

Weight, Related Lifestyle Behaviours and Asthma in Manitoba Children

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## ABSTRACT

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**Background and Rationale:** Asthma and overweight are public health concerns. Lifestyle, including dietary and activity patterns, is associated with overweight and asthma. Moreover, an association between these two diseases has been described. Yet, few studies have considered these associations longitudinally in youth. **Methods:** Based on data from the 1995 Manitoba Birth Prospective Cohort (n=723, 404 [55.9%] boys), we designed a series of studies to address the question: “Do obesity and related lifestyle behaviours influence asthma and airway hyperresponsiveness (AHR) outcomes in children?” Following protocol for a mixed methods sequential explanatory design study, we first

considered this research question using quantitative methods. Exposure variables included weight status (body mass index (BMI); BMI z-scores; normal weight vs. overweight), diet, physical activity and screen time. Outcome variables included asthma and AHR at 8-10 years old and at 12-13 years old. Quantitative findings provided direction for the qualitative investigations. That is, we sought to further explain some of the quantitative findings using qualitative methods. For the qualitative portion of this dissertation, 15-16 year old youth were purposively selected (Winnipeg residency, asthma status, gender) from the 1995 Manitoba Prospective Birth Cohort. Due to recruitment challenges, participation was supplemented with youth from the Canadian Asthma Primary Prevention Study, using the same purposive selection criteria.

**Quantitative Results:** Overweight at 12-13 years old was associated with a two-fold increased odds of persistent asthma in girls. In contrast, boys within the highest BMI quartile at 8-10 years old were nearly twice as likely to have remittent asthma at 12-13 years old. High vegetable intake was protective against allergic asthma and moderate-to-severe AHR by 50% and 42%, respectively. High screen time at 8-10 years old, particularly amongst overweight youth, was associated with an increased odds of asthma, but not AHR at 8-10 years and 12-13 years; there were no associations between physical activity, asthma and AHR.

**Qualitative Results:** Youth spoke of asthma as a condition that neither limits physical activity, nor is an excuse for refraining from physical activity.

**Conclusions:** Modest evidence that some quantitatively-

measured weight and related lifestyle behaviours during the pubertal years is associated with asthma. Yet, qualitative data suggest that youth with asthma believe that physical activity is achievable despite their condition, although some describe that asthma interferes with physical activity.

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Above all, I thank my husband, **Vladan Protudjer**, for his unwavering support in everything that I do. I love you. Je t'aime. Ich liebe dich. Volim te.

This thesis is dedicated to Sara, Jackson and Julia

## ABBREVIATIONS

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AHR	Airway hyperresponsive / airway hyperresponsiveness
BAMSE	Barn Allergi Miljö i Stockholm - en Epidemiologisk undersökning (Children Allergy Environment in Stockholm - an Epidemiological Survey)
BCE	Before Common Era (previously "Before Christ")
BMI	Body mass index
CAPPS	Canadian Asthma Primary Prevention Study
CE	Common Era (previously "AD: anno domini [Latin: the year of our Lord])
CHILD	Canadian Health Infant Longitudinal Development Study
FFQ	Food Frequency Questionnaire

HREB	Health Research Ethics Board
ISAAC	International Study of Allergies and Asthma in Children
MICH	Manitoba Institute of Child Health
NHS	Nurses' Health Study
OR	Odds ratio
s.d.	standard deviation
Q	quartile
YHEI	Youth Healthy Eating Index
yo	years old
95% CI	95 <sup>th</sup> percent confidence interval

## TABLE OF CONTENTS

---

Abstract.....	ii
Acknowledgements.....	v
Dedication.....	vii
Abbreviations.....	viii
List of Copyrighted Materials.....	xx
<b>Chapter One: Introduction.....</b>	<b>21</b>
Asthma.....	21
<i>History</i> .....	21
<i>Modern Definition, Diagnosis and Treatment</i> .....	22
<i>Prevalence and Phenotypes</i> .....	24
<i>Etiology</i> .....	27
<i>The Sex Shift of Asthma</i> .....	29
Childhood Overweight.....	31

<i>History</i> .....	31
<i>Prevalence</i> .....	32
<i>Definition and Diagnosis</i> .....	32
<i>Body Mass Index</i> .....	34
<i>Consequences</i> .....	35
The Link between Asthma and Overweight.....	35
Limitations of Previous Studies.....	38
Aims of the Thesis.....	38
Methodological Improvements Used in this Research.....	43
Organization of the Thesis.....	44
<b>Chapter Two: Methods</b> .....	47
Overarching Study Design and Population.....	47
Study Protocol.....	49
<i>Visit One: 2003-2005</i> .....	49
<i>Exposure Variables</i> .....	49
<i>Outcome Variables</i> .....	51
<i>Confounding Variables</i> .....	52
<i>Visit Three: 2008-2010</i> .....	53
<i>Exposure Variables</i> .....	53
<i>Outcome Variables</i> .....	55
<i>Confounding Variables</i> .....	56

Sample Size Calculations.....	58
Mixed Methods Design.....	60
<i>Defining Mixed Methods</i> .....	60
<i>Worldview: Pragmatism</i> .....	60
<i>Ethical Approval</i> .....	62
Quantitative Component.....	62
<i>Statistical Analysis</i> .....	62
Qualitative Component.....	64
<i>Rationale for Focus Groups</i> .....	65
<i>Participant Selection and Recruitment</i> .....	66
<i>Study Design</i> .....	68
<i>Implementation</i> .....	69
<i>Analysis</i> .....	71
<i>Thematic Coding</i> .....	71
Merging of Data.....	72

### **Results: Quantitative Studies**

Chapter Three: <i>Associations between Weight and Asthma in Manitoba Youth</i> .....	77
Chapter Four: <i>Low Vegetable Intake is Associated with Allergic Asthma and Moderate-to-Severe Airway Hyperresponsiveness</i> .....	95
Chapter Five: <i>High Screen Time is Associated with Asthma in Overweight</i>	

<i>Manitoba Youth</i> .....	134
<b>Results: Qualitative Study</b>	
Chapter Six: “ <i>Asthma isn’t an excuse, it’s just a condition</i> ”: <i>Perceptions of Physical Activity and Screen Time</i> .....	163
<b>Chapter Seven: Summary and Discussion</b> .....	189
Summary.....	189
Discussion.....	191
<b>Chapter Eight: Integration of Findings</b> .....	199
<b>Chapter Nine: Knowledge Translation</b> .....	208
<b>Chapter Ten: Conclusions</b> .....	214
Study Limitations.....	214
Study Strengths.....	218
Conclusion.....	218
<b>Chapter Eleven: Future Directions</b> .....	220
General Comments.....	221
Quantitative Investigations.....	223
Qualitative Investigations.....	223
Relating Future Directions to Two Existing Cohorts.....	224
Policy Implications.....	230
<b>References</b> .....	230

## Appendices

Appendix A. <i>Letter of Permission from Canadian Respiratory Journal</i> .....	252
Appendix B. <i>Letter of Permission from Journal of Continuing Education for Health Professionals</i> .....	254
Appendix C. <i>Certificates of Ethical Approval from the University of Manitoba Health Research Ethics Board</i> .....	256
Appendix D. <i>Qualitative Study Consent Form</i> .....	259
Appendix E. <i>Qualitative Study Assent Form</i> .....	265
Appendix F. <i>Food Frequency Questionnaire Administered at Visit Three; adapted from the Nurses' Health Study</i> .....	268
Appendix G. <i>Focus Group Interview Guide for Parents of Youth with Asthma</i> .....	273
Appendix H. <i>Focus Group Interview Guide for Youth with Asthma</i> .....	276
Appendix I. <i>Manuscript: Sex Hormone Levels are Not Associated with Asthma in Early Puberty</i> .....	280
Appendix J. <i>Manuscript: Asthma is a Low Priority Among the Layers of Experience Faced by Adolescents</i> .....	307

## LIST OF TABLES

---

1.1	Currently Used Methods of Asthma Diagnosis.....	25
1.2	Asthma Phenotypes.....	28
1.3	Overarching Aims of the Thesis.....	46
2.1	Demographic Characteristics of Participants of the 1995 Manitoba Birth Prospective Cohort Study.....	53
2.2	Data Collection from the 1995 Manitoba Birth Prospective Cohort Study Pertinent to the Thesis.....	56
2.3	Adaptation of the Youth Healthy Eating Index (YHEI) and Dichotomization of Low vs. High Scores.....	57
2.4	Sample Size Calculations Based on Various Beta and Odds Ratio Estimates.....	59

2.5	Specific Quantitative Variables and Questions.....	63
2.6	Characterization of Focus Groups.....	69
3.1	Participant Characteristics.....	79
3.2	Associations between Weight Status and Asthma.....	82
3.3	Associations between Weight Status and Airway Hyperresponsiveness.....	84
3.4	Associations between Weight Change from 8-10 years old to 12-13 years old and Asthma and AHR Outcomes at 12-13 years old.....	86
4.1	Adaptation of the Youth Healthy Eating Index (YHEI) and Dichotomization of Low vs. High Scores.....	117
4.2	Participant Characteristics.....	118
4.3	Logistic Regression Models of Diet Quality and Asthma in Manitoba Children.....	119
4.4	Logistic Regression Models of Diet Quality in Children with Non-Allergic and Allergic Asthma Phenotypes compared to Healthy Children.....	122
4.5	Multivariate Logistic Regression Models of Diet Quality in Children with Mild and Moderate/Severe Airway Hyperresponsiveness compared to Healthy Children.....	124
5.1.	Participant Characteristics: 1995 Manitoba Birth Prospective Cohort Study.....	153
5.2.	The Effect of Physical Activity on Asthma and Airway	

	Hyperresponsiveness.....	154
5.3.	The Effect of Screen Time on Asthma and Airway Hyperresponsiveness.....	155
6.1	Characterization of Focus Groups and Interviews.....	182
6.2	Themes Common to Youth with and without Asthma, and Unique to Youth with Asthma.....	183
8.1	Three Ways of Mixing Data in Mixed Methods Research.....	200
AI-1.	Participant Characteristics.....	302
AI-2.	Logistic Regression of Log Levels of Sex Hormones and Asthma at 12-13 Years Old.....	304
AJ-1:	Selected Questions Posed to Youth during Focus Groups/Interviews to Better Understand Perceptions of Asthma.....	327

## LIST OF FIGURES

---

1.1	Asthma Management Continuum (2010).....	27
1.2	The Increasing Prevalence of Asthma and Overweight/Obesity amongst Canadian Children.....	33
2.1	Design of the 1995 Manitoba Birth Prospective Cohort Study.....	49
2.2	Merging Quantitative and Qualitative Data.....	74
2.3	Procedural Summary of the Present Study.....	76
8.1	Merging Quantitative and Qualitative Data.....	207
	A. Theoretical Representation	
	B. Study Representation	
10.1	Knowledge to Action Cycle (Graham et al., 2006).....	210

AI-1. Box Plot of Boys' Testosterone Levels and Asthma Status at  
12-13 Years old.....305

AI-2. Box Plot of Girls' Estrogen Levels and Asthma Status at 12-13  
Years old.....306

## LIST OF COPYRIGHTED MATERIALS

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### **Figure 1.1 Asthma Management Continuum (2010)**

**Lougheed et al., 2010**

This information was originally published in *Can Respir J.* 2010;17(1):15-24.

See Appendix A for letter of permission

### **Figure 11.1 Knowledge-to-Action Cycle**

**Graham et al., 2006**

This information was originally published in *J Cont Educ Health Prof.*

2006;26:13-24.

See Appendix B for letter of permission

## CHAPTER ONE: INTRODUCTION

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### I. Asthma

#### *History*

The term asthma (ασθμα) was first used in Ancient Greece to describe "panting" or "exhaling with open mouth" (Costra, 2011). In his epic poem, *Iliad*, Homer uses the term "asthma" when describing the siege of Troy. The *Corpus Hippocraticum*, written by Hippocrates (460-360 BCE), contains the first medical reference to asthma, although it remains unclear if the description referred to diagnosis or symptoms. Other mentions of asthma were made by ancient Greek and Middle Eastern philosophers and historians. Through the ages, asthma was

believed to result from bronchial obstruction. Ironically, and as recently as 1930-1950, asthma was perceived as a psychosomatic illness, of psychological etiology. Historically, asthma therapies have included owl's blood in wine (Galen, 130-200 CE), medication, ample rest and chicken soup (Moses Maimonides, 1135-1204 CE) (Costra, 2011) and treatment for concurrent depression (Opolski & Wilson, 2005). It was not until the 1960s that asthma was recognized as an inflammatory disease, and that anti-inflammatory medications were introduced as appropriate treatment (Costra, 2011).

### *Modern Definition, Diagnosis and Treatment*

Asthma remains a disease that is difficult to characterize. Accordingly, the definition put forth by Boulet, Becker, Bérubé, Beveridge and Ernst (1999) over a decade ago remains both current and descriptive.

"Asthma is characterized by paroxysmal or persistent symptoms such as dyspnea, chest tightness, wheezing, sputum production and cough, associated with variable airflow limitation and a variable degree of hyperresponsiveness of airways to endogenous or exogenous stimuli."

(Boulet et al., 1999)

This is the definition of asthma that will be adopted for this dissertation. However, it warrants noting that the terms "asthma" and "wheeze" are often used interchangeably, particularly in studies involving pediatric populations, including the International Study of Asthma and Allergies in Children [ISAAC] (ISAAC, 2011).

Moreover, there are various methods of diagnosing asthma, all of which have unique merits (Table 1.1). General practitioner diagnosis is also common, but is prone to overdiagnosis by the physician and underdiagnosis due low presentation by the patient to the physician. The most robust method for asthma diagnosis is (pediatric) allergist or respirologist assessments as these diagnoses are made by sub-specialists with extensive training in asthma and other respiratory conditions. However, both general practitioner and (pediatric) allergist or respirologist assessments are resource-intensive methods to assess asthma status. Many population-level studies have relied on questionnaires (e.g. ISAAC, Global Initiative for Asthma) and more recently, healthcare administrative database records (e.g. Liem, Huq, Ekuma, Becker & Kozyrskyj, 2007; Kozyrskyj, Mustard & Becker, 2004). Such methods are limited by an understanding of what is meant by “wheeze” or filling of prescriptions for asthma medications, respectively. This latter point is particularly important, as asthma prescriptions may be prohibitively expensive for some families. Given that asthma rates vary by income strata (Garner & Kohen, 2008), healthcare databases may underestimate asthma prevalence. The multiple ways of diagnosing asthma may result in different descriptions of asthma. From a clinical perspective, asthma has been well characterized in terms of its potential physiological consequences.

As asthma is clinically diagnosed based on numerous criteria (described above; Becker, Lemièrre, Bérubé, Boulet, Ducharme, FitzGerald, et al., 2005), it is

not surprising that this condition also has numerous physiological consequences, including contraction of the bronchial smooth muscle, airway constriction, expiratory flow limitation, fibrosis and structural changes of the airway walls (Andreoli, Carpenter, Griggs & Loscalzo). Asthma is characterized by three underlying features: airway inflammation, AHR to various stimuli, and airway obstruction that is at least partly reversible via treatment or spontaneously (Becker et al., 2005). Asthma is also characterized by persistent or paroxysmal symptoms, which include dyspnea, chest tightness, wheezing (Becker et al., 2005). Asthma presence or absence is a binary outcome. But, the presence of asthma exists along a continuum, from controlled to uncontrolled. Not surprisingly, asthma treatment, which includes inhaled corticosteroids, also exists along a continuum (Lougheed, Lemièrre, Dell, Ducharme, Fitzgerald, Leigh, et al., 2010; Figure 1.1)

### *Prevalence and Phenotypes*

Due to array of definitions used to diagnose asthma and the oft-synonymous interpretation of wheeze and symptoms, ascertaining the prevalence of asthma in a given population is challenging. However, what remains clear despite variations in definition or diagnosis is that the prevalence of asthma has increased significantly over the past three decades.

The prevalence of asthma increased in developed countries by three- to fourfold during the latter part of the 20<sup>th</sup> century and the first several years of the

**Table 1.1 Currently Used Methods of Diagnosis**

Diagnostic Method	Benefits	Limitations
(Pediatric) Allergist or Respirologist	specialists familiarity with current guidelines, testing and education	lengthy wait times limited number of specialists
General Practitioner	relative ease of access	underdiagnosis <sup>a-c</sup> or overdiagnosis
Questionnaires	low cost easy to access large populations anonymous	not equivalent to a clinical exam <sup>e</sup> Overdiagnosis <sup>f,g</sup>
Health Administrative Databases	establishes longitudinal trends <sup>g</sup> low cost anonymous	based on prescription data; may underestimate true prevalence

<sup>a</sup>Kolnaar, Beisseln, van den Bosch, Folgering, van den Hoogen & van Weel, 1994

<sup>b</sup>Raherison C, Aboulefath A, Le Gros V, Taytard A & Molimard M, 2006

<sup>c</sup>van Schayck CP, van der Heijden FM, van den Boom & Tirimanna PR, van Herwaarden, 2000

<sup>d</sup>Aaron, Vandemheen, Boulet, McIvor, Fitzgerald, Hernandez  
et al. 2008

<sup>e</sup>Masoli, Fabian, Holt & Beasley, 2004

<sup>f</sup>Hederos, Janson, Bornehad & Hedlin, 2002

<sup>g</sup>International Study of Asthma and Allergies in Childhood

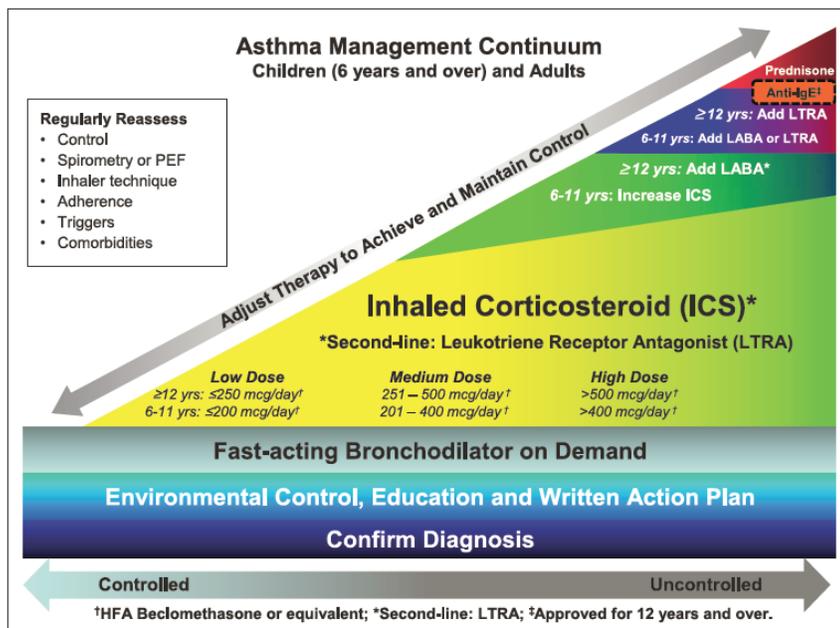
<sup>h</sup>Huzel, Roos, Anthonisen & Manfreda, 2002

21<sup>st</sup> century (Burney, Chin & Rona, 1990; Ninan & Russel, 1992; Manfreda, Becker, Wang, Roos & Anthonisen, 1993; Garner & Kohen, 2008). This increase can be explained almost entirely by the rise in asthma prevalence in children (Garner & Kohen, 2008). In Canada, approximately 12% of children have asthma of varying severities (Garner & Kohen, 2008) based on a composite score of parent/guardian-reported answers to questions about diagnosis of asthma, the number of asthma attacks in the previous 12 months, use of asthma inhalers, and presence of whistling/wheezing in the chest in the past 12 months. Nearly half of the children in the general population who received at least one prescription for asthma medications had a mild form of the disease (Kozyrskyj, Mustard & Simons, 2002). However, any degree of asthma severity has the potential to be problematic if not properly controlled.

Several phenotypes of wheezing, based on timing of onset and persistence of symptoms, have been described (Table 1.2). In children, the most common phenotype is allergic asthma. Those at greatest risk for developing this phenotype are children with a family (particularly maternal) history of atopy or asthma, with onset typically before 12 years of age. The timing of onset is suggestive of a genetic-environmental interaction influencing the innate and adaptive immune systems (Kylie, Smith & Noel, 2007). Other phenotypes include various forms of wheeze (Table 1.2). As the label of wheezing implies, these conditions may not be asthma as defined by a pediatric allergist. They are nonetheless important characterizations, as they may be predictive of future

asthma (Wright, 2002).

**Figure 1.1 Asthma Management Continuum (2010)**



(This information was originally published in Can Respir J. 2010;17(1):15-24.)

The prevalence of asthma remains high. Numerous attempts have been made to understand the etiology of asthma, but its true origins remain elusive. This is likely because it is a disease that is not the result of a single insult.

### *Etiology*

Asthma is a multi-factorial inflammatory disease of unclear etiology, but which likely results from both genetic and environmental insults. By birth, a genetic predisposition towards asthma has already been established. Genetic predisposition may involve innate immunity and immunoregulation, T-helper

**Table 1.2 Asthma Phenotypes**

Phenotype	Age of Onset	Description
Allergic Asthma	By 12 years	Most common phenotype of asthma in children Risk factors include family (maternal) history atopy/ asthma Characterized by a concomitant positive skin prick test to common allergens
Non-Allergic Asthma	Early life	Asthma diagnosis in the absence of a positive skin prick tests to common allergens
Transient Wheeze	0-5 years	Remittance by school age
Late-Onset Wheeze	6-9 years	Onset in school age
Intermittent Wheeze	0-9 years	≥ 1 wheezing episode during preschool or primary school
Persistent Wheeze	0-9 years	≥ 2 wheezing episode during preschool or primary school; usually atopic asthma Predictive of reduced lung function in adulthood

(Th) 2 cell differentiation and effector functions, epithelial biology and mucosal immunity, and function, airway remodeling and asthma severity. Given these various groups of genes, it is not surprising that there have been numerous inconsistencies in identifying the genes associated with asthma (Vercelli, 2008). An international genome wide association study, which included data from participants of the 1995 Manitoba Prospective Birth Cohort, provided strong evidence that asthma is a heterogeneous disease that has outcomes that cannot be predicted solely on genetics (Moffatt, Gut, Demenais, Strachan, Bouzigon, Heath, et al., 2010). Environmental insults, particularly in early life, interact with this genetic predisposition, such that those who go on to develop asthma are both genetically predisposed and also receive an appropriate environmental

stimulus. For this reason, a clinical assessment of early life events associated with asthma development must include a comprehensive history.

Queries should address environmental stimuli associated with asthma susceptibility and exacerbation, including but not limited to environmental tobacco smoke (ETS) (Landau, 2008), indoor allergen exposure such as mould (Arshad, Tariq, Matthews & Hakim, 2001), maternal distress (Kozyrskyj, Mai, McGrath, HayGlass, Becker & Macneil, 2008), nutrition (Lands, 2007), including duration of breast-feeding (Fredriksson, Jaakkola & Jaakkola, 2007), and overweight (Castro-Rodríguez, Holberg, Morgan, Wright & Martinez, 2001; Gold, Damokosh, Dockery & Berkey, 2003; Guerra, Wright, Morgan, Sherrill, Holberg & Martinez, 2004).

There has been some investigation into how genetics and the built environmental influence asthma outcomes. However, the role of lifestyle behaviours, including weight, nutrition and activity, that potentiate childhood asthma remains unclear. Further confounding our understanding of asthma etiology is the shift in asthma prevalence from male to female predominance during puberty.

### *The Sex Shift of Asthma*

Sex plays an interesting role in the timing of asthma onset. In the post-pubertal years, there is a shift towards a higher prevalence of asthma amongst females both due to an increased incidence amongst females and resolution of

asthma symptoms amongst males. This pubertal shift has been documented in numerous populations (Tollefsen, Langhammer, Romundstad, Bjermer, Johnsen & Holmen, 2007; Nicolai, Pereszlenyiova-Bliznakova, Illi, Reinhardt & von Mutius, 2003), including Manitoba children (Manfreda et al., 1990). This may result from lung development beginning *in utero*, where females exhibit more rapid lung maturity than males (Fleisher, Kulovich, Hallman & Gluck, 1985). The female prenatal lung has higher levels of surfactant than males, which may assist in reducing surface tension, preventing alveolar and airway collapse, and facilitate the transition to air breathing (Mendelson, 2000). The delay in males' production of lung surfactant is partly a result of androgens (Neilsen, Kirk, Sweezey & Torday, 1990). From puberty onward, the prevalence of asthma shifts to female predominance (Manfreda, 1990). This sex shift coincides with female development of higher levels of body fat (Katzmarzyk, Srinivasan, Chen, Malina, Bouchard & Berenson, 2004) and female sex hormones progesterone and estrogen.

Several sex-specific shifts during puberty may influence this shift. For example, females gain five times the fat mass of males during the pubertal years (Bitar, Vernet, Coudert & Vermorel, 2000). Gender-specific lifestyle, including physical activity and dietary patterns, changes also occur. Physical activity amongst girls, but not boys, is reduced by 50% (Goran, Gower, Nagy & Johnson, 1998). Similarly, boys have a higher daily energy expenditure and energy intake (Bitar et al, 2000; Kemper, Post, Twisk & van Mechelen, 1999) but lower fruit and

vegetable intake than girls (De Boudeaudhuij, te Velde, Brug, Due, Wind, Sandvik et al, 2008) while girls are more likely to report dieting behaviours (Fonseca & Matos, 2011). Ironically, girls who diet are more likely to have higher vegetable intake than girls who do not diet (Bas & Kiziltan, 2007). Few longitudinal studies have examined the influence of these factors as determinants of the sex-specific shift in asthma rates.

## **II. Childhood Overweight**

### *History*

Unlike asthma, which dates from ancient times (Costra, 2011), childhood overweight is a modern disease. Fifty years ago, there were only a few studies in which childhood overweight and/or obesity were considered (Lloyd, Wolff & Whelen, 1961). Within the past half-century, rates of childhood overweight and obesity have reached epidemic highs (Shields, 2004). For the first time in recorded history, "today's children will be the first generation for some time to have poorer health outcomes and a shorter life expectancy than their parents" (Standing Committee on Health, 2007). Interestingly, rates of overweight and obesity increased in parallel with rates of asthma in youth, suggesting a potential association (Figure 1.2). In the 1980s, the prevalence of childhood asthma and overweight were 3% and 20%, respectively. These rates rose to 10% and 29%, respectively in the mid 1990s. By the 21<sup>st</sup> century, the prevalence of asthma amongst Canadian children was estimated at 11% and the prevalence of

childhood overweight was 31% (Tremblay & Willms, 2000; Dik, Anthonisen, Manfreda & Roos, 2006; Shields, 2006; Garner & Kohen, 2008).

### *Prevalence*

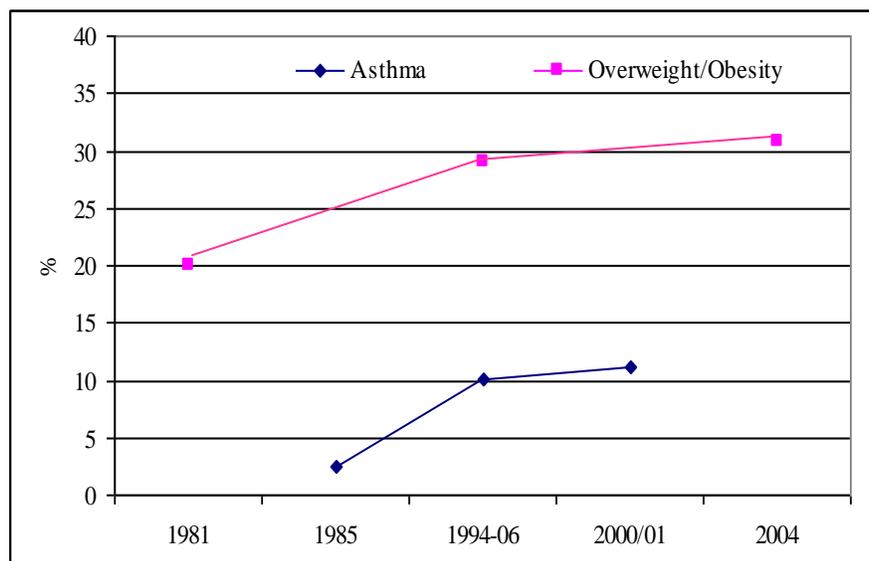
Childhood obesity has reached epidemic proportions in developed nations, and amongst privileged populations in developing countries. The obesity epidemic in high-income countries (Tremblay, Pérez, Ardern, Bryan & Katzmarzyk, 2005; Shields, 2006) and amongst the urban and privileged populations of developing nations (Poskitt, 2009) is the most pressing pediatric public health concern in several countries, including Canada. In Canada, 26% of adolescents aged 12-17 years are overweight or obese, while one in 10 adolescents is considered to be obese, a rate three-fold higher than the rates from 1978-79 (Shields, 2006). Manitoba youth are disproportionately affected by this trend (Shields, 2006), where 35% of 12-17 year-olds are either overweight or obese (Yu, Protudjer, Anderson & Fieldhouse, 2010). While a genetic influence has been described as a causal factor (Wardle, Carnell, Haworth & Plomin, 2008), these increases have been widely attributed to changes in the familial, socio-cultural and built environments (Anderson & Butcher, 2006). The rapid rise in childhood overweight is a significant public health concern.

### *Definition and Diagnosis*

The World Health Organization (WHO) defines childhood obesity as

“excessive body fat with high morbidity” of epidemic proportions (WHO, 2000). There are numerous consequences of childhood obesity (see *Consequences*, pages 35-36), including an increased likelihood of being an obese adult (Freedman, Khan, Serdula, Dietz, Srinivasan & Berenson, 2005). The reader will note that I use childhood overweight and childhood obesity interchangeably. By definition, these are discrete terms (Dietitians of Canada, 2004). But, throughout this thesis, I do not distinguish between the two unless explicitly stated.

**Figure 1.2. The Increasing Prevalence of Asthma and Overweight/Obesity amongst Canadian Children**



(Adapted from Tremblay & Willms, 2000; Dik, Anthonisen, Manfreda & Roos, 2006; Shields, 2006; Garner & Kohen, 2008)

While clinically evident obesity can be easily diagnosed, overweight is much more difficult to diagnose (WHO, 2000). Ideally, a diagnosis is based on knowledge of total fat mass. This measure can be best obtained via indirect measures, such as hydrodensitometry or dual-energy x-ray absorptiometry (DEXA). However, these measures are invasive, expensive and require special equipment. As such, they are not commonly used to define obesity at the population-level (WHO, 2000). Rather, anthropometric measures, such as indices based on weight and height, are more commonly used in the diagnosis of childhood obesity. These measures are less invasive and less costly than measures of body fat, and do not require special equipment (WHO, 2000).

### *Body Mass Index*

The most common variable used to diagnose obesity is the body mass index (BMI). BMI is a calculation of weight [kilograms (kg)] divided by height [metres squared ( $m^2$ )], which, in children, is based on age- and sex-specific percentiles or statistically-derived values that represent that adult cut-points for overweight ( $\geq 25 \text{ kg}/m^2$ ) and obesity ( $\geq 30.0 \text{ kg}/m^2$ ) (46). Using percentile criteria, overweight and obesity are defined as  $\geq 85^{\text{th}}$  and  $\geq 95^{\text{th}}$  percentiles, respectively, for age and sex. These measures are accepted by many Canadian associations, including the Canadian Pediatric Society (Dietitians of Canada, 2004). While BMI is not without limitations, not the least of which is an inability to assess body fat (WHO, 2000), it is widely used. Self-/parent-reports of height

and weight continue to be employed (Okabe, Itazawa, Adachi, Yoshida, Ohya, Odajima, et al., 2011), despite the fact that such reports of height and weight are often over- and under-reported, respectively (Maximova, McGrath, Barnett, O'Loughlin, Paradis & Lambert, 2008). This may result in an inaccurate portrayal of weight status (e.g. overweight, BMI quartiles). An objective description of weight status is critical, given the multitude of adverse events associated with childhood overweight.

### *Consequences*

Excess weight in childhood also has numerous physiological consequences. In his classic review, Dietz (1998) identified that that obese children and youth exhibit cardiovascular abnormalities, including hyperlipidemia, hypertension and abnormal glucose tolerance that persist to adulthood. Other conditions associated with childhood obesity include early female puberty (Lee, Appugliese, Kaciroti, Corwyn, Bradley & Lumeng, 2007) and type 2 diabetes mellitus (Young, Dean, Flett & Wood-Steiman, 2000), amongst others (Agranat-Meged, Deitcher, Goldzweig, Leibenson, Stein & Galili-Weisstub, 2005; Cindik, Baskin, Agras, Klinik, Turan & Saatci, 2005; Dunn & Schwimmer, 2008).

### **III. The Link between Asthma and Overweight**

Both asthma (Garner & Kohen, 2008) and overweight (Yu et al., 2010)

disproportionately affect youth. Numerous studies have explored the concurrent increase in (e.g. Schachter, Peat & Salome, 2003; Spathopoulous, Paraskakis, Trypsianis, Tsalkidis, Arvanitidou, Emporiadou, et al., 2009; Tai, Volkmer & Burton, 2009; see Figure 1.2), and common mechanisms (e.g. Canöz, Erdened, Uzun, Müderrisoglu & Aydin, 2008; Mai, Chen & Krewski, 2009; Shore, 2008; Sood, Qualls, Arynchyn, Beckett, Gross, Steffes, et al., 2009) of asthma and obesity. This association is most pronounced in girls who reach puberty at an early age (Castro-Rodríguez et al., 2001; Herrera-Trujillo, Barraza-Villarreal, Lazcano-Ponce, Hernández, Sanín & Romieu, 2005).

The importance of physical activity and nutrition in the prevention of overweight are perhaps obvious. Daily fruit and vegetable intake and physical activity are protective against overweight, while more time spent in sedentary behaviours increases the risk of overweight (Yu et al., 2010). But, similar parallels have also been made between diet, physical activity and sedentary behaviour and asthma (Lucas & Platts-Mills, 2005; Rosenlund, Kull, Pershagen, Wolk, Wickman & Bergström, 2011).

To date, all of the works investigating the link between asthma and overweight have been quantitative in design. Many have relied on questionnaires to determine the presence of asthma (Castro-Rodríguez et al., 2001; Chu, Chen, Wang, Tseng, Wu & Ko, 2009; Tai et al., 2009; Vázquez-Nava, Morales Romero, Cordova Fernandez, Saldívar-González, Vázquez-Rodriguez, Barrientos Gomez Mdel, et al., 2010; Ho, Lin, Caffrey, Lin, Hsu, Myers et al.,

2011; Okabe et al., 2011) and/or cross-sectional designs (Chu et al., 2009; Tai et al., 2009; Vázquez-Nava et al., 2010; Okabe et al., 2011).

Both obesity and asthma both have physical impacts, as previously discussed. But, these conditions also have psychological effects, including decreased quality of life (Chiang, 2005; de Beer, Hofsteenge, Koot, Hirasing, Delemarre-van de Waal & Gemke, 2007; van Gent, van Essen, Rovers, Kimpen, van der Ent, de Meer, 2007), decreased school performance (Falkner, Neumark-Sztainer, Story, Jeffrey, Beuhring & Resnick, 2001; Silverstein, Mair, Katusic, Wollan, O'Connell & Yunginger, 2001) and substance abuse (Bender, 2007; Farhat, Iannotti & Simons-Morton, 2010). In order to truly gain a better understanding of these psychological effects, which may ultimately be ways of coping with asthma and overweight, it is necessary to heed participants' voices. This is achieved through qualitative methods (Patton, 2002). Thus, an enhanced understanding of asthma and overweight will be realized through a combination of quantitative and qualitative approaches. This is the rationale for mixed methods research. This emerging method is described extensively in Chapter 2. For the moment, I simply provide the reader with a definition of mixed methods:

Mixed methods research is a research design with the *philosophical assumptions* as well as *methods of inquiry*. As a methodology, it involves philosophical assumptions that guide the direction of the collection and analysis of data and the mixture of qualitative and quantitative approaches in many phases in the research process. As a method, it focuses on collecting, analyzing, and mixing both quantitative and qualitative data in a single or a series of studies. Its central premise is that *the use of quantitative and qualitative approaches in combination provides a better understanding of research problems than either approach alone*.

(Creswell & Plano Clark, 2007; emphasis added)

#### IV. Limitations of Previous Studies

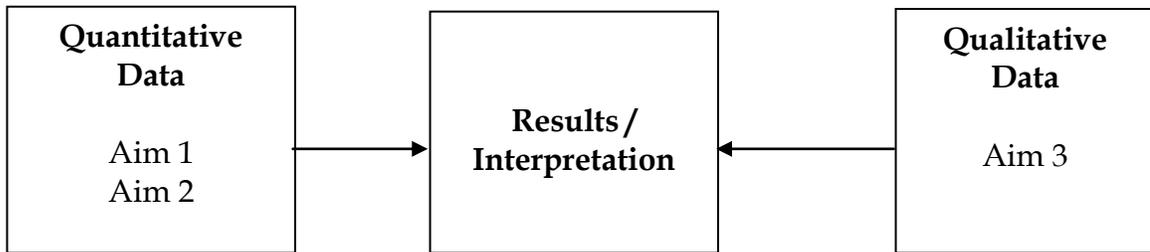
1. Studies addressing weight and asthma in youth have been solely quantitative in design. Recommendations on addressing weight and asthma are made without understanding of the perceptions of those living with asthma.
2. Many studies investigating the association between asthma and weight were cross-sectional in design, which pre-empts findings on causality.
3. Self-/parent-reports of height and weight continue to be used, while this methodology may result in inaccurate interpretations of weight status (e.g. overweight, BMI quartiles) in the study population.
4. Many studies have relied on asthma outcomes based on questionnaire reports, which may overestimate asthma prevalence due to differences in interpretation of the questions.
5. Few studies have considered objective assessments of AHR.

#### V. Aims of the Thesis

**To address these limitations we have developed the following aims that will guide the current thesis:**

**Comprehensive Research Question:**

Do obesity and related lifestyle behaviours influence asthma and airway hyperresponsiveness outcomes in children?



## A. QUANTITATIVE

### **Aim 1. To describe the association between weight and asthma**

*What is known:*

- Youth, particularly girls, who are overweight are more likely to also develop (present with) asthma.

*What is missing:*

- The association between weight, asthma and AHR.

*Hypothesis:*

- 1) Overweight/obesity is associated with a risk of asthma and AHR among youth 8-14 yo.

*Study Design:*

- To address this particular aim, we will rely on cross sectional, plus data from a single prospective cohort of youth assessed at 8-10 yo and 12-13 yo.
- Cross-sectional:
  - Weight, AHR and asthma at 8-10 yo
  - Weight, asthma (presence, persistent, remittent, incident) and AHR

at 12-13 yo

- Longitudinal:
  - Weight at 8-10 yo, asthma (persistent, remittent, incident) and AHR at 12-13 yo
  - Weight change ( $\Delta$  z-scores from 8-10 yo to 12-13 yo), asthma (persistent, remittent, incident) and AHR (12-13 yo,  $\Delta$  AHR from 8-10 yo to 12-13 yo)
- Exposure: Weight (lean vs. overweight, BMI quartiles) at ages 8-10 and 12-13 yo.
- Outcomes: Asthma status at 12-13 yo, persistent asthma, remittent asthma, incident asthma, AHR at 12-13 yo

**Aim 2. To determine if lifestyle patterns, specifically diet quality, physical activity and screen time are associated with asthma.**

*What is known:*

- Collectively, there is some evidence that certain nutrients (Vitamins A, D, E), foods (fruits) and a Mediterranean-style diet are protective against asthma, while other foods (e.g. fast foods) may be associated with an increased odds of asthma

*What is missing:*

- The association of diet quality beyond “Mediterranean-style” vs. western-style diet has not been well described in children.

