Asthma in First Nations Adults:

Prevalence and Associated Factors

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By

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Abstract

Background: Asthma is a significant cause of morbidity worldwide. Research suggests that Indigenous people experience a higher asthma burden than non-Indigenous Canadians. However, few studies have examined the prevalence of asthma and associated factors in adult First Nations people by phenotype and through a sex/gender lens. The study aimed to determine the prevalence of atopic and non-atopic asthma in First Nations women and men and whether the correlates of asthma varied by atopic status and by sex/gender.

Methods: The data source was the First Nations Lung Health Project (FNLHP), a community-based participatory study in two First Nation communities in rural Saskatchewan, Canada. Participants were 648 women and 647 men 18 years of age and older. Data were obtained via interviewer-administered questionnaires and clinical testing. The dependent variable, asthma phenotype, was a categorical variable with three response options (no asthma, atopic asthma, non-atopic asthma) and derived from a combination of self-reported asthma and allergy testing. The independent variables included personal, environmental, and social/economic factors. Multinomial logistic regression was the primary analysis.

Results: Atopic and nonatopic asthma prevalence was 11.4% and 5%, respectively. There were no significant sex differences in asthma prevalence; however, the results of the multivariable analysis indicated a significantly higher occurrence of non-atopic asthma in women 40 years of age and older compared to same-age men. Only one variable was associated with atopic asthma: those with depression had 2.9 times higher odds of atopic asthma than those without depression (95%CI: 1.38, 6.20). Statistically significantly associated with an elevated odds of non-atopic asthma were home dampness (OR=1.83, 95%CI: 1.08-3.11), ever alcohol use (OR=2.21, 95%CI: 1.09-4.48) and the presence of a co-morbidity (OR=1.77, 95% CI: 1.17, 2.68). Financial strain was related to an increased odds of nonatopic asthma in women and decreased odds in men.

Conclusion: The results from this study suggest the possibility of intriguing differences in the correlates of asthma by phenotype and sex. Future research incorporating a longitudinal design and enhanced measurement is required to advance understanding of the complex interrelationships between sex, asthma phenotype, and various risk factors in First Nations adults.

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Dedication

This thesis is dedicated to the most influential person in my life, my daughter Suhayla Zoufishan Islam is the superstar and biggest inspiration of my life

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List of Abbreviation

IgE	Immunoglobulin E
FEV_1	Forced Expiratory Volume in one Second
BMI	Body Mass Index
OR	Odds ratio
COPD	Chronic Obstructive Pulmonary Disease
CHD	Coronary Heart Disease

Definition of terms

Indigenous group - According to Statistics Canada (1): "***Indigenous group*** *quotes whether the person is First Nations (North American Indian), Métis and/or Inuk (Inuit). A person may comprise more than one of these three groups. Indigenous peoples of Canada are defined in the Constitution Act, 1982, Section 35 (2) as including Indian, Inuit and Métis peoples."*

First Nations- According to the Canadian Encyclopedia (2): "***First Nations*** *is a term used to describe Indigenous peoples in Canada who are not Métis or Inuit*. In Saskatchewan, 175,015 Indigenous people make up 16.3% of the population, with nearly two-thirds of First Nations origin (3).

Sex/gender- According to the Canadian Institutes of Health Research (CIHR) (4): *"**Sex** refers to a set of biological attributes in humans and animals. It is fundamentally associated with physical and physiological features, including chromosomes, gene expression, hormone levels and function, and reproductive/sexual anatomy. Sex is usually categorized as female or male, but there is variation in the biological attributes that comprise sex and how those attributes are expressed." "**Gender** specifies the socially assembled roles, behaviours, expressions and recognitions of girls, women, boys, men, and gender diverse people. It controls how people perceive themselves and each other, how they act and interact, and the distribution of power and resources in society. Gender is usually explicated as a binary (girl/woman and boy/man), yet there is considerable diversity in how individuals and groups understand, experience, and express it."*

Chapter 1

Introduction

Asthma is a chronic lung disease that restricts airflow into the lungs, resulting in wheezing, breathlessness, chest tightness, and cough (5). Asthma is not generally considered a single disease but rather comprised of *multiple, separate syndromes that overlap*, with atopic/non-atopic asthma among the most commonly recognized phenotype (6)**.** Correspondingly, asthma is believed to be caused by a complex interaction of genetic and environmental factors over the life course, and both unique and shared risk factors may be involved in the etiology of the various asthma phenotypes (7,8).

Asthma results in significant individual and societal costs: worldwide, 262 million individuals had asthma in 2019, 461,000 asthma-related deaths occurred, and 24.8 million disability-adjusted life years (DALYs) were attributable to asthma (9). In Canada, asthma is the third most common chronic disease, with over 3.8 million people diagnosed (10). An estimated $2.1 billion are direct and indirect related costs of asthma occur in Canada annually (11). Direct costs included hospitalization, healthcare professional services and medication, while indirect costs included decreased and loss of productivity (11). By 2030, the expected cost of asthma to the Canadian economy will climb to $4.2 billion annually (11).

Although asthma is most common in childhood (12,13), asthma from early life may persist into adulthood (14,15) and can also begin in later life with no prior history (15). In Canada, approximately 8.6% of adults have been diagnosed with asthma (16), with a higher prevalence and incidence among women than men (16,17). The importance of sex (biological) and gender (social and economic) concerning asthma-related prevalence, risk, treatment and prognosis is increasingly recognized in the scholarly literature (18).

The burden of adult asthma in Canada is more pronounced among Indigenous people (19) and similar to the general population, more so among Indigenous women than men (20). However, understanding of asthma among adult Indigenous people in Canada is quite limited as the majority of research has focused on children (21,22) and those living off-reserve (20,23,24). Sex and/or

gender are often not explored (25–28)[1]. Nor has there been adequate attention paid to asthma phenotype in Indigenous adults, an important gap, given that risk factors may vary by phenotype (25,29,30), thus having implications for more targeted prevention and treatment of asthma.

To address these limitations, the overall aim of the study was to determine the occurrence of asthma and its correlates in a sample of First Nations adults living on reserve in rural Saskatchewan, Canada, incorporating a sex/gender-based analysis and taking into account asthma phenotype. Two research questions guided the study:

1. What is the prevalence of atopic and non-atopic asthma in First Nations women and men?
2. What factors are associated with atopic and non-atopic asthma in First Nations women and men?

[1] The effects of sex and gender on human health are interwoven and difficult to disentangle; however, for brevity's sake, I will use the term sex throughout most of the thesis rather than "sex and/or gender", except when specifically referring to gender.

