Outdoor Air Pollution and Children´s Asthma in the Census Metropolitan Area of Edmonton, Alberta: the Influence of Place of Residence and Socioeconomic Position

by

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Abstract

Background: Asthma is the most common chronic respiratory disease in children and air pollution has been implicated in its development and exacerbations worldwide. The Census Metropolitan Area of Edmonton (CMAE), Alberta, has unique air pollution sources (traffic and industrial related air pollution) compared to other Canadian cities. Previous studies conducted in the Edmonton area between 1992 and 2002 indicated that ED visits for asthma were associated with day-to-day increases in almost all the main air pollutants and that these associations were stronger among children, and older adults. Since that time, sources of air pollution and asthma management have changed. The short-term effect of multiple air pollutants on ED visits for asthma, its variation at intra-urban scale, and the effect of traffic and industrial pollution sources remain unclear in the CMAE. Similarly, the capacity of the socioeconomic position (SEP) to modify these relationships has not been explored.

Objectives: To determine how place of residence and SEP influence the association between short-term variations in outdoor air pollution and ED visits for children with acute asthma in the CMAE, between April 1, 2004 and March 31, 2010 by: (1) conducting a literature review of the effect-modifier role of the SEP on the relationship between outdoor air pollution and ED visits for asthma in children; (2) analysing the relationship between the exposure to multiple air pollutants and ED visits for asthma and the effect measure modification by the SEP at individual level; (3) analysing the relationship between traffic-related air pollution, SEP and ED visits for asthma at small-area level; and (4) exploring the relationship between proximity to industrial sources of air pollution and ED visits for asthma in children.

Methods: For objective 1, a systematic review of the literature was conducted. For objective 2, a case-crossover study was conducted using the Air Quality Health Index (AQHI) as a

composite air quality measure, and NO_2, O_3, and $PM_{2.5}$ as single pollutants. For objective 3, a small-area case-crossover study was conducted at the dissemination area level using estimations of NO_2 concentration, a proxy of traffic air pollution exposure, applying a city-specific land use regression model. For objective 4, a spatial cluster analysis of disease was conducted around the two main industrial areas in the CMAE. Records of ED visits for asthma were obtained from hospital ED facilities in the Edmonton area and daily air pollution data were obtained from Environment Alberta. Health premium subsidy status was used as an individual proxy for SEP and the Chan's Canadian socioeconomic index as an area-level SEP variable.

Results: The ED visits for asthma in children, the AQHI values and the air concentrations of NO_2, $PM_{2.5}$ all decreased during the study period compared to the previous decade. Day-to-day increase in the city-wide AQHI values or in the traffic-related air pollution at dissemination area level did not increase hospital ED visits for asthma. The SEP, measured at individual or small-area level, did not modify the effect of air pollution on ED visits for asthma, in concordance with the results of the systematic review of existing literature. A cluster of ED visits for asthma was identified in close proximity to the coal-fired power plants in the Wabamum area; however, similar clustering was not identified in close proximity to Alberta's Industrial Heartland.

Conclusions: There are two key factors that potentially explain these results: the decreased ED visit rates for children with acute asthma and the decreased concentration and variability of air pollutants, compared to reports in the previous decade. The decreased ED visits may be explained, in part, by improved access to primary care and changes in asthma management over time. This dissertation results add to the available literature by suggesting that there might be children's health benefits associated with better air quality conditions and adverse effects of industrial pollution from coal-fired power plants on hospital ED visits for asthma in children.

Preface

This thesis is an original work of Laura Andrea Rodríguez Villamizar. The research project, of which this thesis is a part, received research ethics approval from the University of Alberta Health Research Ethics Board – Health Panel, Project Name " Outdoor air pollution and socioeconomic status: Their influence on asthma in Alberta", No. Pro00049816, January 28, 2015 (Appendix A).

Chapter 2 of this thesis has been accepted for publication in the *Reviews on Environmental Health* journal as Rodriguez-Villamizar LA, Berney C, Villa-Roel C, Ospina MB, Osornio-Vargas A, Rowe BH, "The role of socioeconomic position as an effect-modifier of the relationship between outdoor air pollution and children's asthma exacerbations: An equity-focused systematic review".

To my loving parents José and Cecilia

and

the four men of my life: Gustavo, Santiago Andrés, Juan Diego, and Francisco

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List of Abbreviations (Alphabetical)

ACCS	Alberta Ambulatory Care Classification System
AEMERA	Alberta's Environmental Monitoring, Evaluation and Reporting Agency
AH	Alberta Health
AHCIP	Alberta Health Care Insurance Plan
AHS	Alberta Health Services
AQHI	Air Quality Health Index
CAP	Criteria Air Pollutants
CCO	Case-crossover
CI	Confidence Interval
CIHR	Canadian Institutes of Health Research
CMAE	Census Metropolitan Area of Edmonton
DA	Dissemination Area
DSR	Directly Standardized Rates
ED	Emergency Department
FEV_1	Forced expiratory volume in one second
FVC	Forced vital capacity
GINA	Global Initiative for Asthma
HREB	Health Research Ethics Board
ICD	International Classification of Diseases
ICD-10	International Classification of Diseases, Tenth Revision
ICS	Inhaled Corticosteroids
LABA	Long-Acting $Beta_2$-Agonist

List of Abbreviations (continued)

LUR	Land Use Regression
NO_2	Nitrogen Dioxide
OR	Odds Ratio
O_3	Ozone
PM	Particulate Matter
$PM_{2.5}$	Particulate Matter with mean aerodynamic diameter of 2.5μm
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RR	Risk Ratio/ Rate Ratio
SABA	Short-Acting $Beta_2$-Agonist
SD	Standard Deviation
SEP	Socioeconomic Position
SES	Socioeconomic Status
SMR	Standardized Morbidity Ratio
US	United States of America

CHAPTER 1. Introduction

1.1. Dissertation Overview

Although much is known about the clinical and epidemiological aspects of asthma, it continues to be a very prevalent chronic respiratory disease commonly associated with air pollution worldwide (1, 2). Outdoor air pollution is known to be an important trigger for asthma exacerbations (3) and contributor for asthma incidence (4), and different individual (e.g., sex, atopy) (5) or social factors (e.g., family income, education) (6, 7) can modify the effect of air pollution on asthma in children. Furthermore, the mixture of air pollutants differ across and within cities, so city-specific information is needed to inform local asthma programs (8).

The city of Edmonton has seen increased traffic over the last decade (9). In addition, the Census Metropolitan Area of Edmonton (CMAE) has specific pollution sources from the petrochemical industry (northeast) and the coal-fired power plants (west) (9). Those conditions make the CMAE a unique location to assess the effects of air pollution from different air pollution sources on asthma in children and their interaction with individual and social conditions. Previous studies conducted in the CMAE found that ED visits for asthma were associated with an average daily increase of almost all major air pollutants' concentrations, mainly nitrogen dioxide (NO_2), carbon monoxide (CO) and particulate matter (PM), and that these associations were stronger among children and older adults (10, 11).

Traditional epidemiological assessments of the effects of air pollution on health have used models for a single pollutant at a time. In real conditions, however, air pollutants interact to produce health effects (12). Moreover, the distribution of air pollutants, especially those traffic-related such as NO_2, CO, and $PM_{2.5}$, vary spatially within cities depending on sources, weather conditions and dispersion patterns (13, 14). In addition, concentrations for most air pollutants

have steadily decreased in Canada and the city of Edmonton since 2000 (9, 15). The short-term effect of multiple air pollutants on ED visits for asthma in children, its variation at intra-urban scale, and the effect of traffic and industrial pollution sources remain unclear in the CMAE. Similarly, the capacity of the socioeconomic position (SEP) to modify these relationships has not been explored.

This thesis dissertation presents the results of a systematic review of the literature and three population-based ecological and mixed (individual and ecological) analytical studies based on the linkage of data collected from hospital ED facilities, census and environment databases. The general objective of this research was to determine how the place of residence and the SEP, influence the association between short-term variations in outdoor air pollution and ED visits for children with acute asthma in the CMAE, between April 1, 2004 and March 31, 2010.

The remainder of the Chapter 1 presents a synthesis of key concepts related to pediatric asthma, SEP, outdoor air pollution, and the relationships among them. The conceptual synthesis includes the definition, burden, risk factors, diagnosis, and treatment of pediatric asthma; concepts about social determinants of health and the clarification of the SEP definition; concepts and measurements of outdoor pollution; and a review of the effects of outdoor air pollution on children's asthma. After the conceptual synthesis, the study rationale, questions, objectives and significance of this dissertation are presented in detail.

Chapter 2 presents the results of a systematic review of the literature that synthesized the existing research-based evidence related to the effect measure modification of the SEP on the relationship between outdoor air pollution and health service use for asthma in children. This manuscript has been accepted for publication in the *Reviews on Environmental Health* journal.

Chapter 3 presents the results of a case-crossover study of the association between short-term effect of multiple outdoor air pollutants exposure, measured by the Air Quality Health Index (AQHI), and ED visits for asthma and the modification effect by SEP.

Chapter 4 presents the results of a small-area case-crossover study assessing the association between short-term effect of traffic-related air pollution and ED visits for asthma in children and the modifier role of SEP. Small-area estimations of NO_2 by dissemination area (DA) level in the Edmonton area were obtained from an existing city-specific Land Use Regression (LUR) model and calibrated daily to obtain a spatio-temporal resolution of the traffic-related air pollution exposure.

Chapter 5 presents the results of a spatial focused cluster analysis of the effects of air pollution on the ED visits for asthma in children around two industrial zones: the Alberta's Industrial Heartland area at northeast and the coal-fired power plants at west (Wabamum area).

Chapters 3 through 5 are presented in a paper-based format. Each chapter has standard paper sections (e.g., introduction, methods, results, discussion and references), which are written as stand-alone manuscripts for future publication. Therefore, there might be some overlap in the description of study population, some procedures, and references among these chapters.

Chapter 6 provides a general summary of results, discussion with strengths and limitations, and conclusions from the thesis dissertation. This chapter also provides a discussion of the significance of the findings and their implications for health care professionals, researchers and policy makers in the region.

Finally, appendices include materials that support some important procedures used in this dissertation as well as the letters of ethical approval and renewal from the University of Alberta Health Research Ethics Board (HREB).

1.2. Children´s Asthma

1.2.1. Definition and characteristics of pediatric asthma

Asthma is the most common chronic respiratory disease among children worldwide characterized by recurrent attacks of breathlessness and wheezing, which vary in severity and frequency from person to person and over time within the same individual (16). In childhood, asthma is a leading cause of morbidity, health services use, health service costs, and school absenteeism (17, 18). Currently, asthma is considered a common but complex respiratory disease resulting from the interaction of genetic, social and environmental factors (19).

In the recent Global Initiative for Asthma (GINA) Guidelines (1), asthma is defined as "a heterogeneous disease, usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation". This definition is employed in the following sections.

Asthma is characterized by a chronic inflammatory disorder that leads to airway obstruction that is typically fully or nearly fully reversible, either spontaneously or with treatment. The chronic inflammation increases the airway hyperresponsiveness that leads to recurrent episodes of wheezing, chest tightness, breathlessness, and coughing, particularly at night or early in the morning, usually following exposure to an irritant (1, 20). Therefore, children with asthma may develop exacerbations characterized by increased inflammation of the airway and worsening airway obstruction (21, 22), and increased symptoms related to these pathophysiological mechanisms.

1.2.2. Burden of pediatric asthma

According to World Health Organization (WHO) estimates, 235 million people currently suffer from asthma (16). The Global Asthma Report 2014 (23), however, estimates this number may be as high as 334 million. Data on children's asthma prevalence are frequently out of date and comparisons of the prevalence among countries still rely on the International Study of Asthma and Allergies in Childhood (ISAAC) conducted between 2000 and 2003 (24). According to ISAAC estimates, 14% of the world's children had asthmatic symptoms during the last year of the study. The highest prevalence (>20%) was observed in Latin America and English-speaking countries of Australasia, Europe and North America, while the lowest prevalence (<5%) was observed in India, Asia-Pacific, Eastern Mediterranean, and Northern and Eastern Europe. ISAAC estimated that asthma symptoms became more common in children from 1993 to 2003 in countries with previous low levels; however, in most high-prevalence countries, the prevalence of asthma changed little or even declined in few countries.

The burden of asthma measured by disability is greatest in children between 10 and 14 years for both females and males (23). The disability adjusted life years (DALYs) for asthma between 5 and 19 years are mainly accounted for the component of years lived with disability (YLD) rather than the component of years of life lost (YLL) and this pattern becomes reversed as age increase (25). For children between 10 and 14 years is estimated that 500 YLD per 100,000 children are attributed to asthma (see Figure 1-1). Moreover, the burden of this condition on the various caregivers of children with asthma is rarely discussed and is clearly important.

Fortunately, deaths from asthma are infrequent; however, when they are examined in detail, many deaths appear to be preventable. Mortality due to asthma accounts for less than 1%

of all deaths in most countries worldwide and most asthma deaths occur in older adults rather than children. Mortality rates in children have fluctuated over the past 50 years, probably related to changes in health system and the availability of new asthma medications (23).

There is a significant positive correlation between mortality and admission rates for asthma at all ages. The relationship between asthma prevalence, severity, admissions, and mortality rates in high-income countries, however, is complex (26). The proportion of asthma attacks that result in hospital admission varies greatly among and within countries, depending mainly on accessibility and affordability of the health care system, the local thresholds for referral among health care levels, and the quality of asthma management. In European countries the age-standardized admission rates for asthma from 2008-2012 vary widely from less than 50 per 100,000 people in Italy to more than 220 per 100,000 in Lithuania (23).

Long-term trends (1955-2010) in high-income countries in Europe, and countries such as the US, Canada, Australia, New Zealand, Hong Kong and Singapore, show that peaks in prevalence of self-reported asthma, asthma admissions and mortality do not match. For self-reported asthma prevalence the long-term trend increased and reached a peak after 2000, for asthma admission a decreasing pattern has been observed after a peak in 1990, and for mortality, following peaks in 1966 and 1985, decreasing trends have been observed (23, 27) (see Figure 1-2).

The economic burden of asthma is difficult to estimate and international comparisons are limited by the lack of information for most low-and middle-income countries (28). Nevertheless, estimates for specific countries and regions suggest that direct and indirect costs of asthma are tremendously high (23). A recent study in US estimated the total cost of asthma to be $56 billion in 2007, or $3,259 per person per year (29).

In Canada, asthma is one of the most prevalent chronic respiratory diseases. Statistics Canada estimates that about three million Canadians have asthma and, in 2014, its prevalence was 8.1% in people aged >12 years; however, regional and provincial variation has also been demonstrated (30). In the province of Alberta, asthma prevalence in the population over 12 years increased from 7.8% in 2008 to 9.5% in 2010, and then decreased to 8.1% in 2014 (30). In children aged 2 to 7 years old, the prevalence estimates of asthma diagnosis in the Prairie provinces, which include Alberta, steadily increased to 11.7% in 2006/2007 and then fell slightly to 9.6% by 2008/2009 (31, 32). Figure 1-3 shows the asthma trends for Canada and the Prairie provinces between 1994/1995 and 2008/2009.

In terms of economic burden of asthma, a recent Canadian study showed that compared to controlled asthma, uncontrolled asthma results in a $184 (in 2012 Canadian dollars) loss of productivity per person a week, 90% of which is attributable to individual loss of function when at work (i.e., presenteeism) (33).

Exacerbations of asthma are a common reason for visits to the ED, in both adults and children; however, sex and age-standardized ED visit rates declined from 9.7/1,000 in 1999/2000 to 6.8/1,000 in 2004/2005 in Alberta. Therefore, asthma ED visits rates seem to be decreasing over time and characterized by a low proportion of follow-up visits, which is the most important predictor for successful asthma control programs (34). The ED visits for children with acute asthma in Alberta have shown disparities being higher in younger boys, Aboriginal children and those living in low SEP measured by health premium subsidy status (35).

1.2.3. Risk factors and susceptibility for pediatric asthma

There are different children's asthma phenotypes with specific etiology and pathophysiology: allergic asthma, non-allergic asthma, late-onset asthma, asthma with fixed airflow limitation, and asthma with obesity (1). All asthma phenotypes, however, are related to three types of risk factors: genetic, host, and environmental factors. Furthermore, gene-by-environment interactions play an important role in children's asthma and likely explain much of the variation in prevalence statistics for asthma as seen worldwide (36).

1.2.3.1. Genetic susceptibility

Genetics susceptibility has been shown to increase the risk of the development of asthma. Genome-wide linkage studies have identified 18 genomic regions and more than 100 genes, mainly in the regions of chromosomes 2, 5, 6, 12, and 13, associated with allergy and asthma in different populations (37). It is known that the likelihood of developing allergic conditions (e.g., allergic rhinitis, eczema, asthma) increases with a family history of allergic conditions. While the exact gene responsible for asthma has been elusive, genetic influence on the incidence of asthma cannot be denied.

1.2.3.2. Host risk factors

Host risk factors in children can be classified according to the time of exposure in prenatal and childhood risk factors (36).

- Prenatal risk factors: Although prenatal risk factors are not strictly conditions of the children (host), they are related mainly to mother's exposure before conception or during pregnancy that may directly affect the fetus development and the asthma susceptibility.

Diet and nutrition: Several studies have demonstrated that higher intake of fish or fish oil during pregnancy is associated with lower risk of atopic wheeze up to age 6 years (38, 39). Similar associations have been found for higher intake of vitamin E and zinc during pregnancy (40, 41).

Stress: Animal and some human models have shown that prenatal maternal stress can affect the regulation of the hypothalamic-pituitary-adrenal axis in offspring and might affect development of allergic wheezing phenotypes (42).

Antibiotic use: Cohort studies have shown an increased risk of persistent wheeze and asthma in childhood associated with increased number and dose of antibiotics during pregnancy (43, 44).

- Childhood risk factors:

Sex: the frequency of asthma by sex is time-dependent: during the first 13-14 years incidence, prevalence and severity of asthma is higher among boys than girls, while after puberty the pattern is reversed with females having greater incidence and severity of asthma (45, 46). It is also important to note that some environmental risk factors may be modified by sex, which suggest different disease mechanism between sexes (47). For instance, the influence of obesity on the development of asthma is greater among women after controlling for caloric intake and physical activity (48, 49).

Race/ethnicity: The prevalence, morbidity and severity of asthma are higher in children from certain ethnic groups. Frequently minority ethnic groups are also the ones with lower SEP; however the effect of ethnicity appears to be independent of SEP (50).

Breastfeeding: The association between breastfeeding and childhood asthma is controversial. Some studies suggest protection (51, 52) whereas others have reported elevated risk of asthma (53, 54). A meta-analysis regarding this topic concluded that breastfeeding for at least three months is associated with lower risk of asthma in early childhood (up to 5 years of age) (55, 56).

Obesity: There is a recent recognition of a positive association between obesity and the development of asthma in children. It is also well recognized that in this relationship, age and sex are important modifiers as obese girls are more likely to have diagnosed asthma than obese boys and early onset asthma is more severe among obese children (57, 58).

Lung function: The presence of airways of decreased caliber has been associated with increased bronchial responsiveness and increased asthma symptoms (59). Prenatal and postnatal exposure to environmental tobacco smoke has been associated with lung dysfunction (59, 60).

Hygiene hypothesis: The "hygiene hypothesis" postulates that an infant's exposure to an important number of infections and diverse types of bacterial endotoxins stimulates the development of the immune system toward non-asthmatic phenotypes (61). Although previously supported by many studies, the theory remains controversial as evidence arising from recent studies demonstrating increasing prevalence of asthma in low- and middle-income countries (e.g., South American countries) where children are exposed to a wider variety of infections (62).

Infections and antibiotics: Lower respiratory tract infections are associated with early wheezing in children, probably by promoting sensitization to aeroallergens (63). Several studies have reported associations between use of antibiotics and early wheezing and asthma (64-66). Given the overuse of antibiotics in children in general, greater antibiotic use might represent a

marker of more frequent upper and lower respiratory tract infections in childhood. Daycare attendance is associated with early wheeze but lower risk of persistent wheeze, probably as a proxy of increased number of viral infections (56, 67).

1.2.3.3. Environmental risk factors

Exposure to environmental tobacco smoke: prenatal and postnatal maternal smoking has been associated with early wheezing and worsening asthma symptoms (56, 59, 68, 69). Prenatal exposure is likely related to decreased caliber in airways and its effects are additive with postnatal exposure (60).

Allergic sensitization: Higher levels of total IgE at birth and in early childhood have been associated with a higher incidence of asthma. Sensitization of aeroallergens, mainly house dust mite, cat and cockroach allergens, have been associated with asthma (70).

Exposure to animals: The association between exposure to domestic cats and dogs and development of asthma is controversial. Some studies have supported the fact that exposure to farm animals in early life is associated with lower risk of atopy and asthma (71, 72); however, other studies report increased risk of allergic sensitization with exposure to domestic cats (73). On the other hand, exposure to domestic dogs has been associated with decreasing general sensitization (74).

Socioeconomic position: Several studies have reported that children from parents with lower SEP have greater morbidity due to asthma (35, 56, 75, 76). A recent systematic review concluded that asthma prevalence is also associated with lower SEP whereas prevalence of allergies is associated with higher SEP (77). The SEP also may interact with other risk factors including gene-by-environment interactions (50).

Exposure to outdoor air pollutants: There has been strong evidence that outdoor air pollution may exacerbate asthma symptoms resulting in increased outpatient visits, ED visits, and hospitalizations (2, 3, 78-80). Two systematic reviews have summarized results from studies around the world to conclude that exposure to air pollution, mainly NO_2 and $PM_{2.5}$, is also positively associated with incidence of asthma in children (4, 81).

1.2.3.4. Gene-by-environment interactions

Interactions between genes and environmental conditions are complex. Genetic studies have shown that polymorphism in antioxidant enzyme genes may have a direct effect on increasing airway inflammation and oxidative stress induced by air pollutants. For example, people with GSTM1 null genotype have reduce glutathione-S-transferase (GST) activity and therefore higher inflammation response after O_3 exposure (82). Furthermore, one study demonstrated that some genotype variants in the GSTM1 and GSTP1 genes place children at increased risk of developing asthma after exposure to O_3 or smoke (83). Cumulative evidence available in a systematic review, however, found different patterns of interactions when polymorphisms were analyzed alone or together with other genes (84).

In general, epigenetic modification of DNA is the main mechanism behind phenotypic differences that develop over time between monozygotic twins (82). Recently, Rossnerova et al. found that DNA methylation varies across locations with higher gene expression in children living in more polluted areas (85).

1.2.4. Diagnosis of pediatric asthma

The diagnosis of asthma is mainly based on the clinical characteristics of the respiratory symptoms, and the objective measure of lung function showing variable expiratory airflow limitation (1, 86). Overall, making the diagnosis of asthma includes the assessment of: 1) the patterns of respiratory symptoms, 2) individual and family history, 3) physical examination, and 4) lung function testing (1). The three former assessments are common for all age groups; however, due to the inability of most children 5 years and younger to perform lung function tests based on expiratory effort, the asthma diagnosis in this age group relies largely on the symptoms pattern, family history, response to a therapeutic trial, and the absence of important clinical signs that suggests an alternative diagnosis (1, 87). In terms of clinical or epidemiological criteria for asthma diagnosis, the individual and family history corresponds to the epidemiological criteria based on specific variables that if present have shown to increase the risk of asthma. The remaining three criteria are mainly clinical assessments.

Some specific features in the pattern of respiratory symptoms have been identified that increase the probability that a child has asthma. Those clinical features are (1):

- Number: More than one of the following symptoms: wheeze, shortness of breath, cough, chest tightness;
- Timing: symptoms are usually worse at night or early in the morning;
- Variability: symptoms vary during the day, over time and in intensity;
- Response to triggers: usually symptoms appear after exposure to specific triggers such as: viral infections, exercise, cold air or changes in weather, allergens, respiratory effort (loud laughing or crying), smoke, or chemical irritants (e.g., paints, traffic fumes or industrial emissions). In children 5 years or younger, any cough usually is non-productive

and frequently accompanied by wheezing. In infants and toddlers the shortness of breath during crying or laughing is equivalent to exercise in older children. In children under 5 years the physical activity is an important trigger of asthma symptoms.

Regarding lung function testing, spirometry is considered the most reliable lung function test that can be used in patients 5 years or older. The forced expiratory volume in one second (FEV_1) and the forced vital capacity (FVC) are the lung measurements that help confirm the presence of airflow limitation: the reduction of the FEV_1/FVC ratio below 0.90 in children 6-11 years and 0.80 in 12 years or older is considered as diagnostic of airflow limitation. In addition, the asthma diagnosis should document the excess variability in lung function, which is defined as a variability of FEV_1 >12% of predicted value after reversibility testing with bronchodilator or an exercise challenge test. Lung measurements can also be obtained using a peak flow meter; however, when available, the spirometry is recommended due to a wide variability in peak expiratory flow (PEF) and reference values (22). Table 1-1 summarizes the main diagnostic criteria for children and adolescents by age group.

1.2.5. Management of pediatric asthma

According to current GINA and Canadian Thoracic Society Guidelines, the long-term goals of asthma management for both adults and children are (1, 88): 1) To achieve a good control of symptoms and maintaining normal activity levels, and 2) To minimize future risk of exacerbations, fixed airflow limitation and side-effects of medications. Since asthma is a chronic condition, a close relationship between the care provider and the patient with asthma (or parent/caregiver for young children) is beneficial in achieving these long-term goals. In fact,

there is evidence to support that a shared-care approach and self-management education promoted by the health provider reduces asthma morbidity in children (89, 90).

Asthma management is control-based. Pharmacological and non-pharmacological treatments are adjusted regularly following a continuous and flexible cycle that involves three steps: assessment, adjust treatment and review responses (1). The assessment step includes diagnosis but also symptoms and risk factors control, inhaler technique, adherence to treatment plans, and patient's preferences. Treatment adjustment includes modification of asthma medications, non-pharmacological strategies and treatment of modifiable risk factors. The review response step involves checking of symptoms, exacerbations, side effects, patient satisfaction, and lung function (for children 6 years or older).

In terms of asthma medications, there are three main categories of pharmacological options for long-term treatment of asthma (1): 1) Controller medications: used for regular maintenance treatment; 2) Reliever medications: used as-needed symptoms relief during exacerbations; and 3) Add-on therapies for severe asthma: used for patients with persistent symptoms and/or exacerbations despite optimized treatment. Controller medications are the core of the long-term treatment and should be initiated as soon as the asthma diagnosis is made. Low dose of inhaled corticosteroids (ICS) are the first choice of controller medication in most children with asthma and when initiated early and continuously there is evidence of greater improvement in lung function (91, 92). The intermittent use of low dose ICS is ineffective and is not recommended even for the treatment of intermittent wheezing (87).

After starting initial controller treatment, asthma management follows a stepwise approach based on the above-mentioned continuous cycle that involves assessment, adjust

treatment and review response. The stepwise approach for asthma medications involves the following 5 steps (1):

-Step 1: As-needed reliever inhaler. The preferred option is a short-acting beta$_2$-agonist (SABA), which are in general highly effective for the quick relief of asthma symptoms.

-Step 2: Low dose controller medication plus as-needed relief medication. The preferred option is a regular daily low dose ICS plus as-needed SABA.

-Step 3: One or two controllers plus as-needed relief medication. Preferred option for adolescents (12 year and older) is a combination of low dose ICS with a long-acting beta$_2$-agonist (LABA) as maintenance treatment plus as-needed SABA or combination of low dose ICS/formoterol as both maintenance and relief treatment. For children 6-11 years the preferred option is a moderate dose ICS plus as-needed SABA. For children 5 years and younger the preferred option is moderate dose ICS (double the low daily dose).

-Step 4: Two or more controllers plus as-needed relief medication. Preferred option for adolescents (12 year and older) is a combination of low dose ICS/formoterol as maintenance and relief treatment or combination of medium dose ICS/LABA plus as-needed SABA. For children 6-11 years the preferred option is to have an expert assessment and advice. For children 5 years and younger the preferred option is to refer the child for expert advice and further investigation and there is not step 5.

-Step 5 for children 6 years and older: Higher level care and/or add-on treatment. At this step the preferred option is to refer the patient to an asthma specialist and consider add-on treatment. Add-on treatments may include anti-immunoglobulin E (anti-IgE), sputum-guided treatment, bronchial thermoplasty, and low dose of oral corticosteroids.

The stepwise approach also involves step down asthma medications once good asthma control has been achieved and maintained at least for three months. Figures 1-4 and 1-5 present the stepwise approaches for asthma management in children 5 year and younger and children 6 years and older, respectively.

Identifying and treating modifiable risk factors may improve asthma control and reduce exacerbation frequency. Non-pharmacological interventions should be considered where relevant to improve asthma control. Non-pharmacological interventions include cessation of smoking (in older children), elimination of exposure to second-hand smoke, avoidance of occupational exposures, indoor and outdoor allergens, outdoor air pollutants, and the promotion of physical activity and healthy diet, among others.

Current asthma management also includes guided asthma self-management education and skills training as core action to achieve long-term goals (1). These actions are most effective through a partnership between the health care provider and the patient (or parents/care givers) and involve four essential components:

-Skills training to use inhaler devices effectively

- Encourage adherence with asthma medications

-Asthma information

-Training in guided self-management: including self-monitoring of symptoms, a written asthma action plan (to recognize and respond to worsening asthma), and regular review by a health care provider.

Currently, all patients with asthma should have asthma education and a written asthma action plan in addition to the pharmacological treatment based on the stepwise approach (1).

1.3. Children´s Asthma and Social Determinants of Health: Socioeconomic Position

Social determinants of health (SDH), refer to specific features and pathways by which, societal conditions affect health. Assessing SDH in health studies introduces the potential to alter them by informed action (93). According to the WHO conceptual framework for action on SDH there are three elements in the SDH: the socio-economic and political contexts; the structural determinants and socioeconomic position; and the intermediary determinants. The structural determinants refer to the interplay between socio-economic-political contexts, structural mechanisms generating social stratification and the resulting socioeconomic position of individuals. These structural determinants include income, education, occupation, social class, sex and gender, and race/ethnicity and are considered the main social determinants of health inequities. The intermediary determinants refer to more downstream factors related to differences in exposure and vulnerability to health-compromising conditions and include material physical conditions (living and work-place conditions, food availability), behaviours and biological factors, and psychosocial factors (94).

The most common SDH acting as mechanisms for inequalities are sex, race/ethnicity, age, social class, and geography. As defined by Krieger, social class refers to "social groups arising from economic interdependent relationships among people" (95). Geography refers to spatial analysis, and maps, which are as powerful as numbers to guide strategies and policy (96). Socioeconomic position (SEP) is a surrogate measure of social class and is defined as the social and economic factors influencing the position that individuals or groups hold within the structure of the society. Socioeconomic position takes into account not only privileged status, but also resource-based measures linked to social class position. This makes SEP a preferred concept and measure to study SDH and address health inequities (97). Variables that act as

components of SEP and that yield a variety of possible SEP measures are education, income and occupation (97). In Canada, socioeconomic status (SES) is used synonymously with SEP.

The SEP is known to modify the effect of different exposures on health (96, 98, 99), which is known as effect-measure modification (100). It means that the association between an exposure (e.g., air pollution) and the health outcome (e.g., ED visits for asthma) will be different across the categories of the effect modifier (e.g., health premium subsidy level). Asthma studies have shown that low SEP is associated with increased effects on severity of childhood asthma prevalence (77), ED visits (101), hospital admissions (102), and ambulatory physician visits (103).

There are three main mechanisms that could explain those disparities (104): (1) Unequal air pollution exposure related to SEP, as populations with low SEP could be exposed to higher levels of outdoor air pollution (closer to high traffic and/or industrialized areas). (2) Susceptibility directly related to SEP, as populations with low SEP could face lower levels of health care access, nutrition, and increased levels of indoor air pollution, alcohol use and/or stress (e.g., violence). (3) Susceptibility from predisposing health conditions, behaviours or traits already associated with low SEP, such as diabetes, dietary content, obesity, sleep, and/or smoking. As implied by 2) and 3) above, the magnitude of a single SEP's effect is difficult to tease out of other conditions, as they are likely to interact in a complex manner to affect asthma outcomes (105). Thus, taking into account SEP disparities related to asthma as a whole concept should help reduce asthma burden in children by providing guidance for clinical follow-up and local health policy actions in specific locations (50).

Measuring SEP is complex, controversial and varies across studies. Single variables of education, occupation or income have been used as proxies for SEP (97). In studies using

population-based administrative databases the use of area-based SES indexes based on census data offer a valid alternative for exploring health effects by SEP (106). The Pampalon deprivation index was developed for the Province of Quebec and takes into account six variables: employment, income, education, marital status, single parent family, and living alone (107). While this index has been the most commonly used in Canada, it doesn't account for Canada-wide social variations. Recently, Chan et al (108) proposed and validated the Canadian Socioeconomic Index (Chan's SES Index) which is a tool designed to be a comprehensive socioeconomic index for the Canadian population which can be used for research involving environmental pollution and health outcomes. Chan's SES Index includes 22 variables from the Census Canada 2006 based on cultural identities, housing characteristics, variables identified in environmental injustice studies, and the variables included in the Pampalon's deprivation index. The Chan's SES index was compared to the Pampalon's Index by assessing the prevalence of low weight birth, preterm birth, and small for gestational age and $PM_{2.5}$ exposure in Edmonton between 1999 and 2008. There was a more consistent gradient in prevalence of those variables by quintile of Chan's Index, especially for low birth weight ($p<0.0001$ versus $p<0.01$). The Chan's SES Index is available at the DA level across Canada (108).

1.4. Outdoor Air Pollution concepts and measurement

Air pollution is defined as the contamination of the indoor or outdoor environment by any chemical, physical, or biological agent that modifies the natural characteristics of the atmosphere (109). Sources of outdoor air pollution may be natural or anthropogenic, so air quality changes constantly and, though it is linked to changes originated by natural phenomena;

changes are most commonly attributed to industrial development, human behaviour, urban development and transportation (109).

In 2013, it was estimated that approximately 80% of the world population was exposed to air pollution levels that exceeded World Health Organization (WHO) guidelines for annual average concentrations of criteria air pollutants (109). Air pollution is a complex mixture of compounds, and the composition varies greatly, depending on the sources of emission and weather conditions. Pollutants of major public health concern include carbon monoxide (CO), ground-level ozone (O_3), nitrogen dioxide (NO_2), sulphur dioxide (SO_2) and particulate matter (PM) with mean aerodynamic diameter of 10 μm (PM_{10}), or 2.5 μm ($PM_{2.5}$). These pollutants are called "criteria air pollutants". Interestingly, PM itself represents a complex mixture of particles of various sizes and different components. While PM size ranges from ~100 μm to < 0.1 μm in aerodynamic diameter, the most commonly monitored are PM <10 μm (PM_{10}) and PM <2.5 μm ($PM_{2.5}$). As the size of the particles decreases the risk of penetrating the airways increases. PM includes different concentrations of soil, metals, organics, inorganics, elemental carbon, ions and endotoxins, among other contaminants (110).

Sources of outdoor air pollutants are diverse. The majority of CO emissions, especially in urban areas, come from automobiles (111). The O_3 is a secondary pollutant resulting from ground-level chemical reactions between oxides of nitrogen (NO_x) and volatile organic compounds (VOC); these reactions occur when pollutants emitted by cars, power plants, refineries, chemical plants, among others, react in the presence of sunlight. The most common sources for NO_2 are emissions from vehicles (cars, trucks or buses), power plants, and off-road equipment; NO_2 contributes not only to the formation of O_3 but also $PM_{2.5}$ (111). The largest sources of SO_2 emissions are from fossil fuel combustion in power plants (especially coal-

burning power plants) and other industrial facilities (e.g., ore smelters). PM is not a unique chemical but a mixture of small particles and liquid droplets; the PM size and shape can vary widely depending on the composition and sources. Primary particles are emitted directly from a specific source such as construction site, fields or fires; secondary particles are formed from complicated reactions of SO_2 and NO_x in the atmosphere and are important contributors of the $PM_{2.5}$.

1.4.1. Air Quality Surveillance Systems

The criteria air pollutants are monitored almost worldwide by air quality surveillance (monitoring) systems, which use specialized equipment and analytical methods to measure air pollutant concentrations. In general, the air quality surveillance systems work as networks of monitoring stations located at specific sites according to the interest of the local environmental agency. Each monitoring station should have valid sampling methods and devices for one or more air pollutants of interest. The local government and/or environmental agency defines the chemicals to be monitored, the sampling methods, the ambient air monitoring locations, the monitoring schedules, and the data quality parameters for the network (112). The US Environmental Protection Agency (US-EPA) has published a list of sampling devices that are capable of measuring concentrations both accurately and precisely for comparison to its national ambient air quality standards (113).

The US-EPA (114), the Canadian Council of Ministers of the Environment (115), and the WHO (116) have defined national and international air quality standards and guidelines, respectively, for the criteria air pollutants and the US and Canadian standards include

permissible limits. Although some limits differ between standards and guidelines, both are intended to minimize the adverse effects of air pollutants on human health.

In Canada, the National Air Pollution Surveillance (NAPS) program is regulated by Environment and Climate Change Canada and many of these air quality-monitoring networks are managed in cooperation with provincial governments or university researchers. Currently, there are 286 monitoring sites in 203 communities located in every province and territory (117). Concentrations of SO_2, NO_2, O_3, $PM_{2.5}$ and CO are monitored continuously. Continuous monitoring provides immediate measurements of pollutant concentrations that are stored in one-hour average time blocks. Continuous samplers capture air from outdoors and use a commercial analyzer calibrated to produce a measure that is proportional to the ambient pollutant concentration. Continuous monitoring is accurate but expensive in terms of device and operational costs.

In Alberta, there are nine airsheds monitoring air pollutants and providing data to the Alberta's air quality data warehouse (118). The Alberta Capital Airshed includes the CMAE and 11 monitoring stations. From those, four active fixed stations are owned by Alberta Environment and provide continuous monitoring for air pollutants in the CMAE: Edmonton Central (active since 3 December 1976), Edmonton East (active since 1 October 1972), Edmonton South (active since 21 September 2005), and Edmonton McIntyre (active since 20 January 2006; provides PM monitoring only). The Edmonton Northwest station was active from 12 July 1973 to 12 December 2005. In Alberta, the air pollutants are monitored continuously by using the following methods (119): CO is monitored by either non-dispersive infrared photometry or gas filter correlation methods; NO_x are measured by the principle of chemoluminescence; O_3 is measured by using ultra-violet (UV) light; PM_{10} and $PM_{2.5}$ are

monitored using Beta attenuation or most commonly using the Tapered Element Oscillating Microbalance (TEOM).

1.4.2. Intra-urban air pollution exposure models

Air pollutants measurements based on fixed monitoring stations are the most classical method to estimate outdoor air pollutant concentrations. Their limited locations, costs and logistics, however, prevent their use to assess exposure on a small intra-urban scale (120). Alternatives designed to estimate air pollutants concentration at intra-urban scale have been developed from geographic and dispersion exposure methods that combine geographic information systems (GIS) with short-term monitoring information to develop exposure models with the ability to capture small-area variations in air pollutants concentrations (13).

In general, intra-urban air pollution exposure models can be classified in seven types of models with specific characteristics (13):

1. Proximity models: represent the most basic approach by measuring the proximity of a subject to a specific pollution source (e.g., major road or industrial facility) and often use buffers at different distances to estimated risk related to distance.
2. Interpolation models: the model uses measurements of the pollutant(s) obtained from fixed monitoring stations distributed through the target area and then deterministic and stochastic geostatistical techniques are used to generate a continuous surface of estimates of the pollutant at sites other than the locations of the fixed stations.
3. Land Use Regression (LUR) models: the method uses measured pollution concentrations at specific locations as the response variable in a regression model that uses land use types and traffic characteristics as predictors of the measured

concentrations. The measurement of pollutants concentration are usually obtained from a short-term monitoring campaign that uses a moderate to large number of monitoring stations through the study area. The LUR models are used to capture spatial variations of long-term exposure to air pollutants.

4. Dispersion models: this method uses data on emissions, meteorological conditions, and topography for estimating spatial exposure of air pollutant concentrations using Gaussian plume equations.
5. Integrated Meteorological-Emission (IME) models: the method combines meteorological and chemical modules to simulate dynamics of atmospheric pollutants requiring high implementation costs and data requirements.
6. Satellite-based models: this method uses data on high-resolution remote sensing systems based on satellite images of the surface and is usually applied to larger scale estimations than the ones produced by the other methods.
7. Hybrid models: refers to those methods that combine personal or regional monitoring with other of the above-mentioned air pollution exposure methods.

1.4.3. The Air Quality Health Index

In Canada, Health Canada and Environment Canada developed the Air Quality Health Index (AQHI) as a risk communication tool that captures the overall health risk related to three key pollutants (NO_2, $PM_{2.5}$, and O_3) within a no-threshold index standardized in a scale from 1 to 10. The AQHI is calculated based on the linear combination of concentration-response coefficients for the three pollutants from a time-series analysis of air pollution and mortality from multiple Canadian cities (121, 122). Therefore, the AQHI is a composite air quality

measure that combines the effects of the three pollutants with more consistent associations of adverse health effects: NO_2, $PM_{2.5}$ and O_3 (2). Recent Canadian studies have reported that the AQHI is associated with ED visits for asthma and stroke (123-125).(69–71)

1.5. Outdoor Air Pollution and Asthma in Children

The causes of childhood asthma are still subject of intensive research since multiple individual, social, and environmental factors are involved and the connections among them are not completely understood. Some specific factors related to increased susceptibility to asthma are well known and include "inhaled triggers" such as allergens, tobacco smoke, and chemical irritants in outdoor air (126). Outdoor air pollution can affect children with asthma, increasing the risk of asthma exacerbations and impairing asthma control (78). Furthermore, recent evidence suggests that outdoor air pollution might play an important role also in inducing new cases of asthma in children, especially those with specific social or environmental susceptibility (4, 127). A simple causal diagram of the relation between outdoor air pollution and asthma, summarizing current knowledge, is presented in Figure 1-6. Common findings related to the short-term effects of air pollution include an increased severity of symptoms with a consequent increase in the use of medication, an increased number of exacerbations that result in ED visits and hospital admissions, and a decrease in acute and chronic lung volumes (lung function) measured by decreased FVC and FEV_1 (3, 128).

Three principal mechanisms have been postulated as explanations for these exposure-outcomes relationships: (1) airway inflammation producing neutrophilic inflammation and cytokines, activating oxidative-stress pathways and altering anti-oxidant mechanisms; (2) allergy sensitisation (co-adjuvant of allergens in producing IgE stimulation); and (3) epigenetic

regulation of genes (heritable changes in gene expression without physical DNA change that could induce airway inflammation pathways) (82, 129). Animal and human *in vitro* and *in vivo* exposure studies have demonstrated the ability of air pollutants to produce airway inflammation and oxidative stress, being both mechanisms the main pathological explanation for the associations of air pollution and respiratory diseases, specifically asthma (2, 80, 82).

In 2014, our research team published a systematic review of epidemiological studies related to outdoor air pollution and children's respiratory health in Canada and found 27 studies conducted in the last 11 years (79). Fifteen of the 27 studies had asthma-related outcomes: nine with outcomes related to health services use (hospitalizations, ED visits and outpatient visits), five with respiratory symptoms and lung function measures in asthmatic children and one assessing incidence of asthma diagnosis. Overall, the included studies reported adverse effects of outdoor air pollution at concentrations that were below Canadian and US standards, and heterogeneous effects of air pollutants were reported by city, sex, socioeconomic status, and seasonality. Figure 1-7 summarizes the association between air pollutants and asthma-related health service use (ED visits and hospitalizations) reported by the original Canadian studies. This systematic review summarizes the adverse effect of outdoor air pollution on children's asthma in Canada for the last decade. In addition, the study identified knowledge and methodological gaps related to: 1) deepening the understanding of the factors behind the differences in the observed adverse effects for some pollutants and socioeconomic conditions across cities; 2) exploring the combined effect of air pollutants; 3) expanding the study of the health effects of other air pollutants; and 4) strengthening the advances in epidemiological, spatial, statistical and social analysis applied to air pollution studies, aiming for a more integrated approach between the physical and social environment.

1.6. Objectives and Scope of Dissertation

1.6.1. Study rationale and significance

Although much is known about the clinical and epidemiological aspects of asthma, it continues to be a very prevalent chronic respiratory disease commonly associated with air pollution worldwide (1, 2). In the province of Alberta, children's asthma is a common cause of health care service utilization involving ED visits (35, 130). These are potential indicators of existing higher exposure to triggers, more susceptible populations, poor asthma control or a combination of all. Outdoor air pollution is known to be an important trigger for asthma exacerbations and a contributor to asthma incidence. Different individual and local contextual conditions such as sex, atopy, or the social conditions, can modify the effect of air pollution on asthma exacerbations in children (5, 98). Furthermore, the mixture of air pollutants differ across and within cities, so city-specific information is needed to inform regional or local asthma programs (8). According to the latest GINA report, the challenge for the next decades is to work locally to design, implement and evaluate asthma care programs to meet local needs (1). This implies the need to understand the distribution of local determinants of asthma and the identification of susceptible population groups, in order to address appropriate local asthma control and prevention plans.

The CMAE is a unique region in Canada in terms of having characteristic air pollution sources and social environments. Overall, CMAE has an increasing traffic volume associated with economic and population growth forces and corresponding social changes. In addition, the CMAE has specific pollution sources from the petrochemical industry (northeast) and the coal-fired power plants (west). Those conditions make the CMAE a unique location to assess the

effects of air pollution from different air pollution sources on children's asthma and their interaction with individual and social conditions. Previous studies conducted in the CMAE found that ED visits for asthma were associated with day-to-day increase of ambient air pollutants, mainly NO_2, CO, PM, and that these association were stronger among children and older adults (10, 11).

Traditional epidemiological assessments of the effects of air pollution on health have used models for a single pollutant at a time. In real conditions, however, air pollutants interact among them to produce health effects (12). Moreover, the distribution of air pollutants, especially those traffic-related such as NO_2, CO, and $PM_{2.5}$, vary spatially and strongly within cities depending on sources, weather conditions and dispersion patterns (13, 14). In addition, concentrations for most air pollutants have steadily decreased in Canada and the city of Edmonton since 2000 (9, 15). The short-term effect of multiple air pollutants on children's asthma ED visits, its variation at intra-urban scale, and the effect of traffic and industrial pollution sources remain unclear in the CMAE. Similarly, the capacity of the socioeconomic position (SEP) to modify these relationships has not been explored. This information is needed to advance knowledge, to tailor asthma control and prevention programs to local and individual conditions, and to inform public policy.

The main research question addressed in this project is: How do the place of residence and the SEP, influence the association between short-term variations in outdoor air pollution and ED visits for children with asthma in the CMAE?

The results of this research will contribute to the evaluation, recognition, and better comprehension of the interaction among outdoor air pollution, ED visits for asthma, and SEP. They will also help advance in the challenge of identifying susceptible groups of children and

tailoring local asthma control and prevention programs to local and individual conditions. Furthermore, the results will raise awareness of the importance of addressing social disparities in political and clinical decision-making in the CMAE. The final target of this research is the incorporation of air pollution sources, place of residence, and social conditions specific for the CMAE into regional and individual actions plans as additional guidance to prevent asthma exacerbations.

1.6.2. Research objectives

General

To determine how the place of residence and the SEP, influence the association between short-term variations in outdoor air pollution and children's ED visits for asthma in the CMAE, Alberta, between April 1, 2004 and March 31, 2010.

Specific

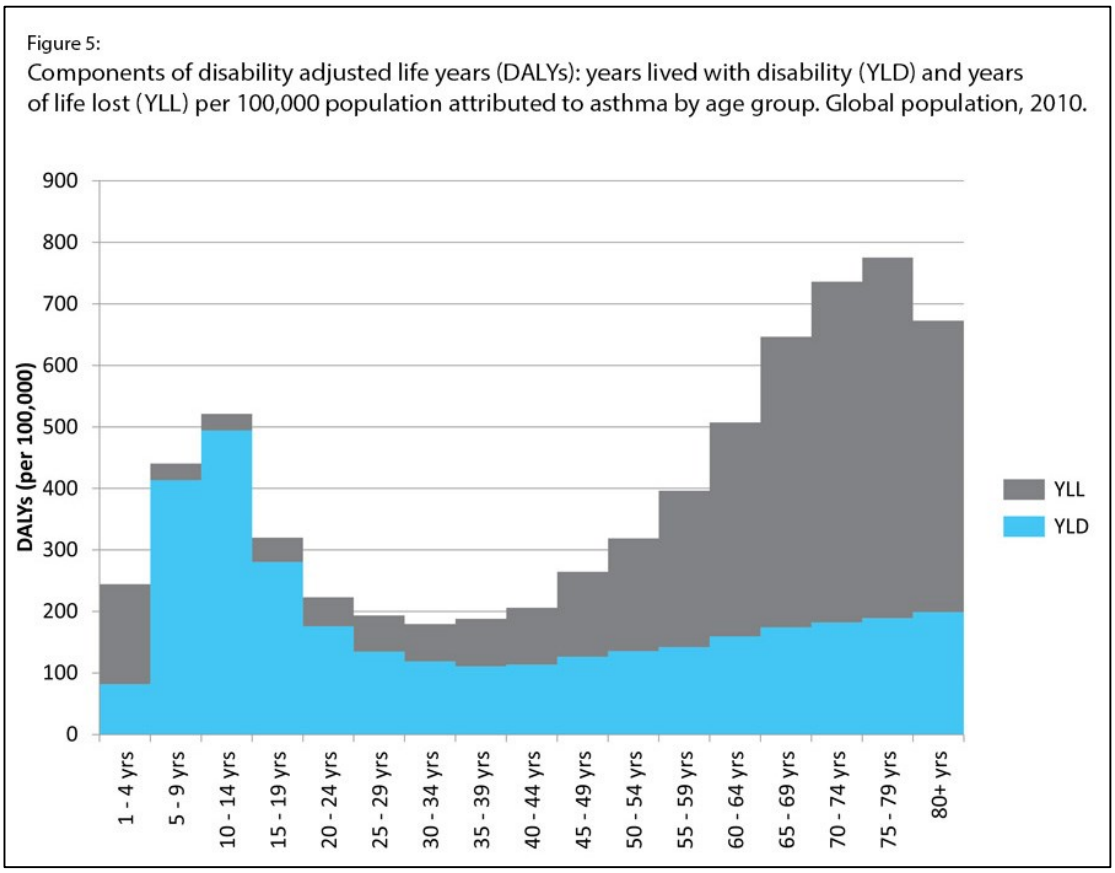
1. To conduct a literature review of the effect-modifier role of the SEP on the relationship between outdoor air pollution and children's ED visits for asthma.
2. To analyse the association between multiple air pollutants exposure, measured by the AQHI, and ED visits for asthma and the effect measure modification by the SEP at individual level.
3. To analyse the association among traffic-related air pollution, measured by NO_2LUR, SEP and children's ED visits for asthma at small-area level.
4. To explore the relationship among ED visits for asthma in children and the proximity to the main industrial sources of air pollution in the CMAE: the Alberta's Industrial Heartland and the coal-fired power plants at Wabamum.

Table 1-1. Main diagnosis criteria for asthma in adolescents and children.

Diagnostic feature	Diagnostic criteria[a]		
	Children 5 years or younger	**Children 6-11 years**	**Children 12 years or older**
Pattern of respiratory symptoms			
Wheeze Shortness of breath Chest tightness Cough	Same criteria for children 6 year or older but other common triggers are laughing or crying. Reduced activity due to get tired easily.	-Number: More than one of the following symptoms: wheeze, shortness of breath, cough, chest tightness - Timing: symptoms are usually worse at night or early in the morning -Variability: symptoms vary during the day, over time and in intensity -Response to triggers: usually symptoms appear after exposure to specific triggers such as: viral infections, exercise, cold air or changes in weather, allergens, respiratory effort, smoke, or chemical irritants (e.g., paints, traffic/industrial emissions).	
Confirmed variable expiratory airflow limitation			
1. Documented airflow limitation	N/A	At least once during diagnostic process when FEV_1 is low, confirm that FEV_1/FVC is reduced (normally >0.75–0.80 in 12 years or older, >0.90 in children 6 -11 years)	
2. Documented excessive variability in lung function[b]			
2.1. Positive reversibility test with bronchodilator (10–15 minutes after 200–400 mcg albuterol or equivalent)	N/A	- Increase in FEV_1 of >12% predicted	- Increase in FEV_1 of >12% and >200 mL from baseline
2.2 Variability over time -Variability in twice daily PEF over 2 weeks	N/A	- Average daily diurnal PEF variability >13%	-Average daily diurnal PEF variability >10%
-Increase in lung function after 4 weeks of anti-inflammatory treatment		-N/A	- Increase FEV_1 by >12% and >200 mL (or PEF by >20%) from baseline, outside of respiratory infections
-Variation in lung function between visits (less reliable)		-Variation in FEV_1 of >12% in FEV_1 or >15% in PEF between visits (may include respiratory infections)	-Variation in FEV_1 of >12% and >200 mL between visits, outside of respiratory infections
2.3. Positive exercise challenge test	N/A	-Fall in FEV_1 of >12% predicted, or PEF >15%	-Fall in FEV_1 of >10% and >200 mL from baseline
2.4. Therapeutic trial 2-3 months with low dose of ICS and as-needed SABA	Clinical improvement during treatment and worsening when stopped	N/A	N/A

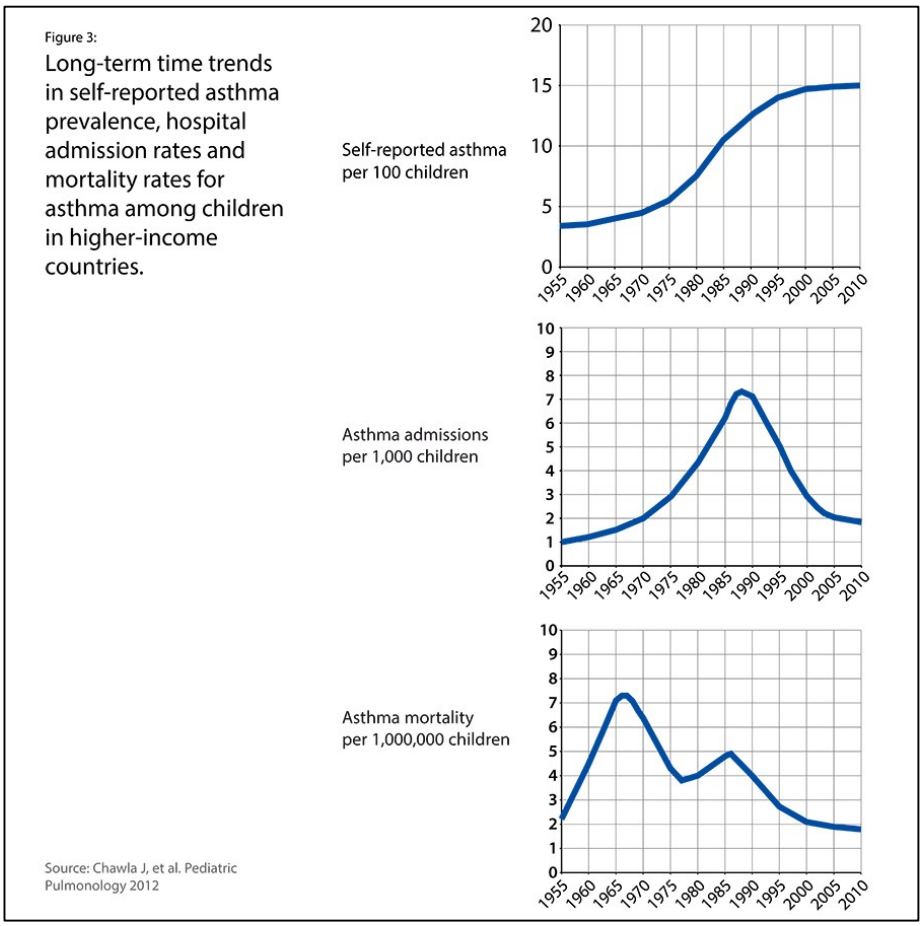
[a]Table based on diagnostic criteria tables from GINA 2014.
[b]The greater the variation, the more confident the diagnosis

Figure 1-1. Burden of asthma measured by components of disability adjusted life years (DALYs)



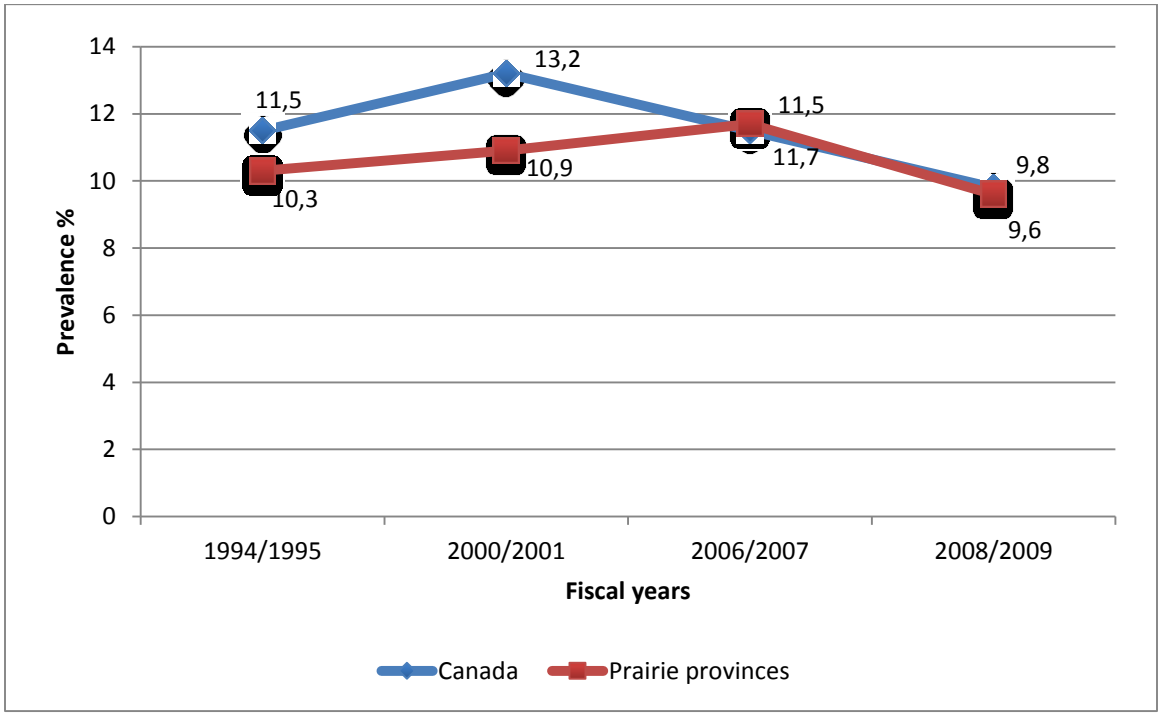
Source: Global Asthma Report 2014. Available from: http://globalasthmareport.org.

Figure 1-2. Long-term trend in self-reported asthma prevalence, hospital admission rates and mortality rates for asthma among children in higher-income countries



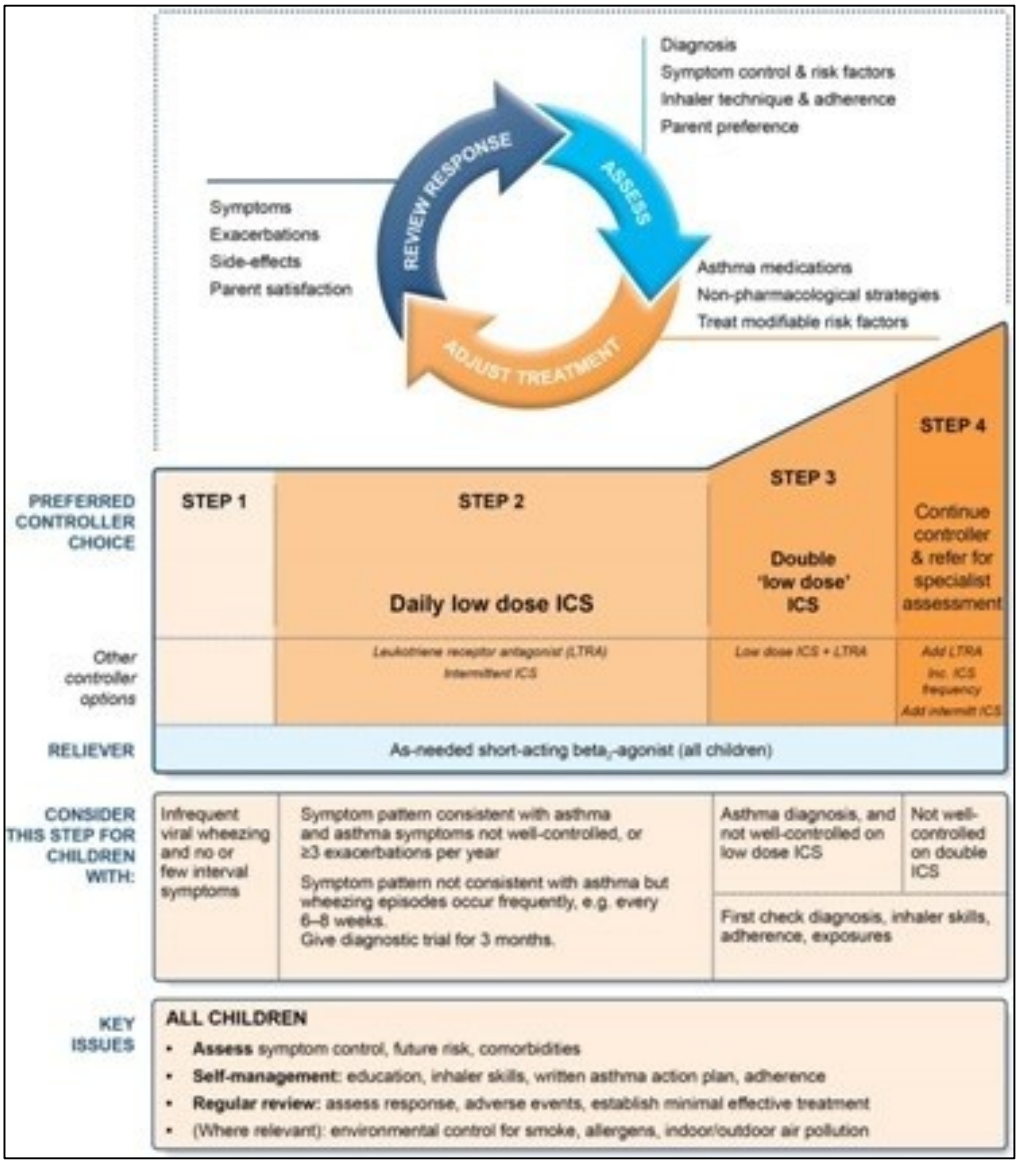
Source: Chawla J, et al. Pediatric Pulmonology 2012 cited in The Global Asthma Report 2014. Available from: http://globalasthmareport.org.

Figure 1-3. Prevalence of asthma diagnosis in children aged 2 to 7 years, Canada and Prairie provinces, 1994/1995 to 2008/2009



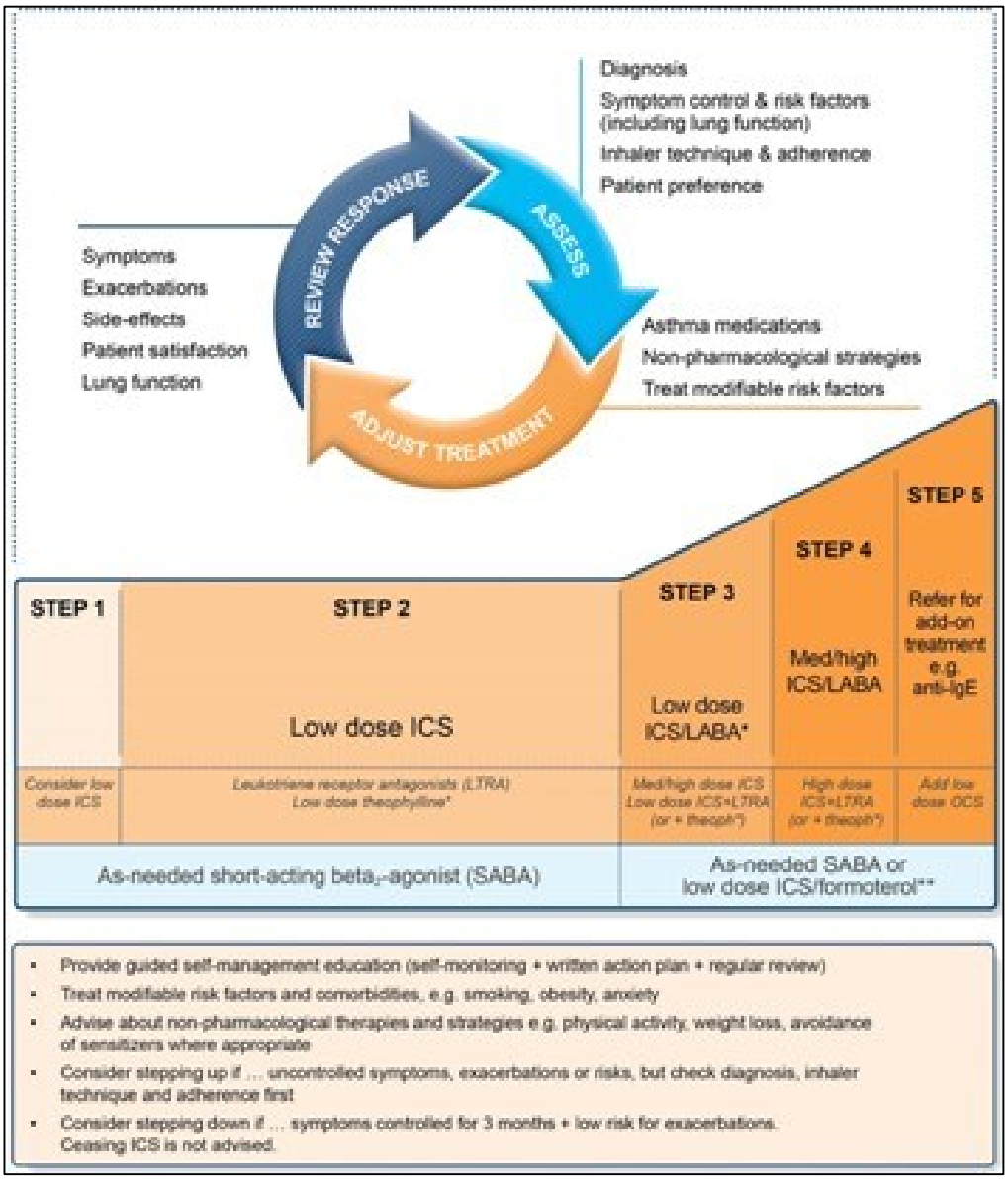
Source: Thomas E. Recent trends in upper respiratory infections, ear infections and asthma among young Canadian children. Health Reports Statistics Canada. 2010;21(4):1-6.