- Associations between diet quality and different asthma phenotypes have not been reported.
- Associations between physical activity/sedentary (screen) time and asthma in children are collectively inconclusive.

*Hypotheses:*

Among youth 8-13 yo,

- 1) There is an inverse association between diet quality and asthma, in particular with allergic asthma.
- 2) Diet quality is also inversely associated with AHR.
- 3) High levels of physical activity and low levels of screen time are associated with less asthma and normal airway responsiveness.

*Study Design:*

A. Diet Quality and Asthma

- Cross-sectional: Exposures and outcomes all based on data collected at 12-13 yo (NOTE: The method of dietary assessment used at 8-10 yo prohibited testing for longitudinal associations between diet quality (exposure at 8-10 yo) and incident asthma (outcome at 12-13 yo).
- Exposure: Diet quality at 12-13 yo as calculated based on food frequency questionnaire (FFQ) and Youth Healthy Eating Index.
- Outcomes: Asthma status at 12-13 yo, asthma phenotypes (non-allergic asthma and allergic asthma) at 12-13 yo

## B. Physical Activity, Screen Time and Asthma

### *Study Design i*

- Cross-sectional: Exposures and outcomes all based on data collected at 8-10 yo
- Exposure: Asthma status at 8-10 yo
- Outcome: Physical activity and screen time, based on parental report, at 8-10 yo

### *Study Design ii*

- Cross-sectional: Exposures and outcomes all based on data collected at 8-10 yo
- Longitudinal: Exposures based on data at 8-10 yo; outcomes based on asthma and AHR at 12-13 yo
- Exposure: Physical activity and screen time, based on parental report, at 8-10 yo
- Outcome: Asthma and AHR at 8-10 yo and 12-13 yo

## **B. QUALITATIVE**

**Aim 3. To describe the lived experience of youth with asthma, specifically by comparisons of perceptions of physical activity and screen time by asthma status.**

*What is known:*

- Youth with asthma strive to normalize their lives by engaging in physical

activity, although perceptions of physical activity amongst youth with asthma are collectively inconclusive.

*What is missing:*

- Perceptions of asthma amongst teen-aged youth.
- Description of themes relating to physical activity and screen time common to, and disparate between youth with and without asthma.

*Research Questions:*

1. How do youth with and without asthma perceive physical activity and screen time?

*Study Design:*

- Framework: Pragmatism
- Interviews and focus groups of youth now aged 15-16 yo and their parents, by asthma status and gender

## **VI. Methodological Improvements Used in this Research**

This study has five characteristics that contribute to its strength and uniqueness.

1. (Pediatric) allergist/respirologist assessment for asthma is the gold standard for asthma diagnosis. We can confidently state that those participants in our study truly have the disease.
2. Oversampling for asthma in this study (34%), a rate approximately three

times greater than the Canadian prevalence of asthma in youth (Garner & Kohen, 2008), provides the opportunity to “tease” apart subtle differences (including by asthma phenotype) that would not have been otherwise identifiable in a sample of this size.

3. Measured heights and weights provide a clear and accurate description of the weight status of participants. The rate of overweight in our study was 34%. This is comparable to the rate of overweight/obesity in Manitoba youth (31%), also based on measured heights and weights (Yu et al., 2010). In this respect, our findings can be considered generalizable.
4. A mixed methods design offers insights into asthma and youth that cannot be gleaned from a single research paradigm. The integration of these findings provides a unique explanation of the studies (Chapter 8).
5. Methacholine challenges to objectively determine AHR provide a reflection of heightened airway sensitivity to inhaled agonists that may be used to characterize asthma particularly among individuals with asthma-like symptoms but who do not exhibit obvious airflow obstruction.

## **VII. Organization of the Thesis**

This thesis is composed of 11 chapters. In addition to this introductory chapter, there is a chapter on methods (Chapter 2; Methods), a chapter in which the associations between weight, asthma and AHR are described (Chapter 3; Associations between Weight and Asthma in Manitoba Youth) as well as three

chapters of manuscripts based on Aims 2 and 3 of this dissertation (Table 1.3). These manuscripts have either been submitted for publication (Chapter 4), or will be submitted for publication in the near future (Chapters 5 and 6). Given the 'sandwich-style' of this thesis, each of the three manuscripts is 'stand alone;' that is, each contains a brief introduction, methods, results, conclusions, references, tables and figures specific to the purpose of each manuscript. I have made attempts to avoid excessive redundancy between the introductory information provided in this chapter and the introduction of each manuscript. No doubt that there is some repetition of content. It is my hope that this repetition serves to contextualize the information in the methods section, rather than distract the reader.

Chapter 7 is a summary and discussion of the key findings of each of the studies.

Chapter 8, *Integration of Findings*, serves to merge the findings of each study. But, more importantly, it synthesizes the findings of the quantitative and qualitative findings, as is the purpose of mixed methods studies, to glean greater insight than either method alone.

**Table 1.3 Overarching Aims of the Thesis**

Aim	Corresponding Chapter
1 To determine the association between asthma, AHR and weight weight status	3
2 To determine if lifestyle pattern changes, specifically diet quality, physical activity and screen time are associated with the development of asthma and AHR	4 5
3 To describe the lived experience of asthma at ages 12-13, specifically by comparisons of physical activity and screen time by asthma status	6

Chapter 9, titled 'Knowledge Translation,' focuses on putting these findings into action. This is done in the context of the Canadian Institutes of Health Research-endorsed knowledge-to-action (KTA) cycle (Graham, Logan, Harrison, Straus, Tetro, Caswell, et al., 2006).

Chapter 10 provides conclusions based on the findings of this thesis, while Chapter 11 is a discussion of future directions.

## CHAPTER TWO: METHODS

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### **Overarching Study Design and Population**

This dissertation is a series of four studies based predominantly on data collected from the 1995 Manitoba Prospective Cohort Study, which has been described elsewhere (Kozyrskyj, HayGlass, Sandford, Paré, Chan-Yeung & Becker, 2009). This overarching cohort is reflective of a component of time with the data collection, and repeat measurements of the same outcome (Young, 2005; Dr. Robert Tate, Associate Professor and Director of the Manitoba Follow-Up Study, University of Manitoba, personal communication, Thursday 18 August 2011)). This study is analytic and observational in nature and features no

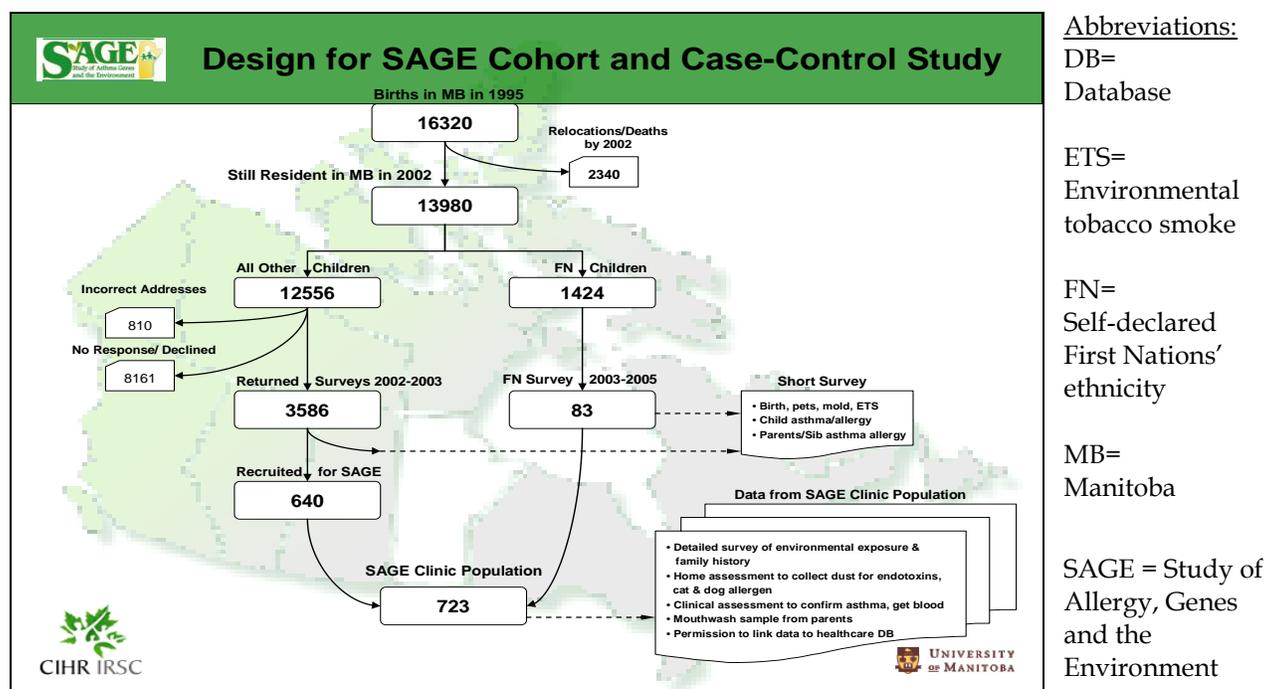
randomization or intervention. End-points include asthma and AHR outcomes, both cross-sectionally and prospectively.

This dissertation is based on data collected from children enrolled in the 1995 Manitoba Prospective Cohort Study. In that year, all of the healthcare databases in Manitoba became interactive. Manitoba database studies have been conducted, and continue to be conducted, using data collected prospectively from birth. This makes Manitoba an ideal location in which to develop prospective cohorts and subsequently studies, such as the one on which this thesis is based.

Briefly, and with regard to the present study, in 2002, letters were sent to families of children born in Manitoba in 1995 and who still resided in the province. Of the ~14000 letters sent, approximately 3500 were returned (Figure 2.1). Those families who reported that their child had a previous physician diagnosis of asthma were invited to participate ("cases"), along with controls matched for sex, region of residence (urban [Winnipeg, Brandon], southern rural, and northern) and ethnicity (First Nations vs. non-First Nations). This yielded a study population of 723 children, including 246 (34.0%) cases (of which 149 [60.5%] were boys) and 477 (66.0%) controls (of which 255 [53.5%] were boys). Children were invited to attend an initial clinic visit in 2003-05, and have been followed prospectively on an approximately biennial basis since that time. To date, this has resulted in three clinic visits: Visit One in 2003-2005, Visit Two in 2005-2007, and Visit Three in 2008-2010. No assessments were made for asthma

or AHR at Visit Two, nor were any data on diet and activity collected at this time point. As such, this thesis is based only on data collected at Visit One and Visit Three. Although numerous questionnaire data and biological samples were collected, and multiple clinical assessments were made at Visit One and Visit Three, only those pertinent to this thesis are discussed below.

**Figure 2.1 Design of the 1995 Manitoba Prospective Cohort Study**



## Study Protocol

### Visit One: 2003-2005

#### *Exposure Variables*

Trained nurses and/or research assistants measured, in triplicate, participants' heights (stadiometer; Holtain Ltd., Crymych, Dyfed, UK) to the

nearest 0.1 cm and weights (scale; Health O Meter; Mettler-Toledo, Inc., USA) to the nearest 0.1 kg, and then took the mean of these three measures, from which children's body mass indices (BMI) were derived using the formula developed by Adolphe Quetelet (1796-1874):  $BMI = \text{weight [kg]} / \text{height [metres squared]}$ . As well, BMI z-scores were calculated using the Centers for Disease Control and Prevention criteria (2011). Children were subsequently classified as normal weight or overweight based on age- and sex-appropriate BMI cut-offs at a stratification threshold of the 85<sup>th</sup> percentile for normal weight vs. overweight (Cole, Bellizzi, Flegal & Dietz, 2000); these are the criteria accepted by the Canadian Pediatric Society (CPS, 2004).

Parents answered closed-ended responses about the frequency of their child's physical activity levels and screen time frequency. Moderate-to-vigorous physical activity frequency was determined from a close-ended parental responses to the following question: "In the last 12 months, how many times a week does your child engage in vigorous or competitive physical activity long enough to make him/her breathe hard?" Possible responses included: never/only occasionally, 1-2 times per week, or most/all days. Physical activity was treated as a binary outcome of inactive (never/only occasionally + 1-2 times per week) or active (most/all days), representing youth that did or did not meet the CPS's (CPS, Healthy Living Statement) recommendation of achieving  $\geq 90$  minutes per day of total physical activity. Frequency of screen time was also assessed with a close-ended response to the following question: "Currently,

during a normal week, how many hours a day does your child watch television or play on the computer before or after school?" Possible responses included <1 hour, 1 to <3hours, 3 to <5hours, or  $\geq$ 5hours. Screen time was treated as a binary outcome with a threshold of screen time above or below 3 hours daily. While the CPS recommends  $\leq$  2 hours of television per day (CPS, Media Statement), we chose to be aggressively conservative in interpreting the effects of screen time. Potential confounding variables for both physical activity and screen time included sex, parental socio-economic status, weight status, region of residence and ethnicity.

### *Outcome Variables*

All 723 children were assessed by a pediatric allergist for asthma. Asthma status was ascertained based on the Canadian Asthma Consensus Guidelines (Becker et al., 2006).

Trained nurses and/or research assistants conducted methacholine (Methapharm Inc.) challenges using the Cockcroft technique (Cockcroft, Killian, Mellon & Hargreave, 1977). AHR was treated as a binary outcome. Children were classified as having normal airway responsiveness if the provocative concentration of methacholine required to decrease participants' forced expiratory volume in one second [FEV<sub>1</sub>] by 20% (PC<sub>20</sub>) by greater than 8 mg/ml, or AHR if their PC<sub>20</sub> was equal to or less than 8mg/ml. Those with AHR were subsequently subclassified as mild (PC<sub>20</sub>: 8-2 mg/ml), moderate (PC<sub>20</sub>: 2-0.25

mg/ml) or severe (PC<sub>20</sub>: <0.25 mg/ml).

### *Confounding Variables*

Parents completed numerous questionnaires with regards to other exposures and potential confounders. Those pertinent to the present study include breastfeeding (binary [never vs. ever]; duration), region of residence (urban, rural, northern); annual family income (in \$10000 increments to a maximum of \$80000 or more); parental education (less than high school, high school, college/trades, university); ethnicity (Caucasian, First Nations, Métis, Asian, other), parental health history, including smoking and maternal history of asthma (Table 2.1). To ensure rigorous data analysis, several of the parent-reported data were collapsed. For example, income was dichotomized as >\$30000 vs. ≤\$30000, parental education as at least some post-secondary training vs. high school or less, and ethnicity, which is presented as Caucasian vs. First Nations due to a low number of participants of other ethnicities.

**Table 2.1 Demographic Characteristics of Participants of the 1995 Manitoba Birth Prospective Cohort**

	Visit One		Visit Three		
	n	%	n	%	
N	723	100.0	489	100.00	
Boys	404	55.9			
Age (years)*	8.6 ± 0.5		12.6 ± 0.5		
Asthma	Overall	246	34.0	151	30.9
	Boys	149	60.5	83	55.0
AHR†		270	39.7	211	43.4
	mild	135	50.0	110	41.1
	moderate/severe	135	50.0	151	57.9
Weight Status	normal	491	67.9	335	68.9
	overweight	232	32.1	151	31.1
Region of Residence	urban	374	51.7	271	55.8
	southern rural	266	36.8	177	36.4
	northern	83	11.5	38	7.8
Annual Family Income	<\$30000	193	26.7	57	13.1
	≥\$30000	530	73.3	378	86.9
Ethnicity	Caucasian	522	72.2	371	81.9
	First Nations	150	20.7	82	18.1

\*mean ± standard deviation

†Airway hyperresponsiveness

### Visit Three: 2008-2010

#### *Exposure Variables*

Trained nurses and/or research assistants measured participants' heights and weights, using the same protocol and equipment described in the section, "Visit One."

Information on children's diets at was collected via parent/guardian- and child report using a 39-item food frequency questionnaire (FFQ) adapted from

the Nurses' Health Study (Willett, 1990) administered at Visit 3 (Appendix F). Subsequently, we determined diet quality via an adapted version of the Youth Healthy Eating Index (YHEI) (Feskanich, Rockett & Colditz, 2004). The YHEI is derived from the USDA's Dietary Guidelines for Americans (Willett, 1990). These guidelines (USDA, 2005) are similar to those outlined in Canada's Food Guide to Healthy Eating (Health Canada, 2007). The FFQ used in the present study was not originally designed to assess diet quality using the YHEI. Thus, some adaptations to component and overall scores were necessary (Table 2.4). Some of these excluded foods included cottage cheese, hard cheese and liver (attempts to reduce number of questions and thus participant burden; not anticipated to greatly alter diet quality scores), coffee and tea (comparable aged children consume only modest amounts [ $<250\text{mL}$ ] of such beverages per day (Wrieden, Longbotton, Adamson, Ogstom, Payne, Haleem, et al., 2008), and alcoholic beverages.

The FFQ were completed primarily by participants. Although it is not possible to say definitively, we suspect that some of the questions were completed solely by the parents. These would have included questions regarding the types of oil used for cooking, use of n-3 enriched eggs, and intake of calcium-fortified orange juice. Notably, parental recall of adolescents' diets via FFQ has been validated, albeit modestly ( $r=0.30$  [range 0.10-0.61] for foods; higher for nutrients) (Maruti, Feskanich, Colditz, Frazier, Sampson, Michels, et al., 2005).

Given the food items that were contained in this FFQ, the following components were excluded from our adaptation of the YHEI: soda and drinks, consumption of visible animal fat (fat on meat; skin on poultry), regularity of breakfast consumption and regularity of eating dinner with family. We also chose to include food items that were not part of the NHS FFQ given the recent interest in asthma and the role of these foods, nutrients and dietary patterns (Litonjua, 2009; Burns, Dockery, Neas, Schwartz, Coull, Raizenne, et al., 2007; de Luis, Armentia, Aller, Asensio, Sedano & Izaola, 2005; Bakolis, Hooper, Thompson & Shaheen, 2010). Examples of such foods included calcium-fortified orange juice, vitamin D-fortified orange juice, n-3 enriched eggs, as well as queries of vegetarianism or veganism. These exclusions and additions resulted in an adapted YHEI maximum possible score of 85; this is 15 points less than the total possible score of the original YHEI (Feskanich et al., 2004). From these totals, two dichotomous groups (low vs. high consumption) were created using the 50<sup>th</sup> percentile of total and component diet scores as cut-offs (Table 2.4).

### *Outcome Variables*

In 2008-10, pediatric allergists reassessed 489 children who continued with the study through to Visit Three. This represents 67.6% of the participants seen at Visit One. Using the same criteria as Visit One, a binary outcome of asthma (presence vs. absence) was established. For the purposes of this study, “persistent asthma” refers to a pediatric allergist diagnosis of asthma at both

Visit 1 and Visit 3, while “remittent asthma” refers to pediatric allergist diagnosis of asthma at Visit 1, but not Visit 3, and “incident asthma” refers to pediatric allergist diagnosis of asthma at Visit 3, but not Visit 1.

Trained nurses and/or research assistants also conducted methacholine (Methapharm Inc.) challenges. Using the criteria described in the section “Visit One,” AHR was first classified as a binary outcome (presence vs. absence). Presence of AHR was subsequently classified as having normal airway responsiveness or mild, moderate or severe AHR.

### *Confounding Variables*

In addition to the confounding variables described under Visit One: Confounding Variables, weight status (overweight vs. normal weight) at Visit One was considered a confounder in Visit Three.

**Table 2.2. Data Collection from the 1995 Manitoba Prospective Cohort Pertinent to the Thesis**

<b>Data collection</b>	<b>Visit 1</b>	<b>Visit 3</b>
Sex	X	
Ethnicity	X	
Geographic region of residence	X	X
Pediatric allergist assessment for asthma	X	X
Measured weights and heights	X	X
Family socio-economic status	X	X
Parental health history	X	X
Dietary habits and patterns		X
Physical activity patterns	X	

**Table 2.3. Adaptation of the Youth Healthy Eating Index (YHEI) and Dichotomization of Low vs. High Scores**

YHEI Component	Criteria for Maximum Score	Criteria for Minimum Score	Maximum Score	Cut-Offs for Scores	
				Low	High
Total YHEI Score	Maximum for all components	0	85	0.00-33.45	>33.45
1. Whole Grains	>2x/day	0	10	0.00-6.50	>6.50
2. Vegetables	>2x/day	0	10	0.00-4.6	>4.60
3. Fruits	>2x/day	0	10	0.00-5.33	>5.33
4. Dairy	>2x/day	1-3x/month or less	10	0.00-4.50	>4.50
5. Meat ratio <sup>a</sup>	>2x/day	0	10	0.00-0.36	>0.36
6. Snack foods <sup>b</sup>	0	≥2x/day	10	0.00-4.25	>4.25
7. Soda and drinks	NA	NA	-	-	-
8. Multivitamin use <sup>c</sup>	Daily	Never	5	0.00-0.25	>0.25
9. Margarine and butter	Never	≥2x/day	5	0.00-2.83	>2.83
10. Fried foods outside home <sup>c</sup>	Never or <1x/month	≥1x/day	5	0.00-3.00	>3.00
11. Visible animal fat	NA	NA	-	-	-
12. Eat breakfast	NA	NA	-	-	-
13. Dinner with family	NA	NA	-	-	-
14. Fish	>2x/week	Never	10	0.00-1.50	>1.50

<sup>a</sup>Lean meat + vegetable protein / dark meat

<sup>b</sup>Salty snacks (e.g. potato chips, nachos, pretzels, crackers, canned soup) and snacks with added sugar (e.g. cakes, doughnuts, cookies)

<sup>c</sup>Dichotomized as low or high consumption due to low range of scores for this component score

Adapted from Feskanich et al., 2004 and Health Canada

### Sample Size Calculations

A power analysis was conducted to determine the minimum sample size required to reasonably expect that a difference of an effect between groups will be detected for a given sample size. Key parameters include:

Alpha ( $\alpha$ ): Probability of a Type I error (false positive); a  $\alpha=0.05$  is widely accepted

Beta ( $\beta$ ): Probability of a Type II error (false positive); a  $\beta=0.20$  is generally accepted

OR: Odds of the outcome occurring; an OR between 1.50 and 2.50 is generally accepted

Actual power ( $1-\beta$ ): 1 - the probability of a Type II error; generally accepted as 0.80 (1-0.2)

Sample sizes were calculated based on different combinations of the above parameters (Table 2.4). Based on a two-sided normal distribution of two independent outcomes (presence vs. absence of asthma), and where the prevalence of asthma at baseline (34%) vs. absence of asthma at baseline (66%) is sampled at a ratio of 1:2, we can make the following statement about a required sample size, assuming  $\alpha=0.05$ :

This study was adequately powered to detect continuous independent associations between ( $\beta$  0.1 and 0.4) and odds ratios of 2.0-2.5. Based on  $\beta=0.20$

and an OR ranging between 2.0 and 2.5, our sample sizes at Visit One (n=723) and Visit Three (n=489) are sufficiently large to detect a true differences based on asthma outcomes (Table 2.X; bolded and framed text).

**Table 2.4 Sample Size Calculations Based on Various Beta and Odds Ratio**

**Estimates**

Beta ( $\beta$ )	OR	Actual Power (1- $\beta$ )	N
0.10	1.50	0.801	2079
0.10	2.00	0.800	648
0.10	2.50	0.802	248
0.15	1.50	0.800	1497
0.15	2.00	0.802	477
0.15	2.50	0.800	258
0.20	1.50	0.801	1218
<b>0.20</b>	<b>2.00</b>	<b>0.801</b>	<b>393</b>
<b>0.20</b>	<b>2.50</b>	<b>0.800</b>	<b>216</b>
0.25	1.50	0.800	1059
0.25	2.00	0.802	348
0.25	2.50	0.804	195
0.30	1.50	0.800	963
0.30	2.00	0.801	321
0.30	2.50	0.805	183
0.35	1.50	0.800	906
0.35	2.00	0.801	306
0.35	2.50	0.806	177
0.40	1.50	0.801	876
0.40	2.00	0.801	300
0.40	2.50	0.804	174

## Mixed Methods Design

### *Defining Mixed Methods*

An abundance of attention has been paid to the physiological consequences or biomarkers of chronic disease in youth. Yet, very little attention is paid to the impact of a diagnosis on youth. Given the relatively recent emergence of mixed methods research, there remains much debate as to a definition of this method. Numerous definitions have been put forth (Johnson, Onwuegbuzie & Turner, 2007; Tashakkori & Teddlie, 1998; Creswell & Plano Clark, 2007). As noted in Chapter 1, the definition of mixed methods that I have adopted for this dissertation is:

Mixed methods research is a research design with the *philosophical assumptions* as well as *methods of inquiry*. As a methodology, it involves philosophical assumptions that guide the direction of the collection and analysis of data and the mixture of qualitative and quantitative approaches in many phases in the research process. As a method, it focuses on collecting, analyzing, and mixing both quantitative and qualitative data in a single or a series of studies. Its central premise is that *the use of quantitative and qualitative approaches in combination provides a better understanding of research problems than either approach alone*.

(Creswell & Plano Clark, 2007; emphasis added)

### *Worldview: Pragmatism*

The philosophical assumption (or worldview) of the mixed methods

researcher must be carefully considered prior to commencing a study. Herein, the term “worldview” has been used in place of “paradigm,” as the latter has numerous definitions, while the former can be succinctly described as a basic set of beliefs or assumptions that guide inquiry (Guba & Lincoln, 1994) rooted in personal beliefs, culture and history (Creswell & Plano Clark, 2007). Further, worldviews are dynamic and flexible (Creswell & Plano Clark, 2007). In my PhD research proposal, I identified that the worldview to which I would ascribe for this project is pragmatism. Pragmatism is characterized by a problem-centered approach oriented in real-world practice. It recognizes that there are multiple realities (Creswell, 2007), rather than a single connection in the data. For example, a single method alone may miss important connections within the data; in contrast, a mixed methods approach can minimize single connections and maximize the ability to build multiple connections. In other words, this worldview allows for the expansion of our understanding of the data. And, although the conclusion may be the same, the explanation of the conclusion may be very different.

**The comprehensive research question of this thesis is: Do obesity and related lifestyle behaviours influence asthma and airway hyperresponsiveness outcomes in children?**

### *Ethical Approval*

This study was granted ethical approval by the University of Manitoba HREB (H2009:146; see Appendix C). Parents/guardians provided written consent and children provided written assent prior to commencement of data collection at each visit (Appendices D and E, respectively).

### Quantitative Component

The quantitative component of this mixed methods study had two distinct aims:

- 1. To determine the association between weight and asthma.**
- 2. To determine if lifestyle patterns, specifically diet quality, physical activity and screen time, are associated with asthma.**

The specific questions, and exposure and outcome variables are noted in Table 2.5.

### *Statistical Analysis*

Descriptive statistics were used to illustrate participant characteristics for each of the quantitative studies. This included sample sizes and percentages for categorical variables, and sample sizes, percentages, means, and standard deviation [s.d.] for continuous variables. Analyses for skewness and kurtosis were also conducted for continuous outcome variables to assess Gaussian

distribution. As all of these variables followed a Gaussian distribution, no log transformation was necessary.

**Table 2.5. Specific Quantitative Questions and Variables**

	Question	Exposure Variable(s)	Outcome Variable(s)
1	Is there an association between weight and asthma?	Overweight *at 8-10 yo *at 12-13 yo BMI z-score *at 8-10 yo *at 12-13 yo $\Delta$ BMI z-score	Asthma at 8-10 yo Asthma at 12-13 yo Asthma: *persistent *remittent *incident AHR at 8-10 yo AHR at 12-13 yo Persistent/Incident AHR
2	Does diet quality differ those with asthma and those without asthma at 12-13 yo?	Diet quality data from 12-13yo based on food frequency questionnaire from Visit 3	Asthma at 12-13 yo AHR at 12-13 yo
3	Does physical activity/screen time differ between those with asthma and those without asthma at 8-10 yo?	Physical activity/screen time data from Visit 1	Asthma at 8-10 yo Asthma at 12-13 yo AHR at 8-10 yo AHR at 12-13 yo

Abbreviations:

yo: years old

AHR: airway hyperresponsiveness

To address potential confounding variables (e.g. SES, maternal asthma, environmental tobacco smoke), we collected relevant information via

questionnaire from participants' parents. Tests for association were conducted to identify variables that would otherwise influence the association/relationship between the exposure and outcome variables. Variables that were found to be associated ( $p < 0.05$ ) were included in various logistic regression models as confounders. Logistic regression was used to identify the magnitude of the effect of an exposure variable on a given outcome variable. This was completed in various steps, or models. First, we considered the unadjusted relationship (exposure-outcome, without consideration to any confounding variables. Next, adjustment for confounders was made, first in partially adjusted model/s, then in a fully adjusted model. For both unadjusted and adjusted regression analyses, we report the odds ratios (OR), 95<sup>th</sup> percent confidence intervals (95% CI) and p-value. Statistical significance was set at  $p < 0.05$ , although smaller p-values are reported herein, as appropriate. Data were analyzed using SPSS 18.0 (IBM Corporation, Somers, NY).

### Qualitative Component

The aim of the qualitative component of this study was to describe the lived experience of asthma in youth 15-16 years old via focus groups. Qualitative methods provide an opportunity to better understand how people perceive phenomena from their own frames of reference and are complimentary to quantitative methods.

Qualitative data, including those gleaned from focus groups, are useful in explaining phenomena via in-depth means about quantitative results, including significant, non-significant or unexpected findings (Creswell & Plano Clark, 2007). Focus group discussions require participants to reveal personal feelings and experiences. The ultimate aim of focus groups is self-disclosure. As this requires individuals to feel comfortable with other participants, three cornerstones to focus group success have been put forth: 1) keeping the purpose of the focus group as the driving force; 2) establishing an environment conducive to discussion; and 3) creating skilled personnel through training, via modeling, rehearsal and feedback, on how to constructively moderate group discussions. This last cornerstone requires the researcher to self-critique after each focus group and make any necessary changes for subsequent focus groups (Côté-Arsenault & Morrison-Beedy, 2005).

### *Rationale for Focus Groups*

The purpose of focus groups is to get a variety of perspectives and increase confidence in emergent themes. As older children and youth increasingly rely on their peer groups (Atwater, 1996), focus groups are a logical forum for peers to discuss topics of interest. Furthermore, focus groups provide an opportunity to discuss sensitive topics (e.g. perceptions of transition to adolescence, living with asthma) because the responsibility for answering such

questions is shared by the group (Morgan & Keuger, 2005). In her review of the usefulness of focus groups with middle school-aged children, Horner (2000, p. 516) noted that “data that emerge through group discussions can provide poignant insights into middle school children’s beliefs, attitudes and behaviors that can affect their lives.”

In contrast to interviews, focus groups provide an opportunity for participants to respond to others’ comments during the discussion. The intent of focus groups is not within-group consensus, although idea sharing is strongly encouraged (Patton, 2002).

At this point, it should be noted that our intent was to conduct focus groups only. However, due to low recruitment and attendance, we conducted some interviews in addition to focus groups. The decision to conduct interviews as necessary is in keeping with a pragmatic worldview, or “doing what works” (Creswell & Plano Clark, 2007).

### *Participant Selection and Recruitment*

Children were purposefully chosen from two established asthma-centric studies: the 1995 Manitoba Prospective Cohort Study and from the Canadian Asthma Primary Prevention Study (CAPPS; detailed below), based on the criteria described in the next paragraph. Participants for the qualitative component were selected via a stratified purposive sample, such that they represent combinations

of different variables (Teddlie & Yu, 2007).

For the qualitative study, participants were purposively selected based on the following criteria. Inclusion criteria for the qualitative component of this mixed methods study included Winnipeg residency (for logistical purposes), assessment for asthma by a pediatric allergist, and previously obtained written consent to re-establish contact. Exclusion criteria were co-morbidities or conditions that interfere with physical activity.

Prospective participants were called and/or emailed to determine interest in, and availability for this study. Initially, only participants from the 1995 Manitoba Prospective Cohort Study were contacted. In contrast to an early qualitative study with this cohort (Protudjer et al., 2009), recruitment for the present study proved challenging. Of the eligible participants, we were able to recruit 10 boys and 7 girls. This was fewer than the estimated number of participants required to complete a sufficient number of focus groups to achieve theoretical saturation. As such, additional participants were recruited from CAPPS.

CAPPS is a randomized controlled trial of 545 children, which has been elsewhere described (Chan-Yeung, Manfreda, Dimich-Ward, Ferguson, Watson & Becker, 2000). Briefly, children in Vancouver and Winnipeg at high risk for asthma based on immediate family history were identified during mothers' third trimesters of pregnancy. Families were recruited randomly assigned to a control

(266; 48.8%) or to multi-faceted intervention (279; 51.2%) group. Intervention occurred during pregnancy (Visit 1) and the first year of life (Visit 2) and consisted of avoidance of exposure to house dust mites, pets and environmental tobacco smoke, promotion of breastfeeding and delayed introduction of solid foods. Other visits (at ages 2 years and 7 years) were also conducted, but are not described herein as they are not pertinent to this qualitative study.

At Visit 5, in 2010, we re-established contact with 134 (75 [56.0% boys) of the original 274 participants residing in Winnipeg. At this visit, data collected relevant to this qualitative study included pediatric allergist assessments for asthma. Purposively selected Winnipeg-based participants who had completed Visit 5 were invited to participate in this qualitative study. The inclusion and exclusion parameters were similar to those described for the purposive selection of participants of the 1995 Manitoba Prospective Cohort Study. Recruitment from this study enabled us to complete the qualitative component of this mixed methods study.

### *Study Design*

Participants were selected for homogeneity within groups (Table 2.6) and heterogeneity between groups. Each focus group was approximately one hour to 90 minutes in duration. This study was initially designed to include four focus groups of children and four focus groups of parents with six to eight individuals

per focus group. However, due to recruitment and scheduling difficulties, focus groups ranged in size from two participants (one focus group from each category detailed in Table 2.6), to three participants (one focus group of boys with asthma; one focus group of parents of girls without asthma) to four participants (one focus group of boys without asthma; one focus group of parents of boys without asthma; one focus group of boys with asthma). We also conducted one-on-one interviews. Interviews were conducted during the same time period as the focus groups (i.e. they were not all conducted prior to commencing focus groups, or following the completion of all focus groups). Interviews were conducted solely to accommodate families' schedules; pre-set times for focus groups were not always convenient for families, yet these families still wished to participate.

**Table 2.6 Characterization of Focus Groups**

<u>Participants</u>	
Girls with asthma*	Boys with asthma*
Girls without asthma	Boys without asthma
<u>Parents of...</u>	
Girls with asthma*	Boys with asthma*
Girls without asthma	Boys without asthma
*or worsened airway hyperresponsiveness if necessary	

### *Implementation*

All interviews and focus groups were conducted at the Manitoba Institute of Child Health (MICH) between September 2010 and February 2011.

Interviews and focus groups were held after regular school hours and/or on weekends/statutory holidays. Upon arrival at MICH, youth and their parents were invited to ask questions about the focus group process and then to complete the assent/consent forms, if they agreed to participate. Parents recessed to another room. Snacks/dinner were made available throughout the focus groups and interviews. Children received two movie passes (value: \$20.50) for their participation. Parents were reimbursed for parking/public transit costs.

At the beginning of each interview/focus group, the moderator (JP) noted that the sessions were being digitally audio recorded. Subsequently, I introduced myself and explained the purpose of the study and the ground rules regarding respect and confidentiality. Subsequently, participants were invited to introduce themselves. Questions were asked one at a time, based on an interview guide (Appendices G and H) until participants had nothing further to discuss about a particular question. If discussion diverged from the topic of interest, the moderator redirected participants to the last relevant topic. This process continued until all questions from the interview guide had been asked. At that time, the moderator provided a two- to three minute summary of the topics discussed during the focus group/interviews. Participants were then given an opportunity to state anything that they had hoped to mention but did not have an opportunity to do so during the course of the focus group. The digital audio recorders were then turned off, and participants were asked to

comment on the process.

### *Analysis*

Verbatim transcripts were generated from digital audio recordings of the interviews and focus groups by a professional transcriptionist who has worked with numerous other qualitative researchers at the University of Manitoba. Additionally, the moderators made notes throughout all interviews/focus group to capture non-verbal interactions and body language which cannot be identified via audio recordings (Côté-Arsennault et al., 2005). Data were analyzed thematically, first by generating initial codes and subsequently by defining and naming themes.

### *Thematic Coding*

Thematic coding is the foundational method in qualitative research. It is independent of theory and epistemology, and thus is compatible with many paradigms, including pragmatism (Braun & Clarke, 2006). Notably, it behooves the researcher to explicitly state his/her chosen paradigm as each theoretical framework has unique assumptions (Braun & Clarke, 2006). Although a very flexible analytic method in qualitative research, thematic coding has requirements to ensure theoretical and methodological soundness. This includes an acknowledgement from the researcher that the chosen framework and

methods are decisions made by the researcher, rather than “emerging” or “discovered” concepts in the data; the latter implies a passive method, while in fact, thematic analysis is an active process (Braun & Clarke, 2006).

Although thematic analysis is a straightforward method of qualitative analysis, pitfalls do exist. These include a failure to analyze all available data, use of interview guide questions as themes, a weak or unconvincing analysis, mismatch between data and analytical claims or between the research questions and type of thematic analysis, or failure to identify theoretical assumptions (Braun & Clarke, 2006). To avoid such pitfalls, precautions have been implemented. This includes 1) triangulating findings from the quantitative component (Aims 1-2) of this study; 2) describing the extent to which the findings enhance our understanding of the topics of interest; 3) placing the findings within the existing literature; and 4) describing the usefulness of the findings for their intended purpose. These are commonly accepted criteria for determining significance of qualitative research (Patton, 2002).

### Merging of Data

**Fundamentally, the methods of inquiry are what make mixed methods research unique.** As the name implies, mixed methods studies consist of two types of data: quantitative and qualitative. However, it is not sufficient to collect and analyze these data independently. The data sets must be “mixed” at some

point during the study, the product of which provides a more comprehensive understanding of the problem than two singular sets of data (Creswell & Plano Clark, 2007).

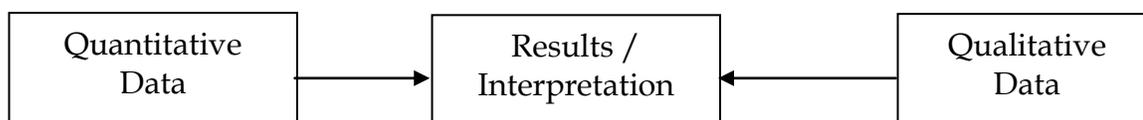
Data collection via each method can occur concurrently or sequentially. The purpose of concurrent data collection is to confirm, cross-validate or corroborate findings obtained via one method with another. Equal or unequal priority can be assigned to each method; weighting of the importance of each method depends on the research question (Creswell & Plano Clark, 2007). The purpose of sequential design is to use data from one method is used to build on another. Data from each method can be given equal or unequal importance during the analysis and interpretation of the study. This study was sequential in design, with an explanatory focus. Sequential explanatory designs occur when qualitative methods are secondary to quantitative methods, commonly denoted as “QUAN” and “qual” to differentiate between the research methods and the respective importance of each method (Creswell & Plano Clark, 2007). In this design, the same individuals are used for each set of data collection, providing an opportunity for the qualitative data to inform the quantitative results. However, the sample sizes need not be the same as the intent is not to merge the data (Teddlie & Yu, 2007).

Quantitative and qualitative data can be “mixed” in three ways: merging, connecting or embedding (Creswell & Plano Clark, 2007). In this study, the two

sets of data were merged in the results and interpretation, shown simplistically in Figure 2.2. In this study, which was sequential in design, inferences from the findings of each method were made and subsequently united in the discussion, thereby creating a meta-inference (Teddlie & Yu, 2007).