Chapter 2

Literature Review

2.1 Asthma defined

Asthma is an 'umbrella term' for a heterogeneous group of obstructive disorders of the lungs that cause wheezing, coughing, chest tightness and dyspnea (5). " Asthma is a chronic inflammatory disorder that affects the airways in the lungs, leading to a repetitive experience of wheezing, breathlessness, chest tightness and coughing with airway hyperresponsiveness, definitely at night or in the flush of the morning," by the Global Initiative for Asthma (31). Genetic and environmental factors trigger asthma, including exposure to allergens and irritants (fumes, gases), exercise, and viral respiratory infections such as cold (8). The Global Strategy for Asthma Management and Prevention identifies three defining features of asthma: chronic inflammation, bronchial hyperresponsiveness (BHR), and airway obstruction (31). However, the signs and symptoms of asthma may differ depending upon specific factors that trigger asthma attacks, the clinical presentation, and patterns of inflammatory responses (32).

Several asthma phenotypes have been identified; however, no established classification system for different asthma subtypes exists (33). Asthma can be classified according to the frequency of symptoms, forced expiratory volume in one second (FEV_1), peak expiratory flow rate (32), or based on atopic or non-atopic status (33). The Severe Asthma Research Program (SARP) identified five distinct clinical phenotypes of asthma that differ in lung function, age of asthma onset and duration, atopy, and sex (34). Wenzel reviewed the literature and identified three broad phenotype groupings of adult asthma based on: 1) clinical or physiological features (e.g., severity, treatment response, age of onset); 2) triggers (e.g., allergens, exercise); and 3) immunopathology (e.g., eosinophilic, neutrophilic) (6,35).

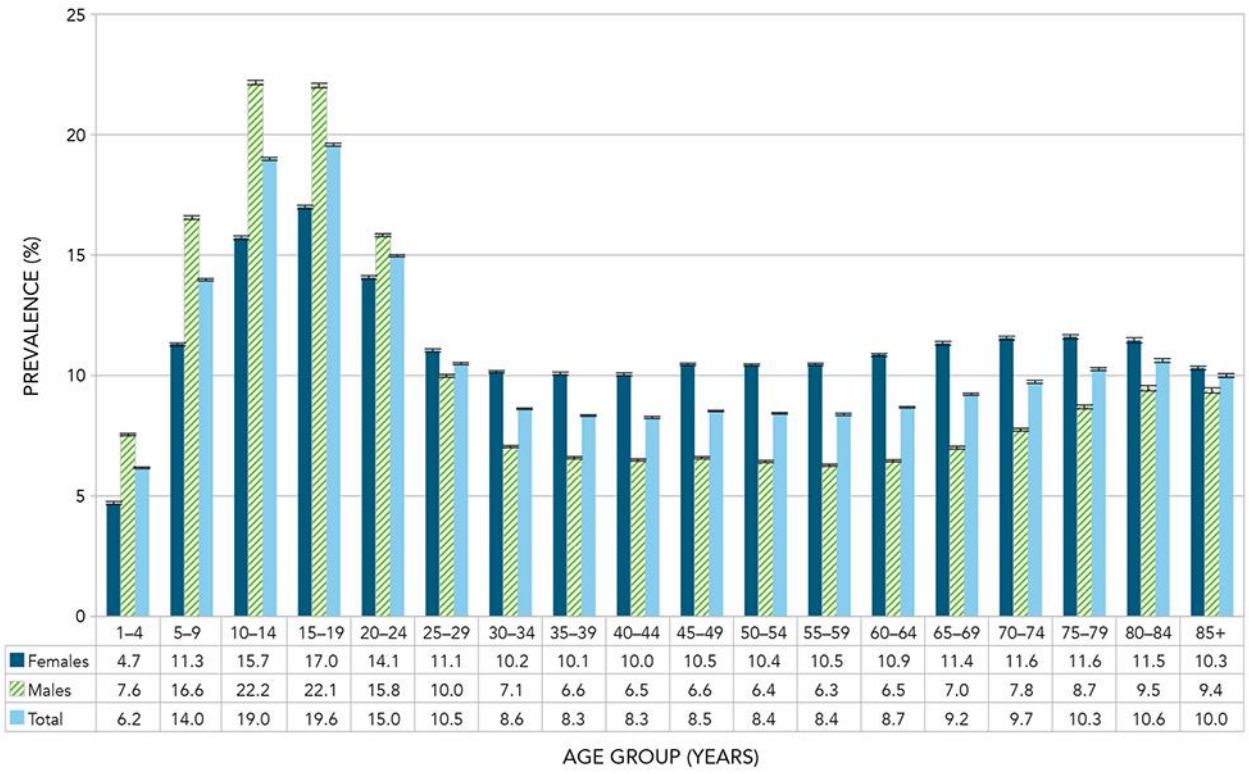
In research, the presence of asthma has been determined in numerous ways, including self-reported diagnosis (36,37), the presence of particular symptoms (38), spirometry (37–40), skin allergen testing (37,39), and health care utilization records (40), or some combination of these methods (37,38,40). Atopic status and/or respiratory symptoms are often used to assess asthma

phenotypes and population-based research. Atopic status is typically determined by the presence of serum immunoglobulin E (IgE) antibodies or a positive skin-prick test for various allergens (41,42). Research suggests that asthma begins during childhood and is more likely to be atopic in nature, whereas the non-atopic type predominates in asthma that originates during adulthood, specifically after age 40 (36). However, few studies in Canada have reported the prevalence and risk factors for atopic versus non-atopic asthma among adults (43,44).

2.2 Epidemiology of asthma

Asthma is a common and serious global health problem, affecting approximately 339 million children and adults worldwide (35). Almost 623 million people live with asthma-related symptoms (45). Although some countries have seen a decline in asthma-related hospitalizations and deaths (46), the global burden of asthma increased by almost 38% in the past 20 years (47), with a similar increase in asthma-like symptoms and allergic rhinitis (48). Even though asthma is increasing in less developed nations, asthma prevalence is currently higher in developed countries, such as Canada (49). At present, approximately 3.8 million Canadians live with asthma (10), and for this reason, asthma is considered among the top three chronic diseases in Canada (50). The prevalence of age-standardized asthma has risen in Canada over time, with approximately 11% of Canadians being diagnosed in 2011-2012, compared to 6.5% in 2000-2001; the steepest increase was observed among those between 10 and 29 years of age (10). In contrast, asthma incidence decreased over the same time period, the latter declining from 904.5 per 100,000 in 2000-01 to 499.0 per 100,000 in 2011-12 (10).