Figure 1-4. Stepwise approach to long-term management of asthma in children 5 years and younger



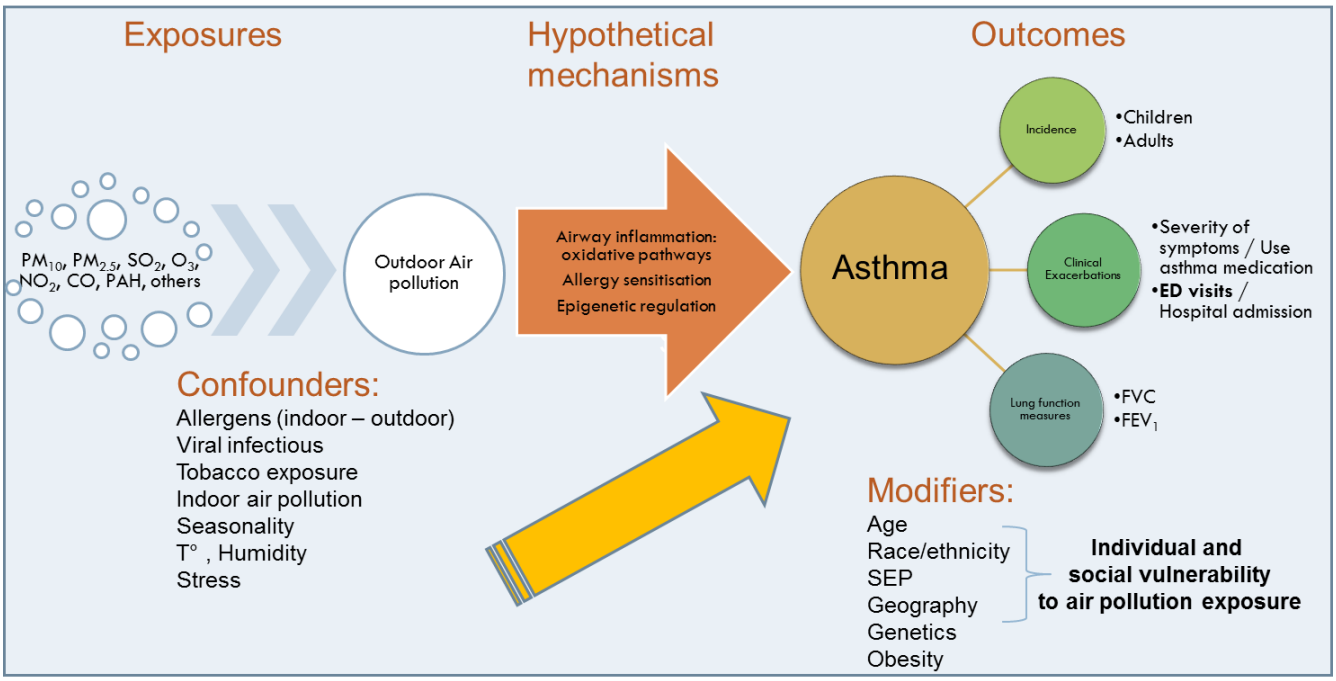
Source: GINA Guidelines 2014. Available at: http://ginasthma.org

Figure 1-5. Stepwise approach to long-term management of asthma in adolescents and children 6 years and older



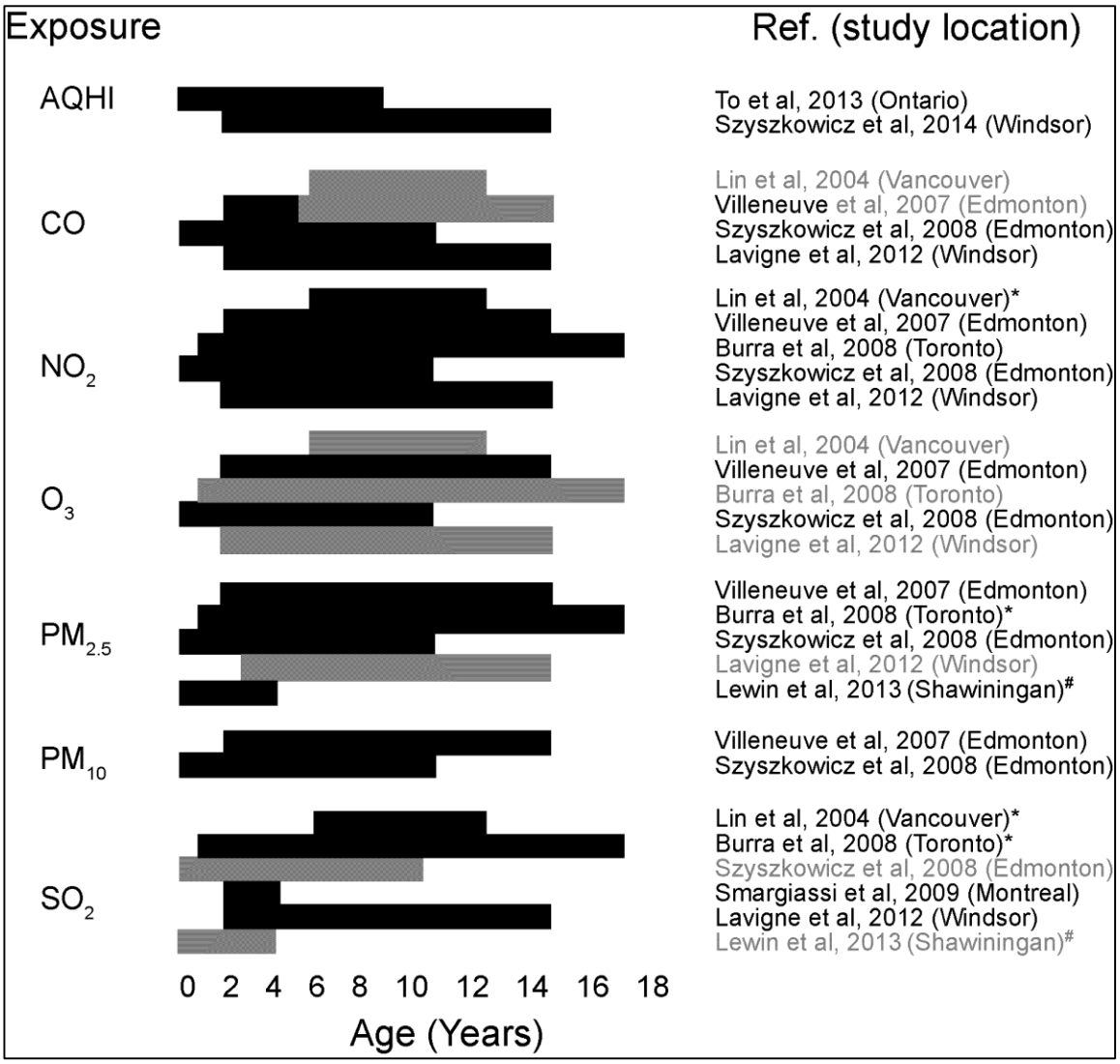
Source: GINA Guidelines 2014. Available at: http://ginasthma.org

Figure 1-6. Epidemiological diagram of the relationship between outdoor air pollution and asthma



Source: original diagram.

Figure 1-7. Association between emergency department (ED) visits and hospitalizations for asthmatic symptoms and pollution exposure in epidemiological studies in Canadian children 2004-2014



Note: The age groups of children tested by each reference were plotted for each air pollutant measure tested. Bars indicate either a statistically significant (black) or non-significant (grey) association between the indicated pollutant and the health effect, for each age group studied by the indicated study.

Source: Figure 3A from: Rodriguez-Villamizar L, Magico A, Osornio-Vargas A, Rowe BH. The effects of outdoor air pollution on Canadian children's respiratory health: a systematic review of epidemiological studies. Canadian respiratory journal : journal of the Canadian Thoracic Society. 2015;22:(5):282-92.

CHAPTER 2. The Role of Socioeconomic Position as an Effect-Modifier of the Association between Outdoor Air Pollution and Children's Asthma Exacerbations: A Systematic Review

2.1. Introduction

The adverse effects of both outdoor air pollution and socioeconomic position (SEP) on respiratory-related outcomes are well documented (2, 50, 131). Outdoor air pollution can affect children with asthma, increasing the risk of exacerbations and limiting asthma control (78). A recent European study estimated that 14% of the cases of incident asthma and 15% of all exacerbations of childhood asthma were attributed to exposure to traffic-related air pollution (132). Recent evidence also suggests that outdoor air pollution might play an important role in inducing new cases of pediatric asthma, especially among children in poor socioeconomic conditions (4, 127).

SEP is a determinant of health that modifies the effect of different exposures on health (96, 104), which is referred to as effect-modification. Three main mechanisms have been proposed to explain this effect related to air pollution exposures: 1) unequal air pollution exposure related to SEP; 2) susceptibility directly related to SEP (e.g., differential levels of health care access, nutrition, stress in low SEP populations); and 3) susceptibility from predisposing health conditions or behaviors already associated with low SEP such as obesity and second-hand smoking (104). Two recent systematic reviews of the literature on socioeconomic gradients in asthma have shown that low SEP is associated with increased prevalence of severe asthma in children and adults (77); however, the role of SEP as a susceptibility factor for asthma incidence is still not clear (133). Despite the availability of literature on social factors, air pollution and respiratory health (77, 104, 133, 134), none of these reviews summarize the

evidence of the modifier effect of SEP on the relationship between air pollution and health services presentations for asthma exacerbations in children or adults. Some studies have reported a strong association between air pollution and use of health services for asthma in children with low SEP (7, 103), whereas other studies (135, 136) have not found a differential effect across SEP categories. To our knowledge, the evidence about the role of SEP as an effect modifier of the association between asthma exacerbations and outdoor air pollution in children has not been synthesized. If consistent evidence of such effect modification exists, it would mean that children with low SEP have a higher risk of poor asthma outcomes and this could be related to their SEP and the adverse effects of air pollution. Understanding the role of SEP on this association could help identify susceptible sub-populations based on SEP and design tailored prevention and control programs (104).

The primary objective of this systematic review was to identify and summarize the evidence regarding SEP as an effect modifier of the association between outdoor air pollution and asthma exacerbations in children.

2.2. Methods

2.2.1. Protocol

An a priori systematic literature review protocol was registered in PROSPERO under the registration number CRD42015022166. The research question addressed in this review was: Is SEP an effect-modifier of the association between outdoor air pollution and asthma exacerbations in children? If yes, what is the magnitude of this effect? Is there any variation of the effect-modification based on SEP measure used?

2.2.2. Search strategy

Comprehensive searches were conducted using five electronic databases: MEDLINE, EMBASE, CAB abstracts, CINHAL, and Scopus. The search strategy was designed by a research librarian and comprised both selected subject headings and key words related to the following terms: “air pollution”, “outdoor air pollution”, “asthma”, “wheez”, “child”, “adolesc”, “youth”, “socioeconomic position”, “socioeconomic status”, “social class”, “poverty”, “social disadvantage” and “deprivation” (see details in Appendix B). No restrictions on language, date, or types of publication were imposed on the searches.

2.2.3. Study selection and data extraction

This review considered studies that evaluated the effect-modifier role of SEP on the association between asthma and outdoor air pollution in children. The review identified SEP measurements and gradients in each publication and compared children living in low SEP with children living in high SEP as defined in the original studies. A stratified analysis of the associations according to SEP category was conducted as an exploratory analysis to identify potential effect-modification; then, the assessment of the statistical significance of the interaction term between air pollutants and the SEP measure was conducted as a confirmatory analysis. The criteria for selecting studies were: 1) observational analytic designs; 2) publication date between January 1 1950 and June 30 2015; 3) population included and reported data separately for children up to 18 years of age; 4) environmental exposure(s) to any non-biological outdoor air pollutant, either measured directly or inferred (i.e., by proximity to roadways), with special interest in criteria air pollutants (CAP): carbon monoxide (CO), nitrogen dioxide (NO_2), sulphur dioxide (SO_2), ozone (O_3) and particulate matter $\leq$10 μm and $\leq$2.5 μm in aerodynamic

diameter (PM_{10} and $PM_{2.5}$, respectively); 5) outcomes related to health service use (i.e., emergency department [ED] visits, physician visits or hospitalizations); and 6) report of measures of association or effect by individual or aggregated SEP measures for one or more SEP categories or report the results of statistical interactions between air pollutants and SEP. We used Krieger's definition of SEP for this review and considered any single or combined measure related to income, education or occupation, as a SEP measure (95). Aggregated SEP measures were defined as area-based SEP measures generally based on census data. The primary outcome was ED visits for asthma and the secondary outcome was asthma-related hospitalizations.

Two members of the team (LR-V; CB) conducted a pilot test to refine the selection criteria and the abstract-title screening form in a sample of 10 randomly selected papers. These two reviewers independently screened titles and abstracts generated from the search strategies to identify potentially relevant articles. Finally, the full text of the articles deemed relevant, and those whose abstracts and titles provided insufficient information were assessed for study eligibility by two independent reviewers. Disagreements on study selection were resolved by a third reviewer (CV-R).

Two reviewers (LR-V; CB) independently extracted data from the included studies using a standardized data abstraction form. The following information was obtained from individual studies: first author, publication year, country, data source, study aim, asthma outcome, outdoor air pollutants included, outdoor air pollution measurement, type of SEP measure (individual or aggregated level of SEP measure), sample size and population, confounders or other factors included in the analysis, results, and reported effect of the association between asthma and outdoor air pollution by SEP category. Disagreements on data extraction were made by consensus.

2.2.4. Risk of bias assessment

Two reviewers (LR-V; CB) independently assessed the risk of bias of included studies, with disagreements being resolved by consensus. We used the risk of bias tool developed for environmental health science assessments by the US National Toxicology Program (NTP)-Office of Health Assessment and Translation (OHAT) (137). This tool includes six bias categories (selection, confounding, performance, attrition/exclusion, detection, selective reporting) and an additional category for other potential threats to internal validity. There are six individual risk-of-bias questions applicable for specific types of study designs (e.g., controlled clinical trials, cohorts) and nine common questions applicable to any study design. The common questions and the ones designed for observational studies were used. Each question of the OHAT tool is answered using one of the following options: definitely low, probably low, probably high, or definitely high risk of bias. Finally, for each outcome, studies were given a confidence rating in terms of the presence or absence of key study design features: High, moderate, low or very low.

2.2.5. Data synthesis

This review follows the recommendations from the PRISMA-Equity extension for systematic reviews with a focus on health equity (138, 139). Descriptive results of the included studies are provided. Agreement between reviewers on inclusion and risk of bias was measured using the kappa (κ) statistic and interpreted according to the magnitude of agreement as poor (≤0), slight (0.01-0.20), fair (0.21-0.40), moderate (0.41-0.60), substantial (0.61-0.80), and almost perfect (0.81-1.00) (140).

Pooled quantitative measures with random effect models were planned for the analysis; however, due to heterogeneity in populations (e.g., children's age), outcomes, and designs

across individual studies, pooling was not conducted. Heterogeneity also precluded meta-regression analyses to assess the effect of the type of SEP measure on the association between asthma and environmental exposures. Risk of bias assessment, data extraction, evidence tables and narrative synthesis of results were documented using Excel (Microsoft Corporation, USA). Forest plots of study results were created using GraphPad Prism version 6 (GraphPad software, San Diego California, USA).

2.3. Results

2.3.1. Search results

The systematic search updated to November 2015 identified 1,335 studies. After removal of duplicates and screening titles and abstracts, 98 studies were selected as potentially relevant, and 10 of them (6, 7, 103, 135, 136, 141-145) were included in the review (Figure 2-1). The complete list of excluded studies and reasons for exclusion is available upon request. Agreement between reviewers was fair for title/abstract screening ($\kappa = 0.35$; 95% CI: 0.26, 0.39) and substantial for full-text study selection ($\kappa = 0.65$; 95% CI: 0.48, 0.81).

2.3.2. Study characteristics

The 10 papers meeting the selection criteria varied by study location, design, participants' age, number and type of air pollutants considered, SEP measure, and type of asthma outcome. Table 2-1 summarizes the main characteristics and results of the included studies.

The studies were mainly conducted in North America (five in the US and two in Canada), two in Korea and one in France. Most of the studies used a time-series design (n=6) (6,

7, 103, 141-143); two were case-crossover studies (135, 136), one a retrospective cohort (145) and one a cross-sectional design (144). Children's age varied widely across the studies, 0-14 years of age being the most common age range. There was also wide variation in the type and number of air pollutants assessed: NO_2 and O_3 were the air pollutants most commonly analyzed (n=6 for each one) (6, 7, 103, 135, 136, 141, 144), followed by PM_{10}, SO_2 and CO (n=4 for each one) (6, 7, 135, 141, 142, 145), $PM_{2.5}$ (n=3) (103, 136, 143), and NO_x (n=1) (145). Asthma-related hospitalization was the most commonly reported outcome (n=5) (6, 7, 141-143), followed by ED visits (n=2) (136, 144), phone calls made to mobile emergency physicians (hereafter ED calls n=1) (135), ambulatory visits (n=1) (103), and repeated hospital encounters (n=1) (145). The majority of studies used area-based SEP measures from census data and only two studies used an individual SEP measure based on health insurance premiums/status (142, 145).

2.3.3. Risk of bias assessment

All included studies had a *probably low risk* of selection, detection and selective reporting bias based on the OHAT risk-of-bias tool. Three studies have a *probably high risk* of confounding, as some important confounding factors were not included in the analysis (e.g., meteorological variables, influenza-related visits) (136, 141, 144). Therefore, for the asthma-related hospitalization outcome, four out of five studies showed a high level of confidence in their evidence based on the key features of the study design. For the asthma-related ED visits/calls outcome, only one of the three studies had a high level of confidence for the associations found.

2.3.4. Effect-modification by SEP

The effect-modifier role of SEP was most commonly assessed for the association between air pollutants and asthma-related hospitalizations in children. Neidell (7) found that the effects of NO_2 and CO in California were larger than other CAPs; however, O_3 had a larger effect on children living in low SEP areas, especially for those aged 3-6 and 12-18 years, for which the interaction terms were statistically significant ($\beta = 0.091$ ($p<0.01$) and $\beta =0.042$ ($p<0.05$), respectively) . Yap et al. (143) analyzed the effect of $PM_{2.5}$ on hospitalizations for asthma in children 1-9 years old in 12 California counties. The analysis of SEP modification-role yielded non-significant interactions; however, the associations between $PM_{2.5}$ exposure and asthma hospitalizations were stronger in areas with higher SEP in the Central Valley region (RR= 0.98 95% CI 0.95-1.01 for low SEP and RR= 1.07 95% CI 1.04-1.09 for high SEP).

Figure 2-2 shows the comparative results of the analysis of the effect modifier role of SEP for five air pollutants in three studies conducted in Canada and Korea that used similar study designs and effect measures (6, 141, 142). When using lags between 0-5 days for NO_2, O_3 and $PM_{10,}$ the associations with asthma-related hospitalizations were higher for children living in low SEP areas; however the 95% CIs for high versus low SEP do overlap. For CO and SO_2, there was no clear pattern of effect-modification by SEP in the included studies. From those three studies, only Lee et al. (141) assessed statistical interaction and found non-significant results.

Three studies assessed the role of SEP as an effect modifier on the association between air pollutants and asthma-related ED visits/calls. Gleason et al. (136) assessed the effect of same-day $PM_{2.5}$ using the proportion of people living in poverty according to the New Jersey census as the SEP indicator. The study did not find any pattern of effect-modification by SEP

level stratification and the interaction terms were not statistically significant. The effect of same day O_3 on asthma ED visits also was not modified by SEP aggregated measures in another study (Figure 3) (135, 136). In Strasbourg, France, the effects of SO_2, PM_{10} and NO_2 on emergency calls were not different by SEP level (Figure 2-3); the interaction terms for SEP and the categorical and continuous variable were not significant (135). In contrast, Shmool et al. (144) used an exploratory ecologic spatial analysis in New York City and found a statistically significant modification effect of NO_2 on asthma ED visits by SEP (i.e., defined as one of the three factors in the factor analysis, mainly characterized by "crowding and poor access to resources"; p value of interaction term <0.05). The negative effect was higher in city areas in which the SEP indicator was above the median (β= 0.055 ±SE=0.026 for low SEP and β =-0.001 ±SE=0.008 for high SEP). The authors, however, reported non-significant interaction terms (absence of effect modification) in the association between NO_2 and ED visits for asthma when using area-level poverty rates as a SEP modifier.

Two studies assessed whether SEP was an effect modifier of the relationship between air pollution exposure and other outcomes of asthma-related health services use. Burra et al. (103) measured social disadvantage and assessed the effect modification on the association between air pollution and ambulatory visits for asthma in an urban setting. For children under 18 years old, there was a significant SEP quintile ratio (Q1/Q5 = 1.006 95% CI 1.000-1.013) using the single day SO_2 exposure. There was also a significant difference in the SEP Q1/Q5 risk ratio using the $PM_{2.5}$ 5-day cumulative average exposure for males and single-day exposure for females (RR=1.017 95% CI 1.002-1.031 and RR=1.012 95% CI 1.001-1.023, respectively). No significant associations were found between O_3 and ambulatory asthma visits. Delfino et al. (145) studied the effect of traffic-related air pollution on repeated hospital encounters for asthma

in urban California. Using different SEP measures at census block level, they found a stronger association with NO_x among children living in higher income areas (HR= 1.07 95% CI 0.98-1.16 for low SEP vs HR=1.14 95% CI 0.006-1.24 for high SEP measured by median household income); however, the assessment of statistical interaction gave non-significant results and the authors suggested that this result might have been attributed to more accurate data collected in this group.

2.4. Discussion

This is the first systematic review summarizing the evidence regarding the role of SEP as an effect modifier of the association between air pollution and asthma-related health services outcomes in children. Ten studies were identified and showed different results of SEP as an effect-modifier. Overall, five out of the 10 studies identified differential effects by SEP in children in important health services outcomes, with stronger negative effects among the low SEP category (6, 7, 141, 142, 144). However, an assessment of statistical interaction was conducted only in three of the five studies (7, 141, 144). Moreover, a statistically significant interaction was reported in one only of these comparisons (7). The effect of O_3 on asthma-related hospitalizations was the association with most consistent differential effects by SEP conditions in Canada, Korea and US (6, 7, 141). In addition to O_3, NO_2 and PM_{10} showed differential associations with asthma-related hospitalizations in children according to SEP in Canada and Korea (6, 141, 142). None of these differential effects by SEP had statistically significant interactions, however, probably related to limitations in sample size.

Despite numerous studies assessing the effects of outdoor air pollution on ED visits for asthma in adults and children (146), only a few have assessed the effect modification of SEP,

especially in children. Overall, three included studies failed to demonstrate any SEP differential effect on the association between pollutant exposure and asthma-related ED visits/calls (135, 136, 144). There are several possible explanations for these findings. First, ED visits may reflect issues related to access to primary health care more than a setting for the delivery of care for the most severe cases (147). From a severity perspective, ED visits for asthma are heterogeneous (range in severity from mild to severe exacerbations), whereas hospitalizations are more homogeneous (moderate-severe exacerbations). Finally, it may be that the effect of pollution is to increase airway inflammation in already inflamed airways (perhaps related to poverty, living conditions, access to medications, etc.) and result in those patients being disproportionally affected.

The current evidence points out a differential effect by SEP on more severe asthma outcomes such as hospitalizations. Furthermore, O_3, NO_2 and PM_{10} are also consistently associated with outdoor air pollution-related mortality (2, 148), including differential effects by SEP conditions (131). As suggested by O'Neill (104), this might support the theory that SEP differentially influences patients through chronic poor living conditions, higher pollution exposures and poor asthma control associated with low SEP. Conversely, these results counter the hypothesis that the gradients are related to differential access to health services during acute asthma episodes, particularly in countries without financial barriers to health care access (e.g., Canada). This hypothesis, however, needs to be verified through additional studies conducted in countries with different health systems and social conditions.

Since SEP is a complex construct, its measurement in these studies requires further discussion. One can define SEP as social and economic factors influencing the position that individuals or groups hold within the societal structure. SEP can be estimated using measures of

occupation, education and income at individual level, or using area-based indices at the aggregated (area) level (95, 97, 106, 149). Most of the studies in this review used aggregated SEP measures at area-level and found differential but non-statistically significant interaction effects by SEP. Only two studies reported individual SEP measures and they also failed to find significant modifier effects by SEP (142, 145). In this regard, Kim et al. compared the role of SEP as an effect modifier on the association between outdoor air pollution and asthma-related ED visits using individual and regional variables from the general population of Seoul, Korea (101). The authors found a modifier effect using only regional-level variables, suggesting that contextual area-level conditions might have a stronger and differential effect than income-related individual conditions. Interestingly, they also reported that all regions included in their study had similar pollutant concentrations and therefore, exposure to higher levels of outdoor air pollution in low SES regions was not the potential mechanism behind the SEP differential effect. Similarly, a nation-wide Canadian mortality study reported that areas with higher percentages of individuals with high education, income and employment have long-term exposure to low concentrations of $PM_{2.5}$ (150); still Canadian studies have also reported stronger effects of air pollution on mortality and respiratory health in populations with lower income and education (98, 151).

Many factors have been proposed to explain the differential effect of air pollution on health outcomes by SEP. Children in low SEP conditions may face important barriers accessing health care services; higher exposure to air pollution sources, violence and stressor factors, poor hygiene and housing conditions, and differential dietary patterns, among other factors (104). Health care use and access may differ by country depending on different factors and, especially, the characteristics of the health care systems. Some studies in this review were conducted in

Canada (6, 103), where there is universal health care coverage. Still, they showed consistent differential effects by SEP categories, suggesting that universal health care may not guarantee equity in access to health care services (152) or that access is not a major determinant of the differential effect by SEP in some settings. For the purpose of this systematic review, differences in access to health care were not considered to introduce a bias in the results. Even in the case of settings with recognized unequal access to health care by SEP conditions (i.e., US jurisdictions), the analysis of effect modification is valid since its purpose is assessing the relationship between air pollution and asthma exacerbations within a given SEP group, and not the frequency/prevalence of health services visits. While the low SEP population seeking health care might be underrepresented in those settings, it is important to note that in the included studies, the number of visits are large in both SEP groups, and frequently higher for people in the low SEP, including the studies from the US (7, 136, 145).

Shmool et al. (26) assessed the effect modification of stressor factors on the association between area-average NO_2 and asthma-related ED visits, identifying a differential effect, albeit non-statistically significant modification effect. Effects were mainly related to factors representing "crowding and poor access to resources", but not to those representing "violent crime or property crime" (144). Therefore, as suggested by Forno, (50) a more practical approach to address inequalities in asthma and environmental health practice may include the use of robust SEP measures to promote interventions in social susceptible populations. Having identified those populations, the mechanisms behind the modifier role of SEP could be addressed locally in order to introduce public health interventions targeting more specific sub-populations.

2.4.1. Strengths and limitations

Some strengths and limitations of this review need to be addressed. The strengths of this systematic review pertain to its *a priori* and registered protocol, its rigor in searching the literature, the criteria-based selection of relevant evidence, the rigorous appraisal of study risk of bias and the evidence-based inferences. The statistical quality of the included studies is also worth mentioning. For example, the commonly used Generalized Additive Models (GAM) for the analysis of time-series studies of air pollution tended to overestimate the relative risk of air pollution on health outcomes. The problem resided in the use of default convergence criteria included in the statistics software S-PLUS that lead to the development of alternative techniques to model GAM convergence (153, 154). Interestingly, the five papers included in this review using GAM described the correction of the convergence criteria; therefore, the results are not likely to be affected by the GAM overestimation (6, 103, 141-143).

There are, however, some limitations. First, the small number of available studies and their heterogeneity precluded the calculation of pooled estimates of the differential effects of SEP. This was particularly true for the ED visits/calls data. Similarly, this review was not able to analyze variations by geographical location. It is well known that the effect-modifier phenomenon is not a condition related to a study design or analysis, but a property of the association between exposure and health outcome that may vary geographically (155). Therefore, it is recommended that SEP differential effects should be routinely assessed in environmental health analyses and if the SEP differential effect is present, the mechanism behind the SEP differential effect should be addressed at local level.

Second, the findings of this systematic review are likely to be affected by the potential confounding effect identified in some studies. This review did not exclude studies with probably

high risk of confounding in the analysis as they still provide important information. Moreover, the main finding of this review related to the weak evidence of SEP as an effect-modifier in children's asthma-related hospitalizations is robust even after excluding the study with potential high risk of confounding.

The findings are likely to be affected also by the SEP variable measurement. Measuring SEP is a complex endeavor (97, 156) and SEP aggregated indicators based on adults' characteristics might facilitate comparison across the studies but not accurately reflect the SEP of children. Further work needs to be performed on SEP measurement in children living in different social settings.

Finally, selection and publication bias are potential limitations of this review. Although a comprehensive electronic search was conducted and identified an important number of potentially eligible studies, many of them were excluded either because SEP was used as a confounding variable, or the analyses were not available specifically for children (Figure 1). The researchers contacted some authors of studies in which SEP modification analyses were conducted; however, data was not published for children and re-analysis of data was not possible in most cases.

2.5. Conclusions

This systematic review synthesized the evidence on the role of SEP as an effect-modifier of the association between air pollutants (mainly O_3, followed by NO_2, and $PM_{10,}$ using lags between 0-5 days) and important asthma-related outcomes. The results revealed that associations between hospitalizations and air pollutants seem to have a stronger negative influence on children living in low SEP conditions. However, confirmation of the effect

modification by statistically significant interactions between air pollutants and SEP was evident only in one out of five studies, probably related to limitations in sample size. Three studies failed to identify effect modification by SEP for asthma-related ED visits. The SEP modifier role was mainly assessed using aggregated measures; however, non-differential effects by SEP were also observed in the two studies that used individual SEP measures. Future studies assessing the association between air pollution exposure and health effects in children should address the differential effect of SEP and, if present, the potential mechanisms behind this phenomenon should be addressed at local level as mechanisms might vary geographically.

Table 2-1. Characteristics and results of included studies

Reference; study location and study period	Study design, study population and size	Pollutants (mean levels[1]) and methods assessing exposure	Asthma-related outcome	SEP measure	Summary of study findings for SEP effect-modification
Lin et al., 2004(6); Vancouver area; 1987-1998	Time series study; hospitalizations of 6-12 year olds; from British Columbia Linked Health Dataset (n = 3 822)	Mean CO (960), SO_2 (4.77), NO_2 (18.65), O_3 (28.02), PM_{10} (NS), $PM_{2.5}$ (NS) from 1995-1998; from monitoring stations	Hospitalizations	Ecological; average household income adjusted for household size by enumeration area defined by 1991 and 1996 Canadian census	1-day lag RR (95% CI): Low SEP / High SEP NO_2 male: 1.13 (1.04-1.23) / 1.04 (0.95-1.14) O_3 female: 1.11 (0.97-1.28) / 0.91 (0.78-1.05) CO male: 1.06 (0.99-1.14) / 1.06 (0.98-1.14) SO_2 female: 1.05 (0.95-1.16) / 1.07 (0.96-1.19) Interaction terms were not tested.
Neidell 2004(7); California, US; 1992-1998	Time series study; hospitalizations of 1-18 year olds from California Hospital Discharge Data (n=38 757)	Mean O_3 (38.91), CO (1777), PM_{10} (34.21), NO_2 (45.95); from monitoring stations	Hospitalizations	Ecological; percentage of high school dropouts by zip code	Linear regression betha coefficients of effect combined for 0-18 year olds: Low SEP / High SEP O_3 0.20 / -0.14 CO 0.17 / -0.04 NO_2 -0.09 / 0.09 PM_{10} -0.03 / 0.002 Interaction terms for CO and O_3 were statistically significant at 5%.
Lee et al., 2006(141); Seoul, Korea; 2002	Time series study; hospitalizations of 0-14 year olds from National Health Insurance Cooperation database (mean 8.09 patients/day)	Mean PM_{10} (135.18), SO_2 (8.74), NO_2= (6.08), O_3 (29.83), CO (6370); from monitoring stations	Hospitalizations	Ecological; average regional health insurance rates	Higher effect from 0-5 day lag RR (95% CI): Low SEP / High SEP O_3 1.32 (1.11-1.58) / 1.12 (1.00-1.25) CO 1.02 (0.85-1.24) / 1.06 (0.96-1.17) NO_2 1.29 (1.05-1.58) / 1.13 (1.01-1.27) PM_{10} 1.31 (1.14-1.51) / 1.16 (1.05-1.28) SO_2 1.29 (1.08-1.53) / 1.08 (0.96-1.22) Interaction terms were not significant.

Reference; study location and study period	Study design, study population and size	Pollutants (mean levels[1]) and methods assessing exposure	Asthma-related outcome	SEP measure	Summary of study findings for SEP effect-modification
Lin et al., 2004(6); Vancouver area; 1987-1998	Time series study; hospitalizations of 6-12 year olds; from British Columbia Linked Health Dataset (n = 3 822)	Mean CO (960), SO_2 (4.77), NO_2 (18.65), O_3 (28.02), PM_{10} (NS), $PM_{2.5}$ (NS) from 1995-1998; from monitoring stations	Hospitalizations	Ecological; average household income adjusted for household size by enumeration area defined by 1991 and 1996 Canadian census	1-day lag RR (95% CI): Low SEP High SEP NO_2 male: 1.13 (1.04-1.23) 1.04 (0.95-1.14) O_3 female: 1.11 (0.97-1.28) 0.91 (0.78-1.05) CO male: 1.06 (0.99-1.14) 1.06 (0.98-1.14) SO_2 female: 1.05 (0.95-1.16) 1.07 (0.96-1.19) Interaction terms were not tested.
Bae 2010(142); Seoul, Korea; 2003-2005	Time series study; hospitalizations of 0-14 year olds from National Health Insurance database (n=23 958)	Mean PM_{10} (62.65) from monitoring stations	Hospitalizations	Individual; based on the national health insurance premium scale and Medic Aim claim data	Percentage increase and 95% CI: Low SEP High SEP PM_{10} 1.78 (0.79-2.78) 0.83 (0.34-1.32) Interaction terms were not tested.
Yap et al., 2013(143); 12 South Coast and Central Valley California counties, US; 2000-2005	Time series study; hospital admissions of 1-9 year olds from California Office of Statewide Health Planning and Development (n=146 224)	Counties mean $PM_{2.5}$ varied between 12.75 and 24.61 from monitoring stations	Hospitalizations	Ecological; Townsend index by zip code areas from US Census 2000.	3-days lag Rate ratio (95% CI): Low SEP High SEP $PM_{2.5}$ South Coast 1.07 (1.03-1.08) 1.07 (1.05-1.09) Central Valley 0.98 (0.95-1.01)1.07 (1.04-1.09) Interaction terms were not significant.
Laurent et al.; 2008(135); Strasbourg, France; 2000-2005	Small-area case-crossover study; emergency calls of 0-19 year olds from emergency health care network (n= 954 phone calls)	Mean PM_{10} (22.6), SO_2 (8.9), NO_2 (36), O_3 (57.7); from ADMS-urban model.	Emergency calls	Ecological; deprivation index based on 1999 French Census	0-1-day lag OR (95% CI): Low SEP High SEP PM_{10} 0.94 (0.81-1.09) 0.97 (0.71-1.33) NO_2 0.93 (0.79-1.09) 0.76 (0.53-1.09) SO_2 0.90 (0.67-1.22) 1.08 (0.52-2.21) O_3 0.93 (0.81-1.08) 1.05 (0.81-1.37) Interaction terms were not significant.

Reference; study location and study period	Study design, study population and size	Pollutants (mean levels[1]) and methods assessing exposure	Asthma-related outcome	SEP measure	Summary of study findings for SEP effect-modification
Lin et al., 2004(6); Vancouver area; 1987-1998	Time series study; hospitalizations of 6-12 year olds; from British Columbia Linked Health Dataset (n = 3 822)	Mean CO (960), SO_2 (4.77), NO_2 (18.65), O_3 (28.02), PM_{10} (NS), $PM_{2.5}$ (NS) from 1995-1998; from monitoring stations	Hospitalizations	Ecological; average household income adjusted for household size by enumeration area defined by 1991 and 1996 Canadian census	1-day lag RR (95% CI): Low SEP High SEP NO_2 male: 1.13 (1.04-1.23) 1.04 (0.95-1.14) O_3 female: 1.11 (0.97-1.28) 0.91 (0.78-1.05) CO male: 1.06 (0.99-1.14) 1.06 (0.98-1.14) SO_2 female: 1.05 (0.95-1.16) 1.07 (0.96-1.19) Interaction terms were not tested.
Gleason et al.; 2014(136); New Jersey, US; 2004-2007	Time-stratified case-crossover design; emergency department visits of 3-17 year olds from New Jersey Department of Health; (n= 21 854 visits)	Mean O_3 (46.18), $PM_{2.5}$ (11.78) from monitoring stations	Emergency department visits	Ecological; proportion of population living in poverty based on 2000 US Census.	Same day OR (95% CI): Low SEP High SEP $PM_{2.5}$ 1.00 (0.98-1.03) 0.99 (0.96-1.02) O_3 1.10 (1.07-1.13) 1.07 (1.04-1.11) Interaction terms were not significant.
Schmool et al.; 2014(144); New York City, US; 2008-2010	Cross-sectional spatial analysis; emergency department visit rates of 0-14 year olds from the New York State Department of Health; (n= mean area-level rate 6.8%)	Mean NO_2 (25.1) from land use regression model.	Emergency department visits	Ecological; Three social stressor factors derived from factor analysis based on 29 administrative indicators at area level.	Betha coefficients (SE) per IQR: Low SEP High SEP F1: "violent crime and physical disorder" NO_2 0.013 (0.008) 0.011 (0.014) F2: "crowding and poor access to resources" NO_2 0.055 (0.026) -0.001 (0.008) F3: "noise complaints and poverty crime" NO_2 -0.013 (0.019) -0.016 (0.016) Interaction term was significant for F2 but not significant interaction was found by area-level poverty rates.

Reference; study location and study period	Study design, study population and size	Pollutants (mean levels[1]) and methods assessing exposure	Asthma-related outcome	SEP measure	Summary of study findings for SEP effect-modification
Lin et al., 2004(6); Vancouver area; 1987-1998	Time series study; hospitalizations of 6-12 year olds; from British Columbia Linked Health Dataset (n = 3 822)	Mean CO (960), SO_2 (4.77), NO_2 (18.65), O_3 (28.02), PM_{10} (NS), $PM_{2.5}$ (NS) from 1995-1998; from monitoring stations	Hospitalizations	Ecological; average household income adjusted for household size by enumeration area defined by 1991 and 1996 Canadian census	1-day lag RR (95% CI): Low SEP High SEP NO_2 male: 1.13 (1.04-1.23) 1.04 (0.95-1.14) O_3 female: 1.11 (0.97-1.28) 0.91 (0.78-1.05) CO male: 1.06 (0.99-1.14) 1.06 (0.98-1.14) SO_2 female: 1.05 (0.95-1.16) 1.07 (0.96-1.19) Interaction terms were not tested.
Burra et al., 2009(103); Toronto, Canada; 1992-2001	Time series study; family physician and specialists service claim records for 1-17 year olds; (n = 1 146 215)	Mean SO_2 (9.7), NO_2 (39.2), O_3 (33.3) and $PM_{2.5}$ (17.9); from monitoring stations	Ambulatory physician visits	Ecological; average household income at census tract level using the 1996 Canadian census.	1-day lag RR (95%CI): Low SEP High SEP Females $PM_{2.5}$ 1.01 (1.01-1.02) 1.00 (0.99-1.01) NO_2 1.03 (1.02-1.03) 1.02 (1.02-1.03) Males SO_2 1.02 (1.02-1.03) 1.02 (1.01-1.02) O_3 0.96 (0.96-0.96) 0.96 (0.96-0.97) Interaction terms were not tested.
Delfino et al., 2009(145); Orange County, California, US; 2000-2003	Retrospective cohort study; admission to the hospital or visits to emergency department of 0-18 year olds; (n= 2 768 patiens and 697 readmissions)	Mean NO_2 cool season (5.24), NO_2 warm season (5.66), NO_x cool (8.10), NO_x warm (6.35), CO cool (114), CO warm (103) from CALINE4 dispersion models	Recurrent hospitalization or emergency department visit	Ecological (poverty level and median household income based on US Census 2000 block group) Individual (insurance status)	Hazard Ratios (95% CI) by IQR: Low SEP High SEP By poverty level NO_x 1.12 (1.03-1.21) 1.08 (0.99-1.16) CO 1.09 (1.00-1.19) 1.06 (0.98-1.13) By median household income NO_x 1.07 (0.98-1.16) 1.14 (0.06-1.24) CO 1.04 (0.96-1.13) 1.12 (1.03-1.21) By insurance status NO_x 1.08 (1.01-1.16) 1.14 (1.04-1.25) CO 1.06 (0.99-1.14) 1.10 (1.01-1.21) Interaction terms were not significant.

[1] parts per billion for gasses, $\mu g/m^3$ for PM; CI, confidence interval; CO, carbon monoxide; F, factor; IQR, interquartile range; NO_x, nitrogen oxides; NO_2, nitrogen dioxide; O_3, ozone; OR, odds ratio; PM, particulate matter; RR, relative risk; SE, standard error; SEP, socioeconomic position; SO_2, sulphur dioxide; US, United States.

Figure 2- 1. PRISMA flow diagram for selected studies.

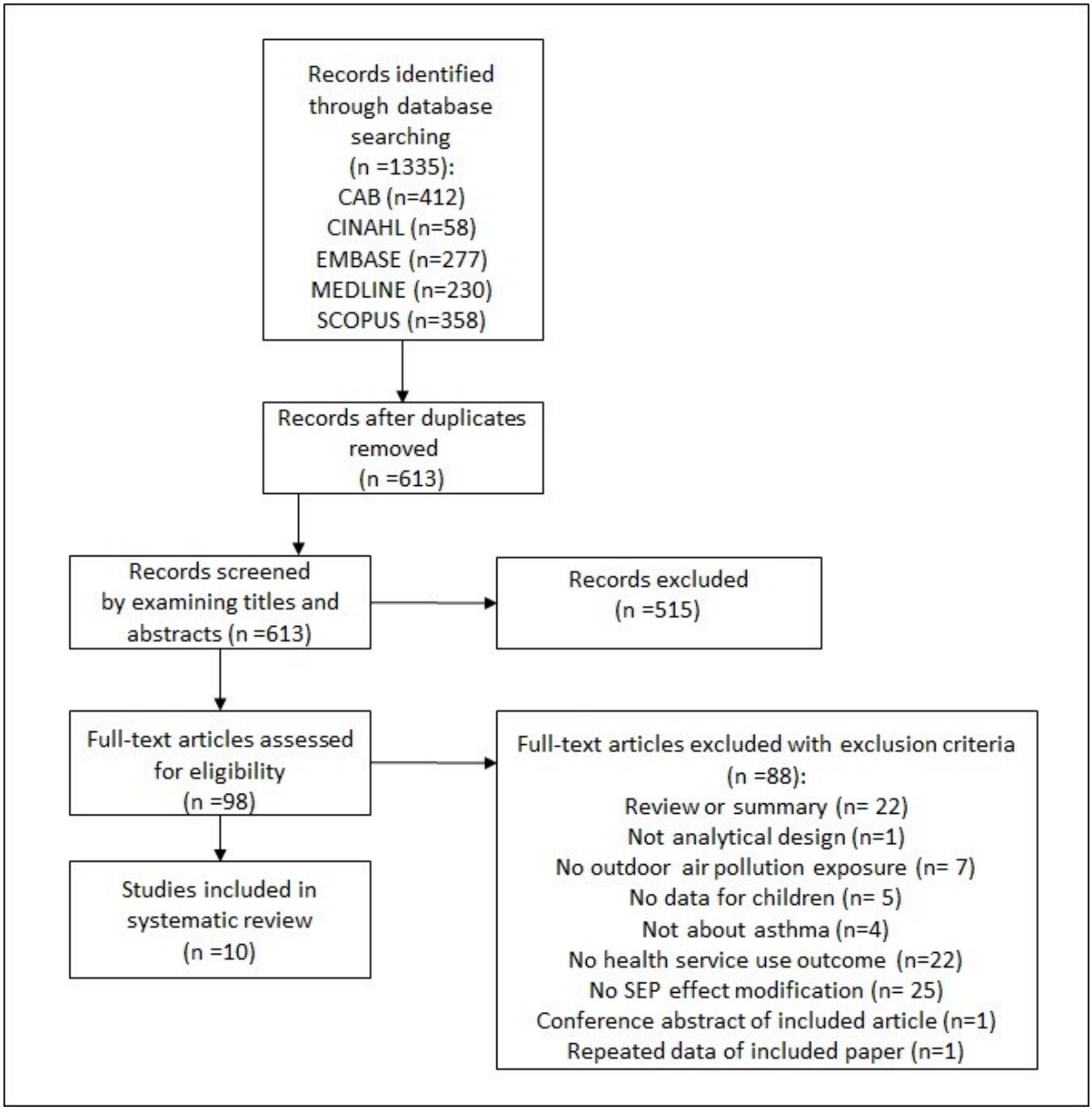


Figure 2- 2. Effect modification by socioeconomic position on the association between air pollutants and hospitalizations for asthma in children.

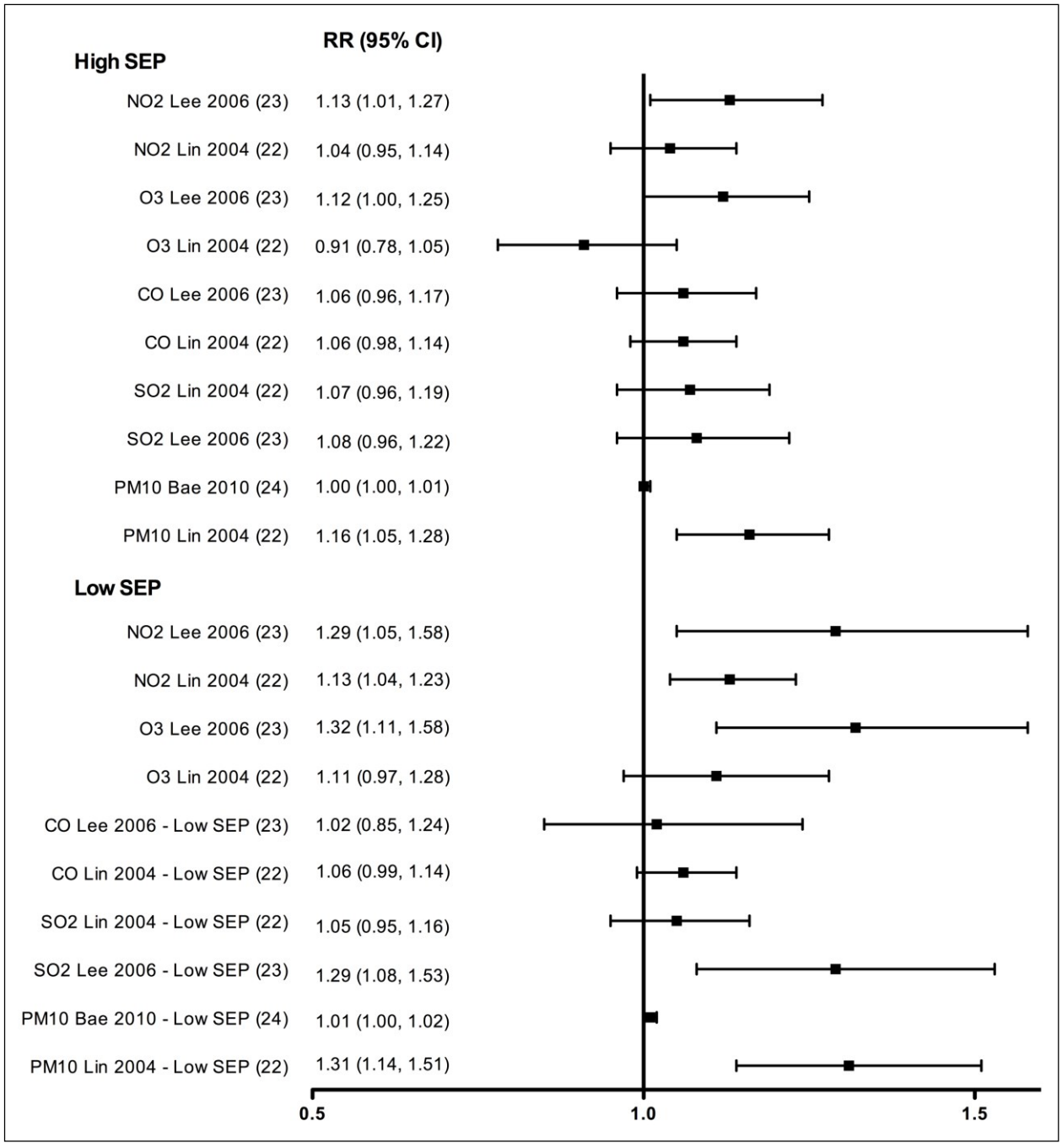
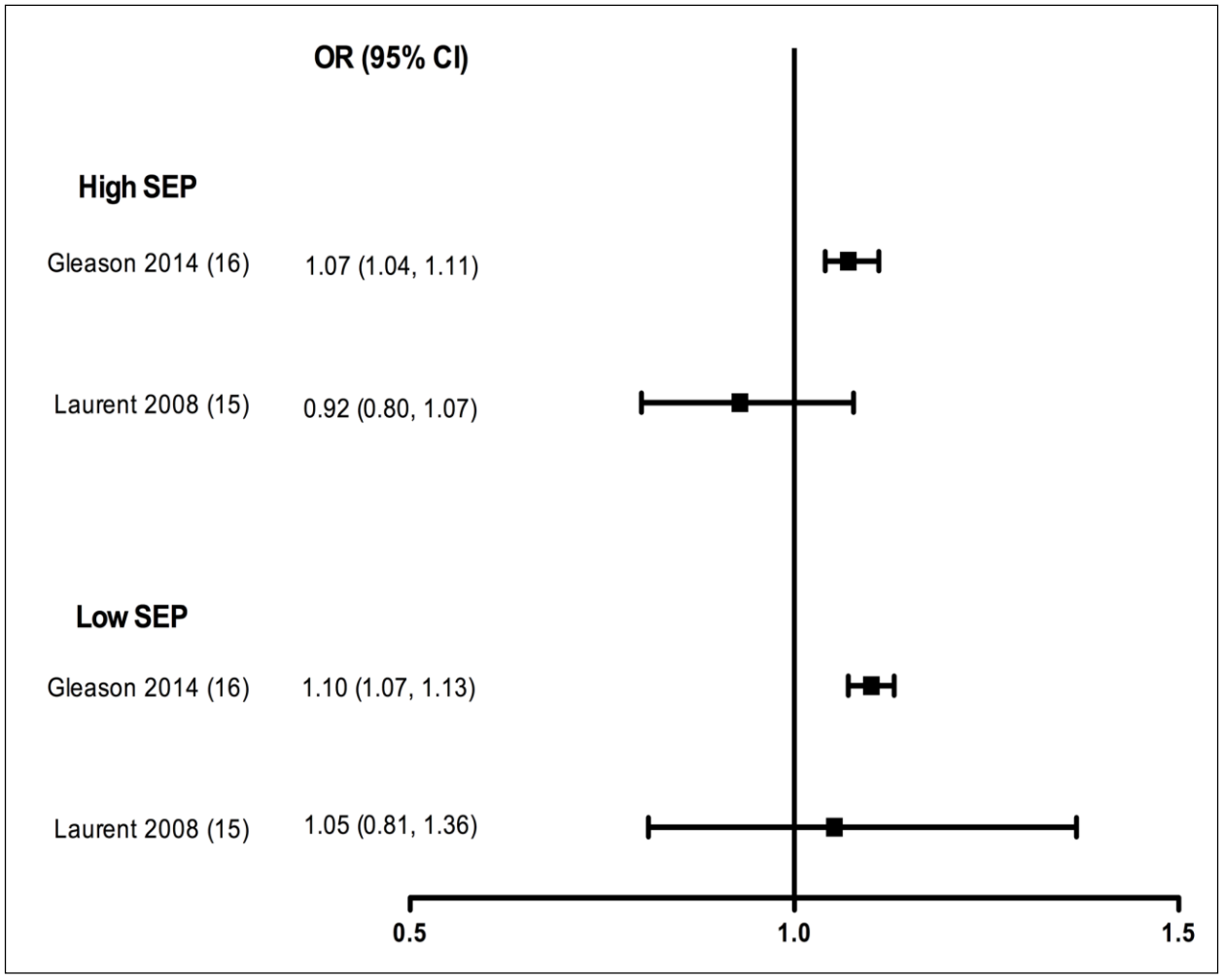


Figure 2- 3. Effect modification by socioeconomic position on the association between ozone and emergency visits/calls for asthma in children.



CHAPTER 3. The Short-term Effect of Multiple Air Pollutants on Children's Emergency Department Visits for Asthma and the Modifier Role of the Socioeconomic Position

3.1. Introduction

Asthma is the most common chronic respiratory disease in children (16). Asthma is also a complex, heterogeneous disease that results from the interaction of genetic, social, and environmental factors, which include chemical irritants in outdoor air (1, 19, 157). Sources of outdoor air pollution may be natural or anthropogenic; anthropogenic sources are most commonly attributed to industrial development and urban traffic (109). Outdoor air pollution has been associated with various health conditions including asthma, cardiovascular diseases, respiratory infections, adverse birth outcomes, and cancer (2, 80, 158). Furthermore, children are considered to be highly susceptible to the effects of air pollution due to physiological factors and physical activity (159, 160). The effects of outdoor air pollution on children's asthma include an increase in its incidence, prevalence, self-reported symptoms, emergency department (ED) visits, hospitalizations, and worsening of lung function measurements (3, 78, 79, 161). It is estimated that 30% of asthma exacerbations in children are related to anthropogenic environmental pollution in air, food, and water (162).

Outdoor air pollution is a complex mixture of compounds (e.g., solid particles, liquid droplets, gases) and its composition varies greatly within and among regions, depending on the sources of emission and weather patterns (14, 110). Air pollutants of major public health concern include carbon monoxide (CO), ground-level ozone (O_3), nitrogen oxides (NO_x), sulfur dioxide (SO_2) and particulate matter with mean aerodynamic diameter of 10 μm (PM_{10}), or 2.5 μm ($PM_{2.5}$). These pollutants are called "criteria air pollutants" and are monitored in most cities

worldwide by air quality surveillance (monitoring) systems (111). Traditional epidemiological assessments of the effects of air pollution on health have used models for a single pollutant at a time. In real conditions, however, air pollutants interact to produce health effects. Currently, the challenge in air pollution and health research is to address this issue using a "multipollutant approach to estimation of health risk", which is defined as research that focuses on estimating the total health effect associated with the exposure to multiple (more than one) pollutants (12, 163). Using multipollutant exposure metrics will advance our understanding of the combined effects on air pollutants (128).

The Air Quality Health Index (AQHI) is an indicator of the short-term health risks associated with air quality, based on the concentrations and associated risks of the three main air pollutants known to adversely affect human health in epidemiological studies (122). The AQHI was developed by Health Canada and Environment Canada, in collaboration with the provinces and key health and environment stakeholders, as a health information tool to help the public adjust their activity levels to minimize their exposure to air pollution, especially for people who may be more susceptible to the effects of air pollution (e.g., people with respiratory or cardiovascular chronic disease). The ultimate goal of the AQHI is to reduce the risk of an adverse health event (164). The AQHI is calculated based on combination of the concentrations and the mortality risks of three pollutants: NO_2, O_3, and $PM_{2.5}$ (122); therefore, the AQHI is a composite measure of air quality. Canadian studies have reported that an increase in AQHI values is associated with an increased number of ED visits for asthma and stroke (123-125).

Socioeconomic position (SEP) is a determinant of health that may modify the effect of environmental exposures on health outcomes (96, 98, 99, 102, 165), which is known as effect-modification (100). Three main mechanisms have been proposed to explain this effect related to

air pollution exposures (104): 1) unequal air pollution exposure related to SEP; 2) susceptibility directly related to SEP (e.g., differential levels of health care access, nutrition, stress in low SEP populations); and 3) susceptibility from predisposing health conditions or behaviors already associated with low SEP such as obesity and second-hand smoking. Understanding the role of SEP on the association between air pollution and children's asthma may help identify susceptible sub-populations to the effect of air pollution (104).

The Census Metropolitan Area of Edmonton (CMAE) has anthropogenic sources of outdoor air pollution arising from both, industry and traffic. Industrial emissions originate mainly from the petrochemical industry in the northeast and the coal-fired power plants in the west. Increased traffic is related to urban development and population growth over the past decade (9, 166). Previous studies conducted in the Edmonton between 1992 and 2002 documented an increase in children's asthma ED visits related to an increase in concentrations of NO_2, CO, O_3, PM_{10}, and $PM_{2.5}$ (10, 11). In addition, asthma ED presentations in children in Alberta were reported to differ by health premium subsidy status, a proxy measure of SEP (35).

The previous chapter of this dissertation summarizes the findings of a systematic review of studies of associations between air pollution and asthma outcomes in children that have assessed the modifier role of SEP. Results showed that there is weak evidence that SEP modifies these associations. Some stronger negative effects on asthma-related hospitalizations were reported for children living in a lower SEP; however, statistical assessment of the modification effect was not routinely conducted. None of the ten included studies used a composite air quality measure (i.e., multipollutants) as pollution exposure and most of them assessed the SEP at ecological level. There were only three studies assessing the modifier role of SEP on asthma ED visits/calls. Two of them failed to control for the effect of important potential confounders (e.g.,

meteorological and influenza seasonality) and the third had a relatively small sample size that may limit interaction analysis. In addition, none of them were conducted in the framework of a universal coverage health system, like the Canadian, that may influence the use or access to health service.

Therefore, this chapter aims to address identified gaps related to exposure to multiple air pollutants, controlling for potential confounders, and using population-based data. The specific objective of the study was to analyse the short-term association between AQHI, as a multipollutant exposure metric, and children's ED visits for asthma and its potential effect modification by SEP, using a case-crossover study design. This chapter also addresses a gap in air pollution and health research in the region with the intention to provide a greater understanding of the relationship among air pollution, asthma, and SEP that could inform regional asthma prevention and control programs.

3.2. Methods

3.2.1. Hospital emergency department visit data

Alberta Health Services (AHS) provided anonymous patient data from the Edmonton zone subdivision required for the study. This Edmonton zone administrative subdivision operates 11 Hospital ED facilities that provide services for children across the CMAE. Appendix C illustrates the geographical location and provides general information of these 11 ED facilities. Appendix D shows the AHS subdivisions and the matching between the AHS Edmonton zone and the CMAE.

Data were obtained for all residents between the ages of 2 and 14 years old in the CMAE, who were diagnosed with asthma in a hospital ED facility from April 1, 2004 to March

31, 2010. Asthma ED visits for children less than 2 years of age were excluded, as the diagnosis of asthma in this age group is less accurate. Asthma ED visits were also restricted for children up to 14 years old to minimize the potential air pollution exposure misclassification in the study of intra-urban variability; children up to 14 years old are usually in primary school and the location of these schools (and therefore their air pollution exposure) is usually close to the children's house area, which was selected as the exposure location for the study.

In the AHS Ambulatory Care Classification System, each ED visit is coded by experienced medical record nosologists using the International Classification of Disease 10th revision (ICD-10) according to the triage information, nursing notes, ED records and consultation notes. Asthma ED visits were identified as those having the ICD-10 code J45 as first discharge diagnosis. Additional variables of the asthma database included a unique patient number, date of the visit, age, sex, health premium subsidy status, Aboriginal status (i.e., First Nations peoples with treaty status), and residential postal code of the patient. Only children whose residential postal code belonged to the CMAE were selected.

The personal health number was anonymized at AHS and instead, a unique number was defined using standard algorithms at AHS. The unique number provided by AHS was used to identify multiple visits from the same child. In total, 10,681 visits belonged to children between 2 to 14 years old residents in the CMAE. Exclusions were made for 229 records corresponding to visits for the same day and patient and 31 records corresponding to visits from the same patient in days corresponding to the same time-strata (month and year). Therefore, the risks estimates presented in this chapter are based on a total of 10,421 ED visits.

In addition to the asthma data, AHS provided information of ED visits with discharge diagnosis of influenza (ICD-10 code J9, J10, and J11). The ED visits with influenza as first

discharge diagnosis were selected and then a database was created with the total number of daily visits for influenza. The influenza data was used to control the AQHI and air pollutants risk estimates for asthma ED visits for the potential confounding effect of viral respiratory seasonal epidemics.

3.2.2. Air pollutants and meteorological measurements

Air pollution data were obtained from the National Air Pollution Surveillance (NAPS) network (117). The fixed monitor stations data for the province was publicly available until 2014 from the Clean Air Strategic Alliance CASA Data Warehouse (httpp://www.casadata.org). Subsequent years' data became available from the Alberta Environmental Monitoring, Evaluation and Reporting Agency (AEMERA), a new provincial authority responsible for the Alberta's ambient air quality data warehouse (118). In the CMAE, continuous data (24 hours data) from air pollutants were available from the five Edmonton stations operated by Alberta Environment during the study period (Figure 3-1): Edmonton Central, Edmonton East, Edmonton Northwest (inactive from 12 December 2005), Edmonton South (active since 21 September 2005), and Edmonton McIntyre (active from 20 January 2006; provides PM monitoring only).

Daily means were calculated as the average of 24 hourly measures in the same day in each station; daily pollution measures were considered as missing if any of the 24 hourly measures were not available at one station. Data were obtained for NO_2, O_3, and $PM_{2.5}$, which are the air pollutants that contribute information to the AQHI. The air pollutants measured by the Alberta Environment monitoring stations use "reference methods" or "equivalent methods" as designed by the US-EPA. NO_2 was measured by the principle of chemoluminescence; O_3 was

measured by using ultra-violet (UV) light absorbance; and $PM_{2.5}$ was monitored using Tapered Element Oscillating Microbalance (TEOM) (119). Overall daily air pollutant levels were represented by the average across the number of monitor stations providing data for NO_2 and $PM_{2.5}$ each day. In the case of O_3, the 8-hour maximum value was used.

Meteorological data for daily mean temperature and relative humidity were obtained from the Environment Canada monitoring station at the Edmonton International airport. These meteorological measurements were used as time-variant potential confounding factors that were controlled for in the multivariable regression models.

3.2.3. AQHI calculation

The AQHI captures the overall risk related to three pollutants (NO_2, $PM_{2.5}$, O_3) within a no-threshold index standardized in a scale from 1 to 10. The AQHI calculation is based on the linear combination of concentration-response coefficients from a time-series analysis of air pollution and mortality from multiple Canadian cities (122, 167). The AQHI calculation uses the rolling 3-hour average pollutant concentrations (i.e., the average of the current and two previous hours), because the 3-hour average had shown to be more stable that 1-hour average (164). The rolling 3-hour average was calculated by hour for each pollutant based on the hourly average concentration across monitoring stations. The following formula was used for calculating the AQHI for every hour (122, 164):

$$AQHI = 10/10.4 \times (100 \times (e^{(0.000871 \times NO_2)} - 1 + e^{(0.000537 \times O_3)} - 1 + e^{(0.000487 \times PM_{2.5})} - 1))$$

where all pollutants are entered as 3-hour moving average concentrations in parts per billion (ppb) for NO_2 and O_3, and $\mu g/m^3$ for $PM_{2.5}$. The daily AQHI was calculated as the average of the 24-hour estimations of the AQHI.

3.2.4. Study design and statistical analysis

Descriptive analysis was conducted by using frequencies and percentages for summarizing categorical data, and mean, standard deviation (SD), median and interquartile range (IQR) for continuous data. Crude ED visit rates for asthma were estimated using the Alberta Health Care Insurance Plan registry total population between 2 and 14 years old for each year. Age-group and sex directly standardized rates (DSR) for ED visits by subsidy status were estimated using the Census 2006 children population in the CMAE as standard population. Pearson coefficients were calculated as correlation measures among pollutants and meteorological variables.

A case-crossover (CCO) study design, with a time-stratified method for selection of control periods, was used to assess the short-term association between the daily average of the AQHI and children's ED visits for asthma. The CCO design was proposed by Maclure in 1991 (168) to identify risk factors for acute events; it is an adaptation of the case-control design where each subject serves as his or her own control by assessing referent exposure at a point in time prior to the event (168, 169). In the CCO design, the referent time periods represent the counterfactual exposure experience of an individual, had he or she not become sick. In the case of air pollution, pre and post-event exposure concentrations of air pollutants are independent of the hazard-period exposure, therefore the post-events can be also appropriated referral periods (170). As a result of its definition, the CCO study controls by design for the influence of

potential confounding variables that remain constant in the subject at both dates (time-invariant confounders at case and referent times), such as sex, age, genetics, obesity, etc. Furthermore, choosing referent intervals that are close in time to the case event, the CCO design also controls for seasonal patterns of disease occurrence (time-variant confounders) by matching. In addition, one advantage of the CCO design is its ability to assess potential effect-measure modification by individual characteristics (171, 172).

The referent selection strategy is a key issue in the CCO design. Selection strategies can be unidirectional versus bidirectional, symmetric and semi-symmetric, or time stratified (171). The time-stratified selection strategy, controls for season and day of the week by restricting referents to the same day of the week, month, and year of the case event. The time-stratified selection strategy is one method of referent selection that controls for time trend bias and for time-variant confounding by design and produces unbiased estimates of association in the conditional logistic regression model (171, 173). In CCO studies of air pollution and acute health events, the exposure is variable, the effect on risk is acute and transient, and the event is abrupt. Under these conditions, the theoretical target population is not the "population at risk" but "the person times at risk", and therefore different events from the same patient at different time windows (case and referent periods) can be considered independent observations (169).

In this study, the day of occurrence of each ED visit for asthma was considered a "case period". By using a time-stratified method, "referent periods" were selected as the days corresponding to the same day of the week, month, and year of the "case period"; therefore, each matched set is composed by a case period and either three or four referent periods. For example, if an ED visits for asthma occurred in Monday, January 11th 2010, the referent periods chosen were all Mondays in January 2010 (January 4th, 18th, and 25th). The ED visits for asthma

for the same person during different days during the study period were included if the case period for a second or subsequent visit was outside the previous referent windows. A program code in Stata 13 (174) was written and used for creating the CCO database with case and referent periods. The Appendix E shows the flowchart of the procedures followed to create the complete database for analysis.

The estimated daily average of the AQHI were compared between case and control periods to estimate a measure of risk of the occurrence of asthma visits associated with variation of AQHI values. Conditional logistic regression was used to calculate Odds Ratios (OR) and their corresponding 95% confidence intervals (CI). The OR represents the change in risk for the occurrence of an ED visit for asthma associated with a daily increase in the AQHI. Multivariable models were used to control for time-varying covariates: temperature, relative humidity, and Canadian holidays; in addition models were adjusted for the daily number of ED visits for influenza controlling for viral respiratory seasonal epidemics.

Meteorological variables (temperature and relative humidity) were modeled as linear and cubic splines; however, there were not notable difference in the risk estimates and the Akaike information criterion (AIC) when using the more complex models (i.e., AIC for models with linear predictors and with cubic splines were 30,679.83 and 30,663.41, respectively); therefore, the multivariable models were adjusted for linear effects of temperature and relative humidity. Risk estimates were also calculated using single pollutants models (for NO_2, O_3, and $PM_{2.5}$) to compare the AQHI risk estimates with the individual pollutants estimated risks.

Following the recommendations from Künzli & Schindler (175), the concentration difference of the AQHI (i.e., the difference between case period and the average of the referent periods) was reported as the relevant exposure term for the CCO analysis. Consequently, the

ORs from all multivariable models are expressed as an increase in the interquartile range (IQR) of the concentration difference distribution over the study period. Risk estimates from multivariable models were provided by age-group, sex, season, and Aboriginal status.

Different exposure lag terms were created to assess the temporal relationship between the AQHI, and single pollutants, and the time when the children presented to the ED for asthma. Considering that most air pollution and children's asthma studies in Canada have found associations with lagged exposures up to 5 days before the presentation of the asthma event (10, 79), lagged exposures from 1 to 5 days and cumulative 3-day and 5-day mean exposure estimates were created. For instance, the cumulative 3-day average exposure refers to the mean air pollutant concentration on the day of the ED visit, the day before, and two days before.

The potential modifier effect of SEP was assessed by using an individual SEP measure. Health premium subsidy status was taken as surrogate measure of individual SEP; children were grouped into subsidy and non-subsidy according to the "alternate subsidy arrangement" variable of the Alberta Health Care Insurance Plan registry file. Children under the categories "A=Aboriginal", "W=Welfare", and "R= Government-sponsored programs" were assigned to the subsidy group and children with "0=resident without subsidy" category were assigned to the non-subsidy group. The subsidy benefit was assigned by the provincial government to people with low family income or for belonging to special protected groups (i.e., welfare and Aboriginals with Treaty status). This variable had been used in previous studies as SEP proxy measure and had shown to be a valid indicator of SEP in Alberta (34, 35).

Effect measure modification by SEP was assessed in multivariable models by using stratified and interaction analyses. Stratified analyses were conducted by building multivariable models for AQHI by subsidy status. Risk estimates that differ in direction and/or magnitude

across SEP categories are an indication of possible effect-modification. Interaction analyses were conducted by creating interaction terms between the SEP measure and the AQHI, and then, adding the interaction term to the multivariable models. A statistically significant interaction term is considered a confirmation of effect-measure modification at multiplicative scale (100, 155, 172). All statistical analyses were performed using Stata 13 (174).

3.2.5. Sensitivity analysis

Sensitivity analyses were conducted to assess the consistency of the results (i.e., risk estimations) when using different statistical analyses or variables. For CCO analyses of air pollution and health effects it has been recommended to conduct a sensitivity analysis by using another type of CCO design or conduct a Poisson time series analyses (172). Based on the equivalence of CCO with time-series methods (176), a conditional Poisson model was used as an alternative analysis. A Poisson conditional time-series model for counts at dissemination area (DA) level with stratum indicators for year-month-day of the week was conducted for different lag periods (177).