**Figure 2.2. Merging Quantitative and Qualitative Data**

[Adapted from Creswell & Plano Clark, 2007]



But, it is not adequate to declare that a study is mixed methods in design once all of the data are collected. Rather, development of a mixed methods study requires integration of quantitative and qualitative data from the study inception. To this end, four overarching steps were considered prior to commencing this mixed methods study (Creswell & Plano Clark, 2007):

- 1) Identifying a worldview.
  - a. The worldview chosen for this project was pragmatism (see page 60-61).
- 2) Understanding the basics of quantitative and qualitative research.
  - a. Throughout my graduate training, I was exposed to these overarching research paradigms. In fact, I have taught a course,

“HMEC 2050: Introduction to Research in Human Ecology” that requires a strong understanding of research methods.

3) Recognizing the common and unique elements to each methodology

a. See 2a above.

4) Deciding on the suitability of mixed methods for a particular study.

a. To best address the comprehensive research question of this study,

Do obesity and related lifestyle behaviours influence asthma and airway hyperresponsiveness outcomes in children? Furthermore,

this association is mediated by nutritional/behavioural factors

including screen time, physical activity and diet quality that

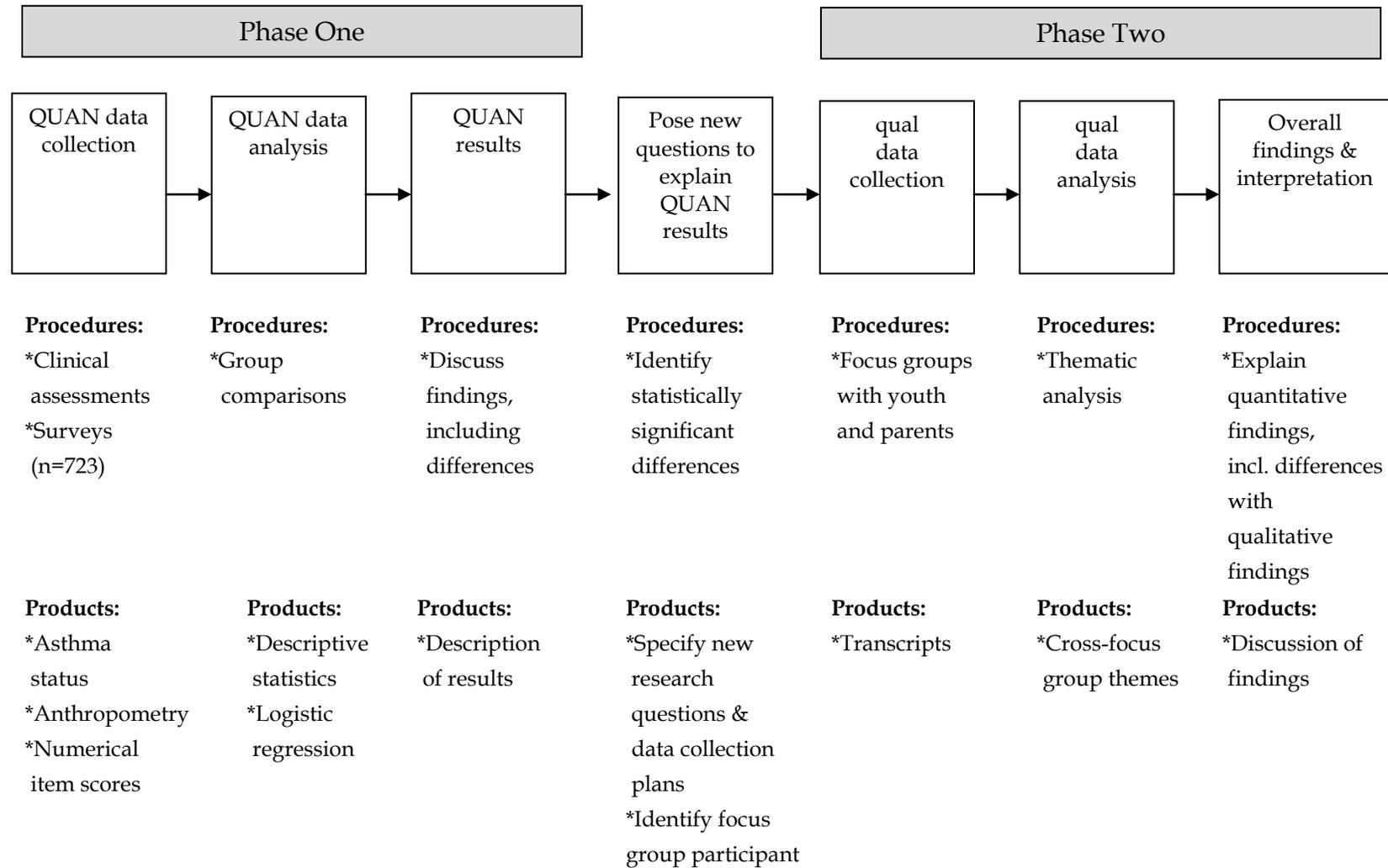
adversely affect airway hyperresponsiveness, both quantitative

methods and qualitative methods are appropriate. Asthma and

obesity have biological and sociological origins, neither of which

can be fully understood from a single research method.

**Figure 2.3. Procedural Summary of the Present Study** (Adapted from Creswell & Plano Clark, 2007)



## CHAPTER THREE: ASSOCIATIONS BETWEEN WEIGHT AND ASTHMA IN MANITOBA YOUTH

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The aim of this chapter is to describe the association between weight status and asthma and AHR. The hypothesis is that weight gain increases the risk of asthma and AHR among youth 8-14 yo.

Weight, the exposure variable, is defined in three ways: 1) a dichotomization of normal weight (BMI <85<sup>th</sup> percentile for age and sex) vs. overweight (BMI ≥85<sup>th</sup> percentile for age and sex) as per CPS (Dietitians of Canada, 2004), 2) BMI z-scores (including  $\Delta$  z-scores from Visit One to Visit Three) and; 3) BMI quartiles (Q1-Q4). The primary outcome variable is asthma

(absence vs. presence at Visit One, and at Visit Three, as well as persistent asthma, incident asthma and remittent asthma). The secondary outcome variable is airway responsiveness, which has been further subdivided into two outcomes: a) normal airway responsiveness vs. AHR, and; b) normal airway responsiveness vs. mild AHR and vs. moderate/severe AHR. Due to the low number of children with severe AHR (Visit One n=5; Visit Three n=26), I created a variable of moderate/severe AHR to ensure adequate power. As the aim of this study was to determine the effect of weight status on asthma/AHR outcomes, I have not considered the association between weight status at Visit Three and asthma/AHR at Visit One.

Participant characteristics are described in Table 3.1. At Visit One, 723 children (aged  $8.6 \pm 0.5$  years; 55.9% boys) were enrolled. At Visit Three, 489 children (aged  $12.6 \pm 0.5$  years) were assessed; this represents 67.6% of the initial prospective cohort, including a comparable sex split (Visit Three: 56.6% boys). At Visit One, 34.0% had asthma, approximately one-third (38.9%) had normal airway responsiveness and 32.0% were of normal weight status. The mean BMI was  $18.4 \pm 3.9$  kg/m<sup>2</sup>. At Visit Three, 30.5% had asthma. This included 24.1% with persistent asthma, 6.3% with incident asthma and 12.3% with remittent asthma. At Visit Three, 44.7% had normal airway responsiveness. The mean BMI was  $20.5 \pm 4.7$  kg/m<sup>2</sup> and 71.3% were within a normal weight range.

**Table 3.1 Participant Characteristics**

Variable	Visit One (N=723)		Visit Three (N=489)	
	n	%	n	%
Sex				
Boys	404	55.9	277	56.6
Girls	319	44.1	212	43.4
Age*	8.6±0.5	-	12.6±0.5	-
Asthma				
no	477	66.0	340	69.5
yes	246	34.0	149	30.5
persistent	-	-	118	24.1
incident	-	-	31	6.3
remittent	-	-	60	12.3
PC20 <sup>†</sup>				
Median (IQR).	5.6 (1.7-8.0)	-	5.38 (1.3-16.6)	-
normal	172	38.9	211	44.7
mild	135	30.5	110	23.3
moderate	130	29.4	125	26.5
severe	5	1.1	26	5.5
BMI* <sup>‡</sup>	18.4±3.9	-	20.5±4.7	-
BMI z-scores*	0.51 ± 1.12		0.38 ± 1.14	
ΔBMI z-score* <sup>§</sup>	-	-	0.08 ± 0.80	
Weight Status				
normal	491	68.0	345	71.3
overweight	231	32.0	139	28.7

\*mean ± standard deviation

<sup>†</sup>PC20: normal >8 mg/ml; mild 2-8mg/ml; moderate 0.25-2mg/ml; severe <0.25mg/ml

<sup>‡</sup>Body mass index based on measured height and weight

<sup>§</sup>Change in body mass index z-scores from Visit One to Visit Three

Few associations were made between weight status and asthma (Table 3.2). Girls who were overweight at 12-13 years old had two-fold increased odds of having persistent asthma (OR 2.22; 95% CI 1.13-4.36;  $p < 0.02$ ) compared to girls within a normal weight range. Similarly, girls in the fourth quartile for BMI at 12-13 years old trended towards an increased odds of persistent asthma, but did not quite reach statistical significance (OR 1.66; 95% CI 0.98-2.81). In contrast, 12-15 year old boys in the fourth quartile for BMI had a greater odds of remittent asthma (OR 1.80, 95% CI 1.01-3.19;  $p < 0.05$ ). An increasing BMI z-score increased the odds of asthma in a cross-sectional analysis of data collected at 8-10 years old children (OR 1.15; 95% CI 1.00-1.32;  $p = 0.05$ ). With consideration to temporal asthma status (asthma status at 8-10 years old and asthma status at 12-13 years old), an increasing BMI z-score at 8-10 years old reduced the odds of incident asthma (OR 0.70; 95% CI 0.50-0.97;  $p < 0.05$ ) but increased the odds of persistent asthma (OR 1.55; 95% CI 1.00-2.42;  $p = 0.05$ ) at 12-13 years old. No such association was found for boys at 12-13 years old. In contrast, a higher BMI z-score amongst 12-13 year old girls was associated with a reduced odds of incident asthma (OR 0.55; 95% CI 0.33-0.93;  $p < 0.05$ ).

Table 3.3 summarized the associations between weight status and AHR. Overweight participants had a reduced odds (OR 0.55; 95% CI 0.32-0.93;  $p < 0.05$ ) of moderate/severe at Visit One. Once stratified by sex, this association did not remain significant. Similarly, a BMI in Q4 at Visit One was inversely associated

with AHR overall (OR 0.57; 95% CI 0.40-0.81;  $p < 0.003$ ) and amongst girls only (OR 0.57; 95% CI 0.33-0.99;  $p < 0.05$ ), and moderate/severe AHR (OR 0.49; 95% CI 0.28-0.84;  $p < 0.003$ ) at Visit One. Several associations persisted to Visit Three. A BMI in Q4 at Visit One was inversely associated with AHR (OR 0.66; 95% CI 0.46-0.85;  $p < 0.05$ ), while a BMI in Q3 or Q4 at Visit One were both inversely associated with moderate/severe AHR (OR 0.56; 95% CI 0.35-0.89;  $p < 0.05$ , and OR 0.54; 95% CI 0.34-0.89;  $p < 0.05$ , respectively). In contrast, girls with a Q3 BMI at Visit Three had an increased odds of mild AHR at Visit Three (OR 2.43; 95% CI 1.01-5.85;  $p < 0.05$ ). No associations were identified between BMI z-scores at 8-10 years old and 12-13 years old and AHR.

We also considered the effect of weight change from 8-10 years old to 12-13 years old on asthma and AHR (presence at 12-13 years old, persistence, incidence and remittance). An increase in BMI z-score was associated with a reduced odds of incident asthma in boys (OR 0.54; 0.31-0.94;  $p < 0.05$ ). No such associations between weight change and asthma outcomes were found for the overall cohort or for girls only. We did not identify any associations between weight change and AHR outcomes, either amongst the entire cohort or by sex.

**Table 3.2 Associations between Weight Status and Asthma**

	Asthma at Visit One (n=246)		Asthma at Visit Three (n=149)		Persistent Asthma (n=118)		Incident Asthma (n=31)		Remittent Asthma (n=60)	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
<b>Overweight*</b>										
<i>Visit One</i>										
Overall	1.23	0.89-1.70	1.17	0.77-1.78	1.20	0.77-1.88	0.99	0.44-2.20	1.24	0.70-2.21
Boys	1.06	0.70-1.62	1.03	0.59-1.78	0.85	0.47-1.55	1.89	0.66-5.38	1.50	0.74-3.05
Girls	1.45	0.86-2.44	1.44	0.75-2.77	1.96	0.99-3.90	0.41	0.09-1.85	0.82	0.29-2.32
<i>Visit Three</i>										
Overall	-	-	1.40	0.92-2.12	1.46	0.93-2.27	1.02	0.46-2.27	1.10	0.61-2.00
Boys	-	-	1.28	0.74-2.23	1.06	0.58-1.92	2.10	0.73-5.98	1.35	0.65-2.81
Girls	-	-	1.58	0.84-3.00	<b>2.22**</b>	<b>1.13-4.36</b>	0.37	0.08-1.70	0.75	0.26-2.12
<b>BMI Quartiles</b>										
<i>Visit One</i>										
Overall										
Q2	1.03	0.79-1.34	1.07	0.78-1.48	1.05	0.74-1.49	1.11	0.61-2.05	0.94	0.58-1.50
Q3	0.85	0.65-1.11	0.98	0.69-1.39	0.97	0.67-1.42	1.04	0.54-2.00	0.73	0.43-1.25
Q4	1.22	0.94-1.58	0.92	0.65-1.30	1.00	0.69-1.45	0.71	0.34-1.49	1.40	0.89-2.19
Boys										
Q2	0.96	0.68-1.35	0.92	0.60-1.42	1.00	0.63-1.59	0.69	0.26-1.82	1.14	0.63-2.05
Q3	0.84	0.59-1.21	1.05	0.66-1.67	1.01	0.62-1.66	1.21	0.50-2.93	0.49	0.22-1.09
Q4	1.15	0.82-1.63	0.86	0.54-1.38	0.81	0.48-1.35	1.17	0.48-2.83	<b>1.80*</b>	<b>1.01-3.19</b>
Girls										
Q2	1.11	0.73-1.70	1.31	0.81-2.14	1.13	0.66-1.92	1.93	0.80-4.68	0.69	0.30-1.61
Q3	0.85	0.56-1.29	0.89	0.63-1.51	0.93	0.53-1.65	1.01	0.35-2.88	1.21	0.57-2.56
Q4	1.30	0.87-1.95	0.99	0.59-1.66	1.29	0.75-2.22	0.32	0.07-1.51	0.98	0.44-2.17
<i>Visit Three</i>										
Overall										
Q2	-	-	0.84	0.60-1.18	0.81	0.56-1.17	1.03	0.55-1.93	1.10	0.69-1.75
Q3	-	-	1.04	0.74-1.45	1.03	0.72-1.48	1.04	0.56-1.94	1.11	0.70-1.76
Q4	-	-	1.16	0.84-1.62	1.27	0.86-1.74	0.90	0.47-1.73	1.03	0.64-1.65
Boys										
Q2	-	-	0.75	0.48-1.19	0.79	0.48-1.29	0.75	0.28-1.98	1.19	0.67-2.11
Q3	-	-	1.07	0.67-1.70	1.02	0.62-1.67	1.24	0.51-3.04	0.88	0.46-1.71
Q4	-	-	1.06	0.68-1.64	0.98	0.61-1.58	1.34	0.58-3.09	1.25	0.70-2.24
Girls										
Q2	-	-	0.98	0.58-1.65	0.85	0.47-1.53	1.50	0.64-3.52	1.00	0.45-2.21
Q3	-	-	1.00	0.62-1.62	1.08	0.64-1.82	0.92	0.38-2.27	1.51	0.77-2.97
Q4	-	-	1.32	0.80-2.18	1.66	0.98-2.81	0.54	0.17-1.68	0.75	0.32-1.75
<b>BMI Z-Scores</b>										
<i>Visit One</i>										
Overall	<b>1.15*</b>	<b>1.00-1.32</b>	0.97	0.82-1.15	1.15	0.90-1.48	<b>0.70*</b>	<b>0.50-0.97</b>	1.09	0.85-1.41
Boys	1.11	0.92-1.33	0.91	0.73-1.14	0.98	0.71-1.34	0.79	0.52-1.20	1.21	0.87-1.66

Girls	1.19	0.95-1.50	1.08	0.81-1.42	<b>1.55*</b>	<b>1.00-2.42</b>	0.60	0.35-1.01	0.90	0.60-1.36
<i>Visit Three</i>										
Overall	-	-	1.03	0.87-1.22	1.00	0.78-1.28	0.85	0.61-1.20	1.16	0.91-1.48
Boys	-	-	1.00	0.80-1.26	0.81	0.58-1.12	1.28	0.78-2.10	1.17	0.85-1.59
Girls	-	-	1.07	0.83-1.39	1.38	0.93-2.07	<b>0.55*</b>	<b>0.33-0.93</b>	1.12	0.76-1.66

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\*p=0.05

**Table 3.3 Associations between Weight Status and AHR**

	AHR at Visit One (n=270)		AHR at Visit Three (n=259)	
	OR	95% CI	OR	95% CI
<b>Overweight*</b>				
<i>Visit One</i>				
Overall	0.72	0.47-1.10	0.79	0.53-1.17
Boys	0.74	0.42-1.30	0.72	0.43-1.20
Girls	0.64	0.33-1.24	0.78	0.41-1.47
<i>Visit Three</i>				
Overall	-	-	0.78	0.52-1.16
Boys	-	-	0.76	0.45-1.28
Girls	-	-	0.74	0.40-1.39
<b>BMI Quartiles</b>				
<i>Visit One</i>				
Overall				
Q2	0.95	0.69-1.30	1.04	0.76-1.43
Q3	0.90	0.65-1.24	0.82	0.59-1.16
Q4	<b>0.57*</b>	<b>0.40-0.81</b>	<b>0.66*</b>	<b>0.46-0.95</b>
Boys				
Q2	1.07	0.71-1.61	1.11	0.74-1.66
Q3	1.00	0.66-1.52	0.82	0.53-1.27
Q4	0.57	0.35-0.93	0.69	0.44-1.09
Girls				
Q2	0.80	0.49-0.32	0.93	0.55-1.57
Q3	0.77	0.47-1.27	0.83	0.48-1.42
Q4	<b>0.57*</b>	<b>0.33-0.99</b>	0.62	0.35-1.12
<i>Visit Three</i>				
Overall				
Q2	-	-	1.02	0.73-1.42
Q3	-	-	0.94	0.67-1.32
Q4	-	-	0.85	0.60-1.21
Boys				
Q2	-	-	1.07	0.71-1.61
Q3	-	-	0.73	0.46-1.15
Q4	-	-	0.86	0.56-1.33
Girls				
Q2	-	-	0.92	0.51-1.64
Q3	-	-	1.33	0.79-2.26
Q4	-	-	0.83	0.46-1.51
<b>BMI Z-Scores</b>				
<i>Visit One</i>				
Overall	0.88	0.77-1.02	0.97	0.82-1.15
Boys	0.87	0.72-1.05	0.91	0.73-1.14
Girls	0.89	0.71-1.10	1.07	0.81-1.42

<i>Visit Three</i>				
Overall	-	-	0.87	0.74-1.03
Boys	-	-	0.85	0.68-1.06
Girls	-	-	0.87	0.68-1.11

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\*p<0.05

**Table 3.4 Associations between Weight Change from 8-10 years old to 12-13 years old and Asthma and AHR Outcomes at 12-13 years old**

		Asthma							
		Presence		Persistence		Incidence		Remittance	
		OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
BMI z-score change									
Overall		0.89	0.70-1.13	1.29	0.91-1.83	0.70	0.47-1.05	0.88	0.59-1.29
Boys		0.85	0.64-1.14	1.34	0.88-2.05	<b>0.54*</b>	<b>0.31-0.94</b>	0.77	0.44-1.35
Girls		0.98	0.65-1.47	1.20	0.64-2.24	1.25	0.52-2.98	0.97	0.52-1.81
		AHR							
		Presence		Persistence		Incidence		Remittance	
		OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
BMI z-score change									
Overall		1.00	0.79-1.26	0.91	0.67-1.24	1.54	0.91-2.63	0.86	0.61-1.21
Boys		0.99	0.75-1.33	0.98	0.65-1.47	1.45	0.73-2.88	0.76	0.44-1.33
Girls		0.97	0.66-1.43	0.80	0.49-1.31	1.73	0.73-4.11	0.96	0.61-1.51

\*p<0.05

Consistent with previous studies (Castro-Rodriguez et al, 2001; Guerra et al, 2004; Herrera-Trujillo et al, 2005), we have shown that overweight amongst girls pre-pubertally and during the pubertal years are associated with an increased odds of persistent asthma. In contrast, boys who were heaviest during their pre-pubertal years had a greater odds of remittent asthma, while a BMI change from pre-puberty to puberty were less likely to have incident asthma.

Overweight girls in the Tucson Children's Respiratory Study were more likely to have wheeze cross-sectionally and prospectively (Castro-Rodriguez et al, 2001; Guerra et al, 2004), particularly amongst girls who began puberty by age 11. Our data precluded stratification by early puberty; data on puberty were not collected until age 11-12 years (a clinic visit not described in this study) and only queried current pubertal stage, not the age at which youth began puberty. The exception to this is an inquiry whether girls had reached menarche prior to age 11 years. Very few girls reported menarche by this age. Notably, we previously showed that pubertal stage, whether assessed by Tanner staging or serum levels of estradiol (in girls) and testosterone (in boys), is not assessed with asthma at 11-12 years old (abstract presented at the American Academy of Asthma, Allergy and Clinical Immunology Annual Meeting, 2009).

Weight gain was not predictive of incident asthma in either boys or girls. Weight gain in this cohort of youth was very small (ChgBMI z-score  $0.08 \pm 0.8$ ), a change which may not have been a large enough to yield statistically significant

results. At a population level, an increase in BMI z-score of 0.08 is not clinically relevant. But, it is important to consider that BMI z-score change as a predictor of incident asthma in girls (and indeed also in boys) tended upwards. It is possible that, with a larger sample, or indeed with a population that had greater weight gain from YR8-10 to YR12-13, ChgBMI z-score may have statistically increased the odds of incident asthma. From a clinical perspective, it is nonetheless important to monitor weight gain in girls especially during the pubertal years. Others have shown (Castro-Rodriguez et al, 2001; Guerra et al, 2004) that weight gain during this period increases the odds of incident asthma. Our results support this, although were not statistically significant.

Participants in our cohort were assessed at 8-10 years old and again at 12-13 years old. Weight gain over as short of a time as 12 months during adolescence may influence asthma outcomes. Amongst Taiwanese adolescents, a one-unit change in BMI was associated with a 1-2% increased odds of asthma (Ho et al, 2011). We did not observe the same phenomenon. In fact, we demonstrated that weight gain amongst boys during this period reduces the risk of incident asthma.

We found that heavier boys were less likely to develop asthma and more likely to outgrow it. This finding is in keeping with the gender shift of asthma. Why this shift was most evident in heavier boys, or boys who got heavier from 8-10yo to 12-13yo is intriguing. Although it is impossible to say conclusively, there are a few potential explanations, the most likely of which is that boys who are

heavier may be in fact, leaner (greater proportion lean mass to total body mass) than boys who are lighter. This may be a proxy for pubertal staging, such that boys who are more physically mature have greater circulating levels of testosterone. This hormone is an immunosuppressant and may serve to protect against immunological and/or inflammatory processes that trigger asthma.

Others have shown that AHR is a strong risk factor for adolescent-onset wheeze or asthma. We know that there is an association between BMI and asthma, particularly amongst girls as they transition through puberty. So, our finding does seem counter-intuitive. And, indeed our findings contradict those of other authors who have shown either no association (Schachter et al, 2001; Wickens et al. 2005) or a positive association (Litonjua et al, 2002) between BMI and AHR. But, at least one group, namely those involved in the Dunedin cohort (Hancox et al, 2005), have shown a that BMI tends towards a positive effect on PC20, although their results were not statistically significant (unlike BMI which increases the odds of asthma). These authors suggest that obese women develop airflow obstruction and respiratory symptoms through non-asthmatic mechanisms. To this end, we propose two possible reasons for our finding, First, we used BMI, rather than a true measure of 'fatness,' such as bio-electrical impedance analysis or dual energy x-ray absorptiometry. It may be that our findings are a function of the measure of the exposure variable, rather than a true finding. This, however, is unlikely. Had this been the case, we could have also

expected similar findings in for quartiles 2 and 3, and also possibly for boys. Second, and more likely, 8-10 year olds girls in quartile four are experiencing a period of weight gain prior to a period of linear growth. Given that height is positively correlated with lung function, our findings may be a reflection of future improvements in lung function (i.e. reduced odds of AHR) rather than our observation that an increase in BMI protects against AHR. This is supported by the fact that we only made the observation cross-sectionally at 8-10yo, but not cross-sectionally at 12-13yo or a temporal association between weight at 8-10yo and AHR at 12-13yo. Notably, Castro-Rodriguez et al (2001) reported that FEV1 was not significantly different between girls who became obese and those with stable or decreasing BMI. This suggests an abnormality in the regulation of airway tone in girls.

The greatest strengths of our study are the use of objective measures of BMI and a physician assessment for asthma at baseline and follow-up. We acknowledge the limitations of our study. The direction of  $\Delta$ BMI change was not considered in the analysis. It is unlikely however, that negative  $\Delta$ BMI would have substantial influence on our findings, given that few children had clinically-relevant weight loss from age 8-10years to 12-13 years. Also, our rate of attrition was highest amongst northern and First Nations youth in our study. As rates of overweight in Manitoba are highest these two groups (Yu et al, 2009), it is possible that these losses may have affected our results.

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This chapter provided a description of the associations between weight status and asthma/AHR amongst participants in the 1995 Manitoba Prospective Cohort Study. Amongst girls, overweight at 12-13 years old is associated with a two-fold increased odds of persistent asthma, while elevated BMI (Q3) is associated with mild AHR. In contrast, 8-10 children with an elevated BMI (Q4) had a reduced odds of AHR and moderate/severe AHR at both 8-10 and 12-13 years old.

Collectively, these findings suggest that the association between weight status and asthma in girls in our cohort parallels findings that have been previously reported in the literature. The association between weight and remittent asthma in boys is contrary to what we had hypothesized.

These findings suggest that the association between weight status and asthma are most pronounced in girls. This reinforces the importance of weight management in girls especially before and during their pubertal years. But, weight status alone may not fully explain this phenomenon. Lifestyle behaviours, such as diet and activity, influence both weight and asthma. Given that these behaviours may change during the pubertal years, most dramatically amongst girls, there is a need to further consider diet, physical activity and

sedentary behaviour, in association with asthma. The subsequent chapters in this thesis will consider the effects of other factors associated with weight status, including physical activity and screen time, and diet quality. As well, youths' perceptions of asthma, physical activity and screen time will also be described so as to provide context, or voice, to the results presented herein.

**CHAPTER FOUR: LOW VEGETABLE INTAKE IS ASSOCIATED WITH  
ALLERGIC ASTHMA AND MODERATE-TO-SEVERE AIRWAY  
HYPERRESPONSIVENESS**

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In recent years, dietary patterns have shifted from a traditional or prudent diet, characterized by fruits, vegetables and grains, to a western or modern diet, which includes processed foods that are high in sugar, fat and salt (Popkin & Gordon-Larsen, 2004). Asthma rates have increased dramatically over a similar time (Bach, 2002). Not surprisingly, the relationship between diet and asthma has received much attention. However, much of this focus has been on adults'

diets or maternal diets during pregnancy. We sought to better understand the association between diet quality and asthma. This chapter is based on cross-sectional analyses of dietary exposures and asthma outcomes. Although longitudinal analyses would have been favourable, data restrictions of the dietary information collected at Visit One precluded this possibility. The aim of this chapter is to determine if lifestyle, for which diet quality is a proxy, is associated with asthma. This chapter is a manuscript, and therefore provides further introduction to the topic, as well as methods (many of which have been previously described in Chapter 2), as well as results and conclusions.

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Low Vegetable Intake is Associated with Allergic Asthma and Moderate-  
to-Severe Airway Hyperresponsiveness

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## ABSTRACT

**Background** In recent decades, children's diet quality has changed and asthma prevalence has increased, although it remains unclear if these events are associated. **Objective** To examine children's total and component diet quality and asthma and airway hyperresponsiveness, a proxy for asthma severity. **Methods** Food frequency questionnaires adapted from the Nurses' Health Study and supplemented with foods whose nutrients which have garnered interest of late in relation to asthma were administered. From these data, diet quality scores (total and component), based on the Youth Healthy Eating Index (adapted) were developed. Asthma assessments were performed by pediatric allergists and classified by atopic status: allergic asthma ( $\geq 1$  positive skin prick test to common allergens  $>3\text{mm}$  compared to negative control) vs. non-allergic asthma (negative skin prick test). Airway hyperresponsiveness was assessed via the Cockcroft technique. Participants included 270 boys (30% with asthma) and 206 girls (33% with asthma) involved in the 1995 Manitoba Prospective Cohort Study nested case-control study. Logistic regression was used to examine associations between diet quality and asthma. **Results** 476 children (56.7% boys) were seen at  $12.6 \pm 0.5$  years. Asthma and airway hyperresponsiveness prevalence were 26.2% and 53.8%, respectively. Few associations were made between total or component diet scores and asthma overall. High vegetable intake was protective against allergic asthma (OR 0.49; 95% CI 0.29-0.84;  $p < 0.009$ ) and

moderate/severe airway hyperresponsiveness (OR 0.58; 0.37-0.91;  $p < 0.019$ ) in fully adjusted models. **Conclusions** Vegetable intake is inversely associated with allergic asthma and moderate/severe airway hyperresponsiveness.

## **Low Vegetable Intake is Associated with Allergic Asthma and Moderate-to-Severe Airway Hyperresponsiveness**

### **INTRODUCTION**

Asthma is the most common chronic disease in children, affecting approximately 12% of Canadian children, a rate which is significantly higher than less than a decade ago (1). Over a similar time period as the increase in allergic disease prevalence, the diets of many people in wealthy nations and individuals in developing countries have also changed considerably. This “western” or more “modern” diet is characterized by high glucose-fructose, and saturated-, trans- and n-6 fats, and is low in fresh fruits, vegetables and n-3 fatty acids (2). This differs from a prudent or traditional diet, which is high in fresh produce and n-3 fatty acids, and which was dominant through to the mid-20th century (3). Many of these diet components, as well as other nutrients, have been considered individually as exposures (reviewed in 4). Yet, most people eat a reasonably diverse diet, not a single food or nutrient (5). Therefore, it may be incorrect to form conclusions about the role of a particular nutrient or food on health outcomes (6).

Although there has been focus placed on maternal diet during pregnancy and subsequent allergic outcomes in the offspring (7-10), little attention has been given to children’s dietary patterns and asthma. Some studies (15-18) have

identified differences in dietary patterns between individuals with asthma and without asthma, however, others indicate no association (11-14). For example, South Asian mothers living in the United Kingdom were more likely to self-report asthma if they had an “entirely English” or “mostly English with Asian” diets, as compared to those with a traditional Asian diet (15). Diets high in fat and low in fibre and carbohydrates are linked with a higher prevalence of bronchial reactivity (16), while vegetarian diets, often high in fibre and carbohydrates, but lower in fat, are associated with lower rates of self-reported asthma in women (17). High salt diets, in contrast to sweet, sour and peppery foods, were identified as being more common amongst Taiwanese adults diagnosed with asthma (18). Although this study was based on a small sample size and does not elaborate on dietary patterns other than what is described herein, it is nonetheless worthy of note as it is one of the first population-based studies in which diet and asthma were considered.

These findings suggest that Western dietary patterns may be associated with a higher prevalence of asthma. As asthma is believed to have origins in childhood (19) or earlier (20), it is logical to address associations between diet quality and asthma in young people. We also report on associations between diet and airway hyperresponsiveness (AHR). AHR is a reflection of heightened airway sensitivity to inhaled agonists (21). It may be used to characterize asthma particularly among individuals with asthma-like symptoms but who do not

exhibit obvious airflow obstruction (21).

The term “diet quality” remains elusively defined, as its interpretation is influenced by the interests of those considering it (6). For the purposes of this study, diet quality is defined as *an indicator of food and beverage intake that is reflective of one’s typical intake patterns*. It is an assessment of total food intake, rather than a specific foods or nutrients. Thus, the present study considers associations between diet quality and asthma, rather than asthma and a particular nutrient. Considering the intake of both nutrients and food/food groups lends itself to addressing the complex etiology of asthma, which has most often been considered from a nutrient perspective. The aim of this analysis was to determine if dietary patterns of 12-13 year old children are associated with asthma. The hypotheses were 1) that an inverse association exists between asthma and diet quality, particularly among those with allergic asthma, and 2) that an inverse association exists between AHR and diet quality.

## **METHODS**

### **Study Design**

This was a nested case-control study of the 1995 Manitoba Prospective Cohort Study of Allergy, Genes and the Environment (SAGE), detailed elsewhere (22). Briefly, study participants were recruited via surveys from ~12000 children born in 1995 and who remained in the province in 2002. Based on the ~3500

returned surveys, 12% of children had parental-reported asthma. These children, along with controls matched for sex, region of residence and socio-economic status (SES), were invited to participate in this study. This yielded a nested case-control study of 723 children; the ethnic and geographic distribution of the participants was comparable to that of Manitoba overall.

Participants and their families have attended clinical visits every two years since 2003. This report is based on data collected at ages 12-13 years, including dietary information, pediatric allergist assessment for asthma and tests for AHR. Consideration was also given to *a priori* confounding variables, including weight status. Height and weight measurements were collected in triplicate, and body mass index (BMI; weight [kilograms]/height [metres<sup>2</sup>]) was calculated from the mean of these measures. Each participant was then categorized as normal weight (<85<sup>th</sup> percentile for age and sex) or overweight (≥85<sup>th</sup> percentile for age and sex), based on the accepted criteria of the Canadian Pediatric Society (23). Other confounding variables included sex, region of residence, SES and maternal history of asthma. In order to add elements of temporality, breastfeeding duration (never breastfed vs. ever breastfed, and <3 months vs. ≥3 months) and children's fast food intake at 8-10 years old (never/occasionally vs. ≥1 time per week) were also considered.

### **Assessment of Diet Quality**

Diet quality was ascertained via an adapted version of the Youth Healthy Eating Index (YHEI) (24). The YHEI is derived from the United States' Department of Agriculture's Dietary Guidelines for Americans (24). These guidelines (25) are similar to those outlined in Canada's Food Guide to Healthy Eating (26). The FFQ used in the present study was not originally designed to assess diet quality using the YHEI. Thus, some adaptations to component and overall scores were necessary (Table 1).

Information on children's diets was at 12-13 years old collected via parent-/guardian- and child report using a 39-item FFQ. All questions were closed-ended; parents and children could select frequency of consumption for each of the foods from various options, depending on the food items. This FFQ was adapted from the validated 72-item FFQ used in the Nurses' Health Study (NHS) (27). Some items included in the NHS FFQ were excluded in our FFQ (Table 1). These included cottage cheese, hard cheese and liver (attempts to reduce number of questions and thus participant burden; not anticipated to greatly alter diet quality scores), coffee and tea (comparable aged children consume only modest amounts (<250mL) of such beverages per day (28), and alcoholic beverages.

The FFQ were completed primarily by the children, although there were some questions that the parent/guardian and child were asked to complete together. Although it is not possible to say definitively, some of the questions

may have been completed solely by the parents. These would have included questions regarding the types of oil used for cooking, use of n-3 enriched eggs, and intake of calcium-fortified orange juice. Notably, parental recall of adolescents' diets via FFQ has been validated, albeit modestly ( $r=0.30$  [range 0.10-0.61] for foods; higher for nutrients) (29).

Given the food items that were contained in this FFQ, the following components were excluded from our adaptation of the YHEI: soda and drinks, consumption of visible animal fat (fat on meat; skin on poultry), regularity of breakfast consumption and regularity of eating dinner with family. We did include were food items that were not part of the NHS FFQ, such as calcium-fortified orange juice, vitamin D-fortified orange juice, n-3 enriched eggs, as well as queries of vegetarianism or veganism. These foods were included given the recent interest in asthma and the role of these foods, nutrients and dietary patterns (30-33). These exclusions and additions resulted in an adapted YHEI maximum possible score of 85; this is 15 points less than the total possible score of the original YHEI (24). From these totals, two dichotomous groups (low vs. high consumption) were created using the 50<sup>th</sup> percentile of total and component diet scores as cut-offs (Table 1).

### **Outcome Measures**

The primary outcome measure in this study was a pediatric allergist

diagnosis of asthma at 12-13 years old. This definition of asthma is more robust than self-/parental-report or general practitioner diagnosis, which tends to over- and under-report asthma, respectively (34,35). Children diagnosed with asthma were further dichotomized as having allergic vs. non-allergic asthma. This dichotomization was made based on a skin prick test (SPT) to one or more common allergens  $\geq 3$  mm in diameter compared to the negative control. Pediatric asthma has several phenotypes. As the presence of atopy may influence the association between diet and asthma/wheeze (36), the phenotypes considered herein were allergic vs. non-allergic asthma.

The secondary outcome measure was AHR. This was measured via the provocative concentration of methacholine required to decrease participants' FEV<sub>1</sub> by 20% (PC<sub>20</sub>), using the Cockcroft technique (37). A 20% drop in FEV<sub>1</sub> yields a measure of the provocative concentration (PC<sub>20</sub>) that can be classified as mild (2.1-8.0 mg/ml), moderate (0.25 - 2.0 mg/ml) or severe (<0.25 mg/ml) AHR as compared to normal (>8mg/ml) controls. An inhaled bronchodilator (e.g. Ventolin or Salbutamol) was subsequently administered to reverse any fall in FEV<sub>1</sub> following the methacholine challenge. This assessment was conducted by trained research nurses and research assistants.

## **Ethics**

This study received ethical approval from The University of Manitoba's

Health Research Ethics Board. Parents/guardians provided written consent and children provided written assent.

### **Study Population**

Of the 489 children seen at ages 12-13, nutritional data were available for 476 children. Pediatric allergist assessments for asthma and PC<sub>20</sub> scores were available for 470 and 460 children, respectively. All children had been involved in the 1995 Manitoba Prospective Cohort Study since its inception in 2002-03. Thus, they were familiar with the research tools and clinical assessments involved in this study.

### **Statistical Analysis**

Descriptive statistics were used to describe the study population. Binary logistic regression analyses were used to identify potential relationships between total and component diet scores (exposure variable; continuous) and asthma (dichotomous outcome variable; categorical). Multivariate logistic regression was used to identify relationships between total and component diets scores and AHR (trichotomous outcome variable [normal, mild, moderate/severe]; categorical). Logistic regression is an appropriate statistical test for two reasons. One, it is a robust test and thus allows for nonlinear associations. Two, it permits the use of dichotomous outcome variables, which are unstable in linear

regression. Although a goodness of fit test should have been done, logistic regression is nonetheless an appropriate analytical technique. If the goodness of fit had been poor, logistic regression would have been appropriate because it allows for nonlinearity. Conversely, if the fit had been good, logistic regression would still be appropriate to use for the second reason.

Results are presented as odds ratios (95% confidence intervals).

Covariates included weight status at 12-13 years old (lean vs. overweight), region of residence (urban, southern rural, northern), income ( $\geq$  or  $<$  \$30000 Canadian annually), physical activity at 8-10 years old ( $>2$  or  $\leq 2$  days per week) and maternal history of asthma.

