

**FACTORS AFFECTING PEDIATRIC ASTHMA IN RURAL
SASKATCHEWAN**

by

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Abstract

Background: Previous research suggests that children living on farms have a lower prevalence of asthma compared to their more urban counterparts. Four potential explanations may underlie this association: personal factors, health care access, health risk behaviours, and the environmental explanation.

Objectives: The objective of this thesis was to first compare the prevalence of asthma between children living on farms and those living in small towns. The second objective was to identify and compare potential risk and protective factors for childhood asthma in rural and farm environments. Finally, we interpreted the findings in light of the above explanations in terms of which is most likely to explain previously observed differences in pediatric asthma prevalence.

Methods: We used cross-sectional data (n=834) from a 2003 study conducted in Estevan, Saskatchewan as well as cross-sectional data (n=2,259) collected as part of the Saskatchewan Rural Health Study in 2011. We determined differences in asthma prevalence and examined the distribution of potential risk and protective factors between farm and small town children. Using multiple logistic regression, we identified a number of potential risk and protective factors for both pediatric asthma and wheeze among these populations.

Results: No differences in prevalence of asthma or wheeze were identified by farm and small town status in both analyses. Risk factors that were identified included: male sex, parental history of asthma, personal history of allergy, home dampness, being overweight or obese, premature birth, living in a single parent home, difficulty accessing routine healthcare, previous daycare attendance, having a mother that previously smoked, having mice in the home, having an air filter in the home and feeding livestock. Protective factors included: previous daycare attendance, having pets in the home and having a dehumidifier present in the home. Farm-specific protective

factors included: filling or emptying grain bins, cleaning or playing in pens, and living on a grain farm.

Conclusions: No differences in asthma or wheeze prevalence were identified between small town and farm children in these study populations. Findings primarily supported the environmental explanation for geographic differences in asthma prevalence identified historically, with modest support for the health care access explanation.

Co-Authorship

This thesis represents the work of Rebecca Barry in collaboration with her supervisors, Dr. William Pickett from Queen's University, and Dr. Joshua Lawson from the University of Saskatchewan, as well as additional co-authors on the two thesis manuscripts.

“Factors Contributing to Risks for Pediatric Asthma in Rural Saskatchewan”.

Ms. Barry, Dr. Pickett and Dr. Lawson were involved in the formation of the research questions as well as the completion of the data analysis, interpretation of results and preparation and revision of the manuscript for the current analysis. Dr. Lawson, Dr. Rennie, Dr. Senthilselvan, and Dr. Cockcroft were involved with the conception and design of the initial study, completion of the data collection, and critical review and editing of the manuscript.

“The Role of Farm Operational Factors As Potential Causes of Asthma among Rural Dwelling Saskatchewan Children”.

The idea of using the Saskatchewan Rural Health Study Children's cohort data to analyze both farm-specific and other risk and protective factors for pediatric asthma was suggested by Dr. Pickett and Dr. Lawson. Ms. Barry, Dr. Pickett and Dr. Lawson were involved in the formation of the research questions as well as the completion of the data analysis, interpretation of results and preparation and revision of the manuscript for the current analysis. Ms. Barry was responsible for partial cleaning of the dataset. Dr. Pickett and Dr.

Lawson provided suggestions, guidance and editorial input into the creation of the manuscript.

Dr. Lawson, Dr. Rennie, Dr. Dosman, Dr. Pahwa, Ms. Hagel, Dr. Pickett, and Dr. Karunanayake were involved with the conception, design and data collection of the children's portion of the Saskatchewan Rural Health Study and will review this manuscript as members of the Saskatchewan Rural Health Study team.

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Abbreviations and Definitions

Abbreviations

ISAAC: International Study on Asthma and Allergies in Childhood

BHR: Bronchial Hyper responsiveness

Definitions

Personal factors explanation: Differences in pediatric asthma prevalence by farm vs. urban status may be the result of differences in personal factors. For example, children that live on farms may be less likely to have parents with asthma because parents with asthma may be less likely to choose farming as an occupation.

Access to Care Explanation: Differences in pediatric asthma prevalence exist due to diagnostic patterns whereby farm children are less likely to become diagnosed with asthma than their more urban counterparts, although they still experience the same symptoms.

Health Risk Behaviours Explanation: Differences in pediatric asthma prevalence arise due to differences in health risk behaviours by geographic location. For example, children living on farms may be less likely to smoke than more urban children and therefore, experience fewer asthma symptoms.

Environmental Explanation: Environmental factors such as dampness or mold in the home or farm-specific factors may be underlying the difference in pediatric asthma prevalence by geographic status. This can be explained by the hygiene hypothesis.

Hygiene hypothesis: The idea that early exposure to environmental agents such as endotoxins influences immune response, primarily by increasing T helper Type 1 cells and decreasing T helper type 2 cells. Therefore, early exposure to endotoxin may subsequently result in decreased risk of developing asthma.

Chapter 1

Introduction

1.1 General Overview

Rural population health is an emerging epidemiological field that is now recognized as a national research priority.¹ One aspect of rural pediatric health worthy of focused attention is childhood asthma. More than 13% of Canadian children have been diagnosed with asthma²; this percentage is increasing both in Canada and globally, and asthma is among the most common chronic childhood diseases.² Yet, a lower prevalence of asthma has been identified among rural children compared to urban children.^{3,4} The lower prevalence is especially evident when comparing children from farming versus more urban environments, such as those from small towns.^{5,6}

While it is unclear why the difference in pediatric asthma rates exists several plausible explanations merit exploration. These are briefly outlined here. The first is called the *personal factors explanation*. This suggests that the distribution of personal factors such as a parental history of asthma may differ between farm children and more urban children. One reason for this might be that parents with asthma or allergies may be less likely to choose to farm as a profession due to factors in the environment which may exacerbate symptoms. The second explanation is the *health care access explanation*. This suggests that children living on farms have less access to health care service or there are differences in health care practices between rural and more urban areas that result in rural children being less likely to be diagnosed with asthma compared to more urban children. It follows that children living on farms have the same risk of experiencing asthma symptoms as those living in more urban areas, but they are less likely to receive an asthma diagnosis.^{7,8} The third explanation surrounds *health risk behaviours*. While more controversial,

this explanation suggests that individual health behaviours, such as smoking or physical activity, may be underlying the association between location of residence and asthma.⁹ A final explanation is *environmental* in nature. This suggests that differences in the environment underlie the differences in asthma prevalence. To illustrate, children living on farms are exposed to more endotoxins in the environment than children living in more urban areas. Endotoxins influence immune response, lowering the risk for asthma and allergic disease. This explanation is typically explained by the hygiene hypothesis, which suggests that early exposure to specific environmental agents have a long-term effect on the immune response which can cause a shift away from the allergic Th2 response.¹⁰

The purpose of the proposed study is to identify and gain a better understanding of specific risk and protective factors that may influence the occurrence of asthma in children living in such rural environments. It will also lead to a better understanding of which explanation(s) accounts for observed geographic differences in pediatric asthma that are typically seen between farm and more urban environments.

1.2 Rationale

As discussed above, previous studies have observed that children in rural environments, especially farms, report reduced asthma and asthma-like symptoms compared to more urban children.^{3,4} Despite this, there is still a relatively high prevalence of asthma in rural Canadian children making asthma an important condition to consider in these areas. Although several explanations have been proposed to explain this phenomenon, more evidence is needed to identify the explanation that is most credible. I will address the aforementioned gaps by taking advantage of an opportunity to compare the prevalence of asthma in farm vs. small town pediatric populations in Saskatchewan, and by identifying which of the above explanations best fits with any observed geographic variation in pediatric asthma. Findings may direct public health

initiatives aimed at reducing asthma prevalence among specific populations by targeting at-risk populations. Findings may also identify specific agricultural exposures that may exacerbate asthma symptoms and direct risk reduction efforts.

1.3 Thesis Organization and Outline

The overall purpose of this thesis is to examine asthma and its risk factors in addressing differences between small town and farm settings. The thesis is organized conceptually around selected aspects of the above explanations that attempt to explain farm vs. small town differences in asthma prevalence.

Two separate manuscripts comprise the thesis. The first manuscript explores potential risk factors (behavioural and environmental) associated with the prevalence of asthma in a region of Saskatchewan made up of both small town and farm children. The second manuscript includes those living on farms and in small towns or villages from four quadrants of rural Saskatchewan. The aim was to identify specific exposures as potential risk and protective factors for childhood asthma and asthma-like symptoms, and to determine which of the four explanations best accounts for geographic variation in pediatric asthma. We also had the ability to examine specific farm-related exposures as potential risk and protective factors. Each manuscript is based on an analysis of an existing, but independent, database.

This thesis involved a number of different experiences consistent with the aims of a Master's thesis in the field of epidemiology. This included: design of hypotheses, preparation of a literature review, designing a questionnaire, data cleaning and management, planning and completion of the analysis, presentation and interpretation of results, and manuscript preparation and submission for publication.

1.4 Objectives and Hypotheses

1.4.1 Manuscript 1

The primary objectives of this study were to: (1) describe the prevalence of asthma and asthma-like symptoms in child populations from a rural area in one region of Saskatchewan, (2) compare children from farms and small towns in this population in terms of key behavioural and environmental factors that might be associated with asthma and asthma-like symptoms, and (3) employ an exploratory approach to examine the associations between these characteristics and asthma and wheeze. Based upon historical findings, it was hypothesized that children living on farms would have a lower prevalence of asthma compared to small town children.^{3-6, 11}

1.4.2 Manuscript 2

The objectives of Manuscript 2 were to (1) compare the prevalence of asthma and wheeze among small town and farm children; (2) to identify risk factors and protective factors for asthma using an exploratory analysis and, while taking into consideration the distribution of these factors, determine which of the explanations for farm vs. non-farm differences in pediatric asthma prevalence is most plausible; and (3) to complete a sub-analysis examining potential farm-specific environmental risk and protective factors for asthma including farm activities and farm type.

1.5 Scientific Importance

Results obtained from this study aid in the understanding of factors that directly and indirectly contribute to the occurrence of pediatric asthma. This understanding may generate hypotheses for more definitive etiological analyses that may lead to focused measures to prevent the occurrence of childhood exposure to risk factors associated with asthma and asthma-like symptoms. Results may also aid in identifying which factors in rural environments exacerbate asthma and asthma-like symptoms in pediatric populations. Therefore, public health interventions

could aim to alleviate and minimize asthma-like symptoms in rural children currently diagnosed with asthma. Finally, results suggest which explanations best describe geographic variation in pediatric asthma, and this knowledge can be used to implement population-based initiatives to reduce asthma prevalence.

1.6 Thesis Outline

The following chapter (Chapter 2) will describe existing literature describing the farm effect and provide evidence for the four explanations that may explain geographic differences in childhood asthma prevalence. Chapter 3 is the first manuscript, and Chapter 4 is the second manuscript. Chapter 5 will discuss both manuscript and summarize key findings, with emphasis on key epidemiological concepts.

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Chapter 2

Literature Review

2.1 Scope of Literature Review

The purpose of this chapter is to explore existing literature that has examined geographic differences in the prevalence of childhood asthma and asthma-like symptoms, as well as factors that might explain such differences. The main geographic difference under study was farm vs. non-farm settings, while asthma and wheeze represent the main outcomes under study.

In this literature review, first I will discuss the urban and rural population distribution in Canada. Second, I will briefly discuss what is known about the natural history and epidemiology of asthma. Third, literature describing general risk factors for pediatric asthma will be reviewed. Fourth, literature examining differences in asthma or wheeze prevalence by geographic location of residence will be summarized. Fifth, I will review the distribution of general risk factors for asthma by urban-rural or small town-farm status. Related to this review, literature supporting four competing explanations that may account for the differences in asthma outcome prevalence by location of residence will be discussed (these represent the core theme of this dissertation). A summary of specific types of farm activities and exposures on farms and their association with childhood asthma and asthma-like symptoms will also be provided.

2.2 Methods

The literature review was conducted between May 2011 and June 2012. I used PubMed, Google Scholar, and the Queen's University Library Summons search engines to identify evidence contained in existing scientific publications and reports. Search terms included combinations of the words "rural", "pediatric", "asthma", "wheeze", "farm", "Canada", "access to care", "environment*", "child*", "behaviour*", and "chores", among others. Additional

scientific articles were identified based on their appearance in the reference section of previously read scientific papers. Papers were only selected if they were published after 1990 and were available in English. Most of the selected publications used a cohort or cross-sectional study design, and originated from North America, Australia, or Europe.

2.3 Rural Living and Farming in Canada

In 2006, the population of Canada was over 31 million, composed of 25 million urban residents and 6 million rural residents.¹ Although the number of farms in Canada is decreasing, the rural population in Canada is growing and depending upon how rural is defined, 19% to 30% of Canadians are living in rural areas.^{1,2} Rural regions adjacent to metropolitan areas have experienced the highest growth, and therefore, a higher percentage of rural Canadians are living within the commuting zone of larger urban centres.² Compared to more urban regions, rural regions demonstrate greater variations in economic attributes such as income level, unemployment and educational attainment.³

Many individuals that live in rural areas also live on farms. Although the number of farms in Canada is declining, the size of Canadian land in agricultural production is increasing. Between 2001 and 2006, the number of farms in Canada decreased from 246,923 to 229,373, while total Canadian farmland area increased by 300,000 acres during this same time period.¹ The largest proportions of Canadian farms are field crop farms (39.8%), followed by beef cattle farms (26.6%). The average net farm revenue in 2007 was \$30,654.¹ Ontario is the province with the most farms, with 57,211 farms in 2006. The province of Saskatchewan had 44,329 farms in 2006.¹ In addition to this, a larger proportion of the Saskatchewan population live in rural areas compared to the rest of Canada.

For both agricultural and non-agricultural populations, rural population health is an emerging epidemiological field that is now recognized as a national research priority.⁴ One

aspect of rural pediatric health worthy of focused attention is childhood asthma, related to farm and small town living.

2.4 Natural history and Epidemiology of Asthma

2.4.1 Symptoms and Natural History

Asthma is a disease characterized by symptoms of wheeze, cough, shortness of breath and chest tightness, which typically occur following exposure to irritants, allergens, respiratory infections or after exercise.⁵ Wheeze is the primary symptom of asthma and is the result of narrowed airways (bronchi) restricting airflow, resulting in turbulent airflow which then causes oscillation of the bronchial walls.⁶ In one study from the US from 1995, although one third of all children aged 3 had respiratory illness with wheezing, almost 60 percent of these children had stopped wheezing by the age of six.⁷ Early episodes of wheeze (before age three) are usually transient, and are not predictive of future diagnoses of asthma, whereas later wheeze is associated with a higher likelihood of future asthma diagnoses. Persistent wheezing beyond early childhood is associated with a family history of allergies and asthma and reduced lung function, and children that wheeze persistently are more likely to display an acute immune response to viruses than children with transient wheeze.^{6,8} Some children, particularly girls, may experience late-onset wheeze as they may only begin to experience wheeze during the transition into adolescence.⁸

2.4.2 Prevalence of Asthma

2.4.2.1 Global prevalence

This chronic health disorder affects an estimated 300 million people worldwide⁹ with the prevalence of pediatric asthma increasing worldwide.^{10,11} The prevalence of asthma is also higher in developed countries characterized by a “westernized lifestyle” than in developing countries,

although the explanation for this trend is still unclear.^{6, 12} In Canada, 13% of children have been diagnosed with asthma.¹¹

2.4.2.2 Saskatchewan prevalence

In the province of Saskatchewan, the prevalence of asthma based on physician billing databases was 4.4% in children aged 5 to 14 years in 1990, an increase from 2.6% in the early 1980s.¹³ The prevalence of asthma also increased between 1991 and 1995, but began to stabilize between 1996 and 1998.¹⁴ Point prevalence estimates from the general pediatric population ranged from 10.0 to 11.2 per 100 in Saskatchewan, as estimated in three cross-sectional population-based studies published in 1996 to 1999.¹⁵⁻¹⁷

Most recently, differences in asthma prevalence have been found between different Saskatchewan communities. Rennie et al. demonstrated in 2000 that in Estevan, a community in Southern Saskatchewan, asthma prevalence in children in grades 1 to 6 was higher than asthma prevalence in another agricultural community (Swift Current) also in Southern Saskatchewan (21.4% compared to 16.2%).¹⁸ This association was largely attributable to higher asthma prevalence observed among girls in Estevan, which is an atypical sex pattern. Although the reasons for differences in prevalence between the communities observed by sex remain unclear, it was posited that the differences may be attributed to earlier diagnosis in Estevan as well as environmental triggers in the environment (e.g., higher air pollution). These differences may also have resulted from regional variation in risk factors for asthma. For example, a significantly higher proportion of children in Estevan compared to Swift Current reported presence of home mould or dampness, gas heating and a dehumidifier in the home.¹⁹

2.4.3 Burden

Asthma contributes to a societal burden that includes a large number of hospital admissions and physician visits each year.⁵ One Canadian survey found that 43% of people with asthma made an unscheduled visit to their physician for asthma and 18% of people with asthma visited the emergency department in the previous 12 months.⁵ Asthma contributed to 10% of all hospital admissions for children ages 5-14 in 1997.⁵ A systematic review of the economic impact of asthma found that high direct costs (e.g., hospitalization and medications) and high indirect costs (e.g., work absenteeism) contribute to a large economic burden.²⁰ In 1990, this burden was between \$504 million and \$648 million in Canada.²¹ In 2010, chronic lung diseases including asthma cost \$3.4 billion in direct costs and \$8.6 billion in indirect costs in Canada.²²

Asthma also contributes to other conditions that affect the health of populations. These health effects may include daily restriction of activities, frequent symptoms and asthma attacks, and impaired overall quality of life. Thirty-five percent of people with asthma report restriction of their daily activities.⁵ Restrictions include absenteeism from school or work and limitations in physical activity.^{5,23} One half of individuals with current asthma have frequent symptoms, and many suffer from asthma attacks.⁵ Asthma attacks are characterized by feelings of suffocation, breathlessness, and loss of control, and these can be life-threatening.⁵ Finally, children with asthma score lower on existing quality of life scales, particularly in the physical dimensions which include bodily pain (average scores of 71 for asthmatic children and 86 for non-asthmatic children) and general health (average scores of 60 and 74, respectively).²⁴ This evidence suggests that asthma reduces the quality of life in children.

2.5 General Risk Factors and Protective Factors for Pediatric Asthma

There are a number of established risk factors for asthma. In the epidemiological and clinical literatures, risk factors are often divided into personal factors (e.g., family and personal

history of asthma), environmental factors (e.g., dampness or mould) and behavioural factors (e.g., physical activity).