The Chan's Canadian Socioeconomic Index was used as an alternative area-based SEP measure. The Chan's Index is a tool designed to be a comprehensive socioeconomic index for the Canadian population, which can be used for research involving environmental pollution and health outcomes. The Chan's SES Index is available at DA level and includes a component related to specific cultural identities (108). The Chan's index score was assigned to each asthma visit by matching the residential DA for each visit with the score of the Chan's index for the same DA. Quintiles of Chan's Index for Alberta were used to assign a quintile of the index to each asthma visit. Sensitivity analyses of the effect modification by SEP using the Chan's Index

quintiles were performed using stratified and interaction analysis as described for subsidy status as individual SEP measure. In addition, using the area-based Chan's index quintiles, a criterion validation of the Chan's index was performed taking the subsidy status individual variable as gold standard.

Finally, AQHI and single air pollutants models were built using the IQR of the daily concentration instead of the IQR of the difference concentration between case and control periods. This sensitivity analysis was conducted because most of the CCO studies of air pollution and asthma report their findings expressing the OR for an IQR of the daily concentration over the study period.

3.3. Results

3.3.1. Descriptive Statistics

A total of 10,421 visits were recorded in hospital EDs for children between 2 -14 years of age living in the CMAE with a primary diagnosis of asthma during the study period. The 10,421 asthma ED visits were made by 6,184 distinct children, with an average of 1.68 visits per child (median=1; IQR=1; 55.9% of children had only 1 ED visit). The ED visits for asthma were more common in boys (64%), in the age group between 5-14 years (62%), and during the warm season (59%). The ED visits from children registered as Aboriginals with Treaty status accounted for approximately 6% of the total visits (Table 3-1).

The CMAE pediatric population increased over the study period and the yearly ED visits for asthma decreased, resulting in a decreasing crude visit rates over time from a maximum of 12.9 per 1,000 children in 2005/2006 to a minimum of 8.1 per 1,000 children in 2009/2010 (Table 3-2). The age and sex directly standardized rates (DSRs) varied greatly by subsidy group.

In most fiscal years, the Welfare and Aboriginal DSRs were on average 50% larger than the DSR for children in the Registrant without Subsidy group (Table 3-3).

One hundred and eighty children (1.7% of the total ED visits) were admitted to the hospital and proportions remain relatively stable over time (Figure 3-2).

The average length of stay in the ED was 208 minutes (median=172; IQR= 157). Timing of the ED visits varied according to month and day of the week. During 2004/2005 to 2009/2010, peaks of ED visits for asthma were observed in September and May (14.7% and 11.2% of the total ED visits). Sunday and Monday were the days of the week with the higher volumes of ED visits. Figure 3-3 shows the timing of ED visits per month and day of the week.

Table 3-4 summarizes the mean, SD, maximum, percentiles (5^{th}, 25^{th}, 50^{th}, 75^{th}, and 95^{th}), and IQR values of daily AQHI, ambient air pollutants (NO_2, O_3, $PM_{2.5}$), and meteorological variables during the study period. For the 2,191 days of the study period, there were at least two monitoring stations with complete hourly concentrations; therefore, daily average of air pollutants were obtained for all days during the study period. The distribution summary measures are presented for the daily concentrations of case events as well as for the concentration difference of the matched pairs of events (i.e., concentration in the case day minus the average of concentrations in the referent days). The average AQHI was 2.63 and the mean concentration difference was -0.01; for the three air pollutants that contribute to the AQHI, the mean and median concentration differences were also negative, which means that on average, the concentration during the referent days was higher than the pollutant concentration during the case days. Table 3-5 presents the same summary measures by season. In general, median AQHI and NO_2 concentrations were slightly higher during the cold season, and median concentrations

for O_3 and $PM_{2.5}$ were higher during the warm season; the median of the concentration differences were negative in both seasons.

Table 3-6 and Figure 3-4 present summary measures for daily concentrations and concentration differences over the calendar years of the study. Overall, the AQHI values were similar between 2004 to 2008 and increased slightly in 2009; NO_2 concentrations decreased over the study period; $PM_{2.5}$ showed a relative stable concentration until 2007 and then started to increase; and O_3 concentrations increased starting in 2006.

The Pearson correlations among air pollutants during the entire study period showed that NO_2 and $PM_{2.5}$ were positively correlated (r=0.46); O_3 was negatively correlated with NO_2 (r=-0.56) and $PM_{2.5}$ (r=-0.20), and $PM_{2.5}$ was positively correlated with temperature (r=0.47).

3.3.2. Association between Exposure to Air Pollution and ED visits for asthma

The adjusted ORs of ED visits for asthma with different pollution exposure lag periods for the AQHI and single air pollutants models by season and for the whole study period are presented in Table 3-7. Adjusted ORs for the AQHI model and NO_2, O_3, and $PM_{2.5}$ single pollutants models exhibit inverse and statistically significant associations with ED visits for asthma during the same day. For instance, an increase in the IQR of the concentration difference during the same day exposure for AQHI was associated with a decrease of 5% in the risk of an asthma ED visit (OR 0.95; 95% CI 0.92-0.98) after controlling for temperature, relative humidity, holiday indicator and daily number of influenza visits. Associations for the remaining exposure lag periods for AQHI exposure, and some lag exposure periods for the single pollutant models were also statistically significant, except for NO_2. During the cold season, AQHI and air pollutants did not exhibit statistically significant associations with children's ED visits for

asthma. In contrast, during the warm season, the AQHI and the three single pollutants models resulted in statistically significant associations with ORs below 1 during the same day and cumulative 5-day lag period. Some of the lagged exposure periods were also statistically significant for O_3 and $PM_{2.5}$, but not for NO_2.

The adjusted ORs of ED visits for asthma for the same day AQHI and single air pollutants exposure by age group, sex, and Aboriginal status are presented in Table 3-8. In AQHI or single pollutant models, the adjusted ORs were not statistically significant for the age group between 2 and 4 years old; for the 5-14 years group ORs were below 1 and statistically significant except for O_3. All models stratified by sex exhibit ORs slightly below 1; however, only the AQHI and NO_2 models exhibit statistically significant ORs for both sexes. The estimated ORs for AQHI and NO_2 models in Aboriginal children exhibit risk associations that were not statistically significant (OR 1.07; 95% CI 0.92-1.24).

3.3.3. Effect Measure Modification by SEP

Table 3-9 display the adjusted OR and 95% CI of the stratified and interaction models assessing the effect modification of the relationship between AQHI and ED visits for asthma by subsidy status. In general, the stratified analysis exhibit similar risk estimates across subsidy status categories for the different exposure lag periods; ORs were slightly below 1 and statistically significant during the same day exposure for both categories but with lower risk for the subsidy-beneficiaries category. The interaction term between AQHI and subsidy status was not statistically significant in the multivariable models using different lag exposure periods, which is against an effect-measure modification of SEP measured at individual level with subsidy status as SEP proxy variable.

3.3.4. Sensitivity analyses results

Results of association between air pollution exposure and ED visits for asthma exhibit similar results, both in direction and magnitude, when using conditional Poisson time series analysis at dissemination area level with a time-stratum indicator. Table 3-10 displays the adjusted ORs and corresponding 95% CI for associations for the whole study period and by season. Odds ratios for the AQHI model and NO_2, O_3, and $PM_{2.5}$ single pollutants models exhibit inverse and statistically significant associations with ED visits for asthma during the same day. For instance, an increase in the IQR of the daily concentration during the same day exposure for AQHI was associated with a decrease of 6% in the risk of an asthma ED visit (OR 0.94; 95% CI 0.91-0.98) after controlling for the effect potential time-variant confounders. Similar findings were seen for single air pollutant models during the same day and cumulative 1-5 days exposure period, with statistically significant estimates for most of the ORs during the whole study period and during the warm season. Therefore, results from the CCO analysis are consistent with results using a time series approach.

Results of association between air pollution exposure and ED visits for asthma also exhibit similar results, both in direction and magnitude, when using IQR of the daily concentration, rather than the IQR of the concentration difference between case and referent periods. Table 3-11 shows the adjusted ORs of ED visits for asthma for AQHI and single pollutants models using same day exposure and IQR of daily concentrations. Therefore, results are consistent when using either exposure term (daily concentrations or concentration difference distributions) for presenting ORs.

Effect modification analysis by SEP using the Chan's Canadian index gave similar results when compared to the analysis using the individual subsidy status. Table 3-12 displays

the adjusted ORs of ED visits for asthma for air pollution exposure using different exposure lag periods and stratified by Chan's index quintiles, where Q1 refers to the lowest SEP level and Q5 to the highest. Interaction models also exhibit no-statistically significant interaction terms between AQHI and Chan's index score, which is against an effect modification by SEP using a small-area level measure. Therefore, lack of effect measure modification by SEP on the relationship between AQHI and asthma ED visits was consistent when using either an individual or area-based SEP measure.

The Chan's index quintiles were compared to the individual subsidy status measure as gold standard. Table 3-13 displays the concordance between the two SEP measurements; according to the table, the Chan's SES Index is misclassifying the individual SES status based on subsidy: only 42% of people with subsidy is in quintile 1 and 65% is in quintiles 1 and 2. In Chan's index quintile 5, 11% of the individuals are misclassified as they are receiving subsidy. Table 3-14 shows the table for criterion validity; based on this table, the estimated sensitivity and specificity of the Chan's index quintiles to classify people was 78.43% and 52.67%, respectively.

3.4. Discussion

This study found that short-term elevations of the AQHI did not increase the risk for children's ED for asthma visits in the CMAE between 2004 and 2010. This finding was more evident during same day exposure and 5-day cumulative lag exposure period and during the warm season when the risk of having an ED visit for asthma decreased between 5% and 13% per one unit increase in the IQR of the AQHI concentration difference, respectively. These findings were consistent when using AQHI as a multi pollutant air pollution exposure or when

individually assessing NO_2, O_3 and $PM_{2.5}$ concentrations. The use of two different study designs, CCO and time series analysis, resulted in similar findings. In addition, the study results revealed that the observed effect was not different across categories of SEP and therefore there is no evidence of the modifier effect of SEP on the relationship between air pollution exposure and asthma ED visits in the study population.

These study findings contrast with results from previous studies conducted in the Edmonton area between 1992 and 2002, which reported associations of short-term elevations of ambient air pollutants with increased risk of ED visits for asthma, especially in children between 2-4 years, and during the warm season (10, 11). Similar findings of increased risk of ED visits for asthma related to elevations in air pollutants had been reported in different cities around the world, including other Canadian cities (3, 78-80). One previous study in Windsor, Canada, using the AQHI as combined air pollution exposure and a similar study design, also found an increased risk of ED visits for asthma up to 11% during the same-day exposure in children aged 2-14 years old between 2004 and 2010 (123). Thus, these study findings counter previous evidence of the adverse health effects of air pollution with apparent no threshold, and create the need and opportunity to explore the specific local conditions that are influencing the change of the relationship between outdoor air pollution and asthma exacerbations in the CMAE.

This study was undertaken, in part, because of the interest of assessing the potential role of SEP as an effect modifier of the relationship between asthma exacerbations and outdoor air pollution. In addition, the study was conducted because there have been few studies that have evaluated how the association changes over time, acknowledging that ED visits for asthma started to decreased slightly after 2002 (35), the concentrations of most air pollutants decreased after 2000 (15), and the pollution mixture may also have changed with changes in pollution

sources in the Edmonton area (9). Therefore, explanations of these changes and their potential role in the study findings are discussed with detail in the following paragraphs.

Children's ED visit rates for asthma decreased over time during the study period. Crude visit rates decrease by 4.8 visits per 1,000 children between 2005/2006 and 2009/2010, which represents a decrease in 37% in the crude rate of ED visits in five years. Similarly, asthma rates reported in Alberta for children under 18 years of age in 2004/2005 were lower than those during the previous five years, which implies that there is a long-term downward trend in asthma rates (35). Asthma ED visits remained more common in boys, 5-14 years of age, and during the warm season, as reported before for Alberta (35). Thus, the number of visits and visits rates decreased over time but the profile of ED visits for asthma remained the same. Considering these findings together suggests that there was a steady decline in the rates of asthma exacerbations in the CMAE between 2004/2005 and 2009/2010. Moreover, the prevalence estimates for children steadily increased up to 13% in 2000/2001 and then fell slightly to 10% by 2008/2009 (31). Therefore, the CMAE had a relatively stable number of children with asthma who experienced fewer asthma exacerbations; the two more probable explanations for this phenomenon rely on better access to health care and improved asthma management.

Health care access and asthma care have both changed in important ways over the last several decades in Canada. The Canadian health care system continues to have universal coverage for all residents (178). Different studies have found that the universal coverage of the Canadian system has been successful in providing access to primary health care (i.e., primary care physician) for people independent of their socioeconomic status; however, it has been less successful at providing access to specialists (179-181), which in turn may result in better

ambulatory care and less ED visits and hospitalizations for conditions sensitive to ambulatory care like asthma (180). In US, there is evidence of a decrease in the number of ED visits for asthma related to an increase in access to primary health care services (147).

Despite the fact that the health care model is based on primary care, the number of family physicians in Canada has been insufficient to respond to the demand of the population; starting in 2000, efforts to increase the primary care workforce have been implemented including reallocation of funds to increase the number of instructional hours for family physicians in the first years of postgraduate training and creating financial incentives and primary care networks (182, 183). In addition, during the same decade, walk-in clinics increased as a response to the scarce availability of primary care facilities and physicians after office hours to provide care for acute non-life threatening conditions (184). Walk-in clinics and urgent care centers are health care options for people who require consultation with a primary care physician for conditions such as an asthma exacerbation when they do not have a family doctor or their family doctor cannot see them in a timely fashion (185). Therefore, during the study period, walk-in clinics emerged as primary care facilities where mild to moderate asthma exacerbations could be treated, thus avoiding the need for hospital ED visits.

Asthma management also changed importantly in Canada during the study period. Starting in 1999 the Canadian Asthma Consensus Report included asthma education as a key recommendation in asthma management (186). In the Asthma Consensus guidelines 2003, the asthma education was defined as an essential component of asthma therapy that should be offered to all patients along with an individual written action plan for self-management. This includes medication adjustment in response to severity or frequency of symptoms, the need for symptoms relief medication or a change in the peak expiratory flow (187).

Educational programs for asthma self-management in children and adolescents have led to improved lung function and feelings of self-control, number of days with restricted activity, and number of visits to ED (89). A community trial of a children's asthma education program conducted in Edmonton among school children with asthma aged 5 to 13 years old reported that after an educational intervention of six weeks administered by health professional in schools, the group receiving the educational intervention improved parent's perceived understanding and ability to cope with asthma, and overall quality of life (188).

Besides asthma education and a written action plan, the Asthma Consensus guidelines 2003, also recommended that the discharge plan for a patient after an ED visit for asthma should reinforce the need for a close follow-up visit within the first week after the ED visit. Fleming et al. (189) in Barrie, Ontario, reported that enrollment in a hospital-based pediatric asthma clinic with a inter-professional care was associated with average decrease of 67% in ED visits for asthma and 85% in admissions in the first year after enrollment.

In addition to the role of improved asthma education and follow-up, increased use of asthma medications have also become more common during the last 15 years. The 1999 Asthma Consensus guidelines recommended the use of pressurized metered-dose inhaler with valve spacer and mouthpiece for children in place of the wet nebulizer with a mask, aiming to maximize the lung deposition of inhaled medications (190). The use of breath-actuated devices such as dry- powder inhalers, was also recommended for maintenance treatment in children over 5 years of age (186).

At the same time, evidence of the effectiveness of new medications such a leukotriene receptor antagonist (191) and long acting β2-agonist (192), as second controller medications, became available for asthma treatment and were included as part of the recommendations for

asthma management (87, 191). The leukotriene receptor antagonist drugs, however, are not provided as a "Regular benefit" in the Alberta Health drug benefit list (193), which means that access to this controller medication may be limited for children with low family income, and may help explain the observed higher rates of ED visits for asthma.

Concentrations of ambient air pollutants decreased during the study period compared to reports of concentration in previous studies. Compared to the daily median concentrations of air pollutants reported by Villeneuve et al (10) during 1992 to 2002, NO_2 median daily concentration decreased from 17.5 to 12.8 ppb (28%) in the warm season, and from 28.5 to 19.3 ppb (32%) during the cold season. The $PM_{2.5,}$ median concentrations decreased from 7.0 to 5.19 $\mu g/m^3$ (26%), and from 7.3 to 3.58 $\mu g/m^3$ (50%) during the warm and cold season, respectively. In contrast, the median concentrations of O_3 increased from 38 to 44 ppb (16%) during the warm season, and from 24.3 to 31 ppb (28%) during the cold season.

The concentration variability also decreased for NO_2 and $PM_{2.5}$ compared to previous reports evidenced by a decrease in the IQR from 13.5 to 8.35 ppb for NO_2, and from 6.3 to 4.38 $\mu g/m^3$ for $PM_{2.5}$. The median value and variability of the AQHI also decreased during the study period compared to another previous study conducted in Edmonton between 1998 and 2002 (124); AQHI median values decreased from 3.20 to 2.58 (19% of the 1998-2002 median value), and IQR decreased from 1.31 to 0.77 (41% of the 1998-2002 IQR), using the same formulae for the AQHI calculation.

Taken together, these data suggest that median concentrations of NO_2 and $PM_{2.5}$ exhibited marked reductions while O_3 exhibited a marked increase during the study period compared to previous studies in the Edmonton area. Interestingly, the risk associations found in children by Villeneuve et al. (10) with ED visits for children with acute asthma aged 2-14 years

in the warm season were stronger for NO_2 and CO than for O_3, especially in the children between 2-4 years for whom the association with O_3 was not statistically significant. In Southern California, Gauderman et al. (194) reported that long-term decrease in levels of NO_2 and particulate pollution ($PM_{2.5}$ and PM_{10}), but not in levels of O_3, were associated with improved lung function development in children between 11 and 15 years of age. Similar health benefits from reduction in air pollution levels have been also described for adults (195, 196). Therefore, improved lung function as a result of a long-term decrease in NO_2 and $PM_{2.5}$ in the Edmonton area is also a potential explanation for these study findings.

Despite the increase of O_3 during the study period, the present study showed no risk association with ED visits for asthma, suggesting that despite the fact that the oxidant capacity of O_3 is larger than that for NO_2 (2), the increase in median O_3 concentrations did not translate into increased ED visits for asthma in children. Similar findings regarding absence of effect of O_3 in children have been reported by different studies of asthma incidence, hospitalizations, lung function, and ED visits (4, 197-200).

It is also worth noting that the outdoor air pollutants concentrations observed in Canadian cities are usually lower compared to most of the concentrations reported in studies from US or Asian cities that have found risk associations with asthma ED visits. Moreover, it is recognized that Canadian studies added to air pollution and asthma research literature in the last decade by demonstrating risk effects on health even at lower concentrations observed in studies conducted in other cities around the world (80).

A systematic review of the literature published in 2015, identified the studies assessing the effects of outdoor air pollution on the respiratory health of Canadian children between 2004 and 2014 (79); the AQHI and single pollutant concentrations reported by the included studies

assessing the effects on ED visits for asthma were higher than the concentrations observed in the present study (10, 11, 123, 125, 201). Thus, the AQHI and air pollutant concentrations reported in this study represent the lowest concentrations of air pollutants in Canadian studies assessing the effect of outdoor air pollution on children's asthma ED visits. Therefore, these study findings suggest that low concentrations coupled with low variability of concentrations of NO_2 and $PM_{2.5}$, and therefore in the AQHI, as the ones reported in CMAE, have no impact on the presentations of children's ED visits for asthma.

The controversial findings of this study, therefore, have potential explanations on the combination of two key evidenced factors: the decreased rates of children's ED visits for asthma and the decreased concentration and variability of NO_2 and $PM_{2.5}$, and therefore the AQHI values, compared to reports in the previous decade. The decreased number of ED visits may be explained, in part, because access to primary care and asthma management have changed over time in the CMAE, and only the more severe cases presented to hospital EDs. It is possible that such asthma cases are more affected by other factors than the studied pollutants, such as allergen exposure in atopic children, indoor air pollution, or epigenetic factors (5, 202). There may be exacerbations after transient elevations in outdoor air pollution that are now better controlled at home or in walk-in clinics. Therefore, this study does not rule out associations of air pollution with mild to moderate asthma exacerbations that did not report to hospital EDs. This study does suggests that patients presenting to hospital EDs, which are likely more severe asthma cases, were not associated with outdoor air pollution levels.

The Aboriginal group, representing First Nations children with treaty status, seem to be a specific population affected by the air pollution exposure. Stratified analysis of the association between AQHI and ED visits exhibited a risk association in the Aboriginal children compared

with no risk in non-Aboriginal children. These associations, however, were not statistically significant and remained unclear due to the small number of Aboriginal children with ED visits for asthma during the study period. Previous studies in Aboriginal children living on reserves and off-reserves have shown that asthma prevalence in children is similar to that reported for the non-Aboriginal Canadian children (203, 204).

Regarding the role of SEP, the study findings support the fact that ED visits for asthma are more common in children receiving health premium subsidy, as a surrogate measure of low SEP. Similar findings have been reported by a previous study of children's asthma presentations to the ED in Alberta (35) and other countries (205, 206). The association between variations of the AQHI and ED visits for asthma, however, did not differ by SEP levels when using individual (subsidy status) or ecological (Chan's Canadian index) SEP measures. Therefore, the study findings do not support the role of SEP as an effect modifier in the relationship between outdoor air pollution and children's ED visits for asthma in CMAE. This finding agrees with the results of the systematic review of the literature presented in Chapter 2, where the three included studies assessing the effect of air pollution on children's ED visits for asthma failed to demonstrate a modifier role of SEP on this relationship (135, 136, 144).

3.4.1. Strengths and limitations

An important strength of this study relies on the study design used. By design, the CCO controls for potential confounders that are invariant in time (e.g., age, sex, social condition, pre-natal and childhood risk factors) (168, 169). The time-stratified method used for selecting the referent periods controls was another strength, which matched for time-variant potential confounders (e.g., meteorological and seasonal variations) (171). Furthermore, the use of an

individual in the CCO design rather than ecological information used in time series analysis, allowed the analysis of the potential SEP modification effect at individual level (172). In addition, this study followed the recommendations for the analysis and presentation of CCO studies regarding the reporting of the relevant exposure term (i.e., the concentration difference), the assessment of the air pollution effect modeling, the statistical interaction, and the sensitivity analysis using a time series analysis (172, 175). Therefore, the results of the CCO analysis are consistent regarding the type of analysis (CCO vs time series) and type of SEP measures (individual vs ecological)

There are also some methodological limitations in this study. The air pollution exposure used in the study was based on a small number of fixed monitor stations located in the city of Edmonton and daily mean concentrations among the stations were assumed as the average of the air pollution exposure in the entire CMAE. There may be a measurement error in the air pollution exposure as the distance to the monitor stations increases due to sources and dispersion patterns of contaminants. Therefore, temporal variations in air pollutant and AQHI concentrations may be well represented at the monitoring stations, but the spatial distribution of the air pollution exposure may be affecting the real air pollution exposure, especially for children living outside the city of Edmonton where there are different traffic patterns and sources of industrial emissions. Assuming that these measurement errors were not differential between case and referent periods, this would usually result in an underestimation of the ORs and would bias the estimate to the null value (207). The AQHI and single pollutant models were not adjusted for the outdoor levels of aeroallergen, however, based in previous findings in Edmonton (10), this lack of adjustment would not lead to an important change in the risk

estimation. This study also lacks statistical power to clearly assess the effect of air pollution exposure by Aboriginal status.

The AHS databases are unable to capture all cases of asthma exacerbations. As discussed before, many children may report to non-hospital ED facilities, for their acute asthma episode. Therefore, the study findings do not rule out risk associations of air pollution with mild to moderate asthma exacerbations that did not report to hospital-ED facilities. Similarly, the AHS databases are unable to identify all Aboriginal children. The proxy variable for Aboriginal status is derived from the health care premium subsidy given by the province to Aboriginal peoples, which is restricted to First Nations peoples with Treaty status and a minority of Inuit Indigenous people living in the province; therefore, the Aboriginal Status variable is systematically excluding children belonging to non-status First Nations and Métis Aboriginal population.

Using administrative health data has several inherent weaknesses for observational studies, such as lack of granular details on the individual and the health care system. Unmeasured factors in this study include information on medication access and use, adherence to medications, exposure to smoke, and mental health, among others. Many of these factors may change over time within the same individual and may have influenced ED visits.

The SEP analysis used the subsidy status as an individual SEP proxy variable. The subsidy premiums were eliminated in Alberta in January 1st, 2009, and since then the registry has a decreasing quality in the registry of Alberta population and the alternate premium arrangement variable where the subsidy status variable is extracted (208). Furthermore, the subsidy status variable accounts mainly for family income and does not have into account the occupational or educational profile of individuals as is recommended for a comprehensive SEP

measure (97). The subsidy status variable, however, had been used in previous studies as proxy measure for SEP and has been shown to be a valid indicator of SEP in Alberta (35, 209-211).

3.5. Conclusions

Children's ED visits for asthma decreased between 2004 and 2010 in the CMAE. This finding may be related to changes in the quality of the asthma health care delivery over the last 15 years, resulting in better access to primary health care facilities and improved asthma management.

The median AQHI values and concentrations of NO_2 and $PM_{2.5}$ decreased 19%, 29%, and 37%, respectively, compared to the median concentrations reported during the decade 1992-2002 in the Edmonton area. These median concentration levels in air pollutants observed during this study are the lowest reported to date in studies assessing the effects of air pollution on asthma ED visits in Canadian children.

Transient elevations in the AQHI values or in the concentrations of NO_2, O_3, or $PM_{2.5}$, were not associated with an increased risk of having an ED visit for asthma in children aged 2-14 years in the CMAE between 2004/2005 and 2009/2010. This study, however, does not rule out risk associations of air pollution with mild to moderate asthma exacerbations that did not report to hospital ED. This study suggests that patients presenting to hospital EDs, which are likely more severe asthma cases, were not associated with outdoor air pollution levels.

In summary, there was a decreased number of hospital ED visits for children with acute asthma in the CMAE and these visits were not associated with transient elevations in the concentration of outdoor air pollutants between 2004 and 2010. Decreased hospital ED visits for asthma may be explained by better access to primary health care facilities and/or improved

asthma management. The decrease in the ED visit rates for asthma, along with a consistent decrease in NO_2 and $PM_{2.5}$ median concentrations compared to the decade 1992-2002, suggest that there might be a health benefit for children with asthma from improved air quality, and that in the CMAE severe children's asthma exacerbation in this age group are now more likely related to other environmental or individual conditions such as individual exposure to allergens, indoor conditions, and asthma mismanagement, among others. There was no evidence of a modifier effect role of SEP in the relationship between outdoor air pollution and children's asthma ED visits in the CMAE during the study period.

Table 3- 1. Number of emergency department visits for asthma in children by age group, sex, season, fiscal year and subsidy status in the Census Metropolitan Area of Edmonton, Alberta, Canada, 2004/2005 to 2009/2010.

Variable	No. visits	%
Age group (years)		
2 – 4	3,946	37.87
5 - 14	6,475	62.13
Sex		
Female	3,749	35.98
Male	6,672	64.02
Seasona		
Cold season	4,229	40.58
Warm season	6,192	59.42
Fiscal year[b]		
2004/2005	1,931	18.53
2005/2006	2,164	20.77
2006/2007	1,793	17.21
2007/2008	1,448	13.90
2008/2009	1,603	15.38
2009/2010	1,482	14.22
Subsidy status[c]		
Aboriginal	576	5.59
Welfare	640	6.21
Government-sponsored program	1,590	15.42
Registrant without subsidy	7,503	72.78

[a] Cold season from October to March and Warm season from April to September.
[b] Fiscal year starts in April 1 of the first year indicated and ends in March 31 of the second year indicated.
[C] Subsidy status based on Alternate premium arrangement variable from the Alberta Health Care Insurance Plan registry. Percentages over 10,309 visits; 112 visits did not have information on subsidy status.

Table 3- 2. Emergency department visits for acute asthma and crude rates for children between 2 and 14 years of age in the Census Metropolitan Area of Edmonton during April 1, 2004 to March 31, 2010.

Fiscal Year	Children population 2-14 years[a]	No. asthma ED visits	Crude visit rate per 1,000
2004/2005	165,030	1931	11.7
2005/2006	167,678	2164	12.9
2006/2007	172,591	1793	10.4
2007/2008	175,733	1448	8.2
2008/2009	179,176	1603	8.9
2009/2010	182,252	1482	8.1

[a] Total population within the Census Metropolitan Area of Edmonton for ages 2-14 from Alberta Health Care Insurance Plan registry.

Table 3- 3. Age-group and sex directly standardized visit rates of emergency department visits for acute asthma for children between 2 and 14 years of age by fiscal year and subsidy group in the Census Metropolitan Area of Edmonton during April 1, 2004 to March 31.

Fiscal year	All DSR[a] (95% CI)	Aboriginal DSR[a] (95% CI)	Government-sponsored program DSR[a] (95% CI)	Welfare DSR[a] (95% CI)	Registrant without subsidy DSR[a] (95% CI)
2004/2005	13.0 (12.4 - 13.6)	17.5 (14.3 – 20.6)	15.6 (13.9 – 17.4)	19.6 (15.8 – 23.4)	11.8 (11.2 – 12.5)
2005/2006	14.2 (13.5 - 14.7)	18.0 (14.7 – 21.2)	15.4 (13.7 – 16.9)	24.6 (20.2 – 28.9)	13.1 (12.3 – 13.7)
2006/2007	11.5 (10.9 - 12.0)	11.0 (8.5 – 13.5)	13.9 (12.4 – 15.4)	18.1 (14.5 – 21.6)	10.4 (9.8 – 11.0)
2007/2008	8.8 (8.4 – 9.3)	11.1 (8.6 – 13.7)	9.1 (7.8 – 10.3)	15.7 (12.4 – 18.9)	8.2 (7.7 – 8.8)
2008/2009	9.8 (9.3 - 10.3)	14.1 (11.3 – 17.0)	10.8 (9.4 – 12.2)	15.2 (12.2 – 18.2)	9.0 (8.5 – 9.5)
2009/2010	8.8 (8.4 – 9.3)	11.4 (8.8 – 14.0)	14.8 (11.3 – 18.2)	12.6 (10.0 – 15.1)	8.2 (7.7 – 8.6)

[a] DSR, directly standardized rates per 1,000 children. Direct standardization used CMAE 2006 Census population as standard population. Subsidy status based on alternate premium arrangement variable from the Alberta Health Care Insurance Plan registry. Subsidy group available for 10,309 visits; 112 visits did not have information on subsidy status.

Table 3- 4. Distribution of daily concentrations and absolute differences between case and control days for air quality health index and selected air pollutants in the Census Metropolitan Area of Edmonton from April 1 2004 to March 31 2010.

Variable (unit)[a]	Mean	SD	Max.	Percentile					IQR
				5th	25th	50th	75th	95th	
Daily concentrations									
AQHI[b]	2.63	0.62	6.64	1.74	2.20	2.58	2.97	3.67	0.77
NO_2 (ppb)	16.71	7.05	61.74	7.90	11.77	15.34	20.12	30.66	8.35
$PM_{2.5}$ (μg/m^3)	6.81	5.56	65.84	2.05	3.57	5.32	7.95	16.45	4.38
O_3 max (ppb)	38.20	12.43	92.00	19.00	30.00	37.00	47.00	59.00	17.00
Mean temperature (°C)	5.64	11.71	29.37	-15.64	-2.10	6.62	15.26	22.03	17.36
Relative humidity (%)	67.15	15.26	100.00	41.75	55.66	67.50	79.00	91.00	23.34
Absolute differences of daily concentrations between case and control days									
AQHI	-0.01	0.55	3.25	-0.86	-0.37	-0.32	0.31	0.91	0.68
NO_2 (ppb)	-0.04	5.47	37.88	-8.38	-3.34	-0.20	2.99	9.32	6.33
$PM_{2.5}$ (μg/m^3)	-0.05	4.52	55.84	-5.59	-2.49	-0.51	1.85	6.91	4.34
O_3 max (ppb)	-0.13	10.20	48.25	-17.25	-6.50	0.00	6.00	16.00	12.5

[a] Daily concentrations for single pollutants were averaged across the three monitor stations.
[b] AQHI, air quality health index; °C, degrees Celsius; IQR, interquartile range; Max., maximum; μg/m^3, micrograms per cubic meter; ppb, parts per billion; SD, standard deviation.

Table 3- 5. Distribution of daily concentrations and concentration differences between case and control days for air quality health index and selected air pollutants in the Census Metropolitan Area of Edmonton from April 1 2004 to March 31 2010 by season.

Variable (unit)	Cold season (October to March)			Warm season (April to September)		
	P 25	Median	P 75	P 25	Median	P 75
Daily concentrations [a]						
AQHI[b]	2.25	2.59	3.02	2.17	2.54	2.93
NO_2 (ppb)	14.55	19.27	24.43	10.14	12.83	15.81
$PM_{2.5}$ (μg/m^3)	5.16	3.58	8.51	3.56	5.19	7.49
O_3 max (ppb)	24.00	31.00	37.00	34.00	44.00	51.00
Absolute differences of daily concentrations between case and control days						
AQHI[b]	-0.34	-0.25	0.32	-0.38	-0.04	0.31
NO_2 (ppb)	-4.67	-0.18	4.35	-2.63	-0.21	2.32
$PM_{2.5}$ (μg/m^3)	-2.78	-0.57	2.15	-2.27	-0.49	1.71
O_3 max (ppb)	-5.16	-0.42	5.13	-4.99	-0.38	4.62

[a] Daily concentrations for single pollutants were averaged across the three monitor stations.
[b] AQHI, air quality health index; °C, degrees Celsius; IQR, interquartile range; Max., maximum; μg/m^3, micrograms per cubic meter; ppb, parts per billion; SD, standard deviation.

Table 3- 6. Distribution of daily concentrations and concentration differences between case and control days for air quality health index and air pollutants by calendar year.

Year[a]	*Daily concentrations*[b]				*Absolute differences of daily concentrations*			
	AQHI	NO_2 (ppb)	$PM_{2.5}$ ($\mu g/m^3$)	O_3 (ppb)	AQHI	NO_2 (ppb)	$PM_{2.5}$ ($\mu g/m^3$)	O_3 (ppb)
2004								
P25	2.14	12.10	3.43	12.17	-0.37	-3.7	-2.48	-4.08
Median	2.53	15.49	5.48	19.32	-0.04	-0.39	-0.29	-0.52
P75	2.92	19.10	7.76	26.81	0.35	3.22	1.84	4.18
2005								
P25	2.10	12.49	3.29	11.08	-0.33	-3.41	-1.96	-4.81
Median	2.51	15.69	4.72	17.98	-0.01	-0.09	-0.43	-0.35
P75	2.79	19.82	7.10	25.10	0.29	2.76	1.73	4.61
2006								
P25	2.23	12.84	3.31	12.63	-0.40	-3.51	-2.66	-5.06
Median	2.54	15.59	4.72	20.76	-0.02	-0.31	-0.70	-0.61
P75	2.90	19.68	7.16	28.25	0.27	2.74	1.45	5.59
2007								
P25	2.19	11.43	3.14	13.93	-0.35	-2.84	-2.16	-5.98
Median	2.51	14.88	4.65	20.06	-0.04	0.08	-0.49	-0.49
P75	2.84	19.42	6.69	26.88	0.31	2.79	1.46	5.06
2008								
P25	2.19	11.17	3.59	13.14	-0.30	-2.77	-2.36	-5.17
Median	2.55	14.51	5.24	21.34	-0.05	0.06	-0.29	-0.29
P75	2.98	19.19	7.17	28.18	0.33	2.93	1.92	5.02
2009								
P25	2.25	9.20	4.71	13.93	-0.40	-3.15	-2.97	-5.03
Median	2.69	14.45	6.82	21.78	-0.05	-0.26	-0.75	-0.36
P75	3.22	22.55	9.77	30.18	0.35	3.14	2.15	5.29
2010								
P25	3.06	15.54	12.11	10.09	-0.73	-6.48	-8.22	-7.16
Median	3.47	22.54	18.24	16.15	-0.02	-0.73	-2.69	0.01
P75	4.03	31.33	26.73	23.59	0.56	7.20	6.07	5.26

[a] 365 days for years except: 2004 (275 days), 2008 (366 days), and 2010 (90 days).
[b] AQHI, air quality health index; P25, percentile 25; P75, percentile 75; $\mu g/m^3$, micrograms per cubic meter; ppb, parts per billion.

Table 3- 7. Adjusted odds ratios of emergency department visits for children with acute asthma per IQR exposure difference increase of the air quality health index and air pollutants by exposure lag period and season.

Pollution exposure	Day lag period							
	Same day	1-day	2-day	3-day	4-day	5-day	1-3 day	1-5 day
All seasons (cases = 10,421) OR[a] (95% CI)								
AQHI	0.95	0.96	0.97	0.96	0.95	0.96	0.94	0.93
	(0.92-0.98)	(0.93-0.99)	(0.94-1.00)	(0.93-0.99)	(0.92-0.98)	(0.93-0.99)	(0.91-0.99)	(0.88-.097)
NO_2	0.98	0.99	1.00	0.99	0.98	0.99	0.99	0.98
	(0.95-1.01)	(0.96-1.01)	(0.98-1.03)	(0.92-1.02)	(0.95-1.00)	(0.97-1.02)	(0.95-1.02)	(0.94-1.02)
$PM_{2.5}$	0.98	0.97	0.98	0.98	0.98	0.98	0.96	0.96
	(0.96-0.99)	(0.95-0.99)	(0.96-1.00)	(0.95-1.00)	(0.96-1.00)	(0.97-1.01)	(0.94-0.99)	(0.93-0.99)
O_3	0.95	0.97	0.94	0.96	0.97	0.93	0.94	0.91
	(0.91-0.98)	(0.95-1.00)	(0.91-0.98)	(0.93-0.99)	(0.94-1.00)	(0.89-0.96)	(0.90-0.99)	(0.87-0.96)
Cold season (cases = 4,229)								
AQHI	1.01	0.99	1.01	1.01	0.97	1.00	1.01	1.01
	(0.96-1.06)	(0.94-1.04)	(0.96-1.06)	(0.96-1.06)	(0.92-1.02)	(0.96-1.06)	(0.94-1.07)	(0.94-1.08)
NO_2	1.00	0.99	1.01	1.00	0.99	1.01	1.00	1.01
	(0.97-1.04)	(0.96-1.03)	(0.97-1.05)	(0.97-1.04)	(0.95-1.02)	(0.97-1.05)	(0.96-1.05)	(0.96-1.06)
$PM_{2.5}$	1.01	1.00	1.01	1.00	0.99	1.02	1.01	1.01
	(0.98-1.04)	(0.97-1.04)	(0.98-1.04)	(0.97-1.03)	(0.97-1.03)	(0.99-1.05)	(0.97-1.05)	(0.96-1.06)
O_3	1.01	1.02	1.01	1.03	0.99	0.94	1.05	1.04
	(0.95-1.08)	(0.96-1.09)	(0.95-1.08)	(0.96-1.09)	(0.93-1.05)	(0.88-1.00)	(0.97-1.15)	(0.95-1.15)
Warm season (cases = 6,192)								
AQHI	0.92	0.94	0.94	0.93	0.94	0.94	0.91	0.87
	(0.87-0.96)	(0.89-0.99)	(0.89-0.98)	(0.88-0.97)	(0.89-0.99)	(0.89-.098)	(0.86-0.96)	(0.81-0.92)
NO_2	0.95	0.97	0.99	0.97	0.96	0.96	0.96	0.93
	(0.89-.099)	(0.92-1.02)	(0.95-1.05)	(0.92-1.01)	(0.92-1.01)	(0.92-1.01)	(0.90-1.02)	(0.86-.099)
$PM_{2.5}$	0.93	0.93	0.96	0.95	0.96	0.96	0.92	0.91
	(0.89-0.97)	(0.89-0.97)	(0.92-1.00)	(0.91-0.99)	(0.93-1.01)	(0.92-1.00)	(0.88-0.97)	(0.85-0.96)
O_3	0.93	0.96	0.91	0.93	0.97	0.93	0.91	0.87
	(0.88-0.97)	(0.91-1.01)	(0.87-0.96)	(0.89-0.98)	(0.93-1.02)	(0.89-0.98)	(0.85-0.96)	(0.81-0.93)

[a] AQHI, air quality health index; CI, confidence interval; OR, odds ratio; ORs were adjusted for temperature, relative humidity, holidays, and daily number of visits for influenza corresponding to the lag exposure period.

Table 3- 8. Adjusted odds ratios of emergency department visits for children with acute asthma per IQR exposure difference increase of the air quality health index and air pollutants by age group, sex and Aboriginal status.

Air pollution exposure[a]	Age group OR (95% CI)		Sex OR (95% CI)		Aboriginal status[b] OR (95% CI)	
	2-4 years (n=3,946)	5-14 years (n=6,475)	Female (n= 3,749)	Male (n=6,672)	Aboriginal (n=576)	Non-Aboriginal (n=9,845)
AQHI	0.96 (0.90-1.01)	0.95 (0.91-0.99)	0.95 (0.89-1.00)	0.95 (0.91-0.99)	1.07 (0.92-1.24)	0.94 (0.91-0.98)
NO_2	1.01 (0.96-1.06)	0.96 (0.93-1.00)	0.95 (0.89-1.00)	0.95 (0.91-0.99)	1.07 (0.92-1.24)	0.94 (0.91-0.98)
$PM_{2.5}$	0.98 (0.94-1.02)	0.97 (0.94-1.00)	0.98 (0.95-1.02)	0.97 (0.94-1.00)	0.99 (0.89-1.09)	0.97 (0.95-0.99)
O_3	0.93 (0.87-0.99)	1.00 (0.95-1.05)	0.99 (0.93-1.06)	0.96 (0.92-1.01)	1.11 (0.95-1.31)	0.96 (0.93-1.00)

[a] AQHI, air quality health index; CI, confidence interval; OR, odds ratio; ORs for the same day exposure adjusted for temperature, relative humidity, holidays, and daily number of visits for influenza.
[b] Aboriginal status based on the category "A=Aboriginal with Treaty Status" from the Alternate premium arrangement variable from the Alberta Health Care Insurance Plan registry.

Table 3- 9. Adjusted odds ratios of emergency department visits for children with acute asthma per IQR exposure difference increase of the air quality health index in stratified and interaction models with individual subsidy status.

Model	Subsidy status[b]	Lag exposure period[a]											
		0 day		1 day		2 day		3 day		4 day		5 day	
		OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Multi-pollutant index models													
AQHI	No subsidy	0.96	0.92-0.99	0.96	0.92-0.99	0.96	0.92-0.99	0.95	0.91-0.98	0.94	0.91-0.98	0.97	0.93-1.01
	Subsidy	0.93	0.86-0.99	0.97	0.90-1.03	0.99	0.92-1.06	0.99	0.93-1.06	0.97	0.91-1.04	0.96	0.90-1.02
	All	0.95	0.92-0.98	0.96	0.93-0.99	0.97	0.94-1.00	0.96	0.93-0.99	0.95	0.92-0.98	0.96	0.93-0.99
AQHI and subsidy status interaction model													
AQHI		0.95	0.92-0.99	0.96	0.92-0.99	0.96	0.93-1.00	0.95	0.91-0.98	0.94	0.90-0.98	0.97	0.93-1.00
AQHI* Subsidy status		0.99	0.93-1.07	1.01	0.94-1.08	1.02	0.95-1.09	1.06	0.99-1.13	1.04	0.97-1.12	0.99	0.93-1.07

[a] AQHI, air quality health index; CI, confidence interval; OR, odds ratio; ORs were adjusted for temperature, relative humidity, holidays, and daily number of visits for influenza corresponding to the lag exposure period.
[b] Subsidy beneficiaries include Aboriginal people with Treaty status, beneficiaries of Welfare social programs, and beneficiaries of social government sponsored programs using the Alternate premium arrangement variable from the Alberta Health Care Insurance Plan registry.

Table 3- 10. Adjusted odds ratios of emergency department visits for children with acute asthma per IQR of daily concentration increase of the air quality health index or single air pollutant by day lags and season using a conditional Poisson time series analysis.

Air pollution exposure	Exposure Lags		
	Same day	2-day	1-5 days
All seasons (2,191 days) IIR[a] (95% CI)			
AQHI	0.94 (0.91-0.98)	0.96 (0.93-1.00)	0.92 (0.87-.097)
NO_2	0.97 (0.94-1.02)	1.00 (0.97-1.04)	0.97 (0.92-1.03)
$PM_{2.5}$	0.97 (0.95-0.99)	0.98 (0.96-1.00)	0.96 (0.93-0.99)
O_3	0.96 (0.90-1.02)	0.93 (0.87-0.98)	0.88 (0.81-0.97)
Cold season (1,093 days)			
AQHI	1.01 (0.95-1.07)	1.02 (0.96-1.07)	1.01 (0.93-1.09)
NO_2	1.00 (0.96-1.05)	1.01 (0.97-1.06)	1.01 (0.94-1.08)
$PM_{2.5}$	1.01 (0.98-1.04)	1.01 (0.97-1.03)	1.01 (0.96-1.06)
O_3	1.00 (0.92-1.09)	0.99 (0.91-1.07)	0.98 (0.86-1.11)
Warm season (1,098 days)			
AQHI	0.91 (0.86-0.96)	0.93 (0.88-0.98)	0.85 (0.79-0.92)
NO_2	0.93 (0.87-.099)	0.99 (0.93-1.06)	0.90 (0.82-0.99)
$PM_{2.5}$	0.93 (0.89-0.97)	0.96 (0.92-1.00)	0.91 (0.85-.096)
O_3	0.93 (0.85-1.01)	0.88 (0.80-.095)	0.82 (0.73-0.93)

[a] AQHI, air quality health index; CI, confidence interval; IRR, incidence rate ratio; IRRs were adjusted for temperature, relative humidity, holidays, and daily number of visits for influenza.

Table 3- 11. Adjusted odds ratios of emergency department visits for children with acute asthma using the IQR of daily concentrations of air pollution exposure.

Air pollution exposure[a]	OR	95% CI
AQHI	0.94	0.91-0.98
NO_2	0.98	0.94-1.01
$PM_{2.5}$	0.98	0.95-0.99
O_3	0.98	0.90-1.01

[a] AQHI, air quality health index; CI, confidence interval; OR, odds ratio; ORs for same day exposure were adjusted for temperature, relative humidity, holidays, and daily number of visits for influenza.

Table 3- 12. Adjusted odds ratios of emergency department visits for children with acute asthma per IQR exposure difference increase of the air quality health index or single air pollutant by lag days and Chan's Canadian socioeconomic index quintiles.

Model	SES index[b] quintile	Lag exposure period[a]											
		0 day		1 day		2 day		3 day		4 day		5 day	
		OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Multi-pollutant index models													
AQHI	Q1	0.89	0.83-0.96	0.94	0.88-1.00	0.93	0.87-0.99	0.94	0.88-1.01	0.93	0.87-0.99	0.92	0.85-0.98
	Q5	0.98	0.91-1.06	0.97	0.90-1.04	0.98	0.91-1.06	0.92	0.85-0.99	0.97	0.90-1.04	1.02	0.95-1.10
	All	0.95	0.92-.098	0.96	0.93-0.99	0.97	0.94-1.00	0.96	0.93-0.99	0.95	0.92-0.98	0.96	0.93-0.99
Single pollutant models													
NO_2	Q1	0.94	0.88-0.99	0.98	0.92-1.03	0.98	0.93-1.04	0.97	0.91-1.02	0.99	0.93-1.04	0.97	0.92-1.03
	Q5	0.99	0.94-1.07	0.99	0.93-1.06	1.02	0.95-1.09	0.97	0.90-1.03	0.99	0.93-1.06	1.02	0.96-1.09
	All	0.98	0.95-1.01	0.99	0.96-1.01	1.00	0.98-1.03	0.99	0.96-1.02	0.98	0.95-1.00	0.99	0.97-1.02
$PM_{2.5}$	Q1	0.97	0.93-1.02	0.97	0.93-1.01	0.96	0.91-1.00	0.97	0.93-1.02	0.98	0.94-1.03	0.97	0.92-1.02
	Q5	0.99	0.95-1.05	0.98	0.93-1.03	0.99	0.95-1.04	0.97	0.92-1.02	0.96	0.91-1.01	1.02	0.97-1.07
	All	0.98	0.96-0.99	0.97	0.95-0.99	0.98	0.96-1.00	0.98	0.95-1.00	0.98	0.96-1.00	0.98	0.97-1.01
O_3 Max	Q1	0.93	0.86-1.00	0.93	0.87-1.01	0.92	0.85-0.99	0.98	0.91-1.06	0.93	0.86-1.01	0.90	0.84-0.98
	Q5	0.96	0.88-1.05	1.02	0.94-1.11	0.97	0.89-1.05	0.88	0.80-0.96	0.94	0.86-1.02	0.94	0.86-1.02
	All	0.95	0.91-0.98	0.97	0.95-1.00	0.94	0.91-0.98	0.96	0.93-.099	0.97	0.94-1.00	0.93	0.89-0.96
AQHI and SES index interaction model													
AQHI		0.95	0.92-0.98	0.96	0.93-0.99	0.97	0.93-1.00	0.96	0.93-0.99	0.95	0.92-0.98	0.96	0.93-0.99
AQHI*SES		1.02	0.97-1.09	1.02	0.96-1.07	1.02	0.96-1.08	1.02	0.96-1.08	1.02	0.96-1.08	1.02	0.96-1.08

[a] AQHI, air quality health index; CI, confidence interval; OR, odds ratio; ORs were adjusted for temperature, relative humidity, holidays, and daily number of visits for influenza corresponding to the lag exposure period.
[b] SES, socioeconomic index quintile; Q1, Chan's Canadian socioeconomic index quintile one (lowest); Q5, quintile five (highest).

Table 3- 13. Comparison between individual subsidy status and Chan's Canadian socioeconomic index at dissemination area.

Subsidy status[a]	Chan's Canadian Index quintiles[b]					
	1	2	3	4	5	Total
No Subsidy	1,336	1,465	1,585	1,336	1,781	7,503
beneficiary	17.81	19.53	21.12	17.81	23.74	100.00
	52.91	69.43	77.32	82.32	89.01	72.78
Subsidy	1,189	645	465	287	220	2,806
beneficiary	42.37	22.9	16.57	10.23	7.84	100.00
	47.09	30.57	22.68	17.68	10.99	27.22
Total	2,525	2,110	2,050	1,623	2,001	10,309
	24.49	20.47	19.89	15.74	19.41	100.00
	100.00	100.00	100.00	100.00	100.00	100.00

[a] Subsidy beneficiaries include Aboriginal people with Treaty status, beneficiaries of Welfare social programs, and beneficiaries of social government sponsored programs using the Alternate premium arrangement variable from the Alberta Insurance Plan Program registry.
[b] SES, socioeconomic status. In each cell results are presented as: number of ED visits, % for row, and % for column

Table 3- 14. Contingency table for criterion validation of Chan's socioeconomic index at dissemination area compared to individual subsidy status as gold standard.

Chan's index quintiles	Subsidy status		
	Beneficiary	Non-beneficiary	Total
1 and 2	1,834	2,801	4,635
4 and 5	507	3,117	3,624
Total	2,341	5,918	8,259

Figure 3- 1. Location of the fixed-monitoring stations with continuous air pollutants data operated by Alberta Environment in the Edmonton area.

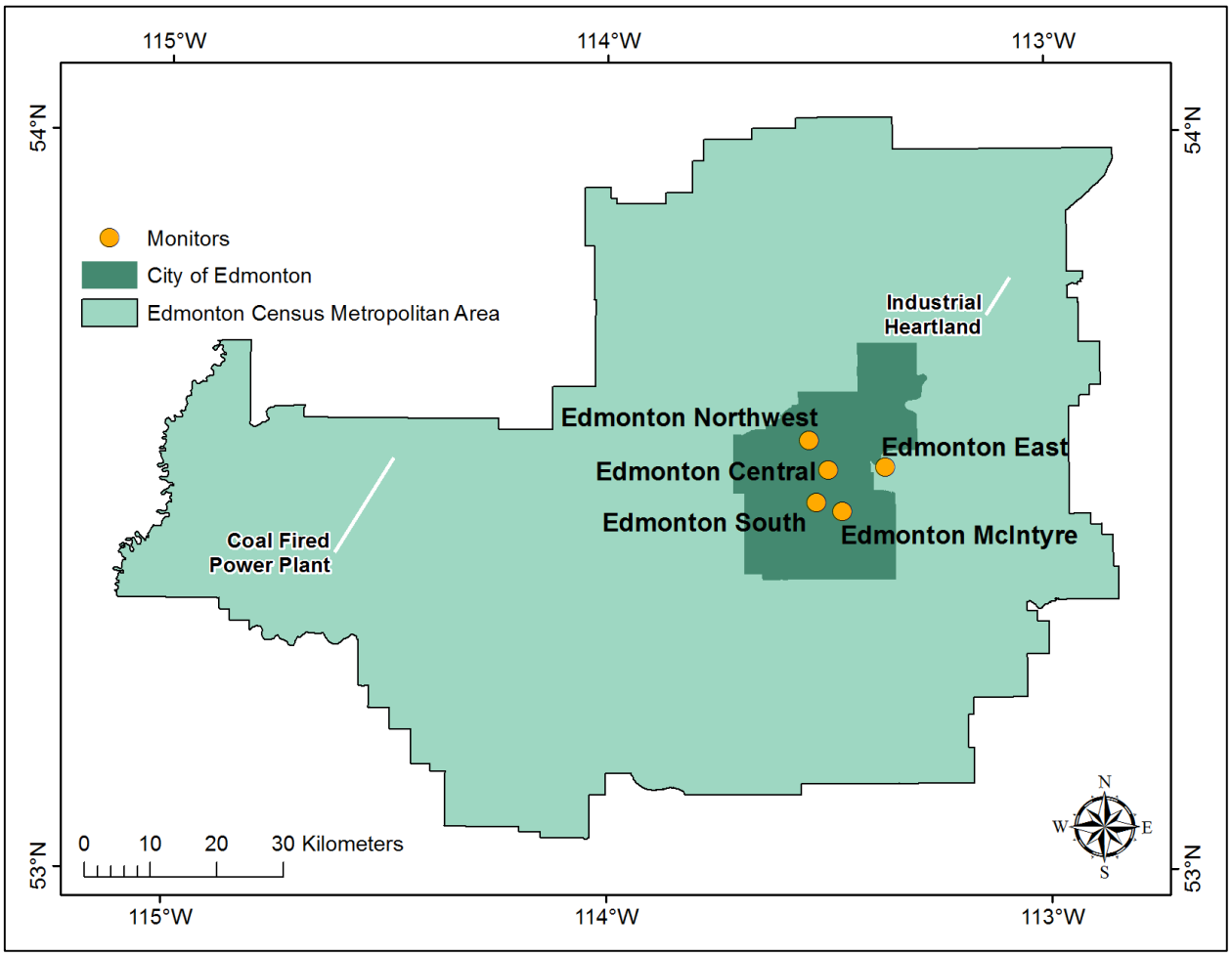


Figure 3- 2. Proportion of admissions from the total emergency department visits for children with acute asthma by fiscal year.

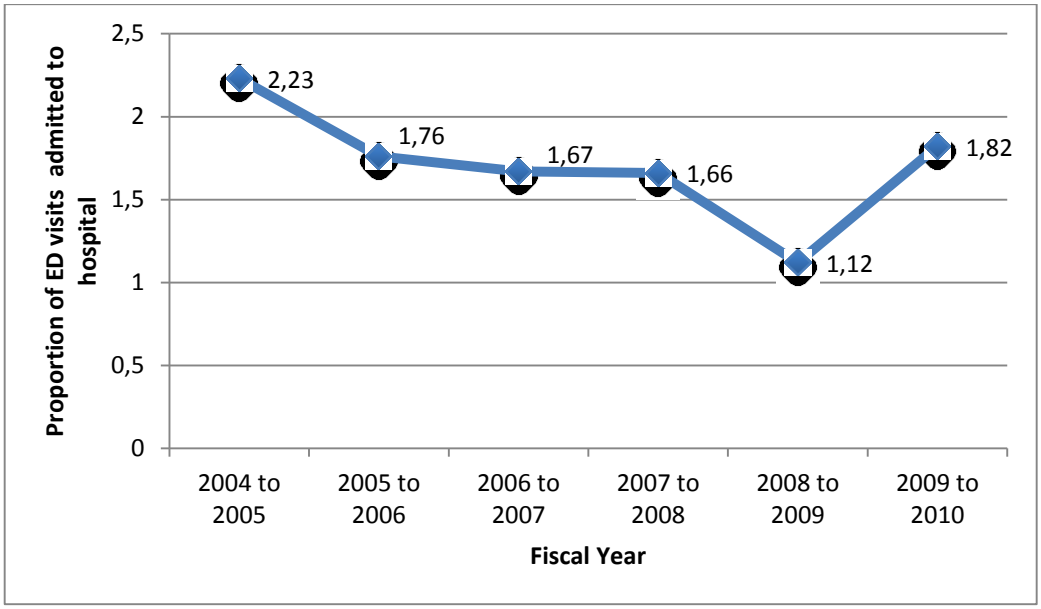
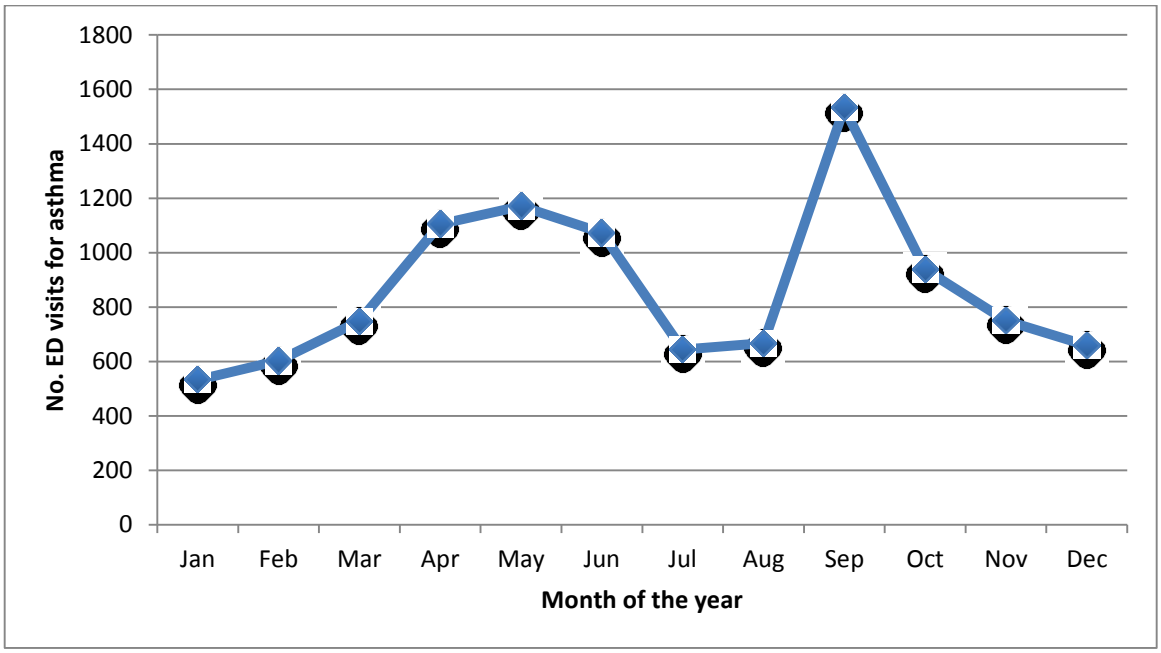


Figure 3- 3. Emergency department visits for children with acute asthma by (a) month of the year, (b) day of the week for the Census Metropolitan Area of Edmonton 2004/2005 to 2009/2010.

a) Month of the year



b) Day of the week

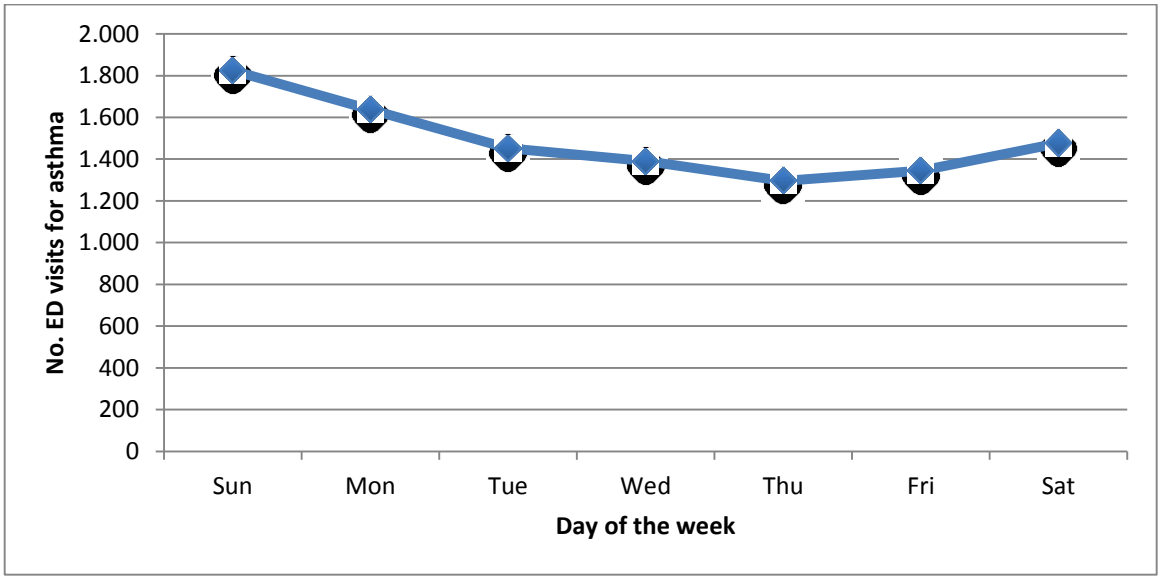
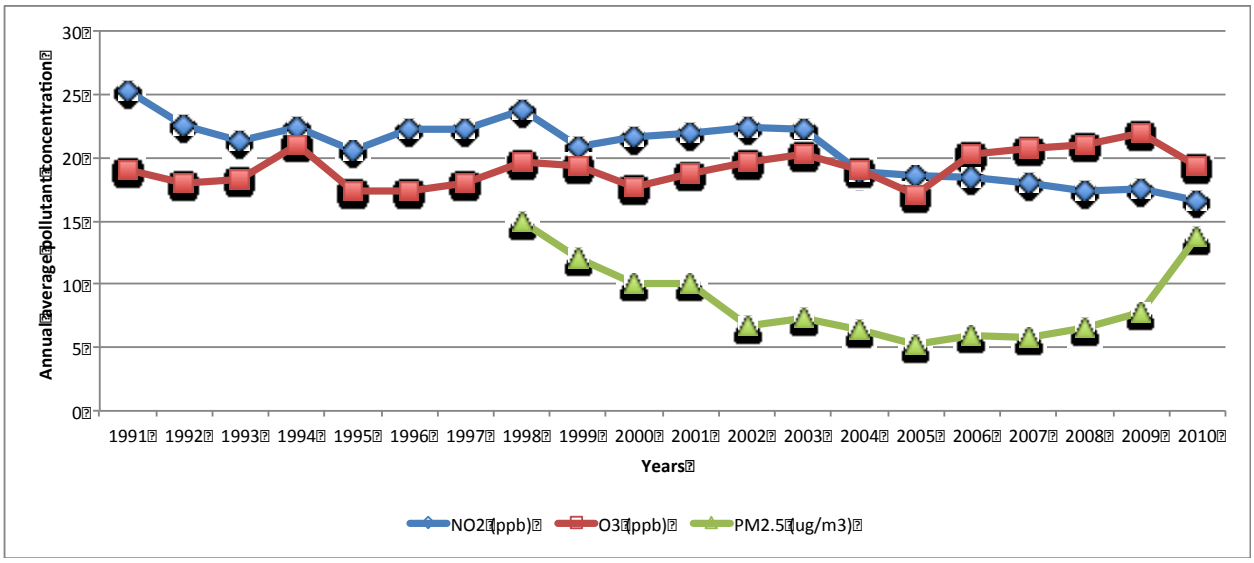


Figure 3- 4. Long trend of selected air pollutants concentrations in Edmonton city between 1991 and 2010.



Source data: airdata.aemera.org Accessed date: January 27, 2016

CHAPTER 4. The Short-term Effect of Traffic-related Air Pollution on Children's Emergency Department Visits for Asthma, its variation at small-area level, and the modifier role of the Socioeconomic Position

4.1. Introduction

The effects of outdoor air pollution on cardiorespiratory morbidity and mortality have been established since the late 1980s (2, 80). Outdoor air pollution is a complex mixture of compounds (e.g., solid particles, liquid droplets, gases) and its composition varies greatly within and among regions, depending on the sources of emission and weather patterns (14, 110). Sources of outdoor air pollution may be natural or anthropogenic; anthropogenic sources are most commonly attributed to industrial activities and urban traffic (109). Children are considered to be highly susceptible to the effects of air pollution due to physiological factors and outdoor physical activity (159, 160). The short-term effects of traffic-related air pollution in children with asthma include acute and chronic changes in lung function, increased risk of asthma exacerbations, increased risk of school absenteeism, and need for rescue bronchodilators (78). Furthermore, the long-term exposure to traffic-related air pollution has been associated with higher incidence of children's asthma (4).

Most of the evidence regarding the short-term effect of air pollution on asthma outcomes is based on time series or case-crossover studies using a common shared pollution exposure by using city-wide pollutant concentrations derived from fixed monitoring stations (3, 78, 79). Traffic-related air pollutant concentrations, however, vary spatially within cities depending on sources, ambient conditions and dispersion patterns (13). Intra-urban spatial variation may be explained mainly by the pollutant mix properties near vehicular emission sources, although the location of other potential sources of pollution (e.g., industrial facilities within urban areas,

unpaved roads, fire smoke) may be also important; the vehicular emission mix includes high concentration of gases such as nitrogen dioxide (NO_2) and carbon monoxide (CO), and large concentrations of fine particulate matter with mean aerodynamic diameter of 2.5 μm ($PM_{2.5}$) (212, 213).

The spatial heterogeneity of NO_2 is recognized to be greater than the other air pollutants and consequently is known to be a valid indicator of urban air pollution generated by traffic (13, 214). Taking into account spatial variation of air pollutants at sub-regional levels may decrease the exposure misclassification and subsequent bias in the study of traffic-related air pollution and asthma (13). In addition, findings from multicity Canadian studies suggest that within-city patterns of exposure to NO_2, rather than between-city contrasts in NO_2, are responsible for associations with cardiovascular and respiratory diseases mortality (215) and that within-city effects are larger than between-city effects when assessing the effect of ambient pollution on ED visits for cardiac and respiratory conditions (167). Therefore, adding spatial variation to the temporal variation in air pollution and asthma studies may help identify subpopulations with stronger short-term effects of traffic-related air pollution.

Socioeconomic position (SEP) is a determinant of health that may modify the effect of environmental exposures on health outcomes (96, 98, 99, 102, 165), which is known as effect-modification (100). Asthma studies have shown that low SEP have increased effects on severity of childhood asthma prevalence (77), ED visits (101), hospital admission (102), and ambulatory physician visits (103). One potential mechanism that has been proposed to explain this effect related to air pollution exposures is the unequal air pollution exposure related to SEP (104). During the last decade, research studies investigating air pollution and health outcomes have shown the uneven distribution of air pollution across population with different SEP. Overall,

studies in US have shown that populations with low SEP are exposed most often to air pollution than those that experience higher SEP (216). In contrast to American studies, some European and Canadian studies have shown an inverse relationship (150, 217). This heterogeneity may be the result of the diversity of the urban pollution distribution across and within countries (218) or it may be due to SEP measurement and exposure variability. The SEP can be measured at individual or regional levels and the development of area-level socioeconomic indexes allow analysis of the SEP effect at small-area level (97, 106, 156).

The Census Metropolitan Area of Edmonton (CMAE) has outdoor air pollution sources arising from both industry and traffic. Based on surrogate data (~20,600 additional motor vehicle registration annually), it has been suggested an increasing role of traffic emissions in the Edmonton Capital Region over the past decade (9). Previous studies conducted in the CMAE between 1992 and 2002 documented an increase in children's ED visits for asthma related to variations in concentrations of NO_2, CO, O_3, PM_{10}, and $PM_{2.5}$ (10, 11). In addition, ED presentations for asthma in children were reported to differ by subsidy status, a proxy measure of SEP in Alberta (35).