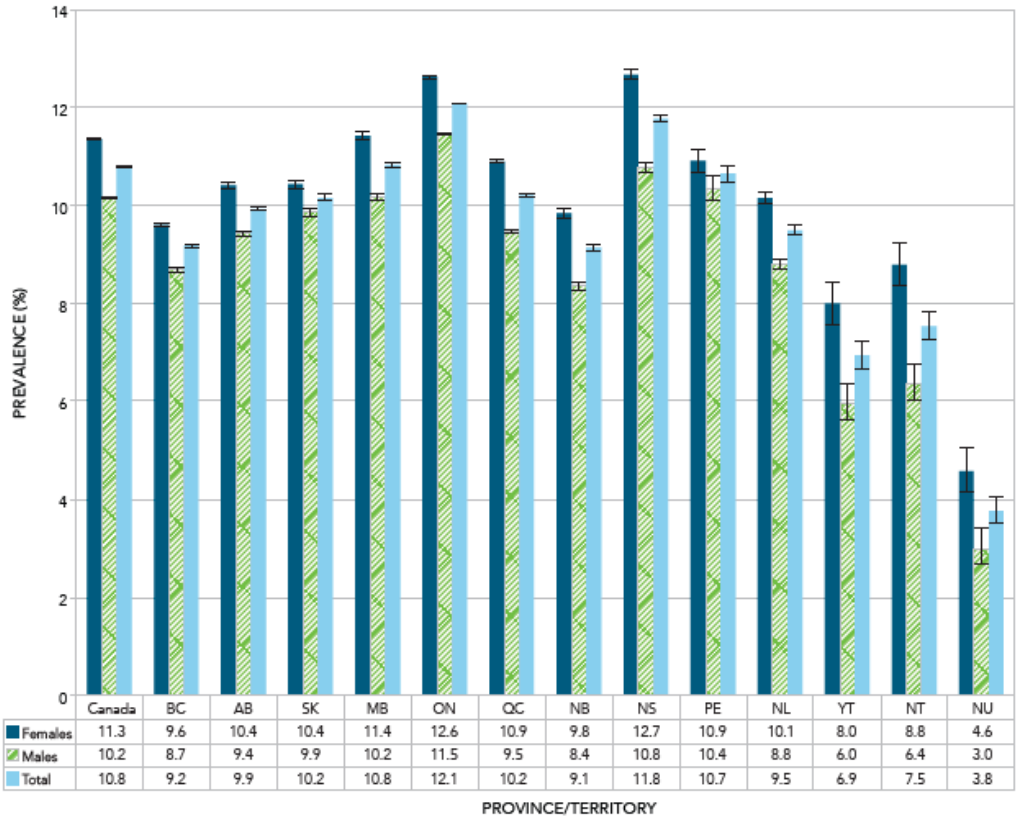
Asthma incidence generally follows an age pattern similar to prevalence but with the highest rates reported at an earlier age (10). As shown in Figure 2.1, the highest prevalence of diagnosed asthma is in 10- to 19-year-old Canadians; after that age, asthma prevalence decreases until age 30-34 years, when a more stable pattern emerges, followed by an increase in prevalence starting in the 60s age range. Males have a higher prevalence and incidence of asthma up until the age of 25-29 years and 15-19 years, respectively, during and after which females dominate (Fig 2.1). New-onset asthma in adulthood is more prevalent among women than men, particularly non-atopic asthma (51–53).



	1–4	5–9	10–14	15–19	20–24	25–29	30–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75–79	80–84	85+
Females	4.7	11.3	15.7	17.0	14.1	11.1	10.2	10.1	10.0	10.5	10.4	10.5	10.9	11.4	11.6	11.6	11.5	10.3
Males	7.6	16.6	22.2	22.1	15.8	10.0	7.1	6.6	6.5	6.6	6.4	6.3	6.5	7.0	7.8	8.7	9.5	9.4
Total	6.2	14.0	19.0	19.6	15.0	10.5	8.6	8.3	8.3	8.5	8.4	8.4	8.7	9.2	9.7	10.3	10.6	10.0

Figure 2.1 Prevalence of diagnosed asthma among Canadians aged one year and older, by age group and sex (2011-2012) (10)

There is a geographical variation in the prevalence of asthma within Canada, with the highest in Ontario and Nova Scotia and the lowest among those in the Yukon, NWT and Nunavut (Figure 2.2) (10). The age-standardized prevalence of asthma in Saskatchewan (10.2%) is slightly lower than the Canadian average (10.8%).



	Canada	BC	AB	SK	MB	ON	QC	NB	NS	PE	NL	YT	NT	NU
Females	11.3	9.6	10.4	10.4	11.4	12.6	10.9	9.8	12.7	10.9	10.1	8.0	8.8	4.6
Males	10.2	8.7	9.4	9.9	10.2	11.5	9.5	8.4	10.8	10.4	8.8	6.0	6.4	3.0
Total	10.8	9.2	9.9	10.2	10.8	12.1	10.2	9.1	11.8	10.7	9.5	6.9	7.5	3.8

Figure 2.2 Age-standardized prevalence of diagnosed asthma among Canadians aged one year and older, by province/territory and sex (2011-2012) (10)

Asthma prevalence is also patterned by ethnicity. Considerable evidence suggests that Indigenous people have a higher prevalence of asthma when compared with their respective country's settler population. In a systematic review and meta-analysis of studies (1994-2010) from four different countries (i.e., Canada, USA, Australia, and New Zealand), Indigenous adults had, on average, a 40% increased prevalence of asthma compared with their non-Indigenous counterparts, and this disparity was most pronounced in Canada (23). More recent research suggests similar findings. Based on administrative data, Metis people (20+ years of age) in Ontario were found to have a higher prevalence of doctor-diagnosed asthma (15.6%) when compared with other residents (11.8%) (54). Indicators other than prevalence also suggest a greater burden of asthma for Indigenous people; higher rates of asthma-related hospitalizations among First Nation people in Canada have been reported (55), and for First Nation people living in Alberta, higher rates of asthma and COPD-related emergency department and physician visits (56).

2.3 Risk factors for asthma

The risk factors for asthma have been extensively researched and point to a complex interaction of biological, personal, and environmental factors over the life course (57). In addition to incorporating some of the main findings from this body of work, the literature review which follows is informed by the Commission on Social Determinants of Health (CSDH) framework (57) on health inequities (Appendix A). According to this perspective, inequities in health, including those patterned by ethnicity and sex, can be viewed as arising due to the influence of various distal structural determinants, which in turn shape exposure and/or vulnerability to a variety of intermediary material, psychosocial, behavioural, and biological factors. The first part of the review will describe risk factors for asthma more generally, followed by a focus on what is known about the correlates of asthma in Indigenous adults.

2.3.1 Sex/gender

Sex and/or gender are hypothesized to have profound effects on asthma over the life course (18). Age-related variation in sex-specific asthma incidence and prevalence rates described previously suggest that sex hormones may play an important role in asthma development (58,59). Epidemiological studies consistently show sex differences in the occurrence of many lung diseases, including asthma, before and after puberty and menopause when sex hormones dramatically change (60–62). Boys experience greater asthma prevalence and related hospitalizations during childhood than girls (63). However, a decline in asthma prevalence for males occurs during adolescence but increases for females (64,65). By early adulthood, asthma is more prevalent among women than men (11), and women are three times more likely to be hospitalized for asthma-related events (66,67). This increasing trend in asthma prevalence in women is maintained until menopause, when there is a decrease in asthma prevalence (68). Other evidence of the potential role of sex hormones in asthma includes the variation in asthma symptoms associated with menstruation (60), use of hormone replacement therapy (60,61), and hormonal contraceptives (60). In addition to hormones, male/female differences in airway size, genetics, and immunology have been suggested as potential pathways to sex differences in asthma (67,69).