Participant data were analyzed collectively, and then stratified for breastfeeding, fast food intake and breastfeeding + fast food intake. In fully adjusted models which were not stratified as such, these variables were considered as confounders.

For all analyses, significance was defined as  $p < 0.05$ . Analyses were conducted using Statistical Package for Social Sciences (SPSS) 17.0.

## RESULTS

Participants' characteristics are noted in Table 2. Four hundred seventy-six children (270 [56.7%] boys) were seen at this assessment. This represents 65.8% of the original nested case-control study, which began in 2002-03. At a

mean age  $12.6 \pm 0.5$  years, approximately 26% of children had asthma, while 53.8% had AHR. There were no differences in rates of breastfeeding, breastfeeding duration, fast food consumption or breastfeeding + fast food consumption (all  $p > 0.05$ ) between those with and those without asthma. No differences were identified between sexes, except for AHR; girls were significantly more likely to have normal AHR than boys. Nearly three-quarters of the children had a BMI within the healthy range. Most lived in urban areas and were from middle-class families. Approximately one in four mothers of participating children had a history of asthma.

Few associations were made between diet scores and asthma. This was true for all participants collectively, as well as after stratification for breastfeeding (never vs. ever), fast food intake (never/occasionally vs.  $\geq 1$  time per week), and breastfeeding + fast food (never breastfed + fast food  $\geq 1$  time per week vs. breastfed at least 3 months + fast food never/occasionally). In model adjusted only for weight status, region of residence, family income and maternal history of asthma, high multivitamin use was protective against asthma in children who consumed fast food at least once per week (OR 0.75; 95%CI 0.56-1.00;  $p < 0.05$ ). This association was lost in a fully adjusted model. Low margarine and butter scores were protective against asthma among those who were never breastfed and who ate fast food at least once weekly (OR 0.22; 95%CI 0.06-0.87,  $p < 0.05$ ). Stratification by duration of breastfeeding ( $< 3$  months vs.  $\geq$

3months) did not reveal any additional significant associations between total diet and diet component scores and asthma (data not shown).

Diet scores of children with allergic asthma (n=107; 22.5%) and non-allergic asthma (n=38; 8.0%) were compared to those of healthy children (n=181; 38.0%). This excluded 150 (31.5%) children from the prospective cohort, who were atopic but who did not have asthma. In unadjusted and partially adjusted models, there was a strong association between low vegetable consumption and low multivitamin intake and allergic asthma. High vegetable intake was protective against allergic asthma persisted in a fully adjusted model (OR 0.49; 95% CI 0.29-0.84;  $p<0.009$ ).

Two hundred four children (44.3%) had normal airway responsiveness, 108 (23.5%) had mild AHR, 123 (26.7%) had moderate AHR and 25 (5.4%) had severe AHR. These latter 2 groups were collapsed to create a moderate/severe AHR category. Vegetable and dairy intakes were identified as protective against moderate/severe AHR in unadjusted and partially adjusted models, including models in which we adjusted for breastfeeding, fast food intake, and breastfeeding + fast food intake (data not shown). Only vegetable intake remained protective against moderate/severe AHR in a fully adjusted model (OR 0.58; 0.37-0.91;  $p<0.019$ ).

## **DISCUSSION**

In this study, total diet scores were not associated with asthma or AHR. In a fully adjusted model, high vegetable intake was inversely associated with allergic asthma, as well as moderate/severe AHR, suggesting that vegetable intake may confer protection for particular asthma phenotypes or severities only. The reasons for phenotype-specific protection remain unclear. However, vegetables may protect against asthma in two different ways. First, vegetables are abundant in antioxidants. The 'antioxidant hypothesis' was first described by Seaton, Godden and Brown (1994) nearly two decades ago. Vitamin C, a potent antioxidant, is known to act on the airways by affecting arachidonic acid metabolites, including prostaglandins. In animal models, Prostaglandin F<sub>2</sub>α induces bronchoconstriction; vitamin C mitigates this reaction. Additionally, vitamin C is the most abundant antioxidant in the extracellular fluid of the lungs (Seaton et al, 1994). Alternatively, vegetable intake may be a proxy for lifestyle factors, including but not limited to variables identified as confounders at Visit 3.

Vegetables queried in the FFQ included green and orange vegetables. Canada's Food Guide (26) suggests both dark green and orange vegetables ought to be consumed at least once daily. These vegetables are rich in numerous antioxidants. The hypothesis that such antioxidants are protective against asthma was first noted in the literature nearly over a decade ago (38). Much of the related literature focuses on fruits, including a recent report in which regular fruit intake over the preceding month reduces the risk of persistent asthma (38).

We were unable to identify a protective effect of fruit intake on asthma outcomes. Nonetheless, this report provides evidence that high vegetable intake, also a proxy for antioxidant intake, may protect against allergic asthma and increasingly severe AHR. Similarly, an inverse association has been reported between green vegetable intake and self-reported wheeze among those living in low/middle income nations, but not high income nations (40). The lack of association between vegetable intake and asthma in developed nations may be due to differences in preparation methods or the variety of available vegetables compared to developing nations (40). However, findings from other work (40-42), including the present study, suggest that vegetable intake may be protective against children from more affluent nations. Also consistent with the present study is work from Menorca, Spain, which was indicative that “fruity vegetables” (tomatoes, green beans, eggplant, zucchini, cucumber) protected against atopic (or allergic) wheeze (35). These types of vegetables were collectively grouped with other vegetables in the present study. The related protective mechanisms of vegetables remain unclear. However, it is plausible that antioxidants, particularly vitamins C and E, and  $\beta$ -carotene play a role.

As a marker of pulmonary function, a decrease in the forced expiratory volume in one second (FEV<sub>1</sub>) has been associated cross-sectionally with a traditional northern European diet, which includes boiled vegetables (44). Although initially high in anti-oxidants, vegetables lose much of their

antioxidant properties in the cooking process, particularly boiling (45). Thus, it is likely that not all vegetables confer a similar protective effect against allergic asthma, AHR and, more generally, lung function. Consideration must also be given to the methods in which these foods were prepared.

As previously noted, allergic disease may begin in fetal (19) and early life (20). As such, the protective effect of vegetable intake against allergic disease has been considered among very young children. High maternal vitamin E consumption in pregnancy is seemingly protective against childhood wheeze (7). While no associations between maternal vegetable intake during pregnancy and asthma in offspring (7,8) have been identified, high maternal vegetable consumption during pregnancy may be protective against wheeze and atopy in school-aged children (9).

These associations provide further evidence that vegetable intake may confer protection against allergic asthma and moderate-to-severe AHR. Although causality cannot be implied due to the cross-sectional nature of this study, the present findings are in accordance with existing literature. Moreover, the inclusion of breastfeeding data and previous fast food consumption data allowed for temporality. Nonetheless, determination of dietary changes resulting from an asthma diagnosis is beyond the scope of this investigation.

There are several limitations to this study. The validated YHEI was adapted, based on available data, for this study, thereby necessitating some

exclusions. Some excluded foods and beverages were likely rarely consumed (e.g. liver, coffee) or would have been inappropriate to query among children aged 12-13 years (e.g. alcohol) and would likely have had little impact on the total dietary score if they had been included. Other excluded foods (e.g. cottage and hard cheeses) were likely more regularly consumed foods. However, these items were not included as part of the FFQ, and thus by necessity, had to be excluded. Second, participants were predominantly from middle class families in Canada. Thus, they likely had greater access to a wider variety of dietary choices and had fewer food security concerns. Last, as with all self-reported dietary data, FFQ have intrinsic limitations. Such limitations range from concerns with variations in nutrient composition and portion sizes of the reported foods (27) to participants' reports based on creating an illusion of a more nutritious diet than is actually consumed. These latter three issues may have been further compounded by the fact that participants were asked to complete numerous questionnaires during the study visit and validity may have been reduced due to participant fatigue/burden. But, many participants actually completed the FFQ prior to the study visit, thereby minimizing participant fatigue.

There are many strengths to this study. Asthma presence, asthma phenotypes and AHR were measured objectively and are considered to be the gold standards. As well, this is one of the largest population-based descriptions

between diet and asthma in an adolescent population. Adolescents tend to have nutritionally-inferior diets (46); this is supported by participants' low total and component diet scores. The sex shift of asthma, from male to female predominance, also occurs during this time (47). As such, examination of potential associations between diet and asthma in this age group is warranted. And, while an adapted version of a validated FFQ was used, the inclusion of foods typically eaten in Manitoba and by adolescents provide an enhanced representation of participants' diets.

These findings have implications for future research and clinical work. The ongoing hypothesis that vegetable intake is inversely associated with allergic asthma and AHR warrant further consideration, as cumulative evidence remains unclear. Moreover, associations between diet and asthma should be considered in a more diverse population. This ought to include children from low-SES and food insecure homes, who are more likely to have a nutritionally-inferior diet than children from more affluent families. Lastly, although it would be premature to advise patients that vegetable intake is protective against allergic asthma and increasingly severe AHR, these nutrients have many other well-documented health benefits. Thus, consumption of these foods ought to be encouraged. In youth, vegetable intake is inversely associated with allergic asthma, and may protect against moderate-to-severe airway hyperresponsiveness.

**Table 4.1. Adaptation of the Youth Healthy Eating Index (YHEI) and Dichotomization of Low vs. High Scores**

YHEI Component	Criteria for Maximum Score	Criteria for Minimum Score	Maximum Score	Cut-Offs for Scores	
				Low	High
Total YHEI Score	Maximum for all components	0	85	0.00-33.45	>33.45
1. Whole Grains	>2x/day	0	10	0.00-6.50	>6.50
2. Vegetables	>2x/day	0	10	0.00-4.6	>4.60
3. Fruits	>2x/day	0	10	0.00-5.33	>5.33
4. Dairy	>2x/day	1-3x/month or less	10	0.00-4.50	>4.50
5. Meat ratio <sup>a</sup>	>2x/day	0	10	0.00-0.36	>0.36
6. Snack foods <sup>b</sup>	0	≥2x/day	10	0.00-4.25	>4.25
7. Soda and drinks	NA	NA	-	-	-
8. Multivitamin use <sup>c</sup>	Daily	Never	5	0.00-0.25	>0.25
9. Margarine and butter	Never	≥2x/day	5	0.00-2.83	>2.83
10. Fried foods outside home <sup>c</sup>	Never or <1x/month	≥1x/day	5	0.00-3.0	>3.000
11. Visible animal fat	NA	NA	-	-	-
12. Eat breakfast	NA	NA	-	-	-
13. Dinner with family	NA	NA	-	-	-
14. Fish	>2x/week	Never	10	0.00-1.50	>1.50

<sup>a</sup>Lean meat + vegetable protein / dark meat

<sup>b</sup>Salty snacks (e.g. potato chips, nachos, pretzels, crackers, canned soup) and snacks with added sugar (e.g. cakes, doughnuts, cookies)

<sup>c</sup>Dichotomized as low or high consumption due to low range of scores for this component score

Adapted from references 26 and 28

**Table 4.2. Participant Characteristics**

	n	% <sup>a</sup>
Sex	476	100.0
Age <sup>b</sup> (n=474)	12.6 ± 0.5	-
Diet Score <sup>b</sup> (n=476)	33.9 ± 7.4	-
Asthma (n=465)		
No	343	73.8
Yes	122	26.2
AHR <sup>c</sup> (n=460)		
Normal	204	42.9
Mild	108	22.7
Moderate	123	25.8
Severe	25	5.3
Breastfeeding (n=471)		
Yes	410	87.0
≥3 months	340	82.9
Fast Food Consumption (n=471)		
Never/Occasionally	217	46.1
≥1 time per week	254	53.9
Physical Activity (n=473)		
≤2 times per week	96	20.3
Most/all days	377	79.7
Weight Status <sup>d</sup> (n=476)		
Lean	342	71.8
Overweight	134	28.2
Region of Residence (n=476)		
Urban	265	55.7
Southern Rural	177	37.2
Northern	34	7.1
Socio-Economic Status <sup>e</sup> (n=476)		
<\$30000	70	14.7
≥\$30000	406	85.3
Maternal History of Asthma (n=475)		
No	343	72.1
Yes	122	25.6

<sup>a</sup>Percentages may not total 100% due to rounding

<sup>b</sup>Mean ± standard deviation

<sup>c</sup>Airway hyperresponsiveness based on methacholine challenge

<sup>d</sup>Weight status based on BMI < or ≥ 85th percentile for age and sex

**Table 4.3. Logistic Regression Models of Diet Quality and Asthma in Manitoba Children**

	All Participants (n=476)	Breastfed		Fast Food		Breastfeeding + Fast Food	
		Never (n=61)	Ever (n=410)	Never or Occasionally (n=217)	≥1 time/week (n=254)	Never Breastfed + Fast Food ≥1 time/week (n=36)	Breastfed ≥ 3 months + Fast Food never or occasionally (n=151)
		OR (95%CI <sup>a</sup> )	OR (95%CI <sup>a</sup> )	OR (95%CI <sup>a</sup> )	OR (95%CI <sup>a</sup> )	OR (95%CI <sup>a</sup> )	OR (95%CI <sup>a</sup> )
<b>Total Diet Score</b>							
<i>Crude</i>	1.02 (0.84-1.24)	1.17 (0.70-2.03)	0.98 (0.80-1.21)	0.84 (0.63-1.12)	1.22 (0.93-1.60)	2.05 (0.95-4.42)	1.22 (0.85-1.76)
<i>Model 1<sup>b</sup></i>	1.01 (0.82-1.24)	1.39 (0.73-2.63)	0.97 (0.78-1.20)	0.83 (0.61-1.13)	1.18 (0.89-1.57)	2.00 (0.82-4.89)	1.13 (0.77-1.65)
<i>Model 2<sup>c</sup></i>	1.01 (0.82-1.24)	1.36 (0.71-2.61)	0.97 (0.78-1.21)	0.83 (0.60-1.13)	1.18 (0.89-1.57)	1.88 (0.77-4.64)	1.17 (0.80-1.73)
<b>YHEI Component</b>							
Whole Grains							
<i>Crude</i>	0.99 (0.77-1.24)	1.37 (0.76-2.46)	0.93 (0.72-1.19)	1.00 (0.71-1.39)	1.00 (0.74-1.37)	1.10 (0.52-2.32)	1.09 (0.73-1.62)
<i>Model 1<sup>b</sup></i>	0.99 (0.78-1.26)	1.61 (0.78-3.33)	0.93 (0.71-1.20)	1.00 (0.69-1.43)	1.02 (0.73-1.41)	1.43 (0.60-3.41)	1.06 (0.70-1.61)
<i>Model 2<sup>c</sup></i>	1.00 (0.79-1.27)	1.56 (0.75-3.27)	0.93 (0.72-1.22)	0.99 (0.69-1.43)	1.03 (0.74-1.43)	1.41 (0.58-3.43)	1.07 (0.70-1.63)
Vegetables							
<i>Crude</i>	0.99 (0.82-1.20)	1.09 (0.63-1.89)	0.98 (0.80-1.21)	1.12 (0.84-1.49)	0.87 (0.67-1.14)	1.00 (0.50-2.02)	0.87 (0.60-1.25)
<i>Model 1<sup>b</sup></i>	0.92 (0.75-1.13)	1.05 (0.55-2.01)	0.92 (0.74-1.15)	1.07 (0.78-1.47)	0.81 (0.61-1.08)	1.04 (0.47-2.31)	0.84 (0.57-1.23)
<i>Model 2<sup>c</sup></i>	0.93 (0.75-1.14)	1.13 (0.58-2.1)	0.93 (0.74-1.16)	1.08 (0.78-1.49)	0.81 (0.61-1.08)	1.03 (0.46-2.30)	0.82 (0.55-1.21)
Fruits							

<i>Crude</i>	0.94 (0.77-1.14)	1.17 (0.70-2.03)	0.90 (0.73-1.11)	0.92 (0.69-1.23)	0.95 (0.73-1.24)	1.18 (0.59-2.38)	0.96 (0.67-1.38)
<i>Model 1<sup>b</sup></i>	0.87 (0.71-1.08)	1.37 (0.70-2.70)	0.83 (0.66-1.04)	0.84 (0.61-1.15)	0.93 (0.70-1.25)	1.45 (0.59-3.55)	0.96 (0.66-1.40)
<i>Model 2<sup>c</sup></i>	0.87 (0.71-1.07)	1.26 (0.63-2.53)	0.83 (0.66-1.04)	0.84 (0.61-1.15)	0.92 (0.69-1.23)	1.29 (0.51-3.24)	0.93 (0.64-1.37)
<b>Dairy</b>							
<i>Crude</i>	0.93 (0.76-1.14)	1.03 (0.58-1.80)	0.93 (0.75-1.15)	0.99 (0.74-1.33)	0.89 (0.68-1.17)	1.00 (0.50-2.02)	0.90 (0.63-1.29)
<i>Model 1<sup>b</sup></i>	0.91 (0.73-1.12)	0.86 (0.43-1.74)	0.91 (0.73-1.15)	0.94 (0.68-1.30)	0.91 (0.68-1.22)	1.08 (0.43-2.73)	0.92 (0.63-1.35)
<i>Model 2<sup>c</sup></i>	0.90 (0.73-1.12)	0.87 (0.43-1.75)	0.91 (0.72-1.14)	0.93 (0.67-1.29)	0.90 (0.67-1.21)	0.90 (0.33-2.43)	0.90 (0.61-1.32)
<b>Meat Ratio</b>							
<i>Crude</i>	1.07 (0.88-1.31)	1.16 (0.67-2.00)	1.06 (0.85-1.30)	1.06 (0.79-1.41)	1.07 (0.82-1.40)	1.00 (0.50-2.00)	1.04 (0.73-1.48)
<i>Model 1<sup>b</sup></i>	1.04 (0.85-1.28)	1.09 (0.56-2.14)	1.04 (0.83-1.29)	0.98 (0.72-1.34)	1.11 (0.84-1.48)	1.12 (0.50-2.52)	1.06 (0.73-1.54)
<i>Model 2<sup>c</sup></i>	1.05 (0.85-1.29)	1.09 (0.56-2.14)	1.04 (0.84-1.30)	0.98 (0.71-1.34)	1.13 (0.85-1.50)	1.08 (0.47-2.44)	1.09 (0.74-1.59)
<b>Snack Foods</b>							
<i>Crude</i>	0.91 (0.75-1.11)	0.96 (0.56-1.67)	0.91 (0.73-1.12)	0.91 (0.68-1.22)	0.90 (0.68-1.18)	1.28 (0.62-2.64)	0.87 (0.61-1.25)
<i>Model 1<sup>b</sup></i>	0.91 (0.74-1.12)	1.12 (0.58-2.17)	0.90 (0.72-1.13)	0.93 (0.68-1.27)	0.89 (0.67-1.19)	1.46 (0.61-3.53)	0.87 (0.59-1.27)
<i>Model 2<sup>c</sup></i>	0.91 (0.73-1.12)	1.13 (0.58-2.20)	0.90 (0.72-1.13)	0.93 (0.68-1.27)	0.89 (0.67-1.18)	1.58 (0.62-4.02)	0.91 (0.62-1.33)
<b>Multivitamin Use</b>							
<i>Crude</i>	0.89 (0.73-1.08)	0.73 (0.40-1.32)	0.93 (0.75-1.15)	1.04 (0.78-1.38)	0.78 (0.59-1.02)	0.91 (0.44-1.89)	0.80 (0.56-1.14)
<i>Model 1<sup>b</sup></i>	0.87 (0.70-1.07)	0.71 (0.38-1.50)	0.91 (0.73-1.13)	1.03 (0.76-1.42)	<b>0.75 (0.56-1.00)<sup>d</sup></b>	1.13 (0.48-2.71)	0.75 (0.51-1.10)
<i>Model 2<sup>c</sup></i>	0.87 (0.71-1.08)	0.78 (0.36-1.67)	0.91 (0.73-1.14)	1.04 (0.76-1.43)	0.76 (0.57-1.01)	1.40 (0.54-3.61)	0.79 (0.54-1.16)
<b>Margarine and Butter</b>							
<i>Crude</i>	0.88 (0.72-1.08)	0.75 (0.43-1.30)	0.93 (0.75-1.14)	0.85 (0.63-1.13)	0.91 (0.69-1.19)	0.62 (0.30-1.28)	0.99 (0.69-1.42)
<i>Model 1<sup>b</sup></i>	0.90 (0.73-1.11)	0.62 (0.30-1.24)	0.95 (0.76-1.19)	0.83 (0.60-1.13)	0.95 (0.71-1.26)	<b>0.26 (0.08-0.87)<sup>d</sup></b>	1.05 (0.72-1.54)
<i>Model 2<sup>c</sup></i>	0.89 (0.73-1.10)	0.53 (0.24-1.13)	0.94 (0.75-1.18)	0.83 (0.60-1.13)	0.93 (0.70-1.24)	<b>0.22 (0.06-0.87)<sup>d</sup></b>	1.03 (0.70-1.51)

Fried Foods Outside of Home							
<i>Crude</i>	0.86 (0.68-1.10)	0.42 (0.14-1.23)	0.91 (0.70-1.18)	0.88 (0.64-1.21)	0.85 (0.58-1.26)	NR <sup>e</sup>	0.88 (0.55-1.41)
<i>Model 1<sup>b</sup></i>	0.87 (0.67-1.13)	0.43 (0.14-1.40)	0.92 (0.70-1.20)	0.93 (0.65-1.32)	0.82 (0.55-1.23)	NR <sup>e</sup>	0.82 (0.50-1.36)
<i>Model 2<sup>c</sup></i>	0.88 (0.68-1.14)	0.48 (0.15-1.51)	0.92 (0.70-1.21)	0.93 (0.65-1.33)	0.83 (0.55-1.25)	NR <sup>e</sup>	0.85 (0.51-1.43)
Fish							
<i>Crude</i>	1.06 (0.87-1.30)	1.01 (0.58-1.76)	1.07 (0.86-1.32)	1.10 (0.82-1.47)	1.03 (0.79-1.35)	1.19 (0.56-2.54)	0.99 (0.69-1.42)
<i>Model 1<sup>b</sup></i>	1.01 (0.82-1.25)	1.18 (0.60-2.30)	1.01 (0.81-1.26)	1.02 (0.74-1.40)	1.02 (0.77-1.36)	1.35 (0.47-3.88)	0.97 (0.67-1.41)
<i>Model 2<sup>c</sup></i>	1.01 (0.82-1.25)	1.30 (0.65-2.61)	1.01 (0.81-1.26)	1.01 (0.74-1.39)	1.01 (0.76-1.35)	1.45 (0.48-4.37)	0.92 (0.63-1.35)

<sup>a</sup>Odds Ratio (95% Confidence Interval)

<sup>b</sup>Adjusted for weight status, region of residence, family income and maternal history of asthma

<sup>c</sup>Adjusted for weight status, region of residence, family income, physical activity at Wave 1 and maternal history of asthma

<sup>d</sup>p<0.05

<sup>e</sup>Not reportable due to small cell counts

Reference group is children with high total diet/diet component scores

**Table 4.4. Logistic Regression Models of Diet Quality in Children with Non-Allergic and Allergic Asthma****Phenotypes compared to Healthy Children**

	Unadjusted OR (95%CI <sup>e</sup> )	Model 1 <sup>a</sup> OR (95%CI <sup>e</sup> )	Model 2 <sup>b</sup> OR (95%CI <sup>e</sup> )	Model 3 <sup>c</sup> OR (95%CI <sup>e</sup> )	Model 4 <sup>d</sup> OR (95%CI <sup>e</sup> )
<b>Total Diet Score</b>					
Non-Allergic Asthma	1.10 (0.55-2.21)	1.10 (0.54-2.24)	1.04 (0.51-2.13)	1.03 (0.50-2.14)	0.98 (0.46-2.06)
Allergic Asthma	0.90 (0.56-1.45)	0.92 (0.56-1.52)	0.88 (0.54-1.44)	0.92 (0.55-1.52)	0.94 (0.56-1.59)
<b>By YHEI Component</b>					
<i>Whole Grains</i>					
Non-Allergic Asthma	0.68 (0.31-1.45)	0.69 (0.32-1.51)	0.75 (0.34-1.65)	0.77 (0.34-1.73)	0.73 (0.32-1.66)
Allergic Asthma	1.28 (0.71-2.30)	1.36 (0.73-2.52)	1.28 (0.70-2.31)	1.39 (0.74-2.60)	1.36 (0.71-2.59)
<i>Vegetables</i>					
Non-Allergic Asthma	0.88 (0.44-1.77)	0.79 (0.39-1.61)	0.89 (0.43-1.82)	0.79 (0.38-1.65)	0.74 (0.35-1.58)
Allergic Asthma	<b>0.55 (0.34-0.90)<sup>g</sup></b>	<b>0.45 (0.27-0.75)<sup>g</sup></b>	<b>0.56 (0.34-0.92)<sup>g</sup></b>	<b>0.47 (0.28-0.79)<sup>g</sup></b>	<b>0.49 (0.29-0.84)<sup>g</sup></b>
<i>Fruits</i>					
Non-Allergic Asthma	0.83 (0.41-1.67)	0.88 (0.43-1.78)	0.83 (0.41-1.70)	0.89 (0.43-1.85)	0.87 (0.41-1.85)
Allergic Asthma	0.94 (0.59-1.53)	1.00 (0.60-1.64)	0.89 (0.55-1.45)	0.97 (0.58-1.61)	1.06 (0.63-1.79)
<i>Dairy</i>					
Non-Allergic Asthma	1.36 (0.65-2.83)	1.32 (0.63-2.77)	1.31 (0.62-2.75)	1.27 (0.59-2.70)	1.35 (0.62-2.94)
Allergic Asthma	1.10 (0.67-1.78)	1.05 (0.63-1.74)	1.12 (0.68-1.85)	1.06 (0.63-1.77)	0.98 (0.57-1.67)
<i>Meat Ratio</i>					
Non-Allergic Asthma	1.00 (0.50-2.02)	1.02 (0.50-2.09)	0.94 (0.46-1.92)	0.97 (0.47-2.00)	0.94 (0.45-1.98)
Allergic Asthma	0.96 (0.59-1.55)	0.97 (0.59-1.60)	0.93 (0.57-1.51)	0.96 (0.58-1.60)	1.00 (0.59-1.69)
<i>Snack Foods</i>					
Non-Allergic Asthma	1.20 (0.59-2.41)	1.16 (0.57-2.36)	1.38 (0.67-2.85)	1.35 (0.65-2.82)	1.26 (0.60-2.66)
Allergic Asthma	1.29 (0.80-2.09)	1.29 (0.78-2.13)	1.40 (0.85-2.29)	1.37 (0.81-2.30)	1.34 (0.79-2.28)

<i>Multivitamin Use</i>					
Non-Allergic Asthma	1.52 (0.75-3.08)	1.38 (0.67-2.82)	1.51 (0.73-3.11)	1.35 (0.65-2.82)	1.17 (0.55-2.49)
Allergic Asthma	<b>1.62 (1.00-2.63)<sup>h</sup></b>	1.38 (0.83-2.28)	<b>1.65 (1.00-2.70)<sup>h</sup></b>	1.42 (0.85-2.37)	1.51 (0.89-2.57)
<i>Margarine and Butter</i>					
Non-Allergic Asthma	0.89 (0.44-1.78)	0.88 (0.44-1.79)	1.04 (0.51-2.13)	1.07 (0.51-2.22)	1.01 (0.48-2.14)
Allergic Asthma	1.16 (0.71-1.87)	1.14 (0.69-1.89)	1.27 (0.77-2.08)	1.27 (0.76-2.12)	1.22 (0.72-2.06)
<i>Fried Foods Outside of Home</i>					
Non-Allergic Asthma	0.93 (0.39-2.20)	0.86 (0.36-2.06)	1.35 (0.54-3.40)	1.28 (0.50-3.25)	1.15 (0.45-2.97)
Allergic Asthma	0.84 (0.47-1.50)	0.78 (0.43-1.44)	0.98 (0.54-1.79)	0.95 (0.51-1.78)	0.91 (0.48-1.73)
<i>Fish</i>					
Non-Allergic Asthma	1.48 (0.73-3.03)	1.43 (0.69-2.94)	1.66 (0.80-3.47)	1.60 (0.76-3.39)	1.48 (0.69-3.19)
Allergic Asthma	1.04 (0.65-1.69)	0.98 (0.59-1.61)	1.05 (0.65-1.72)	0.99 (0.60-1.66)	1.10 (0.65-1.86)

<sup>a</sup>Adjusted for breastfeeding only (never vs. ever)

<sup>b</sup>Adjusted for fast food consumption only (never/occasionally vs.  $\geq 1$  time per week)

<sup>c</sup>Adjusted for breastfeeding + fast food consumption

<sup>d</sup>Adjusted for all the variables in Model 3 plus weight status, region of residence, family income, physical activity and maternal history of asthma

<sup>e</sup>Odds Ratio (95% Confidence Interval)

<sup>g</sup> $p < 0.02$

<sup>h</sup> $p < 0.05$

Reference group is children with low total diet/diet component scores

**Table 4.5. Multivariate Logistic Regression Models of Diet Quality in Children with Mild and Moderate/Severe Airway Hyperresponsiveness compared to Healthy Children**

		Unadjusted OR (95% CI) <sup>c</sup>	Model 1 <sup>a</sup> OR (95% CI) <sup>c</sup>	Model 2 <sup>b</sup> OR (95% CI) <sup>c</sup>
<b>Total Diet Score</b>				
	Mild AHR	0.98 (0.61-1.56)	0.97 (0.61-1.55)	1.07 (0.66-1.72)
	Moderate/Severe AHR	0.92 (0.60-1.40)	0.90 (0.59-1.39)	0.97 (0.62-1.51)
<b>By YHEI Component</b>				
<i>Whole Grains</i>				
	Mild AHR	1.51 (0.84-2.69)	1.45 (0.81-2.59)	1.40 (0.78-2.53)
	Moderate/Severe AHR	0.89 (0.55-1.44)	0.89 (0.54-1.44)	0.90 (0.54-1.49)
<i>Vegetables</i>				
	Mild AHR	0.74 (0.47-1.19)	0.73 (0.46-1.18)	0.68 (0.42-1.11)
	Moderate/Severe AHR	<b>0.62 (0.40-0.94)<sup>d</sup></b>	<b>0.61 (0.39-0.94)<sup>e</sup></b>	<b>0.58 (0.37-0.91)<sup>d</sup></b>
<i>Fruits</i>				
	Mild AHR	0.78 (0.49-1.24)	0.78 (0.49-1.25)	0.77 (0.48-1.25)
	Moderate/Severe AHR	0.93 (0.61-1.43)	0.95 (0.62-1.46)	0.98 (0.63-1.53)
<i>Dairy</i>				
	Mild AHR	0.83 (0.51-1.34)	0.83 (0.52-1.34)	0.83 (0.51-1.36)
	Moderate/Severe AHR	<b>0.63 (0.41-0.98)<sup>e</sup></b>	<b>0.61 (0.39-0.94)<sup>e</sup></b>	0.66 (0.42-1.04)
<i>Meat Ratio</i>				
	Mild AHR	1.05 (0.66-1.67)	1.03 (0.64-1.65)	1.00 (0.62-1.62)
	Moderate/Severe AHR	1.01 (0.66-1.55)	0.97 (0.63-1.50)	0.99 (0.63-1.55)
<i>Snack Foods</i>				
	Mild AHR	1.28 (0.80-2.06)	1.26 (0.78-2.02)	1.37 (0.84-2.23)
	Moderate/Severe AHR	0.95 (0.62-1.45)	0.97 (0.63-1.50)	0.99 (0.63-1.55)
<i>Multivitamin Use</i>				
	Mild AHR	0.85 (0.53-1.35)	0.87 (0.54-1.39)	0.86 (0.53-1.39)
	Moderate/Severe AHR	0.86 (0.56-1.31)	0.88 (0.57-1.37)	0.92 (0.59-1.44)
<i>Margarine and Butter</i>				
	Mild AHR	1.10 (0.69-1.77)	1.10 (0.68-1.76)	1.11 (0.68-1.79)
	Moderate/Severe AHR	1.24 (0.81-1.91)	1.32 (0.85-2.04)	1.39 (0.88-2.18)
<i>Fried Foods Outside of Home</i>				
	Mild AHR	1.34 (0.76-2.36)	1.26 (0.71-2.24)	1.13 (0.63-2.04)
	Moderate/Severe AHR	1.32 (0.79-2.21)	1.40 (0.82-2.38)	1.38 (0.79-2.41)

*Fish*

Mild AHR	1.16 (0.72-1.85)	1.16 (0.72-1.86)	1.12 (0.69-1.82)
Moderate/Severe AHR	0.88 (0.57-1.35)	0.93 (0.60-1.43)	0.94 (0.60-1.47)

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<sup>a</sup>Adjusted for breastfeeding + fast food consumption

<sup>b</sup>Adjusted for variables in Model 1 plus adjusted for weight status, region of residence, family income, physical activity and maternal history of asthma

<sup>c</sup>Odds Ratio (95% Confidence Interval)

<sup>d</sup>p<0.02

<sup>e</sup>p<0.05

Reference group is children with low total diet/diet component scores

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In summary, few associations were made between total or component diet scores and asthma overall. High vegetable intake was protective against allergic asthma and moderate/severe AHR in fully adjusted models.

## **CHAPTER FIVE: HIGH SCREEN TIME IS ASSOCIATED WITH ASTHMA IN OVERWEIGHT MANITOBA YOUTH**

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In the previous chapter, consideration was given to the association between diet quality and asthma. Yet, diet represents only one component of lifestyle. Two other major constituents of lifestyle are physical activity and sedentary behaviour. Low levels of physical activity and high levels of sedentary behaviour are often associated with adverse health outcomes, including but not limited to asthma. To better understand how physical activity and sedentary behaviour influence asthma in youth, we tested for associations between physical activity and screen time, and asthma and AHR in a population-based sample of healthy weight and overweight Canadian youth. Screen time is a proxy for

sedentary time, and also reflects a shift in how youth use their leisure time. More traditionally, screen time was referred to as television time. But, with the advent of video and computer games, on-line social media and the like, the term “screen time” is a more accurately portrayal of this new phenomenon.

The aim of this chapter is to determine if lifestyle behaviours, including physical activity and screen time, are associated with asthma and AHR. Like the previous chapter, this chapter is also a manuscript, and therefore provides further introduction to the topic, as well as methods (many of which have been previously described in Chapter 2), as well as results and conclusions.

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High Screen Time is Associated with Asthma in  
Overweight Manitoba Youth

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Abbreviations:

BMI	Body mass index
CPS	Canadian Pediatric Society
OR	Odds Ratio
95% CI	95 <sup>th</sup> Percent Confidence Intervals

Key Words:

Asthma, overweight, youth, physical activity, screen time

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### Abstract

Low physical activity and high sedentary behaviour are often associated with adverse health outcomes, including but not limited to asthma. To better understand how physical activity and sedentary behaviour influence asthma in youth, we tested for associations between physical activity and screen time, and asthma and AHR in a population-based sample of healthy weight and overweight Canadian youth. In 2003-2005, we conducted a study of children (n=723 [34.0% asthma], 55.9% boys; mean age 8.6±0.5 years, at baseline) within the 1995 Manitoba Prospective Cohort Study. Children (n=489 [30.5% asthma]; 56.2% boys) were reassessed in 2008-2010 (mean age 12.6±0.5 years). Exposure variables, collected at baseline, were parent-reported physical activity and screen time defined as low vs. high with a stratification threshold of most/all days of the week and television/computer use ≥3 hours/day, respectively. At both baseline and follow-up, asthma status was assessed by a pediatric allergist according to standard clinical guidelines. Airway responsiveness was assessed via methacholine challenge using the Cockcroft technique. Airway hyperresponsiveness was defined as a provocative concentration of >8mg/ml methacholine required to induce a 20% fall in FEV<sub>1</sub>. We did not identify any associations between physical activity and asthma or airway hyperresponsiveness. However, youth with high screen time had a greater odds of asthma at baseline (OR 1.40, 95% CI 1.08-1.81, p<0.01) and follow-up (OR 1.45,

95% CI 1.06-1.97,  $p < 0.02$ ). This association was more pronounced among overweight youth (baseline: OR 1.98, 95% CI 1.30-3.01,  $p < 0.001$ ; follow-up: OR 1.81, 95% CI 1.09-3.03,  $p < 0.02$ ). No associations between screen time and AHR were found. High screen time, particularly among overweight youth, increases their odds of having or subsequently developing asthma. These data reinforce the concept that screen time (as a proxy for sedentary time), in addition to physical activity, should be included in clinical assessments of youth with asthma.

## High Screen Time is Associated with Asthma in Overweight Manitoba Youth

### INTRODUCTION

Asthma prevalence has dramatically increased in high income countries in recent decades (1-3), affecting a disproportionate number of youth (4). Asthma is more common in overweight youth compared to healthy weight youth (5), suggesting that overweight is a risk factor for asthma. Risk factors for overweight include low physical activity and high sedentary time (6). In addition to overweight status (7), increased sedentary time is linked with a deterioration of pulmonary function (8) and other cardiometabolic diseases (9). Collectively, these three observations point towards low physical activity and high screen time as risk factors for asthma.

Airway hyperresponsiveness (AHR) is a feature common to many children with asthma (10). AHR may also be present in children without a clinical diagnosis of asthma. High rates of AHR have been described amongst some (11,12), but not all athletes (13). Few studies have considered the association between physical activity, sedentary time and AHR in the general population. Moreover, there is a paucity of evidence regarding longitudinal associations between physical activity and screen time as exposures, and asthma and AHR as outcomes. As overweight youth are at particularly high risk of

chronic diseases, it remains unclear if physical activity and screen time and concurrent overweight status influence asthma and AHR, relative to healthy weight youth. In an effort to address these issues, the purpose of this study was to 1) better understand how physical activity and screen time are associated with asthma and AHR in youth, and 2) determine if these associations were influenced by weight status.

## **METHODS**

### **Study Design, Participant Recruitment**

This was a study of Manitoba youth including 246 youth with asthma and 477 without asthma recruited from the Study of Allergy, Genes and the Environment in Manitoba, Canada, described in detail elsewhere (14). Youth attended study clinic visits in 2003-2005 (baseline) and 2008-2010 (follow-up). The study was approved by the Health Research Ethics Board at the University of Manitoba and the Health Information Privacy Committee of Manitoba. All youth provided written assent and parents provided written consent prior to participation.

### **Assessment of Exposure Variables: Physical Activity and Screen Time**

Physical activity and screen time were determined by parental report. Physical activity frequency was determined from a close-ended response to the

following question: “In the last 12 months, how many times a week does your child engage in vigorous or competitive physical activity long enough to make him/her breathe hard?” Possible responses included: never/only occasionally, 1-2 times per week, or most/all days. Physical activity was treated as a binary outcome of inactive (never/only occasionally + 1-2 times per week) or active (most/all days), representing youth that did or did not meet the Canadian Paediatric Society’s (15) recommendation of achieving “an exercise protocol of at least 90 minutes per day of total physical activity. Frequency of screen time was also assessed with a close-ended response to the following question: “Currently, during a normal week, how many hours a day does your child watch television or play on the computer before or after school?” Possible responses included <1 hour, 1 to <3hours, 3 to <5hours, or ≥5hours. Screen time was treated as a binary outcome with a threshold of screen time above or below 3 hours daily. While the Canadian Paediatric Society recommends  $\leq 2$  hours of television per day (16), we chose to be aggressively conservative in interpreting the effects of screen time on asthma and airway hyperresponsiveness outcomes.

