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A Link Between Paediatric Asthma and Obesity: Are They Caused by the Same Environmental Conditions?

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Abstract

The highly associated paediatric conditions of asthma and overweight have seen dramatic increases over the past few decades. This thesis explored air pollution exposure as a potential underlying mechanism of co-morbid asthma and overweight among adolescents aged 12 to 18 years. Data from the Canadian Community Health Survey were merged with a database containing estimates of air pollution as assessed by particulate matter ≤ 2.5 microns (PM$_{2.5}$) concentrations at the postal code centroid in southwestern Ontario. Logistic regression was used to conduct the analysis. Adolescents were more likely to be overweight as PM$_{2.5}$ concentrations increased. There was no significant association between PM$_{2.5}$ and asthma and co-morbid asthma and overweight. The positive association between PM$_{2.5}$ and overweight found in this study, and the literature supporting a causal relationship between air pollution and asthma, suggests a need to further explore the role of air pollution as a shared risk factor.

Keywords

Adolescents, asthma, overweight, obesity, co-morbid, common risk factor, air pollution, particulate matter, National Pollutant Release Inventory, Canadian Community Health Survey
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<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>Body mass index</td>
</tr>
<tr>
<td>BPA</td>
<td>Bisphenol A</td>
</tr>
<tr>
<td>CAC</td>
<td>Criteria air contaminant</td>
</tr>
<tr>
<td>CAPI</td>
<td>Computer-assisted personal interviewing</td>
</tr>
<tr>
<td>CATI</td>
<td>Computer-assisted telephone interviewing</td>
</tr>
<tr>
<td>CCHS</td>
<td>Canadian Community Health Survey</td>
</tr>
<tr>
<td>CDC</td>
<td>Centers for Disease Control and Prevention</td>
</tr>
<tr>
<td>CI</td>
<td>Confidence interval</td>
</tr>
<tr>
<td>CO</td>
<td>Carbon monoxide</td>
</tr>
<tr>
<td>CRP</td>
<td>C-reactive protein</td>
</tr>
<tr>
<td>IL-6</td>
<td>Interleukin-6</td>
</tr>
<tr>
<td>IOTF</td>
<td>International Obesity Task Force</td>
</tr>
<tr>
<td>NO₂</td>
<td>Nitrogen dioxide</td>
</tr>
<tr>
<td>NOₓ</td>
<td>Nitrogen oxides</td>
</tr>
<tr>
<td>O₃</td>
<td>Ozone</td>
</tr>
<tr>
<td>OR</td>
<td>Odds ratio</td>
</tr>
<tr>
<td>PAH</td>
<td>Polycyclic aromatic hydrocarbon</td>
</tr>
<tr>
<td>PM₉·₅</td>
<td>Particulate matter less than or equal to 2.5 microns</td>
</tr>
<tr>
<td>PM₁₀</td>
<td>Particulate matter less than or equal to 10 microns</td>
</tr>
<tr>
<td>POP</td>
<td>Persistent organic pollutant</td>
</tr>
<tr>
<td>SD</td>
<td>Standard deviation</td>
</tr>
<tr>
<td>SE</td>
<td>Standard error</td>
</tr>
<tr>
<td>SO₂</td>
<td>Sulphur dioxide</td>
</tr>
<tr>
<td>SOₓ</td>
<td>Sulphur oxides</td>
</tr>
<tr>
<td>TPM</td>
<td>Total particulate matter</td>
</tr>
<tr>
<td>VOC</td>
<td>Volatile organic compounds</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
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</table>
Chapter 1

1 Introduction and Literature Review

1.1 Introduction

Asthma and obesity are two of the most common chronic conditions affecting paediatric populations. The prevalence of each condition has seen substantial increases over the past few decades in Canada and worldwide, and both have considerable physical and psychological consequences that plague children and adolescents well into adulthood. The morbidity associated with asthma and obesity causes a reduction in quality of life and productivity, and places a large economic burden on the Canadian healthcare system.

In addition to the parallel increases in asthma and obesity, many studies have found high levels of association between these two conditions. This finding is of great concern because individuals with both asthma and obesity generally have poorer health than those with only one of these conditions. One area of research that is important for the formulation of targeted strategies for co-morbid conditions is that which examines their developmental origins. However, there is no single explanation for how asthma and obesity are linked. Longitudinal studies have indicated that high body mass precedes and increases the risk of asthma, although the reverse has been shown in some studies, suggesting that asthma may lead to the onset of obesity. Since both of these conditions commonly originate in early childhood and proximally in time, a direct causal relationship between asthma and obesity may not be the only explanation for their co-morbid existence. Rather, common risk factors in early life may be contributing to the increasing prevalence of both conditions at such a young age.

Although research to date has examined the role of individual-level predictors associated with each of these health conditions, the role of environmental predictors has been largely unexplored. Addressing the common root causes embedded in the environment has been identified as an important next step in tackling this co-morbid epidemic. Research has shown that air pollution is contributing to the individual growing rates of asthma and
obesity,\textsuperscript{16,17} suggesting this environmental exposure is a common risk factor for both conditions. Assessing the effects of air pollution on asthma and obesity together would therefore be a significant contribution towards understanding the etiology of this co-morbid relationship. This improved understanding may provide vital information to be used in the design of preventive and intervention strategies directed towards children and adolescents who are at a higher risk of having both conditions.

To achieve this research goal, I will first provide an overview of the asthma epidemic (Section 1.2) and overweight/obesity epidemic (Section 1.3) among children and adolescents, by outlining the prevalence, time trends, and health risks associated with each condition. Section 1.4 will discuss the importance of examining asthma and overweight/obesity together by reviewing research that has assessed the association between them, and highlighting the importance of examining common risk factors as underlying mechanisms of this co-morbidity. Section 1.5 discusses potential individual and environmental common risk factors of asthma and obesity, and the need to explore the role of the environment; the end of this section outlines air pollution in particular as a potential environmental cause that needs to be considered (Section 1.5.5). Section 1.6 provides a comprehensive definition of air pollution and highlights children and adolescents as especially susceptible to its health effects. The remainder of this section describes the relationship between air pollution and asthma (Section 1.6.4), overweight/obesity (Section 1.6.5), and co-morbid asthma and overweight/obesity (Section 1.6.6). These sections present the mechanisms through which air pollution causes each condition, reviews of studies assessing these relationships, as well as summarize the limitations of research in these areas. Following this literature review, and an overall summary (Section 1.7), Chapter 2 provides the current plan of study, including specific objectives and hypotheses, followed by methods (Chapter 3), results (Chapter 4), and discussion of findings (Chapter 5).

1.2 The Asthma Epidemic

This section provides the definition of asthma, its prevalence, trends, and associated health consequences. This discussion illustrates paediatric asthma as an increasing public
health problem in Canada that needs to be addressed as the health costs faced by asthmatic children and adolescents are particularly pronounced.

1.2.1 Definition

Asthma is a lung disorder, where inflammation and mucous production causes bronchi swelling and narrowing of the airways. Airflow is restricted resulting in a range of mild to life-threatening breathing difficulties. Asthma symptoms include shortness of breath, coughing, wheezing, and chest tightness, and diagnosis is generally based on presence of these symptoms in addition to respiratory diagnostic testing.

There is no gold standard definition for measuring asthma prevalence. Instead, various measurement instruments are used, such as physician diagnosis, self-reported symptoms via questionnaires, physiological measures like lung function (i.e., the volume and flow of air during inhalation and exhalation) and bronchial responsiveness (i.e., lung function after inhaling chemicals that induce bronchoconstriction), or a combination of these methods. For example, self-reported asthma is validated by testing the questionnaire against results of a physiological investigation, or by comparing self-reported answers with a clinical diagnosis.

Epidemiological prevalence studies should use methods that are simple, inexpensive, practical, and will allow for the comparison of asthma prevalence among diverse populations. Large survey questionnaires of self-reported asthma, preferably validated in the target population, is thus suggested as the method of choice.

1.2.2 Prevalence, Trends, and Health Risks

Overall prevalence in Canada: Asthma is one of the most common chronic diseases in childhood and adolescence. The prevalence of this paediatric illness has substantially increased over the past few decades and its death rates have doubled between 1980 and 1993. In 1978/79, the prevalence of asthma among Canadian children and adolescents aged 0 to 14 years was 2.5% - though this percentage had risen only marginally to 3.1% in 1983/84, by 1994/95, asthma prevalence had increased to 11.2%. In 1994/1995, 11% of children only, aged 0 to 11, had been diagnosed with asthma, whereas by 2000/2001,
the rate had significantly risen to more than 13%. Positive trends were more substantial across periods preceding the year 2001; however, the prevalence rate of asthma still remained high after this time.

Regional differences: Disparities in asthma prevalence have been reported across regions of Canada. While Statistics Canada has demonstrated that the 2008 national average prevalence of asthma for populations aged 12 to 19 years was 11.3%, this prevalence ranged from 6.7% in British Columbia to 16.7% in Prince Edward Island.

Asthma in Ontario: Detailed asthma prevalence trends from 1996 to 2005 have been captured in Ontario through a population-based study conducted by Gershon et al. During this time, the age- and sex-standardized asthma prevalence significantly increased by 55.1%. In children aged 5 to 9 years, this prevalence increased by 19.6% (from 18.8% to 22.5%) and in adolescents aged 10 to 14 years this prevalence increased by 94.7% (from 13.1% to 25.5%). In young adults aged 15 to 39 years, asthma prevalence increased by 81.5% (from 7.1% to 12.9%).

With the exception of Ontario, all estimates of asthma prevalence above were measured using self-reported data from large population-based survey questionnaires. Differences in these estimates may in part be explained by subtleties in the wording of questions across surveys, such as indicating diagnosis by a health professional. It is more difficult to directly compare Ontario estimates with those of Canada, as asthma was alternatively determined using medical records of physician diagnosis. Nevertheless, these findings collectively illustrate a high magnitude of asthma prevalence and growth across time in paediatric populations nationwide.

Health risks: The primary health risk of concern for asthmatics is asthma attacks, where airway inflammation is so severe that the flow of air in and out of the lungs is reduced to a dangerous degree. In many cases, the patient is not equipped with the required medication or the medication they currently use is not effective. Every year in Canada, approximately 146,000 emergency room visits are due to asthma attacks. A population-based cohort study reported the number of children and adolescents aged 2 to 17 years who had an emergency visit for the care of asthma from April 2003 to March 2005 in
Ontario. A total of 32,996 children had at least one asthma-related visit to an emergency department, with 68.5% of these visits classified as with high severity.

Asthma is associated with increased risk of depression, anxiety, and panic attacks, gastroesophageal reflux, sleep disturbances and fatigue, chronic rhinitis and sinusitis, and even the development of heart disease and diabetes later in life. Paediatric asthma is also significantly more likely to persist into adulthood. One prospective study determined that having asthma at age 7 was a strong predictor of having asthma at ages 29 to 32 (OR 1.59, 95% CI 1.10-2.29).

1.3 The Overweight and Obesity Epidemic

In this section, overweight/obesity, its prevalence, trends, and associated health consequences are defined. This discussion illuminates paediatric overweight/obesity as an increasingly important public health problem in Canada as it presents challenges to children and adolescents’ physical, emotional and social well-being and increases the risk of developing chronic diseases in adulthood.

1.3.1 Definition

Overweight and obesity are defined as abnormal or excessive fat accumulation that may impair health. Body mass index (BMI) is the most basic and common method used to identify individuals who are overweight or obese and is calculated by dividing weight in kilograms by height measured in meters squared (denoted as: kg/m²). This convenient and inexpensive measure has been recommended as a screening tool in epidemiological and population-based studies, and is a good predictor of body fatness in children and adolescents. Paediatric body composition varies between different ages and gender. BMI generally follows a J-shaped curve across age and is different for males and females. This curve depicts young children declining in BMI after birth, followed by a gradual increase that begins at approximately 6 years of age (adiposity rebound) and levels out during late adolescence. As a result, the criteria used to determine the BMI at which children and adolescents are overweight or obese are age- and sex-specific.
Several growth curves have been created using different sources of data, resulting in different reference values to define overweight/obesity status in paediatric populations. Growth charts and reference values published by the World Health Organization (WHO), the United States Centers for Disease Control and Prevention (CDC), and the International Obesity Task Force (IOTF) are commonly used. The WHO growth reference defines overweight and obesity as having a BMI one and two standard deviations above the mean, respectively, for age and sex. In contrast, the CDC growth chart defines overweight as having a BMI between the 85th and 94th percentile for their age and sex, while those with a BMI equal to or above the 95th percentile are obese. The IOTF growth chart is based on data from six international surveys. Percentiles corresponding to the adult cut-off points for overweight and obesity (25 and 30 kg/m\(^2\) respectively) were first determined at age 18 years, by sex. For each survey dataset, percentiles were extrapolated across childhood and adolescence with all six curves passing through adult cut-off points at 18 years. The percentiles defining overweight and obesity for each curve were then averaged to obtain age- and sex-specific reference values ranging from 2 to 18 years.

The prevalence of paediatric overweight and obesity in Canada varies considerably when using the IOTF, CDC, and WHO growth curves. This variation is largely due to the different samples and statistical techniques used in the construction of each growth curve, and the criteria used to select the BMI cut-off values. In 2004, the prevalence of overweight and obesity among Canadians aged 2 to 17 was 26.2%, 28.4%, and 34.1% using growth reference defined by the IOTF, CDC, and WHO, respectively. The prevalence of obesity ranged from 8.2% (IOTF) to 12.7% (WHO). Among adolescents only (12 to 17 years), the prevalence of overweight and obesity ranged from 28.0% (CDC) to 33.2% (WHO), and obesity prevalence from 9.4% (IOTF) to 12.4% (WHO). The WHO cut-off points generally yield the highest estimates of excess weight status, and the IOTF cut-off points, the lowest. It has been recommended that the IOTF reference values be used for epidemiological purposes, whereas the CDC and WHO definitions are more useful for monitoring the growth of individual children and adolescents.
1.3.2 Prevalence, Trends, and Health Risks

Overall prevalence in Canada: Paediatric overweight and obesity in Canada has grown rapidly over the last three decades. In 2004, 26% of children and adolescents aged 2 to 17 years were considered overweight or obese, compared with only 15% in 1978/1979. Specifically, the Canadian overweight prevalence had increased from 12% to 18%, while the prevalence of obesity tripled, from 3% to 8%. In adolescents aged 12 to 17 years, the prevalence of overweight notably doubled from 14% to 29%, while obesity prevalence had tripled from 3% to 9%.

Regional differences: There are substantial differences in the prevalence of overweight and obesity across regions of Canada. Data from the Statistics Canada 2008 Canadian Community Health Survey (CCHS) displayed that the national average prevalence of overweight/obesity was 19.3% for adolescents aged 12 to 17 years, ranging from 14.4% in Quebec to 34.8% in Newfoundland and Labrador.

Overweight/obesity in Ontario: In Ontario, during the time period from 2005 to 2014, the overall prevalence of overweight/obesity for adolescents aged 12 to 17 years increased from 19.5% to 23.3%. Though similar patterns were observed for males and females, overweight/obesity prevalence was higher in males across all years.

The numerous standard definitions for paediatric overweight and obesity and different methods of measuring this condition cause difficulties in the comparison of overweight and obesity prevalence across different studies. All prevalence estimates of overweight and obesity above were determined using the BMI growth curve created by the IOTF; however, the overall prevalence in Canada used direct measurements of height and weight to calculate paediatric BMI, whereas provincial-level estimates were based on self-reported height and weight. Despite these inconsistencies, it is evident that the magnitude and growth in the prevalence of overweight/obesity is worrisome in paediatric populations.

Health Risks: The increased prevalence of childhood obesity has been linked to the concurrent rise of many physical health problems. Obese adolescents are more likely to
have risk factors for cardiovascular disease, such as high cholesterol or hypertension. Approximately 70% of obese individuals aged 5 to 17 years in a population-based sample were reported to have at least one risk factor. Overweight/obese adolescents are at higher risk of having pre-diabetes, a condition which places them at high risk of diabetes development. Furthermore, obese children and adolescents are at greater risk for long-term health issues such as musculoskeletal problems, sleep apnea, liver disease, stroke, many types of cancer, and osteoarthritis. Paediatric obesity is also significantly more likely to persist into adulthood. Children who were obese as early as 2 years of age were more likely to be obese as adults.

Obese children and adolescents are more likely to be subject to socio-psychological afflictions such as stigmatization, behaviour problems, social isolation, low self-esteem, anxiety, body dissatisfaction and depression. These psychological impacts are causative of the suicidal and risk-taking behaviours that are more common among this afflicted population relative to normal weight individuals. One study indicated overweight/obese children as having a higher likelihood of ever trying cigarettes, drinking alcohol, using drugs before their last sexual encounter, currently smoking, and smoking before age 13 in comparison to their normal weight peers. Eating disorders, dieting, use of diet drugs, purging (i.e., self-induced vomiting, misuse of laxatives), and conducting other unhealthy weight control behaviours are also more common in this population.

1.4 Looking at Both Asthma and Weight Status

Given the parallel increases in paediatric asthma and obesity, it is questioned whether there is a link between these two health conditions. This section discusses the importance of examining both asthma and overweight/obesity together.

1.4.1 Asthma and Weight Status Association

As described in Sections 1.2.2 and 1.3.2, the prevalence of asthma and overweight/obesity among children and adolescents has been rapidly increasing over the past few decades in Canada. These similar trends suggest that asthma and obesity appear to be increasing alongside one another, indicating an association at the population-level.
However, asthma and obesity have also been established as significantly coinciding with each other at the individual level.

**Child-level association:** Recent studies have shown that asthma has been positively associated with a higher BMI, overweight, and obesity in children and adolescents.\(^{10,11,13,66-79}\) Even in preschool children aged 3-5 years, the prevalence of obesity was reported as higher in asthmatic children than non-asthmatic children.\(^{80}\) This illustrates a strong association between these conditions. Furthermore, when examining the relationship between measures of exacerbations in asthmatics or respiratory symptoms in non-asthmatics and overweight/obesity, a positive association in paediatric populations has been found.\(^{11,81-84}\) Lung function parameters significantly decrease in relation to increased weight status and other measures of fatness, such as tricep skinfold thickness.\(^{75,85,86}\) Examples of studies reporting no association between asthma and weight status\(^{87-92}\) were those conducted in Asian and African American samples of children and adolescents,\(^{93,94}\) where other factors associated with ethnic minorities could have accounted for these results. Overall, all the evidence stated above is indicative of a positive, co-morbid relationship between asthma and weight status at the individual level.

**A Bi-directional relationship:** When examining co-morbid asthma and obesity, there has been lack of agreement on which condition precedes and thus potentially causes the incidence of the other. While many causal explanations in both directions exist, there is more support in the literature for the hypothesis that obesity is preceding asthma. Prospective studies have been conducted in children and adolescents, where those who were obese or overweight at baseline had a higher incidence of asthma in childhood, adolescence, and adulthood than those who were of normal weight.\(^{13,92,95-98}\) These findings are supported by a number of potential causal mechanisms of this relationship: narrowed airways in obese children due to chronic low grade systemic inflammation that modifies airway smooth muscle function, and higher levels of the proinflammatory hormone leptin may, in the end, lead to asthma.\(^{99,100}\) Exercise-induced bronchospasm caused by obesity can subsequently lead to asthma development.\(^{85,101}\) Obesity also causes gastroesophageal reflux and is associated with a poor diet which both contribute to asthma.\(^{102,103}\)
There is also the possibility that in some children, this causal mechanism is reversed. For example, in one study examining children who were both asthmatic and obese, 66.6% were already overweight and obese at the time of asthma diagnosis, indicating that in approximately 33% of these subjects, asthma preceded obesity. These findings can be explained by a number of potential causal mechanisms. Asthmatic patients may develop obesity through the side effects of common systemic corticosteroid use or reduced physical activity resulting from exercise-induced asthma. Children with asthma also have both overall low physical endurance and increased skinfold thickness, indicating physical fitness abnormalities and increased risk of eventual overweight/obesity. Asthma is also a possible causal risk factor for obesity because parents don’t want their asthmatic children exercising, further reducing levels of physical activity.

1.4.2 The Need to Study Co-morbidities in General

This section focuses on the need to study associated diseases, such as asthma and obesity, as co-morbidities rather than separately. When trying to conduct research on, treat, or prevent a condition that is highly correlated with another condition, examining each condition as a co-morbidity will provide further evidence helpful towards achieving these goals more effectively.

Importance for treatment

Co-morbidities may predict a differential clinical outcome than only having one condition. The symptoms and health risks of one condition are thought to worsen those associated with the other condition, and vice versa. Moreover, the increased likelihood of other health problems needs to be considered when assessing a patient and selecting the most suitable treatment method. It has been proven that attention to conditions in the context of their co-morbid state improves prognosis and treatment. Researching co-morbidities may reveal patterns and associations with other risk factors that can contribute to the development of more effective co-morbidity treatment methods. For example, the efficacy of asthma and overweight/obesity treatment may be improved if treatment for depression (associated with both conditions separately) is provided.
Importance for prevention

Prevention programs for co-morbid conditions have traditionally operated separately from one another. As a result, attempts to conduct programs aimed at addressing multiple related conditions in a coalescent manner have been neglected. This disregard presents implications for prevention efforts as it is unclear whether these strategies should be broad or narrow in their target. An understanding of the etiology of co-morbidities is important for identifying targets of prevention. Therefore, to combat the burdens associated with co-morbidities, including asthma and obesity, there is a need to identify the potential disease mechanisms involved through the study of associated conditions together rather than separately. This will be discussed in the following section.

1.4.3 Identification of Potential Disease Mechanisms

The study of co-morbidities acknowledges multiple influential factors and the dynamics of more than one health condition. This approach has the potential to yield important indications about the potential disease mechanisms involved. This section will discuss in more detail the importance of understanding the underlying mechanisms involved in co-morbidity development, and specifically, asthma and overweight/obesity.

If one health condition is more likely to coexist with another, important questions are raised regarding the etiology of these conditions. There are several hypotheses on the reasons why co-morbidity may exist, and are listed as follows: (1) there is a direct causal relationship between the two, with the presence of one condition increasing the likelihood of the other to develop; (2) there is an indirect causal relationship between the two, where one condition affects a mediating variable, which subsequently increases the likelihood of the second condition; and (3) there are common risk factors that increase the likelihood of both conditions.\textsuperscript{116}

Many incidence studies have identified a short period of time elapsed between paediatric overweight/obesity and incident asthma and vice versa (see Section 1.4.1). Since asthma and overweight/obesity frequently originate in early childhood, a direct or indirect causal relationship between the two conditions that have developed so proximally in time may
not be the only explanation for their concurrent existence. Chinn and Rona have reported that the increase in obesity prevalence does not solely explain the increase in asthma from 1982 to 1994. They discuss that a direct causal link between these conditions also cannot be inferred because this coexistence is of recent origin and is inconsistent across various risk factors. These findings are all suggestive of a common risk factor that has contributed to the increasing prevalence of both asthma and overweight/obesity at such a young age. If two associated conditions are primarily the result of a set of common or similar risk factors, this indicates that the pathways by which one condition develops are the same by which the other develops as well. Prioritizing and addressing these risk factors would simultaneously reduce the prevalence of both conditions, indicating this theory as quite useful for intervention. Therefore, by examining asthma and weight status at the same time, it would be easier and advantageous to investigate a potential common risk factor, such as air pollution exposure.