Gender may also play a role in asthma. Some research has focused on how gender may create artifactual sex differences in asthma prevalence by influencing symptom perception (70) and reporting (70), help-seeking behaviour (71), and/or the diagnostic behaviour of health professionals (71), but no definitive findings have emerged. Other research has considered how gender may differentially shape women's and men's exposure to various risk factors. For example, women are more likely than men to use chemical products on their hair and are also more likely to have hair product-related allergies (72). Conversely, men are more likely to be exposed to wood dust than women and have a higher prevalence of wood dust allergy (72,73). However, results such as these appear to be in the minority, as research to date has generally not shown clear and/or direct pathways between exposure to gendered behavioural and/or environmental risk factors and asthma development. More often, research points to more complex relationships, with sex-linked biological factors and/or gender possibly interacting with each other and/or with other exposures to influence asthma risks, such as obesity (74), smoking (75,76), damp housing (77) and inorganic and organic dust (73). The potential role of sex/gender as an effect modifier in the relationship between various risk factors and asthma will be described further below.

2.3.2 Personal factors

A variety of personal factors are associated with asthma. Familial aggregation of asthma and atopic disease has frequently been noted (78), with asthma in one or more first-degree relatives consistently identified as a risk factor for asthma (79). Research has identified numerous candidate genes and chromosomal regions potentially contributing to asthma risk (80). A positive history of asthma on the maternal side of the family has been associated with a two-fold increased risk of new-onset asthma in adulthood (30). Children with two asthmatic parents are over five times more likely to develop late-onset asthma compared to those without such a family history (81). In one study, family history had the strongest association with lifetime asthma prevalence, even after adjustments for other risk factors (82). A family history of allergy and asthma has also been reported to increase the risk of occupational asthma (83).

Research suggests that both active (84,85) and passive forms of cigarette smoking (86,87) are risk factors for adult-onset asthma. The incidence of asthma and frequency of asthma-related emergency room visits could be reduced by eliminating environmental tobacco exposure (88,89). A recent study showed that current smokers with asthma had poorer asthma control and greater acute care needs than lifelong non-smokers or former smokers with asthma (90). While the prevalence of smoking is higher among men than women, the risk of respiratory morbidity due to smoking may be more pronounced in women than men, possibly due to sex differences in airway size (91). Obesity is also considered a major risk factor for developing asthma in adulthood (92,93), with asthma incidence increasing by approximately 50% in overweight and obese individuals compared to those of "normal" weight (94). Abdominal obesity, assessed by waist circumference, may be more strongly associated with the incidence of adult-onset asthma in women than men (95). Regular physical activity has been linked with a lower prevalence and incidence of asthma (96). In a recent meta-analysis examining the association between physical activity and asthma in children, adolescents and adults, those with higher physical activity levels reported a lower incidence of asthma (97). Literature indicates adult asthma is commonly associated with asthma co-morbidity (98), and two-thirds of adult asthma patients have at least one co-morbid condition, whereas 16% of asthma patients have four co-morbidities (99).

2.3.3 Environmental factors

2.3.3.1 Home

There is increasing concern about the health effects associated with indoor dampness and mold, especially concerning asthma (100–102). The results of a meta-analysis of high-quality studies examining the association between damp/mold exposures and new-onset adult asthma strongly supported an association (100). A recent review of 11 cohort studies and five incident case-control studies of respiratory health and indoor dampness/mold concluded that such agents are likely causally associated with asthma, particularly when mold is visible and an odour is present (103). In the United States, it is estimated that approximately 21% of prevalent asthma cases can be attributed to home dampness and mold, equally among nearly 5 million individuals (101). A follow-up study of 16,190 participants from the European Community Respiratory Health Survey

found that living in damp housing was linked with a higher prevalence of respiratory symptoms and asthma but not with asthma risk in longitudinal analyses (104). In Canada, several studies have reported an association between home dampness/mold and an increase in various respiratory symptoms (25,105,106), and in one of those studies (106), women but not men reported elevated wheezing symptoms and respiratory allergies.

In addition to mold/dampness, other agents within domestic environments may be associated with asthma. Long-term exposure to wood heating, gas cooking and heating, and tobacco smoke over ten years were found to significantly contribute to asthma symptoms and accelerated lung function decline in adults (107). Exposure to secondhand smoke has been linked with incident asthma and the exacerbation of pre-existing adult asthma (108). Domestic cooking with biomass fuel and liquefied petroleum gas (LPG) has been found to affect pulmonary function in asthmatics (109). While there is some evidence pointing to an association between pets and increased asthma (110), the majority of research is on children. For example, a recent meta-analysis of case-control and cohort studies on the subject found only four studies that examined adult asthma (110), and of those, only one reported a significant association between pets and asthma, with exposure to any furry pet increasing the risk of asthma by 70% (110). A Canadian longitudinal study found an increased risk of asthma for female smokers who also had pets in their household, showing a 150% increased risk compared to female smokers without pets (75); however, no association between smoking, pets and asthma emerged for men.

2.3.3.2 Work

It has been estimated that between 15% and 55% of all adult asthma is work-related (111–113). The Michigan surveillance program describes trends over 31 years of work-related asthma surveillance and identified 3,634 cases from 1988 to 2018, including nine deaths (114). More than 300 workplace substances have been identified as causally related to incident asthma, including exposure to cleaning agents (115), fragrances (116), isocyanates (117), metalworking fluids (118), and welding fume (119). Also connected to elevated asthma rates are exposures encountered at swimming facilities (120), schools (121), healthcare facilities (122), and wood-processing industries (123).

Research examining sex differences in work-related asthma has produced variable results; while some research suggests higher rates of occupational asthma among women than men (72), other studies suggest no overall differences (124). Some specific occupational allergies appear more prevalent among men than women, such as those related to commercial baking (72,125) and woodworking (72,126). Although women are more likely to be exposed to cleaning products in their work environment, the prevalence of asthma-related to such exposures appears to be similar in women and men (115,127). Researchers face many methodological challenges in their quest to accurately compare women's and men's work exposures (128–130), making it difficult to confidently attribute any sex differences observed to nature, nurture, or some combination of the two.