### **Assessment of Outcome Variables: Asthma and Airway Hyperresponsiveness**

The presence or absence of asthma at either time point is the outcome variable in this analysis. Asthma status was ascertained by pediatric allergist assessment at baseline and follow-up according to the Canadian Asthma

Consensus Guidelines (10). At both baseline and follow-up, trained nurses and/or research assistants conducted methacholine (Methapharm Inc.) challenges using the Cockcroft technique (17). AHR was treated as a binary outcome. Youth were classified as having normal airway responsiveness if the provocative concentration of methacholine ( $PC_{20}$ ) required to decrease participants' forced expiratory volume in one second [ $FEV_1$ ] by 20%) was greater than 8 mg/ml methacholine, or AHR if their  $PC_{20}$  was equal to or less than 8mg/ml methacholine.

To assess the longitudinal influence of physical activity and screen time on asthma and AHR outcomes, we developed variables of incident + persistent asthma and incident + persistent AHR. Although our initial intent was to only consider incident asthma and incident AHR, there were too few cases of either to allow for statistical analysis.

### **Anthropometry**

Trained research assistants measured and recorded weights in light clothing to the nearest 0.2 kg and height to the nearest 0.1 cm using a digital scale and stadiometer, respectively. Body mass index (BMI) was calculated using the standard formula: weight (kilograms) divided by height (meters squared). A BMI value above the Canadian Paediatric Society (18) and Centers for Disease Control and Prevention (19) criteria of the 85<sup>th</sup> percentile for age and sex was

used as a threshold to classify youth as overweight. For the purpose of this study, we did not differentiate between overweight and obesity, due to a relatively low frequency of obese participants.

### **Statistical Analysis**

The outcomes of asthma and AHR were treated as binary outcomes. Differences between youth with and without asthma were assessed with a logistic regression. Multivariable logistic regression, stratified by healthy weight and overweight youth, was then used to determine if the associations remained significant after adjusting for potential confounding variables. Potential confounding variables were addressed via questionnaire, based on *a priori* expectations from the literature including: parental education (high school diploma or less vs. post-secondary education) and income (<\$30000 vs. ≥\$30000 Canadian annually), region of residence (urban, rural or northern), and ethnicity (Caucasian vs. First Nations).

Odds ratios (OR) and 95<sup>th</sup> percent confidence intervals (95% CI) are reported. Statistical significance was set at  $p < 0.05$ , although greater levels of significance are noted if applicable. Data were analyzed using SPSS 18.0 for Windows (Somers, NY).

## RESULTS

Participant characteristics are summarized in Table 1. Of the 723 youth [55.9% boys] seen at baseline ( $8.6\pm 0.5$  years old), 246 (34.0%) had a pediatric allergist diagnosis of asthma, 411/675 (60.9%) had AHR and 232/723 (32.1%) were overweight. Most (51.7%) lived in urban centers, while only a small proportion (11.5%) lived in northern communities. Nearly three-quarters (72.2%) were Caucasian. AHR was more prevalent in First Nations youth than Caucasian youth ( $p<0.05$ ).

Four hundred eighty-nine youth were seen at follow-up. Asthma assessments were not made for three of these youth. Thus, our follow-up sample included 486 youth ( $12.6\pm 0.5$  years old). This represents 67.2% of the sample at baseline. At follow-up, 151/476 (31.1%) of youth had asthma, 411/675 (55.5%) had AHR and 151/486 (31.1%) were overweight.

Table 2 presents the results of logistic regression analyses for the associations between physical activity, asthma and AHR. In the entire cohort and after stratifying on weight status, no significant associations were observed between physical activity, and asthma and AHR at baseline or follow-up, including after adjusting for confounding variables.

In contrast, in an unadjusted model, high screen time significantly increased the odds of asthma, but not AHR, at baseline (Table 3. OR 1.25, 95% CI 1.00-1.55,  $p=0.05$ ). The strength of this association was significantly greater

within the subgroup of overweight youth (OR 1.47, 95% CI 1.05-2.05,  $p < 0.02$ ).

The association between screen time and asthma was strengthened after controlling for differences in demographic variables, including weight status, sex, region of residence, ethnicity, parental income and education. After adjusting for confounding variables, youth with high screen time had 40% greater odds of having asthma compared to those with low screen time (OR 1.40, 95% CI 1.08-1.81,  $p < 0.01$ ). While no associations between screen time and asthma were identified amongst normal weight youth, overweight youth with who engaged in high screen time had a nearly two-fold greater odds of having asthma at baseline (OR 1.98, 95% CI 1.30-3.01,  $p < 0.001$ ) and follow-up (OR 1.81, 95% CI 1.09-3.03,  $p < 0.02$ ). Screen time was not associated with AHR at either baseline or follow-up, regardless of weight status (all  $p > 0.05$ ). Notably, stricter cut-offs of screen time (<1 vs.  $\geq 1$  hour daily) were not associated with a greater odds of asthma than the stratification threshold of 3 hours daily (data not shown).

No associations were identified between physical activity and screen time and incident + persistent asthma and incident + persistent AHR (results not shown).

## **DISCUSSION**

In this study of Manitoba youth, physical activity frequency was not associated with asthma or AHR outcomes either cross-sectionally or

longitudinally. In contrast, youth, particularly those who were overweight at baseline, who engaged in at least three hours daily of screen time had a greater odds of having asthma, but not AHR, at 8-10 years old and at 12-13 years old. The association between screen time and asthma in overweight youth was independent of ethnicity, region of residence and parental socio-economic factors.

The observation that screen time and not physical activity was significantly associated with a diagnosis of asthma reinforces the concept that screen time and physical activity are independent determinants of health in youth. The data presented here also support other observations that youth with asthma are characterized by higher rates of screen time, relative to youth without asthma (20). At least one study supports a dose-response association between television and asthma (21). We were unable to consider such a relationship due to data limitations.

That we did not find an association between physical activity and asthma is encouraging. The Canadian Asthma Consensus Guidelines (10) and the Canadian Paediatric Society's physical activity recommendations for youth with chronic health conditions, including asthma (22), both reinforce the need for regular physical activity, particularly when symptoms are well controlled (22). Notably, improved physical fitness may reduce asthma medication requirements

(23). Yet, many youth fail to reach the minimum daily recommended level of physical activity (24).

Although we identified no differences in asthma outcomes by level of activity, the literature in this area remains ambiguous. Some findings point towards a difference in asthma outcomes by physical activity (26,26), while others, which employed objective measures of physical activity, did not (27,28).

Our data support the latter and extend them by demonstrating that, while physical activity patterns are not associated with or predictive of asthma, youth with high screen time do experience more asthma, compared to youth with low screen time. Furthermore, the observation that the effect size for this association is greater among overweight youth suggests that there may be an interaction between being overweight and high screen time in the development of asthma. That is, being overweight and sedentary is more of a risk factor than either independently.

We also provide evidence that physical activity is not associated with AHR in youth. This finding supports others' findings that AHR rates in youth do not differ by intensity and duration of physical activity (13,29). Interestingly, Pedersen (29) described a high prevalence of AHR in adult athletes. Collectively, these findings indicate that AHR may be a product of the interaction between age and physical activity. Moreover, AHR development in adult athletes may require an additional stimulus; most of the previous work in this field has been

focused specifically on swimmers (13) and cross-country skiers (30), rather than a wide range of activities.

Highly active youth may not exhibit differing objective symptoms of AHR in the presence of activity than their less active peers as the airways of young people may be less susceptible to environmental insults (e.g. chlorine, cold air) than those of adults. With age and multiple years of athletics, respiratory symptoms and airway inflammation may develop. Continued reassessments of our study population will address whether, and if so, when physical activity influences AHR. Consideration to activity type and intensity, as well as the environment in which the activity is carried out is warranted in order to identify if certain activities increase the risk of AHR over other activity choices.

Consideration to the AHR cutoffs used in this and others' work is also warranted. Our cutoff for AHR was  $\leq 8$  mg/ml methacholine. The stratification threshold for AHR varies widely in the literature from 4 mg/ml methacholine to 16 mg/ml methacholine (11,12). Such range in cutoffs makes cross-study comparisons difficult.

Our findings also support an association between screen time and asthma amongst youth. Screen time is also highly predictive of overweight in youth (32). Whether assessed quantitatively (32) or qualitatively (33), overweight youth participate in less in activities. This reduced willingness to be physically active may ultimately be replaced by increased screen time. Continued follow-up of

these youth will provide further insight into the long-term effects of high screen time on asthma and AHR outcomes. Planned qualitative investigations will address perceptions of physical activity and screen time to ascertain similarities and/or differences between groups amongst youth with and without asthma.

There are challenges in determining physical activity patterns accurately and reliably in youth. While direct observation is considered the gold standard for establishing youth's physical and sedentary habits (34), this is not practically- or economically-feasible in population-based studies. We relied on parent-reported data as a surrogate measure with the understanding that individuals frequently over-report physical activity and under-report sedentary time. As youth were involved in a prospective study on asthma, parents of youth with asthma may have promoted regular physical activity. However, this is unlikely as others have reported similar findings (36).

## **Conclusion**

In conclusion, we provide further evidence that physical activity is not associated with a diagnosis of asthma or AHR in youth, while three or more hours daily of screen time nearly doubles the odds of asthma, but not AHR. These data reinforce the concept that, in addition to physical activity, screen time should be monitored in clinical and research settings of asthma in youth. Clinicians need to emphasize that screen time ought to be minimized,

particularly given its association of several chronic diseases, including asthma.

**Table 5.1. Participant Characteristics: 1995 Manitoba Prospective Cohort Study**

	Overall		Asthma at 8-10 yo		Asthma at 12-13 yo		AHR at 8-10 yo		AHR at 12-13 yo	
	n	%	n	%	n	%	n	%	n	%
At 8-10 yo (n=723)	723	100.0	246	34.0	-	-	411	60.9	-	-
At 12-13 yo (n=486)	489	100.0	-	-	151	31.1	-	-	263	55.5
Weight Status										
<i>At 8-10 yo (n=723)</i>										
Normal	491	67.9	160	32.6	103	30.0	171	37.7	143	41.7
Overweight	232	32.1	86	37.1	48	33.6	93	41.9	68	47.6
<i>At 12-13 yo (n=486)</i>										
Normal Weight	335	68.9	-	-	100	29.9	-	-	<b>73</b>	<b>21.8<sup>a</sup></b>
Overweight	151	31.1	-	-	51	33.8	-	-	<b>78</b>	<b>51.7</b>
Region of Residence										
Urban	374	51.7	<b>166</b>	<b>44.4<sup>a</sup></b>	<b>112<sup>a</sup></b>	<b>41.3</b>	<b>113</b>	<b>30.2<sup>a</sup></b>	<b>99</b>	<b>36.5<sup>a</sup></b>
Rural	266	36.8	<b>61</b>	<b>22.9</b>	<b>35</b>	<b>19.8</b>	<b>107</b>	<b>40.2</b>	<b>88</b>	<b>49.7</b>
Northern	83	11.5	<b>19</b>	<b>22.9</b>	<b>4</b>	<b>10.5</b>	<b>44</b>	<b>53.0</b>	<b>24</b>	<b>63.2</b>
Ethnicity										
Caucasian	522	77.7	178	34.1	371	76.3	<b>179</b>	<b>34.3<sup>a</sup></b>	<b>155</b>	<b>41.8<sup>a</sup></b>
First Nations	150	22.3	48	32.0	82	18.1	<b>71</b>	<b>47.3</b>	<b>44</b>	<b>53.7</b>

<sup>a</sup>p<0.05 between groups

**Table 5.2. The Effect of Physical Activity at Age 8-10 years on Asthma and Airway Hyperresponsiveness**

	All Participants			Normal Weight at 8-10 yo			Overweight at 8-10 yo		
	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value
<b>Asthma at 8-10 yo</b>									
Unadjusted	0.91	0.76-1.10	0.34	0.97	0.76-1.25	0.84	0.80	0.59-1.07	0.13
Model 1 <sup>a</sup>	0.93	0.76-1.15	0.50	1.01	0.76-1.33	0.97	0.80	0.58-1.10	0.16
Model 2 <sup>b</sup>	0.91	0.73-1.15	0.44	1.00	0.74-1.36	0.98	0.74	0.52-1.06	0.10
<b>Asthma at 12-13 yo</b>									
Unadjusted	1.03	0.81-1.30	0.82	1.03	0.76-1.39	0.87	0.99	0.68-1.44	0.97
Model 1 <sup>a</sup>	1.07	0.82-1.39	0.64	1.09	0.77-1.55	0.62	0.99	0.66-1.50	0.97
Model 2 <sup>b</sup>	1.03	0.78-1.37	0.83	1.09	0.75-1.58	0.67	0.92	0.59-1.44	0.72
<b>AHR at 8-10 yo</b>									
Unadjusted	0.99	0.82-1.20	0.95	1.04	0.80-1.34	0.77	0.90	0.67-1.20	0.47
Model 1 <sup>a</sup>	0.89	0.72-1.09	0.25	0.95	0.73-1.25	0.73	0.80	0.58-1.10	0.17
Model 2 <sup>b</sup>	0.93	0.74-1.16	0.51	1.00	0.75-1.33	0.98	0.86	0.60-1.22	0.40
<b>AHR at 12-13 yo</b>									
Unadjusted	0.94	0.75-1.17	0.56	0.91	0.68-1.21	0.54	0.91	0.64-1.29	0.39
Model 1 <sup>a</sup>	0.94	0.75-1.20	0.63	0.95	0.70-1.28	0.72	0.93	0.63-1.37	0.72
Model 2 <sup>b</sup>	1.00	0.77-1.28	0.97	0.97	0.70-1.35	0.85	1.07	0.71-1.62	0.73

<sup>a</sup>Adjusted for region of residence and ethnicity

<sup>b</sup>Adjusted for region of residence, ethnicity, parental income and education

**Table 5.3. The Effect of Screen Time at Age 8-10 years on Asthma and Airway Hyperresponsiveness**

	All Participants			Normal Weight			Overweight		
	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value
<b>Asthma at 8-10 yo</b>									
Unadjusted	<b>1.25</b>	<b>1.00-1.55</b>	<b>0.05</b>	1.07	0.79-1.45	0.68	<b>1.47</b>	<b>1.05-2.05</b>	<b>0.02</b>
Model 1 <sup>a</sup>	<b>1.35</b>	<b>1.07-1.72</b>	<b>0.01</b>	1.13	0.82-1.56	0.47	<b>1.61</b>	<b>1.11-2.31</b>	<b>0.01</b>
Model 2 <sup>b</sup>	<b>1.40</b>	<b>1.08-1.81</b>	<b>0.01</b>	1.07	0.75-1.53	0.70	<b>1.98</b>	<b>1.30-3.01</b>	<b>0.001</b>
<b>Asthma at 12-13 yo</b>									
Unadjusted	1.20	0.92-1.57	0.17	1.07	0.75-1.52	0.73	1.41	0.92-2.15	0.11
Model 1 <sup>a</sup>	<b>1.35</b>	<b>1.01-1.81</b>	<b>0.04</b>	1.18	0.81-1.73	0.39	<b>1.62</b>	<b>1.01-2.61</b>	<b>0.05</b>
Model 2 <sup>b</sup>	<b>1.45</b>	<b>1.06-1.97</b>	<b>0.02</b>	1.23	0.82-1.84	0.32	<b>1.81</b>	<b>1.09-3.03</b>	<b>0.02</b>
<b>AHR at 8-10 yo</b>									
Unadjusted	0.95	0.76-1.20	0.67	0.85	0.61-1.19	0.34	1.03	0.74-1.44	0.87
Model 1 <sup>a</sup>	0.89	0.69-1.14	0.35	0.88	0.62-1.24	0.45	0.90	0.63-1.30	0.58
Model 2 <sup>b</sup>	0.90	0.69-1.18	0.45	0.92	0.64-1.32	0.65	0.82	0.54-1.25	0.36
<b>AHR at 12-13 yo</b>									
Unadjusted	0.85	0.66-1.13	0.24	0.70	0.49-1.01	0.06	1.06	0.70-1.61	0.77
Model 1 <sup>a</sup>	0.80	0.60-1.07	0.13	0.69	0.46-1.01	0.06	0.98	0.62-1.54	0.91
Model 2 <sup>b</sup>	0.83	0.61-1.12	0.22	0.69	0.45-1.06	0.09	1.00	0.62-1.62	0.99

<sup>a</sup>Adjusted for region of residence and ethnicity

<sup>b</sup>Adjusted for region of residence, ethnicity, parental income and education

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In summary, low physical activity was not associated with asthma or AHR either cross-sectionally or longitudinally. In contrast, three or more hours of screen time daily is associated with a two-fold greater odds of asthma presence at 8-10 years old and 12-13 years old. No associations between screen time and AHR were identified.

**CHAPTER SIX: “ASTHMA ISN’T AN EXCUSE, IT’S JUST A CONDITION”:  
PERCEPTIONS OF PHYSICAL ACTIVITY AND SCREEN TIME**

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The previous three chapters gleaned further insight into the associations between weight and asthma amongst participants involved in the 1995 Manitoba Prospective Cohort Study. Overweight girls have a two-fold increased risk of asthma and mild AHR. Overweight youth with asthma were significantly more likely to report levels of screen time in excess of current recommended limits. As well, high vegetable intake seemingly confers a protective effect against allergic asthma and moderate/severe AHR.

If high screen time, but not physical activity, increases the odds of asthma (Chapter 5), it begs the question, “How do youth perceive screen time and

physical activity, based on asthma status?" This type of question is best answered using qualitative methods. This qualitative study is based on a series of focus groups and interviews with youth. It is not intended to be viewed as a gender-based analysis, as this was beyond the scope of the study.

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Title: "*Asthma isn't an excuse, it's just a condition*": Youths' Perceptions of Physical Activity and Screen Time

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Running Head (max 50 characters): Youths' perceptions of physical activity and screen time

Key Words (5-7; not in title or journal name): adolescents, exercise, sedentary behavior, sports, qualitative

**Abstract**

During puberty, physical activity patterns begin to decline, while sedentary time increases. These changes may be confounded by asthma. The purpose of this study was to gain insight into youths' perceptions of screen time and physical activity, by asthma status. Four interviews and seven focus groups with boys only or girls only were conducted with 15-16 year old youth enrolled in either of two asthma-focused cohorts in Manitoba, Canada. Using a semi-structured interview guide, youth were asked about their perceptions of physical activity and screen time such as texting, watching television, electronic games, internet chatting, and about their perceptions of the influence that asthma has on these behaviors. Data were analyzed using thematic coding. Two themes were common to youth with asthma and without asthma: 1) sports are an integral part of youths' lives, and 2) screen time is important to youth. Two themes were identified amongst youth with asthma only: 1) physical activity used to be more difficult, and 2) being active and living with asthma. Youth with asthma described physical activity as neither a hindrance to activity nor an excuse for inactivity, although asthma may still present some challenges. They also acknowledged their reliance on screen time for communication and for entertainment. Youth with asthma believe that physical activity has become increasingly easier as they become older, and that being active with asthma, despite its challenges, is a key part of their lives.

*“Asthma isn’t an excuse, it’s just a condition”:*

## **Youths’ Perceptions of Physical Activity and Screen Time**

### **Introduction**

Youth with asthma are encouraged to be as physically active as their peers without asthma (1), but it is not clear whether activity patterns differ between these groups (2-6). To understand behaviour related to physical activity, it may be equally important consider sedentary time. With the recent emergence of social networking and new forms of gaming (e.g. on-line, consoles), youths’ screen time is no longer restricted to television. For this reason, we use the term “screen time” rather than “television time.” This behaviour is a popular way of spending time. Canadian youth engage in an average of three hours of sedentary behaviour per day (7), while only 12% achieved the recommended two hours of daily moderate-to-vigorous physical activity (8).

Before (9) and during puberty (10), physical activity patterns begin to decline, while sedentary time and screen time increase. The role of asthma may further confound these changes. The purpose of the present study was to describe perceptions of screen time and physical activity among youth with and without asthma, because these perceptions may influence the advice about physical activity given to youth with asthma. The research question of this qualitative study was “Do youth with and without asthma perceive physical activity and screen time differently?” For the purposes of this study, screen time

includes leisure time spent texting, watching television, electronic games, internet chatting, and similar activities.

## **Methods**

### *Recruitment and Participants*

Twenty-two participants were recruited via purposive sampling (described below) from two asthma-focused studies: the 1995 Manitoba Birth Cohort study (11) and the Canadian Asthma Primary Prevention Study (CAPPS; 12). Briefly, children in both cohorts were born in 1995 or 1996 in Manitoba, Canada and assessed by a pediatric allergist for asthma at least two times prior to the start of this study. The most recent clinical assessments, on which asthma status was based for the purposes of this study, were made a few months to two years prior to the interviews/focus groups. Despite the time gap between asthma assessment and this qualitative study, it remains very unlikely that all participants had different asthma status from their last assessments to the time of the interviews and focus groups.

For logistical reasons, only participants living in Winnipeg were approached to participate in the present study. Participants were excluded if they had co-morbidities or conditions that may interfere with physical activity. The University of Manitoba's Health Research Ethics Board approved this study. Written consent from the parents and assent from the youth were provided prior to starting the study. All names presented are pseudonyms.

*Interview and Focus Groups, and Analysis*

Interviews and focus groups were undertaken to gain insight into youths' perceptions of living with adolescence, and perceptions of asthma if youth had been diagnosed with this disease.

All 15-16-year-old youth attended focus groups (n=7 focus groups with a total of 18 participants) and interviews (n=4). Focus groups included only boys or only girls and by the presence or absence of asthma. All interviews and focus groups followed a semi-structured interview guide. Questions were discussed one at a time until participants had no further comments. In keeping with a semi-structured format, follow-up questions were asked when the comment of a participant pointed to new aspects of the topic. If discussion diverged from the topic of interest, the moderator redirected participants to the last relevant topic. Snacks/dinner were provided, parking/public transportation costs were reimbursed and two movie passes were offered as incentives. The first author (JP) conducted all focus groups, which were digitally recorded and transcribed. Interviews and focus groups ranged from 32-90 minutes.

Data were collected and analyzed to identify common themes using a constant comparative method, rooted in a pragmatic worldview. Pragmatism is characterized by a problem-centered approach oriented in real-world practice, which allows for the expansion of our understanding of the data (13). It recognizes that there are multiple realities (13), rather than a single connection in

the data. Data collection and analysis continued until constructs were deemed to be saturated when new or additional constructs ceased to be identified with subsequent interview or focus groups.

## **Results**

All sessions were initially designed as focus groups. Due to low recruitment/attendance to some focus groups, interviews were conducted if only one youth arrived at the scheduled time (Table 1). The decision to include focus groups, as well as interviews, was in keeping with a pragmatic worldview, because this worldview is oriented in real-world practice (13) or “doing what works” (14). Regardless of the number of participants, youth were encouraged to share their own experiences and to share ideas as giving voice to participants is an important feature of qualitative research (15).

### **Themes and subthemes common to youth with asthma and without asthma**

#### **I. Sports are an integral part of youths’ lives**

Regardless of their asthma status, most youth spoke of regularly engaging in recreational sports. These activities ranged widely, from dance to football. Regardless of their preferred activity, youth spoke of sports as a “*really important*” part of their lives.

*Sports help keep youth focused*

Sports were a way of abstaining from inappropriate behaviors. Thomas reported that sports “*sports keeps you away from doing other bad things... you can’t skip class, you can’t do drugs or go partying because the coach will kick you off the team.*” Youth with asthma could have perceived sports as form of pressure that could have been threatening given their disease. But instead, they viewed sports as a way of avoiding negative peer pressure and a way in which to spend time with family and friends. This is best exemplified in a comment made by a girl with asthma who said “*it sucks*” that she was unable to participate in school sports because she was already committed to her competitive dance team on most days of the week.

*Striving to improve in their chosen sport*

As a result of viewing sports as an integral part of their lives, youth accepted the pressure to do well in sports. Unlike video or computer games which have a finite skill limit (e.g. youth “beat” the game), youth noted that “*there is no limit to what you can do with your sports.*” Many youth were part of sports teams, clubs or groups. They spoke of wanting to build on their current skills or pursuing a sport to sequentially higher levels. One boy with asthma recalled a recent practice during which he realized that, although he was fit, he could still improve:

*{T}he other day at conditioning football camp I, we were doing wind sprints, it's like sprint there, sprint back. And we had to do six sets of two. So there and back, and, and it was okay not bad, so like the first time I sprinted it was, it was good, all was good, the second time I sprinted back a little bit more tired, the third time I sprinted there, then on like the fourth time I was heading back it was sort of like, like I realized like I guess like I'm conditioned but I'm not necessarily fully ready. I finished all of it but I had to pace myself a lot more... I'm going to obviously have trouble... during a game.*

#### *Activity as a stress release*

Organized and unorganized activities were a way in which youth relaxed and released stressed. These activities varied widely, from traditional to and non-traditional, such as Rock Band, a video game in which participants played drums and “goof[ed] off.” Kyla, who had asthma, noted that “*dance... it's more of like a letting go.. like it's not like stressful like if I'm stressed and I go dance, I'll feel so much better just 'cause it's literally like physical therapy.*”

#### *The choice of sport is a matter of interest*

Some youth were not actively involved in extracurricular sports, due to their personal preferences. This was true of youth with and without asthma. As described above, youth recognized the importance to remain competent at their sport. At the same time, youth neither spoke of challenges in joining a team nor indicated that failure to join a team was socially threatening. For these youth, the decision to be involved in sport was a matter of interest: “*[s]ome people don't care about them, some people don't want to have anything to do with them and some people revolve their whole life around them.*”

### III. Screen time is important to youth

#### *Much of Youths' Leisure Time is Screen Time*

All youth were involved in various forms of screen time. Although our initial interview guide did not include a question on quantifying screen time, we subsequently added a question on the amount of time youth engaged in screen time given the importance of screen time to youth. Some youth commented that their parents set limits screen time use during the school week. However, the majority of youth described engaging in a minimum of three to four hours of screen time daily, outside of school. Screen time consumption increased amongst many youth during the weekends, when some youth spent as many as “eight to nine [hours] maybe... talk[ing] to people on the internet... watch[ing] movies, just lots of things.” Many described their quantity of screen time as being “too much.”

#### *Screen Time as a Source of Communication*

All youth spoke of various types of screen time as a communication tool. The majority of participants had cell phones, which they primarily used for texting rather than talking. All had internet access. The frequency of other forms social media (e.g. Facebook®) as means by which to communicate varied widely, from ranged from occasional to not being able to “live without” it.

Kyla commented that *“like when I’m at home, [being on the computer is] usually what I’m doing. My parents don’t like it when I’m on the phone too long and then I don’t have a cell phone so it’s just like the way I communicate. If I didn’t have it, I think it would be a lot harder to like make plans with your friends and communicate.”*

As such, screen time played a substantial in communication role in these youths’ lives.

#### *Screen Time as a Source of Entertainment*

Screen time was viewed as a form of entertainment, ranging from movies and television, to video games and gaming consoles, with friends. When queried about what they thought would happen if they no longer had screen time access, several youth either explicitly stated or alluded that *“it would be hard for the first while cause it’s pretty addicting to me, but I mean, take away the, take away TV and computer and technology, like, I don’t know.”* Other youth were absolute in their assessment of the role of screen time in their daily lives. Jack, a self-described loner with asthma, commented that the internet and social media were *“his life.”* Interestingly, youth with asthma believed that their current screen time patterns would not be different if they did not have asthma.

## Themes unique to youth with asthma

### I. Physical activity used to be more difficult

Many boys spoke of how their asthma had improved in the years prior to the interviews/focus groups. Miles reported that *“it’s like [his] asthma has gone away”* and that he has not *“really fe[lt] any symptoms of it anymore.”* Jacob stated that he had *“heard that most teenage boys grow out of their asthma”* and many boys’ comments indicated that they believed that they were experiencing a remittance of symptoms.

Therefore, it was not surprising that a common theme to youth with asthma was that physical activity used to be more difficult. James recalled how his asthma used to hinder his physical activity, but that he was now able to participate in sports: *“My asthma’s a lot better. Like, I don’t even have it any more... I got off taking like 20 different inhalers to taking one pill at night. And if I need it, like I have Ventolin® if I need it.”* He attributed this to *“time”* and mentioned how his *“dad used to have it and he grew out of it.”*

### II. Being active and living with asthma

*“Asthma isn’t an excuse, it’s just a condition”*

For these youth, asthma was not an excuse to refrain from physical activity. As described in the previous theme, some youth reported that their asthma symptoms had subsided. Yet, all still had recent clinical diagnoses of

asthma. Few youth explicitly stated that they viewed asthma as an excuse for inactivity. Rather, youth indicated that they believed that they could be as active as they desired in spite of their asthma. As David eloquently stated, *“My asthma was worse when I was younger I guess... I’d just sort of use it as an excuse for my not being conditioned... It was sort of like a, a free pass. Asthma isn’t an excuse, it’s just a condition.”*

In order to achieve this, youth functioned around their symptoms, and acknowledged the role of reliever medications (e.g. Ventolin®) in asthma exacerbation management. Their efforts to control the effects of the disease enough to be socially accepted, as most had networks of very good friends. Youth were asked if they spoke to their peers about asthma. All participants, except for one boy, reported that their friends knew about their asthma and/or that they had taken asthma medications in front of their friends.

#### *Asthma can still get in the way*

No youth described that asthma prevented them from being physically active. But, for a minority, asthma interfered with being active, such that *“breathing... just gets in the way of things.”* Rather than removing themselves from activity altogether, these youth selected sports that demanded less aerobic capacity, such as weight lifting, but still were enjoyable. They also recognized that preventive medications were helpful in maintaining control. For this small group of participants, opting for these types of activities led to other healthy

lifestyle behaviours (e.g. *“eating a bit more healthier”*).

## **Discussion**

Canadian recommendations for the level of physical activity for children and youth have recently been reduced from 90 minutes or more per day of physical activity to 60 minutes of moderate-to-vigorous physical activity (16). However, the recommendation that children with asthma ought to be able to engage in regular physical activity remains unchanged (1). This study found that youth with asthma reported that they are able to participate in their desired physical activities in spite of their asthma. It also suggests that youth with asthma believe that they are better able to engage in physical activity without exacerbation of symptoms, compared to when they were younger. Others have reported similar findings (17).

As with all qualitative work (15), caution should be used when transferring our findings to other populations. Nonetheless, these findings may be transferable to populations with similar social characteristics and experiences (15) with regard to asthma and asthma treatment.

Asthma status was based on assessments when the participants were 12-13 years old. CAPPs participants had been assessed for asthma within several months preceding these interviews and focus groups. . Given the shift of asthma from male to female predominance during early adolescence, it is possible that some boys had outgrown their asthma and some girls had developed asthma.

The fact that we identified fewer themes unique to youth with asthma compared to several common themes based on positive vs. negative asthma assessments reinforces that youth with asthma view themselves in a similar light as youth without asthma. Youth with asthma adopt strategies to normalize their lives. We have previously reported that younger children with seek normalization (18). Normalization includes various steps, not the least of which those affected de-emphasize their condition and emphasize their socially desirable abilities (19). Youth with asthma may view themselves as being normal, and thus seek to be treated by their peers as an average young person (20). As such, youth with asthma recognize that their non-asthmatic peers value screen time as a means of communication or other leisure pursuits (e.g. video games). Youth with asthma may recognize that screen time is not likely to exacerbate their asthma symptoms. Therefore, they seek to become proficient in these pursuits and, in turn, gain recognition or acceptance from their peers. That is, youth with asthma are seen as being normal in this aspect of their lives. However, we suspect that this is not the case, as youth with asthma spoke about the enjoyment and friendships gained from physical activity.

Alternatively, youth with asthma may truly believe that they are no different from their peers without asthma. This is reflected in our finding that there are more common than disparate subthemes amongst youth based on asthma status. Perceptions of asthma, and subsequently internalization of

asthma-related differences may truly be less important than physical activity, screen time and their related benefits to those youth affected by asthma.

We were only able to recruit youth to a total of 11 focus groups and interviews (7 asthma; 4 no asthma). We believe that our data were saturated given the links between the comments made by youth with asthma and youth without asthma, and the consistency in perceptions of asthma across all interviews/focus groups of youth with asthma. There were no new concepts recorded in repeated focus groups for the same asthma/sex group. Interviews were included to accommodate families' schedules. The individual interviews confirmed the concepts recorded in the focus groups, even if some aspects specific to individual participants were uncovered as well.

Healthcare professionals may wish to encourage regular physical activity, amongst youth with asthma, as it is a condition that does permit youth to be active. It behooves clinicians to acknowledge the importance of both physical activity and screen time to youth with asthma, and to reinforce that asthma ought not hinder activity or excuse inactivity.

### **Conclusions/key findings**

Youth with and without asthma describe physical activity as enjoyable, although the nature of the activity varies widely and is a matter of individual choice. They also acknowledge their interest in, and reliance on screen time for interactions with peers and for recreation. Youth with asthma believe that

physical activity has become increasingly easier as they become older, and that asthma does not hinder their abilities to engage in physical activity.

**Table 6.1. Characterization of Focus Groups and Interviews**

	Interviews	Focus Groups*
No Asthma		
Boys	0	2
Girls	1	1
Asthma		
Boys	2	2
Girls	1	2

\*Reflects the number of focus groups, not the number of participants.

**Table 6.2. Themes Common to Youth with and without Asthma, and Unique to Youth with Asthma**

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<b>Themes Common to Youth with Asthma and Without Asthma</b>	
I.	Sports are an integral part of youths' lives
	a) Sports help keep youth focused
	b) Striving to improve in their chosen sport
	c) Activity as a stress release
	d) The choice of sport is a matter of interest
II.	Screen time is important to youth
	a) Much of youths' leisure time is screen time
	b) Screen time as a source of communication
	c) Screen time as a source of entertainment
<b>Themes Unique to Youth with Asthma</b>	
I.	Physical activity used to be more difficult
II.	Being active and living with asthma
	a) " <i>Asthma isn't an excuse, it's just a condition</i> "
	b) Asthma can still get in the way

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In summary, there are more similarities than differences in youths' perceptions of physical activity and screen time by asthma status.

Youth with asthma described how physical activity used to be more difficult during pre- and early puberty, but that asthma is not an excuse to refrain from physical activity.

## CHAPTER SEVEN: SUMMARY AND DISCUSSION

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### *Summary*

The preceding four chapters present the results of my thesis work. This chapter provides a summary of each of these chapters. I begin by restating the comprehensive research question, and then summarizing each of the four chapters with reference to the specific aims of each study.

**The comprehensive research question of this dissertation is “Do obesity and related lifestyle behaviours influence asthma and airway hyperresponsiveness outcomes in children?”**

The first aim of this study was to determine if there was an association between weight status and asthma. Using a longitudinal design, we found that overweight at 12-13 years old was associated with a two-fold increased odds of persistent asthma in girls. In contrast, boys within the highest BMI quartile at 8-10 years old were nearly twice as likely to have remittent asthma at 12-13 years old. Higher BMI z-scores at 8-10 years old increased the odds of persistent asthma in girls.

The second aim of this study was to determine if lifestyle patterns related to weight, specifically diet quality and physical activity and screen time, are associated with asthma. First, with respect to diet quality, we employed a cross-sectional design in which we identified few associations between total or component diet scores and asthma overall. High vegetable intake was found to be associated with a reduced odds of allergic asthma and moderate/severe AHR by 50% and 42%, respectively. Note that, due to limitations with the dietary data collected at 8-10 years old, we were unable to conduct a longitudinal analysis. Second, and with respect to the exposures of physical activity and screen time on asthma and AHR outcomes, we employed both cross-sectional and longitudinal designs. Low physical activity at 8-10 years old did not influence asthma or AHR outcomes. In contrast, high screen time doubled the odds of asthma both at 8-10 years and 12-13 years old, particularly amongst

overweight youth. No associations between screen time and AHR were identified.

The third and final aim of this study was to describe the lived experience of youth with asthma, specifically by comparisons of perceptions of physical activity and screen time by asthma status. To this end, we employed a qualitative study of interviews and focus groups using a pragmatic worldview. We identified that, for youth with and without asthma, sports are an integral part of their lives. Youth described sports as way in which to stay focused, about the need to improve in their chosen sport and that the choice of sport is a matter of interest. Regardless of asthma status, youth also spoke of screen time as being important. Youth spoke of engaging in screen time during much of their leisure time, and that screen time is both a source of communication and entertainment. Two themes specific to youth with asthma were also identified. Youth described how physical activity used to be more difficult. They also spoke of being active and living with asthma, such that asthma ought not to be viewed as an excuse for inactivity although asthma, on occasion, still gets in the way of activity.

### *Discussion*

This section is a brief discussion of the studies presented in the preceding chapters, with references to some of the related existing literature as well as other

projects that I completed during the course of my doctoral training. By no means does this section exhaustively discuss all related literature; this is beyond the scope of this brief discussion as much has already been described in the discussion section of the manuscripts in the preceding chapters.

The first aim of the study was to determine if weight was associated with asthma and AHR outcomes. Using a cross-sectional comparison, we found that being (OR 2.22, 95% CI 1.13-4.36) or in the upper quartile for BMI (OR 1.66, 95% CI 0.98-2.81) at 12-13 years old increased the odds of persistent asthma ~2-fold in girls. No association was found for boys (OR 1.06, 95% CI 0.58-1.92) or within the entire cohort (OR 1.46, 95% CI 0.93-2.27). These findings parallel those of others (Castro-Rodríguez et al. 2001; Herrera-Trujillo et al., 2005) who also demonstrated that asthma risk increases with the degree of adiposity in similar aged youth. Although we did not give consideration to pubertal staging in our analyses, others have described that 11 year old overweight/obese girls who had begun puberty early were significantly more likely to present with frequent wheeze than healthy weight girls. Similar to our results, this group also found no association between asthma and weight status amongst boys (Castro-Rodríguez et al. 2001). In the current study, we chose not to adjust for pubertal staging in the final analysis as only 26 of the 144 (18.1%) girls were pre-pubertal at 12-13 years old (Appendix I). Furthermore, only 2 of these 37 girls (5.4%) were

overweight, we were inadequately powered to repeat our analyses after stratification by weight + pubertal status. However, we did consider weight change. This was achieved by using  $\Delta$ BMI z-scores, which account for expected weight gain in children. In this longitudinal analysis, we identified that weight gain from 8-10 years old to 12-13 years old was associated with a reduced odds of incident asthma (OR 0.54; 95% CI 0.31-0.94;  $p < 0.05$ ). We found no associations between weight gain and asthma outcomes amongst the entire cohort or girls only. We also did not identify any associations between weight gain and AHR outcomes at 12-13 years old.

The sex shift in the prevalence of asthma, from male to female predominance following puberty has been well described (Tollefsen et al., 2007; Nicolai et al., 2003; Manfreda et al., 1990). Participants in the 1995 Manitoba Prospective Birth Cohort have been seen on an approximately biennial basis since the ages of 8-10 years old (i.e. 2003-2005). The most recent time that participants were seen clinically was at ages 12-13 years old (2008-2009). Based on data, including objectively assessed pubertal staging, collected at the most recent clinical visit, we did not identify a dramatic sex shift in the prevalence of asthma by 12-13 years (Appendix I). At that time, many reported being in the early stages of puberty, while very few (especially boys) had completed puberty. This may explain the low rate of change in asthma status between boys and girls.

Alternatively, our oversampling of asthma cases into the original cohort (34% at 8-10 years old; 31.1% at 12-13 years old) may have resulted in a cohort of children more likely to experience remission or incident asthma later into early adolescence.