1.5 What is Causing Asthma and Overweight/Obesity?

This section illustrates how asthma and weight status are linked through the mechanisms of either individual (biological, behavioural, and social) or environmental (physical and social) common risk factors. After providing definitions and evidence of individual and environmental categories as potential common risk factors of asthma and overweight/obesity, the need to examine the environment (especially physical) as a potential predictor of both conditions will be outlined. Finally, air pollution, a component of the physical environment, is introduced as a potential causal factor that needs to be examined.

1.5.1 Classification of Preceding Risk Factors

Several common factors have been hypothesized to explain the increasing rates of asthma and overweight/obesity. These mechanisms are generally of biological, behavioural, social, and environmental nature, or a combination of these factors. Biological determinants are defined as the physical characteristics of individuals, as well as factors related to the genes inherited from their parents. Examples of common biological risk
factors of asthma and overweight/obesity are sex and genetics.\textsuperscript{12,22} Behavioural factors are the manners in which one acts or conducts oneself under normal or specified circumstances. Examples of those associated with asthma and overweight/obesity are physical activity and diet.\textsuperscript{120-122} Social factors are defined as the rank, status, and treatment of an individual in society based on their economic, behavioural, and/or biological attributes. Two examples of social risk factors of asthma and overweight/obesity are income and education.\textsuperscript{12,123} Finally, environmental factors are related to the physical (indoor and outdoor) and social environment in which an individual lives, works, and attends school. Indoor allergens and outdoor air pollution are examples of common physical environmental risk factors of asthma and overweight/obesity, whereas social policies and norms have been proposed as social environmental influences.\textsuperscript{15} A more comprehensive definition and the influence of environmental factors on asthma and weight status will be provided in Section 1.5.3.

These four main groups of possible causal predictors of co-morbid asthma and overweight/obesity can be further collapsed into two categories; individual and environmental (Figure 1). Biological, behavioural, and social factors are considered individual-level predictors as they are all characteristics of a particular person that may explain their health status.\textsuperscript{118} In contrast, physical and social environmental factors are characteristics found in the surroundings or conditions in which a person or group of people live that can collectively influence both individual and group health status.\textsuperscript{15} Evidence for both categories of potential causal predictors of asthma and overweight/obesity will be further discussed in the following two sections.
Figure 1: Categories of shared risk factors for paediatric asthma and obesity.
1.5.2 Individual-level Predictors

The hypothesized underlying mechanisms of co-morbid asthma and overweight/obesity in children and adolescents have mainly been attributed to individual-level predictors. Evidence for the individual risk factors these two conditions have in common is outlined in this section.

**Sex:** There is a higher risk of developing paediatric asthma and obesity in males compared to females. Stingone and colleagues\(^1\) found that the adjusted prevalence odds ratio of asthma and overweight among males was double that of the reference group of females. Another study reported male adolescents had a significant relative risk of developing asthma associated with being overweight or obese, whereas female adolescents had a non-significant risk.\(^9\)

**Age:** Age is positively associated with co-morbid asthma and obesity prevalence. Ahmad et al\(^1\) reported that obese children were significantly more likely to have asthma compared to non-obese children in both 7-12 year olds and 13-17 year olds. However, this association was higher in those aged 13 to 17 years than in those aged 7 to 12 years. This association was non-significant in those aged 0 to 6 years, further confirming a dose-response relationship between these two conditions and age.

**Income:** There is a significant inverse relationship between household income and paediatric asthma and overweight. Stingone et al\(^1\) has reported an adjusted prevalence odds ratio of co-morbid paediatric asthma and overweight of 2.47 (95% C.I.: 1.03 - 5.96), comparing parental annual income of less than $20,000 to $75,000 or more. The odds ratio of paediatric asthma and obesity progressively decreased between these two income categories.

**Physical activity:** Physical activity appears to be a common protective factor against asthma\(^1\)\(^2\) and overweight/obesity.\(^1\)\(^4\) A lack of exercise may lead to reduced stretching of the respiratory airways,\(^1\)\(^3\),\(^1\)\(^2\)\(^5\),\(^1\)\(^6\) causing a greater tendency for the muscles in the airways walls to contract abnormally when in contact with minor irritants. Likewise, each additional kilometer walked per day is associated with a significant reduction in the
likelihood of obesity. It is important to note that while physical activity is exposure protective for both asthma and overweight/obesity, it can be harmful for some individuals by resulting in exercise-induced asthma.

**Second-hand smoking:** Exposure to second-hand (“passive”) tobacco smoke is positively associated with paediatric asthma and overweight/obesity.

**Breastfeeding:** Research has also indicated breastfeeding as a protective factor of paediatric asthma and overweight/obesity independently. The bioactive enzymes, hormones, growth factors, cytokines and immunological agents that are present in the milk help support healthy development.

**Race:** A study conducted by Black et al found a positive association between asthma and obesity that significantly varied by ethnicity. Although black youth were twice as likely and Hispanic youth were 25% less likely to have only asthma compared to white youth, the weight status and asthma relationship was stronger in Hispanic and weaker in black youth. These findings are supported by Stingone et al, where a prevalence odds ratio of co-morbid asthma and overweight of 3.18 (95% C.I.: 1.06 -9.50) comparing Puerto Rican to white children, was reported.

**Other individual factors:** Other common risk factors for asthma and overweight/obesity include, but are not limited to, parental education, prenatal diet, paediatric diet, genetic susceptibility, maternal overweight, levels of adipokines in early life, high birth weight, and rapid weight gain in the first year of life.

### 1.5.3 Environmental Predictors

Environmental factors have two main components: physical and social. This section gives a more detailed definition of the physical and social environment and their corresponding influence on asthma and weight status.

**Physical environment:** Health Canada defines the physical (or “built”) environment as encompassing all buildings, spaces, and products that are created and modified by people. For example, it comprises our homes, schools, workplaces, parks/recreation
areas, business areas, industries, roads, highways, electric transmission lines, and even underground waste disposal sites and subway trains. Constructs of the physical environment impacts factors such as indoor and outdoor air pollution, climatic conditions, allergens, safety and crime, land use and development, and modes of transportation.\textsuperscript{15}

Research indicates that physical environments in which we live, play, and attend school and work influences various health conditions including asthma and weight status.\textsuperscript{15,147-149} For example, one primary causal mechanism for asthma is exposure to indoor and outdoor air pollution, which is increased by industries and automobile use.\textsuperscript{16,150} A principal mechanism for overweight/obesity has been described as a decline in physical activity levels and adoption of a more sedentary lifestyle due to lack of access to safe areas and sprawling neighbourhoods that have increased reliance on automobiles for transportation.\textsuperscript{15} Many other characteristics of the physical environment have been found as common contributors to asthma and overweight/obesity, including housing quality and construction,\textsuperscript{151,152} spatial mobility (neighbourhood walkability/bikeability), land use and development,\textsuperscript{153,154} indoor allergens,\textsuperscript{155,156} safety and crime,\textsuperscript{151,157} and air quality.\textsuperscript{158,159} The paediatric asthma and overweight/obesity association has also been identified as strong particularly in samples residing in urban or highly polluted areas,\textsuperscript{66,75,78,160,161} both key characteristics of the physical environment.

**Social environment:** Many formal definitions of the social environment have been proposed, as it can be difficult to capture such a broad construct. Barnett and Casper\textsuperscript{162} define the social environment as encompassing the social relationships and cultural milieu within which defined groups of people function and interact. They listed its components as social and economic processes, wealth, social, human, and health services, power relations, governments, race relations, social inequality, cultural practices, and beliefs about a place and community. The Public Health Agency of Canada\textsuperscript{163} describes the social environment as the social support from families, friends, and the broader community. This environment is associated with civic vitality, defined as the strength of social networks within a community, region, province, or country, and is subsequently reflected in the organizations, institutions, and informal giving practices that people
create to share resources or build attachments with others. It is then stated that the health and well-being of individuals is influenced by societal norms/values, social stability, recognition of diversity, good working relationships, and cohesive communities, all factors of the social environment. A social environmental factor differs from a social individual-level predictor, where the former is a product of the surroundings in which one operates and affects a group of people (e.g., neighbourhood income), whereas the latter is a product of each individual (e.g., personal income).

Among many health conditions, research has indicated that the social environment in which we operate influences asthma and weight status. For example, Chen et al. discovered that adverse social conditions at the family level impact asthma morbidity by directly affecting the physiological system, whereas adverse social conditions at the community level affects the health behaviours of children and adolescents with asthma. Similarly, Oliver and Hayes reported that Canadian children and adolescents residing in lower socioeconomic status neighbourhoods have a higher risk of being overweight or obese compared to those living in higher socioeconomic status neighbourhoods. Additionally, Brisbon et al. proposed the following characteristics as potential common contributors to the asthma and obesity epidemic: cultural norms, social policies, networks (social cohesion/integration), and the social contexts found in one’s school, work, family, religion, health care system, and geographic location.

1.5.4 The Need to Focus on the Physical Environment

The need to focus on the environment as a potential predictor of co-morbid asthma and overweight/obesity over individual-level common risk factors is first outlined. Reasons are then given for choosing to examine the physical rather than social environment in this context.

Environmental vs. Individual factors: The evidence in Section 1.5.3 illustrates how a number of environmental determinants may predispose individuals to expressing both asthma and overweight/obesity. As such, the coexistence of these two conditions cannot purely be attributed to common individual-level predictors. The fact that research to date has primarily focused on the role of individual-level predictors on co-morbid asthma and
overweight/obesity, elicits the need to explore environmental factors as potential underlying mechanisms of these two conditions. This requirement is supported by Brisbon et al.,\textsuperscript{15} recommending that since asthma and obesity are intricately linked in many complex ways, significant reductions in the incidence and prevalence of these conditions will require an effort to address the common root causes embedded in the environment we have built. Another study reported asthma prevalence as positively associated with BMI in four rural Northern Plains Indian reservation communities, where this association differed across all four locations.\textsuperscript{170} The authors emphasized that these intertribal differences elicits the need for further understanding of the environmental factors associated with paediatric asthma and obesity that differ between these tribes. They further stated that acquiring knowledge on these possible risk factors could benefit disease prevention or management strategies for these co-morbid conditions.

**Physical vs. Social Environment:** When exploring common environmental risk factors, those of the physical environment should be prioritized. After a thorough review on physical and social environmental influences on asthma and obesity, Brisbon et al.\textsuperscript{15} concluded that this co-morbid epidemic would be positively affected through the study and modification of chiefly the physical environment. There is also more concrete evidence on the physical versus social environment as a common risk factor for asthma and overweight/obesity. Though evidence of the social environment influencing both conditions exists, social environmental factors are more difficult to capture, presenting difficulties with obtaining valid and reliable measures of these factors. Finally, Brisbon et al.\textsuperscript{15} has defined the physical environment as having a direct impact on social environmental and even individual-level predictors. The authors additionally illustrated that the physical environment exerts its influence on asthma and overweight/obesity in combination with the causal effects of both individual-level and other environmental (physical and social) factors. Since examining physical environmental risk factors of asthma and overweight/obesity may simultaneously address the role of other common risk factor categories, this further indicates the need to particularly target this macro-level predictor.
1.5.5 Linking Air Pollution to Asthma and Overweight/Obesity

The previous subsection emphasized the need to examine the physical environment as a prospective risk factor for co-morbid asthma and obesity. However, the physical environment has numerous constituents, several of which affect both conditions. Litonjua and Gold\textsuperscript{22} have recommended that since asthma and obesity both have their beginnings in early life, future research studies need to investigate exposures early in life. Air pollution is an early life, and even prenatal period, physical environment factor. It is more difficult for individuals to control their air pollution exposures than those through other environmental routes because it is impossible to carry clean air or stop breathing when exposed to polluted air.\textsuperscript{171} There is also some evidence that environmental air pollution may be contributing independently to the growing rates of asthma and overweight/obesity among children and adolescents.\textsuperscript{16,17} This collectively reveals air pollution as a potential causal risk factor of these co-morbid conditions that needs to be taken into account.

1.6 Role of Air Pollution

In this section, air pollution, its types, and sources are defined. Following this is the discussion of air pollution trends in Canada, and children/adolescents as a particularly susceptible population to its health effects. Lastly, the causal mechanisms and the results of statistical analyses of the relationships between air pollution and asthma, overweight/obesity, and co-morbid asthma and overweight/obesity will be reviewed.

1.6.1 Definition and Sources of Air Pollution

**Definition:** Environment Canada defines air pollution as a broad term applied to any chemical, physical, or biological agent that modifies the natural characteristics of the atmosphere.\textsuperscript{172} It is also the collection of gases, dust, fumes, or odour in amounts harmful to human health. The substances that cause air pollution are known as air pollutants, which Environment Canada has categorized into four main groups: criteria air contaminants (CACs), heavy metals, persistent organic pollutants (POPs), and toxics. Examples of CACs include total particulate matter with a diameter less than 100 microns (TPM), particulate matter with a diameter less than or equal to 10 microns (PM\textsubscript{10}), particulate matter with a diameter less than or equal to 2.5 microns (PM\textsubscript{2.5}), sulphur
oxides (SO₂), nitrogen oxides (NOₓ), ozone (O₃), volatile organic compounds (VOCs), carbon monoxide (CO), and ammonia. Heavy metals include a group of metals with a relatively high atomic mass, such as lead, cadmium, and mercury. POPs are organic compounds that are resistant to environmental degradation and are capable of travelling very large distances, such as dioxins and furans, polycyclic aromatic hydrocarbons (PAHs), and hexachlorobenzene. Finally, toxics comprise a broad class of pollutants toxic or poisonous to human health and the environment (e.g., benzene), essentially overlapping with CACs, heavy metals, and POPs that possess these characteristics. These categories of air pollutants cause broader issues such as smog, acid rain, climate change, indoor air pollution, land use issues, transboundary movement of air pollutants, and poor air quality. They are also detrimental to the environment, economy, and human health due to their bioaccumulation and toxic effects. Out of the four general groups of air pollutants, CACs are definitely the largest contributor to these issues.

The dominant origin of the key air pollutants, especially CACs, is through the combustion of fossil fuels, such as crude oil, coal, natural gas, petroleum, gasoline, diesel, and fuel oils. The sources responsible for the burning of these fuels are categorized as follows:

Motor vehicles: Primarily in urban areas, and progressively more in suburban areas, traffic-related (cars, buses, trucks) emissions are a major source of pollutants. Minor motor vehicle sources include aircraft, locomotives, marine vessels, recreational vehicles (e.g., snowmobiles, ATVs), forklifts, and ice resurfacers. Air pollution can arise specifically through the pumping of gasoline, vehicle exhaust, and the use of engines that are not tuned or working properly. Despite recent efforts to produce cleaner and efficient combustion engines, the increasing use of motor vehicles is leading to a corresponding increase in pollutant levels.

Industry: Another dominant source includes large industrial facilities (e.g., coal-fired power plants), and smaller industries (e.g., dry cleaners). Approximately half of Canadian air pollution is produced by large industry, primarily involving combustion systems. Specifically electricity and industrial energy generation in coal, oil, and gas-fired power
plants is responsible for a large proportion of air pollution emissions.\textsuperscript{172,174} Moreover, industrial emissions from the United States contribute to smog and acid rain in some parts of Canada, where a large proportion of the air pollution in the province of Ontario is transported from the United States.\textsuperscript{172,175}

\textbf{Other minor sources:} Additional sources of fuel combustion include lawn and gardening equipment, kitchen stoves, residential heating using fuel oil furnaces, water heaters, and barbecues.

Other important factors contributing to high air pollution levels are consumer products, agriculture, and transboundary air movements. Some air pollutants are road dust emissions from unpaved surfaces or naturally occurring, produced by forest fires, conifer forests, soil erosion, volcanoes, dust storms, lightning, and sea spray. Although the relative importance of each source listed in this section varies for different pollutants, the principal contributors to the most critical category of air pollutants, CACs, are industries and motor vehicles that burn fossil fuels.\textsuperscript{174}

\subsection*{1.6.2 Trends in Air Pollution}

As mentioned above, CACs have the largest impact on the physical environment, and subsequently, human health. Since they are also chief products of the two largest sources of air pollution, the prevalence and trends of Canadian CAC emissions will be discussed accordingly.

Over the period of 1990 to 2010, the national average of ground-level ozone has significantly increased by 10\%.\textsuperscript{176} From 1990 to 2011, emissions of ammonia increased by 22\%, and TPM (including PM\textsubscript{2.5} and PM\textsubscript{10}) by 35\%.\textsuperscript{177} This trend was based on information reported to the National Pollutant Release Inventory by industrial facilities and emission estimates from other sources such as motor vehicles, agricultural activities, and forest fires.

Conversely, other CACs relatively less critical to human health\textsuperscript{178,179} show a different outlook. From 1990 to 2011, Canadian emissions of a number of CACs have been significantly decreasing. Environment Canada has reported the magnitude of this
decrease as 60% for SO$_2$, 45% for CO, 28% for VOCs, and 21% for NO$_x$. From 1996 to 2010, sulphur dioxide (SO$_2$) levels declined by 62%, and nitrogen dioxide (NO$_2$) by 38%. The reduction in these CAC levels have been mainly attributed to climatic conditions, and more rigorous vehicular emission standards from the government during this time period.

The downward trend of numerous CACs over the last two decades in Canada is viewed as a national feat. However, considering two of the CACs that pose the most widespread health threats are particulate matter and ozone, these corresponding increasing trends are particularly worrisome. Thus, the findings discussed in this section indicate that the declining trends of less harmful CACs cannot reassure that human health is not being compromised by overall air pollution exposure. Certain populations are more susceptible to the health effects associated with these high levels of air pollution. One vulnerable population comprises of children and adolescents, due to reasons outlined in the next section.

1.6.3 Children and Adolescents as Susceptible Populations

Children and adolescents in particular may be more acutely affected by their environments due to their extrinsic mobility restriction which may hinder their ability to choose healthy behaviours. Children and adolescents are susceptible to the effects of specifically air pollution as a result of higher levels of outdoor physical activity. One study comparing activity patterns between children and adults found that children spent more than five times the minutes per day spent by adults engaging in active sports, walking/hiking, or outdoor recreation. To make matters worse, since children/adolescents are less likely to cease activity even when they are symptomatic, they present more severe health risks associated with air pollution exposure relative to older age groups. Children/adolescents also have increased exposure to air pollution due to a greater amount of inhaled pollution per pound of body weight and a higher ventilation rate. Specifically, air intake of a resting infant is twice that of an adult. In one study conducted in the Netherlands, though children were exposed to similar outdoor concentrations as those experienced by adults (38.5 versus 41.5 µg/m$^3$, respectively), children’s personal exposure averaged 66.8 µg/m$^3$ above ambient levels versus only 20.4
\( \mu g/m^3 \) above ambient levels for adults.\(^{182,183}\) These findings confirm the importance of examining air pollution as a common risk factor for co-morbid asthma and overweight/obesity in specifically children and/or adolescents.

Section 1.6.1-3 has elucidated the significance of assessing the role of particular types and sources of air pollution in paediatric populations. In reality, research has focused on the health effects of general air pollution exposure from multiple sources and in many age groups. Thus, in order to gain an overall understanding of the relationship between air pollution exposure and asthma and overweight/obesity, evidence for the role of any air pollutant on the development and prevalence of these two conditions will be reviewed.

### 1.6.4 Air Pollution and Asthma

This section discusses the mechanisms through which air pollution causes asthma, succeeded by a review for the statistical analysis of this relationship.

**Causal Mechanism:** Lung function is a fundamental mediator in the air pollution and asthma pathway. This is likely a result of the course of lung organogenesis. Although this process begins early in fetal life, only eighty percent of the lung alveoli are formed postnatal. Growth and changes are especially rapid in childhood and persist into adolescence.\(^{184}\) The lung epithelium's incomplete development causes greater lung permeability, resulting in more significant damage from air pollution exposure and further alteration in the normal process of paediatric lung development.\(^{171,185-189}\)

Airway inflammation is another significant intermediary step between air pollution exposure and the development of asthma. Research has shown that high air pollution levels have been associated with inflammation of the respiratory system.\(^{190}\) This has been confirmed by evidence of a positive association between air pollutants, such as TPM, PM\(_{2.5}\), PM\(_{10}\), O\(_3\), and SO\(_2\), and inflammatory markers such as interleukin-6 (IL-6), tumor necrosis factor-alpha, fibrinogen, and C-reactive protein (CRP).\(^{191-194}\) In asthma, the lung inflammatory response is also characterized by the recruitment and increased number of these inflammatory substances.\(^{191,195-199}\) Since the peripheral airways of children are more susceptible to inflammatory narrowing than those of adults,\(^{171}\) this suggests that air
pollution is especially likely to cause airway obstruction in asthmatics as a result of these inflammatory effects in paediatric populations.

Other proposed mechanisms by which air pollution could contribute to the development of asthma include oxidative stress/damage, airway wall remodelling, enhancing respiratory sensitization to allergens, affecting immunological responses, and interacting with antigenic proteins.  

**Empirical evidence**: The connection between air pollution exposure and asthma is reviewed as follows: studies examining estimated air pollution exposure and (1) asthma incidence; (2) asthma prevalence; (3) asthma exacerbations; (4) respiratory symptoms in non-asthmatics; and (5) studies examining indirect air pollution exposure and asthma. Considering a broad scope of studies allows for a better understanding of the comprehensive role air pollution has played in asthma status to date.

**Incidence studies**

The majority of studies that have examined the effects air pollution on the incidence of paediatric asthma have revealed a positive association. The prospective design of these studies satisfy the requirement for temporality, allowing the inference of causation between these two variables. A few of the remaining studies illustrating an ambiguous causal relationship between air pollution and incident asthma are those that measure community-level exposure. Measuring pollution exposure at this community level may have attenuated the true association as the grouping of individuals reduces the variation of exposure that exists between individuals within each cluster. In two individual-level studies, there was also no association between air pollution and incident asthma among infants and children respectively.

**Prevalence studies**

Many prevalence studies have shown a strong and positive association between a variety of air pollutants and paediatric asthma. These prevalence studies have captured larger sample sizes and a wider variety of air pollutants than incidence studies, both strengths contributing to the validity of these positive findings. However, more
associations that were not significant have been found in prevalence compared to incidence studies. These findings may be a result of measuring community-level air pollution, or due to measuring prevalence, where it is unknown whether or not study subjects had developed asthma prior to air pollution exposure. Despite the lack of known temporality in prevalence studies, a bi-directional relationship is not of any concern, as it is impossible for asthma to cause air pollution. Moreover, these few null findings are clarified by studies using longitudinal data that primarily confirm a positive association.