Studies examining the relationship between farming and adult asthma have yielded variable results, with Canadian, Netherlands, Denmark and Norwegian (131–134) studies reporting farm living to be protective, while no such associations were found in other European studies (135). Some research suggests that childhood exposures may modify the impact of adult exposures, in that those who live on a farm as a child and as an adult may have a reduced risk of adult atopy (135). Although few studies have considered asthma phenotype, some research suggests that farm exposures might increase the risk of non-atopic asthma while being protective for atopic asthma (43,136,137) . While some studies show farmers are less likely to report asthma symptoms than the general population (45,138,144), pig farmers report a higher prevalence of respiratory symptoms than poultry, cattle, and sheep farmers (137). A study in Saskatchewan, Canada, examined female and male commercial swine workers and non-farming controls (138). Atopic female swine workers showed a significantly greater prevalence of asthma than non-atopic female swine workers, a difference that was not seen in male swine workers or control groups of either sex (138). A meta-analysis on gender differences in respiratory health among workers exposed to organic and inorganic dust in Canada found women had a higher risk of shortness of breath and asthma than men when exposed to inorganic dust (139). In contrast, organic dust exposure was associated with relatively worse lung function in men than in women (139).

2.3.4 Social and economic

Considerable evidence suggests an association between socioeconomic status (SES) and health (140,141), including asthma (142,143). Common indicators of SES, such as income and education, are believed to impact the health of individuals and communities indirectly by influencing their exposure and/or susceptibility to harmful behavioural, environmental, and/or social risk factors (140,144–146). A study of Canadians 12 years and older reported a dose-response relationship between income adequacy and prevalent asthma, with those of lower income reporting more asthma than those of higher income (147). A nationally representative survey in the United States showed a similar association between SES and asthma, with lower income and/or educated participants approximately 25% more likely to report current physician-diagnosed asthma than their higher SES counterparts (146). Basagaña and colleagues (148) reported living in a community with a large percentage of people with low education was associated with increased asthma risk, irrespective of individual-level SES.

In addition to asthma prevalence, research also points to a relationship between lower SES and poorer outcomes among those with asthma. For example, several US studies found that demographic characteristics, such as poverty, low educational attainment, female sex, and African–American heritage, were associated with a greater asthma hospitalization risk (85,143,149,150). In Nordic countries, lower education was a risk factor for uncontrolled asthma in subjects with adult-onset asthma (145).

Recent research has also examined the potential role of social stressors in the development of asthma (142). Often focused on children, stressors associated with an increased odds of asthma include neglect/abuse within the home (151,152) and community violence (151). Chronic stress emanating from experiences of racism may increase the incidence of adult-onset asthma. For example, a cohort study in the United States reported a positive association between racism and incident asthma in a sample of Black women (153). Research with visible minority youth also suggests a link between racist encounters and asthma morbidity (154).

2.4 Asthma in Indigenous people

Indigenous people in Canada, comprised of First Nations, Inuit and Metis groups, make out approximately 4.9% of the population, translating to about 1.67 million people (3). First Nations people form the largest group, representing about 61% of all Indigenous people in Canada. There are 175,015 Indigenous people in Saskatchewan, making up 16.3% of the population, with nearly two-thirds of First Nations origin (3). Nearly one-half of First Nations people in Saskatchewan reside on reserves (3). A large body of research has documented the greater burden of ill health among Indigenous compared to non-Indigenous people in Canada elsewhere (56,155,156), including asthma (23). In the sections which follow, exposures encountered by Indigenous people that may contribute to an increased rate of asthma will be detailed. However, it is important to acknowledge the more distal determinants of Indigenous health not directly measured in this study, such as the legacy of the residential school system, intended to eradicate Indigenous children's language, cultural traditions, and spiritual beliefs and assimilate them into Canadian society (157–160). The continued impact of colonial policies on Indigenous people's physical, economic, social and spiritual well-being has been extensively detailed (161).

2.4.1 Asthma risk factors

Research suggests that exposure to many of the personal, environmental and social/economic risk factors for asthma reviewed in previous sections may occur at higher rates among Indigenous than non-Indigenous people. Denied control over the resources necessary to maximize SES due to colonization, systemic racism and discrimination (161) have resulted in Indigenous people, on average, having lower education attainment, annual incomes, and employment opportunities compared to non-Indigenous populations (162). Indigenous women are, on average, among the most socially and economically vulnerable people in Canada (163). Of the 370 million Indigenous people globally, one-third experienced racism at least once in their lifetime (161). In a recent Saskatchewan study of residents of two First Nations communities, more than two-thirds reported exposure to interpersonal discrimination, with higher levels associated with increased odds of depression (164).

Nearly 30% of housing on Canadian First Nation reserves (165) requires significant repair(s) as poorly constructed or maintained housing can lead to loss of the vapour barrier, allowing areas of dampness that are prone to contamination with mold (166,167). Other indoor exposures may result from secondhand smoke, smoke ceremonies, and cooking practices (168). First Nations homes have demonstrated high values of self-reported (169) and measured (170,171) inhaled air pollutants. Sixty percent of First Nation reserves in Canada intersect or are located within the wildland-urban interface (172) and are over-represented in wildfire evacuations in Canada each year (173). Forest fires produce a high level of fine particulate matter and can cause severe asthma exacerbations, worsen asthma symptoms and reduce lung function (174).

Regarding personal factors, while smoking prevalence has decreased significantly in Canada over the last several decades (12), the rate of cigarette smoking has not substantially declined among First Nations people (175). Current estimates suggest the prevalence of smoking among Indigenous people of about double that of the general population of Canada (176). Regarding alcohol use, among aged 12 years and older, 35% First Nations population are alcohol users compared to only 23% of the general population (177). Compared to those non-Indigenous, Indigenous people have higher rates of overweight/obesity and are less likely to be physically active (178).

A literature search[2] was conducted to identify studies examining the prevalence of and correlates of asthma among adult Indigenous people, with key findings presented in Table 2.1. Eleven studies were identified that examined the prevalence of adult asthma (26,30–34,191–195). Racial and ethnic differences in adult asthma prevalence, problems, and medical care, although several also included some children (age 15+yrs), and one considered only adolescents (age 12-19 yrs.) (179). The United States (27,28,180–182) and Canada (20,24,25,179,183) were the countries of origin for ten studies, the remaining one originating in Australia (26). The vast majority of studies were cross-sectional and assessed the presence of asthma (mostly ever asthma) on the basis of a self-reported doctor diagnosis. Only one study examined atopic asthma (25). Seven of the studies

[2] The scholarly literature was searched from 2000 to 2022 to using PubMed, Medline, Web of Science, Google Scholar, iportal (indigenous Study Portal). Search terms of keywords including "asthma" "respiratory conditions" "lung diseases", "prevalence", "risk factors" "predictors" "exposures", "Indigenous" "Aboriginal" "First Nations" "American Indians" "Alaskan Natives" "Māori", "Adult" "adolescent" in exploring the literature. The search was limited to English language, adult humans.

provided sex-specific estimates of asthma prevalence (20,24,179–183), and except for the study of adolescents (179), all reported asthma to be more prevalent among women than men, which is consistent with the findings from the general population adult samples. In addition, one study found no sex difference in asthma among Inuit participants but did so among participants of First Nation, Metis and multiple ancestries (20).