The previous chapter of this dissertation assessed the association between day-to-day variation of multiple air pollutants, using the Air Quality Health Index (AQHI) as a composite measure of air quality, and children's ED visits for asthma, and the modifier role of the SEP. Using a case-crossover design, the study assessed the effect of temporal variations of AQHI values, and NO_2, O_3, and $PM_{2.5}$ concentrations based on continuous reports of a few monitoring stations; however, the study did not assess whether there is a different effect on ED visits for asthma according to the type of air pollution source or the spatial variations in air pollution exposure. Previous research assessing the short-term effect of spatiotemporal variation of

traffic-related pollution on asthma exacerbations and the role of SEP on this relationship in the CMAE is not available.

The specific objective of this study was to analyse the short-term association between traffic-related outdoor air pollution exposure, using a land use regression model for NO_2, and children's ED visits for asthma, and its potential effect modification by SEP at the dissemination area (DA) level in the CMAE.

4.2. Methods

4.2.1. Hospital emergency department visit data

Alberta Health Services (AHS) provided anonymous patient data from the Edmonton zone subdivision required for the study. This Edmonton zone administrative subdivision operates 11 Hospital ED facilities that provide services for children across the CMAE. Appendix C illustrates the geographical location and provides general information of these 11 ED facilities. Appendix D shows the AHS subdivisions and the matching between the AHS Edmonton zone and the CMAE.

Data were obtained for all residents between the ages of 2 and 14 years old in the CMAE, who were diagnosed with asthma in a hospital ED facility from April 1, 2004 to March 31, 2010. Asthma ED visits for children less than 2 years of age were excluded as the diagnosis of asthma in this age group is less accurate. Asthma ED visits were also restricted for children up to 14 years old to minimize the potential air pollution exposure misclassification; children up to 14 years old are usually in primary school and the location of these schools (and therefore their air pollution exposure) is usually close to the children's house area, which was selected as the exposure location for the study.

In the AHS Ambulatory Care Classification System, each ED visit is coded by trained medical record nosologists using the International Classification of Disease 10th revision (ICD-10) according to the triage information, nursing notes, ED records and consultation notes. The ED visits for asthma were identified as those having the ICD-10 code J45 as first discharge diagnosis. Additional variables of the asthma database included a unique patient number, date of the visit, age, sex, health premium subsidy status, Aboriginal status, and residential postal code of the patient. Only children whose residential postal code belonged to the CMAE were selected.

The personal health number was anonymized at AHS and instead, a unique number was defined using standard algorithms at AHS. The unique number provided by AHS was used to identify multiple visits from the same child. In total, there were 12,439 ED visits for asthma in children between 2 to 14 years old during the study period. From those visits, 10,681 visits belonged to residents in the CMAE. Exclusions were made for 229 records corresponding to visits for the same day and patient and 31 records corresponding to visits from the same patient in days corresponding to the same time-strata (month and year). Therefore, the risks estimates presented in this chapter are based on a total of 10,421 ED visits.

In addition to the asthma data, AHS provided information on ED visits with discharge diagnosis of influenza (ICD-10 code J9, J10, and J11). The ED visits with influenza as first discharge diagnosis were selected and then a database was created with the total number of daily visits for influenza. The influenza data was used to control the traffic-related air pollution risk estimates for asthma ED visits for the potential confounding effect of seasonal viral respiratory seasonal epidemics.

4.2.2. Traffic-related air pollution and meteorological data

Traffic is considered to be responsible for much of the intra-urban variability in outdoor air pollution that cannot be captured by a small number of fixed monitoring stations in an urban area (219). Many intra-urban air pollution exposure models have been developed for the purpose of characterizing the small-scale spatial variations in ambient air pollutants. Land Use Regression (LUR) models are one of the most useful methods for predicting intra-urban air pollution exposure (13). The LUR method predicts pollutant concentrations at a given location based on surrounding traffic, land use, and other air-pollution related indicators; the method collects data for air pollutants using a limited number of mobile monitoring devices across the area of interest during a limited time (13, 120).

Exposures to NO_2 are assumed to be a valid and reliable indicator of traffic pollution due to the greater variability of this pollutant at smaller scale compared to other traffic-related pollutants such as CO, $PM_{2.5,}$ and volatile organic compounds (214, 219). Therefore, a number of LUR models for estimating intra-urban NO_2 concentrations (NO_2LUR) have been developed since 1997 in Europe and North America (120). Allen et al. (220) developed a NO_2LUR for the city of Edmonton, Alberta. The detailed description of the NO_2LUR development for the Edmonton city has been described elsewhere (220). Briefly, 50 Ogawa passive samplers were installed at different locations across the city area during two 14–day sampling campaigns during the winter and spring seasons in 2008. The city-specific Edmonton NO_2LUR model explained over the 80% of the variability in NO_2 and included the following as predictor variables: industrial land use, highways, major roads, all roads, and distance to the city center.

Allen's Edmonton NO_2LUR model was used in this study for estimating the NO_2 concentrations at DA level by averaging the NO_2 estimations given by the model for all postal

codes within the same DA. Following the work from Johnson et al. (221) and aiming to add temporal variation to the spatial NO_2LUR model, a daily calibration factor was used to predict daily concentrations of NO_2 at DA level during the study period. The calibration factor calculation is based on concentrations of NO_2 using fixed monitoring stations. Continuous data (24 hours data) for NO_2 were obtained from four Edmonton stations operated by Alberta Environment during the study period: Edmonton Central, Edmonton East, Edmonton Northwest (inactive since 12 December 2015), and Edmonton South (active since 21 September 2005). Data were publicly available at Clean Air Strategic Alliance CASA Data Warehouse (httpp://www.casadata.org). Daily means were calculated as the average of 24 hourly measures in the same day across the monitoring stations. The following formulae was used for obtaining the daily calibration factor (221):

$$\text{Daily calibration factor} = \frac{\text{daily average of } NO_2 \text{ at fixed monitoring stations}}{\text{seasonal average at the same monitoring sites}}$$

Then, the daily calibration factor was multiplied by the NO_2LUR estimate for each DA to produce an estimated concentration of NO_2 at DA level for the dates of interest. The predicted daily NO_2 concentrations were then used as a proxy for traffic-related air pollution exposure in the multivariable conditional regression models.

Daily meteorological data for mean temperature and relative humidity were obtained from the Environment Canada monitoring station at the Edmonton International airport. These meteorological measurements were used as time-variant potential confounder factors that were controlled for in the multivariable regression models.

4.2.3. Socioeconomic Position data

The Chan's Canadian Socioeconomic Index was used as a small area-based SEP measure. The Chan's Index is a tool designed to be a comprehensive SES index for the Canadian population, which can be used for research involving environmental pollution and health outcomes. The detailed construction of this index has been described elsewhere (108). Briefly, 22 socioeconomic variables from the Canadian 2006 Census were selected based on cultural identities, potential environmental pollutants related to health outcomes, Canadian environmental injustice studies, and variables used in the deprivation index for Canada proposed by Pampalon (222). Principal component analysis was used to synthesize information from these data for 52,974 DA across Canada. Three components were extracted with a cumulative retained variation of 58.9%. A single score index for all DAs was constructed by averaging the components retained. The Chan's Canadian index for Canada shows a relatively normal distribution (median=0.11, mean= 0.0, SD=0.58).

The Chan's Canadian index was validated by examining its association with pregnancy outcomes (i.e., preterm birth, term low birth weight, and small for gestational age) and $PM_{2.5}$ exposures in Edmonton during 1999 to 2008 and then compared to results of association with the Pampalon's index. The associations with the Chan's index exhibited greater statistical significance and more consistent gradient of $PM_{2.5}$ levels and prevalence of pregnancy outcomes (108).

The Chan's Canadian index score was assigned to each asthma visit by matching the residential DA for each visit with the score of the Chan's index for the same DA. Quintiles of Chan's SES Index for Alberta were used to assign a quintile of SES Index to each asthma visit.

4.2.4. Study design and statistical analysis

Descriptive analyses were conducted by using frequencies and percentages for summarizing categorical data, and mean, standard deviation (SD), median and interquartile range (IQR) for continuous data. Age-group directly standardized rates (DSR) for ED visits by DA were calculated using the Census 2006 population for children in the CMAE as standard population. Pearson coefficients were calculated as correlation measures among NO_2LUR and Chan's index.

A case-crossover (CCO) study design, with a time-stratified method for selection of control periods, was used to assess the association between the daily estimation of NO_2 for each DA and children's ED visits for asthma. The CCO design was proposed by Maclure in 1991 (168) to identify risk factors for acute events; it is an adaptation of the case-control design where each subject serves as his or her own control by assessing referent exposure at a point in time prior to the event (168, 169). In the CCO design, the referent time periods represent the counterfactual exposure experience of an individual, had he or she not become sick. In the case of air pollution pre and post-event exposure concentrations of air pollutants are independent of the hazard-period exposure, therefore the post-events can be also appropriate referral periods (170). As a result of its design, the CCO study controls for the influence of potential confounding variables that remain constant in the subject at both dates (time-invariant confounders at case and referent times), such as sex, age, genetics, obesity, etc. Furthermore, choosing referent intervals that are close in time to the case event, the CCO design also controls for seasonal patterns of disease occurrence (time-variant confounders) by matching. An additional advantage of the CCO design is its ability to assess potential effect-measure modification at ecological and individual level (171, 172).

The referent selection strategy is a key issue in the CCO design. Selection strategies can be unidirectional versus bidirectional, symmetric and semi-symetric, or time stratified (171). The time-stratified selection strategy, controls for season and day of the week by restricting referents to the same day of the week, month, and year of the case event. The time-stratified selection strategy is one method of referent selection that controls for time trend bias and for time-variant confounding by design and produces unbiased estimates of association in the conditional logistic regression model (171, 173). In CCO studies of air pollution and acute health events, the exposure is variable, the effect on risk is acute and transient, and the event is abrupt. Under these conditions, the theoretical target population is not the "population at risk" but "the person times at risk", and therefore different events from the same patient at different time windows (case and referent periods) can be considered independent observations (169).

In this study, the day of occurrence of each asthma ED visit was considered a "case period". By using a time-stratified method, "referent periods" were selected as the days corresponding to the same day of the week, month, and year of the "case period"; therefore, each matched set is composed by a case period and either three or four referent periods. For example, if an ED visit for asthma occurred in Monday, January 11th 2010, the referent periods chosen were all Mondays in January 2010 (January 4th, 18th, and 25th). Asthma ED visits for the same person during different days during the study period were included if the case period for a second or subsequent visit was outside the previous referent windows. A program code in Stata 13 (174) was written and used for creating the CCO database with case and referent periods. Appendix E shows the flowchart of the procedures followed to create the complete database for analysis.

The estimated daily average of NO_2 concentrations at DA level were compared between case and control periods to estimate a measure of risk of the occurrence of asthma visits associated with variation of NO_2 concentrations at small-area level. Conditional logistic regression was used to calculate Odds Ratios (OR) and their corresponding 95% confidence intervals (CI). The OR represents the change in risk for the occurrence of an ED visit for asthma associated with a daily increase in the NO_2 concentrations. Multivariable models were used to control for time-varying covariates: temperature, relative humidity, and Canadian holidays; in addition models were adjusted for the daily number of influenza ED visit for controlling for viral respiratory seasonal epidemics. Meteorological variables (temperature and relative humidity) were modeled as linear and cubic splines; however, there were not notable difference in the risk estimates and the Akaike information criterion (AIC) when using the more complex models (i.e., AIC for models with linear predictors and with cubic splines were 30,685.29 and 30,663.38, respectively); therefore, the multivariable models were adjusted for linear effects of temperature and relative humidity.

Following the recommendations from Künzli & Schindler (175) the concentration difference of the NO_2 concentrations (i.e., the difference between case period and the average of the referent periods) is reported as the relevant exposure term for the CCO analysis. Consequently, the ORs from all multivariable models are expressed accordingly as an increase in the interquartile range (IQR) of the concentration difference distribution over the study period. Risk estimates from multivariable models were provided by age-group, sex, season, and Aboriginal status.

Different exposure lag terms were created to assess the temporal relationship between estimated NO_2 concentrations at DA level and the time when the children presented to the ED

for asthma. Considering that most air pollution and children's asthma studies in Canada have found association with lagged exposures up to 5 days (10, 79), lagged exposures from 1 to 5 days and cumulative 3-day and 5-day mean exposure estimates were created. For instance, the cumulative 3-day average exposure refers to the mean air pollutant concentration on the day of the asthma ED visits, the day before, and two days before.

The spatial heterogeneity of the association between estimated concentrations of NO_2 and asthma ED visits during the study period was assessed by building individual conditional logistic regression models by DA. The models did not converge with less than 10 asthma ED visits and therefore models were constructed for the 269 DAs with 10 or more ED visits. A scatter plot of the resulting ORs vs the estimated NO_2 concentrations was used to assess whether the direction and magnitude of the association between traffic-related air pollution and asthma ED visits at DA level was related to the NO_2 estimated levels.

The potential modifier effect of SEP was assessed by using the Chan's socioeconomic index as the small-area SEP measure. Effect measure modification by SEP was assessed in multivariable models by using stratified and interaction analyses. Stratified analyses were conducted by building multivariable models for estimated NO_2 concentrations by quintiles of the Chan's index. Risk estimates that differed in direction and/or magnitude across quintiles, mainly between quintiles 1 and 5, were considered an indication of possible effect-modification. Interaction analyses were conducted by creating interaction terms between the Chan's index score and the estimations of NO_2, and then, adding the interaction term to the multivariable models. A statistically significant interaction term was considered a confirmation of effect-measure modification at multiplicative scale (100, 155, 172). All statistical analyses were performed with Stata 13 (174).

4.2.5. Sensitivity analysis

Sensitivity analyses were conducted to assess the consistency of the results (i.e., direction and magnitude of the risk estimations) when using different measurements of air pollution exposure and SEP variables, as they are variables measured with error.

Hystad et al. (223) created the 2006 national NO_2LUR for Canada. The Hystad's NO_2LUR model includes as predictor variables satellite-based NO_2 concentrations, industrial land use, road length, and summer rainfall. The LUR models estimated population-weighted exposures to NO_2 available at DA level. Estimations of NO_2 at DA level using the Hystad's NO_2LUR model for the CMAE were used to assess the consistency of the risk estimations of the CCO analysis when using this LUR model as exposure air pollution variable. The same procedure described for obtaining predictions of daily concentrations at DA level for Allen's NO_2LUR model were used for Hystad's NO_2LUR models. In addition, a validation of concordance and agreement was conducted for the NO_2LUR models from Hystad and Allen aiming to identify the model that best predicts the NO_2 concentrations at small-area level in the CMAE. The NO_2 daily average concentrations measured at the the Central, East, Northwest, and South fixed monitroing stations from Alberta Environment were compared to the estimated daily concentrations of NO_2 produced by the two models at the DAs where these stations are located. Pearson correlations, Lind's concordance coefficient, mean of the differences with their 95% CI, and the Bland-Altman's limits were calculated as measure of agreement and its variability for each set of comparisons.

The health premium subsidy status was used as an alternative measure of individual SEP. Children were grouped into subsidy beneficiaries and non-beneficiaries according to the

Alternate Subsidy Arrangement variable for the Alberta Health Care Insurance Plan registry file. Children under the categories "A=Aboriginal", "W=Welfare", and "R= Government-sponsored programs" were assigned to the beneficiaries group and children with "0=resident without subsidy" category were assigned to the non-beneficiaries group. The subsidy benefit was assigned by the provincial government to people with low family income or for belonging to special protected groups (i.e., welfare and Aboriginals with Treaty status). This variable had been used in previous studies as proxy measure and demonstrated to be a valid indicator of SEP in Alberta (34, 35). A sensitivity analysis of the effect modification by SEP using the subsidy status as individual SEP measure was performed using stratified and interaction analysis as described for Chan's Canadian index as small area-based SEP measure.

4.3. Results

4.3.1. Descriptive Statistics

A total of 10,421 children between 2 -14 years old, living in the CMAE, presented to the hospital ED facilities with primary diagnosis of asthma during the study period. The 10,421 ED visits for asthma were made by 6,184 distinct children, with an average of 1.68 visits per child (median=1; IQR= 1; 55.9% of children had only 1 ED visit). The ED visits for asthma were more common in boys (64%), in the age group between 5-14 years (62%), and during the warm season (59%). Table 4-1 presents the distribution of ED visits for asthma by the quintiles of the Chan's index. Overall, children living in the lowest quintile (Q1) of the Chan's index accounted for a larger number of ED visits (almost 25% of the total visits); the distribution of ED visits for asthma by age group, sex, season and fiscal year was similar within the five SEP strata. Figure 4-1 presents the distribution of the Chan's Canadian socioeconomic index in the CMAE.

The CMAE pediatric population increased over the study period and the yearly ED visits for asthma decreased, resulting in a decreasing crude visit rate over time from a maximum of 12.9 per 1,000 children in 2005/2006 to a minimum of 8.1 per 1,000 children in 2009/2010 (Table 4-2). The overall crude rate of asthma ED visits was 55.9/1,000 children under 14 years during the 6 years period, which results in a mean crude rate of 9.3/1,000 children population per year. The ED visits for asthma were located all across the CMAE in 1,276 of the total 1,551 DAs during the study period. In 20 records the postal code did not match any DA using the postal code validator so 10,401 visits were used in the small-area analysis. The crude visit rates by DA ranged from 0.00 to 911.11/1,000 children population for the 6-year period (median= 43.61; IQR= 62.98). The directly standardized visit rates ranged from 0.00 to 926.42/1,000 children population (median=44.88; IQR=66.77). Using the lower limit of the 95% CI of the directly standardized rates, 179 DAs (14% of the total DAs with asthma visits) demonstrated significantly higher rates compared to the overall crude rate. Figures 4-2 and 4-3a presents the choropleth maps of the crude and directly standardized rates for asthma ED visits during the entire study period using as cutoff points quartiles of the distributions. The complete list of asthma crude and standardized visit rates for asthma by DA are presented in Appendix F.

Timing of the ED visits varied according to month and day of the week. During 2004/2005 to 2009/2010, peaks of ED visits for asthma were observed in September and May (14.7% and 11.2% of the total ED visits). Sunday and Monday were the days of the week with the highest volumes of ED visits. Figure 4-4 shows the timing of ED visits per month of the year and day of the week.

Figure 4-5 shows the Allen's NO_2LUR model surface for the city of Edmonton that covers 1,231 (79.4%) of the 1,551 DAs in the CMAE; estimated mean concentrations of NO_2 by

DA range between 6.6 and 25.9. Table 4-3 summarizes the mean, SD, maximum, percentiles (5^{th}, 25^{th}, 50^{th}, 75^{th}, and 95^{th}), and IQR values of the daily calculated concentrations of NO_2 at DA level from the Allen's NO_2LUR model with daily calibration for the case days during the study period. The distribution summary measures are presented by season for the daily concentrations of case events as well as for the concentration difference of the matched pairs of events (i.e., concentration in the case day minus the average of concentrations in the referent days). Estimated average NO_2 concentrations were slightly higher during the cold season. The median concentration difference was negative for both seasons, which means that 50% of the cases had NO_2 estimated concentrations that were lower than the average of the concentrations of the referent periods. Spearman correlation between Chan's Canadian index and Allen's NO_2LUR was negative (rho=-0.43; p=0.000) indicating that lower scores of the Chan's index are correlated to exposure to higher estimated levels of NO_2.

4.3.2. Association between ED visits for asthma and traffic-related air pollution

The presentation of ED visits for asthma was not associated, on average, with NO_2 concentrations at DA level in the CMAE. Adjusted ORs of ED visits for asthma for IQR of the same-day concentration difference of NO_2 was marginally significant for the whole period (OR 0.97 95% CI 0.94-1.00) and was not statistically significant when stratified by season. Similar results were found when assessing the effect of lagged day exposure. Table 4-4 presents the adjusted OR and their 95% CI for different exposure day-lag periods by season. Stratification by age group, sex, and Aboriginal status also exhibited absence of association between ED visits for asthma and traffic-related air pollution; risk estimates for the age group between 2 and 4 years old and for girls were positive but statistically non-significant (Table 4-5).

Asthma ED visits were stratified into two groups of exposure using as cut-off value the mean NO_2 exposure concentration during case days; case day concentrations above 13.84 ppb were considered higher exposures and associations with ED visits for asthma were calculated and compared to associations in the group of lower exposure levels. The association between ED visits for asthma and NO_2 concentrations did not differ by the level of LUR-NO_2 exposure. Similar findings were seen when lagged effects were assessed (Table 4-6).

Conditional regression models by DA were built for the 269 DAs with 10 or more ED visits for asthma. Estimated ORs varied widely across DAs ranging from 0.02 to 6.96 (Figure 4-6). Four DA's with ORs of 0.09, 0.23, 0.35 and 3.8 produced statistically significant associations. Figure 4-7 shows the relationship between the ORs and the estimated NO_2 exposure at DA level; plotted data shows that higher or lower ORs were not related to the level of NO_2 exposure at the DA.

4.3.3 Effect-measure modification by SEP

Table 4-7 presents the adjusted ORs of ED visits for asthma associated with one unit IQR increase in the concentration difference of NO_2 stratified by quintiles of the Chan's index and exposure lag periods. Overall, the estimated ORs did not differ by Chan's index quintile and none of them reach statistical significance. Positive but non-statistically significant ORs were obtained for children in the fourth quintile of the SES index, especially for those lagged 2 or more days. The interaction term between NO_2 exposure and Chan's index score was not statistically significant in the multivariable models.

4.3.4. Sensitivity analyses results

Estimations of NO_2 at DA level using the Hystad's NO_2LUR model for the CMAE were used to assess the consistency of the risk estimations observed when using Allen's NO_2LUR model. Figure 4-8 shows the Hystad's NO_2LUR estimations that covers 1,436 (92.6%) of the 1,551 DAs in the CMAE. Table 4-8 summarizes the mean, SD, maximum, percentiles (5^{th}, 25^{th}, 50^{th}, 75^{th}, and 95^{th}), and IQR values of the daily calculated concentrations of NO_2 at DA level from the Hystad's NO_2LUR model with daily calibration for the case days during the study period. Estimated average NO_2 concentrations were slightly higher during the cold season. The median concentration difference was negative for both seasons. Spearman correlation between Chan's Canadian index and Hystad's NO_2LUR was negative (rho=-0.49; p=0.000) indicating that lower scores of the Chan's index are correlated to higher estimated levels of NO_2. The presentation of ED visits for asthma was not associated, on average, with NO_2 concentrations at DA level in the CMAE when using Hystad's NO_2LUR models. Table 4-9 presents the adjusted ORs and 95% CIs for different exposure day-lag periods by season.

Results of concordance and agreement between NO_2LUR models and daily mean concentrations at four fixed monitoring stations in Edmonton during the study period are presented in Table 4-10. Overall, Allen's NO_2LUR model had better concordance with monitoring stations in Northwest and South stations. Similarly, Allen's NO_2LUR model had least mean of differences, especially for the Central and South stations where the means of differences were close to zero. Figure 4-9 present the graphs of the Bland-Altman's limits of agreement for the two NO_2LUR models and stations.

Sensitivity analysis using subsidy status as individual level SEP measure did not exhibit differences with results when using Chan's Canadian index at DA level. Table 4-11 presents the

adjusted OR of ED visits for asthma associated with one unit IQR increase in the concentration difference of NO_2 stratified by subsidy status and lag exposure period. The estimated ORs did not differ by subsidy status and did not exhibit statistical significance. The interaction term between NO_2 exposure and subsidy status was not statistically significant in the multivariable models.

4.4. Discussion

In this study, children's ED visits for asthma were not associated, on average, with short-term effects of traffic-related air pollution exposure measured at the small-area level in the CMAE between 2004/2005 and 2009/2010. Spatial variations in risk estimates, however, were identified. Analyses stratified by age group, sex, and Aboriginal status found, in general, non-statistically significant associations at different lag-day exposures. Girls and younger children had positive, though not statistically significant associations. The SEP measured at the small-area or individual level did not appear to modify this relationship.

Traffic-related air pollution exposure at DA level was measured by using a city-specific NO_2LUR model (220). The LUR modeling had proven to be a valid exposure assessment method for capturing within-city air pollution variations (120, 224, 225). Moreover, measuring air pollution exposure at small-area level minimizes exposure measurement error when compared with ambient concentrations averaged at city level (135, 226). Several previous studies had used NO_2LUR for assessing effects of intra-urban variations of traffic-related air pollution on different asthma outcomes but ED visits (5, 224, 227-230).

The LUR modeling has been mainly used to estimate long-term spatial variation of air pollutants concentrations (120). Concentrations of NO_2 are, however, highly variable in space

and time (228). In this study, a daily calibration factor (221) was applied to the NO_2LUR estimation at DA level to obtain spatio-temporal estimations of NO_2 concentrations across the CMAE during the study period. Temporal calibration of LUR models has been used since 2007 for estimating forward or backward annual trends using data from fixed monitoring stations (228, 231-233).

In Canada, Sbihi et al. (224) used spatiotemporal adjustment of NO_2LUR at two-weeks scale to assess the association of perinatal exposure to traffic-exposure air pollution and atopy in a multi-center birth cohort study. Johnson et al. (221) developed and validated the daily calibration factor used in this study and assessed the association of intra-urban variation of NO_2 pollution with lung function measures in a panel study of patients with asthma in a residential area in Windsor, Ontario. The study validated the temporally refined NO_2 estimations in 50 houses against residential outdoor measurements using Ogawa samplers and found that the refined LUR model explained a greater proportion of the spatial and temporal variance in daily outdoor NO_2 measurements compared with daily concentrations based on fixed monitoring stations (221).

This is the first study to use this calibration factor to produce spatio-temporal NO_2LUR estimations to assess short-term effects of traffic-related air pollution. The main limitation of using the daily calibration factor in the Edmonton area is that it relies on data from a small number of fixed monitor stations across the city and therefore daily estimated concentrations of NO_2 are combining small-area spatial variations with city-wide temporal variations. Despite of the use of a CCO study design that compares daily concentrations for case and control days within the same individuals, the estimated risks from multivariable models stratified by DA

showed that there are spatial variations in risk across the city and therefore the city-wide temporal calibration did not hide spatial variations in risks.

In this study, an internal validation was conducted by comparing the daily-calibrated estimations of NO_2 during the 2,191 days of the study period with the concentrations from four fixed monitor stations located within the city area. Overall, the results showed that means of differences for the calibrated Allen's NO_2LUR estimations are smaller, especially for the central and south monitoring stations. Therefore, the spatio-temporal calibration of NO_2 exposure seems to be adequate to assess short-term effects of traffic-related air pollution on asthma exacerbations.

Children were restricted for ages between 2 and 14 years for two reasons: first, because the diagnosis of asthma is less accurate in young children and may lead to outcome misclassification. Second, because children up to 14 years usually have more limited mobility than adolescents and adults as they spend most of their time at home or attending schools close to their houses. Therefore, restricted mobility of the study population also reduced exposure misclassification.

This study used Allen's NO_2LUR for the city of Edmonton, which covers 79% of DAs of the CMAE, and did not find association between spatio-temporal variations of traffic-air pollution and the occurrence of ED visits for asthma. Furthermore, the sensitivity analysis using national NO_2LUR, which covers 95% of the DAs in the CMAE, produced similar results. These study findings contrasts with findings from previous studies conducted in the Edmonton area between 1992 and 2002, which reported associations of short-term elevations of NO_2 with increased risk of ED visits for asthma, and that this associations were stronger among children between 2-4 years, and during the warm season (10, 11). Similar findings of increased risk of

ED visits for asthma related to elevations in air pollutants had been reported in different cities around the world, including other Canadian cities (3, 78-80).

Since this study's findings counter previous evidence of the adverse health effects of air pollution on children with asthma, with no apparent threshold for exposure, they require efforts to explore the specific local conditions that are influencing the change of the relationship between outdoor air pollution and asthma exacerbations in the CMAE. While the majority of evidence identified risk associations, this is not the first study to report non-statistically significant associations of air pollution and asthma outcomes when assessing effects at small area level. For example, Sahsuvaroglu et al. (5) used a NO_2LUR to assess the effect spatial variability of air pollution on asthma self-report using the ISAAC asthma survey data for Hamilton, Ontario; results did not find associations with asthma except for girls with hay fever with a statistically significant interaction between hay fever and NO_2 exposure in girls. Newman et al. (227) failed to identify associations between NO_2LUR model estimations and readmissions for asthma in a cohort study; positive associations were found only for white children with high exposure to NO_2. Brunst et al. (230) reported that only children with high average exposure to traffic-related air pollution from birth to 7 years had an increased risk of asthma. Using a small-area case-crossover study, Laurent et al. (135), reported positive though non-statistically significant associations between NO_2 and emergency calls for asthma in Strasbourg, France.

There are two important factors that may help explain the lack of association between NO_2 as a proxy for traffic-air pollution and asthma ED visits during the study period in the CMAE: the decrement in asthma visits rates and in the NO_2 outdoor concentrations compared to the ones reported in previous studies (10, 11).

Children's asthma ED visits rates decreased over time during the study period. Crude visit rates decrease by 4.8 visits per 1,000 children between 2005/2006 and 2009/2010, which represents a decrease in 37% in the crude rate of ED visits in five years. Similarly, asthma rates reported in Alberta for children under 18 years of age in 2004/2005 were lower than those during the previous five years, which implies that there is a long-term downward trend in asthma rates (35). Health care access and asthma care have both changed in important ways over the last several decades in Canada and may help explain the decreasing pattern in ED visit for asthma.

The Canadian health care system continues to have universal coverage for all residents (178). While different studies have found that the universal coverage of the Canadian system has been successful in providing access to primary health care (i.e., primary care physician) for people independent of their socioeconomic status, the system has been less successful to provide access to specialists (179-181), which may result in a better ambulatory care and less ED visits and hospitalizations for conditions sensitive to ambulatory care like asthma (180). In addition, during the last decade walk-in clinics increased as a response to the scarce availability of primary care facilities and physicians after office hours to provide care for acute non-life threatening conditions (184). Walk-in clinics and urgent care centers are health care options for people who require consultation with a primary care physician for conditions such as acute asthma exacerbation when they do not have a family doctor or their family doctor cannot see them in a timely fashion (185). Thus, during the study period, walk-in clinics emerged as primary care facilities where mild to moderate asthma exacerbations could be treated avoiding the need for hospital ED visits.

Asthma management also changed importantly in Canada during the study period. Starting in 1999 the Canadian Asthma Consensus Report included asthma education as a key recommendation in asthma management (186). In the Asthma Consensus guidelines 2003, asthma education was described as an essential component of asthma therapy that should be offered to all patients along with an individual written action plan for self-management, which includes medication adjustment in response to severity or frequency of symptoms, the need for symptoms relief medication or a change in the peak expiratory low (187).

The Asthma Consensus guidelines 2003 also recommended that the discharge plan for a patient after an asthma ED visit should reinforced the need for a close follow-up visit within the first week after an ED visit. In Ontario, a hospital-based pediatric asthma clinic with a inter-professional care reported that there was an average decrease of 67% in ED visits for asthma and 85% in admissions in the first year after enrollment (189).

In addition to the role of improved asthma education and follow-up, the increased use of asthma medications have also become more common during the last 15 years. The Asthma Consensus guidelines 1999 recommended the use of pressurized metered-dose inhaler with valve spacer and mouthpiece for children in place of the wet nebulizer with a mask, aiming to maximize the lung deposition of inhaled medications (190). The use of breath-actuated devices such as dry-powder inhalers was also recommended for maintenance treatment in children over 5 years of age (186).

At the same time, evidence of the effectiveness of new medications such a leukotriene receptor antagonist (191) and long acting β2-agonist (192), as second controller medications, became available for asthma treatment and were included as part of the recommendations for asthma management (87). The leukotriene receptor antagonist drugs, however, are not provided

as a “Regular benefit” in the Alberta health drug benefit list (193), which means that access to this controller medication may be limited for children with low family income, and may help explain their higher rates of ED visits for asthma.

On the other hand, concentrations of ambient NO_2 also decreased during the study period compared to reports of concentration in previous studies. Compared to the daily median concentrations of air pollutants reported by Villeneuve et al. (10) during 1992 to 2002, NO_2 median concentration decreased from 17.5 to 12.8 ppb (28%) in the warm season, and from 28.5 to 19.3 ppb (32%) during the cold season. The concentration variability also decreased for NO_2 compared to previous reports evidenced by a decrease in the IQR from 13.5 to 8.35 ppb.

The Allen’s NO_2LUR model used in this study was developed from two sampling campaigns in 2008, almost the mid-term year for the study period, and daily calibrations were made using average city-wide levels of NO_2 from fixed monitoring stations. Therefore, spatio-temporal estimations of NO_2 at DA level are also capturing the decrease in NO_2 concentrations while preserving the spatial distribution across the city. Gauderman et al. (194) reported that long-term decrease in levels of NO_2 in five Southern California communities was associated with improved lung function development in children between 11 and 15 years of age. Similar health benefits from reduction in air pollution levels have been also described for adults (195, 196). Therefore, improved lung function as a result of a long-term decrease in NO_2 in the Edmonton area is also a potential explanation for these study findings.

It is also worth noting that outdoor air pollutants concentrations found in Canadian cities are usually lower compared to most of the concentrations reported in studies from US or Asian cities that have found risk associations with asthma ED visits; moreover, it is recognized that Canadian studies added to air pollution and asthma research literature in the last decade by

demonstrating risk effects on health even at lower concentrations observed in studies conducted in other cities around the world (80). A systematic review of the literature published in 2015, identified the studies assessing the effects of outdoor air pollution on the respiratory health of Canadian children between 2004 and 2014 (79); the NO_2 concentrations reported by the included studies assessing the effects on ED visits for asthma were higher than the concentrations observed in the present study (10, 11, 123, 125, 201). Therefore, the NO_2 concentrations reported in this study represent the lowest concentrations of air pollutants in Canadian studies assessing the effect of outdoor air pollution on children's ED visits for asthma.

The findings of this study, therefore, have potential explanations based on the combination of multiple factors: decreased rates of children's ED visits for asthma, decreased concentration and variability of NO_2 compared to reports in the previous decade, and different methodological approaches among studies. The decreased number of ED visits may be explained, in part, because access to primary care and asthma management have changed over time in the CMAE, being more severe cases the ones that are going to the ED, and those asthma cases are likely influenced by many other factors than pollution, such as different immune activation after allergen exposure, indoor air pollution, or epigenetic factors (5, 202). After transient elevations in outdoor air pollution there may be exacerbations that are now controlled at home or in walk-in clinics. Therefore, this study does not rule out associations of air pollution with mild to moderate asthma exacerbations that did not report to hospital EDs; however, it does suggests that cases attending hospital EDs, which are probably more severe asthma cases, were not associated with outdoor air pollution levels.

Although most ORs were below one and non-significant, the analysis by DA showed some DAs with positive risk estimates, although only one of them was statistically significant.

Interestingly, the magnitude and direction of risk estimates by DA were not related to NO_2 estimated concentrations. Therefore, this study suggests that there are other environmental factors, including allergens distribution, weather factors (e.g., daily temperature change), indoor conditions (e.g., second hand smoking), which may vary over time, and others that may vary spatially (e.g., industrial-related pollutants such as sulphur and volatile organic compounds) and can be more important triggers for an asthma exacerbation (5, 227, 229, 234).

Exposure to outdoor aeroallergens vary seasonally and may be related to seasonality observed in children's ED visits for asthma. In the Edmonton area, however, Villeneuve et al. (10) reported that associations between air pollution and hospital ED visits for asthma were not confounded by exposure to aeroallergens levels. Regarding indoor conditions, a previous study in Alberta identified that second-hand smoking at home and worse parental perceptions of the psychosocial impact of asthma were more common in children with poor asthma control (235). Further research focused on indoor conditions and other social and environmental conditions will be needed to better understand the complex role of air pollution on asthma and potentially incorporate this information into asthma education programs here and elsewhere.

There were also important findings regarding the role of SEP on these relationships. The Chan's Canadian socioeconomic index, used as a small-area SEP measure, was inversely correlated to NO_2LUR concentrations at the DA level. Thus, lower scores of the Chan's index, which represent DAs with people predominantly with low SEP conditions, were correlated with higher NO_2 concentrations. These finding suggests the presence of environmental injustice in air pollution exposure in the CMAE and agree with similar findings that had been reported recently for the cities of Toronto, Montreal, and Vancouver (236). While this study failed to identify a modifier role of SEP, a positive relationship between long-term exposure to air pollution and

SEP had been reported in a Canadian mortality study. This nation-wide study reported that areas with higher percentages of individuals with high education, income and employment have longer exposure to low concentrations of $PM_{2.5}$ (150). Differences in the study findings may be related to the type of air pollutant studied and the within-city variations of air pollution and SEP distributions.

The SEP measured at the small-area or individual level did not modify the association between traffic-related air pollution and ED visits for acute asthma. Despite the presence of environmental injustice in exposure to air pollution, the SEP condition did not change the associations found. Similar results regarding the lack of effect modification by SEP were described in the results of the systematic review that is part of this dissertation (see Chapter 2). The three included studies that assessed the association between air pollution and ED visits for acute asthma failed to demonstrate a modifier role of SEP (135, 136, 144); however, these studies had limitations related to potential confounding and sample size limitations. Therefore, the present study, accounting for short-term spatio-temporal variations in traffic-air pollution exposure, adds to the growing literature reporting absence of effect modification of SEP on relationship asthma exacerbations and air pollution in Canada.

4.4.1. Strengths and limitations

An important strength of this study relies on the study design used. The design of the CCO controls for potential confounders that are invariant in time (e.g., age, sex, social condition, pre-natal and childhood risk factors) (168, 169). The time-stratified method used for selecting the referent periods controls, by matching, for time-variant potential confounders (e.g., meteorological and seasonal variations) (171). Furthermore, the use of individual in the CCO

design rather than ecological information used in time series analysis, allowed the analysis of the potential SEP modification effect at individual level (172).

A city-specific NO_2LUR model was used in this study resulting from a network of 50 sampling sites located across the city of Edmonton during two different seasons in 2008 (220). Several studies have demonstrated that better predictions in NO_2 concentrations result from LUR models that are city-specific, that used between 40 and 80 sampling sites, and were built using samples from more than one season (120, 220, 237). Furthermore, by using daily calibration of the NO_2LUR model this study was able to assess spatio-temporal variations in NO_2 concentrations. The internal validation study showed that daily-calibrated NO_2 concentrations during the study period had median differences close to zero compared to concentrations from four fixed monitoring stations in the city of Edmonton. Therefore, calibrated estimations of exposure at small-area level helped minimize exposure misclassification bias.

This study has important limitations that need to be examined. First, the NO_2LUR city-specific model does not cover the entire CMAE. For this reason, multivariable models were also built using a national NO_2LUR model that covers almost all the DAs in the area; results were consistent using either NO_2LUR model. Traffic volumes are higher in the city of Edmonton compared to the rest of the CMAE, which partially explains why the exclusion of DA's outside the city of Edmonton did not influence the risk estimates.

The internal validation of the estimated spatio-temporal concentrations of NO_2 included only four DAs in the city of Edmonton. No monitoring stations with continuous measurements of air pollutants are available outside the city of Edmonton. The selection of those four DAs corresponds to the location of the fixed-monitoring stations with continuous NO_2 measurements,

and covered different cardinal directions within the city; thus, those four DAs were assumed to be good referents for validation across the city, which may not be true.

The AHS ED databases are unable to capture all cases of asthma exacerbations. As discussed before, many children may report to non-hospital ED facilities, for their acute asthma episode or be self-treated at home using written action plans. Therefore, the study findings do not rule out risk associations of air pollution with mild to moderate asthma exacerbations that did not report to hospital-ED facilities. The definition used for acute asthma cases in this study was the first diagnostic code; and that may differ from some other studies that used the first and second diagnostic codes (35). This may under-estimate the total number of cases of children with acute asthma while at the same time it can make the asthma visits more specific and less biased by other conditions (i.e., acute infections) that may induce an episode of asthma exacerbation.

Similarly, the AHS databases are unable to identify all Aboriginal children. The proxy variable for Aboriginal status is derived from the health care premium subsidy given by the province to Aboriginal peoples, which is restricted to First Nations peoples with Treaty status and a minority of Inuit Indigenous people living in the province; therefore, the Aboriginal Status variable is systematically excluding children belonging to non-status First Nations and Métis Aboriginal population.

Using administrative health data has several inherent weaknesses for observational studies, such as lack of granular details on the individual and the health care system. Unmeasured factors in this study include information on medication access and use, adherence to medications, exposure to smoke, and mental health. Many of these factors may change over time within the same individual and may have influenced ED visits for asthma.

The ecological and individual SEP measures used in this study are not free of potential misclassification bias. The Chan's index, used as small-area SEP measure, relies on socioeconomic data aggregated at DA level and uses averages and percentages across these areas. Therefore, some degree of misclassification may be present when assigning the DA Chan's index score to patients with asthma according to their place of residence. However, the Chan' index was compared to Pampalon's indices and showed more consistent associations with adverse birth outcomes, a group of health outcomes known to have a SEP gradient (108).

The sensitivity analysis used the subsidy status as an individual SEP proxy variable. The subsidy status variable is derived from the Alberta Health Care Insurance Plan registry of the people having subsidy in health care premiums in the province based on the family income or for belonging to special protected groups (i.e., welfare and Aboriginals with Treaty status). The subsidy premiums were eliminated in Alberta in January 1st, 2009, and since then the registry has a decreasing quality in the Alberta population and the alternate premium arrangement variable from the subsidy status variable is extracted (208). Furthermore, the subsidy status variable does not take into account the occupational or educational profile of individuals as is recommended for a comprehensive SEP measure (97). The subsidy status variable, however, had been used in previous studies and has been shown to be a valid indicator of SEP in Alberta (35, 209-211).

4.5. Conclusions

This is the first study to use spatio-temporal calibration of NO_2LUR models to assess short-term effects of intra-urban exposure to traffic-air pollution on ED visits for acute asthma. The results shows that exposure to traffic-related air pollution in the CMAE during 2004/2005

to 2009/2010 was not associated, on average, with increased risk of hospital ED visits for asthma in children between 2 and 14 of age. Furthermore, SEP conditions did not modify this relationship.

Potential explanations to these findings are the steadily decrease in NO_2 concentrations in the area compared to the previous decade, and the decrease in the number and rates of ED visits for asthma. The latter observations may be partially explained by better access to primary health care physicians and facilities, and better asthma management in Canada during recent years.

The results of this study counter previous reports of air pollution effects on asthma in Edmonton, and suggest that there are quantified health benefits that might be associated with the reduction of ambient NO_2 concentrations. At lower exposure levels of traffic-air pollution, the role of other individual (i.e., atopy) or environmental (i.e., indoor second-hand smoke, exposure to industrial pollution) factors may have a greater importance on asthma exacerbations and attenuate the effect of traffic-related air pollution.

Table 4- 1. Number of emergency department visits for acute asthma in children by age group, sex, season, fiscal year and Canadian socioeconomic index quintiles in the Census Metropolitan Area of Edmonton, Canada, 2004/2005-2009/2010.

Variable	Q1 (lowest)[a]		Q2		Q3		Q4		Q5 (highest)		Total	
	n	%	n	%	n	%	n	%	n	%	n	%
Age group												
2 – 4	989	38.38	780	36.65	813	39.24	603	36.90	761	37.86	3,946	37.87
5 - 14	1,588	61.62	1,348	63.35	1,259	60.76	1,031	63.10	1,249	62.14	6,475	62.13
Sex												
Female	954	37.02	760	35.71	717	34.60	593	36.29	725	36.07	3,749	35.98
Male	1,623	62.98	1,368	64.29	1,355	65.40	1,041	63.71	1,285	63.93	6,672	64.02
Season[b]												
Cold season	1,093	42.41	814	38.25	835	40.30	659	40.33	828	41.19	4,229	40.58
Warm season	1,484	57.59	1,314	61.75	1,237	59.70	975	59.67	1,182	58.81	6,192	59.42
Fiscal year[c]												
2004/2005	558	21.65	398	18.70	337	16.26	298	18.24	340	16.92	1,931	18.53
2005/2006	555	21.54	461	21.66	422	20.37	308	18.85	418	20.80	2,164	20.77
2006/2007	412	15.99	378	17.76	330	15.93	299	18.30	374	18.61	1,793	17.21
2007/2008	348	13.50	287	13.49	296	14.29	239	14.63	278	13.83	1,448	13.90
2008/2009	351	13.62	326	15.32	355	17.13	270	16.52	301	14.98	1,603	15.38
2009/2010	353	13.70	278	13.06	332	16.02	220	13.46	299	14.88	1,482	14.22

[a] Chan's Canadian socioeconomic index quintiles; Q1, quintile one; Q2, quintile two; Q3, quintile three; Q4, quintile four; Q5, quintile five.
[b] Cold season from October to March and Warm season from April to September.
[c] Fiscal year starts in April 1 of the first year indicated and ends in March 31 of the second year indicated.

Table 4- 2. Emergency department visits for acute asthma and crude rates for children between 2 and 14 years of age in the Census Metropolitan Area of Edmonton, Canada, 2004/2005-2009/2010.

Fiscal Year	Children population 2-14 years[a]	No. asthma ED visits	Crude visit rate per 1,000
2004/2005	165,030	1931	11.7
2005/2006	167,678	2164	12.9
2006/2007	172,591	1793	10.4
2007/2008	175,733	1448	8.2
2008/2009	179,176	1603	8.9
2009/2010	182,252	1482	8.1

[a] Total population within the Census Metropolitan Area of Edmonton for ages 2-14 from Alberta Health Care Insurance Plan registry.

Table 4- 3. Descriptive statistics for city-specific land use regression model for nitrogen dioxide in the Census Metropolitan Area of Edmonton, Canada, 2004/2005-2009/2010.

Statistic	NO_2 LUR calibrated daily[a]		
	All year	Cold season	Warm season
Daily concentrations for case days (n=10,421)			
Mean	13.84	14.10	13.65
SD[b]	5.66	5.99	5.42
Max.	56.48	56.48	50.81
Percentiles			
5	6.27	6.09	6.42
25	9.74	9.69	9.77
50	12.93	13.17	12.79
75	16.96	17.50	16.59
95	24.48	25.46	23.68
IQR	7.22	7.81	6.82
Absolute difference between case and control days for the same cluster			
Mean	-0.047	0.03	-0.10
SD[b]	4.75	5.31	4.34
Max.	25.89	25.89	25.22
Percentiles			
5	-7.37	-8.32	-6.83
25	-2.91	-3.33	-2.65
50	-0.16	-0.15	-0.17
75	2.59	3.16	2.30
95	8.17	9.12	7.23
IQR	5.5	6.49	4.95
Daily value of metrological variables in the study period (n=2,191 days)			
Temperature ^oC mean (SD)	5.64 (11.71)	-3.37 (8.6)	14.61 (6.22)
Relative humidity % mean (SD)	67.15 (15.26)	72.59 (13.29)	61.73 (15.15)

[a] NO_2LUR: estimations of nitrogen dioxide concentrations in parts per billion averaged at disemmination area level estimated from land use regression model by Allen et al. (2011) and calibrated daily using the calibartion factor described by Johnson et al. (2013).

[b] IQR, interquartile range; Max., maximum; NO_2LUR, land use regression model for nitrogen dioxide; SD, standard deviation.

Table 4- 4. Adjusted odds ratios of emergency department visits for children with acute asthma per IQR exposure difference increase of nitrogen dioxide by day lags and season.

Exposure	All year		Cold season		Warm season	
Lag period	OR[a]	95% CI	OR	95% CI	OR	95% CI
0 day	0.97	0.94-1.00	0.99	0.95-1.04	0.95	0.91-0.99
1 day	0.99	0.96-1.02	1.00	0.96-1.04	0.97	0.92-1.02
2 day	1.01	0.98-1.04	1.01	0.98-1.05	0.99	0.95-1.04
3 day	0.98	0.96-1.01	0.99	0.96-1.03	0.97	0.92-1.01
4 day	0.98	0.95-1.00	0.99	0.95-1.02	0.96	0.91-1.00
5 day	0.99	0.96-1.02	1.00	0.97-1.04	0.96	0.92-1.01
1-3 day	0.99	0.96-1.03	1.01	0.96-1.05	0.96	0.90-1.03
1-5 day	0.98	0.94-1.02	1.01	0.96-1.06	0.93	0.86-0.99

[a] OR, odds ratio; CI, Confidence Interval; ORs for the same day exposure adjusted for temperature, relative humidity, holidays, and daily number of visits for influenza.

Table 4- 5. Adjusted odds ratios of emergency department visits for children with acute asthma per IQR exposure difference increase of nitrogen dioxide by day lags, age group, sex, and Aboriginal status.

Exposure Lag period	Age group OR (95%CI)[a]		Sex OR (95%CI)		Aboriginal status[b] OR (95%CI)	
	2-4 years (n=3,946)	5-14 years (n=6,475)	Female (n= 3,749)	Male (n=6,672)	Aboriginal (n=576)	Non-Aboriginal (n=9,845)
0 day	0.98 (0.93-1.03)	0.97 (0.93-1.00)	0.95 (0.86-0.98)	0.98 (0.95-1.03)	1.00 (0.89-1.13)	0.97 (0.94-1.00)
5 day	0.99 (0.94-1.03)	0.99 (0.96-1.03)	1.00 (0.96-1.05)	0.98 (0.95-1.02)	0.95 (0.85-1.05)	0.99 (0.97-1.02)
1-3 day	1.04 (0.98-1.11)	0.96 (0.91-1.00)	1.02 (0.96-1.09)	0.97 (0.93-1.02)	0.96 (0.84-1.10)	0.99 (0.96-1.03)
1-5 day	1.04 (0.97-1.11)	0.98 (0.92-1.03)	1.06 (0.98-1.13)	0.97 (0.92-1.02)	0.95 (0.82-1.11)	1.00 (0.96-1.05)

[a] OR, odds ratio; CI, Confidence Interval; ORs for the same day exposure adjusted for temperature, relative humidity, holidays, and daily number of visits for influenza.
[b] Aboriginal status based on the category "A=Aboriginal with Treaty Status" from the Alternate premium arrangement variable from the Alberta Health Care Insurance Plan registry.

Table 4- 6. Adjusted odds ratios of emergency department visits for children with acute asthma per IQR exposure difference increase of nitrogen dioxide by day lags and exposure levels.

Exposure Lag period	NO_2LUR[a] lower levels (1.83 to 13.84 ppb)		NO_2LUR[a] higher levels (13.85 to 56.48 ppb)	
	OR	95% CI	OR	95% CI
0 day	0.96	0.91-1.02	0.97	0.93-1.01
1 day	0.99	0.94-1.04	0.99	0.96-1.03
2 day	0.99	0.94-1.03	1.02	0.99-1.06
3 day	0.97	0.93-1.02	0.99	0.96-1.03
4 day	0.96	0.91-1.01	0.99	0.96-1.02
5 day	0.95	0.91-1.00	1.01	0.98-1.04
1-3 day	0.97	0.91-1.03	1.01	0.96-1.05
1-5 day	0.94	0.87-1.01	1.00	0.95-1.06

[a] NO_2LUR: estimated concentrations of nitrogen dioxide from Allen et al. (2011) land use regression model.
CI, Confidence Interval; NO_2LUR, land use regression model for nitrogen dioxide; OR, odds ratio; ppb, parts per billion

Table 4- 7. Adjusted odds ratios of emergency department visits for children with acute asthma per IQR exposure difference increase of nitrogen dioxide by lag days and Chan's Canadian socioeconomic index quintiles.

Exposure lag period	Q1 (lowest)[a]	Q2	Q3	Q4	Q5 (highest)	Total
	OR[b] (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
0 day	0.96 (0.91-1.01)	1.00 (0.94-1.07)	0.95 (0.89-1.01)	0.99 (0.92-1.08)	0.99 (0.91-1.07)	0.98 (0.94-1.00)
1 day	0.99 (0.95-1.04)	0.99 (0.93-1.04)	0.97 (0.92-1.03)	1.01 (0.94-1.09)	0.99 (0.92-1.06)	0.99 (0.96-1.01)
2 day	0.99 (0.96-1.04)	0.97 (0.92-1.03)	1.02 (0.96-1.08)	1.07 (0.99-1.15)	1.03 (0.96-1.11)	1.01 (0.98-1.04)
3 day	0.98 (0.94-1.02)	0.99 (0.94-1.04)	0.98 (0.93-1.04)	1.03 (0.96-1.11)	0.97 (0.91-1.04)	0.99 (0.96-1.01)
4 day	0.99 (0.95-1.04)	0.99 (0.94-1.05)	0.94 (0.89-1.00)	0.96 (0.89-1.03)	0.99 (0.93-1.07)	0.98 (0.95-1.00)
5 day	0.97 (0.94-1.02)	1.00 (0.96-1.06)	0.97 (0.92-1.03)	1.03 (0.96-1.11)	1.02 (0.95-1.09)	0.99 (0.97-1.02)
1-3 day	0.98 (0.93-1.04)	0.97 (0.91-1.05)	0.99 (0.91-1.07)	1.06 (0.96-1.17)	0.99 (0.90-1.09)	0.99 (0.96-1.03)
1-5 day	0.98 (0.91-1.04)	0.98 (0.90-1.06)	0.95 (0.87-1.04)	1.05 (0.94-1.17)	1.00 (0.90-1.11)	0.98 (0.95-1.02)

[a] SES index quintile, socioeconomic index; Q1, Chan's Canadian socioeconomic index quintile one (lowest); Q5, quintile five (highest).
[b] OR, odds ratio; CI, Confidence Interval; ORs were adjusted for temperature, relative humidity, holidays, and daily number of visits for influenza corresponding to the lag exposure period.

Table 4- 8. Descriptive statistics for national land use regression model for nitrogen dioxide in the Census Metropolitan Area of Edmonton, Canada, 2004/2005-2009/2010.

Statistic	NO_2LUR calibrated daily[a]		
	All year	Cold season	Warm season
Daily concentrations for cases (n=10,421)			
Mean	15.88	16.24	15.63
SD[b]	6.77	7.15	6.50
Max.	59.97	51.03	59.97
Percentiles			
5	6.82	6.75	6.85
25	10.94	10.85	11.02
50	14.80	15.10	14.62
75	19.71	20.52	19.15
95	28.46	29.77	27.53
IQR	8.77	9.67	8.13
Absolute difference between case and control days for the same cluster			
Mean	-0.046	0.02	-0.09
SD[b]	5.52	6.15	5.04
Max.	32.63	31.31	32.63
Percentiles			
5	-8.72	-9.68	-7.98
25	-3.33	-3.79	-3.06
50	-0.15	-0.14	-0.16
75	2.98	3.57	2.66
95	9.35	10.39	8.37
IQR	6.31	7.36	5.72

[a] NO_2LUR: estimations of nitrogen dioxide (ppb) concentrations averaged at disemmination area level estimated from land use regression model by Hystad et al. (2011) and calibrated daily using the calibartion factor described by Johnson et al. (2013).
[b] IQR, interquartile range; Max., maximum; NO_2LUR, land use regression model for nitrogen dioxide; SD, standard deviation.

Table 4- 9. Adjusted odds ratios of emergency department visits for children with acute asthma per IQR exposure difference increase of nitrogen dioxide by day lags and season, using national land use regression model.

Exposure	All year		Cold season		Warm season	
Lag period	OR[a]	95% CI	OR	95% CI	OR	95% CI
0 day	0.98	0.94-1.00	0.99	0.95-1.04	0.97	0.93-1.01
1 day	0.99	0.96-1.01	0.99	0.97-1.03	0.97	0.93-1.02
2 day	1.01	0.98-1.04	1.01	0.98-1.05	0.99	0.95-1.04
3 day	0.99	0.96-1.01	0.99	0.97-1.03	0.97	0.93-1.01
4 day	0.98	0.95-1.00	0.99	0.96-1.02	0.96	0.92-1.00
5 day	0.99	0.97-1.02	1.01	0.98-1.04	0.97	0.93-1.01
1-3 day	0.99	0.96-1.03	1.00	0.96-1.05	0.96	0.91-1.02
1-5 day	0.98	0.95-1.02	1.01	0.96-1.06	0.93	0.87-0.99

[a] OR, odds ratio; CI, Confidence Interval; ORs for the same day exposure adjusted for temperature, relative humidity, holidays, and daily number of visits for influenza.

Table 4- 10. Summary of concordance and agreement measures between estimation of NO2 by LUR models and concentrations measured at the monitor stations in Edmonton from April 1, 2004 to March 31, 2010.

Comparison	No. days	Lin's concordance coefficient	Mean of differences[a]	SD[b]	Min.	Max.	95% CI
LUR Hystad – Central station	2,178	0.59	1.14	7.24	-17.11	24.82	-13.06 – 15.34
LUR Allen – Central station	2,178	0.58	-0.37	7.14	-18.24	21.94	-14.37 – 13.62
LUR Hystad – East station	2,181	0.60	-1.03	6.45	-27.61	16.99	-13.67 – 11.62
LUR Allen – East station	2,181	0.53	-2.54	6.60	-31.25	14.11	-15.50 – 10.41
LUR Hystad – Northwest station	620	0.46	5.44	7.54	-19.71	30.80	-9.34 – 20.23
LUR Allen – Northwest station	620	0.52	1.57	7.47	-22.68	23.03	-13.08 – 16.22
LUR Hystad – South station	1,643	0.49	4.53	6.58	-13.98	27.61	-8.38 – 17.45
LUR Allen – South station	1,643	0.53	0.32	6.50	-20.80	19.62	-12.42 – 13.06

[a] Differences were calculated for each day and station as: LUR model estimated – monitor station concentration; therefore, the mean difference is the amount of ppb of the LUR model estimated above or below the concentration in the monitor station.
[b] CI, confidence interval; IQR, interquartile range; LUR, land use regression model; Max., maximum; Min., minimum; SD, standard deviation.

Table 4- 11. Adjusted odds ratios of emergency department visits for children with acute asthma per IQR exposure difference increase of nitrogen dioxide by lag days and subsidy status.

Exposure Lag period	Stratified models by subsidy status[a]		Interaction model	
	No subsidy	Subsidy	NO_2LUR[c]	NO_2LUR*Subsidy status
	OR[b] (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
0 day	0.97 (0.93-1.00)	0.98 (0.92-1.04)	0.96 (0.93-1.00)	1.02 (0.95-1.09)
1 day	0.98 (0.95-1.02)	1.01 (0.96-1.06)	0.98 (0.93-1.02)	1.02 (0.97-1.09)
2 day	1.01 (0.97-1.04)	1.02 (0.97-1.07)	1.00 (0.97-1.04)	1.02 (0.96-1.08)
3 day	0.97 (0.94-1.00)	1.01 (0.96-1.06)	0.97 (0.94-1.00)	1.04 (0.99-1.11)
4 day	0.97 (0.94-1.01)	0.99 (0.94-1.04)	0.97 (0.94-1.00)	1.03 (0.97-1.09)
5 day	0.98 (0.95-1.02)	1.01 (0.96-1.06)	0.98 (0.95-1.01)	1.03 (0.97-1.09)
1-3 day	0.98 (0.93-1.02)	1.03 (0.97-1.10)	0.98 (0.93-1.02)	1.05 (0.97-1.14)
1-5 day	0.96 (0.91-1.01)	1.02 (0.95-1.10)	0.96 (0.98-1.17)	1.07 (0.98-1.17)

[a] Subsidy beneficiaries include Aboriginal people with Treaty status, beneficiaries of Welfare social programs, and beneficiaries of social government sponsored programs using the Alternate premium arrangement variable from the Alberta Insurance Plan Program registry.
[b] OR, odds ratio; CI, Confidence Interval; ORs were adjusted for temperature, relative humidity, holidays, and daily number of visits for influenza corresponding to the lag exposure period.
[c] NO_2LUR: estimations of nitrogen dioxide concentrations in parts per billion averaged at disemmination area level estimated from land use regression model by Allen et al. (2011) and calibrated daily using the calibartion factor described by Johnson et al. (2013).

Figure 4- 1. Distribution of Chan's Canadian Socioeconomic Index in the Census Metropolitan Area of Edmonton, Alberta, Canada, 2006.

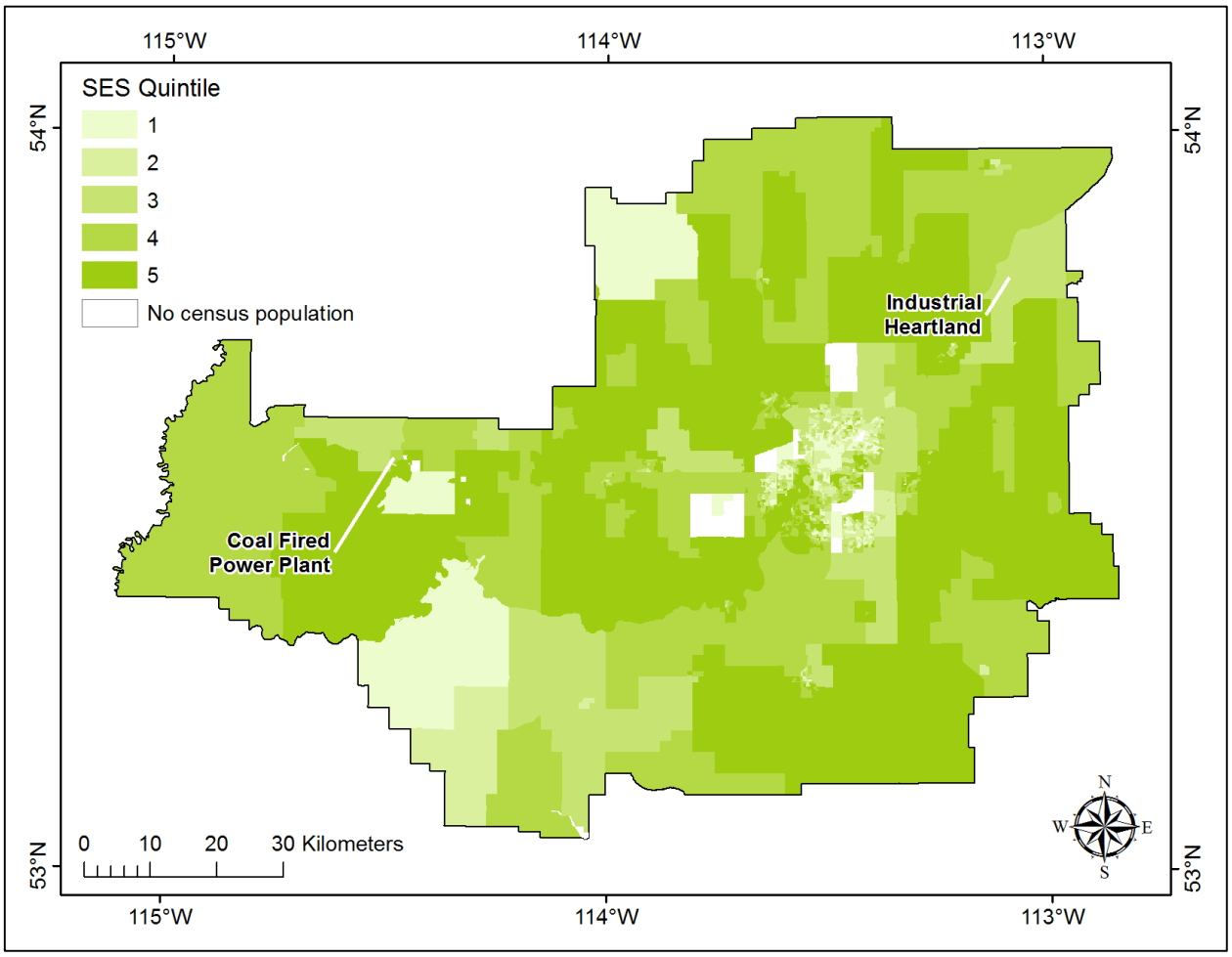


Figure 4-1b. Distribution of Chan's Canadian Socioeconomic Index in the Edmonton city area, Alberta, Canada, 2006.

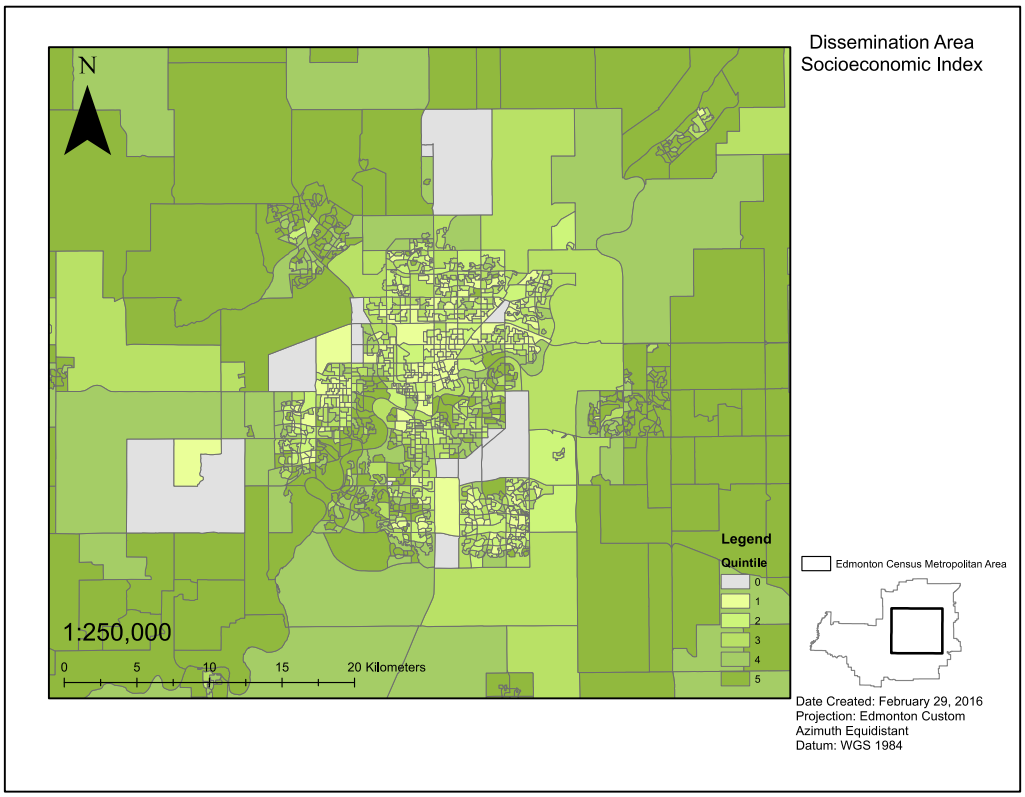


Figure 4- 2. Crude emergency department visit rates for children with acute asthma by dissemination area in the Census Metropolitan Area of Edmonton during 2004/2005 to 2009/2010.