Interestingly, the association between weight status and asthma was reversed among boys. Twelve to 13 year old boys with a BMI in the fourth quartile had a nearly two-fold increased odds of asthma remission compared to same-aged boys in with a BMI in quartile one. The reasons for this observation remain elusive. Here, I simply present one theory, although further investigation is warranted prior to confirming or dismissing it. Overweight boys reach puberty sooner than their normal weight peers (Kleber, Schwarz & Reinehr, 2011). Higher testosterone levels, which are a feature of the progression through puberty, are inversely associated with asthma in boys (Osman, 2003). A remittance of asthma amongst boys during puberty is expected (Tollefsen et al., 2007; Nicolai et al., 2003; Manfreda et al., 1990). But, overweight boys may experience asthma remittance sooner than their normal weight peers due to higher levels of testosterone at an earlier age.

In Chapter One, I noted that asthma is a disease that exists along a continuum from controlled to uncontrolled (Lougheed et al., 2010). Asthma management often involves regular use of inhaled corticosteroids. Youth who

receive inhaled corticosteroids over several years may exhibit delayed linear growth (Sharek & Bergman, 2000). But, there is no reason to believe that low dose inhaled corticosteroids delay weight gain. Thus, youth with asthma may have a higher BMI relative to their peers until such a time that those with asthma achieve their anticipated adult height.

Both diet and activity patterns also influence weight status, which, as we have shown, influences asthma outcomes. Perhaps then, it is not surprising that we also observed associations between diet, screen time and physical activity and asthma. We did not give consideration to diet exposures at 8-10 years old and asthma outcomes cross-sectionally or longitudinally due to diet data limitations at 8-10 years. However, we were able to consider both total diet quality and component diet quality at 12-13 yo. To the best of our knowledge, we are the first to consider total and component diet quality, as well as two phenotypes of asthma (allergic and non-allergic). One component score, vegetable consumption, was protective against allergic asthma and moderate-to-severe AHR. Total diet quality is a better representation of a typical Western diet, which is characterized by high sugar, trans/saturated fat and salt intake and low fruits and vegetables. Mediterranean diets are seemingly protective against asthma (Avaniti, Priftis, Papdimitriou, Papadopoulos, Roma, Kapsokefalou, et al., 2011). This dietary pattern, characterized by high levels of

fish containing ample levels of n-3 fatty acids, fresh fruits and vegetables and olive oil, is common throughout parts of southern Europe. But, this is not a typical dietary pattern in North America. Rather, nutritionists describe North American dietary patterns as being “Western” vs. “prudent.” Like Mediterranean diets, a prudent diet is high in fresh fruits and vegetables. But, the sources (and subsequently the types) of fats differ. In contrast to the Mediterranean diet, which is high in monounsaturated fats from olive oil and long-chain polyunsaturated fats from cold water fish, a prudent diet is high in monounsaturated fats from canola or sunflower oil and low-to-moderate in polyunsaturated fats from cold water fish and flaxseed oil. Had we simply considered a Mediterranean diet vs. a Western diet, very few participants could have been described as having a Mediterranean diet as participants’ fish consumption was very low. Importantly, the consumption of higher amounts of fruit and vegetables in addition to foods high in monounsaturated fat were also protective against asthma and AHR among youth.

Others have described certain foods, including fruit, as being protective (Rosenlund et al., 2011) or a risk factor (e.g. fast food [Wickens, Barry, Friezema, Rhodius, Bone, Purdie, et al., 2005]) for asthma. But, without consideration to total diet quality as well as component diet quality in the same study population, these findings must be interpreted with caution. It is entirely possible that high

fast food intake, for example, may be a proxy for other factors also related to asthma. Such factors include, but are not limited to high salt diets (Burney, 1987) and low socio-economic status (Shankardass, Jerrett, Milam, Richardson, Berhane & McConnell, 2010). Our study extends our current knowledge by demonstrating for the first time, that the initiation of a prudent diet early in life may be protective against diseases of the airway.

Physical activity and screen time could also be considered as proxies for other lifestyle behaviours, including diet quality, influencing asthma outcomes. To overcome this challenge, we adjusted for parental education and income in our logistic regression models. These adjustments had little effect on analyses of physical activity or screen time. This suggests that socio-economic factors have little influence on physical activity or screen time amongst our participants. It also behooves us to acknowledge that the majority of participants were from middle class families (73.3% at Visit One; 86.9% at Visit Three). Thus, these results ought to be generalized with caution to lower-income populations.

The finding that screen time, but not physical activity, increased the odds of asthma is curious, particularly in light of our qualitative findings that youth do not view asthma as an excuse for, or a barrier to physical activity. In the next chapter, I attempt to integrate and interpret these quantitative and qualitative findings. At present, I will simply acknowledge youths' perceptions that asthma

does not hinder activity or excuse inactivity reinforces findings from another qualitative finding that I reported during the course of my doctoral training (Appendix J). Amidst the layers of events youth experience (freedoms and burdens of adolescence; pressures to become involved in inappropriate behaviours), asthma receives little focus.

As we found that screen time is associated with asthma risk both cross-sectionally and longitudinally, it is possible that increased time sitting is a novel risk factor for asthma in youth. Several explanations may exist for this finding. To the best of our knowledge, we are the first to document this association using longitudinal data, classifying asthma directly with a trained physician and an assessment of AHR. Future studies are needed to determine if reducing screen time lowers a child's risk for asthma or AHR.

These findings, presented independently at the beginning of this chapter, are a summary of the key points of the previous four chapters. However, as this is a mixed methods study, it is insufficient to present these summaries as independent entities only. It behooves the researcher to synthesize the findings within the pre-determined design of the mixed methods project. This is the focus of the next chapter.

## CHAPTER EIGHT: INTEGRATION OF FINDINGS

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In Chapter Two, which detailed the methods of this thesis, it is noted that, although “mixed methods studies consist of two types of data: quantitative and qualitative... it is not sufficient to collect and analyze these data independently. The data sets must be “mixed” at some point during the study.” The integration of the previously presented results is the focus of this chapter, as summarized in the preceding chapter.

Prior to collecting and analyzing data, it was decided that this work would follow a sequential explanatory design. It is sequential as the data from

one method (quantitative findings: Chapters 3-5) were collected and analyzed prior to, and ultimately used to inform, the research questions and data collection for the second method (qualitative findings: Chapter 6). As noted in Chapter 2, quantitative and qualitative data can be “mixed” in three ways (Table 8.1; Creswell & Plano Clark, 2007). It was decided to merge the quantitative and qualitative data. The explanatory focus reflected that the quantitative findings were given greater emphasis (denoted “QUAN”), and the qualitative findings were given less emphasis (denoted “qual”). This is not intended to minimize the qual findings. Rather, the qual findings are intended to help explain some of the QUAN findings. All findings, regardless from which method they were gleaned, are united in this chapter, to create a meta-inference (Teddlie & Yu, 2007) and which are represented pictorially in Figure 8.1.

**Table 8.1 Three Ways of Mixing Data in Mixed Methods Research**

Method	Description
Merging	Full integration of both types of data
Connecting	Initial results from first method often inadequate and require additional data for support Link one type of data with results from the other
Embedding	One type of data is supportive of the other Occurs at the design level

Adapted from Creswell & Plano Clark, 2007; Plano-Clark, Huddleston-Casas, Churchill, O’Neil Green & Garrett, 2008

### *Asthma, AHR and Weight*

Based on the findings from Chapter 3, it would have been expected that, youth, and in particular girls, would have described how weight gain hinders, while weight loss improves their asthma symptoms. Or, that they would have commented that heavier girls in the social or peer network seem to experience worse symptoms of asthma than their healthy weight peers. This was not the case. The theme of weight as a factor involved in asthma symptomology or risk was not mentioned during the interviews/focus groups. (An *a priori* decision was made not to include questions such as, "How does your weight influence asthma symptoms?" as questions of this nature are very sensitive, especially given the age range (15-16 years old) of our participants. Furthermore, inclusion of such questions may have led the girls into the topic through in depth interviewing. This line of questioning could also be considered potentially leading, as youth may not have previously considered that weight influences asthma.

Boys were more willing to discuss their weight. This was not done in the context of asthma, but rather changes they experienced while going through puberty. Boys spoke of becoming more muscular and taller, along with non-weight related changes, such as voice changing and hair growth. Nonetheless, neither boys nor girls spoke about weight as having an effect on asthma

symptoms.

That for neither sex weight was described as influencing asthma symptoms is telling. Indeed, it is possible that this topic was simply too sensitive for them to discuss. This is unlikely to be the case. Youth were willing to disclose information regarding drug and alcohol experimentation, about their thoughts on the physical changes related to puberty and their struggles to retain good grades. These statements reflect trust in the moderator, and in the case of focus groups, trust in their fellow participants. It is more likely that youth had not given consideration to weight in the context of asthma. This may be for three reasons.

First, youth who participated in the interviews/focus groups appeared to be within a normal weight range. No anthropometric data were collected at the time of the interviews/focus groups. At the same time, no single boy or girl appeared to be disproportionately heavier than his/her fellow participants. Thus, it is possible that our findings that overweight in girls increases the odds of persistent asthma, while conversely overweight in boys increases the odds of asthma remittance, may not have been relevant to interview/focus group participants. If these interviews/focus groups were repeated with heavier youth or youth who had gained a disproportionate amount of weight during puberty, the findings may differ from those reported herein.

Second, youth involved in the qualitative study spoke of being engaged in various forms of physical activity. Their confidence in their physical abilities and their lack of emphasis on asthma and asthma medications (Appendix J) suggests that they did not give much thought to weight, asthma and related symptoms.

Third, in keeping with the characteristics of our qualitative participants, those who joined an interview or focus group did so voluntarily. It may be that overweight youth who were invited to participate simply declined the invitation. This may have led to a self-selected group of youth who fell within a normal weight range. This is an important observation in and of itself. But, it also serves to reinforce that these findings can only be transferred to populations with similar characteristics, such as middle-income families living in urban areas.

### *Asthma, AHR and Physical Activity and Screen Time*

Youth, and in particular boys, spoke of physical activity as being easier at 15-16 years old than when they were younger. Although physical activity frequency was not associated with asthma outcomes in the quantitative study presented in Chapter 5, this may be due to the way in which the question was worded. Physical activity frequency was based on parental response to “In the last 12 months, how many times a week does your child engage in vigorous or competitive physical activity long enough to make him/her breathe hard?” This

question speaks to intensity, but not endurance or duration of physical activity. Thus, the null findings may be due to a true lack of differences between those with and without asthma, based on parental perceptions of respiratory symptoms. Alternatively, youth who exhibited “hard breathing” soon after commencing activity may have ceased engaging in a given bout of physical activity. Once the short bout of physical activity was over, 8-10 year old youth may have been exposed to high levels of screen time, which predisposed them to asthma outcomes at age 8-10 years and 12-13 years.

### *Asthma, AHR and Diet Quality*

High vegetable consumption was protective against allergic asthma and moderate-to-severe AHR. Although overall diet quality did not differ between those with and without asthma, increased vegetable intake can be viewed as a proxy for greater emphasis on health. Another proxy for health is physical activity level. Youth with asthma described engaging in, and enjoying physical activity, although they also valued screen time, as it was an important way to connect with their peers. Taken together, these findings point towards youth with asthma place some emphasis on health, but that the concept of health is not central to their lives. Rather, much of their focus is on being a “normal” teenager.

### *Summary*

This thesis is a series of studies, which collectively, have been rooted in a sequential explanatory mixed methods design. Using both quantitative and qualitative methods, we have gleaned an understanding of weight and related lifestyle behaviours in youth that could not have been appreciated from a single method.

Quantitatively, we have provided both cross-sectional and longitudinal results, the latter of which contributes to our understanding of the causal association between weight, related lifestyle behaviours and asthma. In this prospective cohort of children born in Manitoba in 1995, there is an association between overweight and persistent asthma in girls, and a greater odds of remittent asthma in overweight boys. Using anthropometric measurements (vs. self-reported data) and the gold standard assessment for asthma, we are confident that our variables were as reliable and accurate as possible. Although we found few associations between weight, related lifestyle behaviours and AHR, we are among the first to extensively report on AHR as an outcome for such exposure variables.

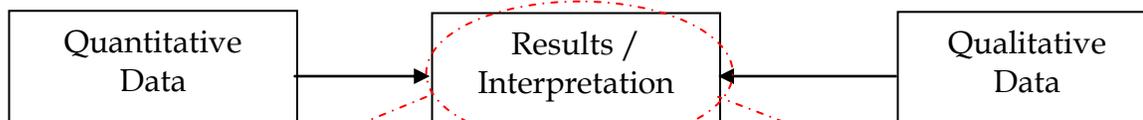
Qualitatively, youth did not view asthma as a barrier to physical activity, although they acknowledged asthma still gets in the way from time-to-time, and that physical activity used to be more difficult. Similar to their peers without

asthma, they viewed sports as an integral part of their lives, while screen time occupied much of their leisure time.

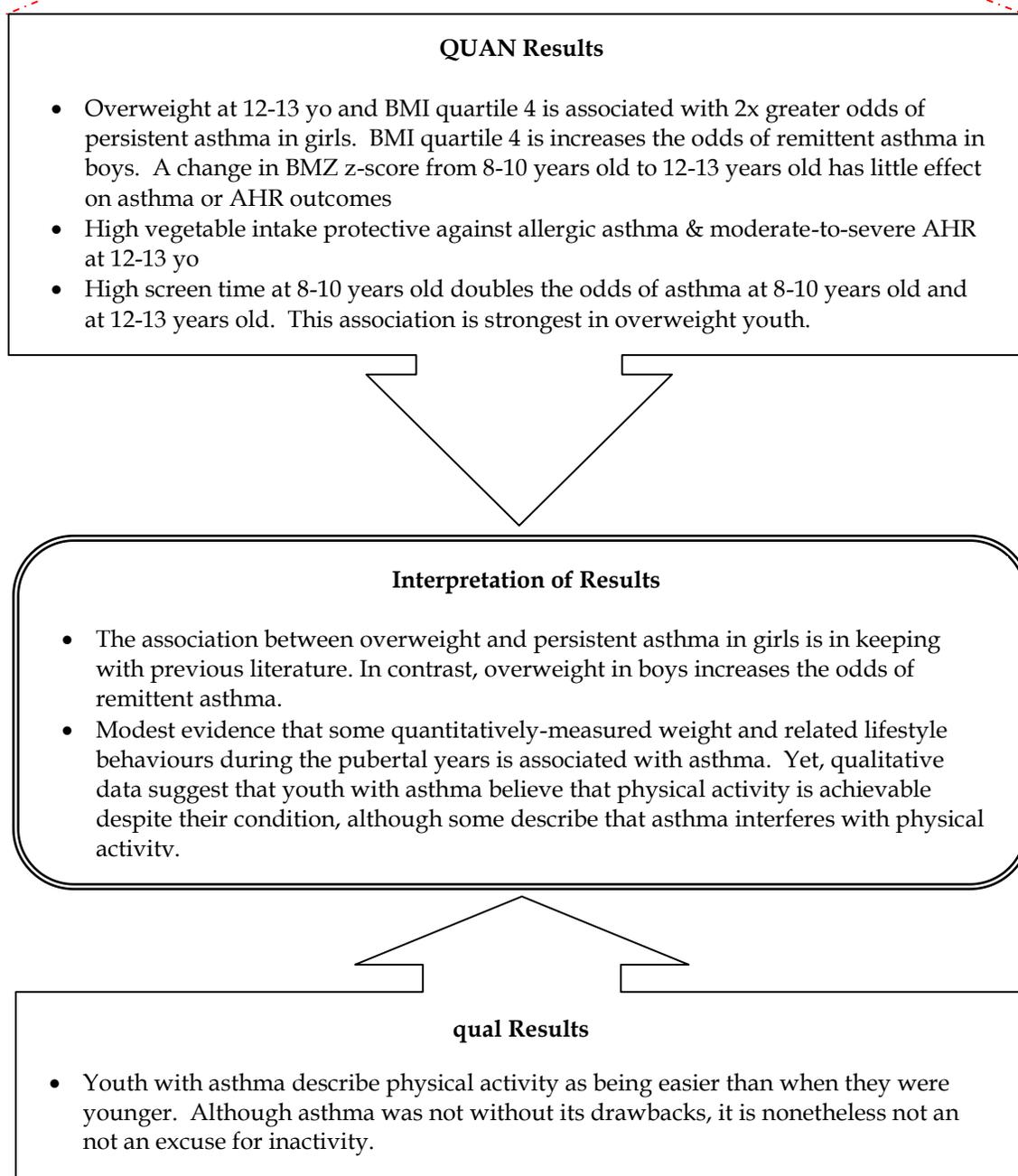
In summary, we provide modest evidence that some quantitatively-measured weight and related lifestyle behaviours during the pubertal years is associated with asthma. Yet, qualitative data suggest that youth with asthma believe that physical activity is achievable despite their condition, although some describe that asthma interferes with physical activity.

**Figure 8.1 Merging Quantitative and Qualitative Data**

**A. Theoretical Representation** [Adapted from Creswell & Plano Clark, 2007]



**B. Study Representation**



## CHAPTER NINE: KNOWLEDGE TRANSLATION

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Findings from this study have provided further insight into asthma, weight status, puberty and sex from both social and biological perspectives. But, the findings of this, or any study is merely the first step. It behooves the researcher to translate his/her findings in a manner that is appropriate for the intended knowledge user. I begin this chapter by providing the currently-accepted definition of knowledge translation (KT):

The exchange, synthesis and ethically-sound application of knowledge – within a complex system of interactions among researchers and users – to accelerate the capture of the benefits of research for Canadians through improved health, more effective services and products, and a strengthened health care system.

Canadian Institutes of Health Research, 2004

KT is a dynamic and iterative process that takes place within a series of interactions between the researcher and knowledge user. These interactions may vary in intensity, complexity and level of engagement depending on the nature of the research and the findings as well as the needs of the particular knowledge user (CIHR, 2011).

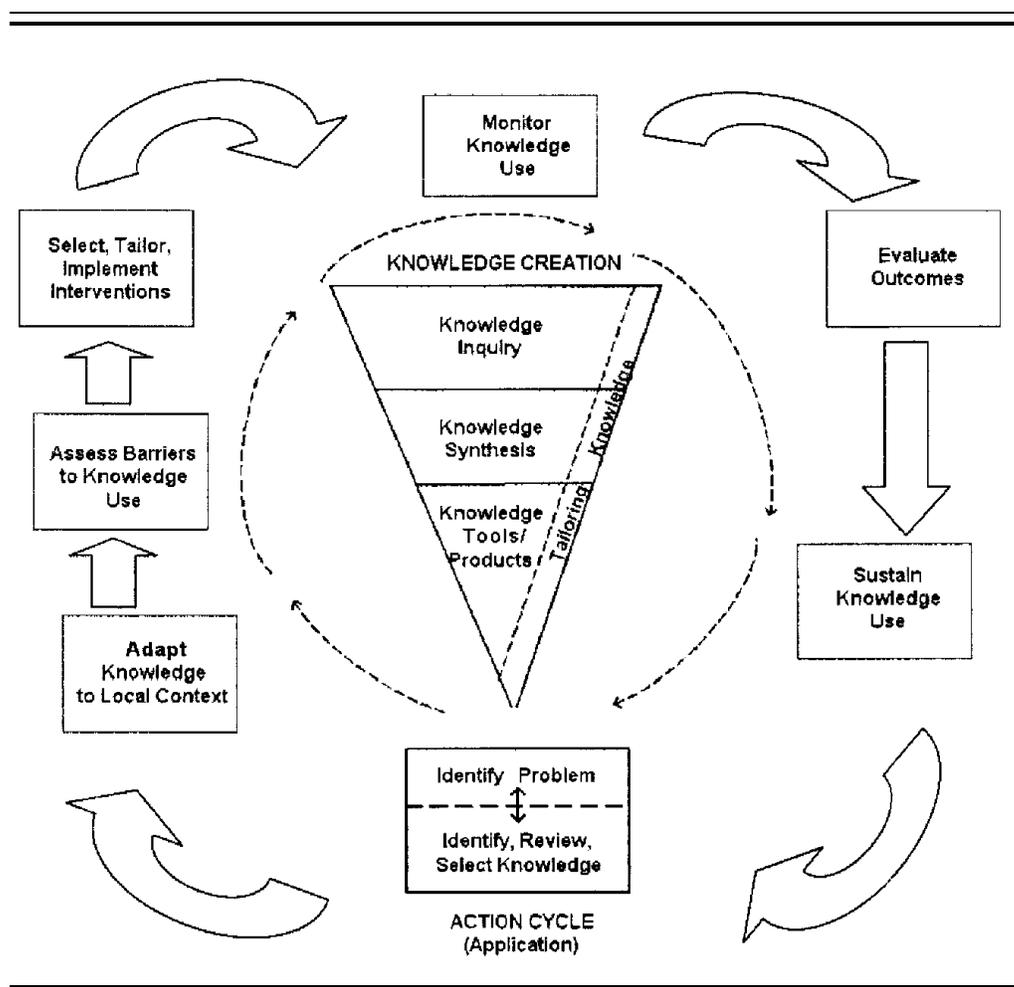
The Canadian Institutes of Health Research (CIHR) strongly encourages KT of the research programs it funds. This is for two overarching reasons:

1. Creation of new knowledge often does not on its own lead to widespread implementation or impacts on health.
2. Increased focus on research governance and accountability from the federal and provincial governments, and from the public, it becomes increasingly important to demonstrate the benefits of investment of taxpayer dollars in health research, and moving research into policy, programs and practice.

Given the CIHR's focus on KT, it is not surprising that a model has been developed to facilitate KT. The KTA cycle (Figure 10.1), originally put forth by Graham et al. (2006), is a conceptualization of the relationships between knowledge creation (research) and knowledge action (use of knowledge). The funnel of the KTA cycle reflects how knowledge must be "distilled" prior to

application, while action implementation and application progress in a cyclical manner.

**Figure 10.1 Knowledge to Action Cycle (Graham et al., 2006)**



This information was originally published in *J Cont Educ Health Prof.* 2006;26:13-24.

The works presented in this thesis can be translated to knowledge users through the KTA cycle. The problem was identified, from which a research

question and specific aims were developed. From this, the works then progressed through the knowledge creation funnel. Data were collected and analyzed (“knowledge inquiries”), regarded collectively (“knowledge synthesis”) and subsequently integrated into four manuscripts and this thesis (“knowledge tools and products”). It must be noted that this last step within the knowledge creation funnel is an on-going process that will extend beyond the timelines of this thesis. In keeping with the pragmatist worldview (see Methods, pp. 45-46), it is not sufficient to disseminate solely via traditional academic means (peer-reviewed journals, conferences, etc) and policymakers (Creswell & Plano Clark, 2007). Dissemination ought to also include informal means. This will include reports to participants and their families, and publications in the lay press. One such example of a non-traditional method of dissemination was the presentation of some of the findings contained herein at a Café Scientifique-style presentation held in Winnipeg on 24 March 2011. Lay summaries of the qualitative studies’ results will be provided to participants and their families, as requested by many who took part in the focus groups/interviews.

Future KT will address two key points:

1. Emphasize disease prevention in adolescents through dissemination of findings to healthcare providers and policy makers. This is vital as both

adolescent-onset asthma (Sears et al., 2003) and overweight (Dietz, 1998) often persist to adulthood.

2. Gain insight into adolescents' strategies for coping with asthma and obesity. This information will be useful in addressing the psychological ramifications of these conditions. As asthma (Krahn, Berka, Langlois & Detsky, 1996) and obesity (Katzmarzyk & Janssen, 2004) are associated with substantial direct and indirect costs, translational research targeting disease prevention and management are paramount.

This will be achieved following the action cycle described by Graham et al. (2006) and will include adaptations of knowledge to local contexts, evaluating outcomes and attempts to sustain knowledge use. This is best illustrated with an example. As was reported in Chapter Six, youth with asthma report that physical activity was more difficult when they were younger. Yet, the collective evidence on physical activity levels in children is inconclusive. We identified that youth place substantial emphasis on their screen time involvement. These findings were based on research involving urban participants, most of who were from middle class families. Qualitative work is considered transferable between congruent situations (Patton, 2002). As such, these findings may or may not be correct for youth involved in the 1995 Manitoba Prospective Cohort Study who

are from rural or northern regions, or who are from less socially advantaged families. This does not mean that our findings should be disregarded for these youth. Rather, caution should be used when transferring the findings to such youth, and adapting them to the local context. Only by being mindful and aware of such differences, and then integrating these differences into the proposed action plan, can these results be most appropriately used.

In summary, KT resulting from this project has made minor contributions to the existing scientific literature, as well as the development/modification of programs aimed at reducing and/or preventing childhood asthma and obesity. On-going translation of these findings, and the knowledge resulting therefrom, ought to follow the non-linear action cycle adopted by the CIHR.

## CHAPTER TEN: CONCLUSIONS

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Even all good things must come to an end. In this second-to last chapter, I provide a description of the study limitations and strengths, and the conclusions drawn from the works presented herein.

### *Study Limitations*

As with any study, the works presented herein are not without limitations. Limitations specific to each of the studies presented in Chapters 3-6 are described in the relevant sections. Here, I present five substantial limitations to the overarching study. These limitations will reduce the generalizability of

this work.

1. Bias, or a systematic error in the design and/or execution of a study that produces results which are constantly distorted in one direction because of non-random factors, is a concern with all observational studies. In the present thesis, two types of bias were of particular concern: confounding bias and selection bias.

Confounding bias results when the exposure being studied is so mixed up with other possible exposures that its single effect on the outcome of interest is very difficult to establish (Bayona & Olsen, 2004). In this thesis, potential sources of confounding bias included region of residence, SES and environmental tobacco smoke. Attempts were made to control for confounding bias using advanced mathematical models.

Selection bias is a concern with all observational studies (Mezei & Kheifets, 2005), including the 1995 Manitoba Prospective Cohort Study. Selection bias occurs when an apparent association develops between an exposure and an outcome due to a common effect of the exposure and the outcome (Mezei & Kheifets, 2005). In other words, an association may develop between weight or lifestyle behaviours (the exposures) and asthma (the outcome) due to genetic predisposition towards both

conditions (the common effect of the exposure and outcome). Selection bias may result in deviation between the measurement of an association in the study and the real magnitude of the association between the exposure and outcome. In turn, this measurement error yields in findings with decreased generalizability and which are unrepresentative of the population (Bayona & Olsen, 2004). We attempted to minimize this form of selection bias by creating a prospective cohort that is consonant with the Manitoba population with regards to geographical distribution. However, we acknowledge the possibility of other forms of selection bias, including a high income population. Participants in these studies are from upper-middle income and high income families. Families in these income brackets have better health and health literacy (Rootman & Ronson, 2005) compared to other income groups. As described in Figure 1.1, asthma management exists along a continuum in which medications play a substantial role. Although Manitoba has universal health care, there are nonetheless some costs associated with medications. These costs may be represent a significant portion of household income for lower income families (Ungar & Witkos, 2005), which may result in poorer asthma control, and therefore perceptions of asthma.

2. Loss of large proportion of First Nations participants in follow-up visits decreases the generalizability of our findings to First Nations communities, and more broadly, to individuals of aboriginal heritage.
3. The drop out rate is concerning among the cohort in general, not just the First Nations.
4. Identifying incident asthma is difficult and limited in a cohort that is select for a large percentage of participants with asthma at baseline.
5. Assessments of diet and activity were based on self- and parent-reported data, respectively. These are not considered gold standard measures. Nonetheless, these analyses were exploratory in nature. In future, consideration of diet and activity would be better assessed using more objective measures.

### *Study Strengths*

1. Oversampling for asthma, at rates three times greater than would be expected in the general population, provides the opportunity to tease apart subtle differences (including phenotypes) that would be

considerably more difficult if the proportion of participants with asthma had been sampled at 12%, the estimated population rate (Garner & Kohen, 2008).

2. Asthma status was determined using the gold standard, a specialist assessment for asthma. As described in Chapter 1, there are multiple methods for determining asthma status. These methods are much less rigorous, albeit validated, as they are based on self-reports or dispensed prescriptions. Our study is one of only a few prospective cohort studies in which asthma status was determined by a specialist.
3. Detailed assessments of atopy and AHR.
4. Involvement of urban-, rural- and northern-dwelling children.
5. Involvement of First Nations children, despite the high loss to follow-up.

### *Conclusion*

Modest evidence that some quantitatively-measured weight and related lifestyle behaviours during the pubertal years is associated with asthma. Yet, qualitative data suggest that youth with asthma believe that physical activity is achievable despite their condition, although some describe that asthma interferes

with physical activity.

## CHAPTER ELEVEN: FUTURE DIRECTIONS

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This is the final chapter of this thesis. Thus far, I have provided evidence that associations between asthma and weight status, puberty diet quality and physical activity exist, although these associations are not as clear as initially hypothesized. Perhaps this lack of clarity has its benefits, for it provides a basis for future directions. If all associations had been clearly defined and linear, future directions resulting from this work may have predominantly involved replication studies. As this is not the case, I offer the following thoughts for

future directions based on my thesis work. I begin with some very general comments, followed by itemizing quantitative and qualitative investigations that I believe are necessary, and finally, I relate these comments to two existing prospective cohorts and offer ways that these suggested future directions could be implemented.

### **General Comments**

To date, participants in the 1995 Manitoba Prospective Cohort Study study have been seen three times, at eight to 10 years old, 11-12 years old (not described in this thesis), and 12-13 years old. The sex shift of asthma (Manfreda et al., 1990) and increased prevalence of overweight (Yu et al., 2010) are most pronounced during adolescence. As such, continued follow-up of these participants through adolescence and beyond is critical to glean an understanding of asthma and weight. Future foci are detailed in the subsections, Quantitative Investigations and Qualitative Investigations, below.

Attempts were made to control for SES in the studies described herein. However, the majority of families (73.3% in Visit One: 86.9% in Visit Three) fell within the upper-middle income adequacy quartile or higher, as outlined by the Government of Manitoba (Government of Manitoba, 2008). But, certain ethnic groups in Manitoba, including First Nations peoples, most of whom live in the

north, have far lower family incomes than other groups (Carter & Polevychok, 2009). Thus, future consideration, and indeed future structuring of cohorts such as the 1995 Manitoba Prospective Birth Cohort, ought to acknowledge differences not only by income strata, but also by region of residence and ethnicity. Future work ought to also target inclusion of a more diverse socio-cultural population.

Yet, we were extremely fortunate to recruit a small sample of on-reserve First Nations participants to the 1995 Manitoba Prospective Cohort Study.

Despite the fact that retention through the second and third waves of many of these participants has proved challenging, the inclusion of First Nations youth adds an interesting and insightful component to our prospective cohort, which would otherwise be lacking. Given the increasing rate of immigration to Manitoba, particularly by individuals from Southeast Asian countries, such as Philippines (Government of Manitoba, 2010), enrolment and retention of such populations would serve to further enhance the generalizability of our future findings. As well, our prospective cohort, particularly those in the urban and southern rural sites, was predominantly from upper-middle class families.

Generalizability would be enhanced by recruiting families from a range of income strata. This challenge is not unique to the 1995 Manitoba Prospective Cohort Study; many studies are characterized by well-educated participants in higher income brackets compared to the general population.

### **Quantitative Investigations**

In this section and the following section, I have itemized several points that I believe ought to be addressed in future works. By no means is this list exhaustive; it is my hope to provide future directions stemming directly from the work presented in this thesis only. These points are listed in no particular order, although some will certainly be much easier to implement than others.

1. Consider methods of food preparation, especially vegetables, as different cooking methods may alter anti-oxidant, vitamin and mineral content.
2. Quantify physical activity intensity and type (organized vs. unorganized), in addition to physical activity duration at 12-13 years old and beyond, to determine if differences exist based on asthma status.
3. Extending these findings to address the associations between weight, diet, physical activity and screen time to lung function.

### **Qualitative Investigations**

1. Consideration of asthma perceptions based on asthma severity.
2. Consideration of asthma perceptions based on weight status.
3. Longitudinal follow-up of participants in early adulthood to determine if perceptions of asthma and asthma management change as they assume primary responsibility for their health.

4. Extend qualitative study to also address youths' perceptions of food allergies.

### **Relating Future Directions to Two Existing Cohorts**

This section provides an overview of how some of the above-described future directions could be integrated into two existing prospective cohorts: the Canadian Healthy Infant Longitudinal Development Study (CHILD) and Barn Allergi Miljö i Stockholm – en Epidemiologisk undersökning (Children Allergy Environment in Stockholm – an Epidemiological Survey; BAMSE).

CHILD is a pan-Canadian study of 5000 infants who will be followed to age five years. Mothers are currently being recruited between 12 and 32 weeks' gestation. This study seeks to address the effects of the environment of child health outcomes, including asthma. Data on numerous variables, including maternal and infant nutrition, are being collected prospectively from the second trimester of pregnancy through to the fifth year of life (CHILD, 2011). Recent evidence, such as that reviewed by Allan and Devereux (2011) is indicative that the effect of diet on asthma may begin *in utero* or in very early life. Given the broad scope of this prospective cohort and the tremendous potential for data collection, nutrition ought to remain a focus of CHILD. If funding is secured to permit study continuation beyond age five years, data on other exposures,

including weight status, physical activity and (at an appropriate time) pubertal markers, ought to be collected. CHILD provides a richness of data likely unparalleled in any other single Canadian study. The findings of my thesis work may inform a small piece of the necessary exposures collected in CHILD, which may further our understanding of the etiology asthma.

Findings from my thesis may also be incorporated with BAMSE (Wickman, Kull, Perhagen & Nordvall, 2002). This prospective cohort of 4093 Swedish children born between February 1994 and November 1996 closely parallels the 1995 Manitoba Prospective Cohort Study. Objective outcomes, such as asthma, lung function, diet and physical activity, and blood samples, allow for comparisons similar to those made in my doctoral work. The advantage of making comparisons between prospective cohorts of same-aged children, and ultimately between two geographically and socially distinct countries, is the ability to draw conclusions that will be generalizable to a broader group of children and youth. This will be a focus of my post-doctoral studies at the Karolinska Institutet in Stockholm, Sweden.

### **Policy Implications**

To be effective and ultimately enduring, policies targeting prevention of asthma and overweight must be aggressive, focused and multifaceted. The rates

of asthma (Garner & Kohen, 2008) and overweight (Shields, 2006; Yu et al, 2010) in Manitoba and Canada remain high. Both diseases disproportionately affect youth from low-income and/or of First Nations origin (Kozyrskyj & Hildes-Ripstein, 2002; Shields, 2006; Yu et al, 2010), although the rates are concerning in all regions. Some weight-focused policies, including the removal of pop vending machines from Manitoba schools and mandatory physical education/health education through to Grade 12, have recently been introduced. It is too soon to determine the effectiveness of such programs in combating overweight.

Although laudable, I speculate that these policies will be insufficient to curtail the obesity epidemic that is plaguing Manitoba youth. Youth eat in excess of 500 kcal daily of low-nutrient, energy-dense foods, most of which are eaten in the home environment (Briefel, Wilson & Gleason, 2009). Provincially-mandated, school-based physical and health education programs offer the possibility of completing 25% of such activities outside of school (Government of Manitoba, 2008), potentially opening up loopholes in the system for youth to not achieve the recommended targets. Yet, even if youth reach the intended targets, these fall far short of the recommended levels of 60 minutes daily of vigorous physical activity (CPS, 2008). Current programs ought to continue. But, for these reasons, additional strategic and multipronged policies are critical. Such policies must target weight and related lifestyle behaviours. The following is a discussion of

three potential policies that may complement existing policies, thereby ultimately beneficially influencing the outcomes of both weight and asthma.

1. Raw vegetables ought to be provided on a daily basis to youth living in low income and northern areas. Similar programs, but which distributed fruit rather than vegetables, have been shown to increase consumption of fresh produce over a three year period. Equally importantly, such programs tended towards a reduced intake of pop, candy and chips consumption (Bere, Veierod, Skare & Klepp, 2007).
2. Region-, income- and age-appropriate after school programs ought to be developed with input from youth collected qualitatively. These programs are intended to encourage youth from reducing screen time by offering a forum in which they can engage with their peers. Fun forms of physical activity will be encouraged, as youth still report such activities as enjoyable. These programs will be provided at no cost to youth or taxpayers, and will be held in community clubs and church basements within walking distance from schools (maximum one kilometer).
3. Asthma medications will be provided free of charge to youth whose

families can demonstrate an inability to pay for such medications.

Concurrently, on-line asthma education programs such as those offered will be made more widely available.

The work described in this thesis has the potential for many other policy implications. An extensive discussion of such policies is beyond the scope of this thesis. Suffice it to say that primary, secondary and tertiary prevention must all receive varying levels of focus. Programs and policies must be innovative and aggressive. Youth must be given the opportunity to express their interests and desires for such policies, for this is what true knowledge translation demands. In addition, health credits must be offered to families who meet objective criteria targeting a healthful lifestyle. These credits may be in the form of reduced taxes, government grants for sports equipment and/or nutritious food, time off work for “family activity” days, or other meaningful incentives for youth and their families. All of these policies will require a paradigm shift in regards to how healthcare is perceived. Many of these policies will not be immediately favourable, or even well received. But the reality is that they, or similar policies, are necessary. Youth who are obese (Kuhle, Kirk, Ohinmaa, Yasui, Allen & Veugelers, 2011) and/or who have poorly controlled asthma (Sadatsafavi, Lynd, Marra, Carleton, Tan, Sullivan et al, 2010) place

tremendous economic and resource demands on Canada's health care system.

As both diseases are likely to persist to adulthood and congregate in families, it is most likely that youth who currently have either condition may continue to present with it throughout their lifespan, but also have children of their own who also present with one or either condition.

These future directions and policy implications highlight that, while this thesis has yielded some interesting and valuable insights into the longitudinal influences on asthma during the pubertal years, much work remains. This work ought to continue. As Charles Darwin noted, "How paramount the future is to the present when one is surrounded by children."

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**Appendix A. Letter of Permission from Canadian Respiratory Journal**

From: [Diana Greiss \[xxxxxxx@pulsus.com\]](mailto:xxxxxxx@pulsus.com) Sent: Wed 30/03/2011 8:01 AM  
To: [Jennifer Protudjer](mailto:jprotudjer@mich.ca)  
Cc:  
Subject: RE: Copyright permission request for figure: Asthma Management Continuum (2010)

Dear Jennifer,

Permission is granted. Please use the credit line: This information was originally published in Can Respir J. 2010;17(1):15-24.

Best regards,  
Diana Greiss  
Account Representative, Reprints & Classifieds  
Pulsus Group Inc  
Tel: 905-XXX-XXXX  
Fax: 905-XXX-XXXX

-----Original Message-----

From: Jennifer Protudjer [<mailto:jprotudjer@mich.ca>]  
Sent: Tuesday, March 29, 2011 9:55 AM  
To: xxxxxxx@pulsus.com  
Subject: Copyright permission request for figure: Asthma Management Continuum (2010)

Tuesday 29 March 2011

Attention: Publisher

I am requesting permission to include in my graduate dissertation following material:

Figure: Asthma Management Continuum (2010), from:  
Lougheed MD, Lemièrè C, Dell SD, Ducharme FM, Fitzgerald JM, Leigh R, Licskai C, Rowe BH, Bowie D, Becker A, Boulet LP. Canadian Thoracic Society Asthma Management Continuum - 2010 Consensus Summary for children six years of age and over, and adults. Can Respir J. 2010;17:15-24.

My thesis, entitled Longitudinal Associations between Obesity and Asthma in Pubertal Children: A Mixed Methods Study, is part of the requirements needed to graduate from the Faculty of Graduate Studies at the University of Manitoba.

My thesis will be available in paper format from the University of Manitoba Libraries. It will also be posted electronically and will be accessible for free to a worldwide audience from the University of Manitoba's digital repository called MSpace located at <http://mspace.lib.umanitoba.ca/index.jsp> <<http://mspace.lib.umanitoba.ca/index.jsp>> and from the Library and Archives Canada's Theses Portal located at <http://www.collectionscanada.gc.ca/thesescanada/index-e.html> <<http://www.collectionscanada.gc.ca/thesescanada/index-e.html>>

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Please reply to confirm whether permission is granted to include the above-mentioned material in my dissertation.