**Exacerbation studies**

Since there is evidence of a linkage between air pollution and asthma, a positive association between air pollution levels and symptom exacerbations in asthmatics is anticipated. This assumption has been strongly supported by several studies, where exacerbations are commonly quantified by the number of hospital admissions and emergency department visits, worsening of asthma symptoms, or increased bronchodilator usage corresponding to different air pollutant levels in asthmatics. Some exacerbation studies have alternatively discovered null and negative associations. However, some of these results may be biased due to reasons such as asthmatics experiencing frequent exacerbations they have become accustomed to, therefore deciding against the very time consuming hospital admission process. While exacerbation studies do contribute to an overall understanding of the air pollution and asthma relationship, asthma diagnosis rather than severity is a more valid measure in this context, reducing the likelihood of inconsistent findings.

**Respiratory symptoms**

Research has shown that increased levels of air pollution are associated with higher levels of respiratory symptom (i.e., wheezing, coughing, shortness of breath, chest tightness) incidence and prevalence in non-asthmatics. Seeing that respiratory symptoms are positively associated with asthma, this evidence supports air pollution as a potential risk factor of this outcome. Zhao et al however, identified that although there were many significant results between air pollution and respiratory symptoms in non-
asthmatics, none of the air pollution and cumulative asthma diagnosis associations were significant. This suggests symptoms in non-asthmatics are not the best proxy measures for being diagnosed with asthma as a consequence of air pollution. A few other respiratory symptom studies have also shown null and even negative associations.\textsuperscript{214,222,234,245}

\textit{Indirect measures of air pollution}

Even air pollution proxy measures are positively associated with paediatric asthma. For example, truck and general traffic density and counts have been noted to increase the likelihood of asthma incidence, prevalence, symptoms, exacerbations, and reduced lung function.\textsuperscript{217,246-253} Children living closer to major roads are more likely to be asthmatic.\textsuperscript{16,240,248,253-260} Though there are null associations between traffic-related measures and asthma,\textsuperscript{220,221,249,255,259,261-266} the difficulty in accounting for different types of roads (e.g., freeway or main roads) in exposure measurement and failure to validate traffic indicators with pollutants may be explanations for inconsistencies in the literature.\textsuperscript{267}

\textit{Summary}

The literature has repeatedly demonstrated a positive association between measures of air pollution and asthma. Though there have been some findings of no association, many of these studies measured air pollution at the community level, whereas individual-level studies, which were able to capture better microscale differences in pollution, have reported a positive association. It is likely that community-level studies fail to capture the microscale variations in air pollution exposure between individuals within each community, resulting in bias towards unity. When assessing the relationship between air pollution and asthma, quantifying air pollution exposure at a smaller level than the community level might then be more useful. In addition, the effects of more directly estimated air pollution on asthma incidence or prevalence rather than exacerbations and symptoms should be of primary focus. Otherwise, there is generally good evidence that air pollution is a potential causative agent of asthma.
1.6.5 Air Pollution and Weight Status

In this section, the mechanisms through which air pollution causes overweight/obesity are elaborated, followed by a review of their association.

Causal Mechanism: The primary mechanisms through which air pollution causes overweight/obesity are potentially systemic inflammation, suppressed adiponectin release, decreased physical activity, and low birth weight followed by early adiposity rebound. These intermediary factors are explained below.

High air pollution levels are causative of systemic inflammation. This has been confirmed by evidence of a positive association between multiple air pollutants and influential inflammatory markers (see Section 1.6.4). Studies have also shown that increased production of adipose tissue inflammatory markers are involved in obesity-associated metabolic syndrome and inflammation.\(^{196,268-270}\) These findings are specifically sustained by a positive association between CRP levels and overweight/obesity, and a positive correlation between IL-6 and percent body fat.\(^{195,271-273}\) Lastly, it has been determined that higher levels of these inflammatory response substances are expressed in the adipose tissue as a result of high air pollution exposure,\(^{274}\) therefore representing potential cellular mediators in the pathway between air pollution and the development of overweight/obesity.

Air pollution has been found to suppress adiponectin release.\(^{275-277}\) Since this protein hormone is negatively associated with triglyceride and intramyocellular lipid content, its suppression results in increased adiposity.\(^{276}\) This outcome is confirmed by studies that have reported lower levels of adiponectin in obese compared to non-obese adolescents,\(^{278}\) indicating adiponectin as a conceivable mediating mechanism through which air pollution causes overweight/obesity.

Another mechanism through which air pollution manifests its effects on overweight/obesity is through lack of physical activity. Increased urbanization has resulted in high-density traffic, low air quality, and high pollution levels, wherefore residing at distances greater than 200 metres from highly travelled main roads are
recommended to support healthy paediatric air consumption. Many children and adolescents live within this advised distance, and are accordingly exposed to high levels of air pollution that irritate the skin, eyes and other body systems. Air pollution specifically causes a decrease in oxygen striation and lower VO\textsubscript{2} max, both impairing exercise performance, and causing adverse symptoms such as pain upon inspiration, shortness of breath, and change in respiratory frequency when exercising. Consequentially, many children stay indoors either by choice or through the concern of their guardians, reducing physical activity. This notion is supported by numerous studies which have consistently reported significant inverse associations between traffic density, parental concerns about traffic, or annual mean PM\textsubscript{2.5} concentration and physical activity, fitness, or active commuting to school. The role of physical activity as a mediator between the air pollution and overweight/obesity relationship is illustrated by studies reporting an increased probability of overweight/obesity, BMI, and skinfold thickness as a consequence of decreased physical activity. In fact each additional kilometer walked per day is associated with a 4.8% reduction in the likelihood of obesity. These findings thus signify a lack of exercise as a more proximal risk factor to the distal effects of air pollution on overweight/obesity development.

A fourth mechanism through which air pollution exerts its effects on overweight/obesity is low birth weight followed by early adiposity rebound in childhood. Prenatal exposure to many air pollutants such as PM\textsubscript{2.5}, PM\textsubscript{10}, O\textsubscript{3}, NO\textsubscript{2}, NO\textsubscript{x}, CO, SO\textsubscript{2}, and PAHs, are inversely associated with fetal size, birth weight, head circumference, and birth length. Higher levels of pollutants also increase the risk of delivering small for gestation age and preterm babies. These measures of low birth weight/size are commonly associated with an earlier than normal adiposity rebound (younger than 6 years of age; see Section 1.3.1), subsequently increasing the risk of paediatric and/or adult obesity.

Empirical Evidence: Considering research on the association between air pollution and overweight/obesity generally differs in the type of exposure quantified, this relationship is reviewed accordingly: studies examining the effects of (1) estimated air pollution...
exposure; (2) early life (prenatal, perinatal) air pollution exposure; and (3) indirect exposure to air pollution, on weight status.

Estimated exposure

The effect of estimated air pollutants on obesity has primarily been investigated using animal models. These studies all discovered a positive association between exposure to CACs and measures of obesity (e.g., adiposity, weight gain).\textsuperscript{274,277,311,312} Alternatively, a connection between estimated air pollution exposure and obesity in adults was displayed in a study conducted by Carwile and Michels,\textsuperscript{313} examining the effects of the environmental contaminant Bisphenol A (BPA). The authors demonstrated that relative to participants in the lowest BPA exposure quartiles, the upper three had cumulatively higher odds of general and central obesity and greater waist circumference. While food, water, and soil are other sources of BPA, the presence of this contaminant in urban ambient outdoor air (especially PM) has been confirmed by many studies,\textsuperscript{314-316} signifying air pollution as a potential risk factor of overweight/obesity. However, much more exposure estimate studies conducted on humans rather than animals is required to strengthen this inference.

Pre/perinatal exposure

Most of the studies indicating causal effects of air pollution on the development of obesity in humans have explored prenatal or perinatal exposure. This type of exposure has been partially ascribed to air pollutants classified as environmental estrogens (e.g., PAHs, BPA, dioxins), due to a recent hypothesis that exposure to these endocrine disrupting chemicals in utero alters metabolic programming early in life\textsuperscript{159} and generates abnormalities in homeostatic control systems necessary for the maintenance of normal body weight throughout one’s life.\textsuperscript{317} These hypotheses were initially guided by in vitro and animal studies showing that brief pre/perinatal exposure to environmental estrogens increased body weight with age and accelerated adipocyte formation.\textsuperscript{318-323} Rundle et al\textsuperscript{159} later confirmed this association in humans when reporting that prenatal exposure to ambient estrogenic PAHs predicted higher BMI z-score and obesity at 5 and 7 years of age, and increased fat mass at 7 years. As previously mentioned, the effects of prenatal
exposure have also been attributed to many CACs (e.g., PM$_{2.5}$, PM$_{10}$, O$_3$, NO$_2$) that increase the risk of low birth weight and subsequent early adiposity rebound, both factors that negatively influence overweight/obesity development.

Indirect exposure

Transport sector activity produces about a quarter of greenhouse gas emissions,$^{324}$ all associated with many adverse health effects.$^{325,326}$ The few studies that accordingly examined the role of this air pollution proxy measure on overweight/obesity reported a positive association.$^{287,324,327-329}$ Most of this effect has been explained by greater distance travelled by motor vehicles in comparison to larger car/engine size and lower active travel$^{324}$; one possibility for this discovery is larger motorized travel distance increases carbon dioxide production, subsequently leading to obesity.$^{330}$ Jerrett et al$^{17}$ recognized that the majority of studies examining the effects of traffic on the current obesity epidemic are cross-sectional, and conducted a longitudinal study following children aged 9-10 years annually until age 18 accordingly. Air pollution exposure was based on traffic density, where increased exposure within 150 metres of the home was associated with a significant increase in BMI at age 18. This study was the first of its kind to measure the effects of a dominant source of critical pollutants on obesity incidence in human adolescents. However, a more direct quantification of air pollution is required to draw more sound conclusions.

Summary

Overall, estimated exposure to key CACs in children/adolescents have not been used to explore the relationship between air pollution and paediatric overweight/obesity. Evidence supporting estimated air pollution exposure as a risk factor for overweight/obesity mainly used animal models, whereas research examining humans have used pre/perinatal or indirect exposure measures. In fact, the study conducted by Jerrett et al$^{17}$ is considered the best illustration of this relationship in children/adolescents to date, where only air pollution proxy measures were used. This is unlike the literature illustrating the air pollution and paediatric asthma relationship, where human exposure to common critical pollutants are more directly quantified (see Section 1.6.4). Otherwise,
the numerous positive associations and their elucidated causal mechanisms provided in this section imply that air pollution increases the risk of developing overweight/obesity.

1.6.6 Air Pollution and Asthma and Weight Status

Overall, the literature has shown that environmental pollution may stimulate the onset and/or exacerbation of asthma and also may separately affect the accumulation of body fat. However, evidence of air pollution as a preceding risk factor of concurrent paediatric asthma and obesity is required to understand its role in their coexistence. In this section, the role the environment and specifically air pollution plays on the simultaneous incidence/prevalence of both asthma and overweight/obesity in children and adolescents will be reviewed.

Causal Mechanism: While the mechanisms through which air pollution causes co-morbid asthma and overweight/obesity have not been identified to date, the causal pathways involved in the separate relationships between air pollution and asthma or weight status are likely to play a role. Some of these mechanisms are common to both independent pathways, such as systemic inflammation. Huang et al.\textsuperscript{331} corroborates the presence of this shared intermediary factor by reporting that inflammatory markers known to increase with high air pollution exposure were significantly elevated in obese asthmatic compared to normal subjects. Additionally, many studies have displayed high levels of inflammatory markers as associated with all three variables. A second potential mechanism common to both independent pathways is decreased physical activity. Airway narrowing caused by air pollution could transiently and permanently decrease exercise capacity and subsequent physical activity.\textsuperscript{283} Reduced physical activity increases the risk of poor respiratory function and obesity, signifying the prospect of this causal pathway. Another shared mechanism is suppressed adiponectin release. Similar to the air pollution and overweight/obesity pathway described in Section 1.6.5, air pollution decreases adiponectin levels,\textsuperscript{275,277} consequently influencing asthma. This is supported by studies demonstrating a lower serum concentration of this hormone in asthmatics relative to controls, after adjusting for BMI.\textsuperscript{332}
A combination of the unshared causal mechanisms (e.g., lung function, low birth weight followed by early adiposity rebound) could also be responsible for the relationship between air pollution and co-morbid asthma and overweight/obesity. It is then likely that the mechanism(s) through which air pollution simultaneously causes both conditions is/are unique to each individual. More research on these specific and novel pathways would be useful towards understanding the etiology of this co-morbidity.

**Empirical Evidence:** Research on the relationship between air pollution, asthma, and weight status can be mainly classified as follows: studies examining (1) if weight status modifies the air pollution and asthma association; (2) the effects of estimated air pollution exposure on asthma and overweight/obesity; and (3) the effects of indirect exposure to air pollution on asthma and overweight/obesity.

*Weight status as an effect modifier*

Research on the air pollution, asthma, and overweight/obesity relationship has largely investigated whether weight status modifies the association between air pollution and respiratory symptoms/asthma. Deposition of fine particles in the respiratory tract is positively correlated with BMI, suggesting that greater weight may increase the risk of asthma from inhalation of pollution particles. This rationale for weight status as an effect modifier of the air pollution and asthma relationship is supported by a study conducted by Bennett et al. The authors revealed that greater BMI and adiposity resulted in greater acute ozone-induced decrements in pulmonary function, in non-asthmatic young adults. Guided by analogous studies conducted on genetically modified obese mice, Bennett et al. discovered this association for the first time in humans. Dong et al. later investigated this relationship in children from Northeast China, where the positive association between PM$_{10}$, SO$_2$, NO$_2$, and O$_3$ and asthma/respiratory symptoms was consistently stronger in those that were overweight or obese than among those of normal weight. The numerous studies illustrating the effect of air pollution on asthma as dependent on weight status is indicative of a significant relationship between these three variables.

*Estimated exposure*
A study conducted by Xu et al.\(^{340}\) evaluated the relationship between estimated short-term exposure to PM\(_{2.5}\) and inflammatory responses in mice during and two months after the 2008 Beijing Olympic Games. Air pollution levels significantly decreased during the Games due to air quality control measures that were implemented by the government. During and after the Games, macrophages and inflammatory markers had significantly increased in the lung and visceral fat with increasing PM\(_{2.5}\). However, these numbers were even higher after compared to those during the Games. The authors noted that the lung inflammatory response in asthmatics is characterized by an increased number of these substances, while adipose tissue macrophages and inflammatory substances accumulate in obesity development, advocating air pollution as a potential causal factor of asthma and obesity. Short-term air quality improvements may even prevent/improve these co-morbid outcomes by reducing systemic inflammation, a key underlying mechanism in this pathway. Although evidence from animal studies are considered weaker, the most widely used animal model of human disease was studied (genetically modified C57BL/6 mice), justifying the review of these results. Still, studies examining the effects of estimated air pollution exposure in humans instead of animals would produce more valid findings. This limitation and the use of lung and adipose tissue inflammatory markers as outcomes rather than asthma and overweight/obesity diagnosis, collectively presents significant gaps to be addressed.

*Indirect exposure*

Many studies have demonstrated that overweight and obesity are positively associated with asthma/respiratory symptoms in children living in highly polluted areas.\(^{66,75,78,160,161}\) However, a direct comparison to less polluted areas is required to determine whether this co-morbidity varies by different exposure levels. This necessity has been addressed by a few studies investigating the effects of indirect measures of air pollution exposure on paediatric asthma and obesity.\(^{341-343}\) For instance, air pollution levels in urban areas are generally higher than in rural areas; Lawson and colleagues\(^{341}\) sought to confirm the existence of an urban-rural gradient in asthma prevalence among Canadian youths and to evaluate whether this gradient was mediated by obesity status. Asthma prevalence became progressively lower as the degree of rurality increased, with a significant
difference between urban and rural regions. Obesity status did not mediate this significant association, indicating asthma occurring as a result of urban/rural status, regardless of obesity. However, obesity was reported as independently and positively associated with asthma, indicating this coexisting relationship is potentially due to a third variable associated with this urban-rural gradient. This hypothesis is supported by Suh et al. where the association between BMI and asthma symptoms in boys was significantly positive among metropolitan, provincial, and industrial areas, whereas null in rural areas. Seeing both studies proposed the environment as a likely mechanism through which this relationship exists, along with a known association between air pollution levels and urban/rural status, a conceivable mechanism is the physical environmental factor, air pollution.

Another example of an indirect exposure study is the comparison of asthma and overweight/obesity across larger geographical regions. Perez-Padilla et al. reported higher obesity prevalence and poorer lung function among Mexican-Americans than Mexicans. Seeing that the United States is generally more polluted than Mexico, air pollution could be one of the factors influencing the geographic difference in these outcomes.

While there is evidence of positive association between air pollution proxy measures and co-morbid asthma and overweight/obesity, comparing the prevalence of these two conditions across large geographic areas (e.g., urban versus rural, countries) is not as effective as the comparison between individuals, as cluster effects need to be taken into account. In addition, examining this co-morbidity across a better urban-rural gradient may capture the influence of air pollution exposure more accurately. Finally, employing a more direct measurement of air pollution would allow for more valid conclusions.

Summary

Although the evidence provided in the above sections indicates air pollution as a potential risk factor of asthma and overweight/obesity separately, it is more difficult to conclude this exposure is a preceding risk factor of these conditions as a co-morbidity. First, there is relatively narrower evidence in the literature regarding the association between air
pollution and co-morbid asthma and overweight/obesity. Existing evidence mostly focuses whether weight status is an effect modifier of the air pollution and asthma relationship, and indirect/proxy measures of air pollution, asthma, and overweight/obesity are frequently used. Short-term air pollution exposure has mainly been quantified, whereas the examination of long-term exposure is required to observe any realistic influence on asthma and obesity development. A number of studies exploring these three variables have also focused on animal models. Most importantly, there is no evidence to date of a study examining the effect of estimated air pollution on the simultaneous development/prevalence of asthma and overweight/obesity in humans. To acquire a better understanding of the etiology of this co-morbidity and explore air pollution as a possible root cause in paediatric populations, there is a distinct requirement to address this significant gap.

1.7 Summary

With the high rates of paediatric asthma and overweight/obesity, it is important that effective efforts are made towards tackling this co-morbid epidemic. Left neglected, these children and adolescents face serious long-term health ramifications more so than children that have only one of these conditions. While many studies support an association between asthma and weight status, the exact nature of this coexistence remains unclear; as a result, identifying a root cause for treatment/prevention strategies is a challenging task. There is currently some evidence that air pollution is potentially contributing to the growing rates of separate asthma and overweight/obesity, suggesting this environmental exposure is a common risk factor of these two conditions as a co-morbidity. Since better understanding of these two separate pathways will contribute to an overall understanding of the potential air pollution and co-morbid asthma and overweight/obesity association, it would be useful to examine the relationships between the following: (1) estimated microscale air pollution exposure and asthma incidence or prevalence; and (2) estimated air pollution exposure (excluding pre/perinatal) and overweight/obesity in paediatric populations. Though the literature indicates that air pollution may stimulate the separate onset of asthma and overweight/obesity, it is more difficult to conclude that this exposure is a preceding risk factor of these conditions as a
co-morbidity. The causal mechanisms involved in this latter pathway are less understood, and there is no evidence to date of a study investigating the effect of estimated air pollution on the simultaneous incidence/prevalence of asthma and overweight/obesity in humans. Future approaches to this co-morbid epidemic need to address this gap to provide insight on the specific disease mechanisms involved and appropriately tailor prevention/intervention strategies.

This thesis begins to explore a potential underlying mechanism of paediatric co-morbid asthma and overweight/obesity in a local Canadian context. It examines the effect of more directly estimated microscale air pollution exposure on the separate and simultaneous prevalence of asthma and overweight/obesity. The objectives of this thesis are further detailed in Chapter 2.
Chapter 2

2 Objectives and Hypotheses

2.1 Overall Objective

This thesis aims to explore a potential underlying mechanism of paediatric co-morbid asthma and overweight/obesity by examining the effect of air pollution on separate and co-morbid paediatric asthma and overweight/obesity. No study has specifically analyzed air pollution as a potential risk factor for both conditions together. Exploring the effect of air pollution on either asthma or overweight/obesity will provide further insight on whether this environmental exposure is a common risk factor for both conditions. For the purposes of this thesis, the word “effect” refers to the association between air pollution and these paediatric outcomes.

Focus on adolescence: The effects of air pollution on paediatric co-morbid asthma and overweight/obesity will be examined among adolescents. Adolescence is an important developmental bridge between childhood and adulthood. The physical and psychosocial changes that occur during this time provide insight on early childhood risk factors, and foresee threats to adult health and quality of life. In addition, asthma and obesity are more associated with one another in adolescents compared to children.10

Both overweight and obesity will be assessed as measures of excess weight status. As such, overweight and obese adolescents are both referred to as overweight for the remainder of this thesis.

Sub-analysis: Lastly, the effect of air pollution on co-morbid asthma and overweight will be analyzed by taking into account factors that are associated with this exposure and paediatric co-morbidity. These potential effect modifiers have been identified as geographic location, income, age, and sex.

Geographic Location
It is important to consider geographic area of residence when examining the relationship between air pollution and co-morbid asthma and overweight. Previous evidence demonstrates that the environmental factors related to air pollution are most prevalent/pronounced in urban areas, resulting in higher ambient air pollution in these areas versus non-urban areas. Furthermore, the highest levels of air pollutants critical to human health are found in urban areas. This is explained by the steady increase of commuting in urban settings, while pollutants of industrial and heating origin have also remained a significant source in these areas. The literature also highlights the asthma and overweight association as strongest in urban areas (see Section 1.6.6). While this evidence collectively advocates a stronger air pollution and concurrent asthma and overweight relationship among those residing in urban areas, this co-morbidity has yet to be examined across an urban-rural gradient.

Urban core status is a measure of geographic location that captures a suitable urban-rural gradient. In this study, the strength of association between the air pollution and co-morbid asthma and overweight will be compared between adolescents living in an urban core and those living outside of an urban core.

Income

Income is another pertinent factor to be taken into account when examining the air pollution and co-morbid asthma and overweight relationship. Air pollution is a factor incorporated into housing prices, where property values are often higher in areas of better air quality. Realtors are aware that, regardless of one’s income, buyers would prefer to live in clean areas that are not detrimental to health. Many families feel more comfortable that these areas offer a cleaner environment for their children to be exposed. However, families with higher levels of income are more likely to actually purchase residences in less polluted areas. This rationale is supported by studies demonstrating low income as associated with poor air quality and higher levels of air pollution that adversely affect individual health. Total household income is found as negatively associated with ozone and particulate matter exposure levels. Likewise, evidence for a significant negative association between household income and co-morbid asthma and overweight
(see Section 1.5.2) indicates that low income is also a risk factor of this paediatric outcome. It is currently unknown whether the air pollution and co-morbid asthma and overweight relationship is affected by household income. This thesis will compare this association between adolescents residing in households of high and low income.