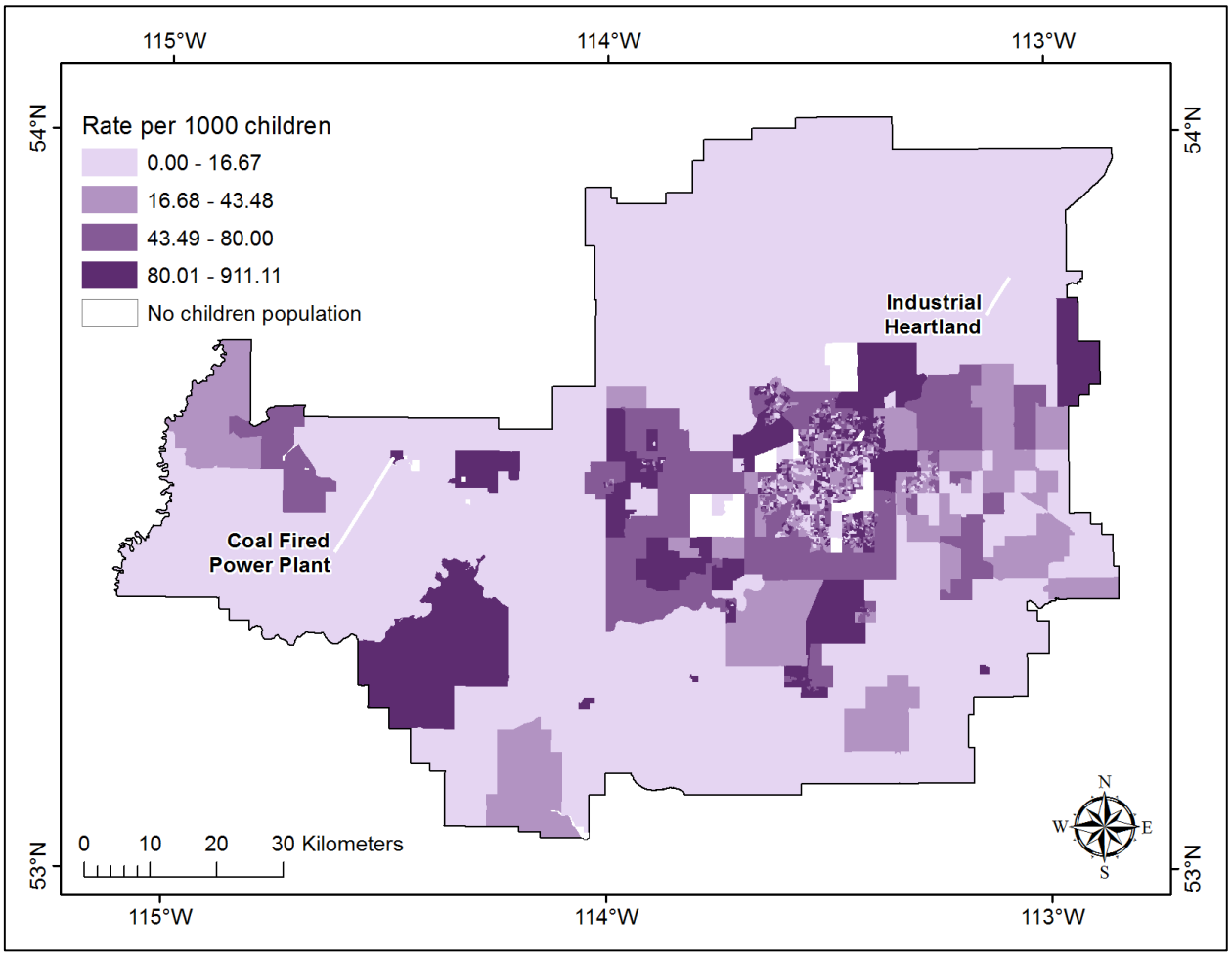


Figure 4- 3. Directly standardized emergency department visit rates of children with acute asthma by dissemination area in the Census Metropolitan Area of Edmonton during 2004/2005 to 2009/2010.

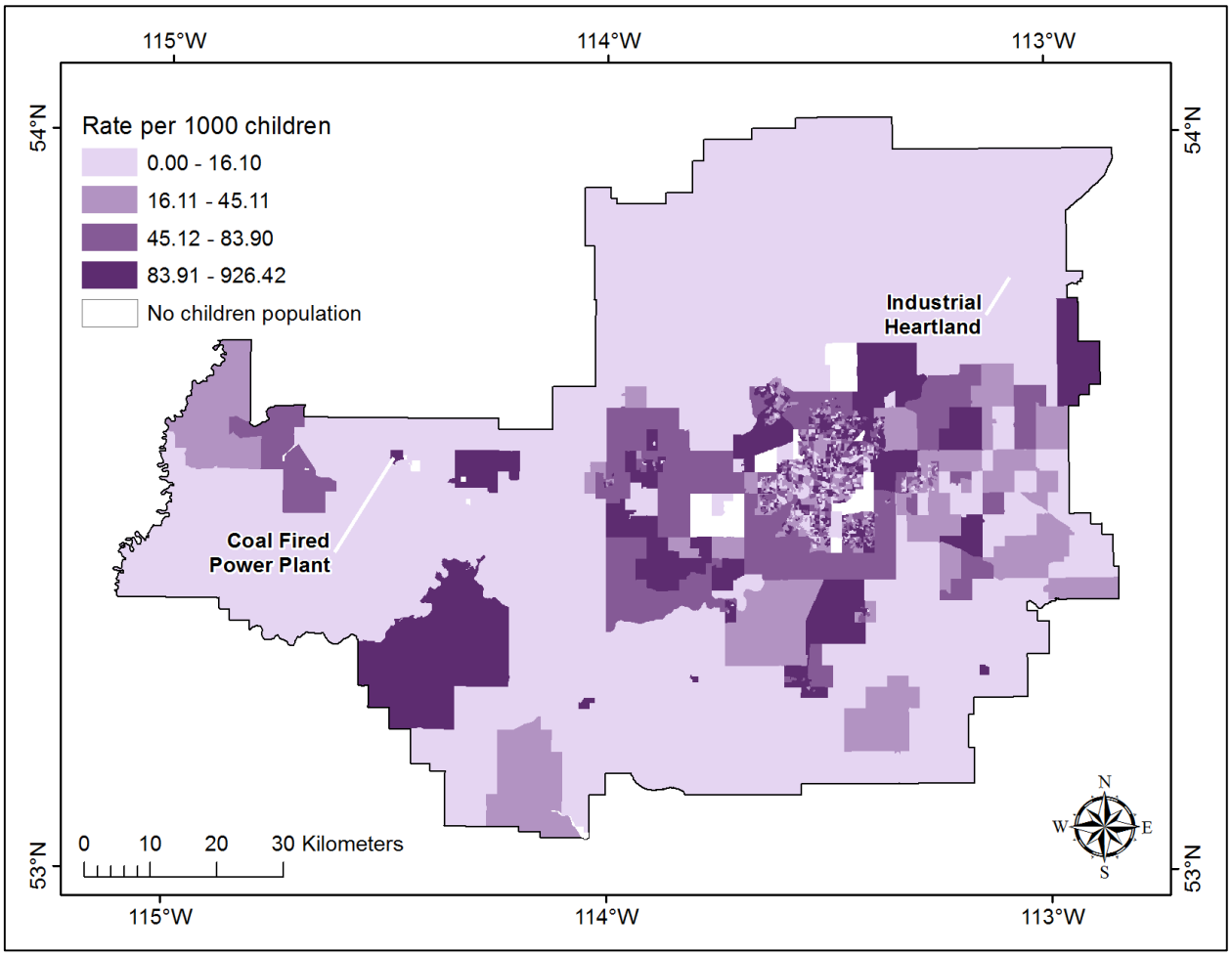
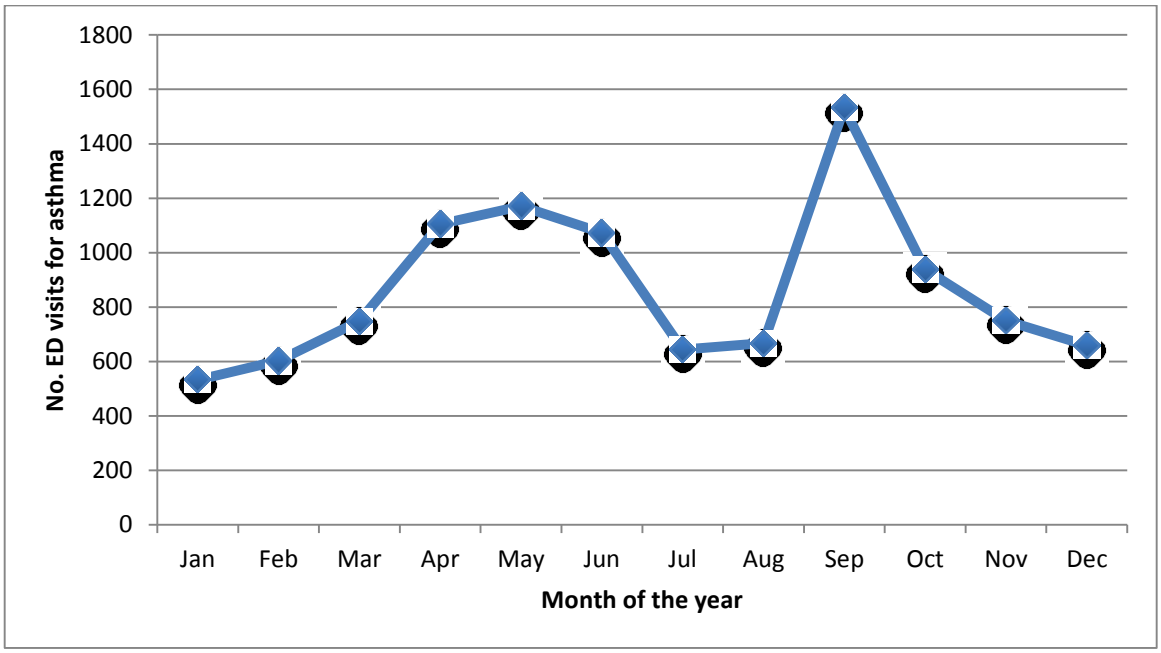


Figure 4- 4. Emergency department visits for children with acute asthma by (a) month of the year and (b) day of the week for the Census Metropolitan Area of Edmonton 2004/2005 to 2009/2010.

c) Month of the year



d) Day of the week

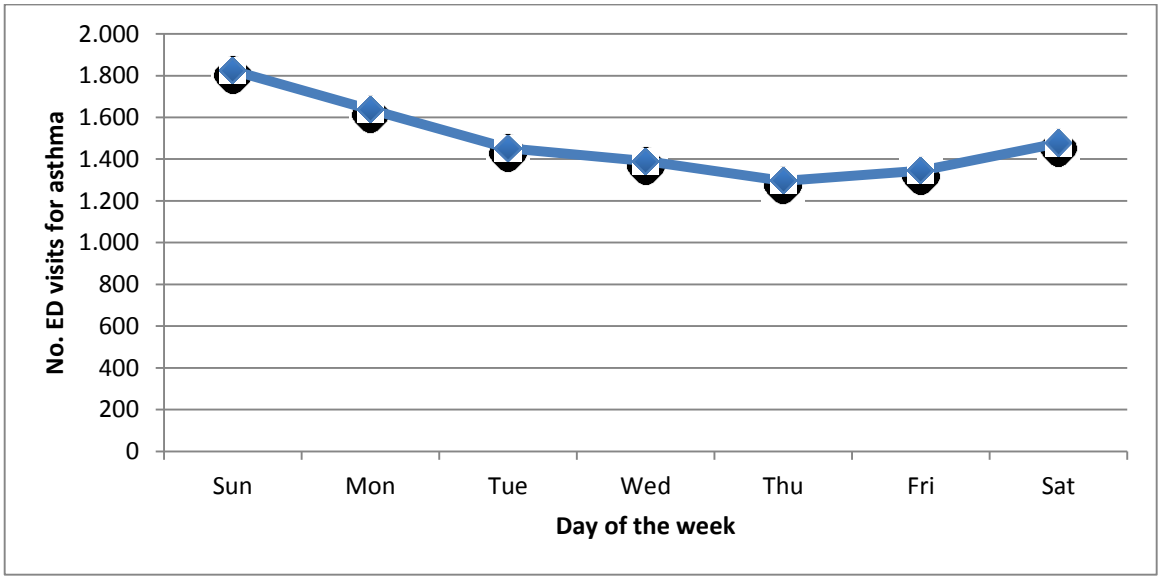


Figure 4- 5. Modeled annual average concentrations of nitrogen dioxide from city specific land use regression model for Edmonton, 2008.

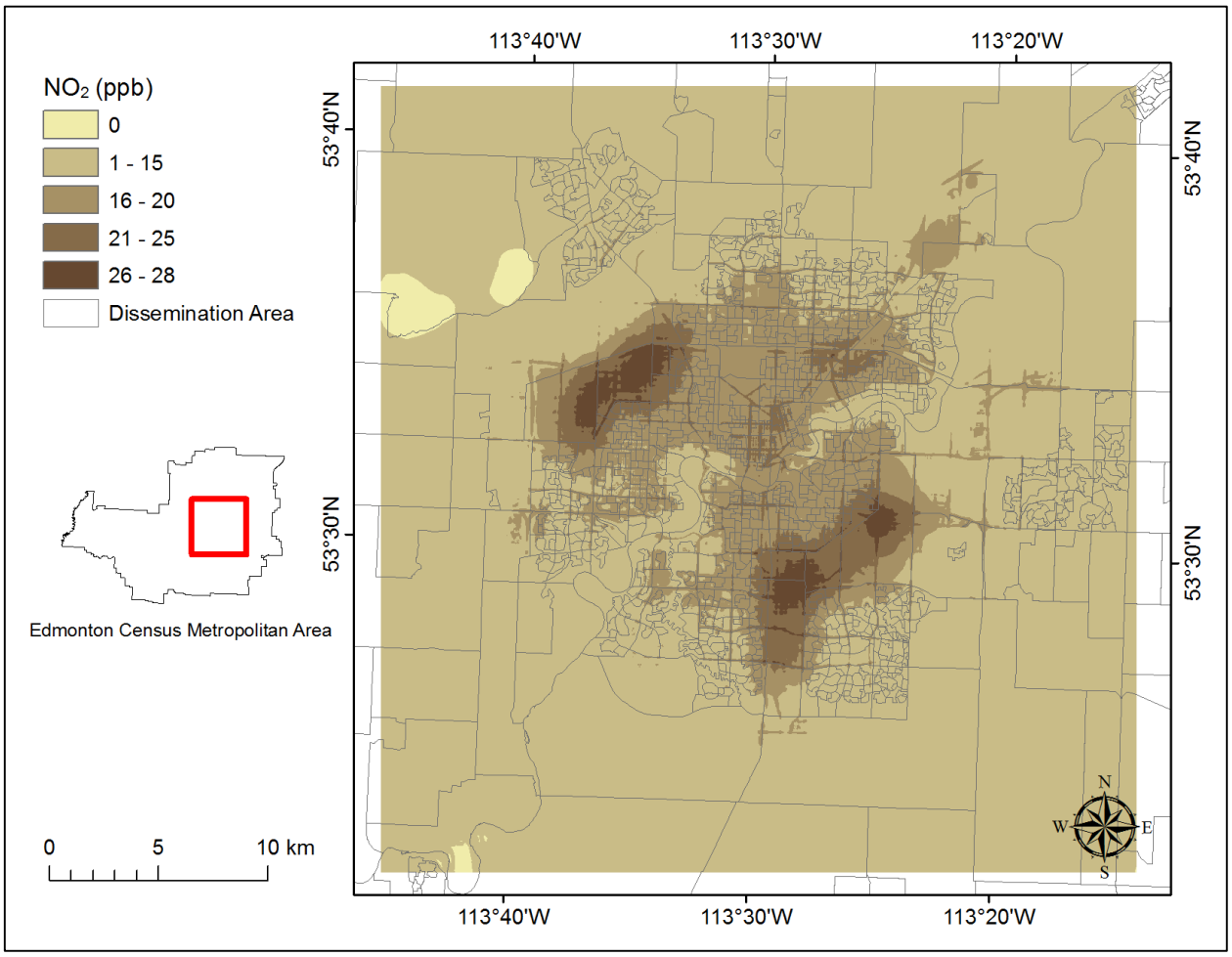


Figure 4- 6. Odds ratios of the association between traffic-related air pollution and emergency department visits for children with acute asthma by dissemination area in the city of Edmonton, 2004/2005 to 2009/2010.

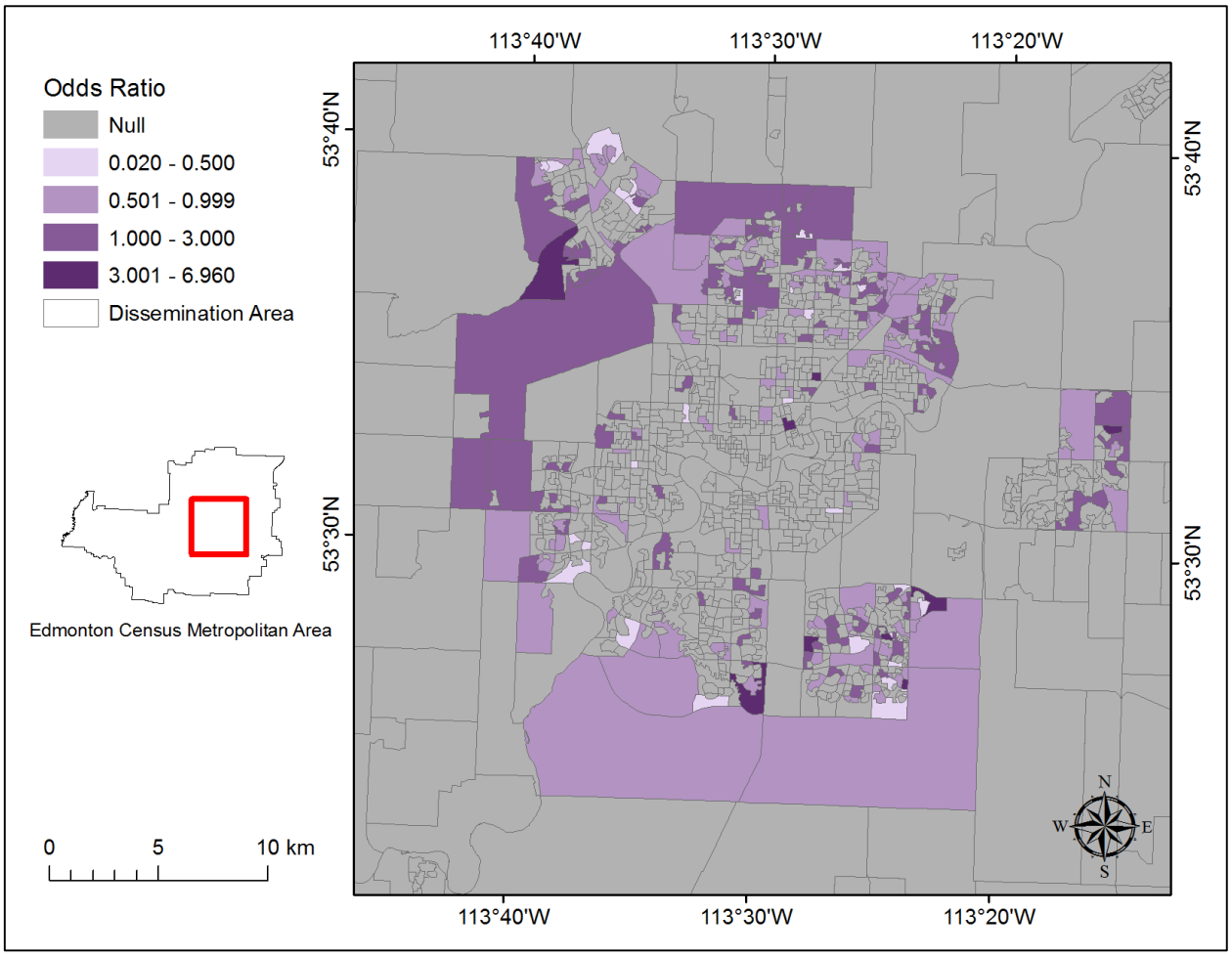
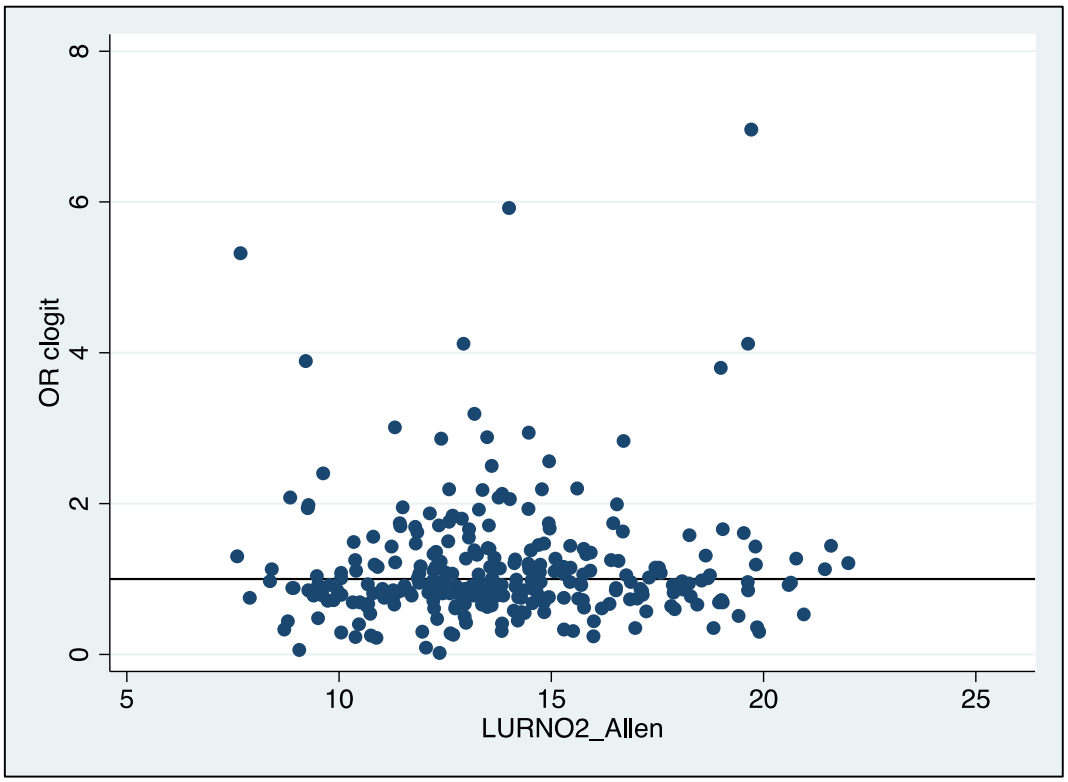


Figure 4- 7. Scatter plot of odds ratios of conditional multivariable regression models versus estimations of nitrogen dioxide by dissemination area.



OR clogit: Odds ratios estimated from multivariable conditional regression models.
NO_2LUR_Allen: estimations of nitrogen dioxide concentrations in parts per billion (ppb) averaged at disemmination area level estimated from land use regression model by Allen et al. (2011) and calibrated daily using the calibartion factor described by Johnson et al. (2013).

Figure 4- 8. Estimated nitrogen dioxide concentrations from national land use regression model in the Census Metropolitan Area of Edmonton, Alberta, Canada, 2006.

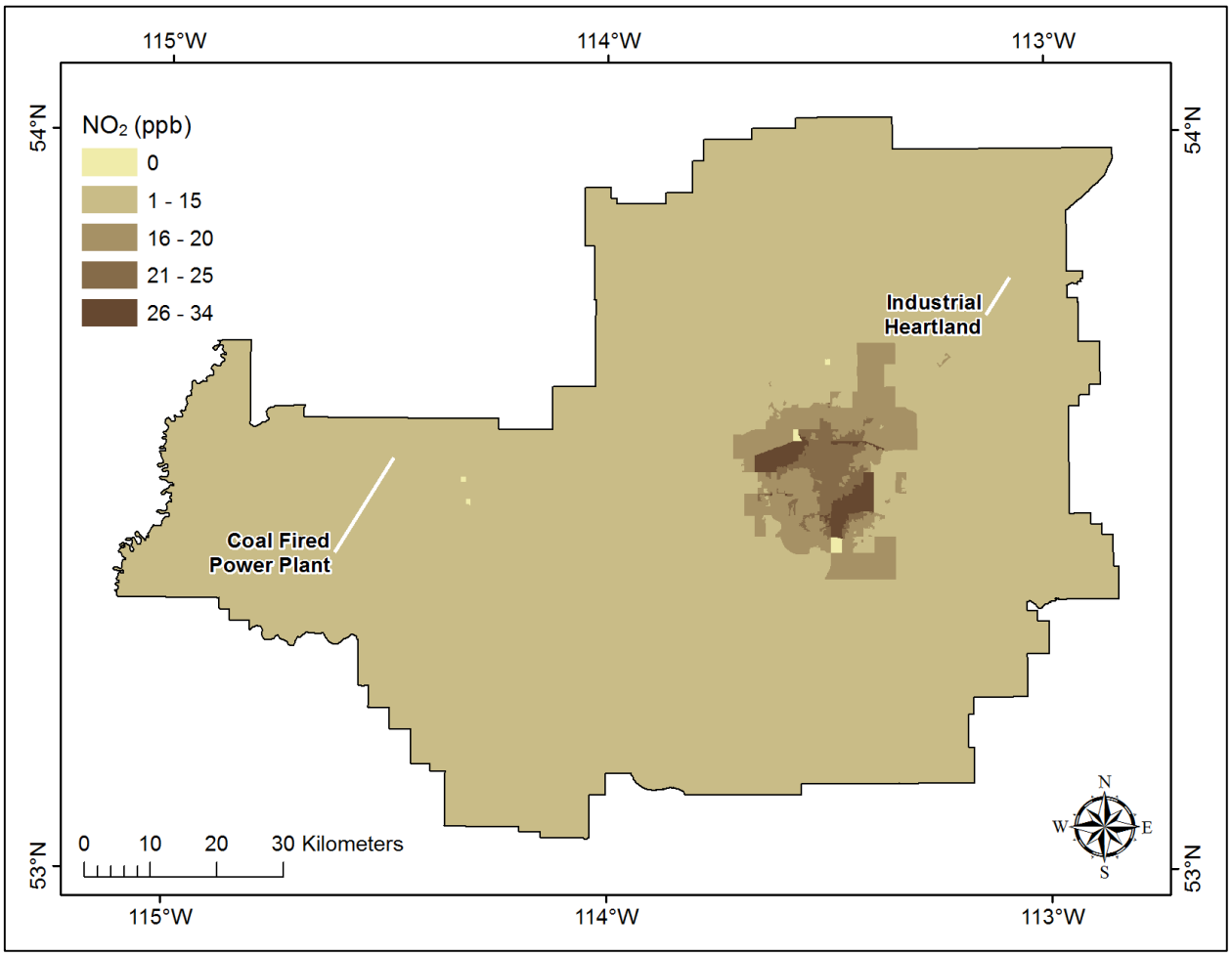
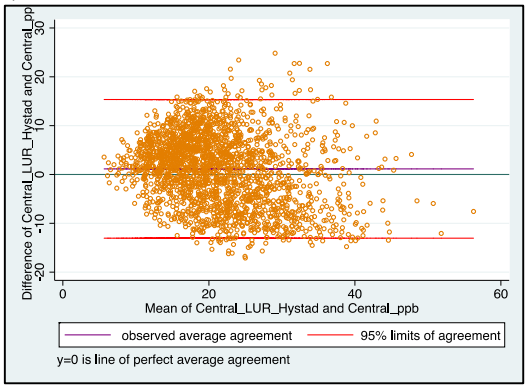
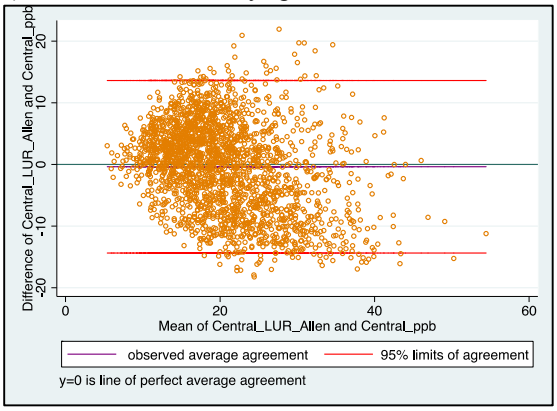


Figure 4- 9. Bland-Altman's limits of agreement between estimation of nitrogen dioxide from land use regression models and concentrations measured at the monitor stations in Edmonton from April 1, 2004 to March 31, 2010.

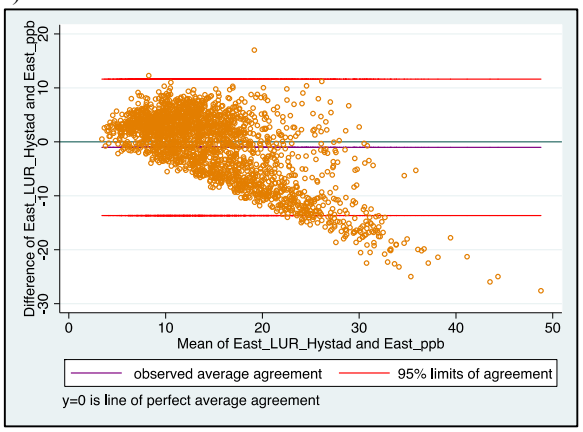
a) Central station vs national LUR model



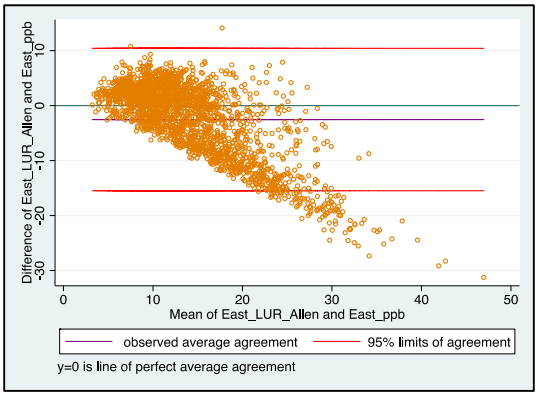
b) Central station vs city-specific LUR model



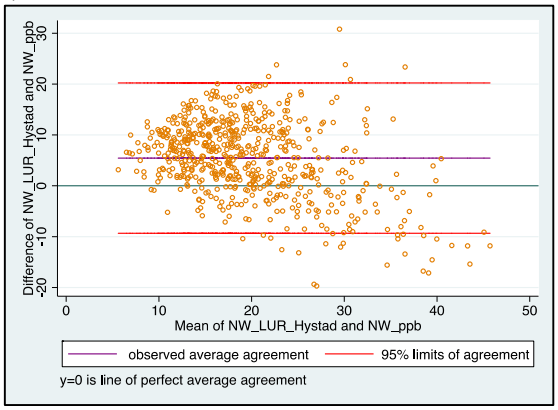
c) East station vs national LUR model



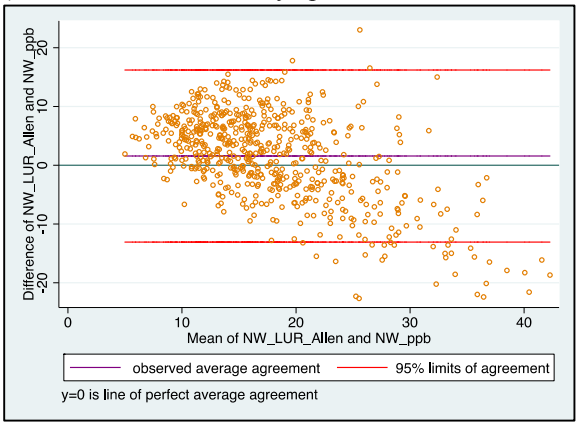
d) East station vs city-specific LUR model



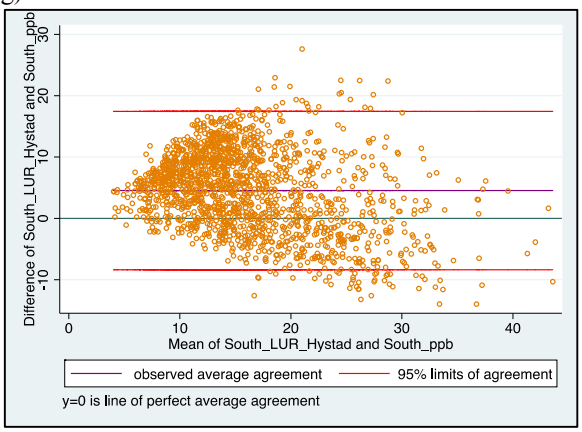
e) Northwest station vs national LUR model



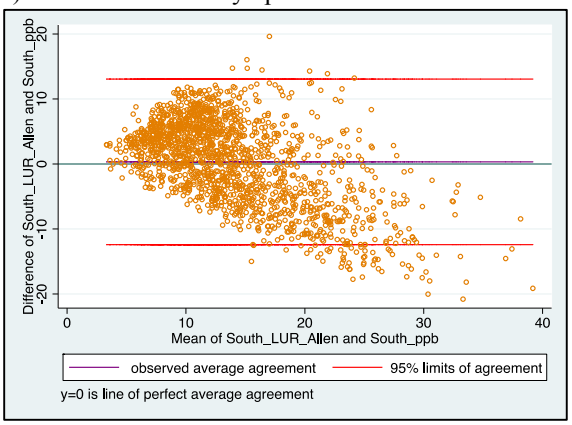
f) Northwest station vs city-specific LUR model



g) South station vs national LUR model



h) South station vs city-specific LUR model



CHAPTER 5. The Effect of Living near to Industrial Sources of Air Pollution on Emergency Department Visits for Asthma in Children

5.1. Introduction

Asthma is the most common chronic respiratory disease in children (16). Asthma is also a complex, heterogeneous disease that results from the interaction of genetic, social, and environmental factors, which include chemical irritants in outdoor air (19, 126). Outdoor air pollution is a complex mixture of compounds, and the composition varies greatly between and within regions, depending on the sources of emission and weather patterns (14, 110). Sources of outdoor air pollution may be natural or anthropogenic; anthropogenic sources are most commonly attributed to industrial development and urban traffic (109). Outdoor air pollution has been associated with various health conditions including asthma, cardiovascular diseases, respiratory infections, adverse birth outcomes, and cancer (2, 80, 158). Furthermore, children are considered to be highly susceptible to the effects of air pollution due to physiological and physical activity factors (159, 160).

The effects of outdoor air pollution on children's asthma include an increase in its incidence, prevalence, self-reported symptoms, emergency department (ED) visits, and hospitalizations, and worsening of lung function measurements (3, 78, 79, 161). In Edmonton, Alberta, studies conducted between 1992 and 2002 documented an increase in children's ED visits for acute asthma related to variations in concentrations of nitrogen dioxide (NO_2), carbon monoxide (CO), ozone (O_3) and particulate matter with mean aerodynamic diameter of 10 μm (PM_{10}), and 2.5 μm ($PM_{2.5}$) (10, 11).

The Census Metropolitan Area of Edmonton (CMAE) has specific pollution sources from the petrochemical industry (northeast) and the coal-fired power plants (west). The Industrial Heartland of Alberta (IHA) is located in the northeast of the CMAE, an area of predominantly petrochemical industries that "upgrade" the northern Alberta oil sands to synthetic crude oil. The IHA is Canada's largest hydrocarbon processing center and concentrations of volatile organic compounds (VOC) in plumes are similar or higher than the world's largest cities and industrial regions (238). The oil sands production in northern Alberta could triple by 2020, and a major industrial expansion is taking place in the IHA as a response to this increasing production (239).

In addition, three major coal-fired power plants (CFPP) are located in the west of CMAE in the Wabamum area. Keephills, Keephills 3, and Sundance are the three active plants located in the Wabamum area operated by TransAlta; the Wabamum plant was closed in 2010. The Sundance power plant is the largest coal-fired electrical generating facility in western Canada, with six generating units (240). Alberta is the leading province in Canada for air pollutants released from industrial sources (241). In 2011, the six coal plants located in Alberta emitted 33% of the sulphur dioxide (SO_2), 10% of the nitrogen dioxides NO_x, 6% of fine particular matter $PM_{2.5}$, and 44% of mercury (Hg) from all anthropogenic sources in the province (242). Despite the presence of these important sources of industrial emissions to the air in the CMAE, the effect of proximity to these facilities on children's asthma is not well known.

The two previous chapters of this dissertation assessed the short-term effect of outdoor air pollution on ED visits for children with acute asthma, with a focus on traffic-related air pollution. This chapter addresses the relationship between proximity to industrial sources of outdoor air pollution and ED visits for asthma in children. The objective of the study was to

explore the presence of clusters of ED visits for acute asthma in children living around the IHA and the CFPP areas, which are the main putative sources of industrial emissions to the air in the CMAE.

5.2. Methods

5.2.1. Study area

The study setting was the CMAE in the Province of Alberta, Canada. Alberta is a culturally diverse province located in western Canada with a 2015 estimated population of about 4.1 million, 83% of whom live in urban centres and 19% of whom are children under 14 years (243). The CMAE is located at the center of the Province of Alberta including its capital city, Edmonton, with a population of approximately 1.2 million, of which 18% are children under 14 years (166). In accordance with the Canada Health Act, Alberta maintains a universal, publicly-funded health care system, the Alberta Health Care Insurance Plan that guarantees Albertans receive universal access to medically necessary hospital and physician services free of charge.

5.2.2. Data sources

Retrospective data on children's ED visits for acute asthma were collected at the dissemination area (DA) level for residents in the CMAE from April 1, 2004 to March 31, 2010.

Asthma data

Alberta Health Services (AHS) provided anonymous patient data. Data were obtained for all residents aged from 2 to 14 year old, who were diagnosed with asthma in a hospital ED facility in the CMAE from April 1, 2004 to March 31, 2010. Asthma data included all children's

ED visits during the study period (i.e., events), therefore might be more than one visit per child (i.e., cases).

The ED visits for asthma in children less than 2 years of age were excluded, as the diagnosis of asthma in this age group is less accurate. Asthma ED visits were also restricted for children up to 14 years old to minimize the potential air pollution exposure misclassification; children up to 14 years old are usually in primary school and the location of these schools (and therefore their air pollution exposure) is usually close to the children's house area, which was selected as the exposure location for the study.

The AHS operates 11 hospital ED facilities within the Edmonton zone that provide services for children across the CMAE. Appendix C illustrates the geographical location and provides general information of these ED facilities. The AHS Edmonton zone is the AHS administrative subdivision that provides health services to the entire CMAE and an additional region in the west region of the CMAE. Appendix D shows the AHS subdivisions and the matching between the AHS Edmonton zone and the CMAE.

In the AHS ambulatory care system, each ED visit is coded by experienced medical record nosologists using the International Classification of Disease 10th revision (ICD-10) according to the triage information, nursing notes, ED records and consultation notes. The ED visits for asthma were identified as those having the ICD-10 code J45 as first discharge diagnosis. Additional variables of the asthma database included the unique number, date of the visit, age, sex, subsidy status, and residential postal code of the patient. Only children whose residential postal code belonged to the CMAE were selected.

Population data

The population data of children by DA were obtained from the Canadian Census Analyzer of the University of Toronto (244). The population estimates were based in the 2006 Canadian Census (245) as this is the census year that provides the population estimates nearest to the middle point of the study period. The projected population data for children under 14 years old were used as the known underlying population at risk to calculate the children's ED visit rates for asthma during the study period.

Geographical data

The CMAE groups 35 census subdivisions and 1,551 DAs. The DA is the smallest standard geographic area for which all census data are disseminated, grouping 400 to 700 persons; each DA is assigned an eight-digit code which identifies the province/territory (2 digits), the census division (2 digits) and a specific DA four-digit code (246). The DA was the geographical unit used in this spatial analysis. Asthma data were linked to this geographical unit by assigning each record's postal code to its corresponding DA using the postal code conversion file from Statistics Canada (247). All asthma cases were aggregated at the DA level over the study period.

The specific locations (latitude and longitude) where the IHA and CFPP are located were defined as the "putative sources". For the IHA, the Shell company location was selected as the referent point as it is the central point within the IHA; for the CFPP Wabamum area the specific location was the Sundance plant. Figure 5-1 shows the location of the two putative sources and the centroids of the all the DAs in the CMAE. To calculate measures from the pollution sources to the DAs, a population-based centroid was calculated for each DA and therefore centroids are not necessarily polygon's geographic centers. Distance and direction between each putative

source location and the centroids of the DAs in the CMAE were calculated using the distance (in meters) and angle (in geodesic grades) calculation tools in ArcGIS ® (248). Distances were then converted to kilometers (km) and angles to cardinal degrees to facilitate interpretations. The DA level polygon map was obtained from Statistics Canada and spatial data layers were created in ArcGIS® using the Edmonton Custom Azimuth Equidistant projection and Datum WGS 1984.

5.2.3. Data analysis

A spatial analysis of disease clusters around putative sources with count (ecological) data was conducted using descriptive, hypothesis testing and multivariable modeling analyses (249).

Descriptive analysis

Crude ED visits rates for asthma for the entire CMAE were calculated by year using as denominator the population of children between 2 and 14 years old living in the Edmonton zone based on the yearly registry of the Alberta Health Care Insurance Plan. The age-sex directly standardized rates (DSR) by DA and their 95% confidence intervals (CI) were calculated using as denominator the Census 2006 population of children between 0 to 14 years in the CMAE. The Census 2006 population of children between 0 to 14 years for the whole CMAE was used as the standard population. The 95% CI of the rates were adjusted for the variance of events (250). The lower limit of the DSR 95% CI for each DA was used to identify areas with statistically higher rates when the overall regional rate was smaller than this limit (251).

Given that the childhood population differs widely in size by DA, some rates may be better estimated than others and the true pattern of risk for ED visits for asthma may be obscured. Therefore, we used a spatial empirical Bayes smoothing technique to reduce

heterogeneity in each DA's risk for the CAME. The empirical Bayes smoothing technique rationale is to "borrow" information from the surrounding areas to calculate a more stable estimator of the Standardized Morbidity Ratios (SMR) for each region and facilitate the visualization of disease's spatial patterns (252, 253). The program gllamm written by Rabe-Hesketh (253) was used to estimate the Bayesian smoothed SMR, using as offset the natural logarithm of expected cases, with options Poisson family and log link. The expected cases by DA were calculated using as reference the overall crude visit rate. Crude, DSR and empirical Bayes smoothed SMR were calculated in Stata 13 (174) and then mapped using ArcGIS 10.3® (248).

Hypothesis testing analysis

The cluster detection methods based on hypothesis testing have demonstrated to have better power to identify the presence of disease clusters compared to CI of rates when the size of the cluster is relatively small (251). The tests that assess the presence of clusters around a predefine location are known as focused cluster detection tests (249). The presence of clusters around the two "putative sources" under study were assessed using three focused tests for cases: Kulldorff circular spatial scan test, Stone's test, Lawson directional score test, and the Chang-Rosychuk spatial scan statistic for events.

The Kulldorff circular spatial scan test (254) uses circular windows centered at the centroid of the area where the putative source is located creating an infinite number of geographical circles until some upper limit of the total population defined by the user is reached. Each circle is evaluated as a potential cluster by calculating the likelihood ratio statistic of observed and expected cases within and outside the circle. Then, the circle with the highest likelihood ratio of being cluster is assigned a P value, which is adjusted by multiple testing. This

method was implemented in SaTScan® (255) using a pure spatial analysis with a Poisson probability model, scanning for high rates, and with maximum spatial cluster size of 25% of the population at risk. Separate analyses were conducted for IHA and CFPP using each time as the focus grid, the latitude and longitude of the DA's centroid where these locations belong.

The Stone's test (256) is a focused test that assesses whether the risk of a disease decreases as the distance increases from a given location. The test's null hypothesis is that relative risks are constant across areas, while the alternative hypothesis is that there is a descending trend in relative risks (RR) as distance to the focus increases. The "DCluster" package coded in R software was used to implement this test with the following specifications: log of expected cases were used as offset under a Poisson sampling model associated with 999 simulations for estimating the p-value (257).

The Lawson directional score test is used to assess directional variation of clusters and uses a score statistic, for a single parameter, that has a χ^2-distribution with 1 degree of freedom (258). The test uses the observed and expected cases for each area and the cosine of the $(\theta - \mu)$ angle, which is the angle between the pollution source point and the mean angle. The mean angle μ is estimated under the null hypothesis of no clustering and in practice should be selected based on pollution dispersion information (i.e., direction of the dominant wind at the contamination site) (258, 259). The calculation of this statistical score was conducted in Microsoft Excel using as inputs the observed and expected cases, the calculated angles from the putative source to each DA's centroid, and the mean angle μ of the wind direction during the study period at the nearest monitor station for each location. For wind data the following reference values were used: 1) IHA, mean wind direction 222° SW = 42° wind dispersion or 0.73 radians, from the Fort Saskatchewan weather station located at 92 Street and 96 Avenue 2)

CFPP, mean wind direction 289° WNW = 109° wind dispersion or 1.90 radians from the Power monitor station located at Wabamum.

The Chang–Rosychuk spatial scan method is the only cluster hypothesis testing tool designed to test events (i.e., children's ED visits for asthma) rather than cases (i.e., children with asthma). The test detects clusters of diseases with the same principles of the spatial scan statistics but also takes into account the correlation of count event data by using a compound representation of the negative binomial distribution (260). This test was implemented using the Hyperev software (261) with counts of cases and events by DA, maximum spatial cluster size of 25% of the population at risk, an alpha value of 0.05 and 999 simulations for estimating P values.

Multivariable modeling analysis

Modelling exposures in multivariable models allows a combination of effects to be assessed (i.e., distance and direction) which are of particular importance when assessing clusters around putative sources of air pollution with contaminant dispersion patterns (249, 259). Following Lawson's approach (262, 263), the ED visits data spatial distribution was explored to define the appropriate model function for the data. The Akaike Information Criterion (AIC) and deviance of the potential models were used for selection of the function model and the Moran's coefficient was calculated to assess spatial autocorrelation (264). Lawson's approach (263) proposes to start a basic model assessing the assumptions of a Poisson model of counts with log of expected cases as offset; then, a multivariable model including the spatial functions (i.e., distance and direction and their interactions) can be built with the following form:

$$\text{Log}(E[Y_i]) = \text{log}E + \beta_0 + \beta_1(X_1) + \beta_2(X_2) + \beta_3(X_3) + \beta_4(X_1 * X_2) + \beta_5(X_1 * X_3)$$

$$\text{With } Y_i \sim \text{Poisson } (E[Y_i])$$

Where,

Y_i = count of observed ED visits for asthma (events) in DA i

$Log(E[Y_i])$ = log of the expected value of Yi

logE = offset term with E= expected visits calculated based on the overall rate 0.0559

β = regression parameter coefficients for spatial functions

X_1 = spatial function of distance from the pollution source point to the DA's centroids

X_2 = spatial function of direction using the sine of the angle from the pollution source point to the DA's centroid

X_3 = spatial function of direction using the cosine of the angle from the pollution source point to the DA's centroid

Generalized linear multivariable (GLM) models for ED visits data were built separately for IHA and CFPP zones assessing independently the effect of the distance and direction from the two putative sources to the DA centroid where visits occurred. Then, a combination of distance-direction effects was included to explore if distance effects could vary with direction of the putative source (249, 262, 263). The mean angle of effects (μ_0) was derived from the sine and cosine of the parameters of the fitted models (262). The potential confounding effect of traffic-related air pollution was assessed in order to define its inclusion into the models. The traffic-related air pollution was measured by using the NO_2 concentrations at DA level estimated by the Hystad's Land Use Regression (LUR) model developed for Alberta in 2006 (223). The deviance of the sequential models was used for model selection. Finally, the standardized deviance residuals of the final fitted models for CFPP and IHA were calculated and plotted into

a map and their Moran's coefficient were calculated to assess residual spatial autocorrelation. The analyses were conducted in Stata 13 and ArcGIS 10.3® (174, 248).

5.3. Results

5.3.1. Descriptive analysis results

During the 6-year study period, 10,421 ED visits for asthma were registered in the ACCS for 6,184 distinct children between 2 and 14 years old living in the CMAE, which resulted in an average of 1.68 visits per child (median=1; IQR=1). The overall crude rate of ED for asthma visits was 55.9/1,000 children aged 2- 14 years during the 6-year period, which results in a mean crude rate of 9.3/1,000 children aged 2- 14 years per year. The overall yearly crude rates decreased from a maximum of 12.9 in 2005/2006 to 8.1 in 2009/2010. Table 5-1 show the total number of ED visits for asthma and the crude rate per 1,000 children by fiscal year during the study period. Regarding age and sex distribution, ED visits for asthma were more common for males than females (64.02% vs 35.98%) and in children between 5 and 14 years compared to children between 2 and 4 years (62.13% vs 37.87%).

The ED visits for asthma were located all across the CMAE in 1,276 out of the 1,524 DAs with children population during the study period; 27 out of the total 1,551 DAs did not have population under 14 years old. In 20 records (<0.2%) the postal code did not match any DA using the postal code validator so 10,401 visits were used in the spatial analysis. The crude visit rates by DA ranged from 0.00 to 911.11/1,000 children aged 2 to 14 years for the 6-year period (median= 43.61; IQR=62.98). The directly standardized visit rates ranged from 0.00 to 926.42/1,000 children aged 2 to 14 years (median=44.88; IQR=66.77). Using the lower limit of the 95% CI of the directly standardized rates, 179 DAs (14% of the total DAs with asthma

visits) has significant higher rates as the overall crude rate is smaller than this limit. The Bayesian smoothed ratios ranged from 0.11 to 30.94 (median= 0.78; IQR=0.82). Figures 5-2, 5-3 and 5-4 presents the choropleth maps of the crude, directly standardized rates and Bayesian smoothed ratios of ED visits for asthma during the entire study period. The complete list of crude, directly standardized visit rates for asthma and Bayesian ratios is presented by DA in Appendix F.

5.3.2. Hypothesis testing analysis results

The Kulldorff circular spatial scan test for cases and the Chang-Rosychuk spatial scan test for events identified a statistically significant cluster of children's ED visits for asthma in the DA (48112023) where the Sundance CFPP is located in the Wabamum area. For this area, the children population at risk was 115, the number of observed cases was 34, the number of observed events was 59, the expected number of cases were 3.8, and the expected number events was 5.7; the estimated relative risk was 8.2 in the spatial scan test for cases and 10.4 for the test of events. Neither of these tests identified a cluster around the IHA area.

The Stone's test identified a statistically significant distance decline effect from both pollution sources but higher in the CFPP compared to the IHA area. The Lawson directional score tests identified directional effects for both pollution sources. The results of the statistics of these tests and their p-values are presented in Table 5-2.

5.3.3. Multivariable modeling analysis results

First, the data distribution was examined to define an appropriate model distribution. The mean and variance of the SMR for the ED visits by DA (outcome variable) shows that its

unconditional mean is much lower than the variance (mean= 1.08; variance= 3.02). Figure 5-5 shows the histogram of the SMR, which is characterized by a right skewed distribution with important over-dispersion. These characteristics of the distribution suggest that the basic Poisson model, where both values are assumed to be equal, could be inappropriate for these data. However, the independence assumption of the Poisson model was met as the Moran's coefficient for SMR was 0.047 ($p<0.001$), which means that there is a low spatial autocorrelation among DAs regarding this indicator and therefore we can assume independence of the SMR measure by DA.

Having count data as the outcome variable, an alternate function model is the negative binomial distribution, which is a Poisson-like distribution for over-dispersed count outcome variables. Therefore, models including distance and directional effects using Poisson and negative binomial distributions were explored and the AIC and deviance of the models were compared. The models using the negative binomial regression resulted in lower AIC and deviance values. For the CFPP, the Poisson model the AIC was 12,396.95 and the deviance 7,941; in the case of the negative binomial model AIC = 8,520.55 and deviance=1,560. Therefore, the negative binomial distribution was selected as more appropriate approach for modeling the ED visits SMR data. In addition, the regression model's standard errors were scaled to the deviance to account for the over-dispersed discrete distribution (263).

The negative binomial multivariable models assessing the effects of distance provided evidence of a significant negative effect with distance for the CFPP models (i.e., the smaller the distance the higher the estimated SMR around the CFPP); for IHA, there was a significant positive effect with distance, which means the estimated ratio increases as the distance increases

from the IHA. Table 5-3 shows the estimated coefficients and their standard errors as well as the p-values of the estimations and the deviance of the fitted models.

The models assessing the directional effect (DIR) alone, showed for CFPP a strong positive coefficient for the sine and a weaker negative coefficient for the cosine function, which suggest that the dominant effects are towards the south-east (SE) from the CFPP. For IHA there was a strong negative coefficient for the sine and cosine function, which suggest that the dominant effects are towards the south-west (SW) from the IHA.

The model assessing the effects of distance and direction (DDIR) for CFPP suggested a significant directional and distance decline effect still with strong SE direction. For IHA, the model confirms the absence of a distance decline effect in presence of directional effects, maintaining the SW preferential effect.

The interaction terms between distance and direction parameters (sine and cosine) were added to the previous model to explore whether the directional effects modify the distance effects. The models with the interaction terms resulted in smaller deviance values when compared with the previous models, indicating that they have better quality compared to previous models. For both models of pollution sources, the interaction terms were statistically significant, which means that the distance effect is modified by the directional effect (i.e., the shorter the distance the stronger directional effect).

For the CFPP, the interaction model showed a discrete but significant decline effect of distance with a stronger radial-directional correlation towards the east (preferred east direction given by the stronger and significant positive distance*sinθ coefficient). For the IHA, the interaction model now showed a significant effect of distance decline and distance-directional correlation towards the west (preferred west direction given by a stronger negative distance*sinθ

coefficient). This model estimated a mean angle (μ_0) of 125.58° (SE) for CFPP and 216.52° (SW) for IHA. The traffic-related air pollution measured by the NO_2LUR was not associated with the children's ED visit rates for asthma at the DA level (coefficient -0.0004; p-value=0.938); therefore, multivariable models were not adjusted for this variable.

Figure 5-6 shows the diagnostic graphs of the fitted models, plotting the standardized deviance residuals against the estimated rate of ED visits from the models for CFPP (a) and IHA (b). In both graphs the majority of the points lies between -2 and 2 values, which means that the fitted models are good models for the data. The Figures 5-7 and 5-8 show the geographical distribution of the standardized deviance residuals of the full fitted models for CFPP and IHA points. In addition, there is a small spatial autocorrelation in the model's residuals as their Moran's coefficients were 0.111 and 0.110 ($p<0.001$) for the CFPP and IHA models, respectively.

Taking together the regression modeling results suggest that there is a significant decline in ED visits for children with acute asthma as distance increases around the CFPP area. This effect is modified in a SE direction (mean angle 125.58°), where the risk increases with distance. In contrast, the regression models for IHA suggested a significant increase in risk for ED visits for children with acute asthma as distance increases around the IHA area. This effect is modified in a SW direction (mean angle 216.52°), where the risk decreases at shorter distances.

5.4. Discussion

Using a large, robust, linked and population-based administrative database covering a six-year study period, this study found consistent findings of increased risk of ED visits for

asthma in children around the CFPP, located at the Wabamum area in the CMAE during 2004-2010. The area with higher risk was identified in the same DA where the Sundance CFPP is located, with a directional effect towards the SE related to predominant wind direction and the location of two other major power plants. In the case of IHA, the analysis failed to identify evidence of a cluster of ED visits for asthma in children in the vicinity of this area; however, an increased risk at shorter distances was observed towards SW of the IHA.

Despite the importance of the CFPP as sources of outdoor air pollution, there has never been an epidemiological study conducted in Canada examining the association of pollution from coal plants with spatial distribution of adult or children's diseases. In 2006, the Wabamum and Area Community Exposure and Health Effects Assessment Program (WACEHEAP) published a summary report of a study conducted in 2004 in 196 participants (53 children) of the Wabamum area to measure exposure to selected air pollutants, assess the role of indoor and outdoor pollution, and examined the relationships between exposure and people's illnesses. Using a pseudo-randomized small sample study, they concluded that the personal exposure to selected air pollutants was low and much related to indoor quality, and identified an increased rate of physician's visits for respiratory illnesses but none related to asthma (265).

In 2008, the Canadian Medical Association published the report with results of the Illness Cost of Air Pollution (ICAP) model, which used population densities, air quality data and known impacts of air pollution to make health and economic damages estimates related to air pollution in the 10 provinces. For Alberta, the ICAP model estimated 894 hospital admissions, 8,638 ED visits and 1,734,300 minor illnesses attributed to air pollution ($PM_{2.5}$ and O_3), and that 8% of the total health impacts from $PM_{2.5}$ were linked to CFPP (266).

The most recent study related to the effects of the CFPP on Albertan's health was published in 2013; this was not an epidemiological study but a compilation of existing literature about the health impacts of coal and used the ICAP model to estimate the magnitude of human health impact and costs related to CFPP in Alberta. The study estimated that in 2008 the asthma sufferers in Alberta faced on average 4,862 days with asthma symptoms severe enough to result in absenteeism from work or school and 223 ED visits for respiratory diseases (242).

The Sundance CFPP located at Wabamum, the pollution source assessed at the west of the CMAE in this study, is the largest of the six plants located in Alberta; the other two CFPP within the CMAE are located at SE of the Wabamum plant where high SMR of ED visits for children with acute asthma were also identified. To the best of our knowledge, this is the first epidemiological study that used spatial analysis of disease clusters around putative sources to assess clustering of asthma around these two pollution sources in the CMAE; the study findings provide epidemiological evidence of the adverse effect of air pollution emitted from CFPP on children's asthma.

The present study also highlights the importance of the descriptive spatial analysis of the potential clusters and the complementary role of hypothesis testing and regression modelling approaches for assessing focused spatial clusters around pollution sources. The descriptive analysis identified specific characteristics of the disease's spatial distribution and identified zones with higher rates within the CMAE. An alternative approach to determine the geographical areas within a region that have disproportionately more cases is using a statistical disease cluster detection method (251). Hypothesis testing methods are preferred when the interest is detecting clustering around specific locations (i.e., around pollution sources - industrial facilities) (252).

Circular spatial scan tests identified a cluster within the DA where the Sundance CFPP is located and did not identify a cluster around IHA. These type of hypothesis tests have been demonstrated to be good tools for identifying clusters of different shapes (267). Usually, these tests are designed for cases, however, their use for events does not take into account dependence of observations. The Chang-Rosychuk spatial scan statistic is the only test designed to identify clusters of events adjusting the correlation through a special compound Poisson representation of the negative binomial distribution (260). In this analysis, both spatial scan tests, for cases and events, agree on their results probably due to most of the children presented only once to the ED during the study period.

Lawson's and Stone's focused tests were also used for assessing the presence and characteristics of the potential clusters. Among different focused cluster tests, the Lawson directional test and Stone's test have demonstrated better power to detect clusters of different shapes and sizes around a point source (259, 268). Both tests agree with multivariable regression models for detecting distance decline and directional effects around pollution sources.

The multivariable models allowed the combined effects of distance and direction to be tested, and estimating the mean angle of effect from the pollution source. For models of directional effects cosine and sine functions are always modeled together for symmetry (262) as cosine function gives information of the latitude of the direction (positive for north and negative for south) and the sine function gives information of the longitude of the direction (positive for east and negative for west). It is assumed in the Lawson's modelling approach that counts of cases of non-infectious diseases in regions follow a Poisson distribution with low spatial autocorrelation which make possible to assume independence and use Poisson heterogeneous process for modelling the disease risk (in the form of SMR) around putative pollution sources

(262, 263). The present analysis showed that event counts of non-infectious diseases (i.e., ED visits for asthma) aggregated at small areas within a region also follow a Poisson-like distribution with spatial independence.

The multivariable models suggest that directional effects modified distance effects. For the CFPP model, the preferred direction of effect modification was towards SE and the estimated mean angle (μ_0) was 125.58°. This mean angle is consistent with the predominant wind blowing from WNW 289° at this point, and is pointing towards two areas that were identified with high risk of ED visits for children with acute asthma at east and SE of the CFPP (Figure 5-4).

For the IHA models, the distance effect model showed a positive and significant effect of the distance coefficient, which is against a cluster effect around the IHA. Despite the predominant SW 222° wind at this point, which assumed the wind was mainly moving to the NE, interaction models showed significant directional effects at shorter distances with SW orientation. A potential explanation to these directional effects is that subdominant winds may have more effect in concentrating pollutants towards SW direction from the IHA. Previous reports of focused cluster analysis around pollution sources in United Kingdom have demonstrated that the dominant wind and speed direction do not necessarily yield a pronounced downwind distribution and that subdominant winds with lower speeds may concentrate air pollutants in different directions (262, 263).

5.4.1. Strengths and limitations

The use of administrative health databases is an important strength of this study as they allow researchers to work with population-based data of ED visits for children with acute asthma aggregated at DA level for this spatial analysis of disease's clusters around pollution

sources. In addition to being the first study to assess the effect of important industrial outdoor pollution sources on children's asthma in the CMAE, the merit of this study is the combination of descriptive, hypothesis testing and regression modeling approaches for assessing the presence and characteristics of clusters of ED visits for children with acute asthma around CFPP and IHA areas.

An important limitation of this study is that asthma data corresponds to visits attending hospital EDs only, where usually more severe cases arrive and therefore asthma exacerbations with mild to moderate symptoms may be underrepresented. For this reason the study results cannot be extrapolated to risk for asthma incidence, prevalence or mild to moderate exacerbations. It is also important to recognize that the asthma data were restricted to visits to the ED of health facilities located within the CMAE corresponding to the AHS Edmonton zone and therefore ED visits of residents in the CMAE to other AHS zones are not included in the analysis. However, the spread distribution of the 11 EDs across the CMAE population makes it less probable that people seek ED attention in health centers outside the region even for those living at the boundaries of the CMAE.

The two pollution sources under study are located at peripheral areas within the CMAE rather than in the center. This geographical location may impose additional considerations to the interpretation of the results of the analytical tools used for detecting focused clusters as they are usually designed for testing disease risks around a central point. The location of the industrial facilities did not seem to affect the capacity of the circular scan tests to detect clusters as the circular scan starts around the source point and increased risks in surrounding areas are immediately detected by the method. The same consideration applies for the Stone's test and regression models assessing distance effects only.

The Lawson directional test and the regression models with directional effects, however, may be biased in terms of having the ability to detect directional effects and interaction between distance and direction within the CMAE only; this study lacks of information to define the directional effects to the far north of the CFPP and the far NE region of the IHA which are beyond the CMAE. Finally, several DAs within the CMAE do not have census estimations of children population; those zones corresponds to less than 1.7% (n=27) of the total number of DAs and except for three Indian Reserves, the remaining locations usually correspond to industrial or environmental reserve areas with no residents and therefore no population at risk. However, there were no cases of ED visits for children with acute asthma located at those zones.

Finally, some degree of measurement error may be present in the estimation of the predominant wind direction at each pollution source. Despite the use of wind data of the nearest fixed monitoring station was used, the wind directions for the specific locations are not known and the aggregation over the 6-year study period may also introduce a measurement error.

5.5. Conclusions

Different methods for detecting cluster of diseases suggested consistently that there is a cluster of hospital ED visits for children with acute asthma around the CFPP although not around the IHA within the CMAE. These results may be explained by air pollutants dispersion as a result of the predominant and subdominant wind direction at each point. These results, however, may also be explained by individual conditions that were not included in this ecological analysis. The use of different approaches to detect clusters of disease is valuable to have a better understanding of the presence, shape, direction and size of clusters of disease around pollution sources.

Table 5- 1. Number of emergency department visits for acute asthma visits and crude rates for children between 2 and 14 years of age in the Census Metropolitan Area of Edmonton during April 1, 2004 to March 31, 2010.

Fiscal Year	Children population 2-14 years[a]	No. asthma ED visits	Crude visit rate per 1,000
2004/2005	165,030	1,931	11.7
2005/2006	167,678	2,164	12.9
2006/2007	172,591	1,793	10.4
2007/2008	175,733	1,448	8.2
2008/2009	179,176	1,603	8.9
2009/2010	182,252	1,482	8.1

[a] Total population within the Census Metropolitan Area of Edmonton for ages 2-14 from Alberta Health Care Insurance Plan registry.

Table 5- 2. Results of focused tests for detection of cluster of emergency department visits for children with acute asthma in the Census Metropolitan Area from April 1, 2004 to March 31, 2010.

Focused test	Coal Fired Power Plants		Industrial Heartland Alberta	
	Statistic	p-value	Statistic	p-value
Kulldorff's circular spatial scan test	7.97 (DA[a] 48112023)	<0.001	No clusters found	
Stone's test for distance decline effect	26.04	0.001	2.87	0.023
Lawson's directional score test	21.72	<0.001	34.61	<0.001
Chang-Rosychuk's spatial scan test for events	22.04 (DA 48112023)	0.001	No clusters found	

[a] DA, dissemination area.

Table 5- 3. Negative binomial multivariable models assessing distance and directional effects of living around two industrial areas in the Census Metropolitan Area of Edmonton from April 1, 2004 to March 31, 2010.

Model type	Variable	Coal-Fired Power Plants[a]				Industrial Heartland Alberta[a]			
		Coefficient	SE	p-value	Deviance	Coefficient	SE	p-value	Deviance
Distance Decline (DD)	distance	-0.01	0.00	0.000	1,592.6	0.01	0.00	0.002	1,600.1
Directional effect (DIR)	cosθ	-0.72	0.17	0.000	1,586.2	-2.42	0.28	0.000	1,517.7
	sinθ	0.93	0.29	0.001		-2.04	0.28	0.000	
Distance Decline plus Directional Effects (DDIR)	distance	-0.01	0.00	0.000	1,560.6	0.01	0.00	0.004	1.509.8
	cosθ	-0.80	0.17	0.000		-2.48	0.28	0.000	
	sinθ	1.29	0.30	0.000		-2.02	0.29	0.000	
Distance Decline plus Directional Effects (DDIR) with interaction terms	distance	-0.11	0.02	0.000	1,530.7	-0.06	0.02	0.006	1,494.6
	cosθ	0.71	0.53	0.180		-2.04	0.02	0.006	
	sinθ	-1.18	0.46	0.010		-0.35	0.59	0.556	
	distance* cosθ	-0.03	0.01	0.000		-0.04	0.02	0.026	
	distance* sinθ	0.09	0.02	0.000		-0.06	0.02	0.000	

[a] cos, cosine; sin, sine; SE, standard error. All models used observed cases at dissemination area as outcome variable, log (expected cases) as offset term, and standard errors were scaled using the square root of deviance-based dispersion.

Figure 5- 1. Location of the Industrial Heartland Alberta, the Coal-fire Power Plants, and the Dissemination Area Centroids in the Census Metropolitan Area of Edmonton.

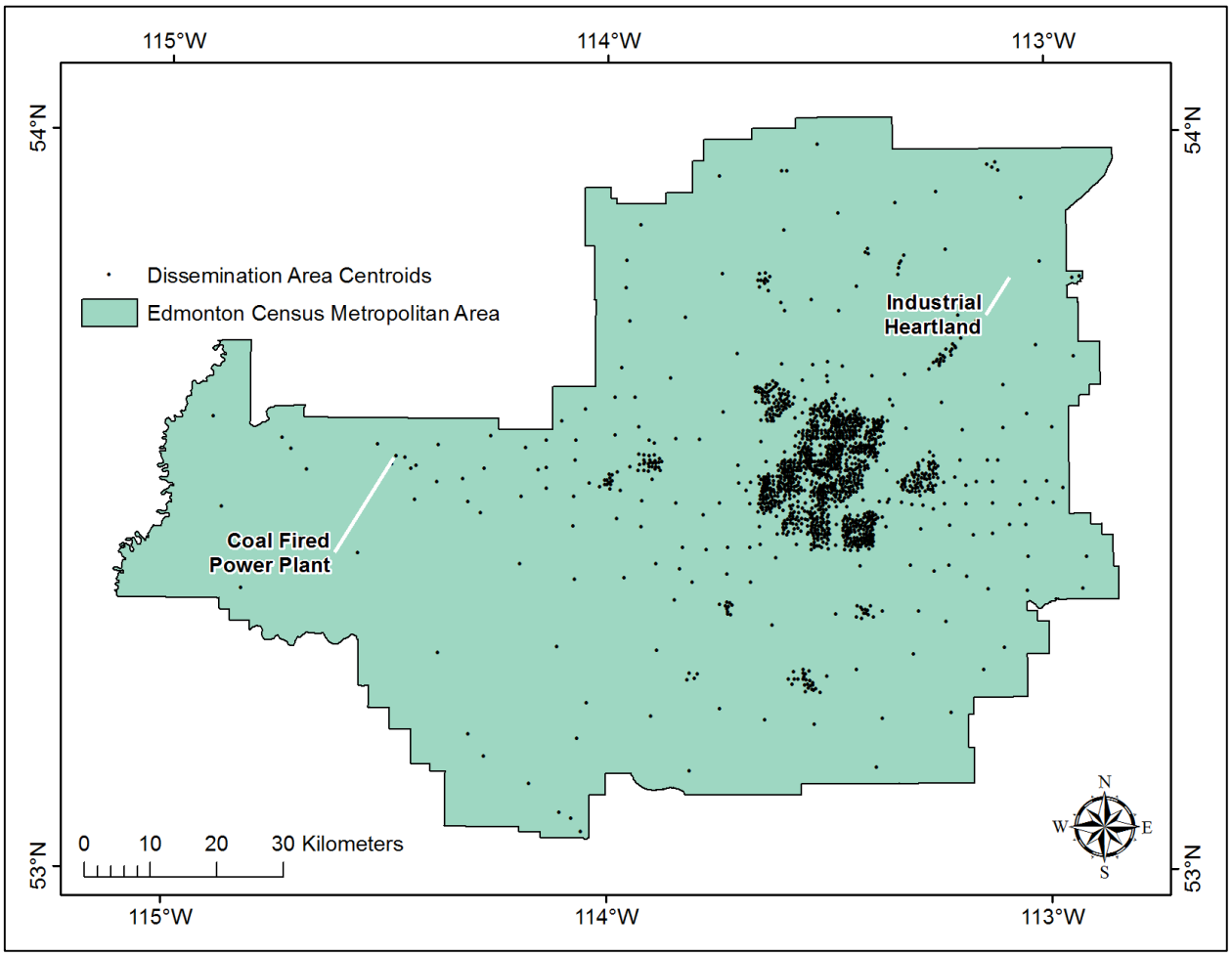


Figure 5- 2. Crude emergency department visit rates for children with acute asthma by dissemination area in the Census Metropolitan Area of Edmonton during 2004/2005 to 2009/2010.