Seven studies examined the correlates of asthma (Table 2.1). Female sex and urban residence emerged as most consistently associated with an increased prevalence of asthma in multivariable analysis (20,24). Obesity was linked to greater asthma prevalence in three studies (20,181,182) and a lower prevalence in one study of Canadian adolescents (179). Indicators of SES were inconsistently associated with asthma prevalence, with some showing a positive association (20,24,179,181) and others with no association (26). In comparison, increased asthma was associated with exposure to 2nd hand smoke in one study (179) and dampness and indoor mold in two other studies (25,181). Orell (181) failed to find any relationship between asthma and smoking, exposure to 2nd hand smoke, work exposures, pets in the home or using wood for fuel in the home.

Only one study examined whether the correlates of asthma varied by sex: Orell (181) reported older age and obesity to be related to a higher prevalence of asthma in both women and men; sex-specific factors for men included unemployment and lower income, and for women, being divorced/separated, living in Alaska's southcentral region, self-reported fair/poor health status, and exposure to indoor mold.

Table 2.1: List of reviewed articles examining asthma prevalence and correlates in Indigenous adults.

Author(s), country, data source	Participant characteristics	Study design	Asthma assessment	Asthma prevalence	Factors associated with an increased prevalence of asthma in Indigenous participants	Comments
Karunanayake et al. (179) Canada 2012 Aboriginal Peoples Survey	First Nations, Metis, or Inuit 12-19 years of age Living off-reserve; urban and rural	Cross-sectional	Self-reported, current asthma diagnosed by a health professional	Unadjusted: Overall=16% Female=15.3% Male=16.8%	Male sex, older age, urban dwelling, living in a Canadian province (compared to Yukon, Nunavut, or NWT), lower guardian education, lower income, smoking allowed in the home, and a history of bronchitis. Being overweight was associated with an increased prevalence of asthma; obesity was associated with a decreased prevalence.	The sample included children and adults. The multivariable analysis did not stratify by sex; however, the authors reported that there were no statistically significant interactions.
Rennie et al. (25) Canada FNLHP (First Nations Lung Health Project)	First Nations 18 to 64 years old Living on-reserve (2 communities)	Cross-sectional	Self-reported, ever asthma is diagnosed by a health professional. Atopic asthma is defined by	Unadjusted: Asthma= 14.9% Atopy= 21.1% The most prevalent SPT responses were to cats (11.1%) and	Adults with atopic asthma were more likely to live in houses with home dampness (adjusted odds ratio: 3.4, 95% CI: 1.41–8.17)	Sex-specific prevalence not reported.

Author(s), country, data source	Participant characteristics	Study design	Asthma assessment	Asthma prevalence	Factors associated with an increased prevalence of asthma in Indigenous participants	Comments
baseline data from 2012			environmental questionnaire followed by clinical assessment of atopy	Cladosporium (7.9%). Of those with asthma, 28.0% were atopic		
Chang et al. (20) Canada 2006 Aboriginal Peoples Survey	NAI (North American Indians), Metis, Inuit, multiple ancestries 15-64 years of age Living off-reserve; urban and rural	Cross-sectional	Self-reported, ever asthma diagnosed by a health professional	Unadjusted: Female: 16.2% Male: 11.2%	Age between 15-34, female sex, urban residence, obesity, lower education, lower family income, difficulties in access to health care.	Female sex was a risk factor for asthma in NAIs, Métis and multiple ancestry groups but not in the Inuit ancestry.
Orell et al. (181) USA Education and Research Towards Health (EARTH) study	American Indian and Alaska Native 18 years and older Alaska (Southcentral, southeastern, southwestern)	Cross-sectional	Self-reported, ever asthma diagnosed by a health professional.	Age-sex adjusted prevalence= 15.4% Female: 12.5% (95% CI: 11.8-13.2)	Male: Older age, unemployment, lower income, obesity. Female: Older age, being divorced/separated, living in Alaska's southcentral region, self-reported fair/poor health	Asthma was not associated with smoking, exposure to 2nd hand smoke, work exposures, pets in the home, or

Author(s), country, data source	Participant characteristics	Study design	Asthma assessment	Asthma prevalence	Factors associated with an increased prevalence of asthma in Indigenous participants	Comments
				Male: 9.5% (95% CI: 8.8-10.2)	status, obesity, and indoor mould.	using wood for fuel in the home.
Cunningham (26) Australia Two National Representative surveys by the 2004-05 Australian Bureau of Statistics (ABS) The National Aboriginal and Torres Strait Islander Health Survey (NATSIHS) and the National Health Survey (NHS).	Indigenous people 18 to 64 years old Major cities, regional (Inner and outer), remote or very remote	Cross-sectional	Self-reported, current asthma diagnosed by a health professional	Unadjusted Overall: 27.5% (95% CI 25.5-29.5) Asthma prevalence decreased with age until age 45 years: after age 45, it increased	Food insecurity was associated with a higher prevalence of asthma. Lower prevalence of asthma in those whose main language was NOT English (compared to those whose main language was English) and those living in remote areas (compared to more urban).	Sex-specific estimates were not provided. Prevalence of asthma was not associated with most traditional indicators of SES (education, employment, income, home ownership and area-level disadvantage).

Author(s), country, data source	Participant characteristics	Study design	Asthma assessment	Asthma prevalence	Factors associated with an increased prevalence of asthma in Indigenous participants	Comments
Crighton et al. (24) Canada 2001 Aboriginal Peoples Survey	First Nations, Metis, or Inuit, other/mixed 15 years and older Living on- and off-reserve; urban and rural	Cross-sectional	Self-reported, ever asthma diagnosed by a health professional	Unadjusted: Female: 13.6% Male: 8.5%	Female sex, older age, no high school diploma, recent health care visit, living off-reserve, urban residence, and living in other regions except northern territories.	Household income is not associated with asthma.
Janz et al. (183) Canada 2006 Aboriginal Peoples Survey	Metis 15 years and older Living off reserve; urban, rural	Cross-sectional	Self-reported, ever asthma diagnosed by a health professional	Female: 17% (15.8–18.2) Male: 11% (9.9–12);	Not reported	Prevalence is highest among 15–19-year-olds (20%) compared to older Metis participants (12%-13%).
Gorman and Chu (27) United States	Native Americans	Cross-sectional	Self-reported asthma diagnosed by a	Unadjusted: 13.1%	Not reported	Sex-specific prevalence not reported.