Typically, personal factors are most consistently identified as important risk factors for asthma. Sex is an important personal risk factor. Boys are more likely to be diagnosed with asthma than girls in childhood, but this trend is reversed in adulthood.^{5, 14} Midodzi et al. found a statistically significant positive association between childhood wheeze and respiratory infection (OR=5.14, 95% CI: 2.29 to 11.5) among Canadian preschool children.⁸ Personal history of allergies has also been implicated as a risk factor for asthma.^{5, 25} Parental history of asthma has been associated with greater airway hyper-responsiveness in children with asthma.²⁶ Midodzi et al. found a statistically significant positive association between childhood wheeze and premature birth (OR=1.64, 95% CI: 1.00 to 2.68), although the validity of this association is still debated. Low birth weight is suggested to be associated with asthma because of immature lungs and immune systems, or due to the fact that the pregnancy complications that may result in low birth weight may also alter the *in utero* environment which can affect immune response patterns.²⁷

Inconsistent associations have been demonstrated between environmental factors and asthma. Established risk factors for childhood asthma include parental history of smoking (particularly, maternal smoking). Weitzman et al. found that maternal smoking was positively associated with higher rates of asthma, increased likelihood of asthma medication use, and earlier onset of the disease.²⁸ Martinez et al. found that children with persistent wheezing were 2.3 times more likely of having a mother that smoked than children without wheeze.⁷ Midodzi et al. also found a similar association between paternal smoking and asthma-like symptoms.⁸ A review by the Canadian Institute for Health Information suggests that high exposures to airborne allergens (including pets, dust mites and mould) during early life are potential risk factors.⁵ A potential protective environmental factor is crowded living areas, as Midodzi et al. found a significant

protective effect for crowding (more than 1.5 persons/bedroom; (OR = 0.63; 95% CI: 0.47 to 0.85).⁸ A more controversial environmental exposure is indoor pets. Exposure to pets may lower risks for asthma and allergies, a phenomenon described as the “protective pet effect”.²⁹ While exposure to dogs has been indicated as a protective factor for asthma, exposure to cats has been indicated as a protective factor for wheeze.²⁹ This effect was found to be stronger among children living on farms.²⁹ However, a prospective cohort study found that indoor pets may be a risk factor for asthma in children with no history of wheeze (RR=1.6, 95%CI: 1.0-2.5).³⁰

Although more controversial, a number of risk factors such as obesity and health behaviours including lack of physical activity have also been found to be associated with asthma.³¹ Breastfeeding has also been implicated as a risk factor for childhood wheeze among Canadian preschool children (OR=1.65, 95% CI: 1.24 to 2.19).⁸

2.6 Geographic Location of Residence

2.6.1 Asthma and Wheeze and the Protective Farm Effect

In the 19th century, Charles Blackley first noticed that children who live on farms have a lower incidence of asthma despite high exposure to pollen and other common allergens.³² More contemporary studies also suggest that living on a farm has a protective effect.^{25, 32-35} This relationship has been observed in a variety of study situations using different exposure assessment techniques. **Table 1** summarizes a selection of research that examines asthma and/or wheeze prevalence by urban vs. rural, urban vs. farm or small town vs. farm children. This table includes studies conducted since 1990 from North America and Europe. Within Canada, Dimich-Ward et al. found that in 4H members aged 8-20 years, those living on farms with livestock had a lower relative odds of asthma compared with members living in a rural area without livestock (OR=0.49; 95% CI: 0.27 to 0.89).³² Although the response rate for the questionnaire was low (50.3%), this study still illustrates that differences may exist even between rural and farm

children. Also within Canada, Ernst and Cormier surveyed 1200 rural adolescent secondary children aged 12-19 years.³⁵ Adolescents raised on farms were less likely to experience wheeze (OR=0.70; 95% CI: 0.52 to 0.95) and less likely to have asthma as defined by self-report of wheeze and airway hyperresponsiveness during a methacholine bronchoprovocation test than adolescents who were not raised on farms (OR=0.59; 95% CI: 0.37 to 0.95).³⁵ An objective measure of allergic disease, the skin prick test, combined with a standardized questionnaire was used in a study on children aged 8-10 in rural Austria.³⁶ Findings indicated that children who live on farms had a lower prevalence of asthma (1.1 vs. 3.9%), and a lower prevalence of positive skin prick reactions (18.8 vs. 32.7%).

There has been some evidence that suggests that asthma prevalence may not differ by farm vs. non-farm status. The Keokuk County Rural Health Study (KCRHS), a longitudinal cohort study with both clinical and survey-based outcome measurements, found that children born on farms and children that currently live on farms did not have a lower prevalence of asthma compared to other children (OR=1.30, 95%CI=0.69 to 2.43; OR=1.03, 95%CI=0.55 to 1.91), respectively).³⁷ Chrischilles et al. did not find that farm children were less likely to have diagnosed asthma compared to town children (OR=0.77, 95%CI: 0.61 to 1.06).³⁸ However, this study did find that farm children were less likely to report ever wheeze (OR=0.85, 95%CI: 0.58 to 0.87) and current wheeze (OR=0.77, 95%CI: 0.60 to 0.98) than town children. A protective farm effect has also been observed for the incidence of asthma in longitudinal studies. One such study followed children without asthma at the baseline (aged 0 to 11 years) living in farming, rural non-farming and urban environments across Canada over a period of 2 years, and found that children living on farms had lower incidence of asthma compared to rural non-farming children (OR = 0.30, 95% CI: 0.24 to 0.65).²⁵ The presence or absence of this association between lower pediatric asthma rates and farm environments may indeed depend upon specific contextual

factors, as well as the comparison populations being studied. Second, where differences in asthma exist by farm vs. non-farm residential status, there are several plausible explanations that merit exploration.

Table 1- Summary of Studies Examining the Relationship between Rural (Farm) vs. Urban (Small town) and Other Geographic Status pediatric asthma prevalence

Study	Year	Place	Population	Study Design	Exposure	Outcome	Major Findings
Senthilselvan et al. ¹⁴	1991-1998	Saskatchewan, Canada	Residents of Saskatchewan covered by universal healthcare (1996 census suggests 976,615 people)	Retrospective cohort	Rural (living in a town or area with fewer than 10,000 people) and urban populations (more than 10,000 people)	Asthma prevalence based on the physician services database of the Saskatchewan Health Department	During the seven year study period, asthma prevalence among rural populations was similar or less than urban populations in all age groups.
Midodzi et al. ²⁵	1994-1997	Canada, across all ten provinces (excluding territories)	13524 children ages 0-11	Cohort	Farming vs. rural non-farming vs. non-rural	Cumulative incidence of asthma based on parental report of physician-diagnosed asthma on interviewer-administered questionnaire	Cumulative incidence of asthma 2.3% in farming rural children, 5.3% in other rural children, and 5.7% in non-rural children. Children living on a farm had a reduced risk of asthma compared to rural non-farming children (OR=0.30, 95%CI:0.24 to 0.65)
Merchant et al. ³⁷	1994-1998	Iowa, United States	644 children ages 0 to 17	Cohort	Currently living on a farm vs. not currently living on a farm; Born on a farm vs. not born on a farm	Diagnosed asthma based on parental report in questionnaire	Children born on farms and children currently living on farms have no differences in prevalence of diagnosed asthma compared to other rural children (OR=1.30,95%CI:69 to 2.43; OR=1.03, 95%CI:0.55-191), respectively)
Riedler et al. ³⁶	1997	Austria (rural areas)	2283 children ages 8-10 years old	Cross-sectional	Farm vs. non-farm	Asthma based on self-report, allergies based on skin prick test	Children who live on farms have a lower prevalence of asthma (1.1% vs. 3.9%), and a lower

prevalence of positive skin prick reactions (18.8 vs. 32.7%).

Adolescents raised on farms were less likely to experience wheeze (OR=0.70; 95% CI: 0.52 to 0.95) and less likely to have asthma than adolescents who were not raised on farms (OR=0.59; 95% CI: 0.37 to 0.95).

Wheeze based on self-report. Asthma as defined by self-report of wheeze and airway hyperresponsiveness during a methacholine bronchoprovocation test

Farm vs. rural non-farm

Cross-sectional

1199 rural secondary school students ages 12 to 19

Rural areas of Quebec, Canada

1999

Ernst and Cormier.³⁵

Those living on farms with livestock had lower relative odds of asthma compared with members living in a rural area without livestock (OR=0.49; 95% CI: 0.27 to 0.89). Those living on farms did not have less reported wheeze than rural areas with no livestock (OR=0.74, 95%CI: 0.41-1.33).

Physician-diagnosed asthma and symptoms of wheeze based on self-report

Farm residence vs. rural, no livestock vs. rural with livestock vs. urban

Cross-sectional

1158 children 4-H club youth ages 8 to 20

British Columbia, Canada

2001-2002

Dimich-Ward et al.³²

Asthma prevalence was lowest in rural regions (metro=17.7%, non-metro-adjacent=15.6%, rural=14.8%). Asthma prevalence was lower in non-metro-adjacent regions (OR=0.81, 95%CI: 0.65 to 1.01) and rural regions (OR=0.76,

Asthma defined as self-report of doctor diagnosis and asthma symptoms or a health care visit for asthma in the past year

Rural regions vs. non-metro but adjacent to metro vs. metro

Cross-sectional

4726 children in grades 6 to 10

Canada

2001-2002

Lawson et al.³⁹

Chrischilles et al. ³⁸	2000-2002	Two rural counties in Iowa, United States	3090 children ages 6 to 12 years	Cross-sectional	Farm vs. rural non-farm vs. town	Asthma and wheeze (ever and current) based on parental report.	95%CI: 0.61 to 0.95) compared to metro regions. Farm children were less likely to report ever wheeze (OR=0.85, 95%CI: 0.58 to 0.87) and current wheeze (OR=0.77, 95%CI: 0.60 to 0.98) than town children. Farm children were not more likely to have physician diagnosed asthma (OR=0.77, 95%CI: 0.61-1.06)
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2.6.2 Distribution of Risk Factors by Location of Residence

Many of the risk factors discussed in section 2.5 may be distributed differently across farming, non-farming rural, and more urban populations. A study from the United States found that children living on farms have been found to be less likely than rural non-farming children to have mothers that smoke (21.2% vs. 29.0%, respectively) and more likely to have parents with more education (14.2 vs. 13.5 mean years of education, respectively).³⁷ Some research from Canada suggests that farm children smoke less often than other rural children (12.7% vs. 21.4%) and although more likely to own pets (76% vs. 36% own a cat; 71% vs. 45% own a dog, respectively), are less likely to allow them in the bedroom (20% vs. 29% allow cats; 21% vs. 27% allow dogs, respectively).³⁵ Children living on farms are more likely than other rural children to have been breastfed (64% vs. 58%), to have pets (88% vs. 79%), and less likely to attend daycare (39% vs. 50%, respectively).⁴⁰ However, another study also found that farm children are more often exposed to wood stoves (31.3% vs. 20.8%, respectively), and conditions that require use of a dehumidifier (54.4% vs. 30.8%, respectively).³⁷

2.6.3 Explanations for Differences by Location of Residence

There are several potential explanations that might explain the lower rates of pediatric asthma observed in farm populations. The first explanation is that children living on farms differ in regard to personal factors, such as parental history of asthma or personal history of allergies (*Personal factors explanation*). The second explanation suggests these differences arise because farm children have less access to healthcare or differences in health care practices, and therefore are simply less likely to become diagnosed with asthma, although they still experience the same symptoms (*Health care access explanation*).^{23, 41} The third explanation is that behavioural differences, such as smoking and physical activity, may account for the observed differences in rates of asthma (*Health risk behaviour explanation*). The fourth explanation is that children living

on farms are exposed to environmental agents such as endotoxins that might influence the immune response (*Environmental explanation*).^{25, 42}

2.6.3.1 Personal Explanation

Personal factors such as parental history of asthma and personal history of allergy are strongly associated with asthma.^{5, 25, 26} Therefore, if there is variation in personal factors between farm children and small town children, this could potentially underlie the observed differences. One reason for this phenomenon may be that people with asthma are more likely to move away from the farm environment in order to decrease symptoms. In a descriptive presentation of case studies occurring in the 1950s, Rackemann and Edwards discussed a number of cases where children with exacerbated asthma grew up and left the farm or country environment and subsequently found that their symptoms mostly vanished.⁴³ Therefore, children living on farms may be less likely to have parents with asthma than those living in town. Other personal factors may also differ by small town and farm status (e.g., premature birth).

2.6.3.2 Health Care Access Explanation

The access to care explanation suggests that the observed geographic differences in the prevalence of asthma arise because farm children have less access to healthcare or engage in different health care practices, and therefore are simply less likely to become diagnosed with asthma, although they still experience the same symptoms.⁴⁴ Chrischilles et al. measured both doctor diagnoses and asthma symptoms and found that less than half of children with frequent symptom of asthma, and less than three-quarters of those with severe symptoms, receive a doctor's diagnosis of asthma.³⁸ Therefore, it is plausible that the potential number of undetected cases may account for observed differences in asthma prevalence between farm and small town children.

Children living in rural areas access medical care for asthma at a lower rate than urban children. Yawn, et al. found that urban children with asthma are twice as likely as rural children with asthma to see an asthma specialist, 2.7 times as likely to receive asthma care in the emergency department, and 1.4 times as likely to receive oral steroid medication to control asthma symptoms.²³ Although this could be a reflection of poorer clinical control of asthma or higher severity in urban populations, it may actually be an indicator that rural children seek specialty care far less often, leading to detection biases. Mortality rates from asthma have also been found to be 4 to 43% higher in rural populations than in urban centres, suggesting that poorer control or higher severity in urban populations may not be the reason for these observed differences in care uptake.³³ The potential number of undetected cases in rural populations, due to lack of access to asthma care, may account for differences in asthma prevalence between rural and urban children, or between small town and farm children.

2.6.3.3 Health Risk Behaviour Explanation

Although a more controversial idea, the health risk behaviour explanation proposes that individual health behaviours, such as smoking and physical activity, may account for the observed differences in asthma prevalence between rural and urban children, as well as among children with and without exposure to farms.

One example of a health behaviour that may influence pediatric asthma is parental smoking. Martinez et al.'s prospective study that aimed to identify factors affecting wheeze found that children who wheezed at age three and at age six were more likely to have mothers that smoke.⁷ However, a cross-sectional study by Lawson et al. found an inverse relationship between childhood asthma and current maternal smoking although this association is likely due to the "healthy smoker effect".⁴⁶ That is, mothers that smoke may cease smoking after their child is

diagnosed with asthma, while those mothers that have children without asthma may continue to smoke. These inconsistent findings suggest that some parents may engage in risk reduction behaviours in order to reduce a child's exposure to suspected risk factors for asthma.

Ernst and Cormier found that secondary students aged 12-19 living on farms had a lower reported smoking prevalence than children living in town.³⁵ They also found that students living on farms, although more likely to have domestic pets, were less likely to allow them into the bedroom. Families in farming environments may have more traditional lifestyles than families in small town environments.³⁶ Therefore, some of these lifestyle and behavioural differences between children living in small town and farm environments may account for the differing prevalence rates of asthma. Finally, Bruner et al. found that rural Canadian adolescents are more likely to be obese than urban adolescents (OR = 1.56, 95% CI: 0.95 to 2.57 for rural regions).⁴⁷ However, there was no significant association between physical activity and unhealthy diet found by geographic location. Similarly, Mitura and Bollman reported that boys in rural areas had higher levels of obesity and girls in rural areas have lower self-rated health.⁴⁸

Despite evidence suggesting that rural and more urban children have differing health behaviour patterns, there is also evidence to suggest that these differences do not actually mediate the association between location of residence and asthma. Lawson et al. found that while being overweight or obese, having a high physical activity level and exposure to passive smoking independently led to greater risk for asthma, these factors did not mediate the relationship between location of residence and asthma prevalence.⁴⁹

2.6.3.4 Environmental Explanation

The environment has been the most common explanation used to explain why farm environments are associated with decreased pediatric asthma. Differences in environmental exposures may alter the immune response. This is typically explained by the hygiene hypothesis.

This hypothesis proposes that early life exposures influence immune system development, lowering risks for asthma and allergic disease.⁵⁰ Early childhood exposures to infectious agents and pathogens are hypothesized to increase production of T helper type 1 cells, and decrease production of T helper type 2 cells. This is thought to result in a decreased reaction to allergens during childhood.⁵⁰

This theory is supported by animal research conducted by Tulic and colleagues.⁵¹ Rats were exposed to aerosol lipopolysaccharides after being sensitized to ovalbumin (OVA) via intraperitoneal injection. Allergic responses to a subsequent exposure to ovalbumin were then assessed. Single exposures to aerosol lipopolysaccharides before and up to four days after the intraperitoneal injection were associated with decreased OVA-specific immunoglobulin IgE. Later exposure to the aerosol (after day six) resulted in increased sensitization to the OVA exposure. Findings from this study lend empirical support for the theory that the timing of some exposures influences the sensitization process. These findings may contribute to differences in pediatric asthma prevalence because endotoxin levels are generally higher in the farm environment than in more urban environments.⁵²

Existing epidemiological studies also support this theory. A cross-sectional study in rural Austria found that early (first year of life) consumption of farm (unpasteurized) milk, and early exposure to stables, were associated with decreased prevalence of asthma (1% vs. 11%).⁵³ The International Study on Asthma and Allergies in Childhood study (ISAAC study) Phase 2 found an inverse relationship between exposure to endotoxin and pediatric asthma across countries.⁵⁴

Endotoxin is an environmental exposure that is thought to help explain the protective effect of farm/rural residential status on the occurrence of asthma. Endotoxin is part of the gram-negative bacteria membrane, and it is found in higher levels in farm dwellings compared to urban settings.⁵² While it is hypothesized that the effects of endotoxin are attributable to early childhood

exposures, as explained by the hygiene hypothesis, a review by Douwes et al. of both human and animal studies suggests that the hygiene hypothesis may be extended beyond early exposure to endotoxin, and that inhibition of atopic sensitization may occur anytime throughout life.⁵⁵

Conclusions based on several studies suggest that endotoxin exposure in adulthood may protect against atopic asthma, and most animal studies also have confirmed this hypothesized association.^{51,55} Therefore, the protective effect of the farming environment on asthma may be attributable to the idea that exposure to environmental microbial matter may determine overall immune status of mammals, and render them less susceptible to the development of T type 2 help cells.

2.7 Farm-specific Environmental Exposures and Respiratory Symptoms

2.7.1 Farm Production Activities

Few previous studies have examined relations between specific farm activities and pediatric asthma, and much of the existing literature provides mixed conclusions. General trends suggest that contact with livestock may be a protective factor for asthma^{32, 36, 56, 57}, while other farm exposures such as grain or dust may be important risk factors.^{56,57}

Several studies suggest that exposure to grain or dust may be a risk factor for pediatric asthma. Farthing et al. conducted a cross-sectional survey conducted in rural Saskatchewan with a population of children aged 6-12 years.⁵⁶ Farm activities that were found to be positively associated with respiratory symptoms included emptying and filling grain bins (OR=2.18, 95% CI: 1.03 to 4.62), playing on or near hay bales (OR=1.89, 95% CI: 1.19 to 3.01), cleaning pens (OR=2.70, 95% CI: 1.05 to 6.97), and exposure to haying activities (OR=2.08, 95% CI: 1.07 to 4.06).⁵⁶ These findings suggest that activities that expose children to grain or other dust may increase risks for asthma. However, a cross-sectional study that examined reports from children living in five European countries found opposite results.⁵⁷ That is, an inverse relationship was found for diagnosed asthma and haying (OR=0.56, 95% CI: 0.38 to 0.81).⁵⁷

A number of studies have demonstrated that exposure to livestock may be a protective factor for asthma and wheeze. Dimich-Ward et al. found an association between living in a farm environment with livestock and poultry and a reduced prevalence of diagnosed asthma compared to living in a rural environment with no livestock among 4-H members aged 8-20 years (OR=0.49; 95% CI 0.27 to 0.89).³² Among rural children, having a dog was identified as a protective factor for asthma (OR=0.4, 95% CI: 0.2 to 0.8).⁵⁸ Ege et al. found a protective effect for both pig-keeping (OR=0.57, 95% CI: 0.38 to 0.86) and frequent stays in animal sheds (OR=0.71, 95% CI: 0.54 to 0.95).⁵⁷ A cross-sectional survey conducted on children ages 6-13 from Austria, Germany and Switzerland, also found protective effects for early life exposure to farm stables (6% vs. 12%).⁵³

Although it is uncertain why exposure to livestock may be associated with reduced atopy, one study found that regular contact with livestock increases endotoxin concentrations within the indoor home environment,⁵⁹ and an inverse relationship between indoor play area endotoxin concentration and school absenteeism due to chest illness has been demonstrated among rural children.^{60, 61}

Other farm-related factors have also been found to be associated with asthma. Ege et al. also found protective farm-related exposures including farm milk consumption (OR=0.77, 95% CI: 0.60 to 0.99) and use of silage (OR=0.55, 95% CI: 0.31 to 0.98).⁵⁷ Riedler et al. also found a protective effect for early life exposure to unpasteurized milk consumption (1% vs. 11%).⁵³

2.7.2 Farm Type

There is limited previous literature examining how pediatric asthma is related to farm production types. However, there is evidence suggesting that residence on a specific type of farm is a greater predictor of respiratory disease than specific farm activities. A study examining 4-H members in British Columbia found that the protective effect of residence on a farm with

livestock was more closely associated with respiratory illness rather than livestock exposure variables such as frequency of contact with animals and barn use.³² A longitudinal study found that living on farm that raised swine and added antibiotics to feed was associated with asthma medication use for wheeze (OR=2.47, 95% CI: 1.29 to 4.74) and cough with exercise (OR=2.72, 95% CI: 1.34 to 5.52).³⁷

2.8 Conclusions

This review discussed existing literature that has examined asthma and wheeze prevalence by rural (farm) versus more urban geographic status, and the distribution of factors that may explain such differences. Current hypotheses that attempt to explain variation in asthma prevalence by location of residence include personal factors, behavioural factors, access to health care and environmental factors. Currently, there is still uncertainty about what is underlying any observed geographic differences in asthma prevalence in populations of children. In the following manuscripts, we will therefore first determine whether there are differences in asthma and wheeze prevalence by small town and farm status within sampled populations of children from Saskatchewan, Canada. We will then examine the distribution of risk factors and protective factors for asthma and wheeze by small town and farm status, and identify which hypotheses most likely underlie any observed geographic differences in asthma.