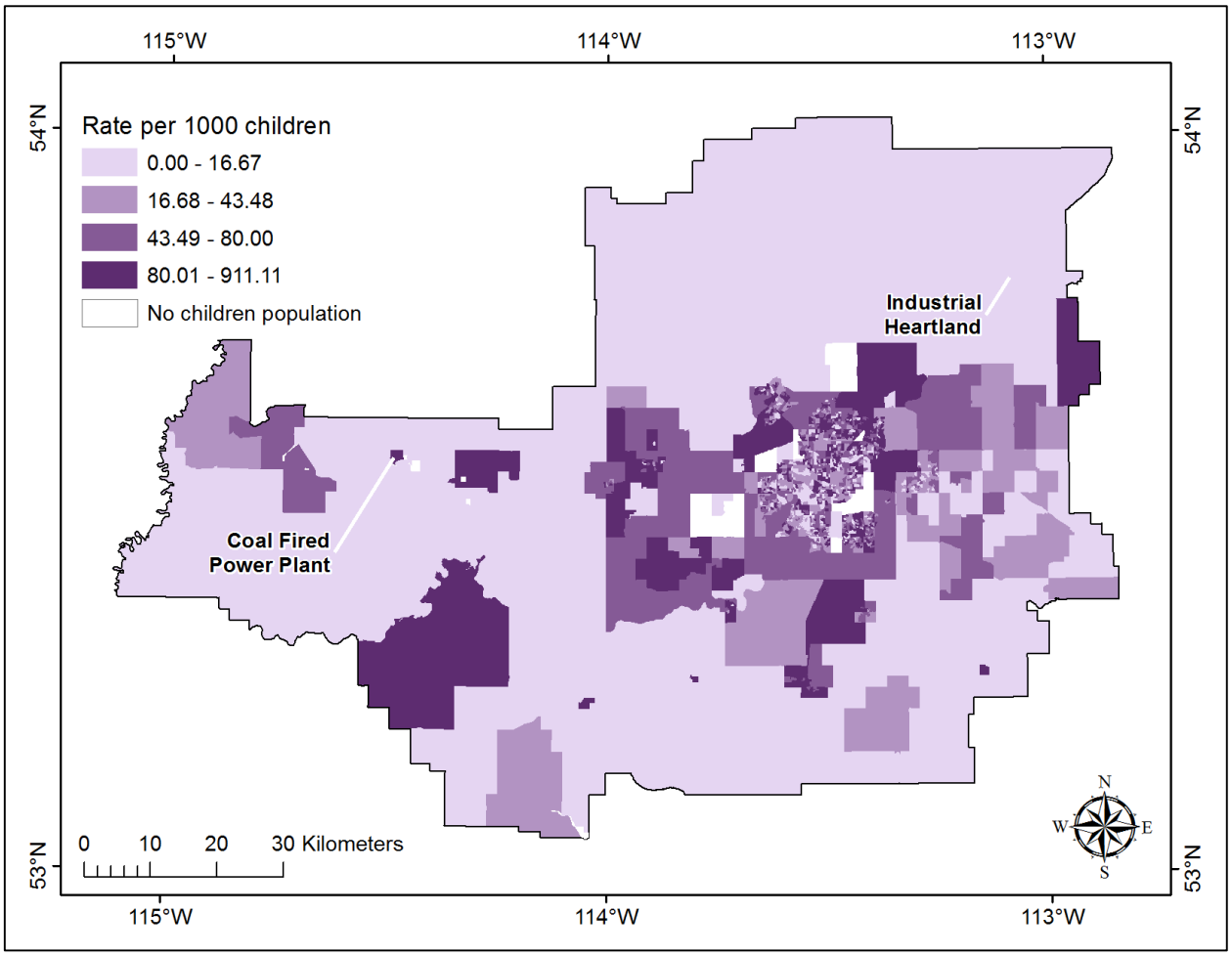


Figure 5- 3a. Directly standardized emergency department visit rates for children with acute asthma by dissemination area in the Census Metropolitan Area of Edmonton during 2004/2005 to 2009/2010.

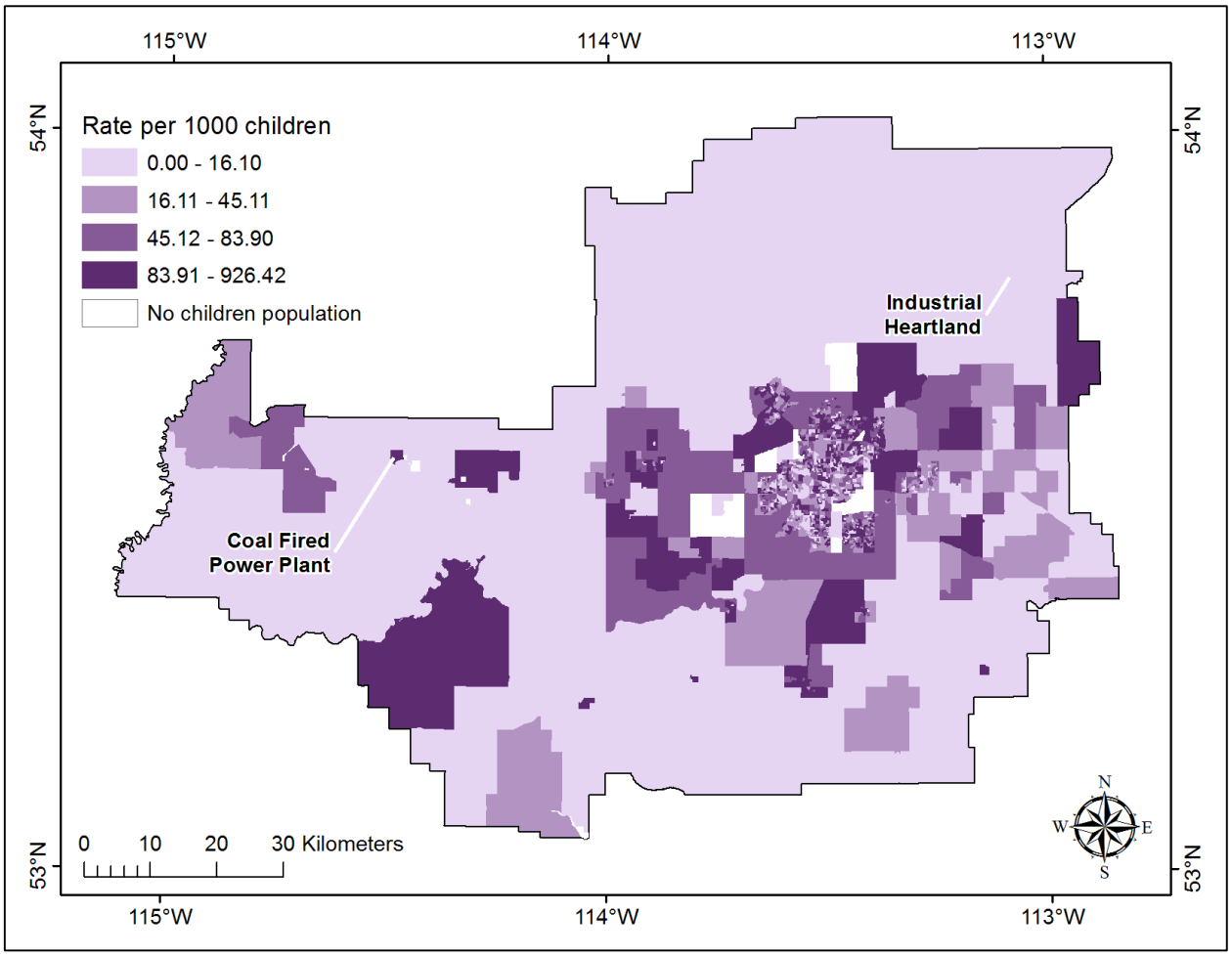


Figure 5-3b. Lower band of the confidence interval of the directly standardized emergency department visit rates for children with acute asthma by dissemination area in the Census Metropolitan Area of Edmonton during 2004/2005 to 2009/2010.

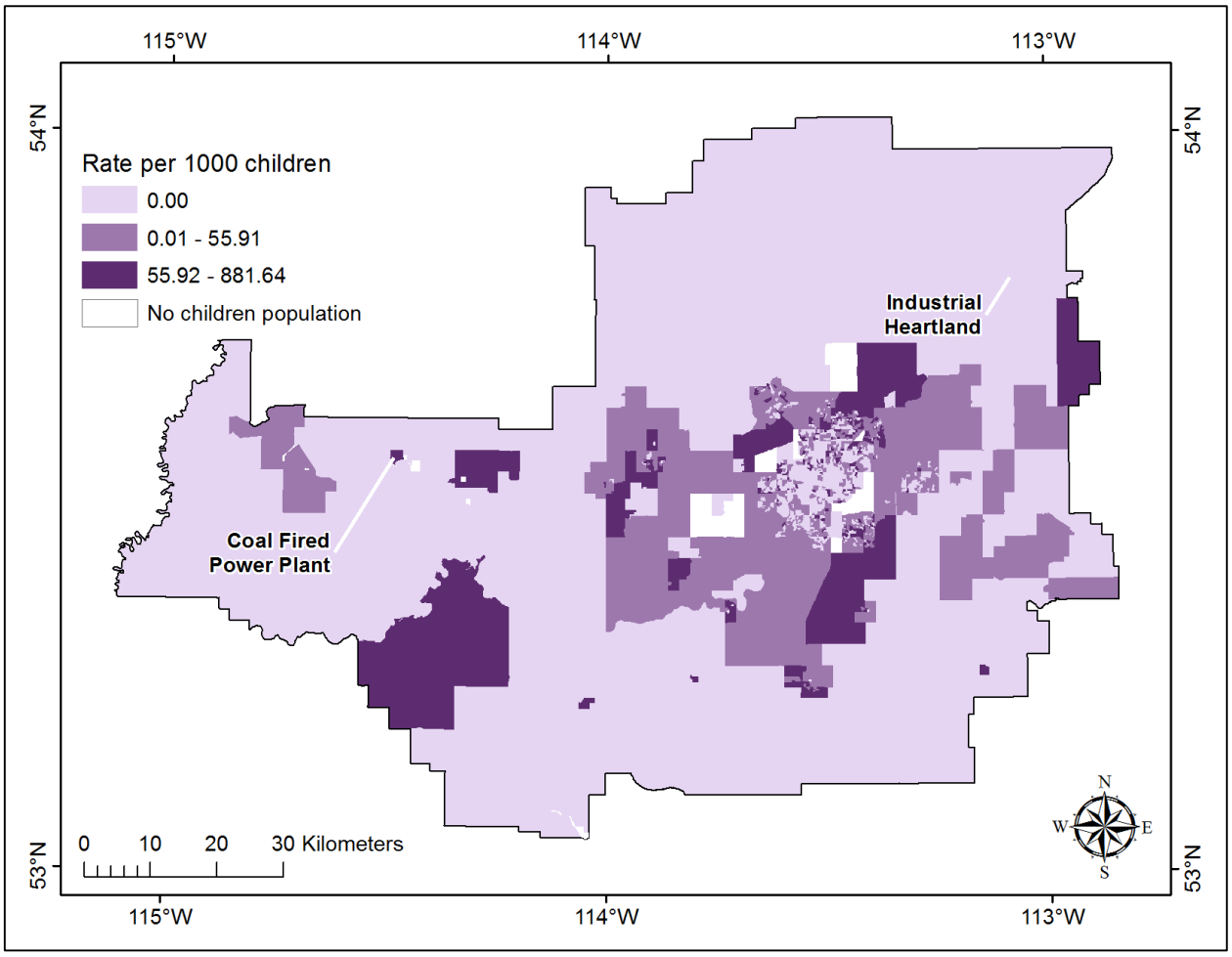


Figure 5- 4. Bayesian smoothed standardized morbidity ratios of emergency department visits for children with acute asthma by dissemination area in the Census Metropolitan Area of Edmonton during 2004/2005 to 2009/2010.

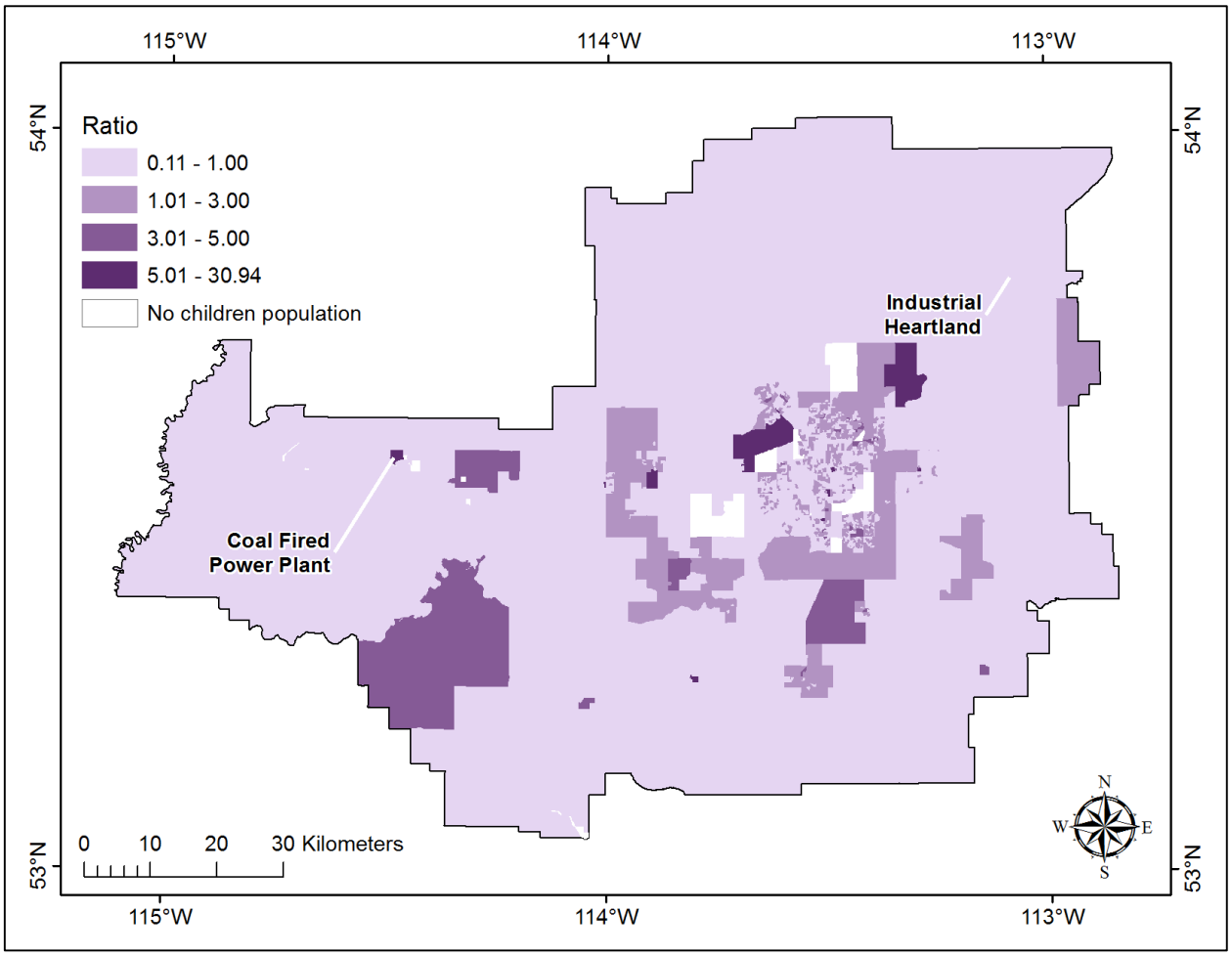


Figure 5- 5. Histogram of the Standardized Morbidity Ratios of emergency department visits for children with acute asthma by dissemination area in the Census Metropolitan Area of Edmonton during 2004/2005 to 2009/2010.

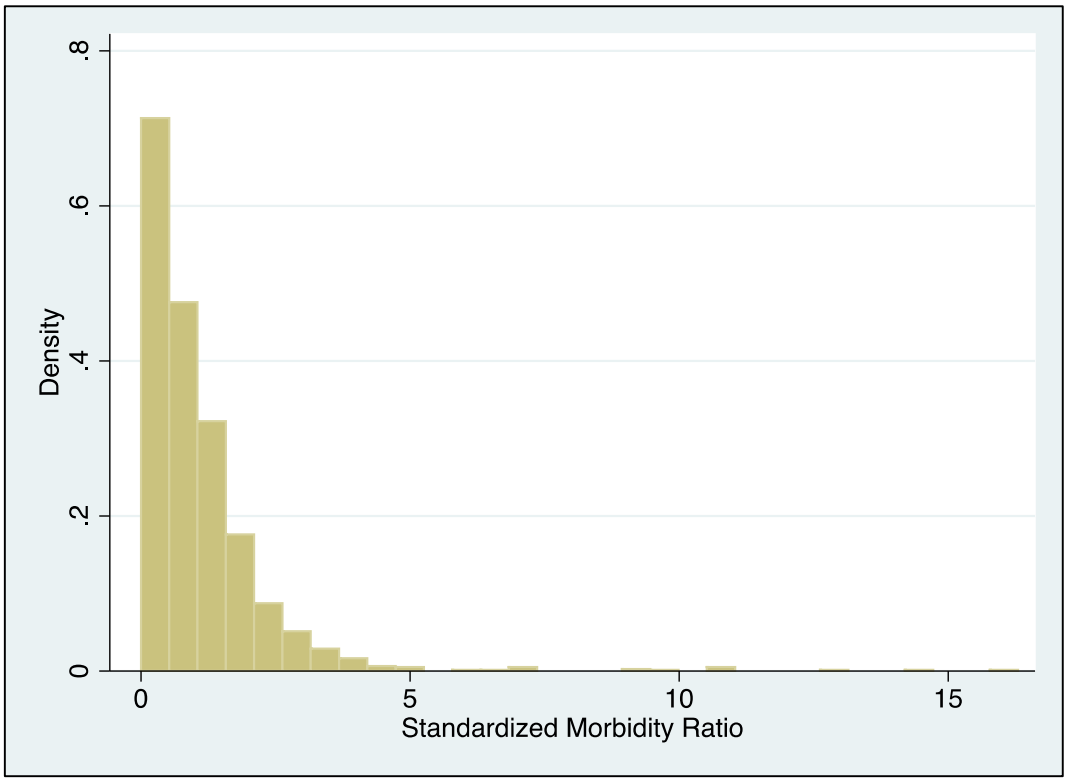
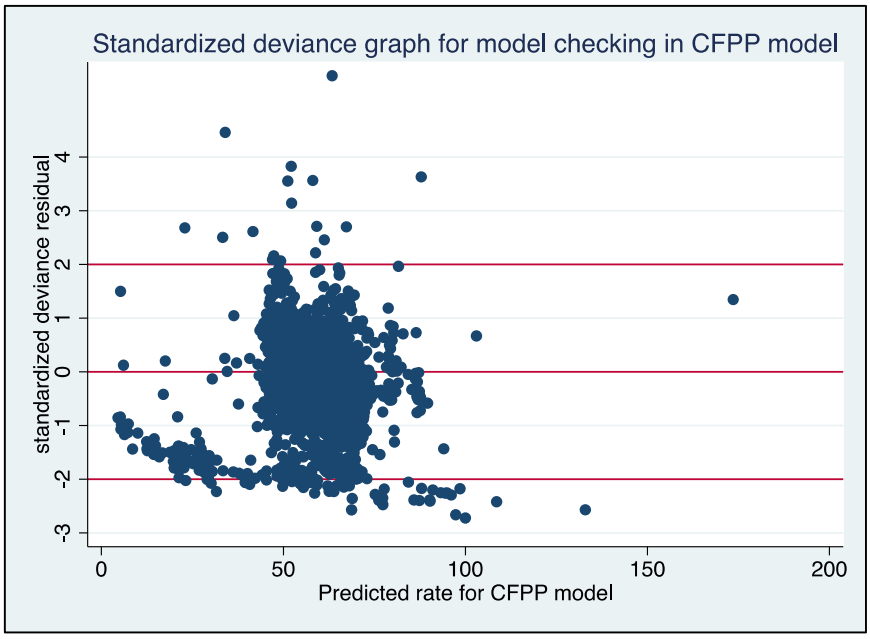


Figure 5- 6. Model diagnostic graphs for the negative binomial models assessing the effects of living near to selected industrial sources of air pollution on the presentation of emergency department visits for children with acute asthma.

a) Diagnostic graph for model of risk around Coal-fired power plants



b) Diagnostic graph for model of risk around Industrial Heartland Alberta

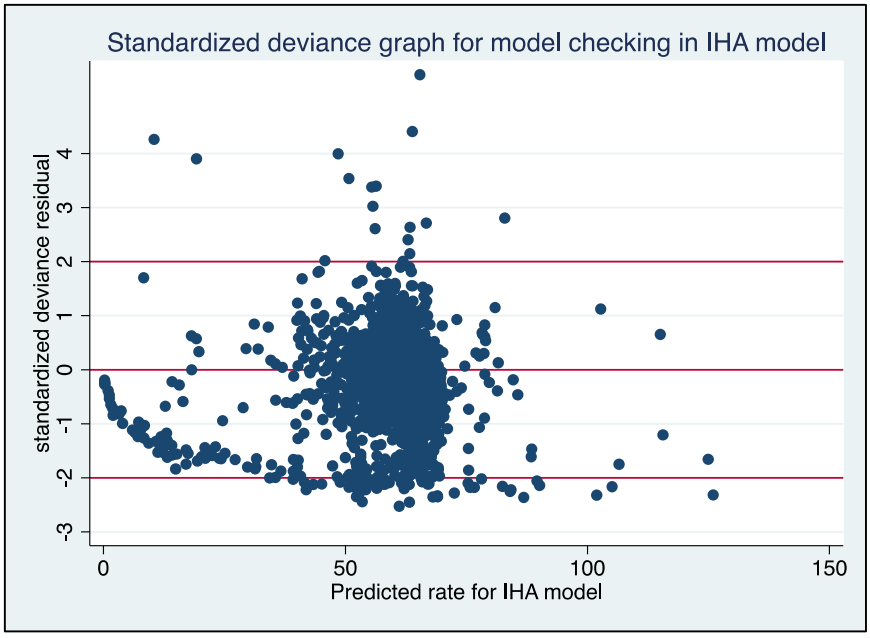


Figure 5- 7. Geographical distribution of the standardized deviance residuals of the regression model of assessing the risk of living around the Coal-fired power plants area for the presentation of emergency department visit for acute asthma in children.

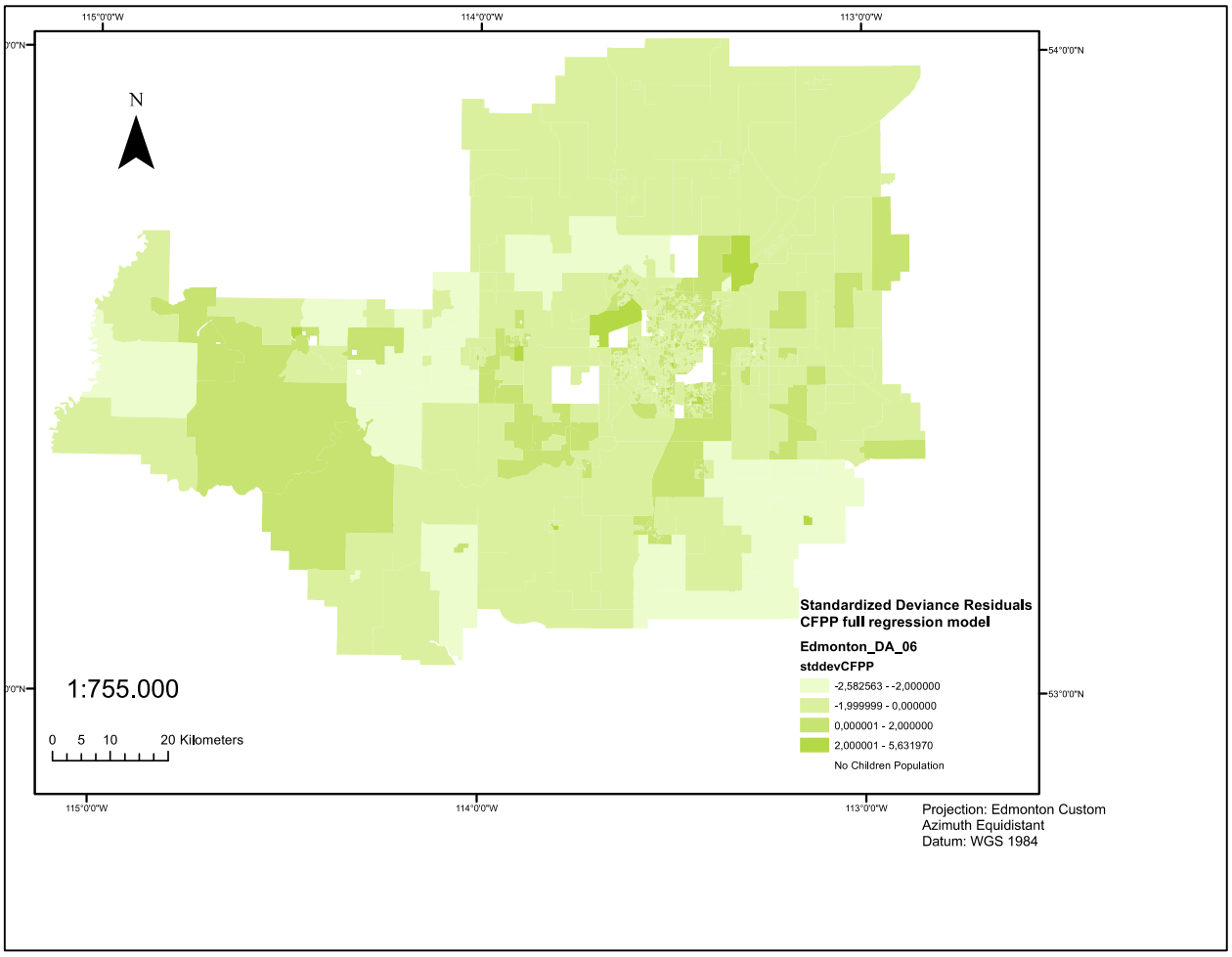
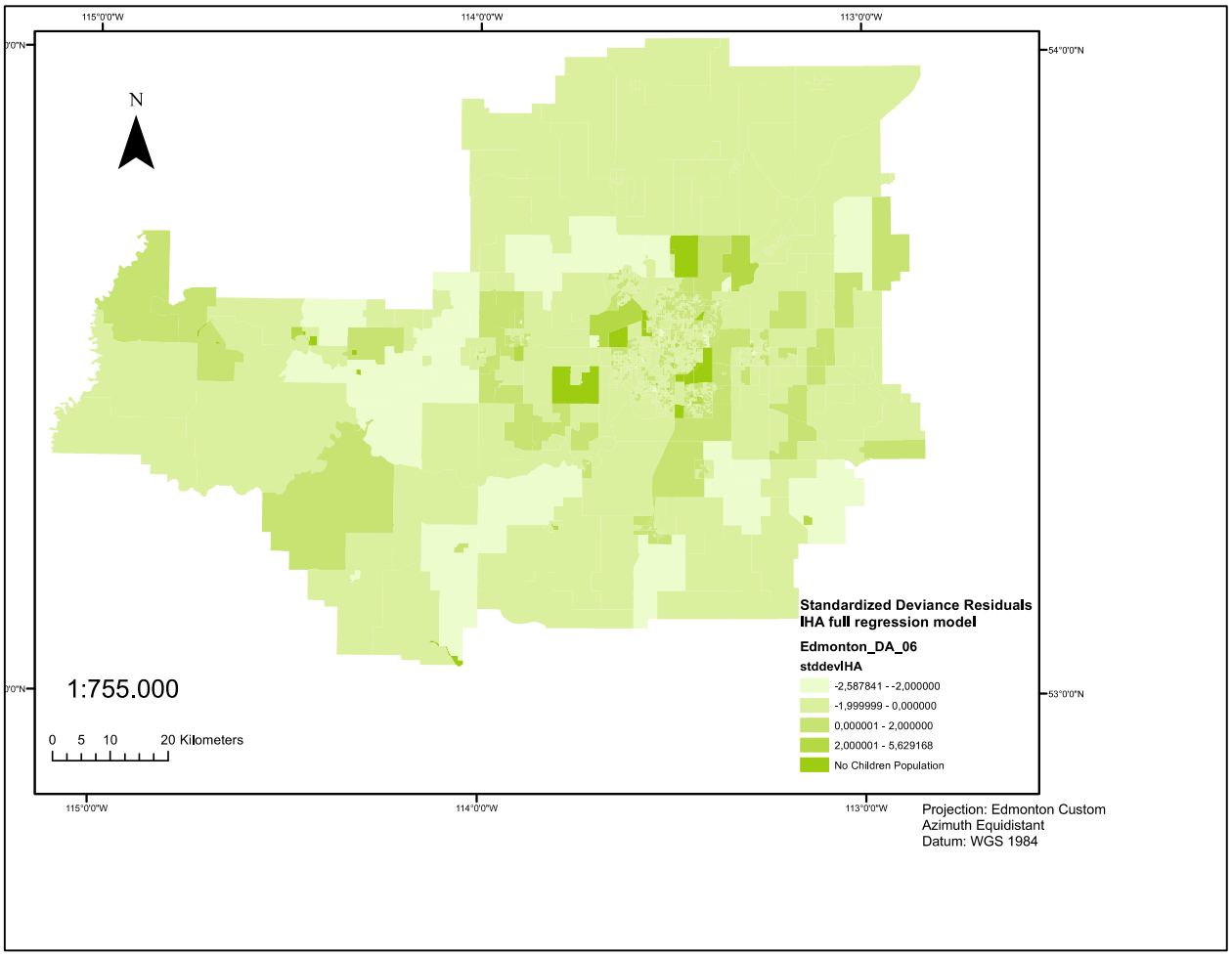


Figure 5- 8. Geographical distribution of the standardized deviance residuals of the regression model of assessing the risk of living around the Industrial Heartland Alberta for the presentation of emergency department visit for acute asthma in children.



CHAPTER 6. Discussion and Conclusions

6.1. Summary and Interpretation of Results

The preceding chapters of this thesis dissertation present the results of research conducted with the objectives of assessing the short-term effects of individual and combined air pollutants on Emergency Department (ED) visits for children with acute asthma, its variation at intra-urban scale, and the effect of traffic and industrial pollution sources in the Census Metropolitan Area of Edmonton (CMAE) between 2004/2005 and 2009/2010. In addition, the research assessed the capacity of the socioeconomic position (SEP) to modify these relationships.

This section summarizes the results and their interpretation based on the systematic review of the literature and the three population-based ecological and mixed (individual and ecological) analytical studies conducted reflecting the objectives of this program of research. The three analytical studies were based on the linkage of data collected from hospital ED visits for children between 2 and 14 years old, census and environment databases.

6.1.1. The systematic review of literature assessing the modifier role of the SEP

Despite the availability of literature on social factors, air pollution and respiratory health (77, 104, 133, 134), none of these reviews summarize the evidence of the modifier effect of SEP on the relationship between air pollution and health services presentations for asthma exacerbations in children or adults.

This is the first systematic review summarizing the evidence regarding the role of SEP as an effect modifier of the association between air pollution and asthma-related health services

outcomes in children. Ten studies were identified and showed different results of SEP as an effect-modifier. The results revealed that associations between hospitalizations and air pollutants seem to have a stronger negative influence on children living in low SEP conditions. However, confirmation of the effect modification by statistically significant interactions between air pollutants and SEP was evident only in one out of five studies, a finding that was postulated to be related to limitations in sample size.

Three studies failed to identify SEP-related effect modification in ED visits for acute asthma. Potential explanations of these findings are that ED visits for asthma are more heterogeneous than asthma-related hospitalizations in terms of severity, and that ED visits may also reflect limitations in accessing primary health care.

The SEP modifier role was mainly assessed using aggregated measures at small-area level; however, non-differential effects by SEP were also observed in the two studies that used individual SEP proxy measures.

6.1.2. The short-term effect of multiple air pollutants and the modifier role of the SEP

Results from the systematic review of literature presented above, showed that there is weak evidence of SEP as an effect-modifier of association between air pollution and health services use for asthma in children. While stronger negative effects on asthma-related hospitalizations occur for children living in a lower SEP, statistical assessment of the modification effect was not routinely conducted. None of the ten included studies used a composite air quality measure as pollution exposure and most of them assessed the SEP modification role at ecological level. There were only three studies assessing the modifier role of SEP on ED visits/calls for acute asthma; two of them had limitations related to potential

confounding factors (i.e., meteorological and influenza effects) and the third one had a small sample size that could limit the analysis of effect modification.

This study assessed the short-term association between the Air Quality Health Index (AQHI), as a multipollutant exposure metric, and ED visits for children with acute asthma and its potential effect modification by SEP, using a case-crossover study design. The AQHI is an indicator of the short-term health risks associated with air quality, based on the concentrations and risks associated with three air pollutants: nitrogen dioxide (NO_2), ground-level ozone (O_3), and particulate matter with mean aerodynamic diameter of 2.5 μm ($PM_{2.5}$) (122, 164).

The analysis revealed that short-term elevations of the AQHI did not increase the risk for children's ED visits for asthma in the CMAE during the study period. These findings were consistent when using AQHI as a composite air quality measure or when individually assessing NO_2, O_3 and $PM_{2.5}$ concentrations. The use of two different study designs, case-crossover and time series analysis, resulted in similar findings. In addition, the study results revealed that the observed effect was not different across categories of SEP when using the health premium subsidy status as an individual SEP proxy measure. Therefore, there is no evidence of the modifier effect of SEP on the relationship between air pollution exposure and ED visits for asthma in the study population.

These study findings contrast with results from previous studies conducted in different cities around the world (2, 80), including other Canadian cities (79, 123, 125), and the results from a previous study conducted in the Edmonton area between 1992 and 2002, which reported associations of short-term elevations of ambient air pollutants with increased risk of ED visits for asthma, especially in children between 2-4 years, and during the warm season (10).

Several considerations may explain these findings with two main mechanisms as the most likely explanations: the decrease in concentrations of ambient air pollutants in the Edmonton area compared to the previous decade, and the consistent decrease of ED visit rates for asthma during the study period.

The median AQHI values, and the NO_2 and $PM_{2.5}$ concentrations decreased 19%, 29%, and 37% compared to the median concentrations observed during the decade 1992-2002 in the Edmonton area (10, 11, 124). In addition, the concentration variability also decreased for the AQHI, NO_2 and $PM_{2.5}$ compared to previous reports (10, 11, 124). The air pollutants median concentration observed in most recent years are the lowest reported to date in studies assessing the effects of air pollution on ED visits for asthma in Canadian children (79).

Crude ED visit rates for children with acute asthma decreased by 37% between 2005/2006 and 2009/2010. Decreased ED visits for asthma may be explained by better access to primary health care services (e.g., walk-in clinics and family physicians) and/or improved asthma management (e.g., asthma education and preventer medications) over the last decade in Canada. Therefore, it may be possible that the expected exacerbations after transient elevations in outdoor air pollution are now assessed and managed at home or in walk-in clinics, rather than in hospital ED facilities. Consequently, while this study does not rule out risk associations of air pollution with mild to moderate asthma exacerbations that did not report to hospital ED facilities, it does suggests that cases attending at hospital EDs, which can be more severe asthma cases, were not associated with outdoor air pollution levels.

The decrease in ED visit rates for asthma, along with a consistent decrease in NO_2 and $PM_{2.5}$ median concentrations in the CMAE, suggest that severe asthma exacerbations in children are now postulated to be related more to other environmental or individual conditions (e.g.,

individual exposure to allergens, indoor conditions, and asthma mismanagement) than to outdoor pollution as reported previously.

Regarding the role of SEP, the study findings confirm that ED visits for asthma were more common in children with low family income who were receiving a health premium subsidy. There was no evidence, however, of a modifier effect role of SEP in the relationship between outdoor air pollution and ED visits for children with asthma in the CMAE during the study period.

Finally, using administrative health data has several inherent weaknesses for observational studies, such as lack of granular details on the individual and the health care system. Unmeasured factors in this study include information on medication access and use, adherence to medications, exposure to smoke, and mental health. Many of these factors may change over time within the same individual and may have influenced ED visits.

6.1.3. The short-term effect of traffic-related air pollution, its variation at small-area level, and the modifier role of the SEP

The previous study assessed the association between day-to-day variation of multiple air pollutants, using the Air Quality Health Index (AQHI) as a composite measure of air quality, and ED visits for children with acute asthma, and the modifier role of the SEP. Using a case-crossover design, the study assessed the effect of temporal variations of AQHI values, and NO_2, O_3, and $PM_{2.5}$ concentrations; however, the study did not assess whether there is a different effect on ED visits for asthma according to the type of air pollution source or the spatial variations in air pollution exposure. Research assessing the short-term effect of spatiotemporal

variation of traffic-related pollution on asthma exacerbations and the role of SEP on this relationship in the CMAE is not available.

This study assessed the short-term association between traffic-related outdoor air pollution exposure and children's ED visits for asthma, and its potential effect modification by SEP at dissemination area (DA) level in the CMAE. Traffic-related air pollution exposure at DA level was measured by using a city-specific land use regression model for NO_2 (NO_2LUR) (220) and calibrated daily based on information from fixed monitor stations (221). The SEP was measured ecologically by using the Chan's Canadian socioeconomic index (108) score at DA level, and individually by using the health premium subsidy status.

This study found that children's ED visits for asthma were not associated, on average, with short-term effects of traffic-related air pollution exposure measured at DA level. Heterogeneity in risk estimations for asthma ED visits by DA, however, were observed across the CMAE. In general, stratified analyses by age group, sex, and Aboriginal status did not identify statistically significant associations when considering different lag-day exposures. In addition, the SEP measured at small-area or individual level did not appear to modify this relationship.

These findings counter previous evidence of the adverse health effects of air pollution with apparently no threshold, and create the need and opportunity to explore the specific local conditions that are influencing the change of the relationship between outdoor air pollution and asthma exacerbations in the CMAE.

In agreement with the results and potential explanation for the study described in section 6.1.2, there are two important factors that may help explain the lack of association between traffic-air pollution and asthma ED visits during the study period in the CMAE: 1) The decrease

in asthma visit rates; and 2) The decrease in NO_2 outdoor concentrations compared to the ones reported in previous studies in the Edmonton area (10, 11).

The ED visits rates for children with acute asthma decreased over time during the study period. The crude visit rates decrease by 4.8 visits per 1,000 children between 2005/2006 and 2009/2010, which represented a 37% decline in ED visits. Similarly, asthma rates reported in Alberta for children under 18 years of age in 2004/2005 were lower than those during the previous five years, which implies that there is a long-term downward trend in asthma rates (35). Health care access and asthma management changed in important ways over the last several decades in Canada and may help explain the steadily decreasing pattern in asthma rates in the CMAE. Different studies have found that the universal coverage of the Canadian system has been successful in providing access to primary health care (i.e., primary care physician and walk-in clinics) for people independent of their socioeconomic status, while the system have been less successful to provide access to specialists (179-181), which may result in a better ambulatory care and less ED visits and hospitalizations for conditions sensitive to ambulatory care like asthma.

Asthma management also changed importantly in Canada during the study period. Starting in 1999 the Canadian Asthma Consensus Report included asthma education as a key recommendation in asthma management (186). Asthma education included the provision of an individual written action plan for self-management that include medication adjustment in response to severity or frequency of symptoms, the need for symptoms relief medication or a change in the peak expiratory low (187). In addition, the use of new asthma medications (i.e., leukotriene receptor antagonist) has also become available during the last 15 years (87, 186).

The access and use of this new medication, however, may be limited for children with low family income in Alberta as they are not part of the provincial regular benefit drug list (193).

On the other hand, concentrations of ambient NO_2 also decreased significantly during the study period compared to reports of concentration in previous studies. Compared to the daily median concentrations of air pollutants reported by Villeneuve et al. (10) during 1992 to 2002, NO_2 median concentration decreased from 17.5 to 12.8 ppb (28%) in the warm season, and from 28.5 to 19.3 ppb (32%) during the cold season. The concentration variability also decreased for NO_2 compared to previous reports evidenced by a decrease in the IQR from 13.5 to 8.35 ppb. The NO_2 concentrations reported in this study represent the lowest concentrations of air pollutants in Canadian studies assessing the effect of outdoor air pollution on children's ED visits for asthma (79). It is also important to note that daily calibrations of the NO_2LUR model were made using average city-wide levels of NO_2 from fixed monitoring stations (221). Therefore, spatio-temporal estimations of NO_2 at DA level are also capturing the decrease in NO_2 concentrations while preserving the spatial distribution across the city.

The results of this study suggest that there are quantified health benefits that might be related to the reduction of ambient NO_2 concentrations. At lower exposure levels of traffic-air pollution, the role of other individual (i.e., atopy) or environmental (i.e., indoor second-hand smoke, exposure to industrial pollution) factors may have a greater influence on asthma exacerbations and attenuate the effect of traffic-related air pollution.

6.1.4. The effect of living near to industrial sources of air pollution in the CMAE

The two previous studies of this dissertation assessed the short-term effect of outdoor air pollution on ED visits for children with acute asthma, with focus on traffic-related air pollution.

The results of these studies failed to demonstrate an increased risk of ED visits for children with acute asthma associated with variations in concentrations of multiple air pollutants, and specifically traffic-related air pollution, during the study period. One of the potential explanations for these findings was the marked decreased in NO_2 and $PM_{2.5}$ concentrations in the CMAE compared to reports in the previous decade. These results suggest that at lower concentrations of traffic-related air pollution it is likely that other individual factors or other air pollution sources (i.e., industrial pollution) may have a greater importance in asthma exacerbations in children. The fourth study of this program of research addresses the relationship between proximity to industrial sources of outdoor air pollution and ED visits for asthma in children.

Specifically, this study explored the presence of clusters of ED visits for children with acute asthma around the Industrial Heartland of Alberta (IHA) and the coal-fired power plants (CFPP) in the Wabamum area, which are the main putative sources of industrial emissions to the air in the CMAE. By using descriptive, hypothesis testing and multivariable analysis, this study found an increased risk for ED visits for asthma in children living around the CFPP during 2004-2010. The area with higher risk was identified in the same DA where the Sundance CFPP is located, with a directional effect towards the SE related to predominant wind direction and the location of the two other CFPPs. In the case of IHA, the study findings failed to identify evidence of a cluster of ED visits for asthma in children in the vicinity of this area.

Despite the importance of the CFPP as sources of outdoor air pollution, there are few studies conducted in Canada examining the association of pollution from coal plants with diseases in children. A previous study conducted in 2004 the Wabamum area enrolled 196 participants (53 children) to measure exposure to selected air pollutants, explored the role of

indoor and outdoor pollution, and examined the relationships between exposure and people's illnesses. Using a pseudo-randomized small sample study, the authors concluded that the personal exposure to selected air pollutants was low, much more related to indoor air quality, and identified an increased rate of visits to physician for respiratory illnesses but none related to asthma (265).

In contrast, the Canadian Medical Association, using the Illness Cost of Air Pollution (ICAP) model, reported in 2008 an estimate of 894 hospital admissions and 8,638 ED visits attributed to air pollution ($PM_{2.5}$ and O_3) in Alberta, and that 8% of the total health impacts from $PM_{2.5}$ were linked to CFPP (266). The most recent study related to the effects of the CFPP on Albertan's health was published in 2013 and using the ICAP model estimated that in 2008 the asthma sufferers in Alberta faced on average 4,862 days with asthma symptoms severe enough to result in absenteeism from work or school to recover and 223 ED visits for respiratory diseases (242).

The present study, conducted as part of this dissertation, is the first epidemiological study conducted in Canada examining the association of living near to the CFPP with the spatial distribution of children's diseases using population-based health databases. This study found evidence of the presence of a cluster of ED visits for children with acute asthma in the vicinity of the Sundance CFPP in the Wabamum area, the largest of the six CFPPs located in Alberta. The other two CFPP within the CMAE are located SE of the Wabamum plant where high SMR of children's asthma ED visits were also identified. Therefore, the study findings suggest the presence of adverse effect of air pollution emitted from CFPP on children's asthma. These results, however, may be also explained by individual conditions that were not included in this ecological analysis.

6.1.5. Summary of dissertation results

Emergency department visits for asthma in children, air concentrations for NO_2, $PM_{2.5}$ and AQHI values all decreased during the study period compared to the previous decade. Day-to-day increase in the city-wide AQHI values or in the traffic-related air pollution at dissemination area level did not increase hospital ED visits for asthma made by children. The SEP, measured at individual or small-area level, did not modify the effect of air pollution on asthma ED visits in this region, in concordance with the results of the systematic review of existing literature. A cluster of ED visits for asthma was identified in children living near to the Sundance CFPP in the Wabamum area; however, similar clustering was not identified in close proximity to Alberta's Industrial Heartland. According to this dissertation results, a proposed diagram of the relationship between outdoor air pollution and children's ED visits for asthma in the CMAE is presented in Figure 6-1.

6.2. Strengths and Limitations

6.2.1. Strengths

There are important strengths of the studies conducted as part of this research that are worth mentioning. Strengths of the systematic review of the literature are presented first, as they are unique to review studies. Then, those related to the analytical studies are presented in terms of the study design, the data sources, and the multiple types of analyses conducted; therefore, some of them may be shared for more than one of the three analytical studies.

Systematic review methods: The strengths of the systematic review conducted pertain to its rigor in searching the literature, the criteria-based selection of relevant evidence by two independent reviewers, the rigorous appraisal of study risk of bias and the evidence-based inferences. Also, the statistical quality of the included studies provided confidence in the summary of the systematic review results. Overall, this review avoided the major biases associated with systematic reviews, such as publication and selection bias, and adhered to the principles required for high-quality and valid reviews (269). This review has been accepted for publication in the *Reviews on Environmental Health* journal.

Case-crossover design: An important strength of the studies assessing the short-term effects of combined (Chapter 3) and traffic-related air pollution (Chapter 4) on ED visits for asthma relays on the study design used. The case-crossover design (CCO) is an appropriate design when the interest is focused on assessing the acute effects (i.e., asthma exacerbations) of transient exposures (i.e., increase in air pollution) (169). The design of the CCO study controls for potential confounders that are invariant in time (e.g., age, sex, social condition, pre-natal and childhood risk factors) (168, 169). Furthermore, the time-stratified method used for selecting the referent periods matches for time-variant potential confounders (e.g., meteorological and seasonal variations) (171). Finally, the use of individual data in the CCO design rather than ecological data used in time series analysis, allowed the analysis of the potential SEP modification effect at individual level (172).

This study followed the recommendations for the analysis and presentation of CCO studies regarding the reporting of the relevant exposure term (i.e., the concentration difference), the assessment of the air pollution effect modeling, the statistical interaction, and the sensitivity

analysis using a time series analysis (172, 175). Moreover, the results of the CCO analysis are consistent based on the type of analysis (CCO vs time series) and type of SEP measures (individual vs ecological).

Population-based asthma data: The three analytical studies used a large, robust, linked and population-based administrative health database covering a six-year period for ED visits for asthma. The codification of asthma visits during the whole study period used the same International Classification of Diseases 10^{th} revision (ICD-10) code (J45) and therefore the studies did not have potential misclassification of asthma due to differences in disease codification. The use of administrative health databases has been widely used in air pollution and health studies and proved to be a reliable data source for identifying asthma visits (270, 271).

Spatio-temporal resolution of the traffic-related air pollution exposure: The analytical study assessing the short-term effect of traffic-related air pollution (Chapter 4) used Allen's land use regression model for NO_2 (NO_2LUR), which is specific for the city of Edmonton and covers 79% of DAs of the CMAE. Allen's NO_2LUR model used in this study was developed from 50 sites during two sampling campaigns in 2008 (220), almost the mid-term year for the study period. Daily calibrations of estimations of NO_2 concentrations by DA were made using the average city levels of NO_2 from fixed monitoring stations. Therefore, spatio-temporal estimations of NO_2 at DA level are also capturing the variations in NO_2 concentrations while preserving the spatial distribution across the city. Furthermore, by using daily calibration of the

NO_2LUR model this study was able to assess spatio-temporal variations in NO_2 concentrations that may help minimize exposure misclassification bias.

This study conducted an internal validation sub-study that demonstrated small median differences between the NO_2 estimated concentrations and the ones measured at fixed monitor stations in four DAs in the city of Edmonton. Therefore, calibrated estimations of exposure at small-area level seem to be valid estimators of exposure at DA level within the city of Edmonton.

The use of spatio-temporal estimations of traffic-related air pollution exposure allowed conducting a small-area case-crossover analysis. Despite the fact that most ORs in the general analyses were below one and non-statistically significant, the stratified analysis by DA, showed some areas with positive risk estimates, although only one of them was statistically significant. Therefore, this small-area analysis was important to show spatial heterogeneity in the risk of ED visits for asthma associated with traffic-related air pollution.

Sensitivity analyses: Sensitivity analyses were conducted in the two CCO studies to assess the consistency of the results (i.e., direction and magnitude of the risk estimations) when using different statistical analyses or different measurements of air pollution exposure and SEP, as they are variables measured with error.

Based on the equivalence of CCO with time-series methods (176), a conditional Poisson model (177) was used as alternative analysis in Chapter 3. In addition, a sensitivity analyses of the AQHI and single air pollutants CCO models were conducted using the IQR of the daily concentration instead of the IQR of the difference concentration between case and control periods. This sensitivity analysis was conducted because most of the CCO studies of air

pollution and asthma report their findings expressing the OR for an IQR of the daily concentration over the study period.

In Chapter 4, the sensitivity analysis using national NO_2LUR (223), which covers 95% of the DAs in the CMAE, was conducted to assess the consistency of the results compared to the ones obtained when using Allen's model which cover a smaller proportion of the CMAE.

For the SEP measurement, the main analysis in Chapter 3 used the subsidy status as a proxy of SEP individual condition and a sensitivity analysis was conducted by using the Chan's Canadian socioeconomic index (108) as SEP ecological variable. In Chapter 4, which focused on small-area estimations, the main analysis was conducted using the Chan's index at DA level and a sensitivity analysis was conducted using the individual subsidy status variable. In addition, using the area-based Chan's index quintiles, a criterion validation of the Chan's index as performed taking the subsidy status individual variable as gold standard.

Use of multiple methods for cluster detection: The study assessing the clustering of ED visits for asthma in children living around industrial pollution sources (Chapter 5) used a combination of descriptive, hypothesis testing and regression modeling approaches. The use of different approaches to detect clusters of disease is valuable to have a better understanding of the presence, shape, direction and size of clusters of disease around specific pollution sources.

6.2.2. Limitations

Similar to the strengths section, there are limitations that are unique to review studies and therefore the limitations of the systematic review of the literature are presented first. The three analytical studies conducted as part of this dissertation are observational in nature, and

there are important limitations related to data sources that are inherent to this type of studies and have to be addressed. Then, the risk of air pollution exposure and SEP misclassification is discussed.

Systematic review limitations: The small number of included studies and their heterogeneity precluded the calculation of pooled estimates of the differential effects of SEP. Similarly, the low number of studies assessing the modifier role of SEP using an individual measure did not permit analyses of variations by type of SEP measure. As in all reviews, selection and publication bias are also potential limitations of the review. Although a comprehensive electronic search was conducted and identified an important number of potentially eligible studies, many of them were excluded either because SEP was used as a confounding variable, or the analyses were not available specifically for children.

Hospital administrative databases limitations: The AHS hospital databases are unable to capture all events of asthma exacerbations. Many children may report to non-hospital ED facilities (e.g., physician offices, walk-in clinics), for their acute asthma episode. Therefore, the study findings do not rule out risk associations of air pollution with mild to moderate asthma exacerbations that did not report to hospital-ED facilities. Similarly, the AHS databases are unable to identify all Aboriginal children. The proxy variable for Aboriginal status is derived from the health care premium subsidy given by the province to Aboriginal peoples, which is restricted to First Nations peoples with Treaty status and a minority of Inuit Aboriginals living in the province; therefore, the Aboriginal Status variable is systematically excluding children belonging to non-status First Nations and Métis Aboriginal population. Finally, the diagnosis of

asthma is often difficult in children and diagnostic misclassification (e.g., bronchitis, wheezy croup, etc) may be occurred; however, it is unlikely this influenced the results.

Inherent to the use of administrative data, there are unmeasured variables at individual level (e.g., access and use of asthma medications, exposure to second-hand smoke) that might change over time and be related to asthma exacerbations. This study used as asthma definition the primary discharge diagnosis, which may limit the comparison with previous studies in the province that used the first two main discharge diagnoses as the asthma definition (35). This study definition, however, represents an advantage for the analysis of the associations under study because it makes the ED visits less biased for primary diseases that trigger asthma exacerbations.

Finally, the subsidy premiums were eliminated in Alberta in January 1st, 2009, and since then the registry has a decreasing quality in the registry of Alberta population and the alternate premium arrangement variable where the subsidy status variable is extracted (208).

Risk for air pollution exposure misclassification: The air pollution exposure used in the CCO study assessing the multi-pollutant short-term effect (Chapter 3) was based on a small number of fixed monitor stations located in the city of Edmonton; daily mean concentrations across the stations were assumed as the average of the air pollution exposure in the whole CMAE. There may be a measurement error in the air pollution exposure as the distance to the monitor stations increases due to variation in sources and dispersion patterns of contaminants. Therefore, temporal variations in air pollutants and AQHI concentrations may be well represented at the monitoring stations, but the spatial distribution of the air pollution exposure may be affecting the true air pollution exposure, especially for children living outside the city of Edmonton where

there are different traffic patterns and sources of industrial emissions. Assuming that these measurement errors were not differential between case and referent periods, this would usually result in an underestimation of the ORs and would bias the estimated to the null value (207).

In Chapter 4, the internal validation of the estimated spatio-temporal concentrations of NO_2 included only four DAs in the city of Edmonton. There are not monitoring stations with continuous measurements of air pollutants outside the city. The selection of those four DAs responds to the location of the fixed-monitoring stations with continuous NO_2 measurements, and covered different cardinal directions within the city; it was assumed that those four DAs represent referents across the city, which may not be a valid assumption.

In Chapter 5, some degree of measurement error may also be present in the estimation of the predominant wind direction at each pollution source. Despite the fact that the wind data of the nearest fixed monitoring station was used, the wind directions for the specific locations are not known and the aggregation over the 6-year study period may also introduce a measurement error.

Risk of SEP misclassification: The CCO analyses assessing the modifier role of SEP used a surrogate individual measure and an area-based SEP measure. Measuring SEP is complex and different individual or ecological measures can be used according to the purpose of the study and the main SEP component most associated with the health outcome (i.e., education, occupation, income) (97, 156). For children's asthma outcomes, parent's level of education and family income are probably the SEP components that need to be better represented in a SEP measure (98).

The CCO studies in this research used the subsidy status as individual surrogated SEP variable. This variable is derived from the Alberta Health Care Insurance Plan registry and classifies people according to type of health care premium subsidy received from the provincial government. The health premium subsidy is provided to people with low family income or people belonging to special protected groups (i.e., welfare and Aboriginals with Treaty status). Therefore, the subsidy status variable accounts mainly for family income and does not take into account the adult's educational profile. The subsidy status variable, however, had been used in previous studies as proxy measure and demonstrated to be a valid indicator of SEP in Alberta (35, 209-211).

This research used the Chan's Canadian SES index as area-based SEP measure. The Chan's index uses aggregated indicators based on adults' characteristics in small areas such as average family income, education level and cultural identities. Despite this is a more comprehensive SEP measure, its ecological nature has inherent measurement error when applied to patients with asthma according to their place of residence. However, the Chan' index was compared to Pampalon's indices and showed more consistent associations with adverse birth outcomes, a group of health outcomes known to have a SEP gradient (108). Therefore, individual and area-based SEP measures used in this research are not free of potential misclassification bias.

Limitations in the interpretation of cluster detection methods: The two pollution sources under study for clustering of ED visits for asthma (Chapter 5) are located at peripheral areas within the CMAE rather than in the center. This geographical location may impose additional considerations to the interpretation of the results of the analytical tools used for detecting

focused clusters as they are usually designed for testing disease's risks around a central point. The location of the industrial facilities did not seem to affect the capacity of the circular scan tests to detect clusters as the circular scan starts around the source point and increased risks in surrounding areas are immediately detected by the method. The same consideration applies for the Stone's test and regression models assessing distance effects only. However, the Lawson directional test and multivariable models assessing direction from the pollution sources have limitations to identify clusters at northeast of the Alberta's Industrial Heartland, and the north of the coal-fired power plants at the Wabamum area as the DAs in these cardinal locations are beyond the CMAE limits.

6.3. Study Significance and Implications for Health Care Professionals and Policy Makers

This is the first study in the CMAE to assess the short-term effect of multiple air pollutants on ED visits for asthma by children, its variation at intra-urban scale, and the effect of traffic and industrial pollution sources.

The results of this research suggest that day-to-day increases in the concentrations of multiple air pollutants were not associated with an increase in hospital ED visits for asthma in children during 2004/2005 and 2009/2010 and that the main potential explanations for these findings are the decrease in the AQHI values, the air pollutants concentrations (mainly NO_2 and $PM_{2.5}$), and the improved asthma care and education compared to the previous decade. The research also identified heterogeneity of effects of traffic-related air pollution exposure at DA level and clustering of asthma ED visits around the CFPP at the Wabamum area. These factors should be taken into account when designing and implementing prevention, diagnosis, treatment and educational programs for children's asthma.

Results of this dissertation have important implications for health care professionals and policy makers in the CMAE. For health care professionals, mainly pediatricians, emergency physicians, family physicians, and respiratory specialists caring for children with asthma, the main message from this dissertation is that the place of residence within the CMAE is an important consideration for asthma management and achieving optimal asthma control. These research results suggest the need to identify children with asthma living around the CFPP in order to adjust asthma follow-up and education programs. A first step towards this change is the dissemination of the summary of this dissertation to pediatricians, family physicians, emergency physicians and respiratory specialists through the Children's Environmental Health Clinic and the AHS Emergency and Respiratory Strategic Clinical Networks.

There are also important implications from this dissertation results for policy makers. Overall, research results provide evidence of health benefits for children with asthma associated with decreased levels of air pollutants concentrations compared to the decade before this study period. Therefore, political efforts in terms of environmental and traffic regulations should be maintained to further reduce the traffic-related air pollution in the Edmonton area. Results from this dissertation also identify an increased risk of hospital ED visits for children with asthma living around areas where CFPP are located. This finding adds to the available evidence of adverse effects of air pollution from power plants and supports recent decisions by the Province of Alberta to impose regulations on this and other industrial pollution sources. Health policy discussion at those areas should include additional benefits for primary health care, and especially asthma care, for people living around CFPP areas.

Finally, another important finding from this research was that children with asthma living in different SEP conditions did not have a differential susceptibility for the effects of

outdoor air pollution on asthma exacerbations conducing to hospital ED visits. The main potential explanation for this finding relates to universal coverage of the Canadian health system and the increased access of population to primary care regardless of their socioeconomic condition. The ED visit rates for children with acute asthma, however, were higher for children from families with low income receiving health premium subsidy. This finding may be related to differential access and use of asthma medications (i.e., leukotriene antagonist receptor that is not included as regular benefit drug in the province). Therefore, health policy makers should continue efforts to improve access to health care (including access to pediatricians, family physicians), asthma education and medications.

6.4. Future Research Directions

Results from this dissertation reveal specific opportunities for future research that include, but are not limited to, the following research topics:

1. To assess the short-term effect of outdoor air pollution on mild and moderate asthma exacerbations that do not report to hospital ED facilities in order to quantify the effect of air pollution exposure on the whole range of asthma exacerbations in children.
2. To assess whether long-term reductions in air pollutants concentrations are associated with continued decreased ED visits for acute asthma in children while controlling for the quality of asthma management.
3. To assess the ecological factors differentiating DAs within the CMAE with high risk of ED visits for asthma in children associated with traffic-related air pollution.
4. To develop and validate and individual SEP measure for children's health studies based on parent's education, occupation and income.

5. To identify and assess the contribution of indoor conditions in children's asthma exacerbations to better understand the role of air pollution on asthma and potentially incorporate this information into asthma education programs.
6. To assess the effect of acute changes in weather conditions (e.g., daily temperature change) on asthma exacerbations in children.
7. To further explore why the Aboriginal group, representing First Nations children with treaty status, seem to be a specific population adversely affected by the air pollution exposure. Stratified analysis of the association between AQHI and ED visits exhibited a risk association in the Aboriginal children compared with lower risk in non-Aboriginal children. These associations, however, were not statistically significant and remained unclear due to the small number of Aboriginal children with ED visits for asthma during the study period that might be explored in detail with a larger sample size (including a broader area of longer study period). In addition, given the limitations of the definition of Indigenous peoples used in this study, expansion of the sub-groups to include non-status First Nations, Inuit and Metis peoples would strengthen the conclusions.
8. To explore the main causes associated with the consistent decrease in concentrations of NO_2 and increase of O_3 in the Edmonton area.
9. To further assess the validity of the daily calibration of city-specific NO_2LUR models in more locations within the Edmonton area.

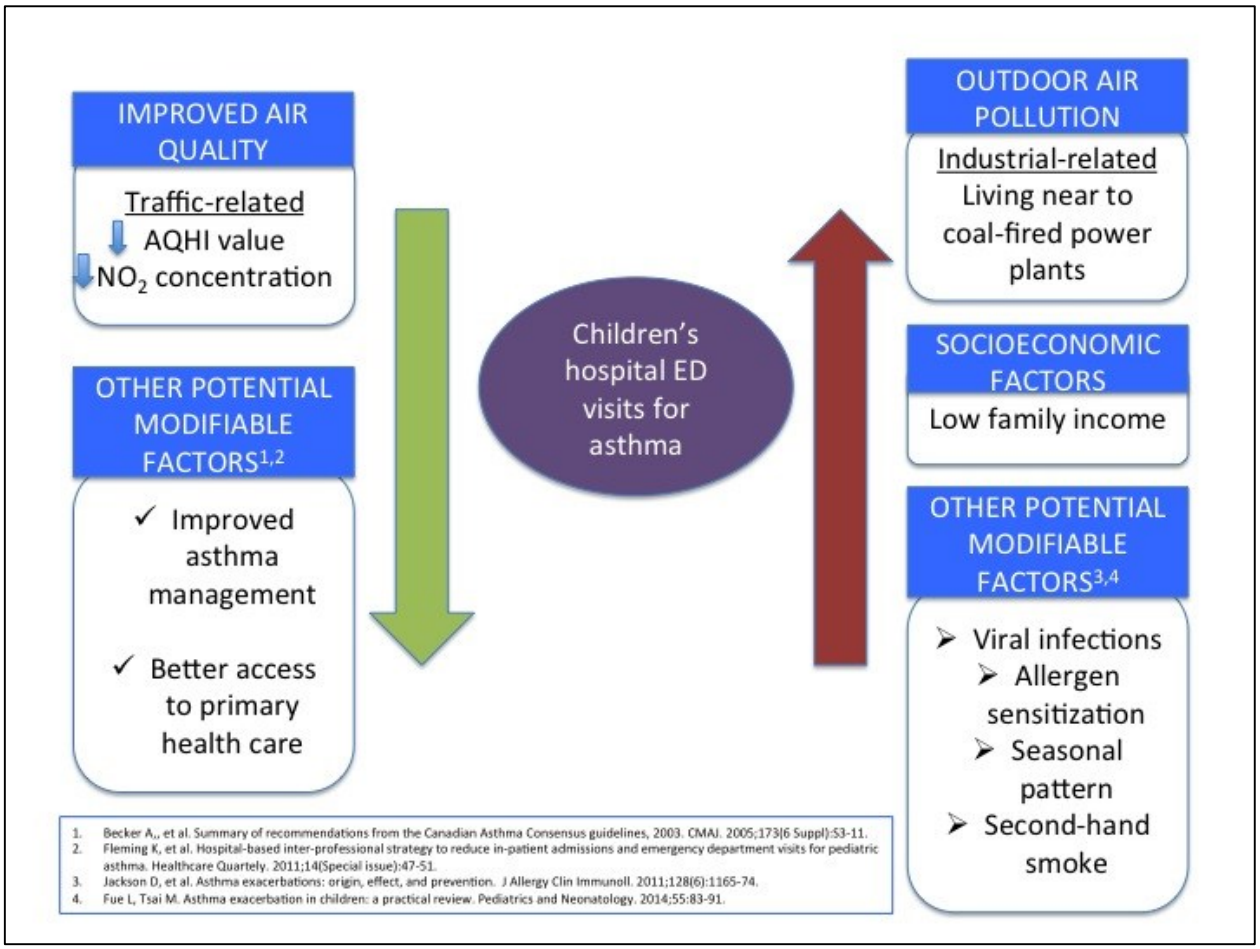
6.5. Conclusions

Day-to-day increase in the city-wide AQHI values or in the traffic-related air pollution at DA level did not increase the risk of hospital ED visits for children with acute asthma. The SEP did not modify these associations despite the fact that ED visits for asthma were more frequent in children with low SEP. In contrast, hospital ED visits for asthma were associated with industrial pollution coming from the CFPP at the Wabamum area.

The findings of this study regarding the lack of short-term adverse effects of increased concentration of air pollutants have potential explanations on the combination of two key evidenced factors: the decreased rates of children's ED visits for asthma and the decreased concentration and variability of NO_2 and $PM_{2.5}$, and therefore the AQHI values, compared to reports in the previous decade. The decreased number of ED visits may be explained, in part, because access to primary care and asthma management have changed over time in the CMAE, with more severe or referred cases attending the hospital EDs, and those asthma cases might be more affected by factors other than pollution (i.e., allergen exposure in atopic children or exposure to second-hand smoke at home).

These dissertation results add to the available literature by providing evidence of the children's health benefits associated with better air quality conditions and the adverse effects of industrial pollution from CFPP on children's asthma.

Figure 6- 1. Proposed diagram of the relationship between outdoor air pollution and Hospital Emergency Department visits for Children with Acute Asthma in the Census Metropolitan Area of Edmonton between 2004/2005 and 2009/2010.



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APPENDIX A. Ethics Approval for the Study and Renewal

Approval Form

Date:	January 28, 2015
Study ID:	Pro00049816
Principal Investigator:	Brian Rowe
Study Title:	**Outdoor air pollution and socioeconomic status: Their influence on asthma in Alberta.**
Approval Expiry Date:	January-27-16

Thank you for submitting the above study to the Health Research Ethics Board - Health Panel . Your application, including revisions received September 3, 2014 and January 27, 2015, has been reviewed and approved on behalf of the committee.

The Health Research Ethics Board assessed all matters required by section 50(1)(a) of the Health Information Act. It has been determined that the research described in the ethics application is a retrospective medical records review for which subject consent for access to personally identifiable health information would not be reasonable, feasible or practical. Subject consent therefore is not required for access to personally identifiable health information described in the ethics application.

In order to comply with the Health Information Act, a copy of the approval form is being sent to the Office of the Information and Privacy Commissioner.

A renewal report must be submitted next year prior to the expiry of this approval if your study still requires ethics approval. If you do not renew on or before the renewal expiry date (January-27-16), you will have to re-submit an ethics application.

Approval by the Health Research Ethics Board does not encompass authorization to access the patients, staff or resources of Alberta Health Services or other local health care institutions for the purposes of the research. Enquiries regarding Alberta Health approvals should be directed to (780) 407-6041. Enquiries regarding Covenant Health approvals should be directed to (780) 735-2274.

Sincerely,

Anthony S, Joyce, Ph.D.
Chair, Health Research Ethics Board - Health Panel

Note: This correspondence includes an electronic signature (validation and approval via an online system).

Health Research Ethics Board

308 Campus Tower
University of Alberta, Edmonton, AB T6G 1K8
p. 780.492.9724 (Biomedical Panel)
p. 780.492.0302 (Health Panel)
p. 780.492.0459
p. 780.492.0839
f. 780.492.9429

Notification of Approval (Renewal)

Date:	January 4, 2016
Amendment ID:	Pro00049816_REN1
Principal Investigator:	Brian Rowe
Study ID:	MS1_Pro00049816
Study Title:	**Outdoor air pollution and socioeconomic status: Their influence on asthma in Alberta.**
Approval Expiry Date:	Tuesday, January 3, 2017

Thank you for submitting this renewal application. Your application has been reviewed and approved.