**Age**

It is important to examine the different stages of adolescence when assessing the air pollution and co-morbid asthma and overweight relationship. Paediatric age is associated with air pollution exposure levels. Section 1.5.2 also discusses a significantly positive association between paediatric age and co-morbid asthma and overweight. As such, this study will examine whether the strength of the association between air pollution and co-morbid asthma and overweight varies across age groups in adolescence. Identifying the specific stage of adolescence where the effects of pollution on this co-morbidity is strongest is crucial for the targeting of disease reduction strategies to a particular narrower age group.

**Sex**

Finally, it is important to consider sex when assessing the relationship between air pollution and co-morbid asthma and overweight. Villarreal-Calderon et al reported that males spend significantly more time outdoors on weekdays and weekends than their female peers, regardless of age. This finding among others reveals air pollution exposure as greater in males relative to females. Section 1.5.2 also discusses the risk of co-morbid asthma and overweight as more likely in males compared to females. Though the evidence as a whole is suggestive of a stronger air pollution and co-morbid asthma and overweight association among males, this relationship has yet to be compared by sex.

### 2.2 Specific Objectives

**Objective 1**

The first goal of this thesis is to assess:

a) The relationship between air pollution concentrations and asthma in adolescents.
b) The relationship between air pollution concentrations and overweight in adolescents.

**Objective 2**

The second objective of this thesis is to assess the relationship between air pollution concentrations and co-morbid asthma and overweight in adolescents.

**Objective 3**

The third objective of this thesis is to assess if the effect of air pollution concentrations on co-morbid asthma and overweight is different for:

(a) Adolescents residing in an urban core and those not residing in an urban core.
(b) Adolescents residing in a high versus low income household.
(c) Younger versus older adolescents.
(d) Males and females.

2.3 Hypotheses

**Objective 1**

Based on previous literature, it is expected that as air pollution concentrations increase, asthma in adolescents is more likely to increase. Similarly, a significant positive association between air pollution concentrations and overweight in adolescents is expected.

**Objective 2**

No previous studies have examined the effect of air pollution on co-morbid asthma and overweight in adolescents. It is hypothesized that as air pollution concentrations increase, co-morbid asthma and overweight is more likely to increase.

**Objective 3**

(a) **Urban core:** It is expected that the association between air pollution concentrations and concurrent asthma and overweight will be different for
adolescents residing in an urban core and non-urban core. Specifically, it is hypothesized that as air pollution concentrations increase, co-morbid asthma and overweight in urban core adolescents is more likely to increase. No such association is anticipated among adolescents living in a non-urban core area.

(b) **Income**: It is hypothesized that the relationship between air pollution and co-morbid asthma and overweight will be positive for both high and low household income adolescents; however, adolescents from low income households are expected to have a higher probability of co-morbid asthma and overweight than high income adolescents across all air pollution concentrations.

(c) **Age**: It is expected that the effect of air pollution concentrations on co-morbid asthma and overweight will be positive in younger and older adolescents; however, it is anticipated that the probability of having both conditions will be higher in older adolescents than among those who are younger, at all pollution concentrations.

(d) **Sex**: It is hypothesized that the association between air pollution and concurrent asthma and overweight will be different for males and females. Specifically, it is expected that as air pollution concentrations increase, co-morbid asthma and overweight is more likely to increase in both males and females; however, this association is expected to be stronger in males than females.
Chapter 3

3 Methods

This thesis assessed the effects of air pollution concentrations on asthma, overweight, and co-morbid asthma and overweight, and whether the air pollution and co-morbid asthma and overweight relationship is modified by urban core status, income, age, and sex. This chapter begins with an overview of the data and study population used in this thesis (Section 3.1). Following is an overview of the measurement instruments used in the analysis (Section 3.2), and a detailed description of all preliminary and regression analyses performed (Section 3.3). This chapter concludes with a discussion in Section 3.4 of other statistical considerations such as the software and estimation method used, measures of model fit, missing data, and survey weights.

3.1 Data Sources and Study Population

Three data sources were used to assess the effect of air pollution on co-morbid asthma and overweight among adolescents: (1) the Canadian Community Health Survey (CCHS) was used to measure the outcome variables of interest and their associated covariates, as well as (2) the Environment Canada 2009 National Pollutant Release Inventory (NPRI) and (3) 1996 to 2000 meteorological data which were used to measure exposure to air pollution at the postal code level.

CCHS: The CCHS is a cross-sectional survey that collects health status, health determinant, and health care utilization information for the population of Canada. The CCHS was conducted biennially from 2001 through 2005, and starting in 2007 data collection was executed annually. For the present thesis, five annual data files from 2007 through 2011 were combined to increase the sample size. The CCHS target population were persons aged 12 years and older living in private dwellings in the 10 provinces and three territories. This target population excluded persons living on Indian Reserves or Crown lands, those residing in institutions, full time members of the Canadian Forces, and those residing in certain remote regions, resulting in 98% coverage of the Canadian population. The survey was predetermined to consist of approximately 130,000
respondents over a two year period. Computer-assisted interviewing was used to collect survey data. CCHS employed two different modes of computer-assisted interviewing: computer-assisted personal interviewing (CAPI) was used to conduct interviews in person, whereas computer-assisted telephone interviewing (CATI) conducted interviews via telephone. More detailed information about the CCHS can be found in publicly available user guides, provided by Statistics Canada.\textsuperscript{360}

**NPRI:** PM\textsubscript{2.5} emissions data were obtained from the Environment Canada 2009 NPRI, a federal inventory of industrial pollutant releases to air, water, and land disposals and transfers for recycling in 2009. This inventory is publicly accessible and includes information collected from facilities that meet compulsory reporting requirements for over 300 substances, including key air pollutant emission estimates.

NPRI data have increasingly achieved and maintained a high level of quality by ensuring data relevance, accuracy, reliability, completeness, understandability, accessibility, and timeliness.\textsuperscript{363} Industries that meet NPRI reporting requirements are necessitated by law to submit information that fit these dimensions of data quality; penalties are given to those that do not report on time and submit false or misleading emissions information.

**Meteorological data:** Meteorological data were obtained from Aermod-ready surface and upper air datasets, created by Environment Canada.\textsuperscript{362} The surface data site was located at the London International Airport in London, Ontario, and the upper air data station was located at White Lake, Michigan. The surface meteorological sites used ceiling height, wind speed, wind direction, air temperature, total cloud opacity, and total cloud amount, while taking into account three different wind independent surface conditions, from 1996 to 2000. These three surface parameters were all set to urban values, a 50/50 mixture of coniferous and deciduous forests, and a 45/45/5/5 mixture of grassland, cultivated land, coniferous forests, and deciduous forests, respectively.

The surface meteorological data were pre-processed to yield a minimum wind speed of about 1 m/s, and to reduce missing data. These pre-processing steps involved setting hours with calm (equal to zero) or very low wind speeds (i.e., less than 4 km/h) to 4 km/h, setting calm wind directions to a “missing” value, and applying linear interpolation
to meteorological elements that had up to six consecutive missing hours. If there were more than 5% missing data after the above processing, imputation was performed using data from the nearest station with similar geographic conditions.

**Study Population:** All analyses were conducted on adolescents between the ages of 12 and 18 years residing in southwestern Ontario, which is defined as a sub region of southern Ontario in the province of Ontario, Canada. The city of London is the geographic center of this region. It extends north to south from the Bruce Peninsula to Lake Erie shorelines and east to south-west from Guelph to Windsor. Its population in 2011 was estimated at approximately 3,514,700, accounting for 32.1% of Ontario’s entire population. The CCHS provides a categorical measure for the health region associated with the postal code residence of each respondent. The 14 CCHS health regions corresponding to southwestern Ontario are the Brant County, Elgin-St. Thomas, Grey Bruce, Haldimand-Norfolk, Halton Regional, Huron County, Chatham-Kent, Lambton, Middlesex-London, Oxford County, Perth District, Waterloo, Wellington-Dufferin-Guelph, and Windsor Essex County health units.

Since paediatric BMI does not hold its usual interpretation during pregnancy due to significant physiological changes, adolescents who were pregnant at the time of the survey were excluded from the analysis. Based on all the above inclusion/exclusion criteria, the sample size and response rates for each survey year are provided in Appendix A. The final sample consisted of selected adolescents residing in southwestern Ontario, who responded to any of the five CCHS survey cycles, 2007 through 2011 (n=2,974).

### 3.2 Measurement Instruments

This section describes how the outcome and exposure variables, and their associated covariates, used in the analysis were measured.

**Asthma:** Across all CCHS cycles, self-reported asthma status was measured using a binary variable representing the question “Do you have asthma?” that can be answered “Yes” or “No”. This variable was re-coded as Yes = 1 and No = 0 (reference category).
Those that responded “Don’t know”, “Refusal”, or chose not to answer the question (all missing data) were excluded from the analysis.

**Overweight:** Overweight was assessed using BMI, which was calculated as weight in kilograms divided by height in metres squared (kg/m\(^2\)). The CCHS provided self-reported values for weight and height (without shoes on). The IOTF growth curve, providing age- and sex-specific BMI cut-off points,\(^{38}\) was then used to determine overweight status. This variable was coded as Yes = 1 and No = 0, indicating not being overweight as the reference category.

Respondents with missing data for height and weight were excluded from the analysis, since their BMI could not be determined. Adolescents with biologically implausible values for height, weight, and BMI as defined by the CDC\(^{364}\) were also excluded from the analysis.

**Asthma and Overweight:** The binary indicator for co-morbid asthma and overweight was created by grouping respondents into two categories. These categories corresponded to being both asthmatic and overweight (coded as Yes = 1) and not being both asthmatic and overweight (coded as No = 0; the reference group). Adolescents with missing data for either of the separate variables, asthma and overweight, were considered “missing” for this co-morbid indicator and excluded from the analysis.

**Air pollution:** For the purposes of this study, air pollution exposure was measured using estimates of PM\(_{2.5}\). PM\(_{2.5}\) exposure estimates were computed by researchers at the Human Environments Analysis Laboratory (HEAL) at Western University Canada.\(^{365}\) Industrial PM\(_{2.5}\) emissions data released from the 2009 NPRI were combined with local meteorological data (1996 to 2000 surface and upper air datasets for southwestern Ontario), and modelled in Aermod.\(^{366}\) Then coupled with ArcGIS,\(^{367}\) the output of this entire modelling process produced a continuous variable estimating 2009 PM\(_{2.5}\) concentration values (µg/m\(^3\)) at the postal code centroid in southwestern Ontario. These values were modelled at a 24-hour averaging period as the Ontario Ministry of the Environment measures the Ambient Air Quality Criteria (AAQC) for particulate matter on a 24-hour averaging time. The AAQC for PM\(_{2.5}\) is 30 µg/m\(^3\) for a 24 hour averaging
period. Although this thesis examined outcome data collected from 2007 to 2011, and exposure data measured in 2009, PM$_{2.5}$ is relatively stable over a five year span.

The PM$_{2.5}$ exposure data are representative of only industrial sources. PM$_{2.5}$ values calculated for each postal code should thus be interpreted as concentrations relative (not absolute) to all other postal code areas in southwestern Ontario.

PM$_{2.5}$ had a considerable positively skewed distribution. Outliers were identified as values beyond four standard deviations (SD) around the weighted mean of PM$_{2.5}$; these comprised of 1.01% (n=27) of the data points. Outliers were then recoded to these cut-off values (mean + 4 SDs = 1.83755 µg/m$^3$). A quadratic variable for PM$_{2.5}$ was computed by squaring the above continuous variable, to explore a potential nonlinear effect of PM$_{2.5}$ concentrations in each study objective.

**Urban Core:** Urban core status was operationalized as a binary variable, based on the CCHS variable measuring urban and rural areas of residence. Each respondent was classified as residing in a rural area, primary urban core, urban fringe, urban area outside a census metropolitan area/census agglomeration, secondary urban core, or mix of urban and rural areas. For this study, the urban core variable was created by collapsing this CCHS variable into two categories: residing in a primary or secondary urban core (coded as Yes = 1), or not residing in these two urban core areas (representative of the remaining four geographic areas of residence; coded as No = 0; the reference category).

**Income:** Income was approximated using the CCHS variable that groups respondents’ total household income into 12 categories in the 2007 and 2008 surveys, 14 categories in the 2009 and 2010 surveys, and 15 categories in 2011. Thus, the original groups were recoded to match the coding of 2007 and 2008, into the following categories: 1 = No income; 2 = Less than $5,000; 3 = $5,000 to $9,999; 4 = $10,000 to $14,999; 5 = $15,000 to $19,999; 6 = $20,000 to $29,999; 7 = $30,000 to $39,999; 8 = $40,000 to $49,999; 9 = $50,000 to $59,999; 10 = $60,000 to $79,999; 11 = $80,000 to $99,999; 12 = $100,000 or more. Respondents with missing values (19.9%; n=592) were assigned to one of 12 income categories based on Statistics Canada 2006 Census data reporting median total household income before taxes and deductions for each forward sortation area in
southwestern Ontario.\textsuperscript{370} This variable was treated as continuous in the present thesis, and was centred around its weighted mean to improve the interpretability of the intercept in the regression analysis.

To assess whether income modifies the association between PM\textsubscript{2.5} and co-morbid asthma and overweight, the continuous indicator for income was also categorized into two groups: less than $60,000 (coded lower = 0; the reference category) and greater than or equal to $60,000 (coded higher = 1). The value of $60,000 was used based on Ontario’s 2005 median total household income before taxes and deductions of $60,455.\textsuperscript{370} Even though this median value was used to measure “higher” versus “lower” income, it is recognized that this value is higher than Canada’s 2005 before-tax low income cut-offs (often used to estimate poverty), ranging from $14,313 to $55,022 according to community and family size.\textsuperscript{371}

\textbf{Age}: The CCHS provided a continuous measure of age in years by computing the difference between the date of interview and respondent’s date of birth. To improve the interpretability of the intercept in the regression analysis, age was centered by subtracting the constant 12 from every value of the variable (redefining the 0 point as the youngest adolescent age).

To assess whether age modifies the association between PM\textsubscript{2.5} and co-morbid asthma and overweight, the continuous indicator for age was categorized into two groups: 12 to 15 years (coded younger = 0; the reference category) and 16 to 18 years (coded older = 1).

\textbf{Sex}: Across all CCHS cycles, this binary variable composed of two categories, Male and Female. Sex was re-coded as Male = 1 and Female = 0 (the reference category).

\subsection*{3.3 Statistical Analysis}

\textbf{Data Linkage}: Before any statistical analyses were carried out, the PM\textsubscript{2.5} exposure and CCHS outcome data were linked using a postal code variable present in both datasets. In the CCHS, this variable represented each respondent’s postal code of residence, and in the PM\textsubscript{2.5} exposure dataset, this variable represented all 58,632 postal codes in
southwestern Ontario at which concentration values of PM$_{2.5}$ were measured. The linkage step was also performed to select adolescents only residing in southwestern Ontario.

**Preliminary Analysis:** The prevalence of asthma, overweight, and co-morbid asthma and overweight was estimated for all adolescents aged 12 to 18 years residing in southwestern Ontario, Ontario, and Canada and compared across urban core residence status, household income levels, adolescent age groups, and sex. Descriptive statistics were computed for the pollution exposure, confounding, and effect modifier variables. This included the calculation of frequencies for categorical variables (urban core status, income, age and sex), and means and standard deviations for continuous variables (PM$_{2.5}$, income and age).

**Regression Analysis:** Logistic regression was used to assess the three study objectives outlined in Section 2.2. This statistical technique models the effect of one or a set of independent variables on the likelihood of a single binary outcome. Independent variables can be continuous or categorical.

The equation for the multiple logistic regression model is as follows:

$$logit(\pi_i) = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \ldots + \beta_n X_n$$

where $\pi_i$ is the probability of the outcome

$X_i$ ($i = 1, \ldots, n$) are the independent variables

$\beta_0$ is the intercept

$\beta_i$ ($i = 1, \ldots, n$) are the slope coefficients (also called regression parameters)

$logit$ is the ln(odds of the outcome); that is, $\ln \left( \frac{\pi_i}{1-\pi_i} \right)$

The intercept ($\beta_0$) denotes the log odds of the outcome when $X_i = 0$ (after centering variables where required). Given the logistic regression equation above, exponentiating the intercept gives us the odds of the outcome when $X_i = 0$. 
When interpreting the effect of a continuous independent variable, exponentiating a regression coefficient ($\beta_i$) estimates the odds ratio of the outcome for every one-unit increase in $X_i$, adjusting for all other independent variables in the model.

For categorical independent variables, $e^{(\beta_i)}$ is the odds ratio of the outcome comparing the higher category of $X_i$ to its reference category (e.g., males vs. females), adjusted for all other independent variables in the model.

**Objective 1**

The first objective examined the relationships between PM$_{2.5}$ concentrations and two outcomes in adolescents: (1) asthma; and (2) overweight. The first set of regression models measured the effect of PM$_{2.5}$ on asthma. The second set of regression models measured the effect of PM$_{2.5}$ on overweight. Past research suggests that air pollution exposure is associated with geographic location, income, age, and sex (see Section 2.1). These four factors are also risk factors of paediatric asthma$^{10,26,341,372-374}$ and paediatric overweight.$^{357,375-377}$ As such, the effects of PM$_{2.5}$ on both outcomes, adjusted for the effects of the covariates urban core status, continuous income, continuous age, and sex, were also estimated. For each crude and adjusted model, the linear effect of PM$_{2.5}$ was evaluated by default. All results (significant or non-significant) from these models will be discussed accordingly. The crude and adjusted quadratic effects of PM$_{2.5}$ were also assessed; however, only statistically significant results from these models will be discussed.

The predicted probabilities of separate asthma and overweight were computed across a range of PM$_{2.5}$ exposure levels. Predicted probabilities were calculated using the intercept and regression coefficients obtained from the unadjusted default linear models for the associations between PM$_{2.5}$ and these two outcomes. Unadjusted, instead of adjusted, probabilities were reported to allow for comparison of probabilities across all study objectives, and because the main effects are the primary focus of this study. For each association, if results from the quadratic model were statistically significant, the predicted probabilities for the unadjusted curvilinear effect were computed in place of those for the linear effect. For each percentile value of PM$_{2.5}$, the sum of the natural logarithm of the
odds was first calculated using the first equation below. Given the second formula below, the result of the previous step was converted to odds by exponentiation, and the odds were then transformed to probabilities.

\[
\logit(\pi_i) = \beta_0 + \beta_1 PM_{2.5_i}
\]

\[
Pr(\text{asthma and overweight}|PM_{2.5} = X_i) = \frac{\exp(\beta_0 + \beta_1 X_i)}{1 + \exp(\beta_0 + \beta_1 X_i)}
\]

The latter formula denotes the probability that an adolescent has asthma and is overweight, separately, at a given PM$_{2.5}$ exposure level. These predicted probabilities were plotted separately for each model.

**Objective 2**

The second objective was to estimate an overall relationship between PM$_{2.5}$ concentrations and co-morbid asthma and overweight in adolescents. This was achieved using logistic regression that measured the effect of PM$_{2.5}$ on the asthma and overweight variable. The effect of PM$_{2.5}$ adjusted for urban core status, continuous income, continuous age, and sex was also evaluated. For all crude and adjusted associations, both the linear and quadratic effects of PM$_{2.5}$ were assessed. The linear models were examined by default, whereas quadratic models were conducted as an additional test.

Using the formulas provided above, the crude predicted probabilities of co-morbid asthma and overweight were calculated and plotted across a range of PM$_{2.5}$ exposure levels.

**Objective 3**

The third objective explored whether the association between PM$_{2.5}$ concentrations and co-morbid asthma and overweight in adolescents was different across four factors: (1) urban core residence status; (2) income; (3) age; and (4) sex. This was accomplished using four sets of unadjusted and adjusted logistic regression models that assessed the presence of interaction between PM$_{2.5}$ and one of the modifiers listed above at a time. The remaining three factors were also kept in the adjusted models as confounders. Models
testing for the interaction between PM\(_{2.5}\) and either income or age used categorical, instead of continuous, measures of these two individual-level characteristics (see Section 3.2). For each set of interaction models, if the results were not statistically significant, then the main PM\(_{2.5}\) and co-morbid asthma and overweight association controlling for the covariate of interest (parallel effect) was tested. Both the linear and quadratic effects of PM\(_{2.5}\) were estimated for all models. The linear models were examined by default, whereas quadratic models were conducted as an additional test.

The predicted probabilities of co-morbid asthma and overweight were computed across a range of PM\(_{2.5}\) exposure levels. Using the log odds obtained from the unadjusted interaction models, probabilities were calculated for the following groups of adolescents: (1) those residing in an urban core and those not residing in an urban core; (2) those residing in a higher income household and those residing in a lower income household; (3) younger and older; and (4) males and females. If the results from an interaction model were not statistically significant (see above), then predicted probabilities for the main association controlling for the covariate of interest (urban core status, categorical income, categorical age, or sex) were computed instead. The formulas used to calculate predicted probabilities are provided in the Objective 1 section above; however, the addition of the regression term for the covariate of interest (e.g., \(\beta_2 sex_i\)) is required, and if significant, the interaction term between PM\(_{2.5}\) and the modifier of interest (e.g., \(\beta_3 PM_{2.5,i} \times sex_i\)). Finally, predicted probabilities were plotted separately for each model, and within each model, separately for the stratified groups of adolescents (e.g., males and females).

3.4 Other Statistical Considerations

Software and Data Access: All preliminary analyses and main analyses were executed using SAS 9.4 software. These analyses were conducted at the Research Data Centres at Western University and York University.

Assessing Model Fit: For the first and second objective, the fit of all sets of analogous crude and adjusted models were compared. For the third objective, all curvilinear interaction models were compared to their nested linear interaction models. Likelihood ratio tests were used to compare the fit of these models.
The likelihood ratio test is a type of chi-square difference test that uses the log likelihood values and degrees of freedom for each of the models being compared. After defining the nested models specified by the null and alternative hypotheses, the likelihood ratio test is calculated via the following formula:

\[ \chi^2_{df} = -2L_O - (-2L_A) \]

where \( L_O \) is the log likelihood for the model specified under the null hypothesis

\( L_A \) is the log likelihood for the model specified under the alternative hypothesis

\( df \) is the difference between the degrees of freedom in the models specified under the null and alternative hypotheses.

The larger the value of the test statistic (greater difference between \( L_O \) and \( L_A \)), the better the fit of the alternative model with respect to the null.

**Missing Data:** A small percentage of respondents, 0.1% (n=3), 9.6% (n=286), and 9.7% (n=289) had missing data for the asthma, overweight, and co-morbid asthma and overweight variables, respectively. Considering these variables are all outcomes of interest, these individuals (n=289) were excluded from all preliminary and main analyses, reducing the final sample size of 2,974 to 2,685 (see Section 3.1). Due to the imputation method implemented using Statistics Canada Census data (see Section 3.2), the indicator for income had no missing data in all analyses. The remaining analysis variables, PM\(_{2.5}\), urban core, age, and sex, had no missing data.

Since almost 10% of the final sample were excluded, respondents with and without missing outcome data (n=289 and n=2,685, respectively) were compared on all covariates. T-tests for continuous variables and Pearson’s chi-square tests for categorical variables were calculated to assess potential differences that could impact the results. Results from this analysis are provided in Appendix B.