Several studies have concluded, albeit with a few inconsistent findings, that living on a farm may be protective for the development of pediatric asthma. The most prevalent explanation used to explain this effect is the environmental explanation. This explanation has been supported by animal research by Tulic et al.,⁵¹ by research suggesting endotoxin levels are higher in the farm environment,⁵² and by studies suggesting that farm-specific factors, such as livestock, may be protective for development of childhood asthma.^{32, 36, 56, 57} However, previous studies have not examined each of the four plausible explanations concurrently. To build upon previous research,

this thesis will examine each of the four plausible explanations that may account for the observed differences in pediatric asthma prevalence by farm versus small town status using two cross-sectional studies involving Canadian pediatric study populations.

2.9 Restatement of Objectives

In order to transition to the next chapters of this thesis, a re-statement of the thesis objectives is warranted. In Manuscript 1, we will describe the prevalence of asthma and wheeze in child populations by farm and small town status, and then compare children from these populations in terms of key factors (e.g., behavioural and environmental) that might explain any observed associations with variations in asthma and also the symptom of wheeze. In Manuscript 2, we will compare the prevalence of asthma and wheeze among small town and farm children in a contemporary study conducted in Saskatchewan. We then identify risk and protective factors for asthma through exploratory analysis and, while taking into consideration the distribution of these factors, determine which of the explanations for geographic differences in pediatric asthma prevalence is best supported by our evidence. We also present a sub-analysis examining potential farm-specific environmental risk factors (e.g., farm activities and farm type) and protective factors for asthma. The overall aim of these manuscripts is to examine asthma and its risk factors and protective factors and by doing so, address differences in asthma and wheeze prevalence between small town and farm settings.

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Chapter 3

Factors Contributing to Risks for Pediatric Asthma in Rural

Saskatchewan

3.1 Abstract

Background: Rural children have lower reported rates of asthma compared to urban children.

While reasons for these differences remain unclear, three possible explanations exist: (1) *environmental* differences, (2) variations in *health care access* and (3) variations in *health risk behaviours*.

Objective: We investigated asthma among children living on farms and in small towns and its potential determinants, including personal, behavioural and environmental factors.

Methods: School children (n=842, ages 6-13; participation rate=72.0%) were involved in a 2003 cross-sectional study. Their parents completed a lung health survey which included questions about asthma, asthma-like symptoms, and potential determinants of asthma (demographic, environmental, health risk behaviours). Participating children were classified into farm dwellers (live on farm or acreage) and small town dwellers. Multiple logistic regression was used to investigate the association between asthma and wheeze with demographic, environmental and behavioural exposures with simultaneous adjustment for confounders.

Results: Asthma and wheeze prevalence was not significantly different between farm and small town areas (current asthma: 16% vs. 13%, respectively; current wheeze: 27% vs. 21%, respectively) and followed consistent patterns. Factors associated with diagnosed asthma were dampness (OR=1.85; 95%CI=1.08-3.17) with enrollment in daycare found to be protective (OR=0.53; 95%CI=0.33-0.85). Being obese or overweight was associated with wheeze (OR=1.77; 95%CI=1.06-2.97).

Conclusions: Given the differences in risk factors between areas and the associations between environmental risk factors and obesity with asthma and wheeze, the study findings support *environment* and *health risk behaviour* explanations for the observed geographic variations.

3.2 Introduction

Asthma is a disease characterized by episodic symptoms of cough, shortness of breath, wheeze and chest tightness which typically occur after exposure to irritants, allergens, respiratory infections or after exercise.¹ More than 13% of Canadian children have been diagnosed with asthma.² With diagnoses increasing in Canada and also globally, asthma has become one of the most common chronic childhood diseases.² A lower prevalence of asthma has been identified among rural compared to urban child populations.^{3,4,5} This lower prevalence is especially evident when comparing children from farming versus more urban environments including small towns.^{6,7}

There are several potential explanations for the variations in asthma prevalence observed between urban and rural children: (1) *Environmental*: farm children may have different exposures⁸ or levels of exposures⁹ to irritants or allergens that could influence asthma prevalence. Farm environments may contribute to differences in asthma prevalence by altering immune responses. This environmental theory is typically explained by the hygiene hypothesis, which proposes that early life exposures influence immune system development, lowering the risk for asthma and allergic disease.¹⁰ (2) *Health care access*: rural children have reduced access to health care or engage less in different health care practices, and therefore are less likely to become diagnosed with asthma, although they experience the same symptoms.^{11,12} However, we are unable to thoroughly examine this explanation in this study. (3) *Health risk behaviours*: while more controversial, individual health behaviours, such as physical activity, could be underlying determinants of differential reported prevalence of asthma.¹³ Personal factors associated with asthma such as male sex and family history of asthma have been fairly well established and are typically consistent between locations.

Based upon the above theories, the aim of this study was to quantify the association between potential demographic, behavioural, environmental and personal risk factors and asthma and wheeze. Through a dedicated comparison of children from small town versus farm status, we explored the association between potential risk factors and asthma and wheeze, in light of the above explanations for observed geographical differences in asthma prevalence. The main hypothesis was that children from farms would exhibit lower risks for asthma and wheeze compared with children who lived in small town settings. We also hypothesized that that the difference in asthma prevalence between farm and small-town dwelling could be explained by exploring a number of risk factors under the explanations outlined above. This would help understand more about mechanisms that may underlie this relationship. Although various farm-related exposures have been implicated as potential risk and also protective factors for childhood asthma, the existing literature has many inconsistent findings and therefore, uncertainty still exists.¹⁴

3.3 Methods

Study Design and Population

We used data from a 2003 cross-sectional study of children conducted in Estevan, Canada. Estevan is a major agricultural centre in Southern Saskatchewan and is situated near a coal mining strip, coal-fired power production, and oil and gas drilling. This cross-sectional study was originally developed to examine lung health in the region and provide a sampling frame for a separate case-control study.¹⁵ In addition, the current analysis builds upon a similar cross-sectional study completed in Estevan in 2000.^{14,16}

All children in Estevan enrolled in grades 1-6 during the 2002-03 academic year were approached to participate. Parents completed questionnaires within a three week period after distribution through the schools in January 2003. A reminder letter was sent 10 days after

distribution. The participation rate was 72.0%, resulting in a sample size of 842 participants. Approvals to conduct the survey were obtained from the school boards and associated school principals in Estevan prior to distribution in the schools. Ethical approval was obtained from the Advisory Committee on Ethics in Biomedical Research at the University of Saskatchewan. Approval to complete this analysis was also obtained from the Queen's Health Science Research Ethics Board (File #6006172).

Study Instrument

Questionnaire content was based on the American Thoracic Society's Children's Respiratory Disease Questionnaire¹⁷, questionnaires used in the Student Lung Health study¹⁴ and an asthma prevalence questionnaire used in a 1992 study conducted in Humboldt, Saskatchewan.¹⁸ The 2003 study questionnaire included items describing demographics, current and previous asthma and asthma-like symptoms, related atopic diseases, other illnesses, home environments, lifestyle factors, and family factors.

Variables Considered in the Study

Respiratory Outcomes

Asthma and wheeze were defined based upon past operational definitions proposed by Rennie and colleagues using data from the 2000 Estevan study.¹⁶ These definitions were similar to those used in other epidemiological studies of childhood asthma^{16,19} and have shown relatively good agreement with other measures of lung health including physician diagnosis, other questionnaires and physiological measures.¹⁹ The outcome definitions are largely based on the ISAAC questionnaire, which has a sensitivity of 0.85 and specificity of 0.81 compared to physician diagnosis of asthma.²⁰ Parent-completed questionnaires optimize cost effectiveness, sensitivity and specificity when measuring pediatric asthma prevalence at a population level.^{21,22}

Ever asthma was assessed by the question, “Has this child ever been diagnosed as having asthma by a doctor?” Current asthma was defined by ever asthma and at least one of the following: an emergency department visit for asthma, a physician’s office visit for asthma, a visit to an intensive care unit for asthma, a self-reported asthma episode or wheeze, and/or medication use for asthma in the past 12 months. Ever wheeze was defined as wheeze or whistling coming from the chest without a cold and/or wheeze with shortness of breath and/or wheeze during or after exercise. Current wheeze was defined as ever wheeze with symptoms reported in the past 12 months.

Location of Residence

Location of residence was based on the question “Where is your home located?” The child was considered to be farm dweller if they lived on a farm or acreage. If it was reported that the child lived in town, they were considered a small town dweller.

Environmental Factors

Environmental factors were also explored as potential risk factors. Unless otherwise specified, operational definitions were chosen based on past precedents as outlined in Lawson et al.¹⁰ House dampness was considered present if there was a positive response to the question “Does your house have any damage caused by dampness (e.g. wet spots on walls or floors)?”. House mold was considered present if there was a positive response to the question “Are there signs of mold or mildew in any living areas in your home?”.²³ Children were considered to have pets in the home if the pet had fur or feathers. Home renovations included those that had occurred during the child’s lifetime. Type of housing unit was defined as single family dwelling or other dwelling. The presence of home fireplaces and dehumidifiers were based on self-report of currently having one in the house. Finally, home crowding was defined using a continuous

variable describing the number of people in the home divided by the number of rooms in the home.¹⁴

Behavioural Factors

Current parental smoking status was defined as parental smoking for the mother or father at the time of questionnaire completion.¹⁰ Ever smoking was defined as parental smoking that occurred in the past, and did not include current smokers.¹⁰ Participation in sports and physical activity was considered high if the answer to “How many times a week does your child engage in vigorous physical activity long enough to make him/her breathe hard?” was “Three or more times per week”, based on the assumption that most children would exercise at a high level.

Personal Factors

Operational definitions were based on past precedents.¹⁰ Age groups were classified as younger (ages 6 to 9), and older (ages 10 to 13).¹² Father’s and mother’s education levels were classified as high school or less vs. any postsecondary education. History of respiratory allergies was considered present if the child had allergies to house dust, grain dust, pollen, trees, grasses, mold or mildew, dogs, cats or birds/feathers. A child was considered low birth weight if parents reported a weight of less than 2.5 kg at birth. Premature birth was defined as being born more than 2 weeks before the expected birth date. A child was considered overweight or obese if their reported height and weight measured more than the adult equivalent of 25kg/m² based on percentile curves derived internationally.²⁴

Statistical Analysis

All analyses were conducted using SAS[®] version 9.2 statistical analysis software (SAS Institute Inc., Cary, NC, USA). We first described the study population using conventional descriptive statistics. We then compared distributions of variables in the two study groups (small

town vs. farm) using chi square tests for categorical variables and independent samples t-tests for continuous measures.

We conducted regression analyses to identify potential risk factors for the asthma outcomes, and to test the focal hypothesis that farm residence status was associated with lower risks for these outcomes. We forced residence type (farm vs. small town) into all models. Other potential determinants were examined individually then collectively using multiple logistic regression analyses. We used generalized estimating equations to account for the clustered nature of the sampling scheme, with students nested within families. We chose to control for clustering by family but not schools because covariance parameter estimates suggested much larger clustering by family (0.025) compared to clustering by school (0.001). We used a purposeful modeling strategy, with consideration of past evidence and theory, as well as statistical criteria (backwards elimination with a liberal alpha level of 0.1) in the selection of covariates. Presented estimates of effect included adjusted odds ratios and their 95% confidence limits.

3.4 Results

A description of demographic factors and environmental, behavioural and personal risk factors stratified by farm vs. small town geographic status are presented in **Tables 1 and 2**. Children from farms were more likely to be female (64% compared to 48%; $p=0.005$), but did not differ statistically ($p>0.05$) by age, and parental education levels. Children from farms were more likely to participate in regular vigorous physical activity compared to children from within town (77.3% vs. 62.9%, respectively; $p=0.01$). While there were no other statistically significant differences between farm and small town children with regard to environmental, behavioural and personal risk factors, children from farms tended ($p<0.10$) to have fewer indoor pets, were more likely to live in a home with renovations, were more likely to live in a single family dwelling,

were more likely to live in a home with a fireplace but were less likely to report past attendance of a daycare, and to have parents that smoked or previously smoked.

Table 3 presents a comparison of asthma and asthma-related outcomes between the groups. While the prevalence of asthma and wheeze was slightly greater in the farm group compared to the small town group, the differences were not statistically significant.

As seen in **Table 4**, the results from the descriptive study are confirmed following adjustment for potential confounders. Associations between each independent variable and the disease outcomes based on the multivariate analysis are also presented in Table 4.

Risk factors for *ever wheeze* included male sex (OR=1.55, 95%CI: 1.07 to 2.25), living in homes with dampness (OR=1.51, 95%CI: 0.99 to 2.31), personal history of allergy (OR=6.24, 95%CI: 4.22 to 9.23), maternal history of asthma (OR=2.06, 95%CI: 1.12 to 3.80), and being overweight or obese (OR=1.53, 95%CI: 0.95 to 2.47). Children with a personal history of allergy (OR=7.66, 95%CI: 4.98 to 11.77), maternal history of asthma (OR=2.45, 95%CI: 1.24 to 4.84), and children who are overweight or obese (OR=1.77, 95%CI: 1.06 to 2.97) were more likely to report *current wheeze*.

Risk factors for *ever asthma* included male sex (OR=2.18, 95%CI: 1.41 to 3.36), living in homes with dampness (OR=1.85, 95%CI: 1.08 to 3.17), being born prematurely (OR=2.37, 95%CI: 1.06 to 5.27), personal history of allergy (OR=7.03, 95%CI: 4.56 to 10.83), paternal history of asthma (OR=2.96, 95%CI: 1.51 to 5.81), and maternal history of asthma OR=3.31, 95%CI: 1.64 to 6.68). A past history of daycare attendance was associated with lower relative odds of ever asthma (OR=0.53, 95%CI: 0.33 to 0.85). Males were more likely to have *current asthma* than females (OR=1.96, 95%CI: 1.16 to 3.25). Children that had attended daycare were less likely to have *current asthma* (OR=0.47, 95%CI: 0.28 to 0.79). Children that reported personal history of allergy (OR=7.80, 95%CI: 4.90 to 12.70), paternal history of asthma

(OR=3.23, 95%CI: 1.42 to 7.37), and maternal history of asthma (OR=2.80, 95%CI: 1.30 to 6.01) were more likely to also report *current asthma*.

3.5 Discussion

The purpose of the current study was to examine differences in asthma and wheeze prevalence by farm and small town status, in light of three potential explanations. We found, unexpectedly, that asthma and wheeze prevalence were similar between small town and farm locations. We did confirm commonly identified personal characteristics associated with asthma and wheeze and identified environmental characteristics that were associated with asthma in this primarily rural region.

The farm and small town groups were almost equally likely to have been given a diagnosis of asthma (ever asthma), but a slightly higher and statistically non-significant proportion of farm children reported current asthma and wheeze, contrary to findings observed in other settings, suggesting that living in a small town does not increase the risk of asthma or wheeze compared to farm children.^{3,4,5} Other contextual risk factors may account for differences in asthma prevalence observed geographically in other studies^{3,4,5}, as well as between different groups in our own study. It is possible that the two geographic groups are too similar to compare, as those children living in town may have been regularly exposed to allergens and irritants commonly experienced in the farm group because: (a) the population and area size of Estevan are relatively small compared to what may be considered a more “urban” center and as such, those in town may have lived in close proximity to farms which surround Estevan and hence shared in their environmental exposures, and (b) other exposures common to the farm and non-farm groups may have affected the entire population and their asthma symptoms and diagnoses, and (c) farm dwellings and farming practices may be different than those from previous studies where associations between farming and asthma have been reported; hence environmental exposures

may be similar among this population. Analogously both groups may have had similar access to health care, or engaged in similar health behaviour patterns given the close proximity of the dwellings.

Our study findings partially support *environmental* explanations for geographic variations in asthma and wheeze prevalence. Environmental factors that were strongly associated with asthma and wheeze were home dampness as a risk factor and prior daycare attendance as a protective factor. Home dampness as a risk factor for asthma and wheeze is consistent with findings reported elsewhere.^{14,15,25} A higher proportion of town children attended daycare than farm children, and this had an apparent protective effect. Midodzi et al. also found that daycare attendance was protective for wheeze among primary school students.²⁶ Environmental factors such as these that differed between our farm and small town groups may be underlying the geographic variations in asthma prevalence.

The *health risk behaviours* explanation was also partially supported by the findings. Being overweight or obese was found to be positively associated with asthma, and a higher proportion of children living on farms were overweight or obese compared to children living in town. Few studies have examined individual health behaviours as risk factors for wheeze and asthma. Lawson et al. (2011) found that although health behaviours and obesity did not mediate the association between geographic region (metro, adjacent to metro, and rural) and asthma, being overweight or obese, having a high physical activity level, and exposure to passive smoke elevated risks for asthma.²⁷ Therefore, differences in levels of various health behaviours may contribute to geographic variation in asthma prevalence.

The present study has limitations. Due to the cross-sectional nature of the survey, it may be difficult to determine temporality in these associations. As no statistically significant prevalence differences were found between groups, future research should include a comparison

group that may be less likely to be exposed to the farming environment. It would also be important to examine specific exposures on the farm that may explain asthma and asthma-like symptom prevalence in rural areas. Finally, there may be response bias as parents of children with asthma or wheeze may be more likely to complete the questionnaire than parents of children without these conditions. Therefore, absolute prevalence rates may be inflated. However, participation was good in our study (72%), and there was no reason to expect the observed effects to differ by residence status, so response bias should be minimal in our setting.

The present study also has strengths. There are few large population-based studies that compare pediatric respiratory outcomes by small town vs. farm status. Furthermore, because all students in Estevan were surveyed, selection bias was minimized because all potential participants were equally likely to be selected for the study. Finally, study results may be generalized to other farm and small town populations within Canada with similar farm and environmental exposures. However, caution must be taken when comparing these results with populations from other countries where both farming procedures and health care practices may differ widely.

Our findings have implications for prevention and further research. Results obtained from this study contribute to a better understanding of factors that directly and indirectly contribute to the occurrence of pediatric asthma. As many of the risk factors found to be associated with asthma and wheeze are personal characteristics (i.e., parent history of allergy and sex), healthcare professionals may be able to closely monitor groups of children that experience higher risks for asthma and asthma-like symptoms. Some exposures, such as home dampness, are modifiable risk factors. It is also important to note that asthma prevalence rates in this study of rural children were higher than the national average of 13%.² Therefore, asthma is still a major concern, even in rural areas where asthma is generally found to be lower.^{3,4,5} The high prevalence is also

concerning because exposures in rural environments may exacerbate symptoms once a child has developed asthma.²⁵ Results may also aid in the identification of factors in rural environments that exacerbate asthma and asthma-like symptoms in pediatric populations.

In summary, this epidemiological study failed to find differences in childhood asthma prevalence by farm and small town status. Results still aid in understanding geographic variation in pediatric lung health outcomes and test potential explanations for geographic variation in asthma and wheeze prevalence. Study findings support both the *environment* and *health risk behaviour* explanations. This information may be used to prevent and reduce the impact of asthma and asthma-like symptoms in rural child populations.