Author(s), country, data source	Participant characteristics	Study design	Asthma assessment	Asthma prevalence	Factors associated with an increased prevalence of asthma in Indigenous participants	Comments
2004 Behavioral Risk Factor Surveillance System (BRFSS)	18 years and older 24 states except Puerto Rico		health professional			
Loveland et al. (182) United States Behavioural Risk Factor Surveillance System (BRFSS) 2001-2006 data	American Indian 18 years and older Montana	Retrospective cohort	Self-reported asthma diagnosed by a health professional	Unadjusted: Female: 14.0% (11.2–17.5) Male:6.7% (4.9-9.2)	Higher (unadjusted) prevalence of asthma associated with: BMI≥30, having health insurance, and older age.	
Pleis and Barnes (28) United States National Health Interview Survey (NHIS) 2000-2003	American Indian/Alaska Native 18 years and older Metropolitan area, Region	Retrospective cohort	Self-reported asthma diagnosed by a health professional	Unadjusted: American Indian or Alaska Native (AIN): 11.7% White & AIN: 19.3%	Not reported.	Sex-specific prevalence not reported.

Author(s), country, data source	Participant characteristics	Study design	Asthma assessment	Asthma prevalence	Factors associated with an increased prevalence of asthma in Indigenous participants	Comments
Dixon et al. (180) USA The Strong Heart Study	American Indian Adults 50 years and older	Cross-sectional	Physician diagnosed Standardized respiratory questionnaire; spirometry; allergen skin testing	Unadjusted: Female: 8.2% Male: 3.2%	Not reported.	Among those with physician-diagnosed asthma: 97% reported trouble breathing, and 52% had severe persistent disease.

2.5 Summary

Asthma is a significant cause of morbidity and disability, with an enormous economic burden on society. In addition to sex, a broad array of factors have been linked with an increased risk of adult asthma. Regarding personal factors, these include a family history of asthma (82,184), obesity (92), and smoking (108,168). Environmental risk factors include housing conditions (e.g., dampness, 2nd hand exposure to smoke) (108,185), outdoor air pollution (186), and various workplace exposures (123). Socioeconomic variables have been related to asthma in the research literature, as have various social stressors, including those arising from racism and discrimination (153,154). Further, a number of studies have found that the relationship between these risk factors and asthma may be modified by sex (73,76,95).

Considerable evidence suggests that Indigenous people in Canada have a higher rate of asthma than non-Indigenous Canadians. However, few studies have been conducted with adults that investigate variation in asthma prevalence *among* Indigenous people, as opposed to differences *between* those Indigenous and non-Indigenous. While the research to date suggests that the sex patterning observed in the general population holds true for Indigenous people, very few studies have examined whether the correlates of adult asthma are modified by sex. In addition, limited research has assessed asthma phenotype. This study will contribute to the scholarly literature by applying sex-specific analyses to identify correlates of adult asthma in First Nations women and men in Saskatchewan, taking into account both atopic and non-atopic variants.

Chapter 3

Methods and Materials

3.1 Study design and participant recruitment

The data source for this study was the Saskatchewan First Nations Lung Health Project (FNLHP, 2012-2017) (187). The FNLHP was a collaboration between University of Saskatchewan researchers and two rural First Nations communities and was developed over two years of "Vision and Relationships" dialogue. Ten consultation sessions took place with community leaders, elders, health workers, and community members to formulate the project, including identifying priority health issues. A Decision Makers Council consisting of band councillors, elders and youth was formed to oversee the FNLHP. Letters of the agreement were received from the two communities, including a commitment to follow the Canadian Institutes for Health Research (CIHR) guidelines for conducting research in Indigenous communities (188). The Biomedical Research Ethics Board approved the study of the University of Saskatchewan (Certificate No. Bio #2942) (Appendix B), and informed consent from all participants was obtained. The complete methodology of this community-based participatory research initiative has been described by Pahwa and colleagues (169).

Baseline assessments were conducted in 2012-2013 through interviewer-based questionnaires and clinical measurements. The Population Health Framework (PHF) was taken into consideration in developing the baseline assessment questionnaires (169). Trained research assistants, who were local First Nations members residing in each community, went door-to-door to explain the project and then invited every adult (18 years and older) to visit the health centre to complete the interviewer-administered questionnaires and clinical assessments. Trained health professionals performed all clinical assessments, which included allergy skin prick testing. During the visit to the health centre, study participants were asked to identify their respective households on the map, and an identification number was assigned to each household using the community map. Data were collected from 406 households (874 individuals: 435 male and 439 female) at baseline, with response rates of 53.9% and 89.9% reported for Community A and Community B, respectively.

Data collection was repeated after four years in 2016 through modified interviewer-based questionnaires and clinical measurements. In this second phase, data were collected from 353 households (839 participants: 405 male and 434 female). Response rates for the follow-up phase were not available.

For this thesis, baseline (874) and follow-up (839) participants were combined into a single cross-sectional sample of 1713 participants. For the 395 individuals who provided data in both study phases, only data from their most recent study (follow-up) involvement were considered, further reducing the potential study population to 1,318 participants.[3] Out of 1,318 participants aged ≥18 years and who completed skin prick testing (SPT), 956 participants made the final study sample size.

3.2 Variables

Dependent variable

Asthma phenotype was a categorical variable with three response options (no asthma, atopic asthma, non-atopic asthma) and derived from a combination of self-reported asthma ("Did a doctor ever tell you that you had asthma?") and allergy testing. Allergy skin tests were performed using the skin prick method with a panel of six non-food allergens: Alternaria (mold), Cladosporium (mold), cat dander, local grasses, aspergillus (wheat dust), and house dust mite. Histamine (10 mg/mL) and saline solution (0.9%) served as the positive and negative control, respectively. Standardized allergen extracts were used as recommended by the Academy of Allergy, Asthma, and Immunology (189) and the allergy skin test procedure was performed according to the recommended protocol (189). Participants were considered positive for atopy if one or more skin prick tests resulted in a raised wheal equal to or greater than 3 mm compared to the saline control. Asthma phenotype was operationalized as follows: 1) no asthma (no self-reported asthma); 2) atopic asthma (self-reported asthma and a positive skin prick test); and 3) non-atopic asthma (self-reported asthma and a negative skin prick test).

[3] For the 395 individuals who provided data in both study phases, only data from their most recent study involvement were considered: 874 (baseline) + 839 (follow-up) = 1,713 - (395) = 1,318.

Independent variables

The exposures of interest can be broadly labelled as demographic, personal, socioeconomic, and environmental. Demographic factors included sex, which was considered a primary exposure of interest in this study, as well as age and marital status. Socioeconomic exposures included household income, educational attainment, employment status and financial strain. Personal factors included physical activity, BMI, alcohol use and smoking. Environmental exposures were those encountered in the home environment and consisted of whether the home required repairs, home dampness, mold, and the presence of pets. Other exposures included racial discrimination (190), depression and comorbidities, the latter being a derived variable assessing the presence of at least one chronic health condition. A more detailed description of each independent variable is presented in Table 3.1.