**Survey Weights:** When sampling individuals to participate in the CCHS, there were unequal probabilities of selection and different proportions of individuals that chose not
to respond across each survey cycle. Statistics Canada provided sampling weights for each cycle to ensure analysis estimates are representative of the Canadian population.

All sampling weights were rescaled after applying the study population inclusion/exclusion criteria, after removing cases with missing data, and prior to merging the CCHS survey files for analysis. For each cycle, weights were adjusted by dividing each individual’s sampling weight by the mean sampling weight of the total eligible respondents. All analyses, including preliminary, and logistic regression analyses assessing the three study objectives, were conducted using these adjusted weights.
Chapter 4

4 Results

Descriptive characteristics of the sample are first presented in this chapter, including the prevalence of asthma, overweight, and both conditions (Section 4.1). Following is a discussion of the association between PM$_{2.5}$ concentrations and asthma and overweight separately and simultaneously (Sections 4.2 and 4.3). This chapter concludes with a discussion of whether the relationship between PM$_{2.5}$ and co-morbid asthma and overweight is modified by urban core status, income, age, and sex (Section 4.4).

4.1 Sample Characteristics

Regional Differences in Outcome Variables: Among the adolescent population aged 12 to 18 years residing in Canada, 11.6% had asthma, 21.7% were overweight, and 3.0% had both conditions, whereas in Ontario, 11.3% had asthma, 22.3% were overweight, and 2.8% had both conditions (Table 1). Among adolescents residing in southwestern Ontario, 11.6% were asthmatic; 25.0% were overweight; 3.2% had both conditions (Table 1). While the prevalence of asthma and both conditions were relatively similar across these three regions, overweight prevalence in southwestern Ontario was higher than that of Ontario and Canada.
Table 1: Separate and co-morbid asthma and overweight prevalence in adolescent respondents to the CCHS in southwestern Ontario, Ontario, and Canada.

<table>
<thead>
<tr>
<th>Region</th>
<th>N</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Southwestern Ontario</td>
<td>Ontario</td>
</tr>
<tr>
<td><strong>Asthma</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>310</td>
<td>(11.6%)</td>
</tr>
<tr>
<td>No</td>
<td>2,375</td>
<td>(88.4%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>2,685</td>
<td></td>
</tr>
<tr>
<td><strong>Overweight</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>671</td>
<td>(25.0%)</td>
</tr>
<tr>
<td>No</td>
<td>2,014</td>
<td>(75.0%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>2,685</td>
<td></td>
</tr>
<tr>
<td><strong>Asthma and Overweight</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>86</td>
<td>(3.2%)</td>
</tr>
<tr>
<td>No</td>
<td>2,599</td>
<td>(96.8%)</td>
</tr>
</tbody>
</table>

**Covariates:** A total of 2,685 respondents between the ages 12 and 18 years residing in southwestern Ontario were analyzed in this study. The descriptive characteristics of these adolescents are provided in Table 2. Fifty-three percent of the sample were male. About two thirds (64.9%) of the respondents resided in an urban core area, and 61.5% of respondents had a household income greater than or equal to $60,000. The average age was 15.1 ± 1.9 years, with 54.7% of adolescents between 12 and 15 years, and 45.3% between 16 and 18 years. The average PM$_{2.5}$ exposure concentration was 0.29 ± 0.29 µg/m$^3$. 
Table 2: Characteristics of adolescent respondents to the CCHS who reside in southwestern Ontario.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urban core residence</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1,742 (64.9%)</td>
</tr>
<tr>
<td>No</td>
<td>943 (35.1%)</td>
</tr>
<tr>
<td>Income</td>
<td></td>
</tr>
<tr>
<td>Higher (Greater than or equal to $60,000)</td>
<td>1,650 (61.5%)</td>
</tr>
<tr>
<td>Lower (Less than $60,000)</td>
<td>1,035 (38.5%)</td>
</tr>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>12-15 years</td>
<td>1,469 (54.7%)</td>
</tr>
<tr>
<td>16-18 years</td>
<td>1,216 (45.3%)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1,426 (53.1%)</td>
</tr>
<tr>
<td>Female</td>
<td>1,259 (46.9%)</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td></td>
</tr>
<tr>
<td>PM$_{2.5}$ exposure</td>
<td>0.29 (0.29)</td>
</tr>
<tr>
<td>Income</td>
<td>9.7 (2.2)</td>
</tr>
<tr>
<td>Age</td>
<td>15.1 (1.9)</td>
</tr>
</tbody>
</table>

**Abbreviations:** SD (standard deviation); PM$_{2.5}$ (particulate matter with an aerodynamic diameter of 2.5 µm or less, µg/m$^3$)

Outcome Variables by Urban Core Indicator: Asthma prevalence was relatively higher in those residing in an urban core area (12.1% versus 10.5% in non-urban core area), whereas overweight prevalence was higher in those residing in a non-urban core area (26.3% versus 24.3%); see Table 3. The prevalence of co-morbid asthma and overweight were similar across urban core and non-urban core areas (3.4% versus 2.9%, respectively). The chi-square tests for differences across urban core status were not statistically significant for asthma ($\chi^2=1.7210$, $p=0.1896$), overweight ($\chi^2=1.2558$, $p=0.2624$), and both conditions ($\chi^2=0.4470$, $p=0.5038$).
Table 3: Separate and co-morbid asthma and overweight across urban core residence status among adolescent respondents to the CCHS residing in southwestern Ontario.

<table>
<thead>
<tr>
<th>Urban Core Status N (%)</th>
<th>Urban core</th>
<th>Non-urban core</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Asthma</strong> $\chi^2=1.7210$, $p=0.1896$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>211 (12.1%)</td>
<td>99 (10.5%)</td>
</tr>
<tr>
<td>No</td>
<td>1,531 (87.9%)</td>
<td>844 (89.5%)</td>
</tr>
<tr>
<td>Total</td>
<td>1,742</td>
<td>943</td>
</tr>
<tr>
<td><strong>Overweight</strong> $\chi^2=1.2558$, $p=0.2624$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>423 (24.3%)</td>
<td>248 (26.3%)</td>
</tr>
<tr>
<td>No</td>
<td>1,319 (75.7%)</td>
<td>695 (73.7%)</td>
</tr>
<tr>
<td>Total</td>
<td>1,742</td>
<td>943</td>
</tr>
<tr>
<td><strong>Asthma and Overweight</strong> $\chi^2=0.4470$, $p=0.5038$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>59 (3.4%)</td>
<td>27 (2.9%)</td>
</tr>
<tr>
<td>No</td>
<td>1,683 (96.6%)</td>
<td>916 (97.1%)</td>
</tr>
<tr>
<td>Total</td>
<td>1,742</td>
<td>943</td>
</tr>
</tbody>
</table>

Outcome Variables by Income Groups: Asthma prevalence for adolescents living in a higher income household was 11.5%, and for those living in a lower income household, 11.7%; see Table 4. The chi-square test for differences across income levels was not statistically significant ($\chi^2 = 0.0467$, $p = 0.8290$). Overweight prevalence in adolescents residing in lower income households was higher than that among adolescents residing in higher income households (27.5% versus 23.4%). The chi-square test for differences across income was statistically significant ($\chi^2 = 5.5948$, $p=0.0180$). The prevalence of co-morbid asthma and overweight was 3.2% and 3.3% in higher versus lower income adolescents, respectively, with a non-significant chi-square test for differences, $\chi^2=0.0530$, $p=0.8179$. 
Table 4: Separate and co-morbid asthma and overweight across household income levels among adolescent respondents to the CCHS residing in southwestern Ontario.

<table>
<thead>
<tr>
<th>Household Income Level</th>
<th>N</th>
<th>(%)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>High</td>
<td>Lower</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Asthma</strong> ((\chi^2=0.0467, p=0.8290))</td>
<td>189</td>
<td>121</td>
<td>11.5%</td>
<td>11.7%</td>
</tr>
<tr>
<td>Yes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1,461</td>
<td>914</td>
<td>(88.5%)</td>
<td>(88.3%)</td>
</tr>
<tr>
<td>Total</td>
<td>1,650</td>
<td>1,035</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Overweight</strong> ((\chi^2=5.5948, p=0.0180))</td>
<td>386</td>
<td>285</td>
<td>23.4%</td>
<td>27.5%</td>
</tr>
<tr>
<td>Yes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1,264</td>
<td>750</td>
<td>(76.6%)</td>
<td>(72.5%)</td>
</tr>
<tr>
<td>Total</td>
<td>1,650</td>
<td>1,035</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Asthma and Overweight</strong> ((\chi^2=0.0530, p=0.8179))</td>
<td>52</td>
<td>34</td>
<td>3.2%</td>
<td>3.3%</td>
</tr>
<tr>
<td>Yes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1,598</td>
<td>1,001</td>
<td>(96.8%)</td>
<td>(96.7%)</td>
</tr>
<tr>
<td>Total</td>
<td>1,650</td>
<td>1,035</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Outcome Variables by Age Groups: The prevalence of asthma for those aged 16 to 18 years, 13.0%, was higher than that among adolescents aged 12 to 15 years, 10.3% (Table 5). The chi-square test for differences across these adolescent age groups was statistically significant \((\chi^2=4.8345, p=0.0279)\). Adolescents aged 12 to 15 years and 16 to 18 years had an overweight prevalence of 26.1% and 23.7%, respectively. The chi-square test for differences in overweight across age groups was not statistically significant \((\chi^2=1.9985, p=0.1574)\). The prevalence of co-morbid asthma and overweight was higher in older versus younger adolescents (4.0% and 2.5%, respectively), with a significant chi-square test for differences, \(\chi^2=4.6757, p=0.0306\).
Table 5: Separate and co-morbid asthma and overweight across adolescent age groups among CCHS respondents residing in southwestern Ontario.

<table>
<thead>
<tr>
<th>Age Group N (%)</th>
<th>12-15 years</th>
<th>16-18 years</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Asthma</strong> ($\chi^2=4.8345, p=0.0279$)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>152</td>
<td>158</td>
</tr>
<tr>
<td>(10.3%)</td>
<td>(13.0%)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1,317</td>
<td>1,058</td>
</tr>
<tr>
<td>(89.7%)</td>
<td>(87.0%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1,469</td>
<td>1,216</td>
</tr>
<tr>
<td><strong>Overweight</strong> ($\chi^2=1.9985, p=0.1574$)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>383</td>
<td>288</td>
</tr>
<tr>
<td>(26.1%)</td>
<td>(23.7%)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1,086</td>
<td>928</td>
</tr>
<tr>
<td>(73.9%)</td>
<td>(76.3%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1,469</td>
<td>1,216</td>
</tr>
<tr>
<td><strong>Asthma and Overweight</strong> ($\chi^2=4.6757, p=0.0306$)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>37</td>
<td>49</td>
</tr>
<tr>
<td>(2.5%)</td>
<td>(4.0%)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1,432</td>
<td>1,167</td>
</tr>
<tr>
<td>(97.5%)</td>
<td>(96.0%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1,469</td>
<td>1,216</td>
</tr>
</tbody>
</table>

Outcome Variables by Sex: Asthma prevalence was relatively higher in females (12.7% versus 10.5%), whereas overweight prevalence was notably higher in males (28.5% versus 21.0%); see Table 6. The prevalence of co-morbid asthma and overweight was similar for males and females (3.3% versus 3.1%, respectively). The chi-square test for differences across sex was not significant for asthma ($\chi^2=3.1967, p=0.0738$), statistically significant for overweight ($\chi^2=20.3906, p<0.0001$), and not significant for co-morbid asthma and overweight ($\chi^2=0.0465, p=0.8293$).
Table 6: Separate and co-morbid asthma and overweight across sex among adolescent respondents to the CCHS residing in southwestern Ontario.

<table>
<thead>
<tr>
<th></th>
<th>Sex</th>
<th>N (%)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Males</td>
<td>Females</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Asthma</strong> (χ²=3.1967, p=0.0738)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>150</td>
<td>160</td>
<td>(10.5%)</td>
<td>(12.7%)</td>
</tr>
<tr>
<td>No</td>
<td>1,276</td>
<td>1,099</td>
<td>(89.5%)</td>
<td>(87.3%)</td>
</tr>
<tr>
<td>Total</td>
<td>1,426</td>
<td>1,259</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Overweight</strong> (χ²=20.3906, p&lt;0.0001)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>407</td>
<td>264</td>
<td>(28.5%)</td>
<td>(21.0%)</td>
</tr>
<tr>
<td>No</td>
<td>1,019</td>
<td>995</td>
<td>(71.5%)</td>
<td>(79.0%)</td>
</tr>
<tr>
<td>Total</td>
<td>1,426</td>
<td>1,259</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Asthma and Overweight</strong> (χ²=0.0465, p=0.8293)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>47</td>
<td>39</td>
<td>(3.3%)</td>
<td>(3.1%)</td>
</tr>
<tr>
<td>No</td>
<td>1,379</td>
<td>1,220</td>
<td>(96.7%)</td>
<td>(96.9%)</td>
</tr>
<tr>
<td>Total</td>
<td>1,426</td>
<td>1,259</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

4.2 Effect of PM$_{2.5}$ on Separate Asthma and Overweight

The first objective of this thesis is to examine the relationship between PM$_{2.5}$ and asthma and PM$_{2.5}$ and overweight among adolescents. For each association, the linear and curvilinear effects of PM$_{2.5}$ were assessed using logistic regression, and their corresponding estimates are provided in Tables 7 and 8. As the linear models were examined by default, their results will be further described throughout this section and illustrated in Figure 2, regardless of statistical significance. Figure 2 was created via the conversion of log odds from the unadjusted linear models to predicted probabilities of asthma and overweight across a range of PM$_{2.5}$ exposure percentiles (see Section 3.3). For ease of interpretation, the figures displayed Sections 4.3 and 4.4 were also created using this method. Since all quadratic models were considered to be an additional test to the default linear models, their corresponding results are shown in Tables 7 and 8, but are not discussed, as none of them was statistically significant.
The effect of PM$_{2.5}$ on adolescent asthma in the unadjusted model was negative (OR 0.93, 95% CI 0.61-1.41; Table 7); see Figure 2. However, this effect was not statistically significant (p=0.7271). After controlling for urban core status, income, age, and sex, the effect of PM$_{2.5}$ on asthma remained non-significant (OR 0.89, 95% CI 0.58-1.37, p=0.5980; Table 7). A likelihood ratio test comparing the crude and adjusted model was also performed, and the results were not statistically significant (0.05 ≤ p < 0.10).

The unadjusted odds ratio for overweight associated with a one µg/m$^3$ increase in PM$_{2.5}$ was 1.47 (95% CI 1.11-1.95; see Table 8), and statistically significant (p=0.0071). Figure 2 presents this positive effect in terms of expected probabilities of overweight, where it is observed that as PM$_{2.5}$ exposure levels increase, the probability that an adolescent is overweight increases. The PM$_{2.5}$ and overweight association remained significant after controlling for the effects of urban core status, income, age, and sex (OR 1.50, 95% CI 1.12-1.99, p=0.0059; Table 8). The likelihood ratio test comparing the crude and adjusted model was also statistically significant (p<0.005).

![Figure 2](image)

*Figure 2: Crude predicted probabilities of separate asthma and overweight across PM$_{2.5}$ exposure percentiles among adolescents residing in southwestern Ontario.*
Table 7: Logistic regression models exploring the effect of PM$_{2.5}$ on asthma among adolescents residing in southwestern Ontario.

<table>
<thead>
<tr>
<th></th>
<th>Linear Effect</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Crude OR (95% CI)</td>
<td>Adjusted$^a$ OR (95% CI)</td>
<td></td>
</tr>
<tr>
<td>PM$_{2.5}$</td>
<td>0.93 (0.61, 1.41)</td>
<td>-0.0745</td>
<td>0.2136</td>
<td>0.7271</td>
</tr>
<tr>
<td>PM$_{2.5}^2$</td>
<td>0.89 (0.58, 1.37)</td>
<td>-0.1168</td>
<td>0.2214</td>
<td>0.5980</td>
</tr>
</tbody>
</table>

|                      | Curvilinear Effect |                   |                   |                   |
|                      |               | Crude OR (95% CI) | Adjusted$^a$ OR (95% CI) |                   |
| PM$_{2.5}$           | 1.29 (0.36, 4.70) | 0.2556            | 0.6587            | 0.6980            |
| PM$_{2.5}^2$         | 0.80 (0.34, 1.87) | -0.2282           | 0.4348            | 0.5997            |
| PM$_{2.5}$           | 0.96 (0.25, 3.69) | -0.0423           | 0.6876            | 0.9510            |
| PM$_{2.5}^2$         | 0.95 (0.40, 2.27) | -0.0507           | 0.4434            | 0.9090            |

**Note:** Results significant at the 5% level (p < 0.05) are highlighted in bold.

**Abbreviations:** OR (odds ratio); CI (confidence interval); SE (standard error); p (probability); PM$_{2.5}$ (particulate matter with an aerodynamic diameter of 2.5 µm or less, µg/m$^3$)

$^a$Adjusted for the effects of urban core status, income, age, and sex.
Table 8: Logistic regression models exploring the effect of PM$_{2.5}$ on overweight among adolescents residing in southwestern Ontario.

<table>
<thead>
<tr>
<th></th>
<th>Log odds</th>
<th>SE</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Linear Effect</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM$_{2.5}$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crude OR (95% CI)</td>
<td>1.47 (1.11, 1.95)</td>
<td>0.3857</td>
<td>0.1434</td>
</tr>
<tr>
<td>Adjusted$^a$ OR (95% CI)</td>
<td>1.50 (1.12, 1.99)</td>
<td>0.4030</td>
<td>0.1462</td>
</tr>
<tr>
<td><strong>Curvilinear Effect</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM$_{2.5}$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crude OR (95% CI)</td>
<td>-0.5361</td>
<td>0.5386</td>
<td>0.4880</td>
</tr>
<tr>
<td>PM$_{2.5}^2$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crude OR (95% CI)</td>
<td>1.83 (1.04, 3.22)</td>
<td>0.6042</td>
<td>0.2886</td>
</tr>
<tr>
<td>Adjusted$^a$ OR (95% CI)</td>
<td>-0.4297</td>
<td>0.5386</td>
<td>0.2998</td>
</tr>
</tbody>
</table>

**Note:** Results significant at the 5% level ($p < 0.05$) are highlighted in bold.

**Abbreviations:** OR (odds ratio); CI (confidence interval); SE (standard error); p (probability); PM$_{2.5}$ (particulate matter with an aerodynamic diameter of 2.5 µm or less, µg/m$^3$)

$^a$Adjusted for the effects of urban core status, income, age, and sex.
4.3 Overall Effect of PM$_{2.5}$ on Co-morbid Asthma and Overweight

The second objective of this thesis is to assess the relationship between PM$_{2.5}$ concentrations and co-morbid asthma and overweight in adolescents. Logistic regression was used to examine the linear and curvilinear effect of PM$_{2.5}$ on co-morbid asthma and overweight, and the corresponding estimates from both models are provided in Table 9. In this section, only results from the default linear models will be further discussed and illustrated in Figure 3 as unadjusted predicted probabilities of co-morbid asthma and overweight, regardless of statistical significance. Results from the curvilinear models are also presented in Table 9; however, none of them was significant.

The crude odds ratio for co-morbid asthma and overweight was 1.18 (95% CI 0.59-2.36; Table 9), but this effect was not statistically significant (p=0.6330); see Figure 3. After controlling for the effects of urban core status, income, age, and sex, the overall effect of PM$_{2.5}$ remained non-significant (OR 1.14, 95% CI 0.56-2.31, p=0.7187; Table 9). A likelihood ratio test was executed to compare the crude and adjusted model. This test also yielded a non-significant result (p>0.10).
Figure 3: Crude predicted probabilities of co-morbid asthma and overweight across PM$_{2.5}$ exposure percentiles among adolescents residing in southwestern Ontario.
Table 9: Logistic regression models exploring the effect of PM$_{2.5}$ on co-morbid asthma and overweight among adolescents residing in southwestern Ontario.

<table>
<thead>
<tr>
<th></th>
<th>Log odds</th>
<th>SE</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Linear Effect</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM$_{2.5}$</td>
<td>Crude OR (95% CI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.18 (0.59, 2.36)</td>
<td>0.1679</td>
<td>0.3515</td>
</tr>
<tr>
<td></td>
<td>Adjusted$^a$ OR (95% CI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM$_{2.5}$</td>
<td>1.14 (0.56, 2.31)</td>
<td>0.1303</td>
<td>0.3617</td>
</tr>
<tr>
<td><strong>Curvilinear Effect</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM$_{2.5}$</td>
<td>Crude OR (95% CI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.57 (0.06, 5.27)</td>
<td>-0.5545</td>
<td>1.1311</td>
</tr>
<tr>
<td>PM$_{2.5}^2$</td>
<td>1.59 (0.42, 6.03)</td>
<td>0.4648</td>
<td>0.6798</td>
</tr>
<tr>
<td></td>
<td>Adjusted$^a$ OR (95% CI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM$_{2.5}$</td>
<td>0.43 (0.04, 4.43)</td>
<td>-0.8396</td>
<td>1.1874</td>
</tr>
<tr>
<td>PM$_{2.5}^2$</td>
<td>1.85 (0.47, 7.33)</td>
<td>0.6156</td>
<td>0.7025</td>
</tr>
</tbody>
</table>

Note: Results significant at the 5% level ($p < 0.05$) are highlighted in bold.

Abbreviations: OR (odds ratio); CI (confidence interval); SE (standard error); p (probability); PM$_{2.5}$ (particulate matter with an aerodynamic diameter of 2.5 µm or less, µg/m$^3$)

$^a$Adjusted for the effects of urban core status, income, age, and sex.
4.4 Stratified Effect of PM$_{2.5}$ on Co-morbid Asthma and Overweight

The third objective of this thesis is to examine whether the effect of PM$_{2.5}$ concentrations on co-morbid asthma and overweight is different for the following groups of adolescents: (1) those residing in an urban core and those not residing in an urban core; (2) those residing in households with higher versus lower income; (3) younger and older; and (4) males and females. This was accomplished using four sets of linear and curvilinear logistic regression models that assess the presence of interaction between PM$_{2.5}$ and one of the following characteristics at a time: urban core status, income, age, and sex. If the interaction effect for each set of models was not statistically significant, then the overall linear and curvilinear PM$_{2.5}$ and co-morbid asthma and overweight relationship controlling for the covariate of interest, was examined. The estimates corresponding to all unadjusted models stated above are provided in Tables 10 to 13. Estimates from the adjusted models are presented in Appendix C. Regardless of statistical significance, results from the default linear models are further described throughout this section and illustrated in Figures 4 to 7 as crude predicted probabilities of co-morbid asthma and overweight. All of the quadratic models yielded non-significant results, and are therefore not discussed. Likelihood ratio tests were also performed to compare all curvilinear interaction models to their nested linear interaction models, and the results were not statistically significant (p>0.10).