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Table 1: Personal characteristics and demographics by geographic status

	Overall (n=834) n(%)	Farm (n=91) n(%)	Small town (n=743) n(%)	P value
Sex				
Male	419 (50)	33 (36)	386 (52)	0.005
Female	415 (50)	58 (64)	357 (48)	
Age Group				
Younger(6-9)	392 (47)	42 (46)	350 (47)	0.83
Older(10-13)	442 (53)	49 (54)	393 (53)	
Father's education				
High school or less	449 (56)	50 (56)	399 (56)	0.99
More than high school	359 (44)	40 (44)	319 (44)	
Mother's education				
High school or less	402 (49)	41 (46)	361 (50)	0.64
More than high school	415 (51)	48 (54)	367 (50)	

Table 2: Environmental and behavioural factors by geographic status

	Overall (n=834) n(%)	Farm (n=91) n(%)	Small town (n=743) n(%)	P value
Environmental Factors				
Homes with dampness	20.5	21.1	20.7	0.49
Homes with mold or mildew	15.3	16.7	15.1	0.46
Homes with indoor pets	59.5	46.1	61.1	0.09
Homes with renovations	42.7	50.6	41.7	0.27
Single family dwelling	89.1	93.4	85.9	0.13
Homes with fireplace	35.3	49.4	33.6	0.23
Homes with dehumidifier	10.7	13.5	11.7	0.41
Crowding (persons/room) (Mean/SD)	0.7 (0.3)	0.7 (0.2)	0.7 (0.3)	0.83
Behavioural Factors				
Children breastfed	74.3	79.8	73.6	0.22
Children that attended daycare	71.5	59.6	72.9	0.09
Mother that currently smoke	23.1	17.1	23.8	0.24
Mother ever smoked	15.2	7.1	16.1	0.09
Mother that smoked during pregnancy	24.6	14.4	25.9	0.07
Father that currently smoke	31.0	24.7	31.8	0.30
Father ever smoked	15.5	6.7	16.5	0.09
Weekly physical activity	64.4	77.3	62.9	0.01
Personal Factors				
Children with allergies	23.5	29.7	22.8	0.22
Fathers with asthma	7.1	12.2	6.5	0.37
Mothers with asthma	7.9	10.0	7.7	0.45
Born underweight (<2500 g)	5.0	3.3	5.3	0.46
Overweight or obese	15.4	20.9	14.7	0.13
Children born premature	10.0	4.4	10.6	0.10

Table 3: Prevalence of asthma and asthma-like symptoms by geographic status

	Overall (n=834) N(%)	Farm (n=91) n(%)	Small town (n=743) n(%)	P value
Current Wheeze	169 (22)	24 (27)	145 (21)	0.28
Ever Wheeze	231 (28)	27 (30)	204 (28)	0.74
Current Asthma	110 (13)	15 (16)	95 (13)	0.48
Ever Asthma	158 (19)	18 (20)	140 (19)	0.94

Table 4: Results of multivariate logistic regression: adjusted odds ratios describing risk factors for asthma and asthma-like symptoms

Covariate	Ever wheeze OR (95%CI)	Current wheeze OR (95%CI)	Ever diagnosed asthma OR (95%CI)	Current diagnosed asthma OR (95%CI)
Demographics				
Farm residence (Ref: small town)	1.02 (0.55, 1.89)	1.20 (0.61, 2.37)	0.87 (0.43, 1.77)	1.00 (0.43, 2.32)
Male sex (Ref: female)	1.55 (1.07, 2.25)	1.31 (0.85, 2.03)	2.18 (1.41, 3.36)	1.94 (1.16, 3.25)
Father education: More than high school (Ref: High school or less)	1.00 (0.69, 1.45)	0.74 (0.47, 1.14)	1.46 (0.94, 2.27)	1.14 (0.68, 1.91)
Environmental Factors				
Dampness	1.51 (0.99, 2.31)	1.54 (0.97, 2.47)	1.85 (1.08, 3.17)	1.25 (0.64, 2.43)
Behavioural Factors				
Daycare	0.91 (0.61, 1.34)	0.77 (0.49, 1.20)	0.53 (0.33, 0.85)	0.47 (0.28, 0.79)
Father current smoker	1.03 (0.70, 1.53)	1.16 (0.75, 1.80)	0.72 (0.43, 1.19)	0.63 (0.35, 1.14)
Personal Factors				
Premature birth	1.05 (0.55, 1.98)	1.12 (0.50, 2.52)	2.37 (1.06, 5.27)	1.76 (0.65, 4.71)
Personal allergies	6.24 (4.22, 9.23)	7.66 (4.98, 11.77)	7.03 (4.56, 10.83)	7.89 (4.90, 12.70)
Father with asthma	1.60 (0.80, 3.23)	1.85 (0.84, 4.08)	2.96 (1.51, 5.81)	3.23 (1.42, 7.37)
Mother with asthma	2.06 (1.12, 3.80)	2.45 (1.24, 4.84)	3.31 (1.64, 6.68)	2.80 (1.30, 6.01)
Overweight or obese	1.53 (0.95, 2.47)	1.77 (1.06, 2.97)	1.08 (0.58, 2.00)	1.63 (0.85, 3.13)
Normal birth weight (Ref: underweight)	1.67 (0.77, 3.65)	1.48 (0.56, 3.87)	0.65 (0.20, 2.13)	0.58 (0.14, 2.42)

Chapter 4

The Role of Farm Operational and Rural Environments as Potential Risk Factors for Pediatric Asthma in Rural Saskatchewan

4.1 Summary

Background: Researchers have historically reported that farm children have a lower reported prevalence of asthma compared to more urban children. Potential explanations include theories surrounding differences in *personal factors*, *access to health care*, engagement in *health risk behaviours*, and differences in *the environment*.

Objective: The aims of this study were: (1) to confirm whether the prevalence of asthma in fact varies between farm and small town residential status among children in the province of Saskatchewan; (2) to identify risk and protective factors for asthma in this mainly rural population, and use this information to infer which of the above theories is most explanatory for any observed geographic variations in pediatric asthma.

Methods: Rural students (grades 1-12) from across the province of Saskatchewan participated in a 2011 cross-sectional study. Parents completed a written survey that included questions about location of residence, asthma (based on physician diagnoses) and wheeze symptoms, potential risk factors for respiratory disease, and exposures to various farm activities. Multiple logistic regression was used to examine relations between respiratory outcomes (asthma, wheeze) with farm type and the various farm activities, while accounting for personal and environmental factors, health care access and health behaviours that may underlie such relations.

Results: A total of 2383 students (42% participation rate) took part. Asthma and wheeze prevalence did not differ by small town and farm status. We found that living on a grain farm (OR=0.64, 95%CI=0.43-0.96), cleaning or playing in pens (OR=0.69, 95%CI=0.46-1.02), filling grain bins (OR=0.56, 95%CI=0.32-0.96), and riding horses (OR=0.65, 95%CI=0.40-1.05) were protective factors for ever diagnosis with asthma.

Conclusions: We identified a number of risk and protective factors for asthma and associated wheeze. This suggests the need to focus on specific environmental explanations, such as exposure

to various farm production activities, in order to better understand previously observed associations between farm residential status and asthma. Our findings also partially supported the health care access explanation for the latter geographic differences.

4.2 Introduction

Asthma is a chronic respiratory disease that is characterized by inflammation and bronchoconstriction resulting in wheeze, cough, shortness of breath and chest tightness.¹ Typically, these symptoms occur after exposure to irritants, allergens or after exercise.¹ The prevalence of asthma that is diagnosed in populations of Canadian children is 13%.² Asthma is a disease that may result in restriction of physical activity, school absenteeism, and reduced quality of life; it also results in a large number of visits to hospital among afflicted children each year.^{1,3} Children living on farms are thought to experience a lower prevalence of asthma and asthma-like symptoms compared to those living in non-farming rural areas and in more urban settings.⁴⁻⁷ Such variations provide an opportunity to examine the specific factors and theories that may contribute to geographic differences in childhood asthma, and provide direction for interventions aimed at reducing asthma in at-risk populations.

There are several plausible explanations for why the rural environment is a protective factor for childhood asthma: (1) *Personal factors explanation*: it is possible that personal factors, such as socio-demographic factors, or parental history of asthma differ by geographic status and therefore underlie the association. (2) *Health care access explanation*: children living on farms have less access to health care services or there are differences in health care practices between rural and more urban areas; these result in rural children being less likely to be diagnosed with asthma, although they still experience the same symptoms.^{8,9} (3) *Health risk behaviour explanation*: such theories suggest that individual health risk behaviours, such as smoking or physical activity, may be mechanisms that underlie the association between location of residence and asthma.¹⁰ (4) *Environmental explanation*: this explanation is typically explained by the hygiene hypothesis which suggests that early life exposures may influence subsequent immune response away from the allergic Th2 response. Farm children are purported to be exposed to

different levels and types of exposures such as endotoxin early in life which influence immune response, lowering the risk for asthma and allergic disease.¹¹ Other environmental exposures that could have an influence of asthma and asthma-like symptoms in agricultural settings include specific farm operational activities. Exposure to dust (e.g., filling grain bins) may be associated with increased risks for pediatric asthma.¹² However, exposure to livestock appears to be protective.¹³

There has been a longstanding interest in childhood asthma experiences on farms, as these settings are felt to be protective.⁴⁻⁷ We had a unique opportunity to confirm whether or not this phenomenon is true in a large geographically diverse sample of children living in rural settings in the province of Saskatchewan, Canada. We also had the chance to simultaneously explore competing theories for possible geographic variations in childhood asthma including personal factors, health care access factors, behavioural factors and environmental factors, including specific activities associated with the farm production settings.^{7, 12}

This study had two main objectives. First, we examined the prevalence of asthma and wheeze in rural children by farm versus small town residential status. Second, we identified potential risk and protective factors (personal, access, behavioural and environmental factors, including specific farm production exposures) for asthma and wheeze within this population. These two objectives were completed in order to provide new evidence that might shed light on the plausibility of the four possible explanations for geographic variations in the frequency of children's asthma.

4.3 Materials and Methods

Study Design and Population

Our primary data source was the child component of the *Saskatchewan Rural Health Study*. This is a large study examining the health of rural dwelling residents in the Canadian

province of Saskatchewan that included both adults and children.¹⁴ Data were initially collected from adults and children in four rural quadrants of the province.

Data collection

Schools that were located within the rural municipalities included in the adult phase of the study were considered the target schools for the child study. The ten divisions that included those schools were approached and all agreed to participate. Forty-three schools within these divisions were chosen to participate based on belonging to the same rural municipalities as the adults in the adult portion of the *Saskatchewan Rural Health Study*. Of the 43 selected schools, 39 of these agreed to participate. Students attending these schools were administered study packages (information letter, questionnaire and return envelope) to be taken home for parents to complete, with completed questionnaires to be returned to the school. A reminder letter was sent out via the school at 2 weeks following the initial package distribution. Questionnaires were distributed to all 5,667 children in grades 1-12 attending one of the 39 schools during the 2010-11 academic year. The participation rate was 42%, resulting in a sample size of 2,383 participants. Of the 2,383 participants, 124 were excluded from the final analysis due to missing data on key variables, resulting in a final sample size of 2,259 participants.

Approval for the full study protocol was obtained from the Biomedical Research Ethics Board at the University of Saskatchewan (Study approval #Bio-10-177). Approval to complete this analysis was obtained from the Queen's Health Science Research Ethics Board (File #6006172). Approvals to conduct the survey were also obtained from the Directors of each school division in June 2010 and from school Principals in December 2010.

Study Instrument

The 2011 child study questionnaire included items describing socio-demographics, current and previous asthma and asthma-like symptoms, related atopic diseases, other illnesses,

the home environment, health risk behaviours, access to healthcare factors, and family factors. It also included items describing farm type and types of farm activities performed on a regular basis.

Questionnaire content was in part based on: (1) the American Thoracic Society's 1979 Children's Respiratory Disease Questionnaire(ATS)¹⁵; (2) the self-administered questionnaires in the Student Lung Health study¹⁶; (3) questionnaires used in a study in Estevan, Saskatchewan in 2000 and 2003^{11, 17, 18}; (4) an asthma prevalence questionnaire used in a 1992 study conducted in Humboldt, Saskatchewan¹⁹; and (5) the International Study of Asthma and Allergies in Childhood Study (ISAAC) questionnaire²⁰.

Variables Under Study

Respiratory Outcomes

Asthma and wheeze were operationally defined based upon standard definitions.^{18,20} Ever asthma was assessed by the question, "Has this child ever been diagnosed as having asthma by a doctor?" Current asthma was defined by ever asthma and at least one of the following: an emergency department visit for asthma, a physician's office visit for asthma, a hospital visit as an inpatient for asthma, at least one self-reported asthma episode or wheeze, and/or medication use for asthma in the past 12 months. Ever wheeze was defined as wheeze or whistling coming from the chest with or without a cold and/or wheeze with shortness of breath and/or wheeze during or after exercise. Current wheeze was defined as ever wheeze with symptoms reported in the past 12 months.

Parent-reported questions related to asthma in the ISAAC survey have a known sensitivity of 0.85 and specificity of 0.81 compared to physician diagnoses of asthma.²¹ Cases of wheeze and asthma identified via this survey have shown relatively good agreement with other measures of lung health including physician diagnoses, other questionnaire-based measures and

physiological measures.²¹ Parent-completed questionnaires have been found to be efficient methods of data collection in terms of cost, and also have high sensitivity and specificity when used to measure pediatric asthma prevalence at a population level.^{22, 23}

Location of Residence

Location of residence was based on the question “Where is your home located?” The child was considered to live on a farm if they reported living on a farm or acreage. If it was reported that the child lived in town, they were considered to live in a small town, as none of the towns in the study had a population greater than 5000.¹⁴

Personal Factors

Operational definitions were based on past precedents.¹¹ Age groups were classified as younger (ages 6 to 9 years), middle (ages 10 to 13 years) and oldest (14 to 18).⁹ Father’s and mother’s education levels were classified as high school or less vs. any postsecondary education. History of respiratory allergies was considered present if there was a positive response to a question asking if the child had allergies to any of the following: house dust, grain dust, pollen, trees, grasses, mold or mildew, dogs, cats, birds/feathers, or farm animals. Premature birth was defined as being born more than 2 weeks before the expected birth date. A child was considered to be born underweight if their reported birth weight was less than 2500g. A child was considered to be overweight if parents responded with *overweight* to the question “Do you consider your child to be underweight, just about right or overweight?”²⁴

Access to Care

We assessed (by parental report on the questionnaire) distance to routine care, distance to emergency care, and if there were any perceived difficulties accessing routine care. Estimated distances to routine medical care were assessed by a response (in km) to the question “How far do you travel (one direction) to receive routine and ongoing medical care for this child?” Estimated

distances to emergency care were assessed by the question “How far do you travel (one direction) to receive 24 hour emergency health care services for this child?”²⁵ It was considered difficult to get routine health care for the child when there was a positive response to the question “In the past 12 months, did you ever experience any difficulties getting the routine or on-going healthcare for this child?”.

Health Risk Behaviours

Current parental smoking status was defined as a report of parental smoking for the mother or father at the time of questionnaire completion.¹¹ Previous smoking was defined as parental smoking that occurred in the past, but did not include current smokers.¹¹ A child was considered to smoke if there was a positive response to the question “Has this child ever smoked tobacco? (at least one cigarette, cigar, or pipe)?” Participation in sports and physical activity was considered high if the answer to “How many times a week does your child engage in vigorous physical activity long enough to make him/her breathe hard?” was “Three or more times per week”.

Environmental Factors

Unless otherwise specified, operational definitions were chosen based on definitions from previous studies.¹¹ Current environmental factors were those considered to be present in the past 12 months. Children were considered to have pets in the home if they reported the presence of a pet that had fur or feathers. Home renovations only included those that had occurred during the past 12 months. Older homes were considered to be those built before 1980. Type of fuel used for heating was defined as natural gas, burning source, or other. Burning sources included wood and coal.

Farm type and farm activities

Farm activities were assessed by the question “In the past 12 months, on average, how often has this child spent 1 hour near or in the following activities”, with response options: “Everyday”, “At least once a week”, “At least once a month”, “Less than once a month” and “Never”. Children were considered to perform an activity regularly if they selected “At least once a month” or more. Activities include: Haying or moving or playing with hay bales, Feeding livestock, Cleaning or playing in barns, Emptying or filling grain bins, Cleaning or playing in pens or corrals, and Riding horses.

Statistical Analysis

All analyses were conducted using SAS[®] version 9.2 statistical analysis software (SAS Institute Inc., Cary, NC, USA). We first described the study population using conventional descriptive statistics. We then compared distributions of variables in two study groups (small town *versus* farm) using chi square tests for categorical variables and independent samples t-tests for continuous measures.

We conducted logistic regression analyses to identify potential risk and protective factors for the asthma and wheeze outcomes, and to test whether farm residence status was associated with these outcomes. We forced residence type (farm vs. small town) and maternal smoking into all models. Other potential determinants were examined individually then collectively using multiple logistic regression analyses. We used a purposeful modeling strategy, with consideration of past evidence and theory, as well as statistical criteria (backwards elimination with an alpha level of 0.05) in the selection of covariates. Presented estimates of effect included adjusted odds ratios and their 95% confidence limits.

Finally, we created individual models to examine the relationship between farm type (grain and livestock) and asthma and wheeze. We also examined the relationship between regular engagement in various farm activities (e.g., haying) and asthma and wheeze. These associations

were adjusted for the same potential confounders identified above. Because there was no available information to identify family units, we were unable to control for clustering by family using generalized estimating equations. Based on the standard error inflation observed in a previous analysis on a similar smaller study population that used generalized estimating equations to control for clustering by family,²⁶ we inflated the variance by an estimated design effect of 4.9%.

4.4 Results

Study population

Key characteristics of the study population are presented in **Table 1**. The population contained a sample of males and females that was roughly equal. There were similar numbers of children in each of the three age groups. The majority of mothers (62.3%) but not fathers (46.7%) had obtained a postsecondary education.

A comparison of those included in the analysis versus excluded from the analysis due to missing data revealed that those that were included were more likely to have parents that had completed postsecondary education (mother: 62.3% vs. 45.7%, $p<0.001$; father: 46.7% vs. 29.1%, $p=0.001$) and were more likely to be Caucasian (90% Caucasian vs. 72.0% Caucasian, $p<0.001$). Those that were included were also more likely to have asthma (*ever* asthma: 15.4% vs. 8.2%, $p=0.03$, *current* asthma: 10.8% vs. 3.3%, $p=0.08$).

Asthma Prevalence

The prevalence of the asthma-related outcomes by location of residence is presented in **Table 2**. There were no statistically significant differences in asthma or wheeze prevalence by farm and small town status ($p>0.05$).

Farm vs. Small town Comparison

There were a number of differences in personal, health care access, behavioural and environmental factors identified by farm versus small town locations of residence (**Table 3**). Considering personal factors, children from farms were more likely to be born premature (12.6% vs. 7.9%, $p<0.001$), were less likely to come from single-parent families (6.4% vs. 14.5%, $p<0.001$), and were less likely to be non-Caucasian (7.1% vs. 12.0%, $p<0.001$) compared to children from small towns.

With regard to health care access, children living on farms were more likely to live more than 30km away from routine care (46.5% vs. 26.4%, $p<0.001$) and more likely to live more than 30km away from emergency care (53.8% vs. 30.4%, $p<0.001$) compared to small town children (**Table 3**).

For the health risk behaviours under study, farm children were more likely to have been breastfed (81.6% vs. 77.3%, $p=0.02$) than small town children. Farm children were less likely to have previously attended daycare (44.8% vs. 59.5%, $p<0.001$), have a mother that previously or currently smokes ($p<0.001$), have a father that previously or currently smokes ($p<0.001$) and were less likely to have a mother that reported smoking during pregnancy (17.4% vs. 23.3%, $p=0.002$) compared to small town children (**Table 3**).

Finally, with regard to environmental factors children living on farms were more likely to have homes with dampness (32.0% vs. 24.6%, $p<0.001$), mold or mildew (24.0% vs. 15.6%, $p<0.001$), renovations in the past 12 months (30.7% vs. 25.0%, $p=0.003$), fireplaces (24.0% vs. 11.7%, $p<0.001$) and mice (20.0% vs. 6.3%, $p<0.001$) than those children living in town. Farm children were also more likely to live in a home with a burning fuel source (21.8% vs. 3.6%, $p<0.001$). However, children living on farms were less likely to have indoor pets (56.8% vs. 68.9%, $p<0.001$) to live in a home built before 1979 (55.7% vs. 65.3%, $p<0.001$), to live in a

home heated with natural gas (45.5% vs. 93.6%, $p < 0.001$) and less likely to live in a home with air conditioner (41.0% vs. 55.0%, $p < 0.001$) compared to small town children (**Table 3**).

Risk Factors and Protective Factors

Table 4 affirms the fact that there were no statistically significant associations between asthma and wheeze outcomes with farm-small town status. In terms of explanatory variables, risk factors for *ever wheeze* include male sex, parental history of asthma, personal history of allergies, being overweight, previous daycare attendance, having mice in the home, having an air filter in the home, or having difficulty accessing routine health care in the past 12 months. Having pets in the home was a protective factor. Risk factors for *current wheeze* include male sex, parental history of asthma, personal history of allergies, living in a single parent home, being overweight, having an air filter in the home, or having difficulty accessing routine health care in the past 12 months.