Thank you.

Jennifer L. P. Protudjer, PhD(c), MSc  
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**Appendix B. Letter of Permission from Journal of Continuing Education for  
Health Professionals**

From: Curtis Olson [xxxxxx@ocpd.wisc.edu] Sent: Wed 30/03/2011 3:25 PM  
To: Jennifer Protudjer  
Cc:  
Subject: Re: Copyright permission request for figure: Knowledge-to-Action  
Cycle

Dear Ms Protudjer: Thank you for your request for permission to use the figure from Graham et al 2006 for the purpose described below. Permission is granted provided a full and accurate citation accompanies the figure. Best of luck with the dissertation. Kind regards, Curt Olson

Curtis Olson, PhD, FACME  
Editor-in-Chief  
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On Mar 29, 2011, at 8:52 AM, Jennifer Protudjer wrote:

Tuesday 29 March 2011

Attention: Publisher

I am requesting permission to include in my graduate dissertation following material: Figure: Knowledge-to-Action Cycle, from:

Graham ID, Logan J, Harrison MB, Straus SE, Tetroe J, Caswell W, Robinson N.  
Lost in knowledge translation: time for a map? J Cont Educ Health Prof.  
2006;26:13-24.

My thesis, entitled Longitudinal Associations between Obesity and Asthma in Pubertal Children: A Mixed Methods Study, is part of the requirements needed to graduate from the Faculty of Graduate Studies at the University of Manitoba. My thesis will be available in paper format from the University of Manitoba Libraries. It will also be posted electronically and will be accessible for free to a worldwide audience from the University of Manitoba's digital repository called MSpace located at <http://mspace.lib.umanitoba.ca/index.jsp> <<http://mspace.lib.umanitoba.ca/index.jsp>> and from the Library and Archives Canada's Theses Portal located at <http://www.collectionscanada.gc.ca/thesescanada/index-e.html> <<http://www.collectionscanada.gc.ca/thesescanada/index-e.html>>

My thesis will be microfiched and although it may be reproduced and made available in various formats by UMI/ProQuest, I do not expect any financial gain. Please reply to confirm whether permission is granted to include the above-mentioned material in my dissertation.

Thank you.

Jennifer L. P. Protudjer, PhD(c), MSc  
Department of Applied Health Sciences  
504J-715 McDermot Avenue  
Manitoba Institute of Child Health  
University of Manitoba  
Winnipeg, Manitoba  
Canada R3E 3P4  
Phone: +1-204-XXX-XXXX  
jprotudjer@mich.ca

## Appendix C. Certificates of Ethical Approval from the University of Manitoba Health Research Ethics Board



UNIVERSITY  
OF MANITOBA

BANNATYNE CAMPUS  
Research Ethics Boards

P126-770 Bannatyne Avenue  
Winnipeg, Manitoba  
Canada R3E 0W3  
Tel: (204) 789-3255  
Fax: (204) 789-3414

### APPROVAL FORM

**Principal Investigator: Ms. J. Protudjer**  
**Supervisor: Dr. G. Sevenhuysen**

**Ethics Reference Number: H2009:146**  
**Date of REB Meeting: May 25, 2009**  
**Date of Approval: June 3, 2009**  
**Date of Expiry: May 25, 2010**

**Protocol Title: Temporal Associations between Obesity and Asthma in Pubertal Children: A mixed Methods Substudy of the Gender-Related Evolution of Asthma Team (GREATice) (Linked to H2004:147 and H2007:050)**

The following is/are approved for use:

- Protocol, Draft 4 submitted June 1, 2009
- Research Participant Information and Consent Form, Version dated May 30, 2009
- Research Participant Information and Consent Form – Assent Form, Version dated May 30, 2009
- Interview Guides dated April 2009
- Letter of Introduction dated April 2009

The above was approved by Dr. John Arnett, Ph.D., C. Psych., Chair, Health Research Ethics Board, Bannatyne Campus, University of Manitoba on behalf of the committee per your submission dated June 1, 2009. The Research Ethics Board is organized and operates according to Health Canada/ICH Good Clinical Practices, Tri-Council Policy Statement, and the applicable laws and regulations of Manitoba. The membership of this Research Ethics Board complies with the membership requirements for Research Ethics Boards defined in Division 5 of the *Food and Drug Regulations of Canada*.

**This approval is valid for one year from the date of the REB meeting at which the study was reviewed.** A study status report must be submitted annually and must accompany your request for re-approval. Any significant changes of the protocol and informed consent form should be reported to the Chair for consideration in advance of implementation of such changes. The REB must be notified regarding discontinuation or study closure.

This approval is for the ethics of human use only. For the logistics of performing the study, approval must be sought from the relevant institution, if required.

Sincerely yours,

John Arnett, Ph.D., C. Psych.  
Chair, Health Research Ethics Board  
Bannatyne Campus

**Please quote the above Ethics Reference Number on all correspondence.**  
Inquiries should be directed to the REB Secretary Telephone: (204) 789-3255 / Fax: (204) 789-3414



**BANNATYNE CAMPUS**  
**Research Ethics Boards**

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Winnipeg, Manitoba  
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Tel: (204) 789-3255  
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**APPROVAL FORM**

**Principal Investigator: Ms. J. Protudjer**

**Ethics Reference Number: H2009:146**  
**Date of Approval: May 25, 2010**  
**Date of Expiry: May 25, 2011**

**Protocol Title: Temporal Associations between Obesity and Asthma in Pubertal Children: A mixed Methods Substudy of the Gender-Related Evolution of Asthma Team (GREATice) (Linked to H2004:147 and H2007:050)**

**The following is/are approved for use:**

- **Annual Approval**
- **Research Participant Information and Consent Form, Version dated May 30, 2009**
- **Research Participant Information and Consent Form, Assent Form, Version dated May 30, 2009**

The above was approved by Dr. John Arnett, Ph.D., C. Psych., Chair, Health Research Ethics Board, Bannatyne Campus, University of Manitoba on behalf of the committee per your submission dated April 29, 2010. The Research Ethics Board is organized and operates according to Health Canada/ICH Good Clinical Practices, Tri-Council Policy Statement, and the applicable laws and regulations of Manitoba. The membership of this Research Ethics Board complies with the membership requirements for Research Ethics Boards defined in Division 5 of the *Food and Drug Regulations of Canada*.

**This approval is valid until the expiry date only.** A study status report must be submitted annually and must accompany your request for re-approval. Any significant changes of the protocol and informed consent form should be reported to the Chair for consideration in advance of implementation of such changes. The REB must be notified regarding discontinuation or study closure.

This approval is for the ethics of human use only. For the logistics of performing the study, approval must be sought from the relevant institution, if required.

Sincerely yours,

John Arnett, Ph.D., C. Psych.  
Chair, Health Research Ethics Board  
Bannatyne Campus

**Please quote the above Ethics Reference Number on all correspondence.**  
Inquiries should be directed to the REB Secretary Telephone: (204) 789-3255 / Fax: (204) 789-3414



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Research Ethics Boards

P126-770 Bannatyne Avenue  
Winnipeg, Manitoba  
Canada R3E 0W3  
Tel: (204) 789-3255  
Fax: (204) 789-3414

APPROVAL FORM

**Principal Investigator: Ms. J. Protudjer**  
**Supervisor: Dr. G. Sevenhuysen**

**Ethics Reference Number: H2009:146**  
**Date of Approval: January 7, 2011**

**Protocol Title: Temporal Associations between Obesity and Asthma in Pubertal Children: A mixed Methods Substudy of the Gender-Related Evolution of Asthma Team (GREATice) (Linked to H2004:147 and H2007:050)**

**The following is/are approved for use:**

- **Posters submitted January 5, 2011**

The above was approved by Dr. John Arnett, Ph.D., C. Psych, Chair, Health Research Ethics Board, Bannatyne Campus, University of Manitoba on behalf of the committee per your submission dated January 5, 2011. The Research Ethics Board is organized and operates according to Health Canada/ICH Good Clinical Practices, Tri-Council Policy Statement, and the applicable laws and regulations of Manitoba. The membership of this Research Ethics Board complies with the membership requirements for Research Ethics Boards defined in Division 5 of the *Food and Drug Regulations of Canada*.

A study status report must be submitted annually and must accompany your request for re-approval. Any significant changes of the protocol and informed consent form should be reported to the Chair for consideration in advance of implementation of such changes. The REB must be notified regarding discontinuation or study closure.

This approval is for the ethics of human use only. For the logistics of performing the study, approval must be sought from the relevant institution, if required.

Sincerely yours,

John Arnett, Ph.D. C. Psych.  
Chair, Health Research Ethics Board  
Bannatyne Campus

**Please quote the above Ethics Reference Number on all correspondence.**

Inquiries should be directed to the REB Secretary **Telephone:** (204) 789-3255 / **Fax:** (204) 789-3414

## Appendix D. Qualitative Study Consent Form



504 John Buhler Research Centre  
715 McDermot Ave  
Winnipeg, MB R3E 3P5  
Phone (204) 977-5613  
Fax (204) 789-3986



### Research Participant Information and Consent Form

**Protocol Title: Longitudinal Associations between Obesity and Asthma in Pubertal Children:  
A Mixed Methods Substudy of the Sex-Related Evolution of Asthma Team**

Protocol Number for SAGE: H2004: 147

**Protocol Reference Number: H2009: 146**

Principal Investigator of Substudy: Jennifer Protudjer

Principal Investigator of GREATice: Dr. Allan Becker

Sponsors: Allergy, Genes and Environment Network of Centres of Excellence (AllerGen)  
Manitoba Institute of Child Health

#### Dear Parent and/ or Legal Guardian:

You and your child have previously participated in a Clinical Trial (Asthma, Genes and the Environment). Your child is being asked to participate in this study. Please take your time to review this participant information and consent form, and discuss any questions you may have with the study staff. You should take your time to make a decision about allowing your child to participate in this study. You may discuss this study with friends, or family before you make a decision. Please ask the study doctor or study staff to explain any words or information that you do not clearly understand.

Participant's Number \_\_\_\_\_

Participant's Initials \_\_\_\_\_

30 May 2009

Version 1

Longitudinal Associations between Obesity and Asthma in Pubertal Children:  
A Mixed Methods Substudy of the Sex-Related Evolution of Asthma Team

**Purpose of Study**

317 children living in Winnipeg are eligible to participate in this study. In total, we hope to have 4 groups of 6-8 children per group ("focus group") and 4 groups of parents (6-8 parents per group) in this study. Each focus group will be sex-specific for the child (boys will be talking with other boys, while girls will be talking with other girls). Children and parents will participate in separate focus groups. Your child does not have to have asthma to participate in a focus group. During the focus group, children and parents will be encouraged to talk about what it is like to become/to have a teenager and how they/their child feel about physical activity. If your child has asthma, he or she will also be invited to talk about what it is like to live with asthma. We will compare any similarities and differences between the perceptions of boys and girls/parents of boys and girls once all the focus groups have been completed and the recordings have been transcribed.

You do not have to consent to participate/have your child participate in this focus group to be involved in other parts of GREATice. You and/or your child has the right to answer only certain questions during the focus group. Please advise your child that he/she does not have to answer any questions that they prefer not to answer. This information and consent form is only for the focus group. You should have already received an information and consent form for the larger study (GREATice). If you did not receive this, or would like another copy, please contact the research team at 204 977-5613.

**If you chose to permit your child to be interviewed, the following topics will be discussed:**

1. Children's perceptions of physical activity, what types of activities they engage in, and how such activities make them feel, and
2. Children's perceptions of becoming a teenager, and
3. If your child has been diagnosed with asthma, how the disease affects their physical activity and relationships with their family, peers, friends, and teachers.

These interviews will be conducted in small groups of children of the same sex. They will be moderated by investigator, Jennifer Protudjer, or an aid. The focus groups will be conducted in a quiet area of the John Buhler Research Centre. Parking costs will be reimbursed and children will be provided with 2 movie passes for their participation. These focus groups will be audio recorded. Cassettes will be locked in a filing cabinet, in 504J John Buhler Research Centre, 715 McDermot, Winnipeg, MB for five (5) years, after which time the audio cassettes will be erased. In the future, we hope to reassess the children in the study. We are now asking your permission to be contacted in the future for your child's participation in this follow-up study. Your decision to allow your child to participate is completely voluntary. Confidentiality of your child's information will be maintained.

Participant's Number \_\_\_\_\_

Participant's Initials \_\_\_\_\_

30 May 2009

Version 1

Longitudinal Associations between Obesity and Asthma in Pubertal Children:  
A Mixed Methods Substudy of the Sex-Related Evolution of Asthma Team

The total time required for this focus group is 1-2 hours. You can stop participating at any time. However, if you decide to stop participating in the study, we encourage you to first talk to the study staff. If you or your child chooses to voluntarily withdraw from this focus group, any recordings of your or his/her comments will not be included in the final transcript.

Any results published from this research will only identify groups, not individual children. Results will be made available to all of the participants and parents/ legal guardians.

**Possible Risks or Discomforts:**

You and your child will be asked questions about becoming a teenager and about his or her relationships with family and friends. In addition, if your child has asthma, you and he/she will be asked what it is like to live with asthma. Any of these questions have the potential to cause you or your child to become upset. If you or your child becomes upset, you/they will be allowed to go to a private room to collect yourself/him- or herself, move on to the next question, and return to the focus group when you/he/she feels comfortable. If necessary, you/he/she can cease to participate in the focus group completely.

**Confidentiality:**

Information gathered in this research study may be published or presented in public forums. However, your name, your child's name, or any other identifying information will never be used or revealed. Medical research records that contain your identity or your child's identity will be treated as confidential in accordance with the Personal Health Information Act (PHIA) of Manitoba. Despite efforts to keep your/your child's personal information confidential, absolute confidentiality cannot be guaranteed. Your child's personal information may be disclosed if required by law. Please note that what is discussed during the focus group must not be repeated once you leave the research lab. Children will be told the same. They will be reminded of this before commencing the focus group.

Organizations that may inspect and/ or copy your child's research records for quality assurance and data analysis include groups such as:

The University of Manitoba Health Research Ethics Board

- This group may review research-related records for quality assurance purposes.

Participant's Number \_\_\_\_\_

Participant's Initials \_\_\_\_\_

30 May 2009  
Version 1

Longitudinal Associations between Obesity and Asthma in Pubertal Children:  
A Mixed Methods Substudy of the Sex-Related Evolution of Asthma Team

**Voluntary Participation/ Withdrawal from the Study:**

Your decision to participate/to permit your child to be part of a focus group is voluntary. Either you or your child may refuse to participate or to withdraw from this study at any time. Your decision or your child's decision to not participate or to withdraw from this study will not affect your other medical care at this site. If the study staff feels that it is in your child's best interest to withdraw from the study, the study staff will remove him or her without your consent.

**Questions:**

You are free to ask any questions that you may have about your child's treatment and your child's rights as a research participant. If any questions come up during or after the study, contact the study staff:

Jennifer Protudjer  
504J John Buhler Research Centre  
715 McDermot Avenue  
Winnipeg, MB  
R3E 3P5  
Telephone: 204 977-5613

For questions about your child's rights as a research participant, you may contact The University of Manitoba Health Research Ethics Board at 204 789-3389.

Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.

Participant's Number \_\_\_\_\_

Participant's Initials \_\_\_\_\_

30 May 2009  
Version 1

Longitudinal Associations between Obesity and Asthma in Pubertal Children:  
A Mixed Methods Substudy of the Sex-Related Evolution of Asthma Team

**Statement of Consent:**

I have read this consent form. I have had the opportunity to discuss this research study with Jennifer Protudjer and/or the study staff. I have had my questions answered by them in language I understand. The risks and benefits have been explained to me. I understand that I will be given a copy of this consent form after signing it. I understand that my participation and child's participation in this study is voluntary and that I or my child may choose to withdraw at any time. I freely agree to participate and to allow my child to participate in this research study.

I understand that information regarding my personal identity and the identity of my child will be kept confidential, but that confidentiality is not guaranteed. I authorize the inspection of my child's medical research records by The University of Manitoba Health Research Ethics Board.

By signing this consent form, I have not waived any of the legal rights that I have as the parent/legal guardian of allowing my child to participate in a research study.

Yes \_\_\_\_\_ No \_\_\_\_\_

Participant's Number \_\_\_\_\_

Participant's Initials \_\_\_\_\_

0 May 2009

Version 1

Longitudinal Associations between Obesity and Asthma in Pubertal Children:  
A Mixed Methods Substudy of the Sex-Related Evolution of Asthma Team

For studies with children, consent should be obtained from the parent/legal guardian, and assent should be obtained from the child.

Parent/ Legal Guardian's Signature \_\_\_\_\_ Date \_\_\_\_\_

Parent/ Legal Guardian's Printed Name \_\_\_\_\_

Witness Signature \_\_\_\_\_ Date \_\_\_\_\_

Witness Printed Name \_\_\_\_\_

As the parent/ guardian, do you give permission to be contacted in the future for your child's potential participation in a follow-up study? Note: This does not mean that you and/or your child has to participate. If you check yes, it only means that you are willing to let us contact you regarding possible participation in the future.

**Yes, I give permission to be contacted about a future study.**

**No, I do not want to be contacted about a future study.**

I, the undersigned, have fully explained the relevant details of this research study to the participant named above, and believe that the participant has understood and has knowingly given their consent.

Printed Name \_\_\_\_\_ Date \_\_\_\_\_

Signature \_\_\_\_\_

Role in the Study \_\_\_\_\_

*[This section must be done by an authorized/ qualified member of the research team i.e. investigator, study nurse, etc.]*

Participant's Number \_\_\_\_\_

Participant's Initials \_\_\_\_\_

30 May 2009  
Version 1

## Appendix E. Qualitative Study Assent Form



504J John Buhler Research Centre  
715 McDermot Ave  
Winnipeg, MB R3E 3P5  
Phone (204) 977-5613  
Fax (204) 789-3986



### **Substudy Title: Longitudinal Associations between Obesity and Asthma in Pubertal Children: A Mixed Methods Substudy of the Sex-Related Evolution of Asthma Team**

Principal Investigator of Substudy: Jennifer Protudjer  
Principal Investigator of GREATice: Dr. Allan Becker

#### **Why you are here:**

We want to tell you about a study about children's perceptions becoming teenagers and the life experiences of children who live with asthma. We hope you will be part of our study. You do not have to have asthma to be in this study. This form tells you about the study. If there is anything that you do not understand, please ask your parent or legal guardian, or the study staff.

#### **Why we are doing this study:**

We want to learn more about what kids think becoming teenagers. If you have asthma, we would also like to learn more about what this experience is like.

#### **What will happen to you:**

If you want to be in this study, you will spend 1-2 hours talking with other children about:

1. The kinds of physical activity (exercise) you do,
2. What it is like to become a teenager, and
3. How asthma affects any of the items listed above, if you have asthma.

This session, called a focus group, will be led by a researcher. The focus group will be tape-recorded.

Longitudinal Associations between Obesity and Asthma in Pubertal Children:  
A Mixed Methods Substudy of the Sex-Related Evolution of Asthma Team

**Will the study hurt?**

No. We will only be talking. Only the other people in the focus group will know what you said. You do not have to answer any questions that you do not want to answer

**Will you get better if you are in the study?**

This study will not make you feel better or get well. But, we may find out something that will help other children later.

**What if you have questions?**

You can ask any questions at any time. You can talk to the research staff during the study. If you have questions after you leave the study, you can call Jennifer at 204-977-5613 or email her at [jprotudjer@mich.ca](mailto:jprotudjer@mich.ca).

**Who will know what you said during the interview?**

Your name will never appear in any paper (other than this form, and the one that your parent/ legal guardian has to sign). Only the other children in your focus group and the researcher will know it was you in this study.

**Do you have to be in this study?**

You do not have to be in this study. No one will be mad at you if you do not want to do this. If you do not want to be in this study, just say so. We will also ask your parents/ legal guardians if they would like you to be in this study. Even if your parents/ legal guardians want you to be in this study, you can still say no. Even if you say yes now, you can always change your mind later. It is up to you.

**Do you have any questions? Please print or write your questions here.**

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504J John Buhler Research Centre, 715 McDermot Avenue  
Winnipeg, MB R3E 3P5  
Telephone: 204 977-5613 Fax: 204 789-3986

Longitudinal Associations between Obesity and Asthma in Pubertal Children:  
A Mixed Methods Substudy of the Sex-Related Evolution of Asthma Team

**ASSENT**

I want to take part in this study. I know I can change my mind at any time.  
I also know that I should not repeat what other children in my focus group said once I leave the research centre.

\_\_\_\_\_  Verbal Assent Given  
Printed Name of Child

If verbal assent is obtained from the child, the process must clearly be documented in the research file.

Written assent if the child chooses to sign the assent.

\_\_\_\_\_                      \_\_\_\_\_                      \_\_\_\_\_  
Signature of Child                      Age                      Date

I confirm that I have explained the study to the participant to the extent compatible with the participant's understanding, and that the participant has agreed to be in the study.

\_\_\_\_\_                      \_\_\_\_\_                      \_\_\_\_\_  
Printed Name of Person                      Signature                      Date

504J John Buhler Research Centre, 715 McDermot Avenue  
Winnipeg, MB R3E 3P5  
Telephone: 204 977-5613 Fax: 204 789-3986

**Appendix F. Food Frequency Questionnaire Administered at Visit****Three; adapted from the Nurses' Health Study**

**The following questions are for parent and child to complete:**

1. What type of milk does your child mostly consume?
  - A) Regular cow's milk (any variety)
  - B) Farm fresh (unpasteurized) milk
  - C) Soymilk
  
2. Does your child drink Calcium fortified orange juice?
  - A) No
  - B) Yes
  
3. Does your child drink vitamin D fortified orange juice?
  - A) No
  - B) Yes
  
4. Does your child eat omega-3 enriched eggs?
  - A) No
  - B) Yes
  
5. What type of cooking oil do you use at home? (Please choose the one(s) you use most often.)
  - A) Lard or Butter
  - B) Vegetable/Olive oil
  - C) Vegetable shortening
  - D) Margarine
  - E) Non-fat cooking spray
  
6. How often does your child take a multivitamin or mineral supplement?
  - A) Often (once a day or more)
  - B) Sometimes (once a week or more)
  - C) Rarely (<1 week)
  - D) Never
  
7. How often does your child take a Vitamin D supplement?
  - A) Often (once a day or more)
  - B) Sometimes (once a week or more)
  - C) Rarely (<1 week)
  - D) Never
  
8. How often does your child take a Vitamin C supplement?
  - A) Often (once a day or more)

- B) Sometimes (once a week or more)
  - C) Rarely (<1 week)
  - D) Never
9. How often does your child take flax seed oil or fish oil?
- A) Often (once a day or more)
  - B) Sometimes (once a week or more)
  - C) Rarely (<1 week)
  - D) Never
10. Has your child ever been told he/she has a gastrointestinal or malabsorptive illness (e.g. Crohn's disease, celiac disease, recurrent diarrhea, cystic fibrosis)?
- A) No
  - B) Yes
11. Has your child ever been told he/she has a bone disease (e.g. Rickets, osteomalacia, Paget's disease)?
- A) No
  - B) Yes
12. How often does your child take acetaminophen (Tylenol)?
- A) Often (once a day or more)
  - B) Sometimes (once a week or more)
  - C) Rarely (<1 week)
  - D) Never
13. How would you describe the condition of your child's mouth and teeth?
- A) Very good
  - B) Good
  - C) Fair
  - D) Poor
  - E) Don't know
14. What was the main reason your child last visited the dentist (please choose the most appropriate answer)? *Applicable responses continued on the following page*
- A) Routine check-up, examination or cleaning
  - B) Something was wrong, bothering or hurting your child
  - C) Treatment for a condition discovered by a dentist at an earlier check-up or examination
  - D) Other
  - E) Don't know
15. Does your child have any cavities or fillings in adult teeth?
- A) No
  - B) Yes
  - C) Don't know

16. Did your child have any cavities or fillings in baby teeth?

- A) No      B) Yes      C) Don't know

17. Currently, how many of your child's teeth have been affected by dental decay/caries (unfilled cavities, filled teeth, extracted teeth)?

- A) 0    B) 1    C) 2    D) 3    E) 4    F) 5    G) 6    H) 7    I) 8    J) 9    K) 10

- L) 11    M) 12    N) 13    O) 14    P) 15    Q) 16    R) 17    S) 18    T) 19    U) 20

**Nutritional Questionnaire:(For child to complete)**

*Please select the correct response to your intake of the following:*

18. In the past year, on average, how often did you eat fast food?

- A) Never/ less than once per month  
B) 1-3 times per month  
C) 1-2 times per week  
D) 5-6 times per week  
E) At least once per day

19. Are you a vegetarian? (no meat, chicken or fish; eat some dairy and/ or eggs)

- A) No    B) Yes

20. Are you a vegan? (no animal products including eggs, dairy or honey)

- A) No    B) Yes

	Food and amounts	Average number times eaten in past year								
		6 + per day	4-6 per day	2-3 per day	1 pe r da y	5-6 per we ek	2-4 per we ek	1 per we ek	1-3 per mo nth	Al mo st nev er
1	Skim or low fat (1% or 2%) milk	A	B	C	D	E	F	G	H	I
2	Whole (homogenized) milk	A	B	C	D	E	F	G	H	I
3	Yogurt	A	B	C	D	E	F	G	H	I
4	Ice cream/frozen yogurt	A	B	C	D	E	F	G	H	I
5	Butter or Margarine	A	B	C	D	E	F	G	H	I
6	Tofu	A	B	C	D	E	F	G	H	I
7	Green vegetables other than lettuce	A	B	C	D	E	F	G	H	I
8	Vegetables with added cheese sauce or butter	A	B	C	D	E	F	G	H	I
9	Orange vegetables [carrots, sweet potatoes, yellow squash (acorn, butternut, spaghetti)]	A	B	C	D	E	F	G	H	I
10	Tomatoes or tomato juice	A	B	C	D	E	F	G	H	I
11	Fruit Citrus fruit [oranges, grapefruit, lemons]	A	B	C	D	E	F	G	H	I
12	Orange or Grapefruit juice	A	B	C	D	E	F	G	H	I
13	Berries (blueberries, strawberries, etc) including cherries	A	B	C	D	E	F	G	H	I
14	Salmon, Tuna	A	B	C	D	E	F	G	H	I
15	Other fish excluding fish sticks	A	B	C	D	E	F	G	H	I

21. For each food listed, select the letter indicating, on average, how often you have eaten the following foods **during the past year**. Although some of these foods listed may be eaten more food was consumed in the past year: frequently or are limited to certain times of the year, please indicate on average how many times that food was consumed in the past year:

	Food and amounts	Average number times eaten in past year								
		6 + per day	4-6 per day	2-3 per day	1 per day	5-6 per we ek	2-4 pe r we ek	1 pe r we ek	1-3 per mon th	Al mo st nev er
16	Hamburgers or hotdogs	A	B	C	D	E	F	G	H	I
17	Pizza	A	B	C	D	E	F	G	H	I
18	Sandwich meats (salami, bologna, sausage, ham, corned beef, soy slices)	A	B	C	D	E	F	G	H	I
19	Eggs	A	B	C	D	E	F	G	H	I
20	Canned legumes (soybeans, lentils, chick peas, black eyed peas, etc)	A	B	C	D	E	F	G	H	I
21	Hot breakfast cereal (not instant), Hot breakfast cereal (instant), Cold breakfast cereal	A	B	C	D	E	F	G	H	I
22	Dark or whole grain bread	A	B	C	D	E	F	G	H	I
23	French Fries	A	B	C	D	E	F	G	H	I
24	Nuts	A	B	C	D	E	F	G	H	I
25	Potato or corn chips	A	B	C	D	E	F	G	H	I
26	Canned soup, canned vegetables or instant noodles	A	B	C	D	E	F	G	H	I
27	Cookies or 1 slice of a 9" pie / cake	A	B	C	D	E	F	G	H	I

## **Appendix G. Focus Group Interview Guide for Parents of Youth with Asthma**

Note:

1. The interview guides for parents of youth without asthma included all statements and questions, other than those pertaining to asthma.

### **Parents of children with asthma**

Good evening and welcome. Thanks for taking the time to join our discussion about having a teenager who is living with asthma. My name is XXXXX and I am a staff member in Dr. Becker's Asthma Study.

You met Jennifer Protudjer when you first arrived. She is working on a project in which she hopes to better understand how parents perceive teens' lives, including their thoughts about asthma. This work will help us better design programs that are more suitable to both them and you.

You were invited because you are all parents of teens who live in Winnipeg and who are involved in our asthma study. We want to tap into these experiences and your opinions about having a teenager.

There are no right or wrong answers. And, I'm not looking for a particular answer. I expect that you may have differing points of view. Please feel free to share your point of view even if it differs from what others have said.

I am recording this session because I don't want to miss any of your comments. No names will be included in any reports. Your comments are confidential.

We have name tents in front of us tonight. They help me remember names, but they can also help you. Don't feel like you have to respond to me all of the time. If you want to follow up on something that someone has said, you want to agree or disagree, or give an example, feel free to do that. Feel free to have a conversation with one another about these questions. I am here to ask questions, listen and make sure everyone has a chance to share. I am interested in hearing from each of you. So, if you're talking a lot, I may ask you to give others a chance. And, if you aren't saying much, I may call on you. We just want to make sure all of you have a chance to share your ideas.

If you have a cell phone or pager, please put it on quiet mode. Feel free to get up

and get more refreshments if you would like.

We want your help in understanding what it's like to have a teen. We want to understand your perceptions on teens' actions on health, asthma and puberty, the foods they eat and activities they do. Let's begin.

### **Opening Question**

1. Let's start with everyone stating their first name, a one- to two-word description of your teenager, and what you enjoy doing in your spare time.

### **Introductory Question**

2. What is the first thing that comes to mind when you hear the phrase, "(s)he's becoming a teenager?"

### **Transition Questions**

3. Think back to when your son/daughter first became a teenager. How is this different than having a kid or a pre-teen?
4. What was it like for you when you first noticed that your child was starting puberty?

### **Key Questions**

5. What is it like to have a teenager?
6. How does having a teen differ from having a pre-teen or a child?
7. What kinds of things do you hear your teen talking about?
8. What kinds of things does your teen do when they hang out with friends?
9. What kinds of peer pressure do you see your teen being faced with? How do they deal with it?

10. Do you think that your teen is concerned about his/her health? Why or why not?
11. What kinds of roles do sports and physical activity seem to have in your teen's life?
12. How do sports and physical activity differ from this age compared to a pre-teen or a child?
13. What kinds of roles do food and nutrition seem to have in your teen's life?
14. How do food and nutrition differ from this age compared to a pre-teen or child?
15. How does your teen talk about his/her asthma?
16. What are your concerns about your teen's asthma?

### **Ending Questions**

17. If you could give one piece of advice to your teen, what advice would you give?

[ 2-3 minute summary by moderator by what was discussed during focus group. ]

18. Is there anything else that I missed? Is there anything that you came wanting to say that you didn't get a chance to say?

## Appendix H. Focus Group Interview Guide for Youth with Asthma

### Notes:

1. The interview guides for youth without asthma included all statements and questions, other than those pertaining to asthma.
2. The interview guide presented here is for girls. The interview guide for boys includes the same questions, but in reference to boys.

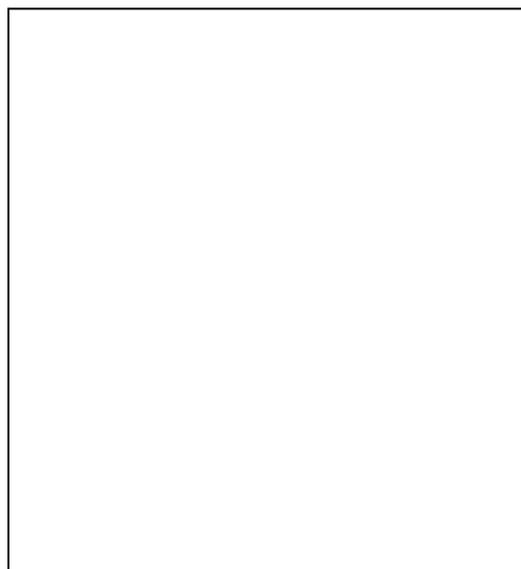
### Focus Group: Girls with asthma

Date: \_\_\_\_\_

Location: \_\_\_\_\_

Seating Arrangement:

Moderator



### Research Question: Girls with asthma

1. To describe girls' experiences of becoming teenagers.
2. To describe girls' experiences of living with asthma

## Girls with asthma

Good evening and welcome. Thanks for taking the time to join our discussion about being a teenager and living with asthma. My name is Jennifer Protudjer and I am a student with Dr. Becker's Asthma Study.

I am working on a project in which I hope to better understand teens' lives, including your thoughts about asthma. This work will help us better design programs that are more suitable to you.

You were invited because you are all teens who live in Winnipeg and who are involved in our asthma study. We want to tap into these experiences and your opinions about life as a teenager.

There are no right or wrong answers. And, I'm not looking for a particular answer. I expect that you may have differing points of view. Please feel free to share your point of view even if it differs from what others have said.

I am recording this session because I don't want to miss any of your comments. No names will be included in any reports. Your comments are confidential.

We have name tents in front of us tonight. They help me remember names, but they can also help you. Don't feel like you have to respond to me all of the time. If you want to follow up on something that someone has said, you want to agree or disagree, or give an example, feel free to do that. Feel free to have a conversation with one another about these questions. I am here to ask questions, listen and make sure everyone has a chance to share. I am interested in hearing from each of you. So, if you're talking a lot, I may ask you to give others a chance. And, if you aren't saying much, I may call on you. We just want to make sure all of you have a chance to share your ideas.

If you have a cell phone, please put it on quiet mode. Feel free to get up and get more refreshments if you would like.

We want your help in understanding teens. We want to know if and how being a teen and/or puberty has changed your thoughts on health, and on the foods you eat and activities you do. Let's begin.

**Opening Question**

1. Let's start with everyone stating their first name, your favourite subject in school and what you enjoy doing most when you are not at school.

**Introductory Question**

2. What is the first thing that comes to mind when you think about becoming a teenager?

**Transition Questions**

3. Think back to when you first became a teenager. How is this different from being a kid or a pre-teen?
4. What were the first changes towards puberty like for you?

**Key Questions**

5. What is it like to be a teenager?
6. What kinds of things do you talk about with your friends? How different do you think this is from other teen girls or is it the same
7. What kinds of things do you do when they hang out with your friends?
8. What kinds of peer pressure do teen girls face? How do they deal with it?
9. Are teens concerned about health?
10. How important are sports and physical activity to teen girls?
11. How important are food choices and nutrition to teen girls?

12. How do your activity habits now compare to your activity habits when you were a kid?
13. What is it like to have asthma?
14. How has having asthma as a teen affected you?

### **Ending Questions**

1. If you had a chance to give advice about being a teen to kids, what advice would you give? What would you tell your parents?  
  
[ 2-3 minute summary by moderator by what was discussed during focus group. ]
2. Is there anything else that I missed? Is there anything that you came wanting to say that you didn't get a chance to say?

**Appendix I. Manuscript: Sex Hormone Levels are Not Associated with  
Asthma in Early Puberty**

NOT FOR CITATION

Target Journal: American Journal of Respiratory and  
Critical Care Medicine

Second Draft Completed: 31 March 2011

Sex Hormone Levels are Not Associated with Asthma in Early Puberty

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## Abstract

**Rationale:** The prevalence of asthma switches from male to female predominance around puberty. This suggests the influence of sex steroids.

**Methods:** Children involved in the 1995 Manitoba Prospective Cohort Study attended study visits at 8-10 yrs (visit 1), 10-12 yrs (visit 2) and 12-13 yrs (visit 3). Children were assessed for asthma by a pediatric allergist at visits 1 and 3.

Serum estrogen, testosterone and dehydroepiandrosterone-sulphate (DHEA-S) levels were assessed based on blood draws at visits 2 and 3. Logistic regression was used to examine the relationship between asthma and sex hormone levels, with adjusting for *a priori* confounders. **Measurements and Main Results:** For this analysis, 271 children (148 [54.61%] boys) were assessed at all study visits.

At visit 1 (8.95±0.55 years old), 104 (56.73% boys) had asthma; at visit 3 (12.51±0.50 years old), 85 (52.94% boys) had asthma. There were no significant sex differences in testosterone or estrogen at visit 2 (10.5±0.38 yrs), while estrogen was higher in girls ( $p<0.001$ ) and testosterone ( $p<0.001$ ) was higher in boys at visit 3 (mean age 12.35±0.37 yrs). No associations were identified between hormone levels at visit 2 or visit 3, and asthma or AR at visit 3 (all  $p$ -values>0.05). **Conclusions:** In this prospective cohort of early pubertal children, no associations were identified between asthma and sex hormones.

## **Sex Hormone Levels are Not Associated with Asthma in Early Puberty**

### **Introduction**

The prevalence of asthma has increased in developed countries by three- to fourfold in the past 30 years (1-3). Although this increase can be explained almost entirely by the increasing rates of asthma in children (4), it remains less clear as to why asthma prevalence and severity switch from male to female predominance beginning in the pubertal years (3,5,6). This change in proportion is commonly referred to the sex shift of asthma and is reflected in hospitalizations rates for asthma at approximately 11-12 years old (7). This suggests that being female is a risk factor for asthma prevalence, and perhaps more importantly, for asthma severity.

Given the sex shift of the prevalence and severity of asthma around puberty, there has been considerable interest in the role of sex hormones. Despite epidemiologic reports (8,9) that suggest a possible role for sex hormones in the sex switch, studies in which the associations between asthma and endogenous sex hormones (10,11) or Tanner pubertal staging scores (12) were considered have collectively yielded no definitive conclusion.

Puberty is a time when there are dramatic hormonal changes, particularly

in estrogen (as estradiol (13)), dehydroepiandrosterone-sulphate (DHEA-S) and testosterone; it is thought that some of these changes may impact on asthma. Estrogen seemingly has a pro-inflammatory effect on lung function, which may be due to the presence of estrogen receptors on mast cells in the airways (14). Notably, it is during puberty, a time characterized by increased levels of estrogen in females, when asthma prevalence shifts to female predominance. Additionally, worsening of asthma symptoms during the luteal phase of the menstrual cycle has been well-documented (15). Also described as perimenstrual asthma, this condition coincides with high levels of estrogen. Additionally, gains in adipose tissue (commonly reported in females from puberty and beyond) may further influence estrogen levels (16), and thus the association between estrogen and asthma.

DHEA-S is believed to have an anti-inflammatory effect on the immune system as evidenced by its ability to mediate NF-KB, which, among other features, downregulates IL-4 and IL-5 (17), although its role in immunoglobulin-E (IgE) regulation and production is unclear (17,18). As well, there is modest evidence to suggest that testosterone has anti-inflammatory properties (14,19). Given the possible roles of these sex hormones on asthma and the conflicting evidence hitherto, we sought to identify possible associations between asthma status and sex hormone levels in early pubertal children. We hypothesized that a

greater prevalence of asthma exists in pubertal vs. non pubertal children.

## **Methods**

This study involves children in the 1995 Manitoba Prospective Cohort Study (20). Manitoba is a province in central Canada, and is heavily populated in the south, while sparsely populated in northern regions (21). In 2002, a short survey was mailed to all families of children born in 1995 not living on First Nations reserves. Participants from First Nations' reserves were recruited via a process deemed acceptable by respective communities' chiefs and councils.

Of the ~3500 returned surveys, 12% of children had parent-reported asthma. This is consistent with the overall proportion and geographic distribution amongst Manitoba children (22). All children with parent-reported asthma and controls matched for sex, location and socio-economic status (SES) were invited to participate in the 1995 Manitoba Prospective Cohort Study. This resulted in a nested case-control prospective cohort of 723 children from which the present study was conducted. Participants have been seen on an approximately bi-annual basis since 2003.