Urban Core Status: The interaction effect between PM$_{2.5}$ and urban core status was statistically significant in the unadjusted linear model (p=0.0138; Table 10); that is, the PM$_{2.5}$ and co-morbid asthma and overweight association is significantly different for adolescents residing in urban core and non-urban core areas. This difference in the main association across urban core status is illustrated in Figure 4. Among adolescents residing in an urban core area, there is a slight increase in the probability of co-morbid asthma and overweight as PM$_{2.5}$ exposure concentrations increase. Conversely, the effect of PM$_{2.5}$ is quite pronounced among adolescents residing in a non-urban core area, where a substantial decrease in co-morbid asthma and overweight across increasing PM$_{2.5}$ levels is observed. The rate of decline in co-morbid asthma and overweight across PM$_{2.5}$ values is
much steeper for non-urban core adolescents than the rate of incline for their urban core peers, further indicating a non-parallel effect. After controlling for the effects of income, age, and sex, this linear interaction remained significant (p=0.0147; Appendix C).

Figure 4: Crude predicted probabilities of co-morbid asthma and overweight across PM$_{2.5}$ exposure percentiles among adolescents residing in urban core and non-urban core areas in southwestern Ontario.
Table 10: Crude logistic regression models exploring whether the effect of PM$_{2.5}$ on co-morbid asthma and overweight is modified by urban core residence status among adolescents residing in southwestern Ontario.

<table>
<thead>
<tr>
<th></th>
<th>OR (95% CI)</th>
<th>Log odds</th>
<th>SE</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Linear Effect</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM$_{2.5}$</td>
<td>0.00 (0.00, 0.28)</td>
<td>-8.0409</td>
<td>3.4600</td>
<td>0.0201</td>
</tr>
<tr>
<td>Urban core (No=0)</td>
<td>0.28 (0.10, 0.80)</td>
<td>-1.2780</td>
<td>0.5356</td>
<td>0.0170</td>
</tr>
<tr>
<td>PM$_{2.5}$*urban core$^a$</td>
<td>5246.94 (5.74, 4796514.18)</td>
<td>8.5654</td>
<td>3.4786</td>
<td>0.0138</td>
</tr>
<tr>
<td><strong>Curvilinear Effect</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM$_{2.5}$</td>
<td>0.00 (0.00, 1.87)</td>
<td>-9.2520</td>
<td>5.0394</td>
<td>0.0664</td>
</tr>
<tr>
<td>PM$_{2.5}^2$</td>
<td>22.11 (0.00, 115629306.70)</td>
<td>3.0961</td>
<td>7.8929</td>
<td>0.6949</td>
</tr>
<tr>
<td>Urban core (No=0)</td>
<td><strong>0.25 (0.07, 0.92)</strong></td>
<td><strong>-1.3933</strong></td>
<td><strong>0.6656</strong></td>
<td><strong>0.0363</strong></td>
</tr>
<tr>
<td>PM$_{2.5}$*urban core$^a$</td>
<td>19335.54 (0.73, 514754167.50)</td>
<td>9.8697</td>
<td>5.1988</td>
<td>0.0576</td>
</tr>
<tr>
<td>PM$_{2.5}^2$*urban core$^b$</td>
<td>0.04 (0.00, 240097.41)</td>
<td>-3.1545</td>
<td>7.9304</td>
<td>0.6908</td>
</tr>
</tbody>
</table>

**Note:** Results significant at the 5% level (p < 0.05) are highlighted in bold.

**Abbreviations:** OR (odds ratio); CI (confidence interval); SE (standard error); p (probability); PM$_{2.5}$ (particulate matter with an aerodynamic diameter of 2.5 µm or less, µg/m$^3$)

$^a$Interaction between linear effect of PM$_{2.5}$ and urban core status.

$^b$Interaction between curvilinear effect of PM$_{2.5}$ and urban core status.
Income: The interaction effect between PM$_{2.5}$ and income was not significant in the crude linear model (p=0.1821; Table 11); that is, the PM$_{2.5}$ and co-morbid asthma and overweight relationship is similar for adolescents residing in higher versus lower income households. Instead there was a non-significant, positive relationship between PM$_{2.5}$ exposure and co-morbid asthma and overweight for both higher and lower income adolescents (OR 1.18, 95% CI 0.59-2.35, p=0.6368; Table 11). However, the odds ratio for co-morbid asthma and overweight comparing higher to lower income adolescents was 0.95 (95% CI 0.61-1.48; Table 11) and not significant (p=0.8262). Figure 5 shows this parallel effect, where adolescents residing in higher income households are slightly less likely to have both conditions compared to lower income adolescents across all PM$_{2.5}$ concentrations. The interaction effect for the linear model remained non-significant after controlling for urban core status, age, and sex (p=0.1771; Appendix C).

![Figure 5: Crude predicted probabilities of co-morbid asthma and overweight across PM$_{2.5}$ exposure percentiles among adolescents residing in a higher and lower income household in southwestern Ontario.](image)
Table 11: Crude logistic regression models exploring whether the effect of PM$_{2.5}$ on co-morbid asthma and overweight is modified by household income among adolescents residing in southwestern Ontario.

<table>
<thead>
<tr>
<th></th>
<th>OR (95% CI)</th>
<th>Log odds</th>
<th>SE</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Model 1</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM$_{2.5}$</td>
<td>0.52 (0.12, 2.38)</td>
<td>-0.6452</td>
<td>0.7708</td>
<td>0.4026</td>
</tr>
<tr>
<td>Income (Lower=0)</td>
<td>0.68 (0.36, 1.29)</td>
<td>-0.3868</td>
<td>0.3269</td>
<td>0.2367</td>
</tr>
<tr>
<td>PM$_{2.5}$*income</td>
<td>3.17 (0.58, 17.32)</td>
<td>1.1551</td>
<td>0.8657</td>
<td>0.1821</td>
</tr>
<tr>
<td><strong>Model 2</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM$_{2.5}$</td>
<td>0.11 (0.00, 6.46)</td>
<td>-2.1630</td>
<td>2.0554</td>
<td>0.2926</td>
</tr>
<tr>
<td>PM$_{2.5}^2$</td>
<td>2.91 (0.24, 35.85)</td>
<td>1.0686</td>
<td>1.2811</td>
<td>0.4042</td>
</tr>
<tr>
<td>Income (Lower=0)</td>
<td>0.54 (0.20, 1.48)</td>
<td>-0.6137</td>
<td>0.5118</td>
<td>0.2304</td>
</tr>
<tr>
<td>PM$_{2.5}$*income</td>
<td>12.21 (0.10, 1511.11)</td>
<td>2.5024</td>
<td>2.4583</td>
<td>0.3087</td>
</tr>
<tr>
<td>PM$_{2.5}^2$*income</td>
<td>0.38 (0.02, 7.39)</td>
<td>-0.9622</td>
<td>1.5114</td>
<td>0.5244</td>
</tr>
<tr>
<td><strong>Model 3</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM$_{2.5}$</td>
<td>1.18 (0.59, 2.35)</td>
<td>0.1661</td>
<td>0.3518</td>
<td>0.6368</td>
</tr>
<tr>
<td>Income (Lower=0)</td>
<td>0.95 (0.61, 1.48)</td>
<td>-0.0491</td>
<td>0.2236</td>
<td>0.8262</td>
</tr>
<tr>
<td><strong>Model 4</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM$_{2.5}$</td>
<td>0.57 (0.06, 5.23)</td>
<td>-0.5662</td>
<td>1.1328</td>
<td>0.6172</td>
</tr>
<tr>
<td>PM$_{2.5}^2$</td>
<td>1.60 (0.42, 6.08)</td>
<td>0.4711</td>
<td>0.6806</td>
<td>0.4889</td>
</tr>
<tr>
<td>Income (Lower=0)</td>
<td>0.95 (0.61, 1.47)</td>
<td>-0.0546</td>
<td>0.2238</td>
<td>0.8071</td>
</tr>
</tbody>
</table>

*Note:* Results significant at the 5% level (p<0.05) are highlighted in bold.

**Abbreviations:** OR (odds ratio); CI (confidence interval); SE (standard error); p (probability); PM$_{2.5}$ (particulate matter with an aerodynamic diameter of 2.5 µm or less, µg/m$^3$)

**Models:** (1) interaction between linear effect of PM$_{2.5}$ and income; (2) interaction between curvilinear effect of PM$_{2.5}$ and income; (3) linear effect of PM$_{2.5}$ controlling for the effect of income; (4) curvilinear effect of PM$_{2.5}$ controlling for the effect of income.
**Age:** The interaction effect between PM$_{2.5}$ and age was not significant in the unadjusted linear model (p=0.0540; Table 12). This indicates a similar effect between adolescents aged 12 to 15 years and 16 to 18 years’ probability of co-morbid asthma and overweight across increasing PM$_{2.5}$ concentrations. As PM$_{2.5}$ exposure levels increase, the probability of co-morbid asthma and overweight increases in both adolescent age groups (OR 1.17, 95% CI 0.58–2.33; Table 12). This overall effect was not significant (p=0.6653). However, the odds ratio for co-morbid asthma and overweight comparing older adolescents to younger adolescents was 1.60 (95% CI 1.04–2.47; Table 12) and statistically significant (p=0.0327). These results are illustrated in Figure 6, where older adolescents have a significantly higher probability of both conditions compared to their younger peers across all PM$_{2.5}$ concentrations. After adjusting for urban core status, income, and sex, the interaction for the linear model remained non-significant (p=0.0505; Appendix C).

![Crude predicted probabilities of co-morbid asthma and overweight across PM$_{2.5}$ exposure percentiles among adolescents aged 12 to 15 and 16 to 18 years residing in southwestern Ontario.](image)

**Figure 6:** Crude predicted probabilities of co-morbid asthma and overweight across PM$_{2.5}$ exposure percentiles among adolescents aged 12 to 15 and 16 to 18 years residing in southwestern Ontario.
Table 12: Crude logistic regression models exploring whether the effect of PM$_{2.5}$ on co-morbid asthma and overweight is modified by age among adolescents residing in southwestern Ontario.

<table>
<thead>
<tr>
<th>Model 1</th>
<th>OR (95% CI)</th>
<th>Log odds</th>
<th>SE</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>PM$_{2.5}$</td>
<td>2.20 (0.97, 4.97)</td>
<td>0.7876</td>
<td>0.4160</td>
<td>0.0584</td>
</tr>
<tr>
<td>Age (Younger=0)</td>
<td>2.51 (1.35, 4.66)</td>
<td>0.9196</td>
<td>0.3157</td>
<td>0.0036</td>
</tr>
<tr>
<td>PM$_{2.5}$*age</td>
<td>0.22 (0.05, 1.03)</td>
<td>-1.4918</td>
<td>0.7743</td>
<td>0.0540</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Model 2</th>
<th>OR (95% CI)</th>
<th>Log odds</th>
<th>SE</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>PM$_{2.5}$</td>
<td>1.36 (0.06, 30.73)</td>
<td>0.3069</td>
<td>1.5910</td>
<td>0.8470</td>
</tr>
<tr>
<td>PM$_{2.5}^2$</td>
<td>1.34 (0.22, 8.11)</td>
<td>0.2902</td>
<td>0.9200</td>
<td>0.7524</td>
</tr>
<tr>
<td>Age (Younger=0)</td>
<td>2.43 (0.92, 6.41)</td>
<td>0.8863</td>
<td>0.4957</td>
<td>0.0738</td>
</tr>
<tr>
<td>PM$_{2.5}$*age</td>
<td>0.26 (0.00, 23.78)</td>
<td>-1.3588</td>
<td>2.3101</td>
<td>0.5564</td>
</tr>
<tr>
<td>PM$_{2.5}^2$*age</td>
<td>0.97 (0.05, 17.64)</td>
<td>-0.0254</td>
<td>1.4773</td>
<td>0.9863</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Model 3</th>
<th>OR (95% CI)</th>
<th>Log odds</th>
<th>SE</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>PM$_{2.5}$</td>
<td>1.17 (0.58, 2.33)</td>
<td>0.1528</td>
<td>0.3531</td>
<td>0.6653</td>
</tr>
<tr>
<td>Age (Younger=0)</td>
<td>1.60 (1.04, 2.47)</td>
<td><strong>0.4714</strong></td>
<td><strong>0.2207</strong></td>
<td><strong>0.0327</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Model 4</th>
<th>OR (95% CI)</th>
<th>Log odds</th>
<th>SE</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>PM$_{2.5}$</td>
<td>0.55 (0.06, 4.94)</td>
<td>-0.6037</td>
<td>1.1235</td>
<td>0.5910</td>
</tr>
<tr>
<td>PM$_{2.5}^2$</td>
<td>1.63 (0.43, 6.11)</td>
<td>0.4874</td>
<td>0.6747</td>
<td>0.4701</td>
</tr>
<tr>
<td>Age (Younger=0)</td>
<td>1.61 (1.04, 2.48)</td>
<td><strong>0.4742</strong></td>
<td><strong>0.2208</strong></td>
<td><strong>0.0318</strong></td>
</tr>
</tbody>
</table>

Note: Results significant at the 5% level (p<0.05) are highlighted in bold.  
Abbreviations: OR (odds ratio); CI (confidence interval); SE (standard error); p (probability); PM$_{2.5}$ (particulate matter with an aerodynamic diameter of 2.5 µm or less, µg/m$^3$)  
Models: (1) interaction between linear effect of PM$_{2.5}$ and age; (2) interaction between curvilinear effect of PM$_{2.5}$ and age; (3) linear effect of PM$_{2.5}$ controlling for the effect of age; (4) curvilinear effect of PM$_{2.5}$ controlling for the effect of age.
Sex: The interaction effect between PM$_{2.5}$ and sex was statistically significant in the unadjusted linear model (p=0.0121; Table 13); that is, the PM$_{2.5}$ and co-morbid asthma and overweight association is significantly different for male and female adolescents. This non-parallel effect is displayed in Figure 7. Among males, there is a slight increase in co-morbid asthma and overweight as PM$_{2.5}$ concentrations increase, whereas among females, there appears to be a considerable decrease in the probability of having both conditions across increasing PM$_{2.5}$ exposure concentrations. Females’ rate of decline in co-morbid asthma and overweight is much steeper than the rate of incline observed in males. After adjusting for the effects of urban core status, income, and age, this linear interaction remained significant (p=0.0114; Appendix C).

![Figure 7](image)

**Figure 7:** Crude predicted probabilities of co-morbid asthma and overweight across PM$_{2.5}$ exposure percentiles among male and female adolescents residing in southwestern Ontario.
Table 13: Crude logistic regression models exploring whether the effect of PM$_{2.5}$ on co-morbid asthma and overweight is modified by sex among adolescents residing in southwestern Ontario.

<table>
<thead>
<tr>
<th></th>
<th>OR (95% CI)</th>
<th>Log odds</th>
<th>SE</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Linear Effect</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM$_{2.5}$</td>
<td>0.05 (0.00, 0.88)</td>
<td>-3.0415</td>
<td>1.4867</td>
<td>0.0408</td>
</tr>
<tr>
<td>Sex (Female=0)</td>
<td>0.40 (0.19, 0.86)</td>
<td>-0.9096</td>
<td>0.3899</td>
<td>0.0197</td>
</tr>
<tr>
<td>PM$_{2.5}$*sex$^a$</td>
<td>46.42 (2.32, 928.62)</td>
<td>3.8377</td>
<td>1.5286</td>
<td>0.0121</td>
</tr>
<tr>
<td><strong>Curvilinear Effect</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM$_{2.5}$</td>
<td>224.33 (0.00, 351457727.90)</td>
<td>5.4131</td>
<td>7.2779</td>
<td>0.4570</td>
</tr>
<tr>
<td>PM$_{2.5}^2$</td>
<td>0.00 (1.09 x 10$^{-19}$, 297836.51)</td>
<td>-15.5393</td>
<td>14.3592</td>
<td>0.2792</td>
</tr>
<tr>
<td>Sex (Female=0)</td>
<td>0.97 (0.17, 5.65)</td>
<td>-0.0304</td>
<td>0.8988</td>
<td>0.9730</td>
</tr>
<tr>
<td>PM$_{2.5}$*sex$^a$</td>
<td>0.01 (0.00, 25801.81)</td>
<td>-4.3383</td>
<td>7.3963</td>
<td>0.5575</td>
</tr>
<tr>
<td>PM$_{2.5}^2$*sex$^b$</td>
<td>4727466.53 (0.00, 8.23 x 10$^{18}$)</td>
<td>15.3689</td>
<td>14.3804</td>
<td>0.2852</td>
</tr>
</tbody>
</table>

**Note:** Results significant at the 5% level (p<0.05) are highlighted in bold.

**Abbreviations:** OR (odds ratio); CI (confidence interval); SE (standard error); p (probability); PM$_{2.5}$ (particulate matter with an aerodynamic diameter of 2.5 µm or less, µg/m$^3$)

$^a$Interaction between linear effect of PM$_{2.5}$ and sex.

$^b$Interaction between curvilinear effect of PM$_{2.5}$ and sex.
Chapter 5

5 Discussion

The prevalence of paediatric asthma and overweight has increased over the past few decades. Children and adolescents who are overweight are more likely to develop asthma, and vice versa, indicating these conditions as co-morbid in paediatric populations. To effectively tackle this increasing co-morbidity, it is pertinent to understand and identify any potential root causes. Research to date has assessed the role of individual-level risk factors (e.g., income, sex). The main goal of this thesis was to alternatively consider the environment, specifically air pollution, as a potential underlying mechanism. This main goal consists of three specific objectives: 1) to examine the associations between air pollution and asthma and between air pollution and overweight in adolescents; 2) to examine the association between air pollution and co-morbid asthma and overweight in adolescents; and 3) to examine whether the association between air pollution and co-morbid asthma and overweight varies by urban core status, household income, age, and sex.

This chapter begins with a discussion of our findings pertaining to the study objectives mentioned above (Section 5.1). Possible mechanisms and explanations for our main findings are also offered in this section. Section 5.2 discusses the strengths of this study and Section 5.3 discusses study limitations. Finally, this chapter concludes with an overall summary of the present thesis and the implications of our work for practice and future research (Section 5.4).

5.1 Overview of Findings

5.1.1 Objective 1

Asthma

We hypothesized that exposure to air pollution would be positively associated with adolescent asthma. Our hypothesis was not confirmed. In our study, there was no association between PM$_{2.5}$ and asthma among adolescents. This finding is inconsistent
with previous literature, which has generally established air pollution as a risk factor for paediatric asthma.\textsuperscript{16,201,207,267,378}

Studies reporting no association between air pollution and asthma have primarily measured community-average levels of pollution,\textsuperscript{200,204,205,208} a limitation said to reduce exposure variation and consequentially drive estimates towards the null. These community-level findings are inconsistent with individual-level studies showing that air pollution, particularly traffic-related, is associated with both the incidence and prevalence of asthma.\textsuperscript{200,208} The present study sought to validate findings from these individual-level studies. However, we did not measure traffic-related air pollution, illustrating a potential reason why our findings were not consistent with those from individual-level studies.

Gasana et al\textsuperscript{16} discussed that any conflicting epidemiological data on the air pollution and asthma association may be a result of using different instruments and indicators to measure air pollution (e.g., motor vehicles vs. industry, PM\textsubscript{2.5} vs. NO\textsubscript{2}). Moreover, literature has suggested that air pollutants may play a part in causing paediatric asthma, mainly amongst those living or attending school in close proximity to areas of high motor-vehicle traffic.\textsuperscript{16,200} Perhaps adolescents residing in closer proximity to industrial sites are also more likely to have asthma\textsuperscript{379-381}; however, we did not explore this possibility.

Despite our findings, the previously mentioned causal mechanisms (e.g., airway inflammation, reduced lung function; Section 1.6.4), and large body of statistically significant results (see Section 1.6.4) generally favour a positive association between air pollution and asthma. More research is needed to determine whether industrial air pollution has a different influence on asthma than traffic-related pollution.

\textbf{Overweight}

We expected that exposure to air pollution would be positively associated with overweight in adolescents. Our hypothesis was confirmed with statistically significant results; that is, as PM\textsubscript{2.5} exposure levels increased, the probability that an adolescent is overweight increased. This study is the first to examine the effect of estimated air pollution on overweight in adolescents. There are, however, animal model studies that
have determined estimated air pollution exposure as a risk factor for overweight,274,277,311,312 consistent with our findings. Our results are also supported by findings from studies that examined the effects of pre/perinatal air pollution exposure or indirect exposure to air pollution (e.g., traffic density) on overweight in humans.17,159,287,317,319,322-324,328,329 Though further research needs to be done in order to validate our findings, based on the current literature (i.e., indirect air pollution, animal models), it is not surprising that we found this relationship to be positive and statistically significant.

Many studies have shown that exposure to PM$_{2.5}$ is associated with a systemic pro-inflammatory response.191-193,382 This response largely takes place in adipose tissue, increasing the risk of obesity development.274,340 Even short-term PM$_{2.5}$ exposure, in the presence of a normal diet, causes an increase in visceral and subcutaneous fat, and an increase in adipocyte size in both types of fat.312 The above scientific data suggest that air pollution exposure alone may potentiate adiposity, and poses a potential mechanism for the findings in our study. Also, industrial pollution is popularly viewed as prominent and detrimental to air quality and general health.383 This perception would likely alter the behaviours of parents and adolescents residing in close proximity to industrial sites, such as decreasing levels of outdoor physical activity to avoid exposure. The risk of overweight would consequently increase. This other possible mechanism is of utmost importance given the confluence of increasing levels of air pollution and shifts in diet/exercise in urban populations.312

Overall, our results and the supporting literature suggest there is a positive association between air pollution and overweight. However, more evidence on the effect of estimated air pollution on adolescent overweight is needed. If air pollution truly causes overweight, this would present a challenge for Canadian public health professionals by introducing yet another target to consider when developing strategies for overweight prevention and management.
5.1.2 Objective 2

We hypothesized that there would be a positive association between air pollution exposure and co-morbid asthma and overweight in adolescents. However, our findings did not support this hypothesis. We observed an increase in co-morbid asthma and overweight as PM$_{2.5}$ levels increased, however, this relationship was not statistically significant. No other study has examined the effect of air pollution on the incidence or prevalence of co-morbid asthma and overweight. Accordingly there is no body of evidence to support our findings.

Despite our non-significant results, there is still reason to believe that a positive association may exist. One of the hypotheses on why co-morbidities develop has been attributed to common risk factors that increase the likelihood of both conditions (Section 1.4.3). Previous literature has shown that environmental pollution may stimulate the onset and exacerbation of asthma, and may separately contribute to the growing rates of overweight (see Sections 1.6.4 and 1.6.5). These findings suggest air pollution is a risk factor that is common to both conditions. It would thus be expected that air pollution is associated with an increase in the prevalence of co-morbid asthma and overweight in paediatric populations. It is important to note, however, that the present study discovered a significant association between PM$_{2.5}$ and overweight, but no association between PM$_{2.5}$ and asthma. Since the presence of significant association between PM$_{2.5}$ and co-morbid asthma and overweight depends on PM$_{2.5}$ being a significant risk factor for each condition separately, it may not be surprising that PM$_{2.5}$ was not associated with co-morbid asthma and overweight in our study.