Risk factors for *ever asthma* included male sex, parental history of asthma, personal history of allergies, previous daycare attendance, having a mother that previously smoked and having difficulty accessing routine health care in the past 12 months. Being overweight and having a mother that currently smokes also tended to be positively associated with ever asthma. Having a dehumidifier in the home was a protective factor. Risk factors for *current asthma* include male sex, parental history of asthma, personal history of allergies, being overweight, previous daycare attendance and having a mother than previously smoked. Having a dehumidifier in the home was a protective factor (Table 4).

Farm-specific Factors

Table 5 presents a sub-analysis of farm-specific environmental risk factors for asthma and wheeze, including both farm activities and farm type. Feeding livestock tended to be positively associated with *ever wheeze*. Filling grain bins was identified as a protective factor for

current wheeze. Cleaning or playing in the barn, cleaning or playing in pens, riding horses, filling grain bins and living on a grain farm tended to show inverse associations with *ever asthma*.

Cleaning or playing in pens and living on a livestock farm tended to be protective for *current asthma*.

4.5 Discussion

This analysis aimed to determine whether asthma and wheeze prevalence differed by small town *versus* farm residential status in this mainly rural study population. We also provided new evidence to support or refute the various theories that explain why the farm environment may be protective for pediatric asthma. This was done through an exploration of risk and protective factors for asthma and wheeze.

No statistically significant differences in asthma or wheeze prevalence were identified between groups of children who live in farm versus small town residential settings. The prevalence values for almost all of the respiratory outcomes were quite similar among children in the two groups. These findings are dissimilar to previous findings that suggested that children living on farms have lower reported asthma.⁴⁻⁷ It is therefore possible that children living in rural non-farming rural areas in this study are exposed to similar allergens and irritants as children living on farms and there may be no true difference in prevalence among this population. It is also possible that past studies have been confounded by some of the identified risk factors, and differences could be explained by uncontrolled confounding. The associations identified in previous studies may have included farms with different farming practices from those in the current study. Furthermore, it is possible that farm homes are becoming increasingly more modern and similar to homes located in town, reducing any effect that would previously have offered protection from asthma and asthma-like symptoms. Although the results did not provide evidence in support of the protective farm theory, they were of considerable value in identifying

risk and protective factors for asthma that may help explain geographic variations in this important childhood disease.

Explanations for the variations in childhood asthma that have been observed historically include variations in personal factors, access to medical care, variations in health risk behaviours, and environmental explanations. In our study, personal factors such as personal history of allergy and parental history of asthma were among the strongest predictors for asthma and wheeze but did not exhibit variations by small town and farm status and therefore, are unlikely to underlie historical variations in asthma and wheeze prevalence.

In contrast, there was modest support for the access to care explanation. This support is largely attributed to access to care being identified as a strong risk factor for wheeze, but not being strongly associated with asthma. This suggests the possible existence of a subgroup of children with symptoms that have not received a diagnosis of asthma due to difficulty or cultural reluctance to access routine health care. Farm children reported longer distances to health care services than small town children, suggesting that access to care may partially underlie variation in childhood asthma prevalence. This explanation is further supported by previous evidence suggesting an inverse relationship between distance to healthcare facilities and prevalence of pediatric asthma in a rural population of children living in Saskatchewan.²⁵

Our findings partially supported the health behaviour explanation. Several behavioural factors were found to be associated with asthma and wheeze, and were also found to differ by small town and farm status. Previous daycare attendance was identified as a risk factor, and children living in small towns were more likely to have attended daycare. Having a mother that previously smoked was identified as a potential risk factor for asthma, and children living in small towns were more likely to have mothers that previously or currently smoke. However, being overweight or obese was also identified as a risk factor for asthma, and children living on

farms were more likely to be obese compared to small town children. Furthermore, research suggests that behavioural factors such as being overweight or obese, exposure to passive smoking and high physical activity levels do not mediate the relationship between location of residence and pediatric asthma prevalence.⁵ Therefore, although health behaviour factors may partially underlie geographic differences in pediatric asthma, it is unlikely that these factors fully underlie the farm protective effect observed elsewhere.

Finally, we considered environmental factors as explanations that may contribute to underlying differences between farm and small town populations. There was evidence to suggest that environmental exposures may explain potential differences: having mice in the home was identified as a risk factor for asthma, and having pets in the home was a protective factor. Children living on farms were less likely to have a pet in the home and more likely to have mice in the home, the opposite of what would be expected if these environmental factors were underlying the association between location of residence and asthma. However, a number of farm specific environmental factors may be underlying the association. A number of protective factors for asthma involved exposure to livestock: cleaning or playing in the barn, cleaning or playing in pens, and riding horses. This is consistent with previous findings.^{7, 13, 27} This protective livestock effect is likely due to increased presence of bacterial compounds such as endotoxin found in areas where livestock are kept compared to hay storage barns.²⁸ Unexpectedly, feeding livestock was identified as a risk factor for wheeze while filling grain bins was associated with decreased presence of ever wheeze. Also unexpectedly, living on a grain farm and filling grain bins was also associated with decreased diagnosed asthma. As most of the farm-specific factors were found to be protective for asthma, it is possible that some of these environmental factors may contribute to geographic variation in pediatric asthma prevalence.

Limitations of this study require consideration. Overall, response rates at the individual student level were modest (42%) and therefore, the absolute prevalence of asthma and asthma-like symptoms may be inflated compared to population norms as parents of children with asthma may have been more likely to complete the questionnaire. A comparison of those included versus excluded for missing data revealed that those that were included were more likely to have asthma. However, this effect likely did not differ by small town and farm status, or by farm activity or farm type, and therefore response bias is unlikely to affect relationships between the exposures and disease outcomes under study. Those excluded for missing data were more likely to have parents that had not completed postsecondary education and more likely to be non-Caucasian. Therefore, results may not be directly generalized to populations with less postsecondary education and with more visible minority groups. Furthermore, as the data were cross-sectional in nature, care must be taken when interpreting temporality and causality. For example, while it is possible that filling grain bins decreases risk of diagnosed asthma, it is more likely that parents of children with asthma may practice risk reduction and be less likely to allow that child to fill grain bins. A longitudinal study may better capture causal relationships between farm-related exposures and asthma outcomes. Finally, there is an increased likelihood of incorrectly rejecting a null hypothesis due multiple comparisons. For example, as we compared multiple factors by farm and small town children, it becomes more likely that these groups may appear to differ by a several risk factors by random chance alone.

However, this study also has strengths. Few studies have examined the relationship between farm exposures and pediatric asthma outcomes with a large sample size and broad age range of children. This study includes a broad study population located across four separate quadrants in Saskatchewan, rather than focusing on one region, decreasing the chance that study results may be heavily influenced by more local factors. Finally, while previous studies have

generally focused on one potential explanation for differences in pediatric asthma, this study examines and compares four plausible explanations concurrently.

Study findings also have relevance to public health. To illustrate, evidence from this study may inform the development of guidelines for child exposure to farm activities. They may also contribute to a better understanding of factors which may exacerbate asthma symptoms, and may aid in preventing asthma symptoms in those children that have an asthma diagnosis. Finally, findings may help explain geographic variation in asthma prevalence among pediatric populations and aid in development of population-based interventions. For example, screening programs could be implemented in communities where children have a high prevalence of identified risk factors for pediatric asthma.

In conclusion, findings from this study suggest that there are no differences in asthma and wheeze prevalence among small town and farm children in our Saskatchewan population. Upon identification of risk and protective factors for asthma while considering geographic variation of factors, we found that geographic variation in asthma is most strongly attributed to the access to care explanation, followed by the environmental explanation. There was mixed support for the behavioural explanation and no support for the personal factors explanation. Future studies may focus on the environmental explanation and the access to care explanation to determine how each contributes to geographic variation in pediatric asthma prevalence.

4.6 References

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Table 1: Personal Characteristics of the Study Population

	Overall (n=2259) n (%)
Sex	
Male	1119 (49.5)
Female	1140 (50.5)
Age Group	
6-9 years	747 (33.1)
10-13 years	875 (38.7)
14-18 years	637 (28.2)
Father's education	
High school or less	1173 (53.3)
More than high school	1029 (46.7)
Mother's education	
High school or less	842 (37.7)
More than high school	1369 (62.3)

Table 2: Prevalence of Asthma and Wheeze by Location of Residence (Farm vs. Small Town)

	Overall (n=2259) n(%)	Dwelling		p-value *
		Farm (n=1024) n (%)	Small town (n=1235) n (%)	
Current wheeze	292 (13.1)	131 (12.9)	161 (13.1)	0.87
Ever wheeze	473 (21.2)	212 (20.9)	261 (21.3)	0.81
Current Asthma	240 (10.8)	104 (10.3)	136 (11.2)	0.48
Ever Asthma	344 (15.4)	145 (14.3)	199 (16.4)	0.18

* Based on comparison of farm and small town groups

Table 3: Personal, Health Care Access, Behavioural and Environmental Factors by Location of Residence (Farm vs. Small Town)

	Overall (n=2259) %	Dwelling		p-value *
		Farm (n=1024) %	Small town (n=1235) %	
Personal Factors				
Children born prematurely	227 (10.1)	129 (12.6)	98 (7.9)	<0.001
Single parent family	244 (10.8)	65 (6.4)	179 (14.5)	<0.001
Fathers with asthma	159 (7.0)	75 (7.3)	84 (6.8)	0.64
Mothers with asthma	180 (8.0)	70 (6.8)	110 (8.9)	0.08
Children with allergies	649 (28.7)	300 (29.3)	349 (28.3)	0.60
Children overweight	196 (8.7)	89 (8.7)	107 (8.7)	0.98
Non-Caucasian	218 (9.8)	72 (7.1)	146 (12.0)	<0.001
Born underweight (<2500g)	202 (8.9)	80 (7.8)	122 (9.9)	0.10
Access to healthcare				
Difficulty accessing routine healthcare (past 12 months)	7.3	7.3	7.3	0.97
Distance routine care >30km	35.9	46.5	26.4	<0.001
Distance to emergency care >30km	41.4	53.8	30.4	<0.001
Behavioural Factors				
Children breastfed	79.3	81.6	77.3	0.02
Children previously enrolled in daycare	52.9	44.8	59.5	<0.001
Mother smoking				
Never smoke	58.1	63.5	53.7	<0.001
Previously smoked	21.8	19.8	23.4	
Currently smokes	20.1	16.7	22.9	
Mothers smoked during pregnancy	20.5	17.4	23.0	0.002
Father smoking				
Never smoke	54.0	60.5	48.6	<0.001
Previously smoked	20.5	18.1	22.5	
Currently smokes	25.5	21.4	28.9	
Children smoking				
Never	91.7	91.4	92.0	0.75
Don't know	2.9	3.2	2.7	
Yes	5.4	5.4	5.3	
Weekly physical activity of > 3 times/week	71.4	72.2	70.7	0.45
Current unpasteurized milk consumption	4.4	4.6	4.2	0.62
Early unpasteurized milk consumption	3.5	4.1	2.9	0.14
Environmental Factors				
Homes with dampness	27.9	32.0	24.6	<0.001
Homes with mildew smell	19.5	21.0	18.2	0.11
Homes with mold or mildew	19.4	24.0	15.6	<0.001
Homes with indoor pets	62.6	56.8	68.9	<0.001
Homes with renovations (past 12 months)	27.6	30.7	25.0	0.003
Homes with mice	12.5	20.0	6.3	<0.001

Single family dwelling	94.1	94.2	94.0	0.81
Older home (built before 1980)	60.8	55.7	65.3	<0.001
Homes with air conditioner	48.7	41.0	55.0	<0.001
Homes with fireplace	17.3	24.0	11.7	<0.001
Homes with dehumidifier	40.5	40.7	40.3	0.89
Homes with humidifier	22.8	23.7	22.1	0.37
Homes with air filter	42.1	40.9	43.0	0.33
Home heated with burning fuel	11.8	21.8	3.6	<0.001
Home heated with natural gas	71.2	45.5	92.6	<0.001
Mean crowding (persons/room) (SD)	1.2 (0.4)	1.2 (0.4)	1.2 (0.4)	0.45

* Based on comparison of farm and small town group

Table 4: Adjusted* associations between asthma and wheeze outcomes and personal, environmental, behavioural, and health care access factors (n=2,259)

	Ever wheeze Odds Ratio (95% Confidence Interval)	Current wheeze Odds Ratio (95% Confidence Interval)	Ever asthma Odds Ratio (95% Confidence Interval)	Current asthma Odds Ratio (95% Confidence Interval)
Farm vs. town residence	1.02 (0.80, 1.31)	1.07 (0.80, 1.43)	0.93 (0.71, 1.23)	1.01 (0.73, 1.39)
Personal factors				
Male sex vs. female sex	1.54 (1.22, 1.94)	1.47 (1.11, 1.95)	1.65 (1.27, 2.14)	1.54 (1.13, 2.10)
Mother with asthma	2.80 (1.93, 4.04)	3.48 (2.33, 5.18)	3.68 (2.50, 5.43)	4.20 (2.74, 6.43)
Father with asthma	2.28 (1.55, 3.37)	2.74 (1.79, 4.19)	2.29 (1.50, 3.50)	2.63 (1.66, 4.18)
History of personal allergies	5.12 (4.05, 6.46)	5.75 (4.34, 7.62)	6.01 (4.62, 7.83)	7.80 (5.68, 10.73)
Single parent home vs. other family structure	1.28 (0.88, 1.80)	1.63 (1.08, 2.45)	1.26 (0.85, 1.88)	1.14 (0.71, 1.83)
Overweight vs. under or normal weight	2.37 (1.65, 3.35)	2.62 (1.76, 3.89)	1.49 (0.99, 2.25)	1.78 (1.12, 2.80)
Access factors				
Difficulty accessing routine healthcare (past 12 months)	2.32 (1.60, 3.39)	1.98 (1.29, 3.05)	1.58 (1.03, 2.44)	1.40 (0.85, 2.30)
Behavioural factors				
Previously or currently enrolled in daycare	1.30 (1.03, 1.65)	1.10 (0.83, 1.46)	1.59 (1.21, 2.08)	1.67 (1.22, 2.30)
Mother smoking (ref=never)				
Previous smoker	1.14 (0.85, 1.52)	1.27 (0.90, 1.78)	1.47 (1.07, 2.02)	1.45 (1.01, 2.10)
Current smoker	1.11(0.82, 1.51)	1.10 (0.76, 1.58)	1.39 (0.99, 1.94)	1.15 (0.77, 1.73)
Environmental factors				
Pets in the home	0.74 (0.58, 0.95)	0.81 (0.60, 1.09)	0.94 (0.71, 1.24)	1.00 (0.72, 1.39)
Mice in the home	1.44 (1.03, 2.02)	1.20 (0.79, 1.82)	1.24 (0.83, 1.84)	1.16 (0.73, 1.85)
Dehumidifier present in home	0.83 (0.65, 1.05)	0.84 (0.63, 1.13)	0.76 (0.58, 0.99)	0.70 (0.51, 0.97)
Air filter present in home	1.29 (1.02, 1.63)	1.35 (1.02, 1.79)	1.21 (0.93, 1.58)	1.27 (0.94, 1.74)

*adjusted for location of residence, sex, parental asthma, personal allergies, single parent vs. two parent home, overweight, daycare attendance, pets in the home, maternal smoking, mice in the home, dehumidifier in the home, air filter in the home, and difficulty accessing health care services

Table 5: Analysis of farm-related environmental exposures (n=2,259)

	Ever wheeze Odds ratio (95% Confidence Intervals)	Current wheeze Odds ratio (95% Confidence Intervals)	Ever asthma Odds ratio (95% Confidence Intervals)	Current asthma Odds ratio (95% Confidence Intervals)
Farm activities				
Haying or playing with or moving hay bales	1.08 (0.79, 1.47)	0.78 (0.53, 1.14)	0.78 (0.54, 1.12)	0.83 (0.55, 1.26)
Feeding livestock	1.34 (0.99, 1.81)	1.20 (0.84, 1.73)	0.90 (0.63, 1.28)	0.97 (0.65, 1.45)
Cleaning or playing in barn	0.91 (0.66, 1.27)	0.92 (0.62, 1.36)	0.73 (0.49, 1.07)	0.72 (0.46, 1.13)
Filling grain bins	0.99 (0.65, 1.50)	0.58 (0.33, 1.02)	0.56 (0.32, 0.96)	0.57 (0.30, 1.07)
Cleaning or playing in pens	0.99 (0.71, 1.37)	0.84 (0.56, 1.25)	0.69 (0.46, 1.02)	0.62 (0.39, 0.99)
Riding horses	0.92 (0.62, 1.37)	0.69 (0.42, 1.14)	0.65 (0.40, 1.05)	0.62 (0.35, 1.09)
Farm type				
Living on a grain farm (ref=farms with no grain production)	1.21 (0.85, 1.71)	1.23 (0.81, 1.86)	0.64 (0.43, 0.96)	0.71 (0.44, 1.12)
Living on a livestock farm (ref=farms with no livestock)	1.05 (0.74, 1.48)	0.80 (0.53, 1.21)	0.75 (0.50, 1.12)	0.65 (0.41, 1.04)

*adjusted for location of residence, sex, parental asthma, personal allergies, single parent vs. two parent home, overweight, daycare attendance, pets in the home, maternal smoking, mice in the home, dehumidifier in the home, air filter in the home, and difficulty accessing health care services

Chapter 5

Discussion

5.1 Bridging the Two Manuscripts

The overall purpose of this thesis was to examine how risk and protective factors for pediatric asthma likely contributed to differences in prevalence observed in the past between farm and small town settings. Manuscripts 1 and 2 compared pediatric asthma and wheeze prevalence by small town and farm status, compared the distribution of potential risk and protective factors, and examined potential risk and protective factors for asthma and wheeze among farm and small town children. Both manuscripts discussed explanations that may account for previously observed geographic variation in pediatric asthma prevalence.

Contrary to our initial hypotheses, neither manuscript found statistically significant differences or strong differences in asthma or wheeze prevalence between small town and farm children. This consistency among both study populations suggests that small town children from Saskatchewan settings are not more likely to have asthma or wheeze than those living on farms. These findings contrast with previous studies conducted elsewhere that found differences in asthma prevalence between farm and small town populations.¹⁻³ Our findings are most likely explained by the fact that small town and farm children from Saskatchewan are actually very similar in regards to exposure to risk and protective factors. The two geographic regions may have been too similar to compare and therefore definitively test our core hypothesis.

With respect to specific risk and protective factors, their distribution by small town-farm status was similar among both studies, suggesting some consistent effects by study. To illustrate, both studies found that farm children were less likely to allow pets in the home, more likely to be exposed to home renovations, and more likely to live in a home with a fireplace. Both studies also

found that children living on farms were less likely to have parents that smoked or previously smoked, and less likely to have attended daycare.

Potential Explanations for Past Geographic Differences in Childhood Asthma Prevalence

In terms of potential explanations for past geographical differences in asthma prevalence, both manuscripts identified risk and protective factors in the rural environment that may be associated with childhood asthma and asthma-like symptoms. *Personal factors* consistently identified in both studies as risk factors for asthma and wheeze included: male sex, parental history of asthma, and personal history of allergies. The latter were the strongest identified risk factors for asthma. However, none of these factors differed by farm versus small town status. It is possible that these factors may differ between farm children and urban children, so it is possible that personal factors may partially account for differences in pediatric asthma. However, our inconsistent findings suggest that it is unlikely that the personal factors explanation accounts for geographic variation in pediatric asthma prevalence in our specific research context.

In terms of *access to healthcare*, the second manuscript suggests that difficulty accessing routine healthcare is a strong risk factor for wheeze, but not as strongly associated with asthma. Furthermore, children living on farms reported longer distances to healthcare services compared to small town children. Therefore, findings suggest that the health care access explanation may partially underlie past geographic differences in asthma prevalence.