This re-approval is valid for another year. If your study continues past the expiration date as noted above, you will be required to complete another renewal request. Beginning at 30 days prior to the expiration date, you will receive notices that the study is about to expire. If you do not renew on or before the renewal expiry date, you will have to re-submit an ethics application.

All study related documents should be retained so as to be available to the Health REB upon request. They should be kept for the duration of the project and for at least 5 years following study completion.

Sincerely,

Anthony S. Joyce, Ph.D.
Chair, Health Research Ethics Board - Health Panel

Note: This correspondence includes an electronic signature (validation and approval via an online system).

UNIVERSITY OF ALBERTA Alberta Health Services Covenant Health

APPENDIX B. Search Strategies for the Systematic Review

MEDLINE®

1. Air Pollution/

2. air pollutants/ or particulate matter/ or sulfur dioxide/ or nitrogen dioxide/ or ozone/ or carbon monoxide/ or polycyclic hydrocarbons, aromatic/ or volatile organic compounds/

3. ("air pollution" or "air pollutant").mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

4. ("ambient air pollution" or "outdoor air pollution").mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

5. 1 or 2 or 3 or 4

6. asthma/

7. ("respiratory sounds" or "asthma").mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

8. ("respiratory symptoms" or "wheez*").mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

9. 6 or 7 or 8

10. Child/

11. ("child*" or "adolesc*" or "teen*" or "youth" or "pediat*").mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

12. 10 or 11

13. socioeconomic position/ or socioeconomic factors/ or exp poverty/ or social class/ or exp Social Marginalization/

14. (social adj (class* or disadvantage*)).mp.

15. (deprivation or poverty or "socioeconomic status" or “socioeconomic*”).mp.

16. 13 or 14 or 15

17. 5 and 9 and 12 and 16

18. limit 17 to yr="1950 -Current"

EMBASE

1. exp Air Pollution/

2. exp air pollutant/ or particulate matter/ or nitrogen dioxide/ or ozone/ or carbon monoxide/ or sulfur dioxide/ or polycyclic aromatic hydrocarbons/ or volatile organic compound/

3. ("air pollution" or "air pollutant").mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

4. ("ambient air pollution" or "outdoor air pollution").mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

5. 1 or 2 or 3 or 4

6. asthma/

7. ("respiratory sounds" or "asthma").mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

8. ("respiratory symptoms" or "wheez*").mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

9. 6 or 7 or 8

10. Child/

11. ("child*" or "adolesc*" or "teen*" or "youth" or "pediat*").mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

12. 10 or 11

13. socioeconomic position/ or socioeconomic factors/ or exp poverty/ or social class/ or exp Social Marginalization/ or exp social status/

14. (social adj (class* or disadvantage*)).mp.

15. (deprivation or poverty or "socioeconomic status" or “socioeconomic*”).mp.

16. 13 or 14 or 15

17. 5 and 9 and 12 and 16

18. limit 17 to yr="1950 -Current"

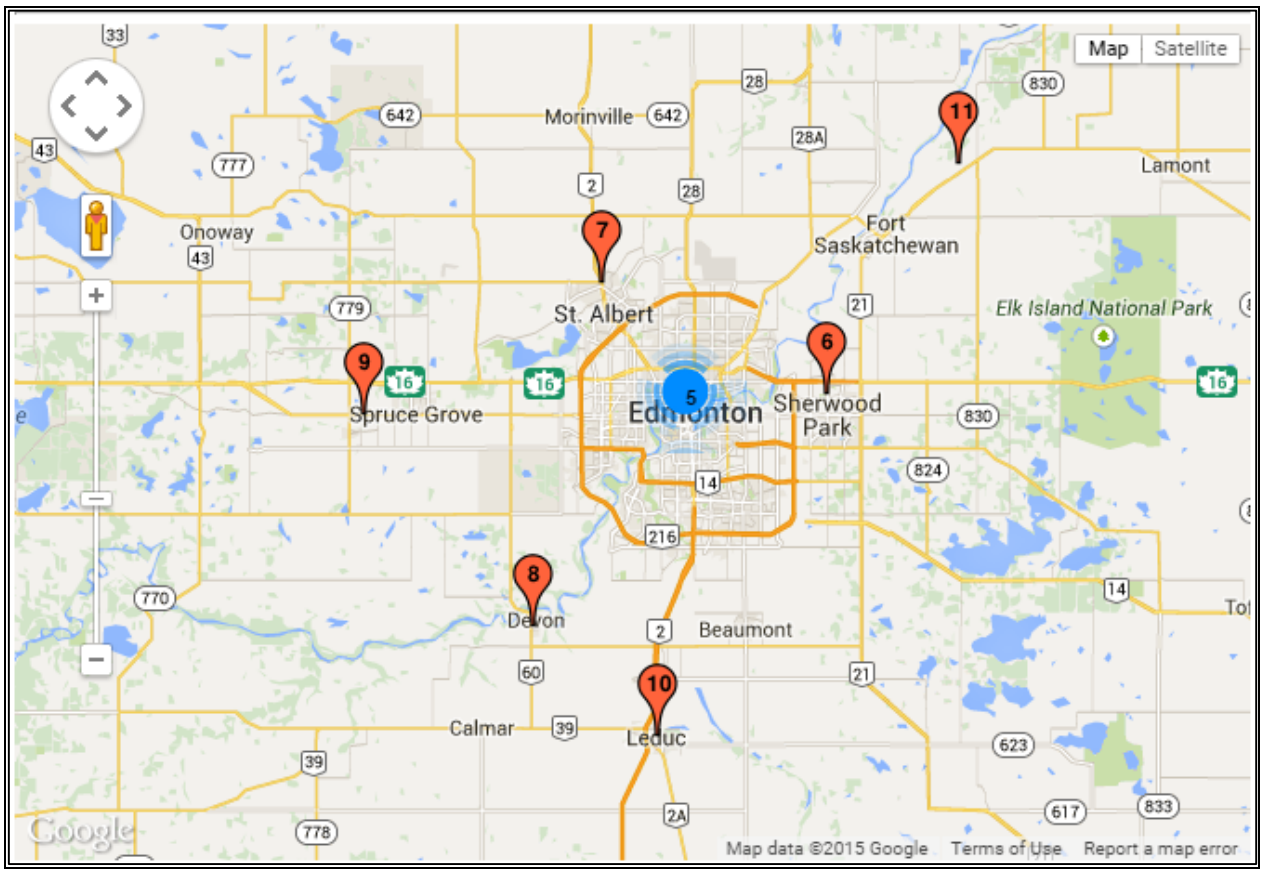
CAB ABSTRACTS, CINAHL, AND SCOPUS

air pollut* OR "ambient air pollution" OR "outdoor air pollution") *AND* **TOPIC:** (asthma* OR wheez* OR "respiratory symptoms") *AND* **TOPIC:** (child* OR adolesc* OR teen* OR pediat*) *AND* **TOPIC:** ("socioeconomic position" OR "socioeconomic status" OR "social class" OR "socioeconomic factors" OR "poverty" OR "social class" OR "social status" OR "social marginalization" OR “socioeconomic*”)

Timespan: 1950-2015.

APPENDIX C. Hospital Emergency Department facilities in the Census Metropolitan Area of Edmonton

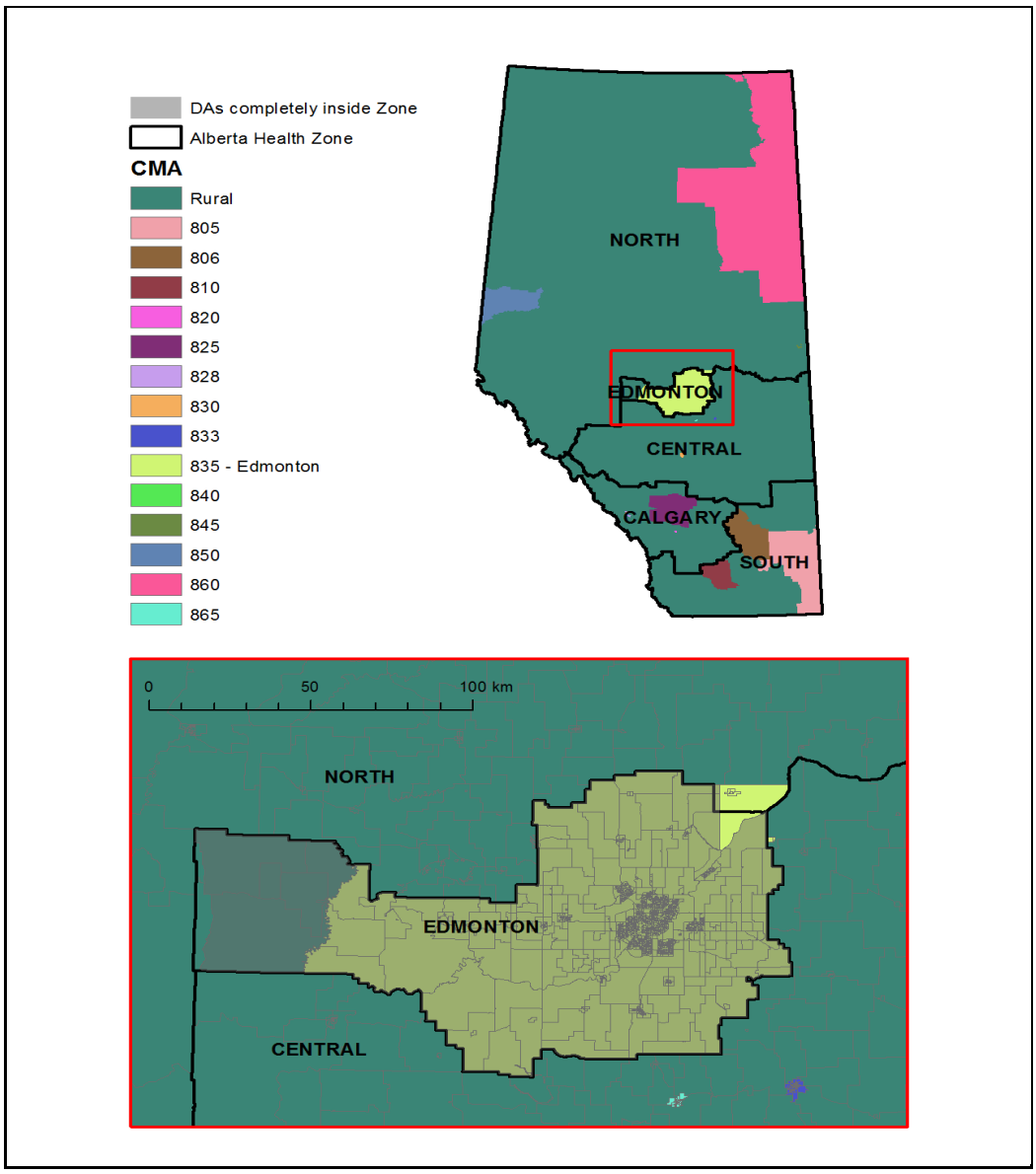
Alberta Health Services (AHS) operates 11 Hospital Emergency Department (ED) facilities within the Edmonton Zone that give services for children. The Stollery Children's hospital provides services for children only and the remaining 10 ED facilities provide services for adults and children. The following map illustrates the geographical location of these EDs:



Source: http://www.albertahealthservices.ca/FacilitySearch/?filter=facilities&city=Edmonton

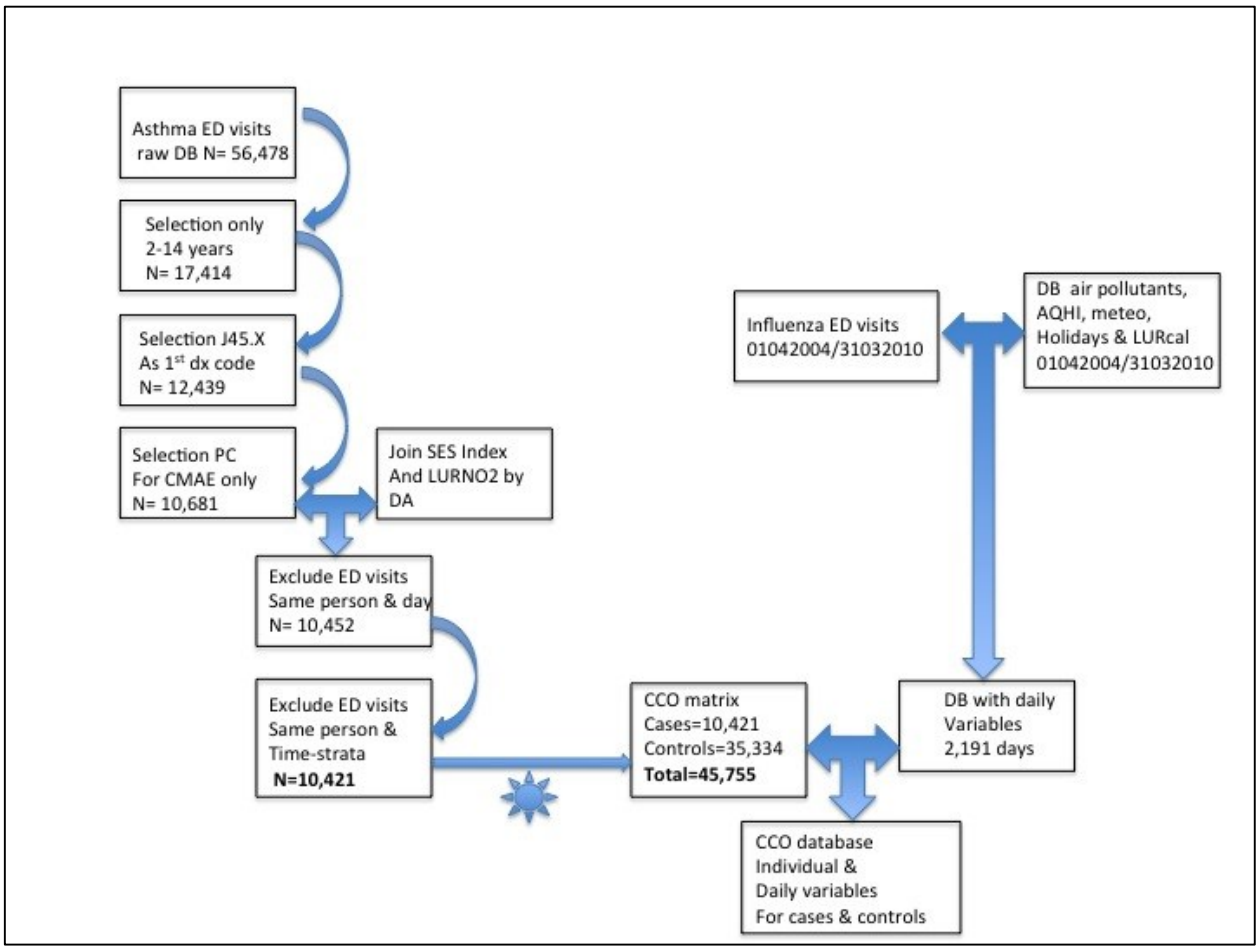
1 Royal Alexandra Hospital 10240 Kingsway Avenue NW Edmonton, Alberta T5H 3V9	**7** Sturgeon Community Hospital 201 Boudreau Road St. Albert, Alberta T8N 6C4
2 Stollery Children's Hospital 8440 112 Street Edmonton, Alberta T6G 2B7	**8** Devon General Hospital 101 Erie Street S Devon, Alberta T9G 1A6
3 Misericordia Community Hospital 16940 87 Avenue Edmonton, Alberta T5R 4H5	**9** WestView Health Centre 4405 South Park Drive Stony Plain, Alberta T7Z 2M7
4 Northeast Community Health Centre 14007 50 Street Edmonton, Alberta T5A 5E4	**10** Leduc Community Hospital 4210 48 Street Leduc, Alberta T9E 5Z3
5 Grey Nuns Community Hospital 1100 Youville Drive NW Edmonton, Alberta T6L 5X8	**11** Fort Saskatchewan Community Hospital 9401 86 Avenue Fort Saskatchewan, Alberta T8L 0C6
6 Strathcona Community Hospital 9000 Emerald Drive Sherwood Park, Alberta T8H 0J3	University of Alberta Hospital 8440 112 Street NW Edmonton, Alberta T6G 2B7 (ED facility within the CMAE but not attending children)

APPENDIX D. The Census Metropolitan Area of Edmonton and the Alberta Health Services Edmonton Zone (Z4)



The map shows the Alberta Health Services subdivisions separated by the black lines and the census metropolitan areas by colours. The zoomed squared in the lower half of the figure shows that the AHS Edmonton zone match almost perfectly the CMAE except for the gray zone located at left and the light green zone located at upper right.

APPENDIX E. Flowchart of the process followed to obtain the databases and case-crossover matrix for analysis.



APPENDIX F. Crude, Directly Standardized Rates and Bayesian Smoothed Morbidity Ratios of Emergency Department Visits for asthma in children by Dissemination Area in the Census Metropolitan Area of Edmonton, Alberta, 2004/2005 – 2009/2010

No.	Dissemination area number	Children population 0-14 years	No. asthma ED visits	Crude rate per 1,000	Directly standardized rates per 1,000[a]			Bayesian smoothed morbidity ratio
					Rate	95% CI		
1	48100190	130	0	0.00	0.00	0.00	0.00	0.22
2	48100191	125	0	0.00	0.00	0.00	0.00	0.22
3	48110083	165	12	72.73	78.55	31.44	137.73	1.23
4	48110084	0	0					
5	48110085	95	9	94.74	95.58	34.95	169.67	1.53
6	48110086	55	0	0.00	0.00	0.00	0.00	0.35
7	48110087	40	1	25.00	21.46	0.00	64.10	0.61
8	48110088	45	1	22.22	21.16	0.00	61.23	0.57
9	48110089	50	1	20.00	21.16	0.00	57.08	0.54
10	48110090	55	1	18.18	14.43	0.00	50.35	0.51
11	48110091	60	5	83.33	83.90	6.91	143.74	1.30
12	48110092	55	4	72.73	63.49	7.84	126.37	1.15
13	48110093	80	1	12.50	12.88	0.00	33.38	0.41
14	48110094	75	5	66.67	67.81	10.88	121.40	1.09
15	48110095	85	1	11.77	10.58	0.00	30.33	0.39
16	48110096	75	1	13.33	12.02	0.00	36.92	0.42
17	48110097	60	7	116.67	140.79	**57.69**	211.13	1.78
18	48110098	70	10	142.86	140.84	**60.77**	264.82	2.22
19	48110099	60	3	50.00	48.29	0.00	95.87	0.86
20	48110100	60	2	33.33	33.18	0.00	72.87	0.66
21	48110101	65	7	107.69	100.66	27.41	193.30	1.67
22	48110102	85	1	11.77	14.43	0.00	30.36	0.39
23	48110103	80	1	12.50	16.10	0.00	34.02	0.41
24	48110104	75	9	120.00	120.00	46.33	220.54	1.88
25	48110105	55	8	145.46	173.37	**61.93**	257.63	2.19
26	48110106	70	2	28.57	25.39	0.00	62.10	0.60
27	48110107	90	5	55.56	60.99	9.18	106.61	0.94
28	48110108	60	6	100.00	98.30	23.37	169.87	1.54
29	48110109	90	8	88.89	121.74	52.20	159.28	1.44
30	48110110	95	3	31.58	28.98	0.00	64.70	0.62
31	48110111	85	4	47.06	60.31	4.86	92.35	0.82
32	48110112	110	2	18.18	19.78	0.00	37.84	0.44
33	48110113	105	9	85.71	85.00	31.89	156.08	1.40
34	48110114	110	9	81.82	77.33	27.67	147.67	1.35
35	48110115	65	4	61.54	59.66	2.40	115.47	1.01
36	48110116	60	2	33.33	21.16	0.00	72.97	0.66
37	48110117	75	11	146.67	150.22	**70.61**	280.75	2.30
38	48110118	70	5	71.43	66.88	11.87	127.74	1.15
39	48110119	75	7	93.33	89.06	30.45	162.51	1.48
40	48110120	100	8	80.00	74.11	24.00	144.32	1.31
41	48110121	115	14	121.74	109.17	**56.14**	230.04	1.99
42	48110122	70	4	57.14	59.31	3.16	108.61	0.96
43	48110123	85	2	23.53	23.43	0.00	55.12	0.52

No.	Dissemination area number	Children population 0-14 years	No. asthma ED visits	Crude rate per 1,000	Directly standardized rates per 1,000[a]			Bayesian smoothed morbidity ratio
					Rate	95% CI		
44	48110124	75	10	133.33	143.25	**61.56**	241.68	2.09
45	48110125	35	2	57.14	48.09	0.00	106.47	0.94
46	48110126	90	0	0.00	0.00	0.00	0.00	0.27
47	48110127	80	1	12.50	14.43	0.00	34.04	0.41
48	48110130	55	1	18.18	10.58	0.00	50.42	0.51
49	48110131	75	0	0.00	0.00	0.00	0.00	0.29
50	48110132	75	5	66.67	69.96	11.03	121.43	1.09
51	48110133	80	0	0.00	0.00	0.00	0.00	0.28
52	48110134	50	5	100.00	105.81	30.08	165.40	1.51
53	48110135	30	0	0.00	0.00	0.00	42.39	0.46
54	48110136	20	0	0.00	0.00	0.00	58.78	0.54
55	48110137	5	3	300.00	190.46	0.00	0.00	4.16
56	48110138	135	3	22.22	28.70	0.00	46.18	0.47
57	48110139	130	2	15.39	15.15	0.00	30.21	0.39
58	48110140	100	6	60.00	64.90	12.59	114.39	1.01
59	48110141	5	4	400.00	288.53	0.00	0.00	6.04
60	48110142	20	1	50.00	15.87	0.00	99.69	0.88
61	48110143	35	2	57.14	64.38	0.00	106.52	0.94
62	48110144	30	0	0.00	0.00	0.00	42.39	0.46
63	48110145	10	1	100.00	63.49	0.00	133.04	1.20
64	48110146	15	1	66.67	63.49	0.00	113.50	1.01
65	48110147	45	0	0.00	0.00	0.00	26.97	0.38
66	48110148	70	3	42.86	51.99	0.00	86.09	0.77
67	48110149	5	1	200.00	120.22	0.00	169.70	1.54
68	48110150	50	0	0.00	0.00	0.00	22.30	0.36
69	48110151	30	0	0.00	0.00	0.00	42.52	0.46
70	48110152	5	0	0.00	0.00	0.00	90.77	0.81
71	48110153	45	8	160.00	257.53	**177.72**	331.38	2.60
72	48110154	25	3	120.00	135.62	0.00	175.37	1.58
73	48110155	30	0	0.00	0.00	0.00	42.53	0.46
74	48110156	5	2	400.00	639.34	**639.34**	335.25	2.65
75	48110157	40	3	75.00	64.38	0.00	126.07	1.15
76	48110158	10	0	0.00	0.00	0.00	75.69	0.68
77	48110159	15	1	66.67	64.38	0.00	113.50	1.01
78	48110160	15	0	0.00	0.00	0.00	62.59	0.60
79	48110161	15	2	133.33	126.97	0.00	170.98	1.55
80	48110163	10	0	0.00	0.00	0.00	75.71	0.68
81	48110164	10	0	0.00	0.00	0.00	75.80	0.68
82	48110165	15	1	66.67	31.74	0.00	113.66	1.01
83	48110166	10	1	66.67	64.38	0.00	133.10	1.20
84	48110167	30	4	133.33	132.19	12.40	213.26	1.81
85	48110168	35	1	28.57	32.19	0.00	72.67	0.66
86	48110169	60	2	33.33	33.18	0.00	73.03	0.66
87	48110170	30	1	33.33	15.87	0.00	80.12	0.72
88	48110171	35	3	85.71	95.23	5.07	140.50	1.26
89	48110172	15	0	0.00	0.00	0.00	62.99	0.60
90	48110173	10	0	0.00	0.00	0.00	75.80	0.68
91	48110174	15	1	66.67	31.74	0.00	113.77	1.01
92	48110176	25	0	0.00	0.00	0.00	48.01	0.50

No.	Dissemination area number	Children population 0-14 years	No. asthma ED visits	Crude rate per 1,000	Directly standardized rates per 1,000[a]			Bayesian smoothed morbidity ratio
					Rate	95% CI		
93	48110177	35	0	0.00	0.00	0.00	37.60	0.43
94	48110178	45	5	111.11	158.71	**60.34**	186.92	1.64
95	48110179	90	16	177.78	170.86	**93.76**	449.87	2.86
96	48110180	65	2	30.77	25.39	0.00	66.94	0.63
97	48110181	75	13	173.33	157.94	**80.39**	351.66	2.73
98	48110182	60	1	16.67	24.04	0.00	46.19	0.48
99	48110183	65	4	61.54	49.78	1.32	115.76	1.01
100	48110184	75	7	93.33	95.68	30.17	162.97	1.48
101	48110185	20	4	200.00	255.74	**61.60**	297.81	2.42
102	48110186	95	7	73.68	90.14	33.48	134.35	1.21
103	48110187	50	2	40.00	56.24	0.00	84.39	0.75
104	48110188	70	4	57.14	58.28	0.00	108.94	0.96
105	48110189	80	3	37.50	31.74	0.00	77.10	0.70
106	48110190	25	0	0.00	0.00	0.00	48.34	0.50
107	48110191	65	10	153.85	167.72	**79.58**	290.11	2.37
108	48110192	45	1	22.22	15.87	0.00	61.23	0.57
109	48110193	85	8	94.12	102.77	32.93	166.84	1.51
110	48110194	40	7	175.00	170.79	**60.83**	314.91	2.50
111	48110195	65	2	30.77	34.63	0.00	67.02	0.63
112	48110196	60	3	50.00	46.65	0.00	95.91	0.86
113	48110197	95	5	52.63	84.83	9.81	101.24	0.90
114	48110198	70	1	14.29	7.94	0.00	39.11	0.44
115	48110199	70	5	71.43	64.38	13.91	128.01	1.15
116	48110200	15	1	50.00	64.38	0.00	114.08	1.01
117	48110201	75	4	53.33	44.62	2.52	103.13	0.91
118	48110202	75	2	26.67	36.07	0.00	59.99	0.57
119	48110203	45	2	44.44	34.16	0.00	89.83	0.80
120	48110204	85	7	82.35	116.57	34.88	145.21	1.33
121	48110205	60	3	50.00	31.74	0.00	96.20	0.86
122	48110206	85	1	11.77	12.02	0.00	30.62	0.39
123	48110207	105	0	0.00	0.00	0.00	0.00	0.24
124	48110208	100	10	100.00	101.20	41.02	184.94	1.62
125	48110209	75	1	13.33	21.46	0.00	37.08	0.42
126	48110210	50	6	120.00	128.17	37.77	211.59	1.79
127	48110211	60	1	16.67	14.43	0.00	46.19	0.48
128	48110212	40	0	0.00	0.00	0.00	31.30	0.40
129	48110213	115	10	86.96	86.65	36.18	159.15	1.43
130	48110214	15	0	0.00	0.00	0.00	63.11	0.60
131	48110215	50	7	140.00	189.55	**71.24**	240.01	2.08
132	48110216	85	10	117.65	114.10	47.05	218.94	1.87
133	48110217	85	8	94.12	96.71	33.63	167.00	1.51
134	48110218	95	3	31.58	26.68	0.00	65.02	0.62
135	48110219	85	2	23.53	25.75	0.00	55.32	0.52
136	48110220	25	3	120.00	127.87	0.00	175.67	1.58
137	48110221	70	10	142.86	147.61	**64.43**	264.82	2.22
138	48110222	50	6	120.00	192.25	**66.76**	211.87	1.79
139	48110223	65	5	76.92	80.03	14.61	136.98	1.22
140	48110224	60	3	50.00	44.89	0.00	96.26	0.86
141	48110225	25	0	0.00	0.00	0.00	48.57	0.50

No.	Dissemination area number	Children population 0-14 years	No. asthma ED visits	Crude rate per 1,000	Directly standardized rates per 1,000[a]			Bayesian smoothed morbidity ratio
					Rate	95% CI		
142	48110226	50	3	60.00	58.79	0.00	111.57	0.98
143	48110227	85	3	35.29	23.81	0.00	73.41	0.67
144	48110228	105	0	0.00	0.00	0.00	0.00	0.24
145	48110229	75	3	40.00	38.27	0.00	81.74	0.73
146	48110230	75	3	40.00	48.29	0.00	81.90	0.73
147	48110231	50	1	20.00	21.46	0.00	57.34	0.54
148	48110232	45	2	44.44	42.92	0.00	89.91	0.80
149	48110233	65	0	0.00	0.00	0.00	0.00	0.32
150	48110234	115	8	69.57	70.97	24.00	130.92	1.16
151	48110235	55	1	18.18	15.87	0.00	50.57	0.51
152	48110236	70	3	42.86	50.22	0.00	86.26	0.77
153	48110237	70	6	85.71	77.26	23.37	149.99	1.36
154	48110238	185	9	48.65	49.14	17.65	95.53	0.85
155	48110239	105	3	28.57	28.80	0.00	61.23	0.57
156	48110240	80	6	75.00	74.83	19.00	136.31	1.22
157	48110241	85	6	70.59	72.64	15.87	129.28	1.16
158	48110242	105	9	85.71	88.64	31.90	156.21	1.40
159	48110243	85	8	94.12	101.71	30.34	167.30	1.51
160	48110244	60	2	33.33	28.85	0.00	73.23	0.66
161	48110245	75	4	53.33	50.65	3.55	103.13	0.91
162	48110246	80	6	75.00	77.68	18.90	136.32	1.22
163	48110247	130	17	130.77	138.60	**78.50**	251.98	2.16
164	48110248	80	0	0.00	0.00	0.00	0.00	0.28
165	48110249	70	10	142.86	133.38	**57.71**	268.75	2.22
166	48110250	80	11	137.50	122.61	**57.35**	255.86	2.17
167	48110251	90	2	22.22	21.31	0.00	49.72	0.50
168	48110252	120	4	33.33	36.17	1.13	67.88	0.63
169	48110253	90	5	55.56	51.52	9.71	106.61	0.94
170	48110254	60	1	16.67	15.87	0.00	46.19	0.48
171	48110255	90	7	77.78	85.56	25.92	141.38	1.27
172	48110256	80	7	87.50	88.56	27.00	154.76	1.40
173	48110257	55	4	72.73	73.40	3.98	126.56	1.15
174	48110258	50	3	60.00	54.10	0.00	111.60	0.98
175	48110259	45	2	44.44	47.84	0.00	89.97	0.80
176	48110260	60	10	166.67	162.68	**75.48**	322.49	2.55
177	48110261	140	14	100.00	94.68	48.67	193.02	1.66
178	48110262	40	1	25.00	63.49	0.00	64.10	0.61
179	48110263	80	3	37.50	36.48	0.00	77.26	0.70
180	48110264	75	7	93.33	94.42	27.64	163.02	1.48
181	48110265	75	1	13.33	16.10	0.00	37.08	0.42
182	48110266	145	8	55.17	57.24	18.06	108.32	0.95
183	48110267	30	2	66.67	67.81	0.00	116.67	1.03
184	48110268	220	12	54.54	55.53	24.63	108.10	0.95
185	48110269	155	3	19.35	18.06	0.00	37.60	0.43
186	48110270	90	3	33.33	36.13	0.00	68.04	0.64
187	48110271	155	12	77.42	80.58	34.79	144.19	1.31
188	48110272	300	28	93.33	95.53	**62.41**	183.95	1.61
189	48110273	40	1	25.00	63.49	0.00	64.20	0.61
190	48110274	155	10	64.52	67.22	27.62	123.48	1.10

No.	Dissemination area number	Children population 0-14 years	No. asthma ED visits	Crude rate per 1,000	Directly standardized rates per 1,000[a]			Bayesian smoothed morbidity ratio
					Rate	95% CI		
191	48110277	150	13	86.67	88.25	43.14	161.20	1.45
192	48110280	275	22	80.00	77.68	46.41	152.75	1.38
193	48110281	125	6	48.00	56.78	13.32	94.11	0.84
194	48110284	85	4	47.06	39.23	1.77	92.45	0.82
195	48110285	485	23	47.42	45.15	26.97	94.88	0.84
196	48110286	140	2	14.29	12.88	0.00	26.47	0.37
197	48110287	65	2	30.77	27.30	0.00	67.08	0.63
198	48110288	175	11	62.86	64.26	27.51	120.44	1.08
199	48110289	45	2	44.44	44.21	0.00	90.23	0.80
200	48110290	100	7	70.00	132.08	34.46	130.01	1.16
201	48110291	245	8	32.65	33.45	10.65	63.34	0.60
202	48110292	55	1	18.18	36.07	0.00	51.52	0.51
203	48110293	165	16	96.97	97.63	52.56	185.39	1.63
204	48110294	90	8	88.89	75.25	21.21	159.30	1.44
205	48110295	155	8	51.61	49.38	15.92	100.23	0.90
206	48110296	210	19	90.48	84.12	49.95	170.86	1.54
207	48110297	55	12	218.18	199.53	**101.24**	0.00	3.33
208	48110298	40	2	50.00	63.49	0.00	98.10	0.86
209	48110299	110	17	154.54	167.81	**100.39**	317.43	2.53
210	48110300	65	9	138.46	139.63	**57.40**	247.96	2.14
211	48110301	45	3	66.67	95.23	5.07	119.13	1.06
212	48110302	55	1	18.18	14.43	0.00	51.99	0.51
213	48110303	275	22	80.00	79.12	47.04	152.79	1.38
214	48110304	25	4	160.00	163.93	10.87	233.96	2.06
215	48110305	185	10	54.05	54.30	22.95	106.30	0.94
216	48110306	65	3	46.15	44.95	0.00	91.19	0.81
217	48110307	50	2	40.00	47.84	0.00	84.42	0.75
218	48110308	165	28	169.70	212.44	**146.24**	415.88	2.86
219	48110309	175	14	80.00	80.64	41.14	149.98	1.36
220	48110310	130	8	61.54	64.89	22.05	117.70	1.04
221	48110311	65	3	46.15	34.13	0.00	91.23	0.81
222	48110312	1395	96	68.82	69.54	**56.12**	136.76	1.22
223	48110314	150	13	86.67	73.96	35.98	161.38	1.45
224	48110315	135	14	103.70	88.63	44.22	202.73	1.72
225	48110316	105	14	133.33	141.82	**76.65**	255.57	2.17
226	48110317	65	17	261.54	270.82	**158.99**	0.00	4.12
227	48110318	165	2	12.12	13.56	0.00	0.00	0.33
228	48110319	190	20	105.26	104.56	**61.69**	210.21	1.78
229	48110320	45	1	22.22	21.46	0.00	61.23	0.57
230	48110321	60	6	100.00	101.64	28.58	170.50	1.54
231	48110322	280	16	57.14	57.11	29.56	113.42	1.00
232	48110323	85	3	35.29	30.48	0.00	73.48	0.67
233	48110324	25	2	80.00	42.92	0.00	128.88	1.15
234	48110325	190	12	63.16	58.95	26.67	120.73	1.09
235	48110326	100	7	70.00	73.41	22.03	130.16	1.16
236	48110327	30	2	57.14	126.97	0.00	116.91	1.03
237	48110328	65	7	107.69	141.85	41.40	193.34	1.67
238	48110329	95	5	52.63	45.08	8.12	102.17	0.90
239	48110330	75	11	146.67	168.24	**71.97**	280.90	2.30

No.	Dissemination area number	Children population 0-14 years	No. asthma ED visits	Crude rate per 1,000	Directly standardized rates per 1,000[a]			Bayesian smoothed morbidity ratio
					Rate	95% CI		
240	48110331	75	7	93.33	97.05	29.00	163.30	1.48
241	48110332	120	5	41.67	40.51	4.98	83.91	0.75
242	48110333	80	7	87.50	86.35	24.67	154.90	1.40
243	48110334	75	6	80.00	86.38	21.78	142.29	1.28
244	48110335	80	3	37.50	47.61	0.00	77.41	0.70
245	48110336	110	11	100.00	88.28	38.01	185.42	1.64
246	48110337	65	11	169.23	186.95	**89.74**	333.86	2.62
247	48110338	90	3	33.33	33.73	0.00	68.11	0.64
248	48110339	75	6	80.00	78.39	14.31	142.47	1.28
249	48110340	90	8	88.89	87.81	33.33	159.75	1.44
250	48110341	70	1	14.29	10.58	0.00	39.75	0.44
251	48110342	105	22	209.52	233.79	**152.68**	0.00	3.44
252	48110343	30	2	66.67	63.49	0.00	117.12	1.03
253	48110344	55	7	127.27	135.62	45.52	222.31	1.92
254	48110345	30	0	0.00	0.00	0.00	42.55	0.46
255	48110346	15	0	0.00	0.00	0.00	63.32	0.60
256	48110347	135	16	118.52	107.36	**56.93**	228.40	1.96
257	48110348	275	7	25.45	29.58	7.11	47.33	0.49
258	48110349	175	0	0.00	0.00	0.00	0.00	0.18
259	48110350	105	7	66.67	65.58	19.62	124.74	1.11
260	48110351	70	0	0.00	0.00	0.00	0.00	0.31
261	48110352	75	1	13.33	15.87	0.00	37.08	0.42
262	48110353	55	12	218.18	224.89	**114.53**	0.00	3.33
263	48110354	75	2	26.67	23.43	0.00	59.99	0.57
264	48110355	100	6	60.00	76.72	19.13	114.39	1.01
265	48110356	80	11	137.50	141.46	**75.01**	257.09	2.17
266	48110357	55	1	18.18	12.70	0.00	52.05	0.51
267	48110358	85	4	47.06	46.06	1.89	92.50	0.82
268	48110359	85	9	105.88	111.50	42.75	198.70	1.69
269	48110360	100	7	70.00	74.51	22.70	130.24	1.16
270	48110361	95	0	0.00	0.00	0.00	0.00	0.26
271	48110362	75	5	66.67	70.37	11.86	121.90	1.09
272	48110363	120	1	8.33	8.02	0.00	0.00	0.31
273	48110364	65	3	46.15	42.77	0.00	91.29	0.81
274	48110365	80	12	150.00	150.02	**73.08**	284.82	2.37
275	48110366	95	8	84.21	88.27	30.97	151.49	1.37
276	48110367	45	0	0.00	0.00	0.00	26.97	0.38
277	48110368	60	9	150.00	138.75	55.19	278.87	2.29
278	48110369	50	2	40.00	31.74	0.00	84.45	0.75
279	48110370	50	5	100.00	114.40	17.21	165.44	1.51
280	48110371	55	1	18.18	21.46	0.00	52.48	0.51
281	48110372	70	7	100.00	105.87	36.08	174.46	1.57
282	48110373	95	14	147.37	180.49	**100.68**	285.09	2.37
283	48110374	175	7	40.00	40.47	11.29	80.38	0.72
284	48110375	265	27	101.89	103.15	**65.80**	204.53	1.75
285	48110376	155	6	38.71	40.45	4.75	78.26	0.70
286	48110377	70	8	114.29	110.44	39.40	207.58	1.78
287	48110378	45	4	88.89	187.18	22.71	145.45	1.34
288	48110379	50	1	20.00	21.16	0.00	57.44	0.54

No.	Dissemination area number	Children population 0-14 years	No. asthma ED visits	Crude rate per 1,000	Directly standardized rates per 1,000[a]			Bayesian smoothed morbidity ratio
					Rate	95% CI		
289	48110380	0	0					
290	48110381	115	21	182.61	192.63	**129.70**	639.34	3.01
291	48110382	95	5	52.63	64.38	13.91	102.21	0.90
292	48110383	55	8	145.46	132.64	52.46	260.30	2.19
293	48110384	70	8	114.29	112.47	40.99	207.92	1.78
294	48110385	75	2	26.67	24.90	0.00	60.21	0.57
295	48110386	80	2	25.00	25.39	0.00	59.15	0.55
296	48110387	465	35	75.27	74.61	51.29	145.11	1.32
297	48110388	115	25	217.39	211.47	**137.85**	0.00	3.60
298	48110389	130	9	69.23	86.93	34.23	131.17	1.16
299	48110390	85	3	35.29	31.74	0.00	73.48	0.67
300	48110391	45	10	222.22	241.69	**85.80**	0.00	3.28
301	48110392	120	7	58.33	59.85	16.82	112.81	0.99
302	48110393	200	17	85.00	84.98	46.26	161.09	1.45
303	48110394	140	5	35.71	31.55	3.88	71.91	0.66
304	48110395	155	26	167.74	154.92	**99.63**	386.40	2.82
305	48110396	105	13	123.81	121.28	**59.33**	230.80	2.01
306	48110397	85	12	141.18	133.63	**59.90**	269.70	2.25
307	48110398	100	1	10.00	8.05	0.00	17.22	0.35
308	48110399	225	11	48.89	48.20	20.42	95.83	0.86
309	48110400	255	19	74.51	74.59	42.58	142.82	1.28
310	48110401	170	14	82.35	78.13	38.77	153.45	1.39
311	48110402	110	9	81.82	79.43	29.59	147.97	1.35
312	48110403	255	15	58.82	60.78	30.87	116.11	1.02
313	48110404	110	10	90.91	92.38	38.62	164.91	1.49
314	48110405	220	22	100.00	96.10	**57.13**	200.33	1.71
315	48110406	150	16	106.67	112.71	**60.02**	206.98	1.78
316	48110408	70	5	71.43	85.54	16.33	128.15	1.15
317	48110410	195	25	128.21	123.35	**78.70**	255.76	2.17
318	48110412	65	7	107.69	133.11	48.77	193.67	1.67
319	48110415	150	8	53.33	52.28	18.30	105.07	0.92
320	48110416	35	4	114.29	178.54	24.34	183.18	1.61
321	48110417	145	6	41.38	47.13	11.30	83.28	0.74
322	48110418	75	10	133.33	134.79	**58.44**	242.30	2.09
323	48110419	135	15	111.11	109.96	**56.91**	215.55	1.84
324	48110420	135	20	148.15	146.14	**85.43**	306.06	2.46
325	48110421	105	7	66.67	63.93	18.49	124.78	1.11
326	48110422	130	12	92.31	82.25	38.43	168.64	1.53
327	48110423	155	2	12.90	12.91	0.00	0.00	0.34
328	48110424	145	0	0.00	0.00	0.00	0.00	0.20
329	48110425	100	5	50.00	56.12	8.92	98.26	0.87
330	48110426	155	13	83.87	88.74	43.21	158.10	1.41
331	48110437	795	69	86.79	83.37	**64.11**	168.75	1.53
332	48110438	50	5	100.00	110.55	18.37	165.45	1.51
333	48110439	285	20	70.18	71.03	41.20	136.74	1.22
334	48110440	425	21	49.41	53.50	31.43	99.62	0.87
335	48110441	70	1	14.29	12.88	0.00	40.50	0.44
336	48110442	160	3	18.75	17.98	0.00	36.46	0.42
337	48110443	115	16	139.13	137.70	**75.06**	278.85	2.28

No.	Dissemination area number	Children population 0-14 years	No. asthma ED visits	Crude rate per 1,000	Directly standardized rates per 1,000[a]			Bayesian smoothed morbidity ratio
					Rate	95% CI		
338	48110444	145	12	82.76	80.97	37.05	153.41	1.39
339	48110445	90	6	66.67	52.95	11.62	123.99	1.10
340	48110446	145	8	55.17	57.59	19.30	108.40	0.95
341	48110447	100	12	120.00	117.01	55.87	225.77	1.94
342	48110448	200	14	70.00	74.55	37.54	132.96	1.20
343	48110449	75	9	120.00	121.02	49.03	220.90	1.88
344	48110450	690	41	59.42	56.58	39.76	118.28	1.05
345	48110451	65	1	15.39	12.88	0.00	43.73	0.46
346	48110630	1410	102	72.34	72.46	**58.39**	143.16	1.29
347	48110633	160	10	62.50	64.54	26.49	120.14	1.07
348	48110634	45	3	66.67	74.51	0.00	119.28	1.06
349	48110635	75	8	106.67	104.38	39.06	196.02	1.68
350	48110636	90	3	33.33	27.21	0.00	68.15	0.64
351	48110637	155	11	70.97	78.29	35.18	133.58	1.20
352	48110638	230	7	30.43	27.89	7.77	59.73	0.57
353	48110639	145	11	75.86	73.49	30.86	142.18	1.28
354	48110640	60	0	0.00	0.00	0.00	0.00	0.33
355	48110641	145	6	41.38	42.98	9.34	83.49	0.74
356	48110642	55	2	36.36	30.52	0.00	78.53	0.70
357	48110643	135	8	59.26	57.96	19.07	115.22	1.01
358	48110644	115	6	52.17	48.75	10.98	100.37	0.90
359	48110645	90	8	88.89	95.68	35.08	159.79	1.44
360	48110646	130	17	130.77	137.00	**78.35**	254.23	2.16
361	48110647	85	5	58.82	61.82	10.14	111.93	0.99
362	48110648	110	10	90.91	95.54	41.10	165.10	1.49
363	48110649	90	4	44.44	54.01	3.63	87.92	0.79
364	48110650	85	10	117.65	120.34	50.83	219.61	1.87
365	48110651	160	17	106.25	110.91	**61.38**	207.21	1.78
366	48110652	165	9	54.54	57.27	21.16	107.88	0.94
367	48110653	130	5	38.46	36.84	5.41	78.15	0.70
368	48110654	235	9	38.30	38.54	13.98	76.49	0.69
369	48110655	70	0	0.00	0.00	0.00	0.00	0.31
370	48110657	155	13	83.87	88.91	41.10	158.12	1.41
371	48110658	280	30	107.14	109.14	**72.89**	216.65	1.85
372	48110659	80	4	50.00	52.28	2.35	96.93	0.86
373	48110660	80	9	112.50	114.58	43.61	206.85	1.78
374	48110661	105	16	152.38	206.90	**128.04**	312.61	2.48
375	48110663	205	13	63.42	66.85	31.39	122.85	1.09
376	48110664	90	5	55.56	56.67	8.81	106.82	0.94
377	48110666	160	4	25.00	25.32	0.84	49.50	0.50
378	48110667	145	10	68.97	73.40	29.26	131.44	1.17
379	48110668	55	1	18.18	21.46	0.00	52.48	0.51
380	48110669	45	5	111.11	110.73	16.93	187.23	1.64
381	48110674	205	16	78.05	80.17	42.71	145.40	1.33
382	48110675	105	10	95.24	99.72	43.37	172.48	1.55
383	48110676	60	14	233.33	204.05	**114.27**	0.00	3.62
384	48110677	65	0	0.00	0.00	0.00	0.00	0.32
385	48110679	205	6	29.27	30.62	6.11	59.22	0.55
386	48110681	125	5	40.00	40.06	5.71	80.76	0.72

No.	Dissemination area number	Children population 0-14 years	No. asthma ED visits	Crude rate per 1,000	Directly standardized rates per 1,000[a]			Bayesian smoothed morbidity ratio
					Rate	95% CI		
387	48110682	150	12	80.00	82.35	36.70	146.79	1.34
388	48110683	140	20	142.86	142.43	**85.35**	292.12	2.38
389	48110684	150	5	33.33	36.22	4.30	66.75	0.62
390	48110685	230	12	52.17	49.42	22.34	104.53	0.91
391	48110686	425	22	51.76	52.04	31.11	104.66	0.91
392	48110687	200	28	140.00	142.56	**93.92**	293.21	2.38
393	48110688	120	8	66.67	63.29	20.19	124.89	1.12
394	48110689	160	14	87.50	81.03	37.67	162.14	1.47
395	48110690	2525	195	77.23	73.68	**63.56**	152.35	1.38
396	48110691	330	20	60.61	63.67	37.43	119.67	1.06
397	48110692	75	2	26.67	25.01	0.00	60.30	0.57
398	48110693	155	12	77.42	82.08	37.55	144.19	1.31
399	48110694	230	14	60.87	59.82	29.33	118.40	1.05
400	48110695	230	8	34.78	36.85	11.87	68.00	0.63
401	48110698	125	1	8.00	9.07	0.00	0.00	0.30
402	48110699	75	3	40.00	53.35	0.00	81.91	0.73
403	48110700	120	11	91.67	79.35	37.93	167.70	1.51
404	48110701	85	4	47.06	46.85	2.53	92.52	0.82
405	48110702	135	16	118.52	120.14	**65.82**	229.13	1.96
406	48110703	160	7	43.75	42.03	11.38	87.33	0.78
407	48110705	100	3	30.00	27.30	0.00	62.10	0.59
408	48110706	140	19	135.71	131.98	**77.04**	273.93	2.26
409	48110707	70	7	100.00	99.12	31.24	174.70	1.57
410	48110708	165	12	72.73	73.03	33.49	137.89	1.23
411	48110709	170	5	29.41	30.02	4.07	59.66	0.56
412	48110711	265	19	71.70	72.19	40.55	139.91	1.24
413	48110712	50	0	0.00	0.00	0.00	23.29	0.36
414	48110713	50	4	80.00	72.33	4.43	138.55	1.24
415	48110714	105	11	104.76	103.60	46.99	199.89	1.70
416	48110715	120	16	133.33	133.05	**71.55**	263.28	2.19
417	48110716	130	0	0.00	0.00	0.00	0.00	0.22
418	48110717	85	2	23.53	31.74	0.00	55.40	0.52
419	48110718	50	4	80.00	64.74	3.40	139.41	1.24
420	48110719	225	22	97.78	90.40	54.77	193.84	1.67
421	48110720	75	2	26.67	28.79	0.00	60.31	0.57
422	48110721	50	1	20.00	31.74	0.00	57.60	0.54
423	48110722	75	2	26.67	25.39	0.00	60.37	0.57
424	48110726	155	9	58.06	55.08	20.32	113.26	1.00
425	48110727	300	24	80.00	77.13	46.85	152.83	1.38
426	48110728	40	6	150.00	190.91	**75.76**	249.89	2.14
427	48110729	95	3	31.58	34.59	0.00	65.03	0.62
428	48110730	230	15	65.22	64.19	32.55	125.05	1.13
429	48110731	90	9	100.00	108.57	41.76	181.54	1.61
430	48110732	70	0	0.00	0.00	0.00	0.00	0.31
431	48110733	70	5	71.43	71.92	11.25	128.36	1.15
432	48110735	225	5	22.22	22.33	2.98	42.13	0.45
433	48110736	220	4	18.18	20.04	0.33	30.21	0.39
434	48110737	185	7	37.84	37.24	10.28	76.15	0.69
435	48110738	80	1	12.50	12.70	0.00	34.07	0.41

No.	Dissemination area number	Children population 0-14 years	No. asthma ED visits	Crude rate per 1,000	Directly standardized rates per 1,000[a]			Bayesian smoothed morbidity ratio
					Rate	95% CI		
436	48110742	75	7	93.33	95.98	26.51	164.07	1.48
437	48110743	95	3	31.58	42.77	0.00	65.76	0.62
438	48110744	95	2	21.05	21.16	0.00	46.81	0.48
439	48110745	90	5	55.56	63.49	13.71	106.86	0.94
440	48110746	65	1	15.39	12.70	0.00	44.08	0.46
441	48110747	70	0	0.00	0.00	0.00	0.00	0.31
442	48110748	85	6	70.59	63.78	15.65	129.42	1.16
443	48110749	50	10	200.00	201.49	**110.86**	587.43	2.99
444	48110750	60	1	16.67	18.03	0.00	46.19	0.48
445	48110751	55	1	18.18	21.16	0.00	52.48	0.51
446	48110752	95	3	31.58	27.21	0.00	65.82	0.62
447	48110753	45	13	288.89	280.08	**160.03**	0.00	4.34
448	48110754	60	0	0.00	0.00	0.00	0.00	0.33
449	48110755	55	0	0.00	0.00	0.00	0.00	0.35
450	48110756	55	1	18.18	31.74	0.00	52.48	0.51
451	48110757	60	3	50.00	45.21	0.00	96.42	0.86
452	48110758	85	3	35.29	37.76	0.00	73.48	0.67
453	48110759	145	2	13.79	13.16	0.00	20.04	0.36
454	48110760	75	2	26.67	32.19	0.00	60.47	0.57
455	48110765	135	12	88.89	88.67	40.59	164.91	1.48
456	48110767	75	12	160.00	153.24	**74.90**	316.81	2.52
457	48110768	55	5	90.91	88.00	17.88	153.90	1.40
458	48110769	60	5	83.33	80.25	16.19	143.95	1.30
459	48110770	105	5	47.62	47.12	6.15	93.39	0.83
460	48110771	80	5	62.50	73.18	11.84	117.13	1.04
461	48110772	95	2	21.05	25.39	0.00	46.82	0.48
462	48110773	70	1	14.29	12.70	0.00	40.62	0.44
463	48110774	65	2	30.77	32.19	0.00	67.21	0.63
464	48110775	45	0	0.00	0.00	0.00	26.97	0.38
465	48110776	75	1	13.33	9.02	0.00	37.08	0.42
466	48110777	135	9	66.67	65.16	22.80	125.11	1.13
467	48110778	105	10	95.24	108.29	46.08	172.61	1.55
468	48110779	90	5	55.56	73.80	13.54	107.16	0.94
469	48110780	165	0	0.00	0.00	0.00	0.00	0.19
470	48110785	65	3	46.15	58.37	0.00	91.41	0.81
471	48110786	45	0	0.00	0.00	0.00	27.63	0.38
472	48110787	95	5	52.63	54.09	7.74	102.30	0.90
473	48110788	50	5	100.00	141.40	41.11	165.45	1.51
474	48110789	85	4	47.06	40.08	1.64	92.67	0.82
475	48110790	0	0					
476	48110791	45	4	88.89	96.13	8.21	145.57	1.34
477	48110792	85	15	176.47	169.60	**91.21**	397.58	2.82
478	48110793	50	5	100.00	127.87	25.41	165.63	1.51
479	48110794	40	0	0.00	0.00	0.00	31.41	0.40
480	48110795	285	10	35.09	30.82	12.24	68.00	0.64
481	48110796	205	11	53.66	53.92	23.26	105.80	0.93
482	48110797	60	0	0.00	0.00	0.00	0.00	0.33
483	48110798	70	8	114.29	113.15	39.72	209.06	1.78
484	48110799	65	1	15.39	16.10	0.00	44.30	0.46

No.	Dissemination area number	Children population 0-14 years	No. asthma ED visits	Crude rate per 1,000	Directly standardized rates per 1,000[a]			Bayesian smoothed morbidity ratio
					Rate	95% CI		
485	48110800	110	3	27.27	26.18	0.00	59.15	0.55
486	48110801	50	2	40.00	53.20	0.00	84.51	0.75
487	48110802	75	2	26.67	25.16	0.00	60.47	0.57
488	48110803	90	4	44.44	40.29	1.74	87.99	0.79
489	48110804	55	7	127.27	125.49	39.49	223.89	1.92
490	48110805	55	6	109.09	114.40	28.82	189.84	1.65
491	48110806	65	1	15.39	14.43	0.00	44.32	0.46
492	48110807	80	2	25.00	25.75	0.00	59.15	0.55
493	48110808	55	9	163.64	163.49	**72.74**	307.86	2.47
494	48110809	55	3	54.54	95.23	5.07	104.70	0.92
495	48110810	55	4	72.73	84.83	7.86	126.61	1.15
496	48110811	75	5	66.67	68.36	8.58	121.93	1.09
497	48110812	95	2	21.05	19.50	0.00	46.84	0.48
498	48110813	80	5	62.50	63.09	8.20	117.22	1.04
499	48110814	45	5	111.11	90.61	16.32	187.86	1.64
500	48110815	70	1	14.29	10.58	0.00	41.18	0.44
501	48110818	70	1	14.29	36.07	0.00	41.67	0.44
502	48110819	85	6	70.59	74.00	14.48	129.55	1.16
503	48110820	55	2	36.36	48.09	0.00	78.62	0.70
504	48110821	80	1	12.50	8.05	0.00	34.19	0.41
505	48110822	75	6	80.00	81.63	18.64	142.53	1.28
506	48110823	80	4	50.00	60.36	0.56	97.29	0.86
507	48110824	55	2	36.36	33.18	0.00	78.84	0.70
508	48110825	45	1	22.22	15.87	0.00	61.23	0.57
509	48110826	70	3	42.86	47.84	0.00	86.32	0.77
510	48110827	85	4	47.06	74.22	6.72	92.77	0.82
511	48110828	80	4	50.00	60.10	1.53	97.35	0.86
512	48110829	75	4	53.33	49.80	2.80	103.13	0.91
513	48110830	95	7	73.68	73.57	20.58	134.51	1.21
514	48110831	75	1	13.33	16.10	0.00	37.08	0.42
515	48110832	35	4	114.29	222.65	**73.78**	183.23	1.61
516	48110833	65	6	92.31	76.54	19.51	160.69	1.44
517	48110834	55	1	18.18	15.87	0.00	52.79	0.51
518	48110835	75	2	26.67	24.04	0.00	60.55	0.57
519	48110836	85	2	23.53	22.60	0.00	55.40	0.52
520	48110837	50	0	0.00	0.00	0.00	23.29	0.36
521	48110838	70	4	57.14	61.38	0.00	109.02	0.96
522	48110839	85	1	11.77	18.03	0.00	30.97	0.39
523	48110840	45	2	44.44	32.19	0.00	90.32	0.80
524	48110841	60	0	0.00	0.00	0.00	0.00	0.33
525	48110842	80	5	62.50	57.50	9.19	117.28	1.04
526	48110843	145	6	41.38	32.89	7.42	83.79	0.74
527	48110844	40	6	150.00	204.77	**67.46**	250.10	2.14
528	48110845	105	2	19.05	18.03	0.00	42.13	0.45
529	48110846	0	0					
530	48110847	55	4	72.73	76.45	4.94	126.72	1.15
531	48110848	60	13	216.67	218.76	**115.03**	0.00	3.34
532	48110849	105	8	76.19	83.95	28.49	140.23	1.26
533	48110850	55	2	36.36	37.33	0.00	79.11	0.70

No.	Dissemination area number	Children population 0-14 years	No. asthma ED visits	Crude rate per 1,000	Directly standardized rates per 1,000[a]			Bayesian smoothed morbidity ratio
					Rate	95% CI		
534	48110851	95	1	10.53	12.88	0.00	23.62	0.36
535	48110852	70	1	14.29	12.02	0.00	41.72	0.44
536	48110853	40	0	0.00	0.00	0.00	31.41	0.40
537	48110854	90	1	11.11	7.94	0.00	26.47	0.38
538	48110855	50	4	80.00	78.39	6.07	139.62	1.24
539	48110856	40	0	0.00	0.00	0.00	31.41	0.40
540	48110857	70	2	28.57	31.97	0.00	62.10	0.60
541	48110858	70	3	42.86	44.89	0.00	86.42	0.77
542	48110859	65	0	0.00	0.00	0.00	0.00	0.32
543	48110860	40	2	50.00	52.16	0.00	98.23	0.86
544	48110861	25	0	0.00	0.00	0.00	49.27	0.50
545	48110862	10	0	0.00	0.00	0.00	75.98	0.68
546	48110866	40	1	25.00	21.16	0.00	64.30	0.61
547	48110867	30	1	33.33	21.16	0.00	80.12	0.72
548	48110868	5	0	0.00	0.00	0.00	90.77	0.81
549	48110869	25	2	80.00	85.54	0.00	129.28	1.15
550	48110870	35	3	85.71	84.95	0.00	140.66	1.26
551	48110871	30	0	0.00	0.00	0.00	42.59	0.46
552	48110872	35	1	28.57	64.38	0.00	72.72	0.66
553	48110873	65	3	46.15	41.26	0.00	91.50	0.81
554	48110874	70	1	14.29	12.88	0.00	42.13	0.44
555	48110875	85	6	70.59	75.51	20.61	129.71	1.16
556	48110876	55	1	18.18	12.70	0.00	52.97	0.51
557	48110877	55	2	36.36	39.49	0.00	79.47	0.70
558	48110878	105	11	104.76	110.68	51.48	199.97	1.70
559	48110879	40	1	25.00	21.16	0.00	64.32	0.61
560	48110880	70	2	28.57	42.32	0.00	62.10	0.60
561	48110881	85	3	35.29	63.49	0.00	73.48	0.67
562	48110882	25	1	40.00	63.49	0.00	89.06	0.79
563	48110883	90	3	33.33	42.47	0.00	68.27	0.64
564	48110884	90	5	55.56	56.73	8.40	107.40	0.94
565	48110885	70	4	57.14	253.94	**142.65**	109.29	0.96
566	48110886	65	5	76.92	76.36	15.47	137.09	1.22
567	48110887	25	4	160.00	253.94	0.00	235.23	2.06
568	48110889	175	5	28.57	30.33	4.19	59.15	0.55
569	48110890	160	11	68.75	73.06	32.45	131.91	1.17
570	48110891	135	2	14.81	15.87	0.00	26.59	0.38
571	48110892	0	0					
572	48110893	310	2	6.45	6.44	0.00	0.00	0.20
573	48110894	75	4	53.33	61.46	3.25	103.33	0.91
574	48110895	45	4	88.89	116.69	17.80	146.13	1.34
575	48110896	80	4	50.00	54.50	3.50	97.35	0.86
576	48110897	75	3	40.00	36.06	0.00	82.05	0.73
577	48110898	220	0	0.00	0.00	0.00	0.00	0.16
578	48110899	150	1	6.67	8.05	0.00	0.00	0.27
579	48110900	105	5	47.62	50.79	7.76	93.73	0.83
580	48110901	50	0	0.00	0.00	0.00	23.29	0.36
581	48110902	130	4	30.77	34.04	0.74	62.02	0.59
582	48110903	80	6	75.00	95.68	22.72	136.47	1.22

No.	Dissemination area number	Children population 0-14 years	No. asthma ED visits	Crude rate per 1,000	Directly standardized rates per 1,000[a]			Bayesian smoothed morbidity ratio
					Rate	95% CI		
583	48110904	105	6	57.14	46.80	10.37	110.54	0.97
584	48110905	110	5	45.46	56.69	6.53	90.66	0.80
585	48110906	100	6	60.00	87.40	25.18	114.86	1.01
586	48110907	135	3	22.22	20.81	0.00	46.18	0.47
587	48110908	45	0	0.00	0.00	0.00	27.81	0.38
588	48110909	60	7	116.67	109.46	33.51	211.48	1.78
589	48110910	85	1	11.77	16.10	0.00	30.97	0.39
590	48110911	15	9	450.00	492.70	**288.22**	0.00	7.52
591	48110912	70	3	42.86	37.33	0.00	86.44	0.77
592	48110913	50	0	0.00	0.00	0.00	23.29	0.36
593	48110921	185	13	70.27	93.57	46.49	133.53	1.20
594	48110923	275	13	47.27	43.91	20.88	93.85	0.83
595	48110924	55	7	127.27	90.14	33.48	224.94	1.92
596	48110929	50	1	20.00	21.16	0.00	57.95	0.54
597	48110930	105	1	9.52	7.94	0.00	0.00	0.34
598	48110931	140	7	50.00	45.93	11.11	99.04	0.87
599	48110932	145	4	27.59	26.80	0.63	59.04	0.54
600	48110933	90	7	77.78	76.11	22.51	141.72	1.27
601	48110934	125	3	24.00	22.16	0.00	49.66	0.50
602	48110935	95	19	200.00	202.11	**125.35**	971.20	3.25
603	48110936	120	7	58.33	56.24	14.37	113.11	0.99
604	48110937	75	8	106.67	120.98	48.62	196.08	1.68
605	48110943	150	2	13.33	14.36	0.00	15.79	0.35
606	48110944	110	6	54.54	66.85	16.21	105.54	0.93
607	48110945	85	1	11.77	10.31	0.00	30.97	0.39
608	48110946	110	5	45.46	45.55	6.65	90.68	0.80
609	48110947	60	2	33.33	28.85	0.00	73.25	0.66
610	48110948	230	4	17.39	18.14	0.88	26.47	0.37
611	48110949	55	0	0.00	0.00	0.00	0.00	0.35
612	48110950	150	6	40.00	39.97	8.38	80.48	0.72
613	48110951	155	4	25.81	26.91	0.85	54.18	0.51
614	48110952	40	0	0.00	0.00	0.00	31.99	0.40
615	48110953	115	8	69.57	57.32	18.03	130.96	1.16
616	48110954	75	1	13.33	12.70	0.00	37.08	0.42
617	48110955	25	4	160.00	96.13	0.00	235.50	2.06
618	48110956	85	2	23.53	23.46	0.00	55.43	0.52
619	48110957	60	4	66.67	64.08	1.88	120.17	1.08
620	48110958	85	16	188.24	232.39	**139.04**	673.29	3.02
621	48110960	110	9	81.82	95.83	38.16	148.03	1.35
622	48110961	65	2	30.77	33.18	0.00	67.21	0.63
623	48110962	160	13	81.25	108.71	55.28	150.98	1.37
624	48110965	70	3	42.86	39.19	0.00	86.52	0.77
625	48110966	60	3	50.00	40.18	0.00	96.60	0.86
626	48110967	75	3	40.00	44.62	0.00	82.84	0.73
627	48110968	85	3	35.29	50.49	0.00	73.48	0.67
628	48110971	170	8	47.06	56.29	17.69	93.35	0.83
629	48110972	1770	106	59.89	55.31	44.78	119.68	1.07
630	48110973	580	29	50.00	45.80	29.52	99.92	0.89
631	48110974	110	3	27.27	22.47	0.00	59.15	0.55

No.	Dissemination area number	Children population 0-14 years	No. asthma ED visits	Crude rate per 1,000	Directly standardized rates per 1,000[a]			Bayesian smoothed morbidity ratio
					Rate	95% CI		
632	48110975	60	0	0.00	0.00	0.00	0.00	0.33
633	48110976	470	10	21.28	21.43	8.50	35.19	0.41
634	48110977	120	3	25.00	34.27	0.00	54.42	0.52
635	48110978	110	2	18.18	17.79	0.00	37.84	0.44
636	48110979	185	7	37.84	39.74	10.06	76.47	0.69
637	48110980	85	1	11.77	16.10	0.00	30.97	0.39
638	48110981	110	2	18.18	17.14	0.00	37.84	0.44
639	48110982	120	1	8.33	8.05	0.00	0.00	0.31
640	48110983	95	2	21.05	42.32	0.00	46.84	0.48
641	48110984	85	0	0.00	0.00	0.00	0.00	0.27
642	48110985	45	1	22.22	31.74	0.00	61.23	0.57
643	48110986	60	1	16.67	16.10	0.00	46.19	0.48
644	48110987	135	4	29.63	34.42	1.83	61.23	0.57
645	48110989	125	1	8.00	6.44	0.00	0.00	0.30
646	48110991	115	4	34.78	39.79	2.32	70.52	0.65
647	48110992	150	13	86.67	85.75	41.49	161.55	1.45
648	48110993	85	0	0.00	0.00	0.00	0.00	0.27
649	48110994	115	6	52.17	51.38	11.35	100.45	0.90
650	48110995	245	5	20.41	19.62	2.78	36.20	0.41
651	48110996	65	3	46.15	80.25	0.00	91.57	0.81
652	48110997	90	1	11.11	6.56	0.00	26.47	0.38
653	48110998	90	0	0.00	0.00	0.00	0.00	0.27
654	48110999	115	4	34.78	38.60	1.13	70.64	0.65
655	48111000	80	2	25.00	23.00	0.00	59.15	0.55
656	48111001	50	4	80.00	202.48	**64.22**	139.80	1.24
657	48111002	115	13	113.04	102.41	46.68	217.45	1.85
658	48111003	130	3	23.08	15.87	0.00	46.84	0.49
659	48111006	155	10	64.52	62.60	22.79	123.70	1.10
660	48111007	145	2	13.79	12.79	0.00	20.73	0.36
661	48111008	90	1	11.11	9.07	0.00	26.59	0.38
662	48111009	80	8	100.00	106.28	34.02	178.54	1.59
663	48111010	115	4	34.78	40.65	0.93	71.20	0.65
664	48111012	280	12	42.86	42.73	18.96	85.16	0.76
665	48111013	70	6	85.71	91.57	23.39	150.12	1.36
666	48111014	230	13	56.52	57.34	26.76	111.90	0.98
667	48111016	110	11	100.00	102.47	45.67	185.49	1.64
668	48111017	40	3	75.00	63.49	0.00	126.29	1.15
669	48111021	100	10	100.00	96.49	40.22	185.39	1.62
670	48111022	80	3	37.50	35.89	0.00	77.57	0.70
671	48111023	70	3	42.86	45.51	0.00	86.54	0.77
672	48111024	60	3	50.00	55.20	0.00	96.76	0.86
673	48111025	235	5	21.28	29.99	4.50	37.60	0.43
674	48111026	90	7	77.78	76.95	19.63	141.94	1.27
675	48111027	115	9	78.26	91.43	31.21	143.58	1.30
676	48111028	230	16	69.57	73.35	39.19	132.60	1.20
677	48111029	140	6	42.86	51.36	12.75	85.64	0.76
678	48111030	210	12	57.14	59.40	26.93	112.57	0.99
679	48111035	90	5	55.56	56.77	9.05	107.48	0.94
680	48111036	105	13	123.81	146.25	**76.94**	230.80	2.01