Thus, more studies are needed to assess the relationship between air pollution and co-morbid asthma and overweight. Our findings can be used as a benchmark for comparison in future studies exploring air pollution as a potential underlying mechanism of this paediatric co-morbidity.

5.1.3 Objective 3

The third objective of this thesis investigated if the association between air pollution and co-morbid asthma and overweight is different across the following four characteristics:
urban core residence status (yes versus no), household income (higher versus lower), adolescent age (12 to 15 years versus 16 to 18 years), and sex (males versus females). There were no studies in the literature that examined these specific research questions. Therefore, inferences made from the results presented in this section must be conjectural, and future research on these questions is needed to validate our respective findings.

**Urban Core Status**

We hypothesized that the effect of air pollution on co-morbid asthma and overweight would be different for adolescents residing in an urban core and for those not residing in an urban core. The effect of air pollution was expected to be positive among urban core adolescents, and no association was anticipated for non-urban core adolescents. The first part of our hypothesis was confirmed; that is, the PM$_{2.5}$ and co-morbid asthma and overweight association was significantly different across urban core status.

For urban core adolescents there was a slight increase in co-morbid asthma and overweight as PM$_{2.5}$ concentrations increased, fairly consistent with what we expected, although, a much larger effect was anticipated. Published evidence has displayed a strong relationship between asthma and overweight particularly in urban settings. Suh et al reported a significant association between asthma symptoms and BMI in male children residing in urban areas, whereas no association was found among their rural peers. Environmental factors that differ between geographic areas are plausible causes of this co-morbid association; air pollution levels are known to be higher in urban areas than non-urban areas. Urban core topography is also dominated by tall buildings, which weaken and calm winds responsible for the dispersal and dilution of pollutants. Therefore in an urban core, air pollution is more concentrated in an adolescent’s breathing zone. It then makes sense that in our study, PM$_{2.5}$ had a positive effect on co-morbid asthma and overweight among adolescents residing in an urban core.

For non-urban core adolescents however, the story is quite different. The present study found a marked decline in co-morbid asthma and overweight across increasing PM$_{2.5}$ levels. That is, the probability of this co-morbidity was highest among adolescents exposed to lower air pollution concentrations. This finding was not expected. It is
important to note that in non-urban areas, increases in adolescent overweight is associated with an increased level of “rurality.” Increasing rurality is also associated with lower ambient air pollution. Since overweight is a risk factor for asthma, the present study might have accordingly captured a higher probability of co-morbid asthma and overweight in areas with the highest level of rurality. It is also possible that our measurement instrument did not capture PM\textsubscript{2.5} concentrations as properly in non-urban core areas compared to urban core areas. Geographic and spatial gaps exist in Canada’s air quality monitoring network, largely because the technical capacity to monitor air pollution is limited in rural areas.

Overall, our findings suggest the effect of air pollution on co-morbid asthma and overweight is quite different across categories of urban core status. Though high pollution exposure may be of greater concern for urban core adolescents, this needs to be verified.

\textit{Income}

We first hypothesized that the association between air pollution and co-morbid asthma and overweight would be positive, regardless of household income. However, adolescents from low income households were expected to have an overall higher probability of co-morbid asthma and overweight than adolescents from high income households, across all air pollution concentrations.

Our findings of a non-significant interaction between PM\textsubscript{2.5} and household income supported our hypothesis that the effect of air pollution on co-morbid asthma and overweight is similar for adolescents from high and low income households. These results may be due to both income groups being equivalently susceptible to the health effects of air pollution, though for different reasons: Children with family incomes less than $50,000 spend more time outdoors on weekdays compared to their higher income peers, increasing their degree of pollution exposure. Air pollution is also generally more prevalent in low income areas. Though it appears that high income buffers children’s exposure to the effects of air pollution, this group may be just as vulnerable as low income children. Many high income families reside in heavily polluted cities; in fact,
large urbanized areas mainly have higher earnings than smaller urban areas and rural areas.\textsuperscript{387} Research has also found that the association between particulate pollution and poor health was higher in wealthier areas compared to more deprived ones.\textsuperscript{388,389} However, it was proposed that wealthier people may appear more vulnerable to air pollution because they are relatively protected from competing risk factors of poor health (e.g., substance abuse) plaguing disadvantaged groups. It is also important to note that these income group differences were not always large enough to provide a statistically significant effect modification by socioeconomic status. Cakmak et al\textsuperscript{390} likewise reported that the association between air pollution and cardiac disease (another systemic inflammatory disease) is not significantly influenced by income, further supporting our hypothesis for a similar effect.

The second part of our hypothesis was not confirmed. Although there was a positive association between PM\textsubscript{2.5} exposure and co-morbid asthma and overweight in higher and lower income adolescents, this effect was not statistically significant. The non-significant association between PM\textsubscript{2.5} and co-morbid asthma and overweight among all adolescents was also not anticipated (see Section 5.1.2), and may explain similar findings across income levels. The final part of our hypothesis was also not confirmed; across all PM\textsubscript{2.5} concentrations, there was no significant difference in the probability of co-morbid asthma and overweight between higher and lower income adolescents, inconsistent with previous evidence of significant inverse relationship between household income and this co-morbidity.\textsuperscript{12} These results may not be surprising since our preliminary analysis revealed that asthma alone was virtually the same across income levels (see Table 4), a finding that also conflicts with previous literature.\textsuperscript{12,372}

Overall, our findings suggest the effect of air pollution is similar across higher and lower income adolescents, and are consistent with previous evidence of a non-significant interaction between air pollution and income.

\textit{Age}

We hypothesized that the effect of air pollution on co-morbid asthma and overweight would not be modified by adolescent age. Instead, a similar positive association was
expected for both younger and older adolescents. Lastly, older adolescents were expected to have a higher probability of co-morbid asthma and overweight across all pollution concentrations.

Our findings of a non-significant interaction between PM$_{2.5}$ and age supported the first part of our hypothesis; that is, the effect of air pollution on co-morbid asthma and overweight is similar for adolescents aged 12 to 15 years and 16 to 18 years. These results are consistent with previous research demonstrating the effect of air pollution on asthma alone as similar across paediatric age, and may be a result of younger and older adolescents having a similar level of vulnerability to the health effects of air pollution, albeit for different reasons. Total time spent outdoors and participation in outdoor sports are higher among adolescents aged 13 to 15 years compared to those aged 16 to 19 years. Individuals participating in sports breathe more deeply and rapidly allowing more air pollution to enter the lungs. Younger adolescents also have a higher breathing rate (i.e., inhale more air per unit of body weight) than their older peers. Though these factors make younger paediatric populations quite susceptible to air pollution, older adolescents may be just as sensitive. Avoidance behaviour (e.g., limiting outdoor physical activity, remaining indoors) is less actively undertaken by the parents of older adolescents, potentially increasing their exposure to poor air quality. Older age is also associated with an increase in low-grade systemic inflammation, which may exacerbate the inflammatory health effects of air pollution. Evidently there is no consensus on which adolescent age group is more susceptible to the effects of air pollution, which may explain our findings of a non-differential PM$_{2.5}$ effect across age.

The second part of our hypothesis was not supported as we found that the association between PM$_{2.5}$ exposure levels and co-morbid asthma and overweight in younger and older adolescents was not statistically significant. These results relate to the non-significant association between PM$_{2.5}$ and co-morbid asthma and overweight among all adolescents (see Section 5.1.2). The final part of our hypothesis however, was confirmed; older adolescents were significantly more likely to have asthma and overweight than younger adolescents. Our results are consistent with a study conducted by Ahmad and colleagues, who reported the strength of the association between asthma and obesity
increases with paediatric age. Possible explanations for these mutual findings include the increased likelihood of systemic inflammation and developing co-morbid illnesses among older age groups.\textsuperscript{393,394}

Overall, the effect of air pollution appears to be similar for younger and older adolescents. Though it may be argued that the age ranges 12 to 15 years and 16 to 18 years are too narrow to detect any significant main effects differences (which is why many studies tend to group all adolescents into just one category), we expect that a number of biological and behavioural factors vary across adolescents of different ages.\textsuperscript{392} It is thus worth further exploring the effect of adolescent age on the relationship between air pollution and co-morbid asthma and overweight.

Sex

We hypothesized that the effect of air pollution on co-morbid asthma and overweight would be modified by sex. The effect of air pollution was expected to be positive for both groups but stronger among males than females. The first part of our hypothesis was confirmed. There was a statistically significant interaction between PM\textsubscript{2.5} and sex, indicating the effect of PM\textsubscript{2.5} on co-morbid asthma and overweight was different for males and females.

Although a much larger effect was anticipated, our study confirmed the second part of our hypothesis and the findings of past studies,\textsuperscript{17,213,342} by suggesting a potential positive association between the air pollutant, PM\textsubscript{2.5}, and asthma and overweight in boys. These findings may be explained by gender-specific behaviours. Boys tend to spend more time outdoors than girls on weekdays and weekends.\textsuperscript{356,357} More boys than girls go outside to hang out/play with friends, participate in sports, and ride-off road vehicles, while girls are more likely to be outside reading or studying.\textsuperscript{356} This high level of outdoor activity may increase the degree of air pollution exposure in adolescent males (via rapid breathing), subsequently elevating their risk of systemic inflammatory conditions.

Among females, however, we found that there was a considerable decrease in the probability of co-morbid asthma and overweight as PM\textsubscript{2.5} exposure concentrations
increased. This finding was not expected. Previous evidence of a positive association between air pollution and asthma, and air pollution and overweight in adolescent females\textsuperscript{17,21,391} contradicts our findings of an inverse relationship between PM\textsubscript{2.5} and these two conditions as a co-morbidity. Current literature suggests that the effect of air pollution on paediatric asthma and overweight may be weaker in females compared to males. Girls are less active than boys when spending time outdoors (see above), decreasing their degree of systemic air pollution exposure. There may be competing risk factors for asthma and overweight in females, making them less susceptible to air pollution. For example, female puberty is marked by hormonal changes such as increased estrogen, shown to increase asthma incidence, physiological and ectopic fat, and serum leptin concentrations.\textsuperscript{82,395} It is also possible that our measurement tool did not capture personal PM\textsubscript{2.5} exposure as properly in females as in males. PM\textsubscript{2.5} exposure values were calculated for each respondent’s neighbourhood area of residence only. However, girls are more likely than boys to visit public places such as the downtown area, movies, and malls, and to use these spaces as alternatives to hanging out in their neighbourhood.\textsuperscript{396} As a result of these behaviours, personal PM\textsubscript{2.5} exposure among females may largely deviate from the ambient levels measured in the present study, and the accuracy of our female findings would be affected accordingly.

Overall, our results suggest the effect of air pollution on co-morbid asthma and overweight is quite different across sex. Though it appears the effect of high pollution concentrations is more worrisome among males, further verification is required.

5.2 Strengths

First of its Kind: Research has primarily attributed the underlying mechanisms of co-morbid asthma and overweight in children and adolescents to individual-level risk factors. However, Brisbon et al\textsuperscript{15} illustrated there are also common root causes embedded in the built environment; these environmental factors need to be addressed in order to significantly reduce levels of this co-morbidity. To our knowledge, the present study is the first to further explore this recommendation by presenting a prevalence estimate of co-morbid asthma and overweight as a result of environmental influences accordingly.
Important insight is provided on the role played by air pollution, providing a potential target for intervention in public health planning.

Representativeness of the CCHS and NPRI: A fundamental strength of this project was the use of a: (1) national population-based survey (CCHS) to measure outcome variables of interest and their associated covariates; and (2) a nationally representative inventory of industrial pollutant emissions (NPRI) to measure the exposure variable of interest.

The central objective of the CCHS was to gather health-related data from a large sample of respondents at the health region level. It can thus be ensured that the CCHS provided a representative sample of the adolescent population residing in the 14 health regions of southwestern Ontario.

The 2008 NPRI contained data on 100% of Canadian operating coal-fired power plants, primary metal smelters, steel mills, oil sands facilities, off-shore oil and gas platforms, crude oil refineries, major automobile assembly plants, Portland cement manufacturing facilities, and pulp and paper mills. These estimates are likely similar for the 2009 NPRI. In addition, Environment Canada’s rigorous efforts towards compliance promotion, expanding reporting requirements, and the maintenance of high quality data, ensures that exposure estimates used in the present study are accurate, reliable, and quite representative of industrial PM$_{2.5}$ emissions in southwestern Ontario.

Air Pollution Exposure Variation: PM$_{2.5}$ exposure was measured in such a way that allowed us to assess differences between individuals at a micro level. This decision takes into account the microscale variations in air pollution exposure that exists between each geographic location in southwestern Ontario. Alternatively measuring pollution exposure at the community level, where individuals would be clustered based on proximal postal code areas, would have eliminated the variation in PM$_{2.5}$ exposure between subjects within each cluster.

The present thesis also selected a study location with sufficient exposure variation. When Zhao et al examined the association between air pollution and paediatric asthmatic symptoms, air pollution concentrations were quantified only in heavily polluted urban
areas of Taiyuan, China. The authors later discussed that the high general air pollution level in their study location may have limited the possibility of acquiring adequate variation in the overall air pollution exposure. The present research project alternatively examined the effect of PM$_{2.5}$ concentrations among adolescents residing across the different geographical areas of southwestern Ontario.

Finally, air pollution concentrations vary with the meteorological conditions in a given area. For example, the degree to which PM$_{2.5}$ is discharged from an industrial source and concentrated into a particular area, depends on wind speed/direction and air temperature. Our study used such parameters in the calculation of PM$_{2.5}$ exposure values for each postal code area in southwestern Ontario, a methodological step that captures the significant impact of meteorology on air pollution exposure variation.

5.3 Limitations

**Temporality**: Due to the cross-sectional design of this study, and temporal mismatch between data sources (see Section 3.1), temporality cannot be assured. This study is unable to determine if PM$_{2.5}$ is a causal factor that leads to the development of asthma, overweight, and co-morbid asthma and overweight. Instead, only an association between PM$_{2.5}$ and these three outcomes can be identified. Though it is unknown whether study subjects had developed asthma and/or overweight prior to when PM$_{2.5}$ exposure was measured, a bi-directional relationship is not of any concern as it is impossible for asthma and overweight to cause or influence air pollution levels. A cross-sectional design allows us to address the primary objective of this study, which is to acquire a better understanding of the etiology of paediatric asthma and overweight.

**Interview Mode**: Interview mode has produced a notable difference in reported key health indicators of the CCHS. A study conducted using the CCHS cycle 2.1 (2003) indicated possible mode effects between using CAPI (in person interviewing) and CATI (telephone interviewing). Significant differences in point estimates were found between both modes for many health indicators including self-reported height and weight. From these measures, obesity (BMI score of 30 or higher) was derived in the mode study for respondents aged 18 years or older, and was determined as significantly higher for CAPI
(17.9%) than CATI (13.2%). CATI underestimation has been attributed to social desirability, whereas in person it is harder to report incorrect values. Although these mode differences in self-reported height and weight were established among adults, the results are likely applicable to adolescents. This bias in reporting presents the possibility of study estimates being representative of CCHS respondents who were interviewed using one mode over the other. Some recommendations were made to improve this discrepancy for future cycles of CCHS, therefore, benefiting the present study. For example, the same area/telephone frames and CAPI/CATI ratios used in cycle 2.1 were implemented in cycle 3.1, and interviewer procedures were reinforced among both collection methods.

Measurement Instruments: Assessing asthma via questionnaire might have resulted in the misclassification of this outcome. This self-reported question did not require a physician diagnosis, and was not tested for reliability or validity in the CCHS. Published studies however, have indicated that there is high accordance between self-reported asthma and medical records; when compared with a clinical diagnosis of asthma, the average sensitivity of self-reported asthma was 68%, and the average specificity was 94%. Overall, obtaining a self-report of physician diagnosis is recognized as a reliable and commonly used method for identifying asthma in epidemiologic studies.

There is also the possibility that asthma was underestimated in the CCHS due to a high prevalence of asthma under-diagnosis in paediatric populations. Siersted et al found that undiagnosed asthma comprised approximately one third of all asthma cases identified among Danish adolescents aged 12 to 15 years. These findings are largely due to two-thirds of those undiagnosed not reporting their symptoms to a doctor. Physicians may also fail to appreciate the importance of respiratory symptoms that are presented to them. For example, these symptoms have been inaccurately ascribed to a lack of physical fitness among those with a high body mass or low physical activity. Undiagnosed asthma is more prevalent in females compared to males, indicating the prospect of differential bias in asthma prevalence by sex in the present study.
This study used BMI to determine adolescent weight status. One limitation of using BMI is its failure to differentiate between fat mass and lean body mass (i.e., muscle and bone). Concern then arises over this screening tool misclassifying weight status. For example, overestimation is likely prevalent among those with high lean body mass for their height, or muscular builds. Individuals with a large body frame (high bone mass) for their height, but very little body fat, may also be erroneously labelled as overweight on the BMI scale. This limitation is quite pertinent in adolescence, where during this developmental period, there can be substantial increases in both muscle and bone mass. BMI’s inability to account for body frame size can alternatively result in overweight underestimation. Namely, adolescents carrying a high level of fat mass for a very small body frame, might have a BMI value that categorizes them as normal weight, when in contrast, they should be considered overweight for their frame. There are several methods, such as dual-energy x-ray absorptiometry, that can assess overall body fat and fat distribution. However, factors such as accessibility, simplicity, cost, and ease of use are restricted with respect to these instruments, making them unsuitable measures of adiposity for the current study. Despite concerns associated with using BMI to identify overweight adolescents, this measure has been recommended for epidemiologic and population-based research due to its feasibility, and positive correlation with direct measures of body fatness, metabolic risk in youth, and disease in adulthood.

Another limitation involves the use of self-reported height and weight to calculate BMI. Most studies have found that individuals generally underestimate their weight and overestimate their height. As a result, the prevalence of obesity based on self-reported data tends to be underestimated. Females underestimate their weight more than males. Inaccurate self-reporting is usually more prevalent among younger youth compared to their older peers. Overweight youth underestimate their weight more than normal weight youth. This reporting bias among higher BMI individuals would affect study estimates of overweight by making them more conservative.

Despite concerns over self-report bias, a high correlation exists between self-reported and measured height and weight. Overall, self-reported height and weight are not likely
to influence conclusions about study estimates in population-based epidemiological studies, and are considered valid measures for these types of studies.411,412

The PM$_{2.5}$ variable has some limitations worth noting. First, the exposure data are representative of emissions from industrial sources alone. These data do not account for other sources of PM$_{2.5}$ that are present in southwestern Ontario’s air-shed such as transboundary pollutants and emissions from transportation and agriculture. In fact, open sources, such as construction operations and dust from paved and unpaved road, emit the majority of PM$_{2.5}$ in Canada but were not accounted for in the present study.174 The concentration values calculated by HEAL are thus only representative of a small fraction of the total amount of PM$_{2.5}$ that could be expected over any 24-hour averaging period within each postal code area. This causes misclassification of the overall PM$_{2.5}$ exposure in the present study. Nevertheless, since the isolated effects of industrial air pollution on asthma and overweight have never been explored, using this measure is a valuable addition to the literature.

Second, the PM$_{2.5}$ data is incomplete as not all industrial facilities report to the NPRI. In 2008, there were lower rates of reporting coverage for facilities such as foundries, pits and quarries, rubber and plastics manufacturing plants, forest product manufacturing facilities, and wastewater facilities. These lower rates are mainly ascribed to falling below compulsory reporting thresholds or a result of certain facilities not reporting to the NPRI as required.397

Third, PM$_{2.5}$ values were created by combining emissions data released from the NPRI in 2009 with local meteorological data in southwestern Ontario from 1996 to 2000 (see Section 3.2). Since atmospheric conditions greatly impact the level of air pollution an area is exposed to,398 obtaining meteorological data closer to 2009 would have been more appropriate. Calculating annual PM$_{2.5}$, averaged over a three year period, would have provided more stable estimates of exposure than a single year average.413 These options were not available at the time of analysis.

Finally, PM$_{2.5}$ values were calculated for each respondent’s postal code area of residence in 2009. However, adolescents spend a large portion of their day in other locations (e.g.,
school, alternative residence) likely exposed to different PM$_{2.5}$ concentrations. This concern is confirmed by Delfino et al.$^{233}$ who demonstrated that personal PM$_{2.5}$ (measured by a portable monitor worn during waking hours) was only moderately correlated with ambient PM$_{2.5}$ ($r=0.64$) among children and adolescents residing in Southern California, and the association between PM$_{2.5}$ and airway inflammation was more robust for personal exposure than ambient exposure. It is also unknown whether respondents to the CCHS before or after 2009 were actually exposed to their assigned concentrations, as some respondents may have resided in a different postal code area than in 2009. Our measurement instrument did not account for pollution exposure in these other postal code areas that may have contributed to their health outcomes. These flaws may collectively misclassify the final sample's true level of exposure, presenting information bias and regression attenuation into the study.

**Missing Data:** A sensitivity analysis compared adolescents with and without missing data (Appendix B). Both groups were significantly different on all covariates, indicating that excluding adolescents with missing data from the analysis may potentially impact study results. These significant differences may be due to comparing very unequal sample sizes ($n=289$ and $n=2,685$). Burton and Altman$^{114}$ discuss that the maximum amount of missingness in any variable is tolerable if there is only a small number of cases with overall missing data (i.e., less than 10%); in the present study, 9.7% of the final sample had missing data.

### 5.4 Implications and Future Research

Our cross-sectional study sought to examine the etiology of co-morbid asthma and overweight in adolescents. Co-morbidity development may be a result of common risk factors that increase the likelihood of both conditions separately. In accordance with Brisbon et al.$^{15}$ who proposed these common root causes are largely components of our environment, the role played by air pollution exposure was explored.

It was revealed that adolescents are more likely to be overweight as PM$_{2.5}$ concentrations increase in areas of residence. However, no significant association was found between PM$_{2.5}$ and adolescent asthma. There was also no association between PM$_{2.5}$ and co-
and overweight in adolescents. It is important to note however, that there is a large body of epidemiological research supporting a causal relationship between air pollution and paediatric asthma (see Section 1.6.4). Due to this evidence, and because we found a significant association between PM$_{2.5}$ and paediatric overweight, there is still reason to believe air pollution may be a shared risk factor for asthma and overweight. Finally, our study showed that the effect of PM$_{2.5}$ on co-morbid asthma and overweight was different across urban core residence status and sex. Adolescents residing in an urban core were more vulnerable to PM$_{2.5}$ than their non-urban core peers, and males were more susceptible than females. Upon targeting specific groups for intervention, perhaps concern should be raised with regard to high air pollution exposure in urban core areas and among adolescent males.

No other epidemiologic studies have measured the effect of air pollution on co-morbid asthma and overweight. Due to the paucity of research on this topic, we are unable to contextualize our findings of no association between PM$_{2.5}$ and co-morbid asthma and overweight, and our recommendation to target specific adolescent groups over others (e.g., urban core areas over non-urban core areas) cannot be conclusive. Clearly, more evidence on the subject is needed. If air pollution is actually a causal factor of this paediatric co-morbidity, the implications could be great.