In terms of the *health risk behaviours* explanation, few behavioural factors were identified as risk or protective factors for asthma. Both manuscripts identified being overweight or obese as a potential risk factor, while the second manuscript identified maternal smoking as a risk factor. However, previous research suggests that obesity and passive exposure to smoking does not mediate differences in pediatric asthma prevalence between rural and more urban areas⁴

suggesting the possibility of inconsistent findings. Overall, the health risk behaviour explanation was not generally supported by our analyses

In terms of the *environmental explanation*, both manuscripts identified risk and protective factors in the rural environment that may be associated with childhood asthma and asthma-like symptoms. The first manuscript identified home dampness as a risk factor for asthma, and daycare as a protective factor, while the second manuscript identified daycare as a risk factor. It is possible that the inconsistent findings for daycare attendance may have arisen due to the age differences between the two study populations. The Saskatchewan Rural Health Study includes older children (ages 6 to 18) compared to those in the Estevan study (ages 6 to 13). Also, it is important to note that a higher percentage of children in the Estevan study reported previous daycare attendance (71.5%) compared to the children in Saskatchewan Rural Health Study (52.9%), and the reason for this difference may also be underlying the inconsistent findings. The second manuscript identified having pets in the home and having a dehumidifier in the home as protective factors, and having mice in the home and air filters as risk factors. Analysis of farm-related environmental exposures revealed feeding livestock as a risk factor, and filling grain bins, cleaning or playing in pens, and living on grain farms as protective factors. The indication that many environmental exposures common to the farm environment are risk factors for pediatric asthma supports the environmental explanation, although the possibility of reverse causation is also recognized due to the cross-sectional nature of our study designs.

5.2 Modeling Strategy

As a brief summary, we conducted regression analyses to identify potential risk factors for the asthma outcomes, and to more generally test the hypothesis that farm residence status was associated with lower risks for these outcomes. We therefore forced residence type (farm vs. small town) into all models. Other potential determinants were examined individually then

collectively using multiple logistic regression analyses in order to explore the four competing explanations for geographic differences in asthma experiences. We used generalized estimating equations to account for the clustered nature of the sampling scheme, with students nested within families. We used a purposeful modeling strategy, with consideration of past evidence and theory, as well as statistical criteria in the selection of covariates.

Our modeling strategy was therefore exploratory as opposed to being based upon a definitive etiological hypothesis. This exploratory approach to modeling allowed us to examine a large number of potential risk and protective factors for pediatric asthma simultaneously. We did not presume a priori focused hypotheses, and instead examined a list of risk and protective factors informed by previous literature. Covariate selection was also informed by previous literature as well as initial exploratory analyses. We included variables as potential confounders if supported as such in the previous literature, and also if they were identified as potential risk factors in any of our initial analyses. We did this in order to come up with a consistent set of covariates to adjust for in each of the many models that were examined.

Unlike predictive modeling, models were not focal in nature and did not test a single exposure or set of exposures relative to a single outcome. Therefore, we did not have a clear focal relationship from which to identify and include confounders and effect modifiers, which may have resulted in residual confounding, or inclusion of factors in some models that were not true confounders for the specific outcomes under study. Our desire to have a standard list of covariates to adjust for may therefore have resulted in some inefficiencies in estimation, for example some loss of power to study main effects. Despite this, we were deliberate in our consideration of various confounders and considered past research and statistical selection processes. A more focused modeling approach would be the next logical step in examining the

focal relationship between identified risk and protective factors and asthma and wheeze outcomes.

5.2 Internal Validity

Internal validity refers to the extent to which the findings of the study reflect the actual situation of the study population.⁵ Five common threats to internal validity include selection bias, information bias, confounding, chance, and reverse causation. Each of these is discussed below, relative to the two study populations and associated analyses.

Selection Bias

Selection bias may occur when there are systematic differences between those included and those excluded from a study, or when comparison groups are selected differently.⁵ The main selection issues to explore are sampling error, response bias, and the “healthy student effect”.

The sampling methods used in our two studies likely did not result in bias. The target population for the first manuscript included all children attending school in Estevan, and our high response rate likely decreases the probability of random sampling error. The sampling methods for manuscript 2 involved schools being chosen from each school district. There may have been some sampling error that arose due to chance. However, all students from a chosen school were asked to participate in the study. It is unlikely that sampling methods contribute to bias in this study.

Response bias is a potential threat for selection bias, as parents of children with asthma or wheeze may be more likely to complete the questionnaire than those parents of children without asthma or wheeze. This response effect is confirmed when we examined parents that completed the entire questionnaire and those that did not in manuscript 2 and found that children of parents that did complete the entire questionnaire were more likely to have asthma than those that only

partially completed the questionnaire and were subsequently excluded from the analysis (ever asthma: 15.4% vs. 8.3%, $p=0.03$; current asthma: 10.8% vs. 3.3%, $p=0.01$). Therefore, absolute prevalence for asthma may be inflated in both manuscripts. However, this response effect is not likely to affect small town vs. farm comparisons as it is unlikely that this response effect differs by small town vs. farm status. Furthermore, the response rate was higher for manuscript 1 than for manuscript 2 (72% versus 42% participation rate, respectively), and findings were similar between the two studies, suggesting that the low participation rate in the Saskatchewan Rural Health Study did not strongly bias the associations.

Another source of selection bias might be that children with serious asthma or other conditions may be more likely to be absent from school than other children,⁶ and therefore, less likely to be included in the study. The possibility of this effect occurring is reduced because students had a period of time in which to have their parents complete the questionnaire, and children would have to be absent from school for an extended period of time to not have the opportunity to take part in the studies. However, it is possible that students with poor health may be more likely to have been excluded from the study than those healthier students with more consistent school attendance. This effect may decrease the overall reported prevalence of asthma and wheeze. It is unlikely that this effect differs by small town and farm status, and therefore, this “healthy student effect” should not influence small town versus farm comparisons.

Information bias

Information bias is an important consideration in the interpretation of epidemiological study findings. These manuscripts both relied on parental report, which is subject to errors in recall. Despite the cross-sectional nature of the study, the findings are also potentially subject to a variation of recall bias (recognizing that the latter is usually associated with case-control

designs), in that relative to parents of non-asthmatic children, parents of children with asthma may be more likely to recall exposures that may have triggered asthma symptoms in the past. This effect would strengthen the association between known risk factors and asthma. Recall bias may also arise due to social desirability. For example, parents that smoke and have a child with wheeze or asthma may be less likely to reveal that they smoke because they experience guilt or fear of social judgment. This effect would bias the odds ratio toward a protective association between smoking and asthma. Finally, the parental reports of physician-diagnosed asthma were not validated through medical or hospital records. However, we were re-assured by the fact that many studies that use large sample populations often rely on self-report of physician diagnoses. A validation of the ISAAC questionnaire reported a sensitivity of 0.85 and a specificity of 0.81 for parent reported physician diagnosis of asthma.⁷ This measure was found to be more optimal than bronchial hyper responsiveness (BHR) test (sensitivity: 0.54; specificity: 0.64) and a combination of the questionnaire and BHR (sensitivity: 0.47; specificity: 0.94) for parent reported physician diagnosis of asthma.⁷

Chance

Due to the large numbers of comparisons involved, there is a possibility that some of the results may have been due to chance. That is, some findings may be the result of a Type 1 error. We reported all p-values in these manuscripts so that the probability of chance playing a role in the findings can be evaluated for each comparison by the reader. The confidence intervals and p-values manuscript 2 were all inflated by a factor of 0.049 due to clustering by family. This decreases the probability of committing a Type 1 error. We did not, however, adjust our p-values for multiple comparisons, which would increase the probability of a type 1 error.

There is also a possibility that some null findings may be the result of a Type II error. One main reason for failing to reject the null hypothesis is due to lack of statistical power. We

completed power analyses for both manuscripts prior to completing the statistical analyses, and found that with the given sample size we did have considerable power to estimate prevalence values and also detect associations among these populations at an alpha set at 0.05 (see appendix D). To illustrate, based upon the sample size in the cohort in Manuscript 1, for proportions of 50% the confidence interval will lie within 4.7% of this proportion, 19 times out of 20. When only 10% are exposed, the 95% confidence interval will be within 2.8% of the estimate. These confidence intervals were inflated by a factor of 1.4 (a conservative estimate) to account for the clustered study design.

Power in manuscript 2 refers to the ability to detect an effect estimate summarizing the association between an exposure variable and asthma outcome, assuming there is a true association. While 2400 surveys were expected to be completed, it was assumed that 5% would have missing answers. Due to the clustered nature of the data, the sample size was also divided by a very conservative design effect of 1.4, as per existing precedents (indeed, this effect was much more conservative than the calculated effect that was eventually used). Therefore, the effective sample size used in these calculations was 1629, with 40% of the sample estimated to be residents of farms.

Measures of effect (OR) varying between 2.0 and 2.5 were used based upon previous literature and minimally important differences in effect.⁸ To illustrate, power to detect an odds ratio of 2.0 between farm type and diagnosed asthma ranged from 44.4% (poultry) to 100% (grain), and this is reflective of the number of children living on each farm type. In general, the vast majority of analyses are powered above 90% to detect such effect estimates, with some exceptions.

Confounding

Although we attempted to control for a variety of factors by using a multivariable analysis, it is possible that there are several additional potential confounders or residual confounding that may affect the results. We did not have information regarding environmental factors outside of the farm and home, such as proximity to industrial waste or other environmental hazards. It is possible that proximity to these areas may increase risks for asthma. It is possible that farm and small town children are not equally likely to live in close proximity to such a risk factor. Therefore, it is possible proximity to large environmental hazards outside of a child's immediate home and/or farm is confounding the association between farm vs. small town status and pediatric asthma. Another variable potentially confounding the small town vs. farm relationship and pediatric asthma is early exposure to farms. The environmental explanation suggests that early life exposures may influence immune response^{9,10} and we did not have adequate information about early exposure to the farm environment nor did we examine the effects of moving to or away from a farm.

It is also possible that poor measurement of confounders resulted in uncontrolled or residual confounding. Confounders were assessed using questions derived from previous research. However, in manuscript 2, we used parental report of a child being "overweight" versus "normal or underweight" rather than body mass index (BMI) which was used in manuscript 1, due to excessive missing data for this variable. Research has demonstrated that most mothers are able to accurately assess their adolescent's weight¹¹, but that many parents did not recognize younger children as being overweight or obese and instead were likely to report overweight children as normal weight.¹² Furthermore, both manuscripts defined BMI using broad categories that combined both overweight and obese children. Therefore, it is possible there is residual confounding in both due to weight.

Reverse Causation and the Cross-sectional Design

Both of the studies in this thesis used a cross-sectional design which presents obvious challenges with respect to interpretation and causal associations between exposures and outcomes in terms of temporality. It is possible that parents of children with asthma removed those children from obvious triggers of their symptoms and this is one potential explanation for an apparent protective effect for some environmental variables.

5.3 External Validity

Generalization

External validity refers to how applicable the results of a study are to populations aside from the study population; that is, whether the results can be generalized to other populations.⁵ One potential threat to external validity might be that children attending private schools or who are homeschooled were not included in the study population. Therefore, results may not be generalized to the latter populations. It is possible that these children may be exposed to different risk factors than those children attending public schools and therefore, they may have different asthma and wheeze prevalence.

Overall, many of the associated risk factors and protective factors may be generalized to other children within Canada with similar farm and environmental exposures, and similar access to healthcare. However, caution must be taken when comparing these results with populations from other contexts and countries where both farming procedures and health care practices may differ widely. For example, these findings may not be generalized to children living on farms in developing countries where farm practices may differ largely from those in Canada.

5.4 Other Strengths and Limitations

Both manuscripts share common limitations. The study population consists of children from rural areas. Children living in small towns may be exposed to similar risk factors and

protective factors as those living on farms, and this is a potential reason why no differences in asthma prevalence were found between the two groups. Another important limitation is that all data is derived from cross-sectional questionnaires and study contexts. Therefore, it is necessary to be careful when interpreting causality and temporality. The ideal study design for examining the causal effects of many potential risk and protective factors would be a prospective cohort study, but this was not feasible in our research setting.

Findings may also be subject to detection bias. It is possible that children with known risk factors for asthma are more likely to become diagnosed with asthma than those without these risk factors, despite experiencing the same symptoms. For example, if a child has parents with severe asthma, perhaps these parents are more likely to bring their child with symptoms of wheeze to a physician compared to parents without asthma. This detection bias may have inflated the odds ratio for this known risk factor.

This thesis also has strengths. The large proportion of farm children in the sample population allowed for the investigation of farm specific factors (e.g., farm activities) as potential risk and protective factors. Although a number of previous manuscripts have examined asthma prevalence by farm and small town environments, this thesis is one of few studies that examines farm specific factors as risk factors and protective factors for asthma. This thesis is also based on a Canadian population, which is somewhat novel to this literature. Uncertainty still exists regarding some potential risk and protective factors (e.g., pets in the home). This study investigated many of these factors simultaneously, which is unique, and results may contribute to future meta-analyses which may be implemented to solve debatable factors. Finally, this thesis is the result of collaboration across universities. These manuscripts benefitted from a variety of feedback and perspectives. This may have enhanced the interpretation and presentation of findings.

5.5 Recommendations

Recommendations include (1) improving surveillance among children with personal risk factors, (2) promotion of risk reduction, and (3) reducing exacerbation of symptoms in children that already have asthma.

First, the strongest identified risk factors for asthma were personal risk factors (i.e., parents with asthma, personal history of allergies, etc.) and these findings highlight the potential clinical importance of surveillance and clinical screening for children with these personal risk factors. Physicians may closely monitor children with these key personal risk factors, increasing the likelihood of diagnosis and subsequent symptom prevention for these children. Screening programs that use questionnaires, spirometry and follow-up with an allergist can identify children with undiagnosed asthma.¹³ Screening programs may be beneficial in communities with pediatric populations that have a high prevalence of risk factors identified in these studies.

Second, by identifying risk factors for asthma, these findings could be applied to the promotion of risk reduction behaviours, particularly for children at high risk for developing asthma. For example, one behavioural factor found to be a risk factor for asthma was maternal smoking. Parents may engage in risk reduction by reducing their smoking. The Canadian Pediatric Asthma Consensus guidelines and Canadian Asthma Consensus guidelines suggest that physicians recommend smoke avoidance for children that are at high risk for developing asthma (i.e., have parents with asthma or have personal allergies) as secondary prevention.¹⁴

Finally, many of the factors associated with wheeze may exacerbate symptoms in children that already have an asthma diagnosis. For example, feeding livestock was positively associated with wheeze (and not asthma) and therefore, could be exacerbating symptoms in children that have asthma. If children with asthma are less likely to be exposed to this farm chore, it may reduce symptoms of wheeze. Current recommendations for asthma control in children

acknowledge the use of environmental control measures.¹⁴ Therefore, these results contribute to literature identifying specific environmental factors that may exacerbate asthma, and that may assist in controlling asthma.

5.6 Future Research Directions

A number of suggestions for future research directions arise from this study. To more carefully examine the healthcare access explanation, future research could examine children with wheeze symptoms but with no asthma diagnosis. Although one of the outcomes in the present study was “ever wheeze”, this included both children with and without an asthma diagnosis. By comparing risk factors for wheeze with no diagnosis to an asthma diagnosis, the healthcare access explanation may be examined more focally.

Important designs for future epidemiological research will include cohort studies, as analyses were limited by their cross-sectional nature. A cohort study could better capture causal relationships between potential risk factors and protective factors and asthma and wheeze. These studies could also examine more focal relationships between specific risk factors and protective factors and asthma and wheeze.

Many of the risk factors and protective factors in the rural environment are still debatable and/or controversial. Meta-analyses of existing data will improve power and may provide more conclusive evidence for which risk factors or protective factors in the rural environment are associated with asthma and asthma-like symptoms.

Future studies should aim to improve exposure assessment. After identifying which farm factors are most strongly associated with asthma, future research may quantify these exposures to examine a dose-response relationship or other patterns. Future research could better assess the timing, frequency and duration of these exposures, and where possible, objectively measure these exposures. For example, if barn dust is identified as a risk factor, it could be collected from barns

and measured and further analysis could identify a dose-response relationship or a threshold exposure level.

Finally, children living in small towns may be exposed to similar allergens compared to those living on farms, and this may be why there were no differences in asthma prevalence between the two groups. Future research should strive to include a comparison group that is less likely to have been exposed to the farm environment, such as a study population that contains both large city and rural farming communities.

5.7 Summary

This thesis uniquely examines each of four existing explanations (*personal factors, access to healthcare, health risk behaviours, environmental*) for geographic variation in pediatric asthma among a large Canadian population of children. Findings suggest that the *access* to health care and *environmental* explanations may underlie the geographic variation in pediatric asthma among farm versus more urban children observed in past studies. Future studies may benefit from using a cohort design (to better capture causal relationships) and from using more heterogeneous exposure groups (e.g., compare farm vs. city children). Findings from this thesis may contribute to recommendations for risk reduction and asthma control.

5.8 References

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Appendix A

The Estevan Cohort Study

The Estevan Cohort study is a cross-sectional study conducted in 2003 in Estevan, a city located in the Canadian province of Saskatchewan. Estevan is a major agricultural centre in Southern Saskatchewan situated near a coal mining strip, coal-fired power production, and oil and gas drilling. This cross-sectional study was originally developed to examine lung health in the region. It also provided a sampling frame for a separate case-control study.¹ The 2003 Estevan study builds upon a similar cross-sectional study completed in Estevan in 2000.^{2,3}

All children in Estevan enrolled in grades 1-6 during the 2002-03 academic year were approached to participate. Children attended one of eight separate schools. Questionnaires were distributed across these eight schools in January 2003, and parents completed questionnaires within a three week period after distribution. A reminder letter was sent 10 days after distribution. The participation rate was 72.0%, resulting in a sample size of 842 participants. Approvals to conduct the survey were obtained from the school boards and school principals in Estevan prior to distribution in the schools. Ethical approval for this study protocol was obtained from the Advisory Committee on Ethics in Biomedical Research at the University of Saskatchewan.

Questionnaire content was based on the American Thoracic Society's Children's Respiratory Disease Questionnaire⁴, questionnaires used in the Student Lung Health study³ and an asthma prevalence questionnaire used in a 1992 study conducted in Humboldt, Saskatchewan.⁵ The 2003 study questionnaire included items describing demographics, current and previous asthma and asthma-like symptoms, related atopic diseases, other illnesses, home environments, lifestyle factors, and family factors.

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Appendix B

The Saskatchewan Rural Health Study

The 2010 *Saskatchewan Rural Health Study* is a prospective cohort study (with cross-sectional components) that seeks to evaluate associations between potential health determinants and respiratory outcomes in rural populations. The study population includes both adults and children living in the four quadrants of rural Saskatchewan, Canada. Our analysis focused on the cross-sectional child component of the study. Drs. Lawson and Pickett are co-investigators on this CIHR grant-funded project, and my CIHR-PHARE scholarship was partially supported by this grant as well (travel).

The municipalities included in the adult phase of the study were chosen to represent each of the four quadrants of Saskatchewan using a multistage stratified random sampling strategy.¹ Schools that were located within the rural municipalities included in the adult phase of the study were the target schools for the child study. The ten divisions that included those schools were approached and all agreed to participate. Forty-three schools within these divisions were chosen to participate. Of the 43 selected schools, 39 of these agreed to participate.

Students attending these schools were administered study packages to be taken home for parents or adult guardians to complete, with completed questionnaires to be returned to their home room teacher at school. The package contained an information letter, study questionnaire, and return envelope. A reminder letter from the school was sent out 2 weeks following the initial package distribution. Questionnaires were distributed to 5667 children in grades 1-12 attending one of the 39 schools during the 2010-11 academic year. The participation rate was 42%, resulting in a sample size of 2383 participants. Of the 2383 participants, 124 were excluded from

the final analysis due to missing data on key variables resulting in a final sample size of 2259 participants.

Ethics approval for the study protocol was obtained from the Biomedical Research Ethics Board at the University of Saskatchewan (Study approval #Bio-10-177). Approvals to conduct the survey were also obtained from the Directors of each school division in June 2010 and from school Principals in December 2010.

The 2011 Rural Health child study questionnaire included items describing socio-demographics, current and previous asthma and asthma-like symptoms, related atopic diseases, other illnesses, the home environment, health risk behaviours, and family factors. It also included items describing farm type and types of farm activities performed on a regular basis.

Questionnaire content was in part based on: (1) the American Thoracic Society's 1979 Children's Respiratory Disease Questionnaire(ATS)²; (2) the self-administered questionnaires in the Student Lung Health study³; (3) questionnaires used in a study in Estevan, SK in 2000 and 2003⁴⁻⁶; (4) an asthma prevalence questionnaire used in a 1992 study conducted in Humboldt, Saskatchewan⁷; and (5) the International Study of Asthma and Allergies in Childhood Study (ISAAC) questionnaire⁸.