No.	Dissemination area number	Children population 0-14 years	No. asthma ED visits	Crude rate per 1,000	Directly standardized rates per 1,000[a]			Bayesian smoothed morbidity ratio
					Rate	95% CI		
681	48111037	45	1	22.22	31.74	0.00	61.23	0.57
682	48111038	80	1	12.50	12.70	0.00	34.36	0.41
683	48111039	50	1	20.00	21.16	0.00	58.05	0.54
684	48111041	85	5	58.82	61.52	11.44	112.29	0.99
685	48111042	60	3	50.00	43.76	0.00	96.79	0.86
686	48111043	115	3	26.09	23.81	0.00	56.46	0.53
687	48111045	120	3	25.00	29.40	0.00	54.48	0.52
688	48111046	215	10	46.51	45.35	19.33	92.14	0.82
689	48111047	125	0	0.00	0.00	0.00	0.00	0.22
690	48111048	175	1	5.71	8.05	0.00	0.00	0.24
691	48111049	90	1	11.11	9.20	0.00	26.59	0.38
692	48111050	90	7	77.78	76.35	19.59	142.18	1.27
693	48111051	85	0	0.00	0.00	0.00	0.00	0.27
694	48111052	90	0	0.00	0.00	0.00	0.00	0.27
695	48111053	55	2	36.36	44.62	0.00	79.47	0.70
696	48111054	55	0	0.00	0.00	0.00	0.00	0.35
697	48111055	55	2	36.36	32.19	0.00	79.47	0.70
698	48111056	105	4	38.10	41.48	0.00	76.63	0.70
699	48111057	95	14	147.37	145.70	**76.67**	285.77	2.37
700	48111058	115	0	0.00	0.00	0.00	0.00	0.23
701	48111059	110	5	45.46	39.11	4.12	90.77	0.80
702	48111060	70	1	14.29	10.73	0.00	42.13	0.44
703	48111061	95	5	52.63	40.24	7.25	102.31	0.90
704	48111062	55	0	0.00	0.00	0.00	0.00	0.35
705	48111063	80	10	125.00	183.86	**86.82**	229.70	1.98
706	48111064	55	1	18.18	24.04	0.00	52.98	0.51
707	48111065	55	1	18.18	31.74	0.00	53.32	0.51
708	48111066	95	3	31.58	26.61	0.00	65.82	0.62
709	48111067	100	5	50.00	49.05	7.64	98.27	0.87
710	48111068	90	2	22.22	21.03	0.00	49.74	0.50
711	48111069	55	0	0.00	0.00	0.00	12.65	0.35
712	48111070	65	3	46.15	55.62	0.00	91.87	0.81
713	48111071	85	8	94.12	94.76	32.10	167.41	1.51
714	48111072	90	11	122.22	135.66	**64.11**	227.95	1.96
715	48111073	75	4	53.33	90.27	0.00	103.74	0.91
716	48111074	65	6	92.31	86.38	21.78	160.90	1.44
717	48111075	65	3	46.15	46.17	0.00	91.93	0.81
718	48111076	75	0	0.00	0.00	0.00	0.00	0.29
719	48111077	100	3	30.00	30.91	0.00	62.10	0.59
720	48111078	45	1	22.22	21.16	0.00	61.23	0.57
721	48111079	85	1	11.77	10.58	0.00	30.97	0.39
722	48111080	75	1	13.33	16.10	0.00	37.08	0.42
723	48111081	30	1	33.33	31.74	0.00	80.12	0.72
724	48111082	70	3	42.86	37.33	0.00	86.72	0.77
725	48111083	115	2	17.39	15.98	0.00	37.08	0.42
726	48111084	105	1	9.52	9.07	0.00	0.00	0.34
727	48111086	95	1	10.53	9.07	0.00	23.62	0.36
728	48111087	90	2	22.22	25.39	0.00	49.74	0.50
729	48111088	115	2	17.39	14.43	0.00	37.08	0.42

No.	Dissemination area number	Children population 0-14 years	No. asthma ED visits	Crude rate per 1,000	Directly standardized rates per 1,000[a]			Bayesian smoothed morbidity ratio
					Rate	95% CI		
730	48111089	85	5	58.82	56.64	8.59	112.39	0.99
731	48111090	75	13	173.33	158.21	**86.38**	354.64	2.73
732	48111091	70	1	14.29	12.02	0.00	42.13	0.44
733	48111092	75	5	66.67	61.34	6.57	122.13	1.09
734	48111093	40	2	50.00	68.26	0.00	98.24	0.86
735	48111094	45	4	88.89	109.46	6.68	146.79	1.34
736	48111095	25	4	160.00	84.65	0.00	238.07	2.06
737	48111096	0	0					
738	48111097	175	15	85.71	83.97	43.94	161.18	1.45
739	48111098	75	8	106.67	78.99	26.81	197.88	1.68
740	48111099	50	2	40.00	35.89	0.00	84.58	0.75
741	48111100	70	2	28.57	30.30	0.00	62.30	0.60
742	48111101	50	4	80.00	75.56	6.01	139.89	1.24
743	48111102	75	10	133.33	139.64	**58.80**	243.66	2.09
744	48111103	85	5	58.82	71.72	11.27	112.42	0.99
745	48111104	65	4	61.54	61.38	1.32	115.89	1.01
746	48111106	0	0					
747	48111107	265	27	101.89	101.50	**65.12**	204.78	1.75
748	48111108	125	8	64.00	65.51	20.92	120.49	1.08
749	48111109	85	3	35.29	38.09	0.00	74.09	0.67
750	48111110	90	2	22.22	24.89	0.00	49.80	0.50
751	48111111	205	14	68.29	66.42	32.47	132.18	1.17
752	48111112	1495	78	52.17	50.49	39.30	105.50	0.93
753	48111113	60	3	50.00	48.06	0.00	96.81	0.86
754	48111114	95	5	52.63	61.82	10.14	102.36	0.90
755	48111115	95	1	10.53	9.20	0.00	23.62	0.36
756	48111116	220	7	31.82	31.29	8.52	61.82	0.59
757	48111117	75	3	40.00	40.00	0.00	82.95	0.73
758	48111118	1025	56	54.63	51.73	38.43	111.21	0.97
759	48111119	155	9	58.06	56.16	20.29	113.38	1.00
760	48111124	10	0	0.00	0.00	0.00	76.04	0.68
761	48111125	75	4	53.33	44.89	2.59	103.82	0.91
762	48111126	75	2	26.67	27.12	0.00	60.97	0.57
763	48111127	70	5	71.43	70.48	10.79	128.37	1.15
764	48111128	70	3	42.86	50.01	0.00	87.07	0.77
765	48111129	90	3	33.33	40.76	0.00	69.20	0.64
766	48111130	95	6	63.16	60.69	13.29	118.66	1.05
767	48111131	100	10	100.00	100.03	39.36	185.39	1.62
768	48111132	105	10	95.24	102.93	40.96	173.09	1.55
769	48111133	50	3	60.00	74.51	0.00	111.64	0.98
770	48111134	5	2	400.00	317.43	**317.43**	337.34	2.65
771	48111135	75	2	26.67	25.17	0.00	60.98	0.57
772	48111136	35	1	28.57	21.16	0.00	72.74	0.66
773	48111137	90	6	66.67	62.68	13.07	124.22	1.10
774	48111138	60	4	66.67	60.60	3.91	120.21	1.08
775	48111139	55	1	18.18	15.87	0.00	53.37	0.51
776	48111140	75	12	160.00	153.44	**77.75**	317.00	2.52
777	48111141	65	3	46.15	41.49	0.00	92.03	0.81
778	48111142	60	1	16.67	14.43	0.00	46.19	0.48

No.	Dissemination area number	Children population 0-14 years	No. asthma ED visits	Crude rate per 1,000	Directly standardized rates per 1,000[a]			Bayesian smoothed morbidity ratio
					Rate	95% CI		
779	48111143	75	6	80.00	68.08	16.47	142.70	1.28
780	48111144	25	0	0.00	0.00	0.00	49.38	0.50
781	48111145	75	2	26.67	28.85	0.00	60.98	0.57
782	48111146	85	6	70.59	64.08	15.75	129.89	1.16
783	48111147	85	2	23.53	25.11	0.00	55.43	0.52
784	48111148	90	3	33.33	30.42	0.00	69.44	0.64
785	48111149	105	2	19.05	18.40	0.00	42.13	0.45
786	48111150	130	8	61.54	55.71	18.44	117.93	1.04
787	48111152	230	25	108.70	105.07	**65.91**	218.57	1.86
788	48111153	190	5	26.32	25.68	3.40	54.06	0.51
789	48111154	155	6	38.71	37.40	7.31	78.35	0.70
790	48111155	50	0	0.00	0.00	0.00	23.55	0.36
791	48111156	65	5	76.92	75.02	12.95	137.12	1.22
792	48111157	270	30	111.11	97.31	**63.66**	222.03	1.91
793	48111158	55	2	36.36	63.49	0.00	79.47	0.70
794	48111159	45	9	200.00	188.82	**71.73**	550.58	2.94
795	48111160	95	19	200.00	211.41	**132.72**	0.00	3.25
796	48111161	0	0					
797	48111162	85	6	70.59	79.30	18.22	129.93	1.16
798	48111163	90	2	22.22	16.10	0.00	49.85	0.50
799	48111164	40	0	0.00	0.00	0.00	32.17	0.40
800	48111165	180	14	77.78	80.86	41.21	145.14	1.32
801	48111167	75	8	106.67	104.98	41.20	198.27	1.68
802	48111168	75	3	40.00	41.73	0.00	82.95	0.73
803	48111169	110	9	81.82	78.65	25.83	148.23	1.35
804	48111171	80	2	25.00	27.30	0.00	59.15	0.55
805	48111172	150	4	26.67	23.75	0.97	56.24	0.53
806	48111173	105	4	38.10	31.74	2.23	76.69	0.70
807	48111174	40	1	25.00	24.04	0.00	64.36	0.61
808	48111176	125	3	24.00	23.81	0.00	49.72	0.50
809	48111180	100	1	10.00	10.31	0.00	18.93	0.35
810	48111181	5	2	400.00	437.65	**245.26**	339.94	2.65
811	48111182	100	0	0.00	0.00	0.00	0.00	0.25
812	48111183	90	3	33.33	38.45	0.00	69.57	0.64
813	48111184	115	4	34.78	41.15	0.93	71.37	0.65
814	48111185	125	1	8.00	7.94	0.00	0.00	0.30
815	48111187	55	1	18.18	15.87	0.00	53.46	0.51
816	48111188	110	4	36.36	44.89	2.59	74.52	0.67
817	48111189	65	2	30.77	30.52	0.00	67.21	0.63
818	48111190	70	3	42.86	38.45	0.00	87.15	0.77
819	48111192	95	3	31.58	38.27	0.00	65.82	0.62
820	48111193	85	4	47.06	46.78	0.69	92.87	0.82
821	48111194	100	10	100.00	101.50	41.92	185.39	1.62
822	48111195	110	1	9.09	15.87	0.00	0.00	0.33
823	48111202	285	12	42.10	55.69	24.14	84.66	0.75
824	48111203	130	6	46.15	56.53	13.15	90.77	0.81
825	48111204	555	20	36.04	36.01	20.50	69.66	0.65
826	48111205	125	6	48.00	53.40	13.44	94.28	0.84
827	48111206	120	6	50.00	57.82	9.04	98.66	0.87

No.	Dissemination area number	Children population 0-14 years	No. asthma ED visits	Crude rate per 1,000	Directly standardized rates per 1,000[a]			Bayesian smoothed morbidity ratio
					Rate	95% CI		
828	48111207	60	3	50.00	42.62	0.00	96.85	0.86
829	48111208	150	22	146.67	209.87	**145.28**	305.91	2.45
830	48111209	105	3	28.57	34.59	0.00	61.23	0.57
831	48111210	90	2	22.22	19.50	0.00	50.11	0.50
832	48111243	2120	122	57.55	53.73	44.15	116.23	1.03
833	48111244	0	0					
834	48111247	135	0	0.00	0.00	0.00	0.00	0.21
835	48111248	60	1	16.67	18.03	0.00	46.19	0.48
836	48111249	165	19	115.15	112.19	**65.24**	225.72	1.93
837	48111250	100	14	140.00	129.42	**65.01**	274.47	2.27
838	48111251	65	2	30.77	28.79	0.00	67.21	0.63
839	48111258	90	25	277.78	282.92	**161.89**	0.00	4.54
840	48111260	25	0	0.00	0.00	0.00	49.40	0.50
841	48111261	135	7	51.85	51.82	14.41	100.33	0.90
842	48111262	70	4	57.14	63.71	5.29	109.38	0.96
843	48111263	80	5	62.50	65.19	9.88	117.42	1.04
844	48111265	140	4	28.57	27.96	0.83	59.41	0.56
845	48111266	105	1	9.52	9.07	0.00	0.00	0.34
846	48111268	95	2	21.05	20.89	0.00	46.84	0.48
847	48111269	80	3	37.50	46.92	0.00	77.61	0.70
848	48111270	65	0	0.00	0.00	0.00	0.00	0.32
849	48111271	65	4	61.54	76.36	7.51	116.10	1.01
850	48111272	50	1	20.00	24.04	0.00	58.18	0.54
851	48111273	155	2	12.90	16.22	0.00	0.00	0.34
852	48111275	65	2	30.77	27.30	0.00	67.28	0.63
853	48111276	45	0	0.00	0.00	0.00	29.07	0.38
854	48111277	50	3	60.00	89.78	0.00	111.70	0.98
855	48111278	90	5	55.56	74.22	14.85	107.50	0.94
856	48111279	70	3	42.86	84.95	0.00	87.18	0.77
857	48111280	90	3	33.33	38.09	0.00	69.57	0.64
858	48111281	85	2	23.53	25.39	0.00	55.49	0.52
859	48111282	105	6	57.14	58.64	12.31	110.58	0.97
860	48111283	50	1	20.00	32.19	0.00	58.35	0.54
861	48111284	60	1	16.67	16.10	0.00	46.19	0.48
862	48111285	70	0	0.00	0.00	0.00	0.00	0.31
863	48111286	10	1	100.00	64.38	0.00	133.35	1.20
864	48111287	30	3	100.00	193.15	54.92	155.54	1.40
865	48111288	15	3	150.00	165.43	0.00	264.51	2.20
866	48111294	50	3	60.00	72.13	0.00	111.86	0.98
867	48111295	25	0	0.00	0.00	0.00	49.50	0.50
868	48111296	10	0	0.00	0.00	0.00	76.06	0.68
869	48111297	40	1	25.00	21.16	0.00	64.44	0.61
870	48111298	45	0	0.00	0.00	0.00	29.71	0.38
871	48111299	40	1	25.00	21.16	0.00	64.44	0.61
872	48111300	50	1	20.00	12.70	0.00	58.36	0.54
873	48111301	75	1	13.33	10.73	0.00	37.08	0.42
874	48111302	80	3	37.50	38.63	0.00	77.86	0.70
875	48111303	45	2	44.44	31.74	0.00	90.46	0.80
876	48111304	75	3	40.00	43.79	0.00	83.05	0.73

No.	Dissemination area number	Children population 0-14 years	No. asthma ED visits	Crude rate per 1,000	Directly standardized rates per 1,000[a]			Bayesian smoothed morbidity ratio
					Rate	95% CI		
877	48111305	55	1	18.18	12.70	0.00	53.53	0.51
878	48111306	25	1	40.00	31.74	0.00	89.22	0.79
879	48111307	35	6	171.43	174.22	48.95	293.84	2.38
880	48111308	5	13	650.00	640.84	**433.64**	0.00	30.94
881	48111309	30	2	66.67	72.13	0.00	117.12	1.03
882	48111310	70	2	28.57	26.68	0.00	62.42	0.60
883	48111311	70	6	85.71	76.90	19.63	150.71	1.36
884	48111312	95	2	21.05	18.03	0.00	46.84	0.48
885	48111313	105	3	28.57	28.82	0.00	61.23	0.57
886	48111314	50	1	20.00	21.16	0.00	58.53	0.54
887	48111315	75	2	26.67	25.01	0.00	61.04	0.57
888	48111316	65	3	46.15	46.83	0.00	92.05	0.81
889	48111317	135	4	29.63	52.98	2.22	61.23	0.57
890	48111318	110	2	18.18	15.87	0.00	37.86	0.44
891	48111319	20	4	200.00	200.00	13.60	299.49	2.42
892	48111320	45	8	177.78	175.96	**65.39**	332.74	2.60
893	48111321	45	3	66.67	63.93	0.00	119.62	1.06
894	48111322	60	1	16.67	15.87	0.00	46.19	0.48
895	48111323	70	4	57.14	57.60	2.81	109.47	0.96
896	48111324	105	5	47.62	46.71	6.98	93.73	0.83
897	48111325	90	1	11.11	21.16	0.00	26.59	0.38
898	48111326	100	2	20.00	19.85	0.00	45.58	0.47
899	48111327	195	6	30.77	33.41	6.45	61.23	0.58
900	48111328	110	1	9.09	9.02	0.00	0.00	0.33
901	48111329	95	2	21.05	21.46	0.00	46.84	0.48
902	48111330	95	7	73.68	95.86	24.30	135.07	1.21
903	48111331	75	2	26.67	44.62	0.00	61.05	0.57
904	48111332	70	0	0.00	0.00	0.00	0.00	0.31
905	48111333	95	2	21.05	21.03	0.00	46.84	0.48
906	48111334	80	3	37.50	33.49	0.00	77.86	0.70
907	48111335	75	9	120.00	105.61	43.93	221.48	1.88
908	48111336	100	8	80.00	76.08	23.79	144.62	1.31
909	48111371	135	21	155.56	177.20	**114.38**	325.74	2.58
910	48111372	90	3	33.33	30.91	0.00	69.57	0.64
911	48111373	100	6	60.00	55.00	13.81	114.86	1.01
912	48111433	140	9	64.29	68.46	26.33	120.76	1.09
913	48111434	30	0	0.00	0.00	0.00	43.15	0.46
914	48111435	155	7	45.16	44.47	12.13	89.75	0.80
915	48111436	150	6	40.00	42.69	9.32	80.48	0.72
916	48111438	150	15	100.00	115.25	**59.52**	194.56	1.67
917	48111442	120	2	16.67	14.37	0.00	35.40	0.41
918	48111443	45	0	0.00	0.00	0.00	30.21	0.38
919	48111444	145	16	110.35	111.97	**60.65**	213.36	1.84
920	48111445	55	12	218.18	224.29	**114.27**	0.00	3.33
921	48111446	150	12	80.00	76.05	34.67	147.43	1.34
922	48111447	170	19	111.76	113.95	**66.12**	220.45	1.88
923	48111448	105	6	57.14	59.38	11.13	110.58	0.97
924	48111449	60	6	100.00	116.84	34.15	170.56	1.54
925	48111451	205	13	63.42	63.41	30.05	123.17	1.09

No.	Dissemination area number	Children population 0-14 years	No. asthma ED visits	Crude rate per 1,000	Directly standardized rates per 1,000[a]			Bayesian smoothed morbidity ratio
					Rate	95% CI		
926	48111452	120	12	100.00	90.17	40.44	188.21	1.65
927	48111453	90	8	88.89	86.11	29.36	159.84	1.44
928	48111454	75	19	253.33	238.08	**142.30**	0.00	4.05
929	48111455	60	1	16.67	15.87	0.00	46.53	0.48
930	48111456	135	9	66.67	66.73	25.58	125.66	1.13
931	48111457	145	16	110.35	125.20	**67.22**	214.74	1.84
932	48111458	70	5	71.43	60.96	8.80	128.60	1.15
933	48111459	70	5	71.43	78.54	12.07	128.65	1.15
934	48111460	65	11	169.23	176.33	**82.96**	334.31	2.62
935	48111461	55	14	254.54	284.95	**154.01**	0.00	3.91
936	48111462	105	4	38.10	39.38	1.65	76.82	0.70
937	48111463	55	2	36.36	64.38	0.00	79.64	0.70
938	48111464	55	2	36.36	39.92	0.00	79.64	0.70
939	48111465	75	7	93.33	92.70	27.29	164.07	1.48
940	48111466	50	0	0.00	0.00	0.00	23.55	0.36
941	48111467	115	3	26.09	31.08	0.00	56.48	0.53
942	48111468	95	8	84.21	95.36	29.12	151.65	1.37
943	48111469	40	8	200.00	202.38	**83.67**	484.63	2.87
944	48111471	125	12	96.00	98.62	49.00	177.25	1.59
945	48111475	195	7	35.90	36.28	9.98	71.56	0.65
946	48111476	95	8	84.21	99.67	29.68	151.67	1.37
947	48111477	105	10	95.24	96.61	39.81	173.18	1.55
948	48111478	265	10	37.74	36.75	14.48	75.66	0.68
949	48111479	65	5	76.92	78.14	13.48	137.26	1.22
950	48111480	40	20	444.44	430.80	**311.02**	0.00	7.71
951	48111495	205	14	68.29	75.47	36.87	132.57	1.17
952	48111496	190	6	31.58	27.17	5.78	61.25	0.59
953	48111497	230	24	104.35	104.14	**64.54**	211.10	1.78
954	48111499	185	10	54.05	54.04	21.76	106.39	0.94
955	48111500	170	4	23.53	21.80	0.00	46.19	0.48
956	48111501	140	5	35.71	39.13	5.40	72.12	0.66
957	48111502	205	33	160.98	162.02	**110.79**	365.24	2.74
958	48111503	175	13	74.29	75.12	36.82	140.90	1.26
959	48111504	250	10	40.00	43.08	16.97	80.08	0.72
960	48111505	100	6	60.00	63.05	14.19	114.93	1.01
961	48111506	75	7	93.33	97.71	31.34	164.11	1.48
962	48111507	140	5	35.71	36.01	4.93	72.31	0.66
963	48111508	255	15	58.82	60.02	31.61	116.13	1.02
964	48111509	85	4	47.06	36.07	2.54	92.98	0.82
965	48111510	55	4	72.73	62.71	5.22	126.99	1.15
966	48111511	155	3	19.35	20.12	0.00	37.60	0.43
967	48111512	115	7	60.87	73.11	21.17	116.65	1.03
968	48111513	165	4	24.24	30.78	0.00	47.50	0.49
969	48111514	165	23	139.39	142.32	**88.63**	284.56	2.34
970	48111515	100	1	10.00	10.31	0.00	18.93	0.35
971	48111516	80	6	75.00	90.54	18.12	136.56	1.22
972	48111517	75	2	26.67	18.40	0.00	61.05	0.57
973	48111518	110	11	100.00	84.04	37.17	185.55	1.64
974	48111519	55	0	0.00	0.00	0.00	14.38	0.35

No.	Dissemination area number	Children population 0-14 years	No. asthma ED visits	Crude rate per 1,000	Directly standardized rates per 1,000[a]			Bayesian smoothed morbidity ratio
					Rate	95% CI		
975	48111520	40	0	0.00	0.00	0.00	32.21	0.40
976	48111521	90	0	0.00	0.00	0.00	0.00	0.27
977	48111522	75	1	13.33	9.02	0.00	37.08	0.42
978	48111523	55	3	54.54	45.51	0.00	104.80	0.92
979	48111524	40	1	25.00	18.03	0.00	64.44	0.61
980	48111525	65	0	0.00	0.00	0.00	0.00	0.32
981	48111526	75	5	66.67	87.11	14.92	122.28	1.09
982	48111527	20	1	50.00	32.19	0.00	99.86	0.88
983	48111528	195	3	15.39	15.19	0.00	19.29	0.36
984	48111529	200	19	95.00	94.38	54.53	184.05	1.61
985	48111530	30	10	333.33	346.80	**151.83**	0.00	4.68
986	48111531	200	18	90.00	95.01	53.71	168.00	1.53
987	48111532	110	3	27.27	27.42	0.00	59.15	0.55
988	48111533	55	10	181.82	160.96	**90.42**	371.52	2.75
989	48111534	115	22	191.30	204.47	**130.09**	703.18	3.15
990	48111536	30	1	33.33	72.13	0.00	80.38	0.72
991	48111537	185	4	21.62	22.27	0.82	42.13	0.45
992	48111538	115	4	34.78	34.16	0.32	71.37	0.65
993	48111539	125	5	40.00	38.76	5.39	80.77	0.72
994	48111540	285	9	31.58	34.54	12.27	61.23	0.58
995	48111541	230	10	43.48	42.08	16.28	87.23	0.77
996	48111542	740	56	75.68	75.06	**56.28**	145.45	1.34
997	48111543	200	3	15.00	13.80	0.00	15.27	0.35
998	48111544	155	2	12.90	11.71	0.00	0.00	0.34
999	48111545	155	15	96.77	96.00	50.05	184.29	1.62
1000	48111546	140	4	28.57	29.90	1.26	59.41	0.56
1001	48111547	95	0	0.00	0.00	0.00	0.00	0.26
1002	48111548	150	0	0.00	0.00	0.00	0.00	0.20
1003	48111549	140	0	0.00	0.00	0.00	0.00	0.21
1004	48111550	140	0	0.00	0.00	0.00	0.00	0.21
1005	48111551	90	0	0.00	0.00	0.00	0.00	0.27
1006	48111552	140	0	0.00	0.00	0.00	0.00	0.21
1007	48111553	155	0	0.00	0.00	0.00	0.00	0.19
1008	48111554	80	0	0.00	0.00	0.00	0.00	0.28
1009	48111555	115	0	0.00	0.00	0.00	0.00	0.23
1010	48111556	75	0	0.00	0.00	0.00	0.00	0.29
1011	48111557	125	0	0.00	0.00	0.00	0.00	0.22
1012	48111558	155	0	0.00	0.00	0.00	0.00	0.19
1013	48111559	140	0	0.00	0.00	0.00	0.00	0.21
1014	48111560	105	0	0.00	0.00	0.00	0.00	0.24
1015	48111561	140	0	0.00	0.00	0.00	0.00	0.21
1016	48111562	110	0	0.00	0.00	0.00	0.00	0.24
1017	48111563	150	0	0.00	0.00	0.00	0.00	0.20
1018	48111564	75	0	0.00	0.00	0.00	0.00	0.29
1019	48111565	75	0	0.00	0.00	0.00	0.00	0.29
1020	48111566	275	0	0.00	0.00	0.00	0.00	0.14
1021	48111567	80	0	0.00	0.00	0.00	0.00	0.28
1022	48111568	50	0	0.00	0.00	0.00	23.62	0.36
1023	48111569	65	0	0.00	0.00	0.00	0.00	0.32

No.	Dissemination area number	Children population 0-14 years	No. asthma ED visits	Crude rate per 1,000	Directly standardized rates per 1,000[a]			Bayesian smoothed morbidity ratio
					Rate	95% CI		
1024	48111570	110	0	0.00	0.00	0.00	0.00	0.24
1025	48111571	195	0	0.00	0.00	0.00	0.00	0.17
1026	48111572	145	0	0.00	0.00	0.00	0.00	0.20
1027	48111573	170	0	0.00	0.00	0.00	0.00	0.18
1028	48111574	160	0	0.00	0.00	0.00	0.00	0.19
1029	48111575	220	0	0.00	0.00	0.00	0.00	0.16
1030	48111576	95	0	0.00	0.00	0.00	0.00	0.26
1031	48111577	145	0	0.00	0.00	0.00	0.00	0.20
1032	48111578	80	0	0.00	0.00	0.00	0.00	0.28
1033	48111579	100	0	0.00	0.00	0.00	0.00	0.25
1034	48111580	150	0	0.00	0.00	0.00	0.00	0.20
1035	48111581	345	0	0.00	0.00	0.00	0.00	0.12
1036	48111582	250	0	0.00	0.00	0.00	0.00	0.14
1037	48111583	85	45	529.41	613.46	**523.73**	0.00	8.85
1038	48111584	500	45	90.00	90.32	**64.74**	174.78	1.58
1039	48111585	125	0	0.00	0.00	0.00	0.00	0.22
1040	48111586	70	0	0.00	0.00	0.00	0.00	0.31
1041	48111587	175	4	22.86	23.03	0.76	45.29	0.47
1042	48111588	215	7	32.56	31.04	8.76	63.57	0.60
1043	48111589	100	2	20.00	23.50	0.00	45.58	0.47
1044	48111590	70	6	85.71	86.44	20.09	150.98	1.36
1045	48111591	80	7	87.50	98.56	24.64	155.54	1.40
1046	48111592	350	38	108.57	109.52	**76.51**	220.49	1.88
1047	48111593	200	22	110.00	95.47	53.97	218.73	1.87
1048	48111594	260	20	76.92	65.25	37.99	145.20	1.33
1049	48111595	110	11	100.00	95.32	39.15	186.57	1.64
1050	48111596	195	18	92.31	92.55	50.94	174.78	1.57
1051	48111597	140	22	157.14	151.79	**92.47**	333.22	2.62
1052	48111598	115	3	26.09	26.18	0.00	56.48	0.53
1053	48111599	185	5	27.03	28.05	4.11	55.98	0.52
1054	48111600	55	5	90.91	152.57	11.93	154.67	1.40
1055	48111601	85	3	35.29	35.45	0.00	74.25	0.67
1056	48111602	195	5	25.64	25.27	3.21	49.72	0.50
1057	48111603	155	6	38.71	36.29	7.55	78.53	0.70
1058	48111604	110	0	0.00	0.00	0.00	0.00	0.24
1059	48111605	110	5	45.46	49.48	8.30	90.77	0.80
1060	48111606	90	4	44.44	46.99	1.53	88.03	0.79
1061	48111607	80	6	75.00	86.24	22.51	136.72	1.22
1062	48111608	135	0	0.00	0.00	0.00	0.00	0.21
1063	48111609	85	3	35.29	38.27	0.00	74.41	0.67
1064	48111610	105	3	28.57	26.41	0.00	61.23	0.57
1065	48111611	125	2	16.00	17.13	0.00	30.97	0.40
1066	48111612	105	0	0.00	0.00	0.00	0.00	0.24
1067	48111613	110	2	18.18	18.40	0.00	38.05	0.44
1068	48111614	195	6	30.77	30.92	6.53	61.23	0.58
1069	48111615	225	15	66.67	65.41	34.02	126.33	1.15
1070	48111616	90	1	11.11	21.16	0.00	26.59	0.38
1071	48111617	285	9	31.58	33.39	12.12	61.25	0.58
1072	48111618	215	8	37.21	55.41	18.68	74.52	0.67

No.	Dissemination area number	Children population 0-14 years	No. asthma ED visits	Crude rate per 1,000	Directly standardized rates per 1,000[a]			Bayesian smoothed morbidity ratio
					Rate	95% CI		
1073	48111619	240	12	50.00	50.01	22.42	99.68	0.88
1074	48111620	215	6	27.91	27.99	5.86	56.40	0.53
1075	48111621	85	0	0.00	0.00	0.00	0.00	0.27
1076	48111622	215	8	37.21	44.89	13.98	74.52	0.67
1077	48111623	580	19	32.76	32.99	18.47	62.10	0.59
1078	48111624	90	1	11.11	9.07	0.00	26.59	0.38
1079	48111625	100	2	20.00	18.03	0.00	45.58	0.47
1080	48111626	70	4	57.14	55.29	1.12	110.07	0.96
1081	48111627	100	4	40.00	41.06	1.74	81.37	0.73
1082	48111628	80	1	12.50	9.02	0.00	35.19	0.41
1083	48111629	100	1	10.00	10.73	0.00	18.93	0.35
1084	48111630	60	2	33.33	42.62	0.00	73.36	0.66
1085	48111631	65	2	30.77	37.26	0.00	67.33	0.63
1086	48111632	75	9	120.00	138.40	**57.18**	221.86	1.88
1087	48111633	120	3	25.00	22.75	0.00	54.67	0.52
1088	48111634	135	3	22.22	22.32	0.00	46.19	0.47
1089	48111635	90	4	44.44	58.35	0.00	88.10	0.79
1090	48111636	80	1	12.50	21.16	0.00	35.19	0.41
1091	48111637	65	5	76.92	121.63	24.31	137.41	1.22
1092	48111638	125	6	48.00	56.15	12.44	94.62	0.84
1093	48111639	55	1	18.18	14.43	0.00	54.05	0.51
1094	48111640	65	1	15.39	15.87	0.00	45.13	0.46
1095	48111641	115	2	17.39	17.08	0.00	37.08	0.42
1096	48111642	80	1	12.50	12.88	0.00	35.19	0.41
1097	48111643	145	0	0.00	0.00	0.00	0.00	0.20
1098	48111644	80	0	0.00	0.00	0.00	0.00	0.28
1099	48111645	95	2	21.05	25.39	0.00	46.84	0.48
1100	48111646	115	2	17.39	15.26	0.00	37.31	0.42
1101	48111647	145	1	6.90	10.58	0.00	0.00	0.28
1102	48111648	170	7	41.18	49.78	14.40	83.22	0.74
1103	48111649	230	7	30.43	33.23	9.13	59.87	0.57
1104	48111650	135	1	7.41	12.70	0.00	0.00	0.29
1105	48111651	90	5	55.56	58.79	9.27	107.51	0.94
1106	48111652	145	1	6.90	5.55	0.00	0.00	0.28
1107	48111653	155	2	12.90	18.14	0.00	0.00	0.34
1108	48111654	125	3	24.00	21.58	0.00	49.72	0.50
1109	48111655	170	2	11.77	14.11	0.00	0.00	0.32
1110	48111656	850	40	47.06	45.11	31.19	93.94	0.84
1111	48111657	150	4	26.67	21.93	0.00	56.28	0.53
1112	48111658	125	1	8.00	5.85	0.00	0.00	0.30
1113	48111659	180	4	22.22	19.53	0.99	42.39	0.46
1114	48111660	185	5	27.03	26.35	2.84	56.24	0.52
1115	48111661	170	2	11.77	8.47	0.00	0.00	0.32
1116	48111662	110	4	36.36	34.11	1.44	74.52	0.67
1117	48111663	125	7	56.00	65.51	17.25	110.13	0.96
1118	48111664	120	3	25.00	33.18	0.00	55.08	0.52
1119	48111665	110	1	9.09	9.20	0.00	0.00	0.33
1120	48111666	120	5	41.67	44.33	7.42	84.16	0.75
1121	48111667	120	0	0.00	0.00	0.00	0.00	0.23

No.	Dissemination area number	Children population 0-14 years	No. asthma ED visits	Crude rate per 1,000	Directly standardized rates per 1,000[a]			Bayesian smoothed morbidity ratio
					Rate	95% CI		
1122	48111668	100	4	40.00	42.28	0.17	81.55	0.73
1123	48111669	115	3	26.09	22.16	0.00	56.65	0.53
1124	48111670	75	4	53.33	104.25	12.41	103.89	0.91
1125	48111671	90	4	44.44	54.50	3.50	88.43	0.79
1126	48111672	115	3	26.09	32.04	0.00	56.65	0.53
1127	48111673	115	2	17.39	15.45	0.00	37.31	0.42
1128	48111674	90	4	44.44	45.26	2.66	88.95	0.79
1129	48111675	115	4	34.78	34.16	0.32	71.39	0.65
1130	48111676	185	2	10.81	11.14	0.00	0.00	0.30
1131	48111677	110	2	18.18	23.89	0.00	38.08	0.44
1132	48111678	115	0	0.00	0.00	0.00	0.00	0.23
1133	48111679	105	3	28.57	26.68	0.00	61.23	0.57
1134	48111680	115	0	0.00	0.00	0.00	0.00	0.23
1135	48111681	85	0	0.00	0.00	0.00	0.00	0.27
1136	48111682	90	0	0.00	0.00	0.00	0.00	0.27
1137	48111683	95	1	10.53	12.70	0.00	24.73	0.36
1138	48111684	105	5	47.62	50.68	0.13	93.81	0.83
1139	48111685	100	0	0.00	0.00	0.00	0.00	0.25
1140	48111686	85	2	23.53	24.72	0.00	55.51	0.52
1141	48111687	125	9	72.00	103.31	44.10	134.16	1.20
1142	48111688	155	6	38.71	40.69	8.66	78.53	0.70
1143	48111689	75	0	0.00	0.00	0.00	0.00	0.29
1144	48111690	115	8	69.57	72.98	25.79	131.15	1.16
1145	48111691	160	1	6.25	7.05	0.00	0.00	0.26
1146	48111692	135	0	0.00	0.00	0.00	0.00	0.21
1147	48111693	195	0	0.00	0.00	0.00	0.00	0.17
1148	48111694	85	22	258.82	256.97	**166.18**	0.00	4.20
1149	48111695	95	0	0.00	0.00	0.00	0.00	0.26
1150	48111696	170	0	0.00	0.00	0.00	0.00	0.18
1151	48111697	170	0	0.00	0.00	0.00	0.00	0.18
1152	48111698	125	0	0.00	0.00	0.00	0.00	0.22
1153	48111699	270	7	25.93	26.68	7.31	47.97	0.49
1154	48111700	165	12	72.73	73.50	33.59	138.11	1.23
1155	48111701	125	9	72.00	68.42	24.97	134.17	1.20
1156	48111702	150	10	66.67	90.16	38.94	126.06	1.13
1157	48111703	85	17	200.00	199.32	**114.57**	848.03	3.21
1158	48111704	105	10	95.24	100.83	44.88	173.23	1.55
1159	48111705	85	4	47.06	56.30	3.59	93.13	0.82
1160	48111706	360	33	91.67	89.03	**60.01**	180.24	1.59
1161	48111707	585	26	44.44	44.40	27.83	89.75	0.79
1162	48111708	100	2	20.00	16.10	0.00	46.04	0.47
1163	48111709	140	5	35.71	33.05	3.80	72.65	0.66
1164	48111710	215	12	55.81	61.07	26.60	110.13	0.97
1165	48111711	115	25	217.39	247.39	**161.56**	0.00	3.60
1166	48111712	80	0	0.00	0.00	0.00	0.00	0.28
1167	48111713	135	8	59.26	59.71	19.78	115.25	1.01
1168	48111714	80	5	62.50	76.40	15.40	117.49	1.04
1169	48111715	55	6	109.09	110.73	17.32	191.21	1.65
1170	48111716	145	30	206.90	208.05	**142.16**	0.00	3.47

No.	Dissemination area number	Children population 0-14 years	No. asthma ED visits	Crude rate per 1,000	Directly standardized rates per 1,000[a]			Bayesian smoothed morbidity ratio
					Rate	95% CI		
1171	48111717	90	9	100.00	94.86	35.05	182.70	1.61
1172	48111718	25	4	160.00	131.29	18.93	238.38	2.06
1173	48111719	130	7	53.85	55.37	15.44	105.48	0.93
1174	48111720	35	5	142.86	108.69	24.32	229.84	1.99
1175	48111721	25	3	120.00	127.87	0.00	177.25	1.58
1176	48111722	105	15	142.86	154.58	**83.39**	284.08	2.32
1177	48111723	110	8	72.73	70.73	23.76	134.28	1.21
1178	48111724	165	10	60.61	62.43	25.53	117.54	1.04
1179	48111725	140	7	50.00	46.87	13.65	99.04	0.87
1180	48111726	400	55	137.50	139.20	**105.23**	295.42	2.40
1181	48111727	155	12	77.42	85.75	39.60	144.22	1.31
1182	48111728	170	18	105.88	105.18	**58.30**	207.37	1.78
1183	48111729	100	7	70.00	78.81	25.05	130.41	1.16
1184	48111730	155	27	174.19	178.20	**118.34**	541.76	2.93
1185	48111731	120	6	50.00	43.82	9.77	98.66	0.87
1186	48111732	105	9	85.71	86.34	32.79	156.27	1.40
1187	48111733	285	46	161.40	171.32	**126.00**	377.31	2.79
1188	48111734	80	8	100.00	101.08	38.06	178.79	1.59
1189	48111735	100	7	70.00	71.39	20.49	130.67	1.16
1190	48111736	160	8	50.00	47.12	15.88	99.16	0.87
1191	48111737	135	15	111.11	112.10	**58.75**	215.58	1.84
1192	48111738	65	0	0.00	0.00	0.00	0.00	0.32
1193	48111739	105	0	0.00	0.00	0.00	0.00	0.24
1194	48111740	115	2	17.39	19.25	0.00	37.60	0.42
1195	48111741	85	0	0.00	0.00	0.00	0.00	0.27
1196	48111784	0	0					
1197	48111785	0	0					
1198	48111786	90	2	22.22	31.74	0.00	50.15	0.50
1199	48111787	0	0					
1200	48111788	85	0	0.00	0.00	0.00	0.00	0.27
1201	48111789	210	56	266.67	293.28	**231.93**	0.00	4.58
1202	48111790	95	0	0.00	0.00	0.00	0.00	0.26
1203	48111791	80	0	0.00	0.00	0.00	0.00	0.28
1204	48111792	135	0	0.00	0.00	0.00	0.00	0.21
1205	48111793	110	65	590.91	585.77	**498.25**	0.00	10.07
1206	48111794	125	0	0.00	0.00	0.00	0.00	0.22
1207	48111795	60	0	0.00	0.00	0.00	0.00	0.33
1208	48111796	110	0	0.00	0.00	0.00	0.00	0.24
1209	48111797	120	0	0.00	0.00	0.00	0.00	0.23
1210	48111800	120	5	41.67	40.14	6.03	84.22	0.75
1211	48111801	385	56	145.46	147.47	**110.01**	317.74	2.53
1212	48111802	175	29	165.71	167.71	**113.94**	382.65	2.80
1213	48111803	120	3	25.00	24.14	0.00	55.08	0.52
1214	48111804	125	9	72.00	80.04	30.18	134.22	1.20
1215	48111805	75	8	106.67	128.76	**59.65**	198.58	1.68
1216	48111806	75	10	133.33	135.14	**56.93**	243.75	2.09
1217	48111807	130	8	61.54	64.28	22.10	117.97	1.04
1218	48111808	100	14	140.00	139.01	**73.23**	278.64	2.27
1219	48111809	125	18	144.00	156.24	**91.94**	290.37	2.38

No.	Dissemination area number	Children population 0-14 years	No. asthma ED visits	Crude rate per 1,000	Directly standardized rates per 1,000[a]			Bayesian smoothed morbidity ratio
					Rate	95% CI		
1220	48111810	85	0	0.00	0.00	0.00	0.00	0.27
1221	48111811	125	1	8.00	8.05	0.00	0.00	0.30
1222	48111812	130	13	100.00	102.17	50.43	191.27	1.66
1223	48111813	130	4	30.77	32.69	0.67	62.07	0.59
1224	48111814	105	11	104.76	86.29	38.24	200.14	1.70
1225	48111815	110	2	18.18	25.39	0.00	38.21	0.44
1226	48111816	100	22	220.00	196.01	**123.27**	0.00	3.60
1227	48111817	75	7	93.33	135.88	37.81	164.53	1.48
1228	48111818	130	9	69.23	72.40	29.58	131.22	1.16
1229	48111819	115	6	52.17	69.48	14.23	100.86	0.90
1230	48111820	100	5	50.00	59.33	8.02	98.30	0.87
1231	48111821	125	10	80.00	86.44	36.14	145.39	1.33
1232	48111822	70	12	171.43	185.10	**89.74**	340.74	2.68
1233	48111823	85	0	0.00	0.00	0.00	0.00	0.27
1234	48111824	405	34	83.95	83.57	**56.57**	161.79	1.46
1235	48111825	285	15	52.63	55.02	28.14	105.45	0.92
1236	48111826	105	9	85.71	94.07	36.48	156.78	1.40
1237	48111827	75	4	53.33	50.31	2.39	104.39	0.91
1238	48111828	85	4	47.06	50.16	2.06	93.28	0.82
1239	48111829	90	3	33.33	32.19	0.00	69.57	0.64
1240	48111830	70	4	57.14	43.30	0.74	110.10	0.96
1241	48111831	155	11	70.97	78.70	34.78	133.58	1.20
1242	48111832	290	15	51.72	51.84	26.28	104.52	0.91
1243	48111833	160	12	75.00	89.82	39.85	142.18	1.27
1244	48111834	285	17	59.65	57.42	30.55	117.63	1.04
1245	48111835	90	4	44.44	41.26	2.52	89.04	0.79
1246	48111836	80	4	50.00	54.49	2.47	97.75	0.86
1247	48111837	240	11	45.83	56.63	24.21	90.77	0.81
1248	48111838	90	82	911.11	926.42	**881.64**	0.00	15.58
1249	48111839	110	4	36.36	31.74	2.23	74.93	0.67
1250	48111840	110	0	0.00	0.00	0.00	0.00	0.24
1251	48111841	105	0	0.00	0.00	0.00	0.00	0.24
1252	48111842	95	1	10.53	9.07	0.00	26.45	0.36
1253	48111843	120	0	0.00	0.00	0.00	0.00	0.23
1254	48111844	130	0	0.00	0.00	0.00	0.00	0.22
1255	48111845	95	0	0.00	0.00	0.00	0.00	0.26
1256	48111846	120	0	0.00	0.00	0.00	0.00	0.23
1257	48111847	180	0	0.00	0.00	0.00	0.00	0.18
1258	48111848	185	0	0.00	0.00	0.00	0.00	0.17
1259	48111849	175	0	0.00	0.00	0.00	0.00	0.18
1260	48111850	250	0	0.00	0.00	0.00	0.00	0.14
1261	48111851	155	13	83.87	77.85	36.43	158.13	1.41
1262	48111852	165	3	18.18	14.92	0.00	32.54	0.41
1263	48111853	145	5	34.48	32.31	4.96	68.04	0.64
1264	48111854	185	14	75.68	78.15	39.65	143.54	1.29
1265	48111855	240	30	125.00	137.43	**92.17**	247.99	2.14
1266	48111856	165	0	0.00	0.00	0.00	0.00	0.19
1267	48111857	215	10	46.51	45.36	17.70	92.35	0.82
1268	48111858	90	4	44.44	58.35	0.00	89.05	0.79

No.	Dissemination area number	Children population 0-14 years	No. asthma ED visits	Crude rate per 1,000	Directly standardized rates per 1,000[a]			Bayesian smoothed morbidity ratio
					Rate	95% CI		
1269	48111859	70	9	128.57	148.48	**58.57**	230.33	2.00
1270	48111860	145	25	172.41	191.25	**126.74**	527.84	2.88
1271	48111861	100	8	80.00	85.48	27.43	144.87	1.31
1272	48111862	95	15	157.90	150.50	**80.55**	320.01	2.55
1273	48111863	70	7	100.00	100.27	29.68	174.78	1.57
1274	48111864	200	13	65.00	58.62	28.18	124.86	1.12
1275	48111865	100	9	90.00	91.08	36.71	161.80	1.47
1276	48111866	190	30	157.90	159.09	**106.31**	347.76	2.68
1277	48111867	450	37	82.22	77.56	52.95	160.43	1.44
1278	48111868	90	1	11.11	12.88	0.00	26.59	0.38
1279	48111869	140	24	171.43	179.63	**115.51**	403.95	2.86
1280	48111870	105	6	57.14	66.47	12.50	110.65	0.97
1281	48111871	225	14	62.22	62.19	30.44	120.15	1.08
1282	48111872	205	9	43.90	43.32	16.12	87.36	0.78
1283	48111873	90	34	377.78	385.29	**285.95**	0.00	6.25
1284	48111874	130	18	138.46	129.81	**74.12**	280.45	2.29
1285	48111875	105	6	57.14	59.88	12.27	110.80	0.97
1286	48111876	125	12	96.00	90.35	42.97	178.15	1.59
1287	48111877	210	21	100.00	102.04	**60.13**	199.53	1.70
1288	48111878	225	27	120.00	124.25	**80.81**	231.58	2.05
1289	48111879	140	12	85.71	101.06	50.26	158.15	1.43
1290	48111880	125	0	0.00	0.00	0.00	0.00	0.22
1291	48111881	135	19	140.74	142.41	**81.33**	284.15	2.33
1292	48111882	85	9	105.88	110.94	41.53	199.52	1.69
1293	48111883	130	7	53.85	51.64	12.50	105.50	0.93
1294	48111884	140	6	42.86	43.88	9.49	85.87	0.76
1295	48111885	100	5	50.00	50.22	7.94	98.66	0.87
1296	48111886	215	1	4.65	4.29	0.00	0.00	0.21
1297	48111887	130	1	7.69	6.44	0.00	0.00	0.30
1298	48111888	780	44	56.41	56.83	40.41	113.43	1.00
1299	48111889	125	9	72.00	65.84	24.52	134.26	1.20
1300	48111890	105	8	76.19	100.28	35.10	140.38	1.26
1301	48111891	140	10	71.43	72.75	28.84	134.07	1.20
1302	48111892	95	8	84.21	86.93	28.99	151.86	1.37
1303	48111893	95	4	42.10	50.14	1.61	85.07	0.76
1304	48111894	80	5	62.50	84.52	14.15	117.49	1.04
1305	48111895	110	9	81.82	88.79	34.01	149.63	1.35
1306	48111896	265	24	90.57	94.38	**58.83**	173.52	1.56
1307	48111897	140	1	7.14	7.15	0.00	0.00	0.28
1308	48111898	235	15	63.83	71.31	37.08	124.73	1.10
1309	48111899	105	9	85.71	111.43	35.64	157.14	1.40
1310	48111900	105	9	85.71	95.87	34.24	157.41	1.40
1311	48111901	345	32	92.75	97.68	**65.11**	182.96	1.61
1312	48111902	140	14	100.00	109.26	54.00	193.07	1.66
1313	48111903	170	1	5.88	5.36	0.00	0.00	0.25
1314	48111904	190	4	21.05	22.99	0.86	37.60	0.44
1315	48111905	135	0	0.00	0.00	0.00	0.00	0.21
1316	48111906	185	0	0.00	0.00	0.00	0.00	0.17
1317	48111907	925	18	19.46	16.99	9.25	23.62	0.36

No.	Dissemination area number	Children population 0-14 years	No. asthma ED visits	Crude rate per 1,000	Directly standardized rates per 1,000[a]			Bayesian smoothed morbidity ratio
					Rate	95% CI		
1318	48111908	155	11	70.97	66.38	28.25	133.58	1.20
1319	48111909	100	12	120.00	115.72	47.15	226.97	1.94
1320	48111910	70	12	171.43	150.67	**73.39**	342.08	2.68
1321	48111911	195	10	51.28	50.63	19.51	100.13	0.90
1322	48111912	80	1	12.50	9.02	0.00	35.19	0.41
1323	48111913	115	5	43.48	45.21	0.00	87.24	0.77
1324	48111914	185	19	102.70	95.93	54.32	203.49	1.74
1325	48111915	95	5	52.63	55.20	8.04	102.41	0.90
1326	48111916	75	15	200.00	207.23	**124.08**	718.47	3.17
1327	48111917	50	6	120.00	125.33	31.94	212.25	1.79
1328	48111918	105	9	85.71	86.82	32.74	157.49	1.40
1329	48111919	70	5	71.43	79.58	16.00	128.88	1.15
1330	48111920	55	4	72.73	111.32	16.07	127.74	1.15
1331	48111921	70	2	28.57	40.76	0.00	62.54	0.60
1332	48111922	90	8	88.89	102.41	34.26	160.20	1.44
1333	48111923	190	18	94.74	94.64	52.96	181.48	1.61
1334	48111924	80	2	25.00	25.57	0.00	59.15	0.55
1335	48111925	10	0	0.00	0.00	0.00	76.06	0.68
1336	48111926	60	1	16.67	21.16	0.00	46.76	0.48
1337	48111927	55	0	0.00	0.00	0.00	15.18	0.35
1338	48111928	85	52	611.77	616.57	**514.68**	0.00	10.29
1339	48111929	90	6	66.67	61.51	13.73	124.38	1.10
1340	48111930	95	3	31.58	23.81	0.00	65.85	0.62
1341	48111931	110	2	18.18	18.27	0.00	38.57	0.44
1342	48111932	60	1	16.67	31.74	0.00	46.81	0.48
1343	48111933	95	5	52.63	52.08	8.24	102.58	0.90
1344	48111934	190	6	31.58	30.52	6.63	61.68	0.59
1345	48111935	100	6	60.00	76.54	19.51	115.15	1.01
1346	48111936	45	11	244.44	232.64	**148.47**	0.00	3.63
1347	48111937	100	11	110.00	119.39	50.57	205.31	1.78
1348	48111938	150	15	100.00	101.08	52.18	195.64	1.67
1349	48111939	285	13	45.61	47.41	22.16	90.77	0.81
1350	48111940	100	13	130.00	154.47	**78.14**	247.92	2.10
1351	48111941	115	6	52.17	43.82	9.77	101.02	0.90
1352	48111942	110	21	190.91	235.57	**151.14**	697.18	3.13
1353	48111943	135	3	22.22	25.29	0.00	46.19	0.47
1354	48111944	235	8	34.04	34.37	11.13	66.79	0.62
1355	48111945	85	1	11.77	12.70	0.00	30.97	0.39
1356	48111946	110	5	45.46	45.63	7.09	90.77	0.80
1357	48111947	150	6	40.00	45.24	9.71	80.60	0.72
1358	48111948	165	4	24.24	27.01	1.24	47.51	0.49
1359	48111949	135	6	44.44	48.63	10.04	87.77	0.79
1360	48111950	120	6	50.00	65.39	15.54	98.83	0.87
1361	48111951	135	3	22.22	21.58	0.00	46.19	0.47
1362	48111952	120	13	108.33	110.62	54.40	206.58	1.78
1363	48111953	100	2	20.00	25.39	0.00	46.07	0.47
1364	48111954	110	4	36.36	38.23	1.49	74.97	0.67
1365	48111955	90	3	33.33	30.48	0.00	69.60	0.64
1366	48111956	110	4	36.36	54.17	2.89	75.15	0.67

No.	Dissemination area number	Children population 0-14 years	No. asthma ED visits	Crude rate per 1,000	Directly standardized rates per 1,000[a]			Bayesian smoothed morbidity ratio
					Rate	95% CI		
1367	48111957	110	4	36.36	34.63	1.36	75.56	0.67
1368	48111958	95	14	147.37	134.96	**69.79**	286.52	2.37
1369	48111959	70	27	385.71	416.21	**304.58**	0.00	6.25
1370	48111960	525	22	41.90	40.44	23.80	84.28	0.75
1371	48111961	160	14	87.50	80.42	41.22	162.19	1.47
1372	48111962	95	5	52.63	43.36	4.82	102.64	0.90
1373	48111963	195	9	46.15	47.79	16.97	92.05	0.81
1374	48111964	120	4	33.33	31.98	1.54	67.89	0.63
1375	48111965	90	2	22.22	20.61	0.00	50.20	0.50
1376	48111966	125	11	88.00	87.29	43.37	161.60	1.46
1377	48111967	195	16	82.05	84.05	44.61	153.49	1.40
1378	48111968	70	3	42.86	43.79	0.00	87.18	0.77
1379	48111969	380	0	0.00	0.00	0.00	0.00	0.11
1380	48111970	250	14	56.00	52.05	24.10	111.55	0.98
1381	48111971	555	22	39.64	38.13	22.22	80.01	0.71
1382	48111972	180	5	27.78	26.37	3.08	56.82	0.54
1383	48111973	1495	80	53.51	51.52	40.05	108.61	0.95
1384	48111974	165	3	18.18	24.40	0.00	33.14	0.41
1385	48111975	215	3	13.95	15.55	0.00	0.00	0.33
1386	48111976	180	8	44.44	54.76	16.84	87.86	0.79
1387	48111977	210	14	66.67	65.68	32.20	126.07	1.15
1388	48111978	325	21	64.61	64.75	37.92	126.03	1.13
1389	48111979	205	8	39.02	42.96	13.61	80.00	0.70
1390	48111980	80	4	50.00	59.79	2.46	97.93	0.86
1391	48111981	0	0					
1392	48111982	215	0	0.00	0.00	0.00	0.00	0.16
1393	48111983	95	5	52.63	59.24	7.68	102.89	0.90
1394	48111984	145	0	0.00	0.00	0.00	0.00	0.20
1395	48111985	130	0	0.00	0.00	0.00	0.00	0.22
1396	48111986	195	0	0.00	0.00	0.00	0.00	0.17
1397	48111987	185	0	0.00	0.00	0.00	0.00	0.17
1398	48111988	0	0					
1399	48111989	0	0					
1400	48111990	125	0	0.00	0.00	0.00	0.00	0.22
1401	48111991	115	0	0.00	0.00	0.00	0.00	0.23
1402	48111992	160	0	0.00	0.00	0.00	0.00	0.19
1403	48111993	130	0	0.00	0.00	0.00	0.00	0.22
1404	48111994	285	0	0.00	0.00	0.00	0.00	0.13
1405	48111995	115	0	0.00	0.00	0.00	0.00	0.23
1406	48111996	200	0	0.00	0.00	0.00	0.00	0.17
1407	48111997	100	0	0.00	0.00	0.00	0.00	0.25
1408	48111998	20	0	0.00	0.00	0.00	58.85	0.54
1409	48111999	75	0	0.00	0.00	0.00	0.00	0.29
1410	48112000	120	0	0.00	0.00	0.00	0.00	0.23
1411	48112001	170	0	0.00	0.00	0.00	0.00	0.18
1412	48112002	95	0	0.00	0.00	0.00	0.00	0.26
1413	48112003	150	0	0.00	0.00	0.00	0.00	0.20
1414	48112004	175	0	0.00	0.00	0.00	0.00	0.18
1415	48112005	120	0	0.00	0.00	0.00	0.00	0.23

No.	Dissemination area number	Children population 0-14 years	No. asthma ED visits	Crude rate per 1,000	Directly standardized rates per 1,000[a]			Bayesian smoothed morbidity ratio
					Rate	95% CI		
1416	48112006	135	0	0.00	0.00	0.00	0.00	0.21
1417	48112007	105	0	0.00	0.00	0.00	0.00	0.24
1418	48112008	185	0	0.00	0.00	0.00	0.00	0.17
1419	48112009	150	0	0.00	0.00	0.00	0.00	0.20
1420	48112010	130	0	0.00	0.00	0.00	0.00	0.22
1421	48112011	125	0	0.00	0.00	0.00	0.00	0.22
1422	48112012	105	0	0.00	0.00	0.00	0.00	0.24
1423	48112013	130	0	0.00	0.00	0.00	0.00	0.22
1424	48112014	120	0	0.00	0.00	0.00	0.00	0.23
1425	48112015	185	35	189.19	191.14	**134.35**	910.83	3.21
1426	48112016	0	0					
1427	48112017	280	0	0.00	0.00	0.00	0.00	0.13
1428	48112018	190	0	0.00	0.00	0.00	0.00	0.17
1429	48112019	0	0					
1430	48112020	0	0					
1431	48112021	180	2	11.11	11.56	0.00	0.00	0.31
1432	48112022	0	0					
1433	48112023	115	59	513.04	511.23	**435.03**	0.00	8.72
1434	48112024	0	0					
1435	48112025	170	0	0.00	0.00	0.00	0.00	0.18
1436	48112026	150	0	0.00	0.00	0.00	0.00	0.20
1437	48112027	60	0	0.00	0.00	0.00	0.00	0.33
1438	48112028	90	5	55.56	48.20	7.45	107.64	0.94
1439	48112029	0	0					
1440	48112030	0	0					
1441	48112031	130	3	23.08	21.58	0.00	47.32	0.49
1442	48112032	105	0	0.00	0.00	0.00	0.00	0.24
1443	48112033	140	1	7.14	5.15	0.00	0.00	0.28
1444	48112053	105	1	9.52	9.02	0.00	0.00	0.34
1445	48112054	100	0	0.00	0.00	0.00	0.00	0.25
1446	48112055	100	21	210.00	215.71	**136.01**	0.00	3.43
1447	48112056	130	0	0.00	0.00	0.00	0.00	0.22
1448	48112057	170	0	0.00	0.00	0.00	0.00	0.18
1449	48112058	140	1	7.14	12.02	0.00	0.00	0.28
1450	48112059	165	0	0.00	0.00	0.00	0.00	0.19
1451	48112060	0	0					
1452	48112072	120	2	16.67	13.71	0.00	35.93	0.41
1453	48112073	85	3	35.29	38.63	0.00	74.52	0.67
1454	48112074	140	1	7.14	10.58	0.00	0.00	0.28
1455	48112075	240	8	33.33	37.27	12.01	64.03	0.61
1456	48112076	95	1	10.53	9.07	0.00	26.47	0.36
1457	48112077	80	0	0.00	0.00	0.00	0.00	0.28
1458	48112078	125	5	40.00	42.15	6.15	81.23	0.72
1459	48112079	85	15	176.47	183.42	**116.75**	400.13	2.82
1460	48112080	90	0	0.00	0.00	0.00	0.00	0.27
1461	48112081	105	0	0.00	0.00	0.00	0.00	0.24
1462	48112082	120	0	0.00	0.00	0.00	0.00	0.23
1463	48112083	100	0	0.00	0.00	0.00	0.00	0.25
1464	48112084	80	0	0.00	0.00	0.00	0.00	0.28

No.	Dissemination area number	Children population 0-14 years	No. asthma ED visits	Crude rate per 1,000	Directly standardized rates per 1,000[a]			Bayesian smoothed morbidity ratio
					Rate	95% CI		
1465	48112085	110	0	0.00	0.00	0.00	0.00	0.24
1466	48112086	140	0	0.00	0.00	0.00	0.00	0.21
1467	48112087	80	0	0.00	0.00	0.00	0.00	0.28
1468	48112088	205	0	0.00	0.00	0.00	0.00	0.16
1469	48112089	300	14	46.67	35.67	17.16	93.33	0.83
1470	48112090	105	4	38.10	39.24	1.46	77.02	0.70
1471	48112091	685	29	42.34	42.82	27.59	85.05	0.76
1472	48112092	140	3	21.43	21.16	0.00	43.22	0.46
1473	48112093	165	4	24.24	25.76	0.96	47.90	0.49
1474	48112094	230	13	56.52	60.76	28.23	111.92	0.98
1475	48112095	295	10	33.90	34.21	13.33	66.51	0.62
1476	48112096	130	10	76.92	77.04	28.98	142.87	1.29
1477	48112097	190	3	15.79	15.51	0.00	23.62	0.36
1478	48112098	545	25	45.87	46.47	28.64	92.05	0.82
1479	48112099	110	8	72.73	59.79	19.25	134.31	1.21
1480	48112100	160	5	31.25	32.00	3.02	61.98	0.59
1481	48112101	130	0	0.00	0.00	0.00	0.00	0.22
1482	48112102	90	1	11.11	8.02	0.00	26.59	0.38
1483	48112103	135	0	0.00	0.00	0.00	0.00	0.21
1484	48112104	75	6	80.00	64.08	15.75	142.79	1.28
1485	48112105	15	11	733.33	720.12	**529.41**	0.00	9.56
1486	48112106	95	8	84.21	71.44	26.64	152.06	1.37
1487	48112107	0	0					
1488	48112108	65	2	30.77	28.85	0.00	67.49	0.63
1489	48112109	95	1	10.53	10.58	0.00	26.47	0.36
1490	48112110	35	3	85.71	97.53	0.00	140.69	1.26
1491	48112111	105	13	123.81	119.65	**60.51**	231.50	2.01
1492	48112112	95	2	21.05	31.74	0.00	46.84	0.48
1493	48112113	60	3	50.00	79.58	0.00	96.93	0.86
1494	48112114	0	0					
1495	48112115	5	0	0.00	0.00	0.00	90.77	0.81
1496	48112116	75	5	66.67	66.11	9.37	122.61	1.09
1497	48112117	180	11	61.11	56.56	23.86	118.06	1.05
1498	48112118	200	10	50.00	37.10	13.89	99.64	0.87
1499	48112119	165	3	18.18	18.36	0.00	33.22	0.41
1500	48112120	145	10	68.97	65.69	26.72	131.47	1.17
1501	48112121	95	15	157.90	161.32	**88.83**	321.10	2.55
1502	48112122	120	1	8.33	4.88	0.00	0.00	0.31
1503	48112123	150	2	13.33	16.10	0.00	16.34	0.35
1504	48112124	100	8	80.00	73.20	25.66	145.01	1.31
1505	48112125	145	26	179.31	192.79	**127.95**	630.04	3.00
1506	48112126	225	2	8.89	9.28	0.00	0.00	0.26
1507	48112127	85	11	129.41	125.17	**57.03**	233.82	2.06
1508	48112128	185	2	10.81	12.44	0.00	0.00	0.30
1509	48112129	135	4	29.63	38.90	2.11	61.23	0.57
1510	48112130	80	23	287.50	294.90	**212.50**	0.00	4.65
1511	48112131	215	17	79.07	78.01	42.64	149.96	1.35
1512	48112132	145	2	13.79	17.46	0.00	21.02	0.36
1513	48112133	315	29	92.06	98.71	**64.47**	180.35	1.59

No.	Dissemination area number	Children population 0-14 years	No. asthma ED visits	Crude rate per 1,000	Directly standardized rates per 1,000[a]			Bayesian smoothed morbidity ratio
					Rate	95% CI		
1514	48112134	565	56	99.11	98.59	**74.00**	204.14	1.74
1515	48112135	105	2	19.05	25.07	0.00	42.13	0.45
1516	48112136	150	6	40.00	44.92	9.47	80.64	0.72
1517	48112137	90	5	55.56	45.44	6.98	107.74	0.94
1518	48112138	65	5	76.92	83.68	15.01	137.53	1.22
1519	48112139	35	0	0.00	0.00	0.00	37.60	0.43
1520	48112140	100	0	0.00	0.00	0.00	0.00	0.25
1521	48112141	90	0	0.00	0.00	0.00	0.00	0.27
1522	48112142	0	0					
1523	48112143	0	0					
1524	48112144	105	9	85.71	94.63	36.44	157.78	1.40
1525	48112145	85	2	23.53	32.19	0.00	55.63	0.52
1526	48112146	145	1	6.90	6.44	0.00	0.00	0.28
1527	48112147	55	3	54.54	49.78	0.00	104.96	0.92
1528	48112148	195	7	35.90	35.53	10.01	71.91	0.65
1529	48112149	160	8	50.00	52.69	18.05	99.34	0.87
1530	48112150	85	5	58.82	59.94	8.19	112.42	0.99
1531	48112151	75	4	53.33	51.33	3.62	104.49	0.91
1532	48112152	95	22	231.58	246.16	**152.37**	0.00	3.78
1533	48112153	30	0	0.00	0.00	0.00	43.15	0.46
1534	48112154	35	1	28.57	36.07	0.00	72.74	0.66
1535	48112155	30	0	0.00	0.00	0.00	43.15	0.46
1536	48112156	25	1	40.00	15.87	0.00	89.27	0.79
1537	48112157	30	1	33.33	12.70	0.00	80.38	0.72
1538	48112158	40	5	125.00	119.75	17.46	212.82	1.79
1539	48112159	25	3	120.00	95.23	5.07	177.25	1.58
1540	48112160	60	0	0.00	0.00	0.00	0.00	0.33
1541	48112161	20	0	0.00	0.00	0.00	59.02	0.54
1542	48112162	245	9	36.74	35.01	12.59	73.40	0.66
1543	48112163	135	13	96.30	101.51	49.58	181.15	1.60
1544	48112164	270	8	29.63	25.15	7.70	59.15	0.55
1545	48112165	140	6	42.86	48.12	8.25	86.00	0.76
1546	48112166	125	2	16.00	19.72	0.00	30.97	0.40
1547	48112167	145	7	48.28	49.51	13.97	95.29	0.84
1548	48112168	150	14	93.33	85.04	43.36	173.91	1.56
1549	48112169	90	0	0.00	0.00	0.00	0.00	0.27
1550	48112170	135	9	66.67	77.80	27.00	125.94	1.13
1551	48112171	125	8	64.00	63.23	20.16	120.52	1.08

ED, Emergency Department; CI, Confidence Intervals

[a] Children population between 0-14 years old from Census 2006 used as standard population. Lower band of the 95% CI for the directly standardized rates are in bold if they are higher than the overall rate (55.91 visits per 1,000 children).