One such implication is that it is quite difficult for adolescents to control their exposure to air pollution. For one, it is not possible to carry clean air or stop breathing in polluted air. Adolescents also have a higher ventilation rate, inhale a greater amount of pollution per pound body weight, and spend more time outdoors than older age groups.$^{171,181}$ There are certain behaviours that may protect one’s exposure to air pollution. Children and adolescents however, are less health conscious and face extrinsic mobility restriction which may hinder their ability to choose these healthy behaviours. These protective measures may also have minimal benefits and can even lead to other health implications. For example, going indoors is generally advised when air pollution levels are high.$^{415}$ Yet outdoor air pollutants can still penetrate into the indoor environment.$^{416}$ Another recommendation is limiting outdoor physical activity when exposed to poor air quality.$^{415}$ This is because physical activity causes rapid, deeper breathing, allowing more pollutants
to enter the lungs. However, outdoor exercise has a greater effect on physical and mental well-being than exercising indoors.\textsuperscript{417} Television viewing, computer games and other sedentary behaviours would likely increase. This behavioural change may also lead to a reduction in the numerous health benefits of regular exercise such as chronic disease prevention and enhanced strength, self-esteem, and immunity.\textsuperscript{418}

Another implication involves air pollution potentially causing a greater disease burden among adolescents with co-morbid asthma and overweight. Adolescents with this co-morbidity already face greater health consequences than adolescents who have only one of these conditions. Compared to those who have asthma alone or are only overweight, obese asthmatics have more emergency department visits, hospitalizations, and sleep disturbances, lower lung function, and use more medication.\textsuperscript{12,419} Obese asthmatics have more co-morbidities such as gastroesophageal reflux disease, diabetes mellitus, and hypertension.\textsuperscript{419} Obesity alters asthma toward a more difficult-to-control/treat phenotype, and vice versa.\textsuperscript{99,420} Finally, systemic inflammatory markers are more elevated in patients with both conditions. Air pollution, which is known to cause systemic inflammation, may therefore precipitate other chronic diseases associated with systemic inflammation such as cardiac disease, chronic heart failure, diabetes, and arteriosclerosis.\textsuperscript{421} Society is impacted by these endpoints due to increased healthcare and medication costs, school absenteeism, out of pocket expenses, restricted activity days, and eventually, a loss of workplace productivity and lost wages due to sick time. There are also intangible costs such as pain, suffering, and reduced quality of life.

Since it is evident that co-morbid asthma and overweight is difficult to manage at the individual level, more research on the effects of air pollution on this co-morbidity would be beneficial, as these conditions may be easier to control at the environmental level. Research thus far has concentrated on risk factors of asthma and overweight that are not modifiable such as ethnicity, sex, and income.\textsuperscript{12} Alternatively, the level of air pollution has the potential to be modified. For example, a recent study found that the economic value of reducing the health effects of air pollution, by introducing cleaner vehicles and fuels in Canada, was $24 billion over a 24-year period (compared to a cost of $6 billion for implementing this program).\textsuperscript{422} These findings not only indicate that air pollution
levels can be improved, but also that the reduction of this exposure dramatically benefits the well-being of society. Finally, Brisbon et al. stressed that the prevention and management of asthma and overweight in particular will likely be achieved through the study and modification of the built environment.

The results of the current study may be used as a benchmark for future research examining the effects of air pollution or the role of the environment on co-morbid asthma and overweight. Given the public health implications discussed above, we should continue exploring this relationship until we achieve a satisfactory buildup of knowledge to conclude whether air pollution causes this co-morbidity or not. Ideally, future work would use a longitudinal study design with actual measurements of weight and height and validation of reported asthma. To enhance the accuracy of exposure measurement, quantifying air pollution from all sources (e.g., industry, transportation, agriculture, transboundary) needs to be considered. This can be achieved by using ambient air monitoring data, or if feasible, personal exposure monitors for each subject. In addition, research should further investigate whether the effects of air pollution vary by other risk factors such as geographic residency, age, sex, and measures of socioeconomic status, to provide effective targets for intervention. Overall, conducting further studies as such will bring us closer to understanding the etiology of paediatric asthma and overweight, which is important for guiding public health strategies taken towards this co-morbid epidemic.
References


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## Appendices

**Appendix A: Sample size and response rates by year for the Canadian Community Health Survey.**

<table>
<thead>
<tr>
<th>Sample Size (N)</th>
<th>Survey Year</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2007</td>
</tr>
<tr>
<td>All respondents aged 12 years and over – Canada</td>
<td>65,946</td>
</tr>
<tr>
<td>Adolescents only* - Canada</td>
<td>6,201</td>
</tr>
<tr>
<td>Adolescents only* - Ontario</td>
<td>2,065</td>
</tr>
<tr>
<td>Adolescents only* - Southwestern Ontario</td>
<td>556</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Response Rates (%)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>77.6</td>
</tr>
<tr>
<td>By health region</td>
<td>66.3-87.6</td>
</tr>
</tbody>
</table>

*Adolescents who were pregnant at the time of the survey were excluded from the analysis.
Appendix B: Comparison of model covariates between adolescents with and without missing data.

This Appendix compares respondents that had missing data for the asthma and overweight variables (excluded from the analysis; n=289) to respondents that had no missing outcome data (included in the analysis; n=2,685) on all regression model covariates. The means of continuous variables were compared using independent samples t-tests (Table 14), and chi-square tests were used to compare both groups on all categorical covariates (Table 15). All analyses were conducted using rescaled CCHS survey weights. Compared with the included participants, participants who were excluded had a lower mean income (9.3 vs. 9.7; p=0.0028), lower mean age (14.0 vs. 15.1 years; p<0.0001), but a higher average PM$_{2.5}$ exposure concentration (0.34 vs. 0.29 µg/m$^3$; p=0.0138); see Table 14. Participants with missing data were also more likely to live in an urban core (77.4% vs. 64.9%; p<0.0001), more likely to live in a lower income household (47.9% vs. 38.5%; p=0.0025), more likely to be in the younger adolescent age group, (78.7% vs. 54.7%; p<0.0001), and more likely to be female (56.7% vs. 46.9%; p=0.0019); see Table 15.

After excluding adolescents with missing data from the analysis, adolescents who live in an urban core area, reside in a lower income household, who are younger, female, and are exposed to high air pollution concentrations were underrepresented in the sample. Since income and age are not expected to modify the association between air pollution and asthma and overweight, an underrepresentation of lower income and younger adolescents in the sample may not have impacted the results. However, considering that the main association is expected to be weaker among females than males, an underrepresentation of females in the sample may have caused in our results to appear stronger than they actually are. On the other hand, urban core adolescents are expected to have a stronger association between air pollution and asthma and overweight than their non-urban core peers; as a result, their underrepresentation in the sample may have made the main association appear weaker than it truly is. Since each of these covariates likely affect the main association in a different way, it is hard to determine how excluding respondents with missing data would have affected the results as a whole.
Table 14: Independent samples t-test comparing continuous covariates between adolescents with and without missing data.

<table>
<thead>
<tr>
<th>Missing Data</th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>PM$_{2.5}$ exposure</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>289</td>
<td>0.34</td>
<td>0.34</td>
<td>-2.46</td>
<td>0.0138</td>
</tr>
<tr>
<td>No</td>
<td>2,685</td>
<td>0.29</td>
<td>0.29</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Income</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>289</td>
<td>9.3</td>
<td>2.1</td>
<td>2.99</td>
<td>0.0028</td>
</tr>
<tr>
<td>No</td>
<td>2,685</td>
<td>9.7</td>
<td>2.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>289</td>
<td>14.0</td>
<td>1.8</td>
<td>9.53</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>No</td>
<td>2,685</td>
<td>15.1</td>
<td>1.9</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Note:** Results significant at the 5% level (p<0.05) are highlighted in bold.

**Abbreviations:** SD (standard deviation); t (test statistic for independent samples t-test); p (probability); PM$_{2.5}$ (particulate matter with an aerodynamic diameter of 2.5 µm or less, µg/m$^3$)
Table 15: Chi-square test for categorical covariates comparing adolescents with and without missing data.

<table>
<thead>
<tr>
<th></th>
<th>Missing Data N (%)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td><strong>Urban core residence (χ²=17.5358, p&lt;0.0001)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>77.4%</td>
<td>64.9%</td>
</tr>
<tr>
<td>No</td>
<td>22.6%</td>
<td>35.1%</td>
</tr>
<tr>
<td><strong>Income (χ²=9.1082, p=0.0025)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Higher</td>
<td>52.1%</td>
<td>61.5%</td>
</tr>
<tr>
<td>Lower</td>
<td>47.9%</td>
<td>38.5%</td>
</tr>
<tr>
<td><strong>Age (χ²=58.6481, p&lt;0.0001)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12-15 years</td>
<td>78.7%</td>
<td>54.7%</td>
</tr>
<tr>
<td>16-18 years</td>
<td>21.3%</td>
<td>45.3%</td>
</tr>
<tr>
<td><strong>Sex (χ²=9.6832, p=0.0019)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>43.3%</td>
<td>53.1%</td>
</tr>
<tr>
<td>Female</td>
<td>56.7%</td>
<td>46.9%</td>
</tr>
</tbody>
</table>

**Note:** Results significant at the 5% level (p<0.05) are highlighted in bold.

**Abbreviations:** $\chi^2$ (chi-square test statistic); p (probability)
Appendix C: Adjusted logistic regression models exploring whether the PM$_{2.5}$ and co-morbid asthma and overweight relationship is modified by urban core residence status, income, age, and sex.

The following provides estimates from adjusted logistic regression models that assessed the presence of interaction between PM$_{2.5}$ and one of the following modifiers at a time: urban core residence status (Table 16); income (Table 17); age (Table 18); and sex (Table 19). Each model is adjusted for the effects of the remaining three covariates. Seeing that the linear and curvilinear interaction effects between PM$_{2.5}$ and income and PM$_{2.5}$ age were not statistically significant, Table 17 and Table 18 also present adjusted estimates from models testing for a parallel effect (i.e., main association controlling for the covariate of interest - income and age, respectively).
**Table 16: Adjusted logistic regression models exploring whether the effect of PM$_{2.5}$ on co-morbid asthma and overweight is modified by urban core residence status among adolescents residing in southwestern Ontario.**

<table>
<thead>
<tr>
<th></th>
<th></th>
<th>Log odds</th>
<th>SE</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Linear Effect</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM$_{2.5}$</td>
<td></td>
<td>0.00 (0.00, 0.31)</td>
<td>-7.9425</td>
<td>3.4500</td>
</tr>
<tr>
<td>Urban core (No=0)</td>
<td>0.28 (0.10, 0.80)</td>
<td>-1.2700</td>
<td>0.5349</td>
<td>0.0176</td>
</tr>
<tr>
<td>PM$_{2.5}$*urban core$^a$</td>
<td>4744.78 (5.30, 4249449.49)</td>
<td>8.4648</td>
<td>3.4682</td>
<td>0.0147</td>
</tr>
<tr>
<td><strong>Curvilinear Effect</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM$_{2.5}$</td>
<td></td>
<td>0.00 (0.00, 2.53)</td>
<td>-9.1126</td>
<td>5.1228</td>
</tr>
<tr>
<td>PM$_{2.5}^2$</td>
<td></td>
<td>19.77 (0.00, 210837868.40)</td>
<td>2.9844</td>
<td>8.2564</td>
</tr>
<tr>
<td>Urban core (No=0)</td>
<td>0.25 (0.07, 0.94)</td>
<td>-1.3749</td>
<td>0.6701</td>
<td>0.0402</td>
</tr>
<tr>
<td>PM$_{2.5}$*urban core$^a$</td>
<td>16202.16 (0.52, 508105672.20)</td>
<td>9.6929</td>
<td>5.2824</td>
<td>0.0665</td>
</tr>
<tr>
<td>PM$_{2.5}^2$*urban core$^b$</td>
<td>0.05 (0.00, 558829.67)</td>
<td>-3.0209</td>
<td>8.2933</td>
<td>0.7157</td>
</tr>
</tbody>
</table>

**Notes:** (1) Results significant at the 5% level (p<0.05) are highlighted in bold; (2) Both models are controlled for the effects of income, age, and sex.

**Abbreviations:** OR (odds ratio); CI (confidence interval); SE (standard error); p (probability); PM$_{2.5}$ (particulate matter with an aerodynamic diameter of 2.5 µm or less, µg/m$^3$)

$^a$Interaction between linear effect of PM$_{2.5}$ and urban core status.

$^b$Interaction between curvilinear effect of PM$_{2.5}$ and urban core status.
Table 17: Adjusted logistic regression models exploring whether the effect of PM$_{2.5}$ on co-morbid asthma and overweight is modified by household income among adolescents residing in southwestern Ontario.

<table>
<thead>
<tr>
<th>Model</th>
<th>OR (95% CI)</th>
<th>Log odds</th>
<th>SE</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Model 1</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM$_{2.5}$</td>
<td>0.49 (0.10, 2.32)</td>
<td>-0.7064</td>
<td>0.7903</td>
<td>0.3714</td>
</tr>
<tr>
<td>Income (Lower=0)</td>
<td>0.68 (0.36, 1.30)</td>
<td>-0.3855</td>
<td>0.3300</td>
<td>0.2427</td>
</tr>
<tr>
<td>PM$_{2.5}$*income</td>
<td>3.29 (0.58, 18.48)</td>
<td>1.1894</td>
<td>0.8813</td>
<td>0.1771</td>
</tr>
<tr>
<td><strong>Model 2</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM$_{2.5}$</td>
<td>0.78 (0.00, 5.32)</td>
<td>-2.4455</td>
<td>2.1005</td>
<td>0.2443</td>
</tr>
<tr>
<td>PM$_{2.5}^2$</td>
<td>3.35 (0.27, 41.73)</td>
<td>1.2078</td>
<td>1.2875</td>
<td>0.3482</td>
</tr>
<tr>
<td>Income (Lower=0)</td>
<td>0.55 (0.20, 1.50)</td>
<td>-0.6046</td>
<td>0.5161</td>
<td>0.2414</td>
</tr>
<tr>
<td>PM$_{2.5}$*income</td>
<td>12.26 (0.10, 1560.72)</td>
<td>2.5064</td>
<td>2.4727</td>
<td>0.3108</td>
</tr>
<tr>
<td>PM$_{2.5}^2$*income</td>
<td>0.39 (0.02, 7.40)</td>
<td>-0.9492</td>
<td>1.5058</td>
<td>0.5285</td>
</tr>
<tr>
<td><strong>Model 3</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM$_{2.5}$</td>
<td>1.14 (0.56, 2.32)</td>
<td>0.1315</td>
<td>0.3614</td>
<td>0.7159</td>
</tr>
<tr>
<td>Income (Lower=0)</td>
<td>0.96 (0.62, 1.49)</td>
<td>-0.0382</td>
<td>0.2242</td>
<td>0.8648</td>
</tr>
<tr>
<td><strong>Model 4</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM$_{2.5}$</td>
<td>0.44 (0.04, 4.48)</td>
<td>-0.8256</td>
<td>1.1862</td>
<td>0.4864</td>
</tr>
<tr>
<td>PM$_{2.5}^2$</td>
<td>1.84 (0.46, 7.27)</td>
<td>0.6075</td>
<td>0.7019</td>
<td>0.3868</td>
</tr>
<tr>
<td>Income (Lower=0)</td>
<td>0.96 (0.62, 1.49)</td>
<td>-0.0419</td>
<td>0.2243</td>
<td>0.8518</td>
</tr>
</tbody>
</table>

Notes: (1) Results significant at the 5% level (p<0.05) are highlighted in bold; (2) All models are controlled for the effects of urban core status, age, and sex.

Abbreviations: OR (odds ratio); CI (confidence interval); SE (standard error); p (probability); PM$_{2.5}$ (particulate matter with an aerodynamic diameter of 2.5 µm or less, µg/m$^3$)

Models: (1) interaction between linear effect of PM$_{2.5}$ and income; (2) interaction between curvilinear effect of PM$_{2.5}$ and income; (3) linear effect of PM$_{2.5}$ controlling for the effect of income; (4) curvilinear effect of PM$_{2.5}$ controlling for the effect of income.
Table 18: Adjusted logistic regression models exploring whether the effect of PM$_{2.5}$ on co-morbid asthma and overweight is modified by age among adolescents residing in southwestern Ontario.

<table>
<thead>
<tr>
<th>Model</th>
<th>OR (95% CI)</th>
<th>Log odds</th>
<th>SE</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Model 1</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM$_{2.5}$</td>
<td>2.13 (0.93, 4.86)</td>
<td>0.7549</td>
<td>0.4215</td>
<td>0.0733</td>
</tr>
<tr>
<td>Age (Younger=0)</td>
<td>2.56 (1.37, 4.79)</td>
<td>0.9394</td>
<td>0.3200</td>
<td>0.0033</td>
</tr>
<tr>
<td>PM$_{2.5}$*age</td>
<td>0.21 (0.04, 1.00)</td>
<td>-1.5570</td>
<td>0.7961</td>
<td>0.0505</td>
</tr>
<tr>
<td><strong>Model 2</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM$_{2.5}$</td>
<td>1.07 (0.04, 26.09)</td>
<td>0.0723</td>
<td>1.6271</td>
<td>0.9646</td>
</tr>
<tr>
<td>PM$_{2.5}^2$</td>
<td>1.51 (0.24, 9.43)</td>
<td>0.4091</td>
<td>0.9363</td>
<td>0.6621</td>
</tr>
<tr>
<td>Age (Younger=0)</td>
<td>2.51 (0.94, 6.73)</td>
<td>0.9203</td>
<td>0.5031</td>
<td>0.0674</td>
</tr>
<tr>
<td>PM$_{2.5}$*age</td>
<td>0.22 (0.00, 21.39)</td>
<td>-1.5297</td>
<td>2.3431</td>
<td>0.5139</td>
</tr>
<tr>
<td>PM$_{2.5}^2$*age</td>
<td>1.08 (0.06, 19.75)</td>
<td>0.0791</td>
<td>1.4818</td>
<td>0.9574</td>
</tr>
<tr>
<td><strong>Model 3</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM$_{2.5}$</td>
<td>1.12 (0.55, 2.27)</td>
<td>0.1090</td>
<td>0.3637</td>
<td>0.7645</td>
</tr>
<tr>
<td>Age (Younger=0)</td>
<td>1.60 (1.04, 2.47)</td>
<td>0.4717</td>
<td>0.2208</td>
<td>0.0327</td>
</tr>
<tr>
<td><strong>Model 4</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM$_{2.5}$</td>
<td>0.40 (0.04, 4.12)</td>
<td>-0.9073</td>
<td>1.1858</td>
<td>0.4442</td>
</tr>
<tr>
<td>PM$_{2.5}^2$</td>
<td>1.91 (0.48, 7.53)</td>
<td>0.6456</td>
<td>0.7009</td>
<td>0.3570</td>
</tr>
<tr>
<td>Age (Younger=0)</td>
<td>1.61 (1.04, 2.48)</td>
<td>0.4765</td>
<td>0.2210</td>
<td>0.0311</td>
</tr>
</tbody>
</table>

**Notes:** (1) Results significant at the 5% level (p<0.05) are highlighted in bold; (2) All models are controlled for the effects of urban core status, income, and sex.

**Abbreviations:** OR (odds ratio); CI (confidence interval); SE (standard error); p (probability); PM$_{2.5}$ (particulate matter with an aerodynamic diameter of 2.5 µm or less, µg/m$^3$)

**Models:** (1) interaction between linear effect of PM$_{2.5}$ and age; (2) interaction between curvilinear effect of PM$_{2.5}$ and age; (3) linear effect of PM$_{2.5}$ controlling for the effect of age; (4) curvilinear effect of PM$_{2.5}$ controlling for the effect of age
Table 19: Adjusted logistic regression models exploring whether the effect of PM$_{2.5}$ on co-morbid asthma and overweight is modified by sex among adolescents residing in southwestern Ontario.

<table>
<thead>
<tr>
<th></th>
<th>OR (95% CI)</th>
<th>Log odds</th>
<th>SE</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Linear Effect</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM$_{2.5}$</td>
<td>0.04 (0.00, 0.79)</td>
<td>-3.3520</td>
<td>1.5914</td>
<td>0.0352</td>
</tr>
<tr>
<td>Sex (Female=0)</td>
<td>0.38 (0.17, 0.84)</td>
<td>-0.9685</td>
<td>0.4071</td>
<td>0.0174</td>
</tr>
<tr>
<td>PM$_{2.5}$*sex$^a$</td>
<td>60.61 (2.52, 1456.95)</td>
<td>4.1045</td>
<td>1.6223</td>
<td>0.0114</td>
</tr>
<tr>
<td><strong>Curvilinear Effect</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM$_{2.5}$</td>
<td>93.86 (0.00, 195037030.80)</td>
<td>4.5418</td>
<td>7.4220</td>
<td>0.5406</td>
</tr>
<tr>
<td>PM$_{2.5}^2$</td>
<td>0.00 (3.24 x 10$^{-19}$, 1039239.76)</td>
<td>-14.3596</td>
<td>14.3949</td>
<td>0.3185</td>
</tr>
<tr>
<td>Sex (Female=0)</td>
<td>0.90 (0.15, 5.38)</td>
<td>-0.1103</td>
<td>0.9148</td>
<td>0.9041</td>
</tr>
<tr>
<td>PM$_{2.5}$*sex$^a$</td>
<td>0.03 (0.00, 60306.79)</td>
<td>-3.6582</td>
<td>7.4825</td>
<td>0.6249</td>
</tr>
<tr>
<td>PM$_{2.5}^2$*sex$^b$</td>
<td>1603180.46 (0.00, 2.86 x 10$^{18}$)</td>
<td>14.2875</td>
<td>14.3937</td>
<td>0.3209</td>
</tr>
</tbody>
</table>

**Notes:** (1) Results significant at the 5% level (p<0.05) are highlighted in bold; (2) Both models are controlled for the effects of urban core status, income, and age.

**Abbreviations:** OR (odds ratio); CI (confidence interval); SE (standard error); p (probability); PM$_{2.5}$ (particulate matter with an aerodynamic diameter of 2.5 µm or less, µg/m$^3$)

$^a$Interaction between linear effect of PM$_{2.5}$ and sex.

$^b$Interaction between curvilinear effect of PM$_{2.5}$ and sex.
Curriculum Vitae

Name: Phylicia Gonsalves

Post-secondary Education and Degrees:
The University of Western Ontario
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2010 B.M.Sc. Honors (Physiology and Medical Cell Biology)
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2013

Children’s Health Research Institute Travel Fund
2013

Children’s Health Research Institute
Quality of Life Initiative Grant
2012-2013

Schulich School of Medicine and Dentistry, Western University
Schulich Graduate Scholarship
2011-2013

Western University Dean’s Honor List
2006, 2009, 2010

Western Scholarship of Excellence
2005-2006

Related Work Experience:
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Middlesex-London Health Unit
2013