Numerous data were collected during each visit. Pertinent to this study are: Visit 1: sex; all visits: height and weight (measured in triplicate at each study

visit); Visits 1 and 3: pediatric allergist-assessed asthma, Visits 2 and 3: blood samples from which we analyzed serum estradiol, DHEA-S and testosterone via electrochemiluminescence at visits 2 and 3, and self-reported Tanner staging.

Mean height and weight measurements were used to calculate age- and sex-appropriate body mass index (BMI) for each participant. Subsequently, each participant was categorized as either normal weight or overweight, based on a stratification threshold of 85<sup>th</sup> percentile (23). As childhood overweight has been identified by some as predictive of early puberty (reviewed in 24), we also considered the effect of pre-pubertal weight status. Tanner staging was treated as a binary outcome: non-pubertal (stage 1) or pubertal (stage 2 or higher). To address potential confounding variables (e.g. SES, maternal asthma, environmental tobacco smoke), we collected relevant information via questionnaire from participants' parents.

### *Statistical Analysis*

Data analysis involved descriptive statistics, correlation and regression and were analyzed first, for all participants and second, by sex. Logistic regression was used to test for associations between the independent (continuous) variable, sex hormone levels, and the dependent (categorical) variable, asthma status. To facilitate interpretation, odds ratios (OR) are

presented as the inverse logs of the coefficients of determination (25).

Simple and multiple linear regression was used to test for associations between the independent variable, sex hormone levels, and the dependent variable, airway responsiveness. P-values < 0.05 were considered statistically significant. All analyses were conducted using SPSS 18.0 (26).

## Results

We saw 271 children at both ages 8-10 (visit 1) and 12-13 (visit 3) years old (Table 4.1). No significant differences were identified in the prevalence of asthma or overweight between visits 1 and 3. By visit 3, nearly all boys and girls were pubertal based on self-reported Tanner staging of 2 or higher. No significant differences in confounding variables were identified, with the exception of family income. Significantly more girls than boys were from low-income homes.

The mean ages of participants were  $8.95 \pm 0.55$  years at visit 1,  $10.53 \pm 0.38$  years at visit 2 and  $12.51 \pm 0.50$  years at visit 3 (Table 4.1). At visit 1, 59/104 (56.73%) of the children with asthma were boys. This ratio remained relatively unchanged at visit 3; 45/85 (52.94%) of the children with asthma were boys. More boys than girls were overweight. Boys' mean (standard deviation [SD]) testosterone and DHEA-S levels were  $5.67 \pm 5.67$  nmol/L and  $3.44 \pm 1.73$   $\mu$ mol/L,

respectively, at visit 3. Girls' mean  $\pm$  standard deviation (s.d.) levels of estradiol and DHEA-S were  $203.50 \pm 188.14$  pmol/L and  $3.07 \pm 1.16$   $\mu$ mol/L, respectively, at the same time point. These levels are in good agreement with documented normal ranges for same-aged children (27).

We constructed box plots (Figures 4.1 and 4.2) to visually compare sex hormone levels and asthma status. In unadjusted and partially adjusted models, estrogen levels in girls and testosterone levels in boys were significantly associated with asthma. However, these associations were lost in fully adjusted models (Table 4.2). Only DHEA-S in boys was significantly associated with asthma status (OR 0.64; 95% CI 0.47-0.88;  $\beta$  0.159; SE  $\beta$  0.159,  $p < 0.01$ ) in a fully adjusted model.

## Discussion

In this longitudinal study of pre- and early-pubertal children, we were unable to identify associations between asthma status or airway responsiveness, and estradiol and testosterone levels and in girls and boys, respectively. Although we anticipate no selection bias given as this was not a clinical population, our population-based prospective cohort was designed to be weighted towards children with asthma. Thus, these results may be more pronounced than would be expected in a random sample of similar-aged

children with and without asthma. In keeping with others' findings (11), we did not identify a sex shift in the prevalence of asthma during the pubertal years. This provides further evidence that the switch from male to female predominance may not entirely be a pubertal-related phenomenon, and thus cannot solely be attributed to changes in sex hormones.

Yet, this remains a contested debate in the literature. Reports stemming from the Tucson Children's Respiratory Study indicate an association between parental-reported puberty before 11 years old and wheeze amongst overweight/obese girls, compared to those within a normal weight range (8,9); this association held true for both sexes combined (19) and girls only (8). Moreover, although Castro-Rodriguez et al (8) did not provide any data on asthma, puberty and overweight, they noted that weight gain from ages 6-11 years was associated with a nearly nine-fold increased odds of incident asthma/asthma-like symptoms at age 13. This is an important observation, given that childhood overweight may predict early puberty in females (28). In contrast, Salam et al (10) noted that girls who reported menarche before age 12 (an indicator of early puberty) had a two-fold increased likelihood of developing asthma in the year(s) following puberty, as compared to girls who those who reached menarche at >12 years, even after adjusting for BMI, among other confounders.

Our finding that testosterone levels are not associated with asthma status supports others' findings. Nicolai and colleagues (11) reported that androstenediolgluconoride (a marker for peripheral testosterone metabolism) levels did not predict asthma status in boys or in girls. Moreover, they were unable to identify associations between indicators of late puberty (voice change in boys; menarche in girls) and asthma status (11). These authors concluded that the sex shift of asthma happens either very late in puberty or post-pubertally (11). We also demonstrated no sex shift of asthma in early puberty. At present, we cannot comment as to when the sex shift in our birth prospective cohort will occur. However, we hope to reassess these children during their late pubertal years (~15-16 years old); this follow-up will enable us to glean further information about the sex shift of asthma, including the role of sex hormones.

DHEA-S was associated with a reduced odds of asthma in boys only. Others have described low levels of DHEA-S amongst a small sample of hospitalized asthmatic individuals, including those who had and those who had not been taking oral steroids (29). DHEA-S may play a role in mediating inflammatory responses (30). Although the mechanism by which this occurs is poorly elucidated, DHEA-S has been shown to mediate NF-kB activation and decrease interleukin (IL)-4 to undetectable levels in a mouse model (31). In humans with atopic dermatitis, DHEA (the active form of DHEA-S) reduced

peripheral blood mononuclear cell production of IL-4, although not IL-5 (32).

These two cytokines, along with IL-9 and IL-13, are elevated amongst individuals with asthma (33). IL-4 may be particularly important as it is involved in immunoglobulin (Ig)-E production, which plays a major role in allergic reactions (34).

In the present study, pubertal status was obtained based on serum hormone levels. As the majority of children in our study were in the early stages of puberty, we were unable to differentiate between pubertal stage and asthma status. However, this distinction may be important. Although a sex divergence in airway responsiveness amongst children with asthma has been identified as early as Tanner stage 2, this difference is not significant until Tanner stage 4, or late puberty (12).

We acknowledge several limitations of our study. Although estrogen levels fluctuate on a diurnal and lunar cycle (13), our study design did not permit us to capture these data. In a recent paper, changes in FEV<sub>1</sub> in similar-aged girls over a two-week time period (reflective of menstrual vs. non-menstrual status) were shown statistically significant (35). However, these differences cannot be considered clinically significant. Thus, such fluctuations may have less impact on girls compared to women, whose menstrual cycles and thus, estrogen fluctuations, are more regular. Also, we only considered endogenous sex

hormone exposure. Despite a lack of data on oral contraceptive use by participating girls and steroid use in boys and girls, we suspect that exogenous exposure to such hormones is low amongst girls of this age, as suggested by other reports (36). We also did not consider the use of glucocorticoids or corticosteroids amongst children with asthma. Kannitso et al. (37) demonstrated that, in children, budesonide and fluticasone propionate decreased serum DHEA-S concentrations in a dose-dependent manner. Similar biological results have been published by others (38). Yet, these authors noted that drug type (budesonide vs. fluticasone propionate) and delivery method (dry powder inhaler, nebulizer suspension, pressurized metered dose inhaler) yielded no clinical differences, based on FEV<sub>1</sub>, between children who passed vs. failed a corticotrophin stimulation test (38). Thus, despite not accounting for glucocorticoid or corticosteroid use amongst participants in the present study, we do not anticipate that these medications would have yielded clinical differences in DHEA-S levels.

Our study also had several strengths. Asthma was ascertained by a pediatric allergist, and airway responsiveness was objectively measured. Pubertal status was determined via hormone levels and self-reported Tanner staging. As participants were involved in a longitudinal prospective cohort, we were able to consider associations between asthma and hormone levels/Tanner

staging differences at two different time points during early puberty. And, to our knowledge, this is one of the largest study populations in which hormone levels have been analyzed. Although other studies of hormonal effects on asthma have also involved large sample sizes, puberty was based on Tanner staging only (12), or participant-reported breast development (9) or menarche (9-11) in girls and voice change in boys (9,11).

#### *Clinical Relevance*

Early-stage pubertal onset is occurring in children at increasingly younger ages (41). Clinicians ought to be aware that, while estrogen and testosterone may not play a significant role in the sex shift of asthma, adolescent girls without a childhood history of asthma may present with asthma-like symptoms at an increasingly younger age. This may be particularly true amongst girls who are overweight, given the associations between early puberty and overweight (28), overweight and asthma (8) as well as the potential for obesity-related wheezing due to a lack of fitness to be misdiagnosed as asthma (42).

#### *Conclusion*

The sex switch of asthma during the late pubertal years and beyond is a well-documented phenomenon. Yet, the role of sex hormones in the change of

asthma prevalence from male to female predominance during early puberty remains controversial.

**Acknowledgments**

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**Table AI-1. Participant Characteristics**

	Overall		Boys		Girls	
	n	%*	n	%*	n	%*
Sex (n=271)			148	54.60	123	45.40
Age†						
Visit 1	8.95 ± 0.55		8.96 ± 0.55		8.94 ± 0.54	
Visit 3	12.51 ± 0.50		12.5 ± 0.50		12.52 ± 0.50	
Body Mass Index†						
Visit 1	18.03 ± 3.73		18.45 ± 4.17		17.53 ± 3.07	
Visit 3	20.52 ± 4.77		20.71 ± 4.89		20.28 ± 4.63	
Sex Hormones at Visit 3†						
Estradiol (pmol/L)	-		-		203.5 ± 188.14	
Testosterone (nmol/L)	-		5.67 ± 5.67		-	
DHEA-S (umol/L)	-		3.44 ± 1.73		3.07 ± 1.16	
Asthma						
Visit 1 (n=271)	104	38.40	59	56.73	45	43.27
Visit 3 (n=271)	85	31.40	45	52.94	40	47.06
Overweight						
Visit 1 (n=271)	69	25.50	43	62.32	26	37.68
Visit 3 (n=271)	75	27.70	46	61.33	29	38.67
Tanner at Visit 3 (n=312)						
Pre-Pubertal‡	97	31.09	71	73.20	26	26.80
Pubertal§	215	68.90	97	45.12	118	54.88
Region of Residence (n=271)						
Urban	175	64.60	95	54.29	80	45.71
Rural	89	32.80	52	58.43	37	41.57
Northern	7	2.60	1	14.29	6	85.71
Ethnicity (n=270)						
Caucasian	229	84.80	128	55.90	101	44.10
First Nations/Métis	28	10.40	12	42.86	16	57.14
Other	13	4.80	7	53.85	6	46.15
Breastfed (n=270)						
No	30	11.10	15	50.00	50	50.00
Yes	240	88.90	132	55.00	108	45.00
Family Income <sup>  </sup> (n=238)						
< \$30000 Canadian	15	6.30	6	40.00	9	60.00
≥ \$30000 Canadian	222	99.60	128	57.66	94	42.34
Maternal Asthma (n=267)						
No	190	71.20	110	57.89	80	42.11
Yes	77	28.80	37	48.05	40	51.95
Mould in Home (n=271)						
No	104	38.40	62	59.62	42	40.38

Pets in Home (n=268)	Yes	167	61.60	86	51.5	81	48.5
	No	101	37.70	59	56.44	42	41.58
Smokers in Home (n=271)	Yes	168	62.30	88	52.38	79	47.02
	0	215	79.30	118	54.88	97	45.12
	1	35	12.90	21	60.00	14	40.00
	2 or more	21	7.70	9	42.86	12	57.14

\*percentages may not total 100.00% due to rounding

†mean ± standard deviation

‡Pre-pubertal; Self-Reported Tanner stage 1

§Pubertal; Self-reported Tanner Stage 2 or higher

||Significantly different between sexes (p<0.02)

**Table AI-2. Logistic Regression of Log Levels of Sex Hormones and Asthma at 12-13 Years Old**

	Odds Ratio <sup>†</sup>	95% CI	B	SE of B	p-value
<b>Girls</b>					
<i>Estradiol</i>					
Crude	0.998	0.996-0.999	-0.002	0.001	0.01
Model 1 <sup>§</sup>	0.998	0.996-1.000	-0.002	0.001	0.05
Model 2 <sup>  </sup>	0.999	0.997-1.001	-0.001	0.001	0.30
Model 3 <sup>**</sup>	1.001	0.998-1.003	0.001	0.001	0.66
<i>DHEA-S</i>					
Crude	0.793	0.702-0.895	-0.232	0.062	0.001
Model 1 <sup>§</sup>	0.780	0.675-0.902	-0.248	0.074	0.001
Model 2 <sup>  </sup>	0.815	0.685-0.968	-0.205	0.088	0.02
Model 3 <sup>**</sup>	0.893	0.665-1.197	-0.114	0.150	0.45
<b>Boys</b>					
<i>Testosterone</i>					
Crude	0.913	0.865-0.964	-0.091	0.028	0.001
Model 1 <sup>§</sup>	0.933	0.882-0.987	-0.069	0.029	0.02
Model 2 <sup>  </sup>	0.938	0.883-0.997	-0.064	0.031	0.04
Model 3 <sup>**</sup>	0.956	0.877-1.042	-0.045	0.044	0.31
<i>DHEA-S</i>					
Crude	0.762	0.684-0.849	-0.272	0.055	0.001
Model 1 <sup>§</sup>	0.735	0.638-0.846	-0.308	0.072	0.001
Model 2 <sup>  </sup>	0.683	0.571-0.818	-0.381	0.092	0.001
Model 3 <sup>**</sup>	0.644	0.472-0.880	-0.440	0.159	0.01

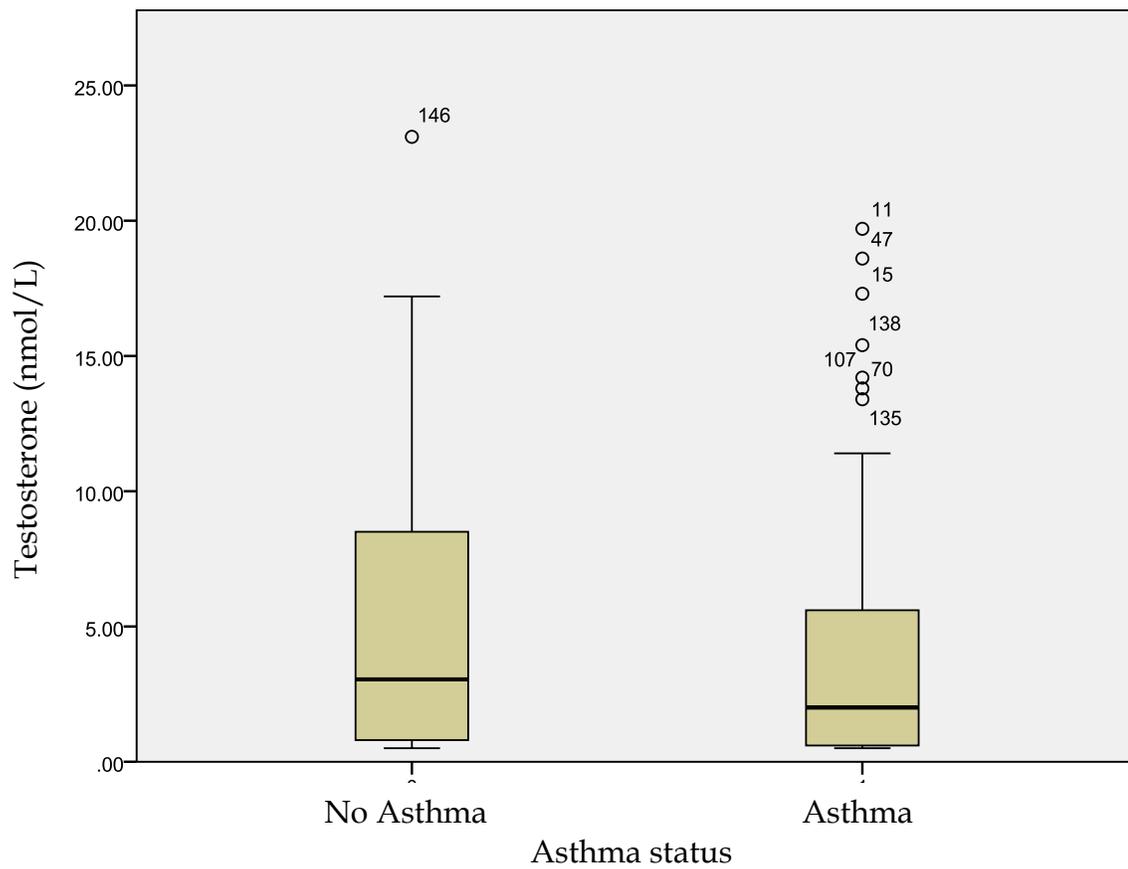
<sup>†</sup>Visit 3: Ages 12-13 years

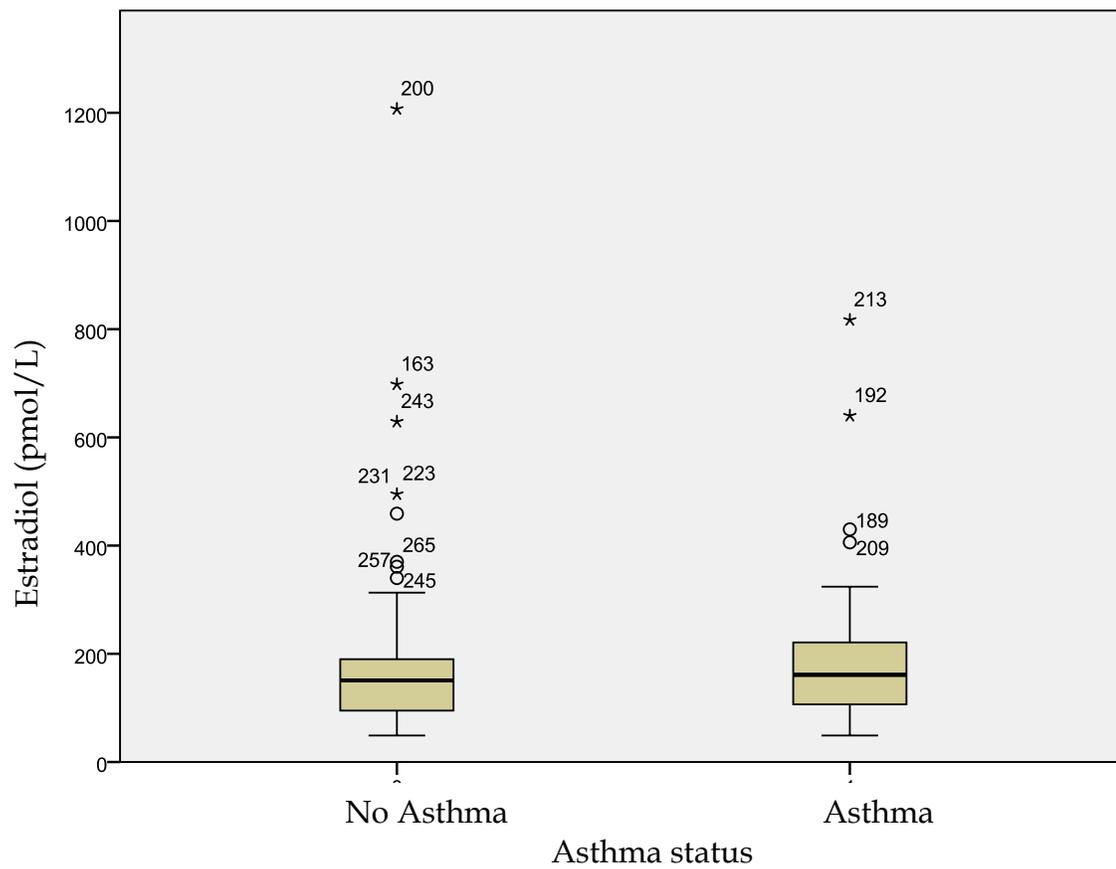
<sup>‡</sup>Reference group is those without asthma at 12-13 years old

<sup>§</sup>Model 1: Adjusted for overweight at ages 8-10 years old and 12-13 years old

<sup>||</sup>Model 2: Also adjusted for maternal history of asthma, ethnicity and environmental tobacco smoke

<sup>\*\*</sup>Model 3: Also adjusted for breastfeeding, family income, and mould and pets in home

**Figure AI-1. Box Plot of Boys' Testosterone Levels and Asthma Status at 12-13****Years old**

**Figure AI-2. Box Plot of Girls' Estrogen Levels and Asthma Status at 12-13****Years old**

**Appendix J. Manuscript: Asthma is a Low Priority Amidst the Layers  
of Complexity Faced by Adolescents**

NOT FOR CITATION

Target Journal: Pediatrics

## **Asthma is a Low Priority Amidst the Layers of Complexity Faced by Youth**

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Short Title: Asthma is a Low Priority for Youth

JLPP collected and analyzed the data, and wrote the manuscript. All authors contributed to conception and design and interpretation of data; critically revised the manuscript for important intellectual content; and approved the final version to be published.

### Abstract

**Rationale:** The social impacts of adolescence and the physiological changes associated with puberty may change asthma presentation and the perception youth have of the disease. The characteristics of adolescence and these perceptions influence youths' ways of living with asthma. **Objectives:** To document the perceptions, and management behaviours towards asthma of youths and parents in order to understand the role of the disease in the lives of youth. **Patients and Methods:** Patients with pediatric allergist-diagnosed asthma, aged 15-16 years, were recruited using purposive sampling from the 1995 Manitoba Birth Cohort and the Canadian Asthma Primary Prevention Study. All were residents of Winnipeg, MB. None had co-morbid conditions except other allergic diseases (atopy, environmental/food allergies). **Study Design:** Focus groups and interviews, held between September 2010 and February 2011, were conducted separately by sex. All focus groups (n=4 with patients; n=5 with parents) and interviews (n=3 with patients; n=2 with parents) followed a semi-structured interview guide and were recorded and transcribed. Data were analyzed using thematic coding. **Main Results:** Patients described social demands experienced during adolescence and the pre-occupation with social relationships, including pressures to engage in inappropriate behaviors (e.g. drugs, alcohol). Only when prompted did patients talk about asthma, even

in focus groups with patients with asthma. **Conclusions:** The social demands related to adolescence appear to overshadow the burden of asthma. The perceived importance of these demands appears to reduce the importance of sustained asthma management in youth.

### **Asthma is a Low Priority Among the Layers of Complexity Faced by Youth**

#### **Introduction**

Adolescence is a time of emerging independence and developing one's identity (1). Youth face conflicting pressure from family and peers in building independence. At the same time, the need for youth to comprehend the long-term results of their behaviours and actions diminishes and they tend to focus on their immediate situation (1). Asthma introduces additional complications in this period of life. Physiological changes during puberty may change asthma presentation, including a shift from male to female predominance (2), and in girls, worsening symptoms during the luteal phase of the menstrual cycle (3). Achieving increased autonomy is more challenging when the person has to adhere to routine asthma management and treatment (4). These changes, coupled with characteristics of youth, may influence youths' perceptions of, and ways of living with asthma. At the same time, parents of youth with asthma struggle to establish a balance between disease control and the increased

autonomy of their youth (5).

The lived experience can be described using qualitative methods (6). By giving opportunity to those directly affected by a chronic illness, such as asthma, to talk about experience it should be possible to understand its impact. The purpose of our study was to expand the understanding the perceptions and management behaviours towards asthma of youths and their parents. The research question was, "How do youth with asthma, as well as their parents, perceive and manage asthma?"

## **Patients and Methods**

### *Recruitment and Participants*

Youth and their parents were recruited using purposive sampling from two existing asthma-focused studies, the 1995 Manitoba Birth Cohort (7) and the Canadian Asthma Primary Prevention Study CAPPS; 8). Purposive sampling provides an opportunity for discussion about the topic of interest, in this case asthma, from those most directly affected by it. Gaining insight about a phenomenon from such key informants is one of the aims of qualitative research (6). Letters of invitation were mailed to families of youth who met the following criteria: asthma diagnosed by a pediatric allergist, Winnipeg residency (for logistical purposes), and no co-morbidities or conditions that interfere with

physical activity. All those who consented to be part of the study were invited to participate in focus groups. We also included the option of one-on-one interviews in order to compare and, where appropriate, confirm data from focus groups.

#### *Focus Groups, Interviews and Analysis*

Focus groups and individual interviews with youths were undertaken to gain insight into youths' perceptions of living with asthma. The individual interviews and focus groups with parents provided independent descriptions of selected physical and psychological contexts in which the youth made decisions about asthma.

All 15-16-year-old youth and their parents attended focus groups and interviews at the same time, but in separate rooms. Each youth focus group included either boys only or girls only. All interviews/focus groups followed a semi-structured interview guide, which included introductory and transition questions, followed by asthma-related questions (Table 1). Questions were discussed one at a time until participants had no further comments. In keeping with a semi-structured format, follow-up questions were asked when the comment of a participant pointed to new aspects of the topic. If discussion diverged from the topic of interest, the moderator redirected participants to the

last relevant topic. Snacks/dinner were provided throughout the focus groups, parents were reimbursed for parking and youth received two movie passes for their participation. The first author (JP) conducted all focus groups with youth and trained research assistants conducted the focus groups with parents.

Interviews and focus groups were digitally recorded and transcribed, and ranged from 32-90 minutes in duration. Verbatim transcripts were generated from digitally recorded interview and focus groups.

Data were analyzed using thematic coding. Thematic coding is the foundational method in qualitative research. Although a very flexible analytic method in qualitative research, thematic coding has requirements to ensure theoretical and methodological soundness. This includes an acknowledgement from the researcher that the chosen framework and methods are decisions made by the researcher, rather than “emerging” or “discovered” concepts in the data; the latter implies a passive method, while in fact, thematic analysis is an active process (9). Thematic analysis is independent of theory and epistemology, and thus is compatible with many theoretical frameworks, including pragmatism (9). Pragmatism is characterized by a problem-centered approach oriented in real-world practice, which allows for the expansion of our understanding of the data (10). Content analysis was used to help identify constructs that provided insight into youths’ perceptions of being an adolescent and living with asthma, as well

as parental perceptions on these topics. Constructs were deemed to be saturated when new or additional constructs ceased to be identified with subsequent interview or focus groups.

This study was approved by the University of Manitoba's Health Research Ethics Board. All youth and their parents provided written consent, respectively, prior to participation. All names are pseudonyms.

## **Results**

Four focus groups, involving nine youth, and three interviews with youth were held. All were 15-16 years old and in Grade 10. Two parents' interviews and five focus groups of parents were attended primarily by mothers. Three focus groups also involved four fathers; this includes one focus group with a mother and father whose youth participated in an interview. All were residents of Winnipeg.

The analysis of verbatim transcripts identified four themes for youth (freedoms and burdens of adolescence; pressures to become involved in inappropriate behaviors; asthma as a minor issue, and; drawbacks of the disease) and three themes for parents (parents have genuine admiration for youth; youth demand, and are given greater freedoms, and; asthma as a minor issue). For both youth and parents, themes are provided in order of importance, from

highest to lowest, based on the frequency and intensity of participant discussion. Intensity of discussion was determined based on extemporaneous comments (participant discussion about a given topic without prompting from the moderator), non-verbal cues (body language, eye contact with the moderator, or in the case of focus groups, with other participants) and tone of voice (animated or excited speech, for example).

### *Youths' Perceptions*

#### 1. Freedoms and burdens of adolescence

Youth understood that they were in an age of transition from children to adults. Although they were eager to experience their independence, they were also aware of the increasing responsibilities and expectations. This was the most common theme, or layer of experience. Freedoms included earning increased trust from parents, expressed as being given a later curfew or being permitted to go to social events with their peers, and from social institutions, such as passing a driver's test. However, they also understood that increased freedom came with a cost.

Youth also spoke of the increased burdens of school and oft-unfounded stereotypes. Such pressures caused varying degrees of anxiety, and influenced

their social lives. As Victoria stated, *“School gets harder. I never hang out with my friends anymore ‘cuz I have no time. I’m always doing homework... I really want to do my best, but it’s hard.”* Other youth described how they believed that they had been stereotyped as menaces because of their age. Many of these youth, particularly boys, described how they believed that this was an unfair assumption even though youth were more likely than adults to be involved in such activities: *“[S]ome of the stereotypes are deserved because teens do cause a lot more trouble than adults and I don’t think that’s it is right to assume that all teens are going to be causing trouble”*.

## 2. Pressure to become involved in inappropriate behaviours

Consonant with newfound freedoms and burdens, youth also spoke of pressures to become involved in inappropriate behaviors, including drugs and alcohol. Most acknowledged that alcohol and drugs were easily accessible, although few had experimented with either. Comments such as *“there’s drinking and stuff [at parties]”* were commonly made. Jacob was more candid, noting that he had *“had joints shoved in [his] face, people trying to sell [him] joints.”* Some youth acknowledged that they had experimented with alcohol. A small number also commented that they had tried street drugs.

### 3. Asthma as a minor issue

Only when youth were queried about their asthma did most speak to it, despite the fact that they had previously been told that all participants had asthma. Youth spoke of asthma as a minor issue compared to other complexities, such that *“asthma’s not something that overtakes [a teen’s] life that much”* and that *“[a]sthma is something you can control.”* Comment such as these reflect youths’ assertions that, within the context of other events in their lives, asthma is not a major focus.

#### a. Asthma medication has a place, but is not top-of-mind

Although youth recognized that asthma medication has a place, it was not top-of-mind. Youth knew that their rescue medications would provide relief from symptoms, but most reported that they were not diligent about carrying their inhalers. Preventive or controller medications were used by few participants. But, even for those youth on inhaled corticosteroids, their disease and its management were not central to their lives. Yet, despite their comments that they placed little emphasis on asthma medication, youth recognized the benefits of such drugs. Micah, who had previously had limited pulmonary function as a result of his asthma, described how his pulmonary function tests had improved since he had been regularly using a higher dose of inhaled

corticosteroids.

#### 4. Drawbacks of the disease

That youth perceived asthma as a low priority in the context of their lives is not to suggest that youth viewed no drawbacks. A minority of participants described how asthma *“just gets in the way of things”* despite their attempts to view it as a minor issue. Only one boy mentioned his asthma without being prompted. But, his statement was made in context of what he viewed as a drawback of asthma. Rather than focusing his discussion on asthma, he contextualized how asthma was a hindrance to experimenting with drugs. His description of his involvement in inappropriate behaviors led him to mention his asthma: *“I’ve smoked pot... I couldn’t breathe right for like the rest of the night, so I’m never doing pot again.”* This statement is ironic, as it suggests that asthma, as a disease with its own consequences, was a hindrance to behaviours that were socially acceptable to his peer group, but potentially also had social consequences.

## *Parents' Perceptions*

### 1. Parents have genuine admiration for youth

Parents' spoke about their youth with pride and satisfaction. Although the adolescent years involved transitions (e.g. school, puberty) and determination of identity, parents generally enjoyed their youth and were proud of the individuals they were becoming. Comments such as sons and daughters who were *"quite interesting to talk to... [she]/he's a good kid"* were expressed by many parents. Although parents did not agree with all of their youth's views, they were learning to respect the difference in opinion. Christine was candid about this experience: *"I found it hard accepting [David] as a young man with an opinion that's different than mine, so you know we, we disagree on things and its okay to have different opinions and that was a little hard for me to swallow."* Parents also acknowledged how different their youths' lives were, compared to their own experiences of adolescence. Parents commented how well their youth appeared to be coping with the pressures of adolescence for the current generation. It is perhaps for this reason that parents also spoke about giving their youth greater freedoms.

## 2. Youth demand, and are given greater freedoms

Parents also spoke of how their youth demanded, and were given greater freedoms. Deanne described how her daughter, Kyla, was trying to *“assert more independence... spread [her] wings a bit”* and how she, as a mother, had been *“allowing her a little bit more freedom”* Although youth demanded, and were often given greater freedoms, parents spoke of the transition from childhood to adulthood as a challenge. Such comments were not made only by mothers. Fathers described *“power struggle[s]” [because] they’re trying to stake out their territory... but emotionally, they aren’t prepared to handle the responsibilities and decisions that come with [adulthood].”* As such, parents acknowledged that their youth needed increased freedom, but also continued guidance.

### a. Parents have a responsibility to mentor their youth

Although parents realized that their youth were becoming increasingly independent and had increased freedoms, they still viewed themselves as mentors. Parents spoke of *“giving more choices and encouraging [him]/her to look at the choices that [he]/she is making,” “put[ting] the moral lecture”* and making decisions based on what youth desired for their futures.

These parents also recognized that their youth were faced with burdens to which they had not been exposed when they were younger. Paula, whose son,

Jacob, spoke of drugs, confirmed that the common peer pressures "*at the moment is smoking and drinking and drugs.*" No parents spoke of being unaware of these pressures. Many believed that youth would drink alcohol, for example, whether it was condoned by the parents or not. A small group of parents talked about their mentoring role as including a responsibility to ensure their youth consumed alcohol in a safe environment so as to minimize the potential for undesired outcomes.

### 3. Asthma as a minor issue

Like youth, parents viewed asthma as a minor issue in the context of adolescence. Few parents spoke of their youth's asthma without being asked directly. Parents described how asthma had not hindered their youth. Rather, they described how youth participated and excelled in activities that were of interest to them. For example, one mother spoke with pride about how her son had become a top-ranked football player on his team despite the fact that his "*asthma was so severe that that wasn't even an option for him*" in the past. Parents also reported having fewer conversations now than in the past, regardless of the severity of their youth's asthma. Paulina, whose son, Micah, had asthma, stated, "*Once [asthma] became under control, it was less of a problem so we stopped talking about it as much... he doesn't talk about it as much.*" This comment was made

despite the fact that Micah had nearly been hospitalized as a result of his limited pulmonary function the previous autumn and was still concerned about his health. Parents contextualized a reduction in asthma-related conversations within the framework of youths' increased responsibility for their own health. Paulina further commented that, *"you need to leave him alone now, he needs to make his own [asthma management-related] choices... he knows when he's to take his inhaler."*

## **Discussion**

Asthma disproportionately affects youth (11,12). Moreover, asthma-related fatality rates increase in late childhood (12) and healthcare system contact subsequent to emergency department visits are high (13). Yet, this study provides evidence that youth do not prioritize their asthma. In all aspects of their lives, youth spoke of gaining increased autonomy. This was juxtaposed against their comments about placing little priority on asthma management. Youth candidly spoke about forgetting their inhalers and not viewing asthma as a chronic condition. Unlike findings in other studies, participants in our study did not compare their condition to other chronic diseases, such as diabetes (14). This lack of comparison is very telling for two reasons. Our participants may not have recognized that asthma, much like diabetes, is a chronic condition that warrants regular management. Or, they have minimized their condition under

the multiple demands of adolescence and peer pressure. Either way, the result is the same: for today's youth with asthma, asthma is a low priority amidst the layers of experience faced by youth.

Youth willingly discussed inappropriate behaviours (described above). This suggests that they were comfortable in discussing sensitive topics when assured of confidentiality. As such, their asthma-related comments are taken as true reflections of their beliefs on the topic; youth would have been comfortable discussing more sensitive asthma issues had they deemed them important.

Previously, we reported that youth aged 12-13 years developed strategies to normalize their asthma (15). Younger youth developed strategies to normalize their lives, such as minimizing the health impact of asthma, stressing normality, emphasizing abilities, making adaptations and managing symptoms with medication (13). The present findings confirm our earlier work. During adolescence, when youth have gone through processes to normalize the disease, they will acknowledge their asthma, but talk about it as an issue that can be controlled, in contrast to the other experiences of adolescence that feel less controllable.

Layers of experience faced by today's youth overshadow the burden and management of asthma. Youth have numerous demands on their time and rarely recognize the importance of sustained asthma management (16). Asthma

needs to be contextualized within these layers, but not minimized.

Understanding that youth do not prioritize their asthma management (16) is an important first step in asthma education. Healthcare professionals need to acknowledge these layers of experience when discussing asthma action plans and management with youth so as to improve their asthma outcomes and quality of life. Studies are required to define the most effective approach(es) with these youth and to communicate these findings to healthcare providers and policy makers.

A common theme to both youth and parents was increasing freedoms and burdens, which has also been reported by others (4,5). Along with greater responsibility, youth with severe asthma noted confusion about their treatment, which resulted in unintentional non-adherence (4,5). Nonetheless, they desired independence and privacy when dealing with healthcare providers (4). Parents of youth with chronic conditions, including asthma spoke of struggling with their youth's increasing autonomy, while youth both acknowledged, and were irritated by parental involvement (5). Although some youth in the present study spoke of tensions between themselves and their parents that were the result of youths' newfound freedoms, none of these participants spoke of such tensions in relation to asthma.

As with other reports (14), youth involved in the current study reported

requiring less asthma medication compared to when they were younger. They attributed this to “growing out” of their asthma. Although participants’ asthma status was last assessed as long as two years prior to this qualitative investigation, it is unlikely that all youth involved in our study had outgrown their asthma. The majority, if not all youth participants, will still have had asthma at the time of the interviews/focus groups. Indeed, no youth reported being told by a physician that their asthma had resolved.

We acknowledge the limitations of our study. Although we were only able to recruit 12 youth with asthma, we believe that our data were saturated given the links between youths’ comments, parents’ comments and the comments of these two groups collectively. The major themes resonated across all focus groups and interviews. The apparent lack of interest in participating in focus groups for this study may be a proxy for the low priority youth in general ascribe to their asthma, even for youth who had been involved in our asthma studies for many years. Such involvement, including contact with asthma experts, may have given them a greater sense of control over their asthma, whereby they were able to de-emphasize its impact. As with all qualitative work (6), caution should be used when transferring our findings to other populations. Nonetheless, these findings may be transferable to populations with similar social characteristics and experiences (6) with regard to asthma and asthma

treatment.

The qualitative approach in this study provides insights into perceptions that may ultimately influence health behaviors and outcomes, but which cannot be quantified (17). By understanding that youth place little priority on their asthma given the other demands of daily life, healthcare professionals can develop treatment and education plans in a way that is more suitable, and thus may be better received by youth and their families.

### **Conclusion**

More predominant themes, or “layers of experience” faced by today’s youth overshadow the burden and management of asthma. Although youth recognize the importance of asthma medication, it is not top-of-mind. For both youth and their parents, asthma is a minor issue in the context of their daily lives.

**Table AJ.1: Selected Questions Posed to Youth during Focus****Groups/Interviews to Better Understand Perceptions of Asthma\***

- 
- 1 What is it like to be a teenager?  
What do you talk about with your friends? Do you think this is different from
  - 2 other teens?
  - 3 What kinds of things do you do when they hang out with your friends?
  - 4 What kinds of peer pressure do teens face? How do they deal with it?
  - 5 Are teens concerned about health?
  - 6 How important are sports/nutrition to teens?
  - 7 What is it like to have asthma?
  - 8 How has having asthma as a teen affected you?
  - 9 If you had a chance to give advice about being a teen to kids, what advice would you give? What would you tell your parents?
- 

\*Similar questions were posed to parents about their youth

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