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Appendix C

Relevant Portions from the Estevan Cohort Questionnaire

5. Has this child ever had a wheeze or whistling noise that comes from the chest?

No ___ Yes ___ Don't know ___

If yes tick all that apply

___ Yes, past 12 months

___ Yes, before last 12 months

6. Does the wheezing or whistling in the chest occur

___ apart from colds?

___ with colds?

___ both apart from colds and with colds?

9. Has this child ever been short of breath with wheezing? (speech limited to one or two words between breaths) *Tick all that apply*

___ Yes, past 12 months

___ Yes, before last 12 months

___ No

15. Has this child ever been diagnosed as having asthma by a doctor?

No ___ Yes ___ Don't know ___

18. In the past 12 months, how many times has your child required services for asthma from:

Number of times

___ Emergency department

___ Doctor's office

20. In the past 12 months, how many asthma episodes has your child had?

___ (number of episodes)

21. In the past 12 months, was this child admitted to an intensive care unit for asthma? No ___ Yes ___ Don't know ___

22. Which of the following statements best describes this child's asthma medication use **in the past 12 months:**

___ Never in the past 12 months

___ At least once in the past 12 months

___ At least once per month

___ At least once per week

___ Every day

30. Has this child ever had an allergy (hives, runny nose, swelling, itchiness and/or wheezing) to any of the following:

House dust No ___ Yes ___

Grain dust No ___ Yes ___

Pollen No ___ Yes ___

Trees No ___ Yes ___

Grasses No ___ Yes ___

Mold or mildew No ___ Yes ___

Dog No ___ Yes ___

Cat No ___ Yes ___

Birds/feathers No ___ Yes ___

Farm animals No ___ Yes ___

Chemicals No ___ Yes ___

Foods No ___ Yes ___

Other (please name) _____

41. How many times a week does your child engage in vigorous physical activity long enough to make him/her breathe hard?

___ Never or occasionally

___ Once or twice per week

___ Three or more times per week

44. What is your child's current height?

___ feet ___ inches

45. What is your child's current weight?

___ pounds

47. Where is your home located?

___ Farm

___ Acreage

___ In town

50. Which best describes the type of housing unit in which you live?

one family house _____

a duplex _____

a building for 3 or more families _____

a mobile home or trailer _____

52. Have renovations been done to your home?

No ___ Yes ___ Don't know ___

If YES, in what years? _____

53. How many rooms are in your home (not including bathrooms, porches, balconies, halls, or entrance ways) Rooms _____

54. How many people live in your home?

Number _____

56. Do you have any of the following in your home?

Air conditioners No ___ Yes ___

Air filter No ___ Yes ___

Humidifier No ___ Yes ___

Dehumidifier No ___ Yes ___

Fireplace No ___ Yes ___

57. Does your house have any damage caused by dampness (e.g., wet spots on walls, floors)?

No ___ Yes ___

58. Are there any signs of mold or mildew in any living areas in your home?

No ___ Yes ___

59. Do you currently have pets living inside your home? No ___ Yes ___

If YES, please specify kind (s) _____

61. Has this child's father ever smoked?

No ___ Yes ___

Does this child's father currently smoke?

No ___ Yes ___

If NO, what year did he quit smoking?

62. Has this child's mother ever smoked?

No ___ Yes ___

Does this child's mother currently smoke?

No ___ Yes ___

If NO, what year did she quit smoking?

63. Did the mother smoke during the pregnancy?

No ___ Yes ___

68. Child's sex:

Male ___ Female ___

69. Date of Birth:

___ ___ ___

Mo. Day Yr.

70. What was the baby's birth weight?

___ pounds ___ ounces

71. Was this child born before the mother's due date?

No ___ Yes ___ Don't know ___

73. Was this child breastfed?

No ___ Yes ___ Don't know ___

74. Did this child ever go to a daycare, child care facility, or nursery school?

No ___ Yes ___

75. Does the child's natural mother have any of the following conditions? *Tick any that apply*

___ Asthma

___ Hayfever

___ Allergies

___ Eczema

___ Don't know

76. Does the child's natural father have any of the following conditions? *Tick any that apply*

- Asthma
- Hayfever
- Allergies
- Eczema
- Don't know

78. What is the highest level of education completed by the child's mother?

- Public school
- Grade 12
- Technical school
- University degree

79. What is the highest level of education completed by the child's father?

- Public school
- Grade 12
- Technical school
- University degree

80. Type of household

- Single parent home
- Two parent/partner home

81. What is this child's ethnic background?

- Caucasian
- Aboriginal
- Other Please specify

Appendix D

Relevant Questions from the Children's Questionnaire of the Saskatchewan Rural Health Study

5. Has this child ever had a wheeze or whistling noise that comes from the chest?

No ___ Yes ___ Don't know ___

6. **In the past 12 months**, has this child had a wheeze or whistling noise that comes from the chest?

No ___ Yes ___ Don't know ___

10. Has this child ever been short of breath with wheezing? (speech limited to one or two words between breaths) *Tick all that apply*

___ Yes, past 12 months

___ Yes, before last 12 months

___ No

12. Has this child ever been diagnosed as having asthma by a doctor?

No ___ Yes ___ Don't know ___

15. **In the past 12 months**, how many asthma episodes has your child had?

___ (number of episodes)

16. Which of the following statements best describes this child's asthma medication use **in the past 12 months**:

___ Never in the past 12 months

___ At least once in the past 12 months

___ At least once per month

___ At least once per week

___ Every day

20. Has this child ever had an allergy (hives, runny nose, swelling, itchiness and/or wheezing) to any of the following:

House dust No ___ Yes ___

Grain dust No ___ Yes ___

Pollen No ___ Yes ___

Trees No ___ Yes ___

Grasses No ___ Yes ___

Mold or mildew No ___ Yes ___

Dog No ___ Yes ___

Cat No ___ Yes ___

Birds/feathers No ___ Yes ___

Farm animals No ___ Yes ___

Chemicals No ___ Yes ___

Foods No ___ Yes ___

Other (please name) _____

41. How many times a week does your child engage in vigorous physical activity long enough to make him/her breathe hard?

- Never or occasionally
- Once or twice per week
- Three or more times per week
- Don't know

46. Do you consider your child to be

- Underweight?
- Just about right weight?
- Overweight?

47. Where is your home located?

- Farm
- Acreage
- In town

If you answered "FARM", from the list above, please check each commodity that is **produced for sale** on your farm or ranch (*Check all that apply*).

- Grain crops
- Cattle (beef)
- Cattle (dairy)
- Pigs
- Poultry
- Vegetable/fruit
- Other: Please specify:

45. **In the past 12 months,** on average, how often has this child spent 1 hour near or in the following activities (*Please check the box that best applies*):

	Everyday	At least once a week	At least once a month	Less than once a month	Never
Haying or moving or playing with hay bales					
Feeding livestock					
Cleaning or playing in barns					
Emptying or filling grain bins					
Cleaning or playing in pens or corrals					
Riding horses					

50. Which best describes the type of housing unit in which you live?
one family house _____
a duplex _____
a building for 3 or more families _____
a mobile home or trailer _____

51. Which category of years do you think most closely matches when this building was built?
1980-present _____
1979 or before _____
Don't know _____

52. **In the past 12 months**, have major renovations been done to the home?
No ___ Yes ___ Don't know ___

53. How many bedrooms do you have in your home? Number _____

54. How many people live in your home?
Number _____

55. In your house, what fuel is usually used for heating?

___ Natural gas
___ Propane
___ Electricity
___ Fuel oil
___ Coal
___ Geo-thermal
___ Solar energy
___ Wood
Other, specify _____
___ Don't know

56. **In the past 12 months**, have you had any problems with mice or rats in your home?
No ___ Yes ___ Don't know ___

57. Do you have any of the following in your home?

Air conditioners No ___ Yes ___
Air filter No ___ Yes ___
Humidifier No ___ Yes ___
Dehumidifier No ___ Yes ___
Wood fireplace No ___ Yes ___

58. Does your house have any damage caused by dampness (e.g., wet spots on walls, floors)?
No ___ Yes ___

59. **During the past 12 months**, has there been water or dampness in your home from broken pipes, leaks, heavy rain, or floods?
No ___ Yes ___ Don't know ___

60. Does your home (including basement) frequently have a mildew odor or musty smell?
No ___ Yes ___ Don't know ___

61. Are there signs of mold or mildew in any living areas in your home?
No ___ Yes ___

62. **In the past 12 months**, have you had any of the following pets living in your home? (*Please check yes or no for each type of pet*).

Cat No ___ Yes ___

Dog No ___ Yes ___

Bird No ___ Yes ___

Any other pet No ___ Yes ___

64. Has this **child's father** ever smoked?
No ___ Yes ___

If Yes, what year did he start smoking?

65. Does this child's father currently smoke?
No ___ Yes ___

If No but he has smoked, What year did he quit smoking? _____

66. Has this **child's mother** ever smoked?
No ___ Yes ___ **If Yes**, what year did she start smoking? _____

67. Does this child's mother currently smoke?
No ___ Yes ___

If No but she has smoked, What year did she quit smoking? _____

73. Has this child ever smoked tobacco? (At least one cigarette, cigar or pipe)
No ___ Yes ___ Don't know ___

77. Child's sex: Male _____
Female _____

78. Date of Birth: _____
Mo Day Yr.

79. Child's age: _____

80. How tall is this child? (*For best results please use a tape measure against a wall*)
_____ feet _____ inches

81. How much does this child weigh?
_____ pounds

82. What was the child's weight at birth?
___ pounds ___ ounces or ___ kg

83. Was this child born before mother's due date?

No ___ Yes ___ Don't know ___

If **YES**, how many weeks early?

_____ weeks

85. Was this child breastfed?

No ___ Yes ___ Don't know ___

86. Did this child consume unpasteurized milk (raw milk, farm milk) regularly **in the first year of life**?

No ___ Yes ___ Don't know ___

87. Does your child **currently** drink unpasteurized milk regularly?

No ___ Yes ___

92. Did this child ever go to daycare?

No ___ Yes ___ Don't know ___

93. Does the child's natural mother have any of the following conditions? *Tick any that apply*

___ Asthma

___ Hayfever

___ Allergies

___ Eczema

___ Don't know

94. Does the child's natural father have any of the following conditions? *Tick any that apply*

___ Asthma

___ Hayfever

___ Allergies

___ Eczema

___ Don't know

96. What is the highest level of education completed by the child's mother?

___ Public school

___ Grade 12

___ Technical school

___ University degree

97. What is the highest level of education completed by the child's father?

___ Public school

___ Grade 12

___ Technical school

___ University degree

98. Type of household

Single parent home

Two parent/partner home

99. What is this child's ethnic background?

Caucasian

First Nation/Metis

African, African-American

Other Please specify

Appendix E

Statistical Power Calculations

P	Q	N	Lower	Upper	R
0.1	0.9	842	0.072	0.128	0.028
0.2	0.8	842	0.162	0.238	0.038
0.3	0.7	842	0.257	0.343	0.043
0.4	0.6	842	0.354	0.446	0.046
0.5	0.5	842	0.453	0.547	0.047

Table 1: Power analysis for manuscript 1.

P = proportion exposed

Q = proportion unexposed

n = sample size

$r = P \pm (1.96 * (P * Q / N)^{1/2})$

	N_{adjusted}	% exposed*	N_{exposed}	R	OR	p**	p⁰	p¹	d	z_{a/2}	z(1-B)	Power
<i>Grain</i>	1629	0.172	280.188	4.813953	2	0.13	0.110922	0.221843	0.110922	1.96	3.063708	99.9%
	1629	0.172	280.188	4.813953	2.5	0.13	0.103339	0.258347	0.155008	1.96	5.060412	100%
	1629	0.112	182.448	7.928571	2	0.13	0.116906	0.233813	0.116906	1.96	2.464695	99.3%
<i>Cattle</i>	1629	0.112	182.448	7.928571	2.5	0.13	0.111301	0.278253	0.166952	1.96	4.358828	100%
	1629	0.02	32.58	49	2	0.13	0.127451	0.254902	0.127451	1.96	0.181413	57.2%
<i>Pig</i>	1629	0.02	32.58	49	2.5	0.13	0.126214	0.315534	0.18932	1.96	1.220934	88.9%
	1629	0.01	16.29	99	2	0.13	0.128713	0.257426	0.128713	1.96	-0.42302	33.6%
<i>Poultry</i>	1629	0.01	16.29	99	2.5	0.13	0.128079	0.320197	0.192118	1.96	0.334116	63.1%
	1629	0.06	97.74	15.66667	2	0.13	0.122642	0.245283	0.122642	1.96	1.535476	93.8%
<i>Fruit/Vegetable</i>	1629	0.06	97.74	15.66667	2.5	0.13	0.119266	0.298165	0.178899	1.96	3.138905	99.9%
	1629	0.02	32.58	49	2	0.13	0.127451	0.254902	0.127451	1.96	0.181413	57.2%
<i>Other</i>	1629	0.02	32.58	49	2.5	0.13	0.126214	0.315534	0.18932	1.96	1.220934	88.9%
	1629	0.132	215.028	6.575758	2	0.13	0.114841	0.229682	0.114841	1.96	2.705229	99.7%
<i>Livestock</i>	1629	0.132	215.028	6.575758	2.5	0.13	0.108514	0.271285	0.162771	1.96	4.65232	100%
	1629	0.4	651.6	1.5	2	0.13	0.092857	0.185714	0.092857	1.96	3.499466	100%
<i>Farm/Nonfarm</i>	1629	0.4	651.6	1.5	2.5	0.13	0.08125	0.203125	0.121875	1.96	5.205549	100%

Table 2: Estimated power for detecting Farm Type and Diagnosed Asthma Associations

* Statistics Canada

** Garner and Kohen

N_{adjusted} is the sample size adjusted for non-responders and missing answers

N_{exposed} is the number of children exposed

r is the ratio of unexposed to exposed

OR is the detectable odds ratio

p is the proportion of students who have the outcome (i.e. reported wheeze or diagnosed asthma)

p₀ is the prevalence of outcome in the unexposed

p₁ is the prevalence of outcome in the exposed

d is the difference between p₁ and p₀

Z_{α/2} is the level of significance

$$\text{Power} = F Z_{(1-\beta)} = F \{d [(nr)/p(1-p)(1+r)]^{1/2} - Z_{\alpha/2}\}$$

Appendix F
Additional Tables for Manuscript 1

Appendix Table 1: Descriptive Covariates and 4 Outcomes: 2003 Child Asthma Study in Estevan, Saskatchewan (n=834)

Covariates	Ever Wheeze (n=233) n(%)	Current Wheeze (n=170) n(%)	Current Wheeze (n=170) N(%)	Ever Asthma (n=161) n(%)
Demographics				
Location				
Farm	27 (12)	24 (14)	18 (11)	15 (14)
Small town	204 (88)	145 (86)	140 (89)	95 (86)
Sex				
Female	101 (43)	81 (48)	64 (40)	45 (40)
Male	132 (57)	89 (52)	97 (60)	67 (60)
Father education				
High school or less	122 (55)	98 (61)	75 (48)	56 (52)
More than high school	100 (45)	62 (39)	80 (62)	51 (48)
Environmental Factors				
Dampness				
Absent	172 (74)	125 (26)	114 (72)	84 (76)
Present	59 (26)	44 (74)	45 (28)	27 (24)
Behavioural Factors				
Daycare				
No	67 (29)	52 (31)	56 (35)	42 (38)
Yes	162 (71)	116 (69)	102 (65)	68 (62)
Father current smoker				
No	180 (71)	105 (65)	116 (74)	82 (76)
Yes	73 (29)	59 (35)	40 (26)	26 (24)
Personal Factors				
Premature birth				
No	207 (89)	151 (13)	139 (86)	99 (88)
Yes	26 (11)	19 (87)	22 (14)	13 (12)
Personal allergy				
No	115 (49)	75 (44)	70 (43)	41 (37)
Yes	118 (51)	95 (56)	91 (57)	71 (63)
Father with Asthma				
No	204 (88)	146 (86)	132 (83)	88 (79)
Yes	27 (12)	23 (14)	27 (17)	23 (21)
Mother with Asthma				
No	198 (85)	141 (83)	125 (78)	85 (76)
Yes	34 (15)	29 (17)	35 (22)	27 (24)

Overweight or obese				
No	187 (80)	131 (77)	135 (84)	89 (79)
Yes	46 (20)	39 (23)	26 (16)	23 (21)
Birthweight				
Normal	217 (93)	159 (94)	152 (94)	107 (96)
Underweight	16 (7)	11 (6)	9 (6)	5 (4)

Appendix Table 2: Bivariate Regression: Crude Odds Ratios

Covariate	Ever Wheeze	Current Wheeze	Ever Diagnosed Asthma	Current Diagnosed Asthma
Demographics				
Farm residence (Ref: small town)	1.09 (0.64, 1.89)	1.37 (0.77, 2.42)	0.97 (0.50, 1.91)	1.18 (0.55, 2.53)
Male sex (Ref: female)	1.49 (1.09, 2.03)	1.28 (0.90, 1.81)	1.82 (1.29, 2.58)	1.81 (1.21, 2.74)
Father education: More than high school (Ref: less than highschool)	1.02 (0.74, 1.41)	0.79 (0.54, 1.14)	1.39 (0.96, 2.01)	1.14 (0.674, 1.74)
Environmental Factors				
Dampness	1.45 (1.01, 2.09)	1.49 (0.99, 2.23)	1.71 (1.14, 2.56)	1.26 (0.78, 2.02)
Behavioural Factors				
Daycare	0.97 (0.69, 1.35)	0.88 (0.61, 1.27)	0.69 (0.47, 1.01)	0.63 (0.42, 0.95)
Father current smoker	1.10 (0.79, 1.53)	1.29 (0.89, 1.87)	0.71 (0.48, 1.05)	0.69 (0.43, 1.12)
Personal Factors				
Premature birth	1.20 (0.73, 1.97)	1.19 (0.66, 2.13)	1.60 (0.96, 2.67)	1.20 (0.65, 2.23)
Personal allergies	6.85 (4.77, 9.83)	8.34 (5.62, 12.37)	7.33 (5.02, 10.71)	8.57 (5.58, 13.15)
Father with asthma	2.27 (1.26, 4.07)	2.67 (1.42, 5.00)	3.95 (2.19, 7.13)	4.71 (2.52, 8.81)
Mother with asthma	2.73 (1.70, 4.39)	3.20 (1.91, 5.37)	5.22 (3.17, 8.62)	4.89 (2.87, 8.33)
Overweight or obese	1.65 (1.11, 2.46)	2.08 (1.37, 3.15)	1.15 (0.72, 1.86)	1.69 (1.03, 2.79)
Low birth weight (Ref: normal weight)	1.62 (0.87, 3.03)	1.54 (0.75, 3.19)	1.16 (0.56, 2.37)	0.91 (0.38, 2.21)

Appendix G

Additional Tables for Manuscript 2

Table 1: Bivariate association between asthma and wheeze outcomes and personal factors. The 2010 Saskatchewan Rural Health Study-Children (n=2,259)

Covariates	Ever wheeze Odds ratio (95% Confidence Intervals)	Current wheeze Odds ratio (95% Confidence Intervals)	Ever asthma Odds ratio (95% Confidence Intervals)	Current asthma Odds ratio (95% Confidence Intervals)
Personal Factors				
Sex (Ref: female)	1.45 (1.18, 1.79)	1.40 (1.09, 1.81)	1.54 (1.22, 1.96)	1.48 (1.22, 1.96)
Age Group (Ref: ages 6-9 years)	1.14 (0.89, 1.46)	1.09 (0.81, 1.46)	1.17 (0.89, 1.55)	1.09 (0.79, 1.50)
ages 10-13				
ages 14-18 years	1.05 (0.80, 1.38)	0.99 (0.72, 1.38)	1.04 (0.77, 1.42)	0.82 (0.57, 1.18)
Father with postsecondary education (Ref: highschool or less)	1.05 (0.85, 1.30)	0.94 (0.73, 1.21)	1.15 (0.90, 1.46)	1.13 (0.86, 1.50)
Mother with postsecondary education (Ref: highschool or less)	1.10 (0.89, 1.37)	0.95 (0.73, 1.23)	1.07 (0.84, 1.37)	1.11 (0.83, 1.48)
Child born prematurely	1.12 (0.80, 1.57)	1.29 (0.88, 1.90)	2.14 (1.54, 2.98)	1.81 (1.23, 2.67)
Single parent family	1.39 (1.01, 1.90)	1.68 (1.17, 2.39)	1.48 (1.05, 2.09)	1.32 (0.88, 1.99)
Fathers with asthma	2.62 (1.86, 3.70)	3.20 (2.20, 4.65)	2.63 (1.81, 3.82)	3.04 (2.03, 4.55)
Mothers with asthma	2.94 (2.12, 4.08)	3.57 (2.51, 5.09)	3.65 (2.60, 5.13)	4.06 (2.81, 5.86)
Children with allergies	5.10 (4.09, 6.35)	5.88 (4.50, 7.68)	5.97 (4.65, 7.67)	7.75 (5.73, 10.50)
Child overweight	2.44 (1.77, 3.35)	2.64 (1.85, 3.77)	1.65 (1.14, 2.39)	1.90 (1.26, 2.85)
Non-Caucasian	0.80 (0.55, 1.17)	1.07 (0.70, 1.63)	1.03 (0.69, 1.53)	1.04 (0.66, 1.65)
Born underweight (<2500g)	1.07 (0.75, 1.54)	1.17 (0.76, 1.78)	1.39 (0.95, 2.03)	1.28 (0.82, 2.01)

Table 2: Bivariate association between asthma and wheeze outcomes and environmental factors. The 2010 Saskatchewan Rural Health Study-Children (n=2,259)

Covariates	Ever wheeze		Current wheeze		Ever asthma		Current asthma	
	Odds ratio (95% Confidence Intervals)							
Homes with dampness	1.21 (0.96, 1.51)	1.04 (0.78, 1.37)	1.11 (0.86, 1.44)	1.01 (0.74, 1.37)	1.31 (0.96, 1.77)	1.08 (0.80, 1.45)	1.21 (0.87, 1.69)	
Homes with mildew smell	1.35 (1.05, 1.74)	1.48 (1.10, 1.98)	1.08 (0.80, 1.44)	1.31 (0.96, 1.77)	1.08 (0.80, 1.45)	1.08 (0.80, 1.45)	1.31 (0.94, 1.82)	
Homes with mold or mildew	1.30 (1.01, 1.67)	1.31 (0.96, 1.77)	1.08 (0.80, 1.45)	1.31 (0.96, 1.77)	1.08 (0.80, 1.45)	1.08 (0.80, 1.45)	1.21 (0.87, 1.69)	
Homes with indoor pets	1.38 (1.10, 1.72)	1.30 (0.99, 1.69)	1.14 (0.89, 1.46)	1.06 (0.80, 1.41)	1.14 (0.89, 1.46)	1.06 (0.80, 1.41)	1.06 (0.80, 1.41)	
Homes with renovations (past 12 months)	1.00 (0.79, 1.26)	1.06 (0.80, 1.40)	0.84 (0.64, 1.10)	0.83 (0.60, 1.14)	0.84 (0.64, 1.10)	0.83 (0.60, 1.14)	0.83 (0.60, 1.14)	
Single family dwelling	0.70 (0.46, 1.05)	0.76 (0.46, 1.24)	0.74 (0.46, 1.17)	0.72 (0.42, 1.22)	0.74 (0.46, 1.17)	0.72 (0.42, 1.22)	0.72 (0.42, 1.22)	
Older home (built before 1980)	1.25 (1.00, 1.56)	1.32 (1.00, 1.74)	1.10 (0.85, 1.41)	1.09 (0.81, 1.46)	1.10 (0.85, 1.41)	1.09 (0.81, 1.46)	1.09 (0.81, 1.46)	
Homes with air conditioner	0.95 (0.77, 1.17)	0.95 (0.74, 1.22)	1.13 (0.89, 1.43)	1.06 (0.81, 1.40)	1.13 (0.89, 1.43)	1.06 (0.81, 1.40)	1.06 (0.81, 1.40)	
Homes with fireplace	1.10 (0.84, 1.44)	1.17 (0.85, 1.61)	1.01 (0.74, 1.38)	0.92 (0.63, 1.33)	1.01 (0.74, 1.38)	0.92 (0.63, 1.33)	0.92 (0.63, 1.33)	
Homes with dehumidifier	0.89 (0.72, 1.10)	0.91 (0.70, 1.18)	0.85 (0.67, 1.08)	0.83 (0.63, 1.11)	0.85 (0.67, 1.08)	0.83 (0.63, 1.11)	0.83 (0.63, 1.11)	
Homes with humidifier	1.27 (1.00, 1.62)	1.37 (1.03, 1.81)	1.47 (1.13, 1.92)	1.38 (1.02, 1.88)	1.47 (1.13, 1.92)	1.38 (1.02, 1.88)	1.38 (1.02, 1.88)	
Homes with air filter	1.31 (1.06, 1.61)	1.36 (1.06, 1.75)	1.27 (1.00, 1.61)	1.35 (1.03, 1.78)	1.27 (1.00, 1.61)	1.35 (1.03, 1.78)	1.35 (1.03, 1.78)	
Burning fuel source	1.11 (0.81, 1.52)	1.30 (0.90, 1.87)	0.97 (0.67, 1.39)	0.93 (0.60, 1.43)	0.97 (0.67, 1.39)	0.93 (0.60, 1.43)	0.93 (0.60, 1.43)	
Natural gas fuel source	1.04 (0.83, 1.31)	1.04 (0.78, 1.37)	1.08 (0.83, 1.40)	1.01 (0.75, 1.37)	1.08 (0.83, 1.40)	1.01 (0.75, 1.37)	1.01 (0.75, 1.37)	

Table 3: Bivariate association between asthma and wheeze outcomes and behavioural factors. The 2010 Saskatchewan Rural Health Study-Children (n=2,259)

Covariates	Ever wheeze		Current wheeze		Ever asthma		Current asthma	
	Odds ratio (95% Confidence Intervals)		Odds ratio (95% Confidence Intervals)		Odds ratio (95% Confidence Intervals)		Odds ratio (95% Confidence Intervals)	
Children breastfed	0.91 (0.71, 1.17)		0.89 (0.65, 1.20)		0.79 (0.60, 1.04)		0.84 (0.61, 1.17)	
Children previously enrolled in daycare	1.28 (1.04, 1.58)		1.12 (0.87, 1.44)		1.52 (1.20, 1.94)		1.58 (1.19, 2.10)	
Mother smoking (ref: no)								
Mother currently smoke	1.29 (0.99, 1.68)		1.35 (0.98, 1.86)		1.55 (1.15, 2.07)		1.35 (0.95, 1.92)	
Mothers previously smoked	1.24 (0.96, 1.46)		1.38 (1.02, 1.88)		1.56 (1.17, 2.08)		1.57 (1.14, 2.18)	
Mothers smoked during pregnancy	1.34 (1.05, 1.72)		1.37 (1.02, 1.83)		1.33 (1.01, 1.76)		1.33 (0.96, 1.83)	
Father smoking (ref: no)								
Fathers currently smoke	1.11 (0.86, 1.43)		1.12 (0.82, 1.52)		1.17 (0.89, 1.56)		1.11 (0.79, 1.55)	
Fathers previously smoked	1.29 (0.99, 1.68)		1.19 (0.86, 1.64)		1.22 (0.90, 1.65)		1.30 (0.92, 1.83)	
Child smoking (ref: no)								
Yes	1.83 (1.21, 2.75)		2.03 (1.29, 3.22)		1.42 (0.89, 2.29)		1.31 (0.75, 2.29)	
Don't know	0.81 (0.41, 1.60)		0.74 (0.31, 3.22)		0.57 (0.24, 1.36)		0.41 (0.12, 1.34)	
Weekly physical activity	1.09 (0.86, 1.38)		1.04 (0.78, 1.39)		0.94 (0.72, 1.22)		0.90 (0.66, 1.22)	
Early unpasteurized milk consumption	0.69 (0.36, 1.31)		0.77 (0.36, 1.64)		0.96 (0.49, 1.87)		0.87 (0.39, 1.95)	
Current unpasteurized milk consumption	0.96 (0.58, 1.61)		1.42 (0.82, 2.47)		0.93 (0.52, 1.68)		1.07 (0.56, 2.07)	

Table 4: Bivariate association between asthma and wheeze outcomes and wheeze outcomes and health care access factors. The 2010 Saskatchewan Rural Health Study-Children (n=2,259)

Covariates	Ever wheeze		Current wheeze		Ever asthma		Current asthma	
	Odds ratio (95% Confidence Intervals)		Odds ratio (95% Confidence Intervals)		Odds ratio (95% Confidence Intervals)		Odds ratio (95% Confidence Intervals)	
Difficulty getting routine health care	2.65 (1.89, 3.72)		2.35 (1.59, 3.47)		1.93 (1.31, 2.85)		1.77 (1.13, 2.77)	
Distance to routine care >30km	1.21 (0.97, 1.50)		1.18 (0.90, 1.53)		1.10 (0.85, 1.41)		1.31 (0.98, 1.74)	
Distance to emergency care >30km	1.00 (0.80, 1.24)		0.97 (0.75, 1.27)		0.92 (0.72, 1.18)		0.92 (0.69, 1.22)	

Table 5: Bivariate association between asthma and wheeze outcomes and environmental farm-specific factors (farm activities and farm type). The 2010 Saskatchewan Rural Health Study-Children (n=2,259)

Covariates	Ever wheeze Odds ratio (95% Confidence Intervals)	Current wheeze Odds ratio (95% Confidence Intervals)	Ever asthma Odds ratio (95% Confidence Intervals)	Current asthma Odds ratio (95% Confidence Intervals)
Farm Activities				
Haying or playing with or moving hay bales	1.14 (0.89, 1.47)	0.91 (0.67, 1.25)	0.86 (0.63, 1.16)	0.92 (0.65, 1.31)
Feeding livestock	1.30 (1.03, 1.65)	1.24 (0.93, 1.65)	0.96 (0.72, 1.23)	1.06 (0.77, 1.46)
Cleaning or playing in a barn	0.96 (0.73, 1.26)	0.97 (0.70, 1.36)	0.74 (0.53, 1.03)	0.75 (0.51, 1.11)
Filling grain bins	1.10 (0.77, 1.59)	0.73 (0.44, 1.21)	0.64 (0.39, 1.04)	0.65 (0.37, 1.16)
Cleaning or playing in pens	1.03 (0.78, 1.35)	0.93 (0.67, 1.31)	0.73 (0.52, 1.02)	0.70 (0.47, 1.04)
Riding horses	0.94 (0.67, 1.32)	0.79 (0.51, 1.22)	0.70 (0.46, 1.06)	0.73 (0.44, 1.18)
Farm Type				
Living on a grain farm (ref.=farms with no grain production)	1.18 (0.86, 1.61)	1.25 (0.86, 1.82)	0.74 (0.52, 1.06)	0.82 (0.54, 1.24)
Living on a livestock farm (ref.=farms with no livestock)	1.14 (0.83, 1.55)	0.95 (0.65, 1.38)	0.85 (0.59, 1.23)	0.78 (0.51, 1.19)

Table 6: Included vs. excluded in analysis due to missing key variables: The 2010 Saskatchewan Rural Health Study-Children
(n=2,383)

Variable	Included in analysis (n=2259) %	Excluded in analysis (n=124) %	p-value
Farm children	45.3	39.6	0.290
Male sex	49.5	46.0	0.450
Age group			
6-9 years	33.1	28.2	0.524
10-13 years	38.7	40.3	
14-18 years	28.2	31.4	
Father with postsecondary education	46.7	29.1	0.001
Mother with postsecondary education	62.3	45.7	<0.001
Non-Caucasian	9.8	28.0	<0.001
Single parent household	10.8	16.7	0.080
Ever wheeze	21.2	18.6	0.499
Current wheeze	13.0	7.5	0.083
Ever asthma	15.4	8.2	0.034
Current asthma	10.8	3.3	0.010

Appendix H

Ethical Approval



QUEEN'S UNIVERSITY HEALTH SCIENCES & AFFILIATED TEACHING HOSPITALS RESEARCH ETHICS BOARD-DELEGATED REVIEW

August 02, 2011

Ms. Rebecca Barry
Department of Community Health and Epidemiology
Queen's University

Dear Ms. Barry

Study Title: EPID-351-11 Factors Contributing to Risks for Pediatric Asthma in Rural Saskatchewan
File # 6006172
Co-Investigators: Dr. W. Pickett and Dr. J. Lawson

I am writing to acknowledge receipt of your recent ethics submission. We have examined the protocol (June 2011) for your project (as stated above) and consider it to be ethically acceptable. This approval is valid for one year from the date of the Chair's signature below. This approval will be reported to the Research Ethics Board. Please attend carefully to the following listing of ethics requirements you must fulfill over the course of your study:

Reporting of Amendments: If there are any changes to your study (e.g. consent, protocol, study procedures, etc.), you must submit an amendment to the Research Ethics Board for approval. Please use event form: HSREB Multi-Use Amendment/Full Board Renewal Form associated with your post review file # 6006172 in your Researcher Portal (https://eservices.queensu.ca/romeo_researcher/)

Reporting of Serious Adverse Events: Any unexpected serious adverse event occurring locally must be reported within 2 working days or earlier if required by the study sponsor. All other serious adverse events must be reported within 15 days after becoming aware of the information. Serious Adverse Event forms are located with your post-review file 6006172 in your Researcher Portal (https://eservices.queensu.ca/romeo_researcher/)

Reporting of Complaints: Any complaints made by participants or persons acting on behalf of participants must be reported to the Research Ethics Board within 7 days of becoming aware of the complaint. Note: All documents supplied to participants must have the contact information for the Research Ethics Board.

Annual Renewal: Prior to the expiration of your approval (which is one year from the date of the Chair's signature below), you will be reminded to submit your renewal form along with any new changes or amendments you wish to make to your study. If there have been no major changes to your protocol, your approval may be renewed for another year.

Yours sincerely,

Albert J. Clark

Chair, Research Ethics Board
August 02, 2011

Investigators please note that if your trial is registered by the sponsor, you must take responsibility to ensure that the registration information is accurate and complete

QUEEN'S UNIVERSITY HEALTH SCIENCES AND AFFILIATED TEACHING HOSPITALS ANNUAL RENEWAL

Queen's University, in accordance with the "Tri-Council Policy Statement, 1998" prepared by the Medical Research Council, Natural Sciences and Engineering Research Council of Canada and Social Sciences and Humanities Research Council of Canada requires that research projects involving human subjects be reviewed annually to determine their acceptability on ethical grounds.

A Research Ethics Board composed of:

Dr. A.F. Clark, Emeritus Professor, Department of Biochemistry, Faculty of Health Sciences, Queen's University (Chair)

Dr. H. Abdollah, Professor, Department of Medicine, Queen's University

Dr. R. Brison, Professor, Department of Emergency Medicine, Queen's University

Dr. M. Evans, Community Member

Dr. S. Horgan, Manager, Program Evaluation & Health Services Development, Geriatric Psychiatry Service, Providence Care, Mental Health Services Assistant Professor, Department of Psychiatry

Ms. J. Hudacin, Community Member

Dr. B. Kisilevsky, Professor, School of Nursing, Departments of Psychology and Obstetrics and Gynaecology, Queen's University

Mr. D. McNaughton, Community Member

Ms. P. Newman, Pharmacist, Clinical Care Specialist and Clinical Lead, Quality and Safety, Pharmacy Services, Kingston General Hospital

Ms. S. Rohland, Privacy Officer, ICES-Queen's Health Services Research Facility, Research Associate, Division of Cancer Care and Epidemiology, Queen's Cancer Research Institute

Dr. B. Simchison, Assistant Professor, Department of Anaesthesiology and Perioperative Medicine, Queen's University

Dr. A.N. Singh, WHO Professor in Psychosomatic Medicine and Psychopharmacology Professor of Psychiatry and Pharmacology Chair and Head, Division of Psychopharmacology, Queen's University

has reviewed the request for renewal of Research Ethics Board approval for the project **Factors Contributing to Risks for Pediatric Asthma in Rural Saskatchewan** as proposed by **Ms. Rebecca Barry** of the **Department of Community Health and Epidemiology**, at Queen's University. The approval is renewed for one year, effective **August 02, 2012**. If there are any further amendments or changes to the protocol affecting the participants in this study, it is the responsibility of the principal investigator to notify the Research Ethics Board. Any unexpected serious adverse event occurring locally must be reported within 2 working days or earlier if required by the study sponsor. All other adverse events must be reported within 15 days after becoming aware of the information.

Allan F. Clark

Date: July 18, 2012

Chair, Research Ethics Board

Renewal 1 Renewal 2 Extension Code# EPID-351-11 Romeo file# 6006172

QUEEN'S UNIVERSITY HEALTH SCIENCES AND AFFILIATED TEACHING HOSPITALS ANNUAL RENEWAL

Queen's University, in accordance with the "Tri-Council Policy Statement, 1998" prepared by the Medical Research Council, Natural Sciences and Engineering Research Council of Canada and Social Sciences and Humanities Research Council of Canada requires that research projects involving human subjects be reviewed annually to determine their acceptability on ethical grounds.

A Research Ethics Board composed of:

Dr. A.F. Clark, Emeritus Professor, Department of Biochemistry, Faculty of Health Sciences, Queen's University (Chair)

Dr. H. Abdollah, Professor, Department of Medicine, Queen's University

Dr. R. Brison, Professor, Department of Emergency Medicine, Queen's University

Dr. M. Evans, Community Member

Dr. S. Horgan, Manager, Program Evaluation & Health Services Development, Geriatric Psychiatry Service, Providence Care, Mental Health Services Assistant Professor, Department of Psychiatry

Ms. J. Hudacin, Community Member

Dr. B. Kisilevsky, Professor, School of Nursing, Departments of Psychology and Obstetrics and Gynaecology, Queen's University

Mr. D. McNaughton, Community Member

Ms. P. Newman, Pharmacist, Clinical Care Specialist and Clinical Lead, Quality and Safety, Pharmacy Services, Kingston General Hospital

Ms. S. Rohland, Privacy Officer, ICES-Queen's Health Services Research Facility, Research Associate, Division of Cancer Care and Epidemiology, Queen's Cancer Research Institute

Dr. B. Simchison, Assistant Professor, Department of Anaesthesiology and Perioperative Medicine, Queen's University

Dr. A.N. Singh, WHO Professor in Psychosomatic Medicine and Psychopharmacology Professor of Psychiatry and Pharmacology Chair and Head, Division of Psychopharmacology, Queen's University

has reviewed the request for renewal of Research Ethics Board approval for the project **Factors Contributing to Risks for Pediatric Asthma in Rural Saskatchewan** as proposed by **Ms. Rebecca Barry** of the **Department of Community Health and Epidemiology**, at Queen's University. The approval is renewed for one year, effective **August 02, 2012**. If there are any further amendments or changes to the protocol affecting the participants in this study, it is the responsibility of the principal investigator to notify the Research Ethics Board. Any unexpected serious adverse event occurring locally must be reported within 2 working days or earlier if required by the study sponsor. All other adverse events must be reported within 15 days after becoming aware of the information.

Albert F. Clark

Date: July 18, 2012

Chair, Research Ethics Board

Renewal 1 Renewal 2 Extension Code# EPID-351-11 Romeo file# 6006172

Appendix I

Acceptance to Annals of Allergy, Asthma and Immunology



Annals of Allergy, Asthma and Immunology

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Ref.: Ms. No. 12-05-0212R1

Factors Contributing to Risks for Pediatric Asthma in Rural Saskatchewan
Annals of Allergy, Asthma & Immunology

Dear Dr Lawson,

The Editor is pleased to inform you that your manuscript entitled "Factors Contributing to Risks for Pediatric Asthma in Rural Saskatchewan" has been accepted for publication in the Annals of Allergy, Asthma & Immunology.

Please send completed authorship forms, from all authors, to the editorial office (if this has been done, we thank you. Duplicate submission is not necessary but we will inform you if we determine that we do not have a copy of your signed authorship form.) If needed, the authorship form can be found on the EES Log In page.

Authorship forms should be either faxed OR mailed to:

Gailen D. Marshall, MD PhD

Professor of Medicine and Pediatrics

Vice Chair for Faculty Development

Director, Division of Clinical Immunology and Allergy

The University of Mississippi Medical Center

2500 North State Street

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If our automated system has warned us that one or more of your figures are not of publication quality, you will be contacted by the editorial office.

Final acceptance for publication will be contingent upon you providing the editorial office with figures which pass the artwork quality check program.

Sincerely,

Gailen D Marshall, MD, PhD

Editor-in-Chief

Annals of Allergy, Asthma & Immunology