Table 3.1 Independent variables and their operationalization

	Variable name	**Original question and response options**	**Operationalized in this study**
Demographic	Sex	Self-reported	0. Male 1. Female
	Age	Self-reported	1. 18-39 years 2. 40 years and older
	Marital status	Marital status • Married • Common law/living together • Separated • Divorced • Single • Widowed	1. Single (separated, divorced, single, widowed) 2. Partnered (married, common law/living together)
Socioeconomic	Household income (annual)	Please think of your total household income before deductions from all sources last year. We are asking for the total amount of all the money you and the people	1. Less than $20,000 2. More or equal to $20,000 3. Refused/don't know

	Variable name	Original question and response options	Operationalized in this study
		in the household received in the last year. • No income • $1-4,999 • $5,000-9,999 • $10,000-14,999 • $15,000-19,999 • $20,000-24,999 • $25,000-29,999 • $30,000-39,999 • $40,000-49,999 • $50,000-over • Don't know • Refusal	
	Education	Highest level of education • Grade 8 or less • Less than high school • Completed high school • Some university • Completed university • Completed technical school • Some technical school	1. Less than high school 2. High school or greater
	Financial strain	In the past 12 months, did you ever struggle to meet basic living requirements? (i.e., food, housing, power, heating, water, clothing, etc.) • Yes • No	0. No 1. Yes
	Employment status	What is your current employment status? • Employed full time • Employed part-time • Self-employed • Employed seasonally • Disabled on Employment Insurance • Unemployed	1. Employed (Employed full/part-time, self-employed, employed seasonally, student full/part-time) 2. Unemployed (disabled on employment insurance,

	Variable name	Original question and response options	Operationalized in this study
		• Retired • Homemaker • Student part-time • Student full time	unemployed, retired, homemaker)
Personal	Physical activity • Exercise	Do you exercise? • Yes • No	0. No 1. Yes
	• Exercise duration	How long do you usually exercise? • Less than 15 minutes • 15 to 30 minutes • 31 to 60 minutes • More than 60 minutes • Do not know	1. <15 minutes (less than 15 minutes, do not know) 2. ≥15 minutes
	BMI (191)	Body mass index (BMI) = weight in kg/ height in m^2 (Underweight- <18.5 kg/m^2, Normal weight- 18.5 to 24.9 kg/m^2, Overweight-25 to 29.9 kg/m^2, Obese ≥30 kg/m^2)	1. Normal 2. Underweight 3. Overweight/obese
	Alcohol	During the past 12 months, how often did you drink alcoholic beverages? • Never • Less than once a month • Once a month • 2 to 3 times a month • Once a week • 2 to 3 times a week • 4 to 6 times a week • Every day	1. Never drinker 2. Ever drinker

	Variable name	Original question and response options	Operationalized in this study
	Smoking	Have you ever smoked cigarettes? • Current smoker • Ex-smoker • Never smoker	1. Non-smoker (never/ex-smoker) 2. Current smoker
Environmental	Housing in need of repairs	Is this house in need of repairs? • Yes, major repairs • Yes, minor repairs • No, only regular maintenance is required • Refused • Do not know	0. No, regular maintenance (no, only regular maintenance is required/refused/do not know) 1. Yes, repairs needed (yes, major /minor repairs)
	Home dampness	Water or dampness in your house in the past 12 months from broken pipes, leaks, septic tank, heavy rain, or floods? • Yes • No • Refused • Do not know	0. No (no/refused/do not know) 1. Yes
	Mold/mildew in the home	Are there signs of mold or mildew in any living area in your house? • Yes • No • Refused • Do not know	0. No (no/refused/do not know) 1. Yes
	Pet in home	Pet (cat, dog, bird, other) living in your house in the past 12 months? • Yes	0. No 1. Yes

	Variable name	Original question and response options	Operationalized in this study
		• No	
Other	Racial discrimination(190)	Have you ever experienced discrimination or racism, been prevented from doing something, or been hassled or made to feel inferior (badly) in any of the following situations because of your race, cultural group or color?" (at school, getting hired or getting a job, at work, getting housing, getting medical care, getting service in a store or restaurant, getting credit bank loans or mortgages, on the street or public setting, from the police or the courts) • Yes • No	0. No situation 1. 1–2 situations 2. 3 or more situations
	Depression	Has a doctor or primary caregiver ever said you have depression? • Yes • No • Do not know	0. No (no/ do not know) 1. Yes
	Comorbidity	Has a doctor or primary caregiver ever said you have a heart problem, stroke, sleep apnea, tuberculosis, cancer, COPD, chronic bronchitis, emphysema, or diabetes? • Yes • No	0. No 1. Yes

3.3 Statistical Analyses

The frequency distribution of all study variables was determined for the total sample and then by sex. The proportion of participants with asthma phenotypes was calculated overall and then stratified by sex and age; chi-square analyses were applied to identify the presence of sex and/or age differences. Cross-tabulations followed by chi-square tests were then performed between asthma and each independent variable, first for the total sample and then by sex. Fisher's exact test was conducted rather than chi-square if the expected frequencies were less than five.

Hosmer's and Lemeshow's approach to model-building (192) was then used to determine adjusted associations with asthma phenotype. A series of bivariable multinomial logistic regression analyses were conducted to determine the association of asthma with each potential risk factor. The STATA procedure, mlogit, was used to conduct multinominal logistic regression analysis. The STATA post-estimation command mlogtest was used to test the assumption of independence of irrelevant alternatives (IIA). The IIA states that the odds of being in one category compared to the base /reference (no asthma) category would not change if any other category was added. The presence of multicollinearity was assessed by examining pairwise correlation coefficients and variation inflation factors (VIF); a VIF $\geq$10 indicates the presence of potentially harmful collinearity (193). For the multivariable multinomial logistic regression analyses which followed, variables with a p-value <0.25 from the bivariable phase or of biological/theoretical importance were simultaneously entered into the model. Two-way interactions between sex and each independent variable were assessed with cross-product terms; statistically significant interactions were graphed as predicted probabilities. Clustering effects were taken into account with STATA cluster robust standard error estimation (vce (cluster HOUSEUNIQUE)). Variables with a p-value < 0.05 and those of biological/theoretical importance were retained in the final model. STATA version 15 was used for all statistical analyses.

Chapter 4

Results

4.1 Descriptive analyses

Table 4.1 illustrates the frequency distribution of study variables for the total sample and by sex. Similar numbers of women and men participated in the study, and over 64% of participants were in the 18-39 years age group. Just over 60% of respondents were single, and just over one-half were employed. Fifty-two percent of respondents completed less than high school, 38% reported an annual household income of less than $20,000 and 46% experienced financial strain. The majority of participants reported exercising (70%), ever alcohol use (81%), and current smoking (77%) and 52% were normal or underweight. Regarding housing characteristics, just over one-third of participants had a pet in the home, 73% believed their homes needed repairs, and 62% and 50% reported their homes had issues with dampness and mold/mildew, respectively. One-in-five respondents reported having been diagnosed with depression, and 47% had at least one other comorbidity. Finally, 67% of participants had experienced racial discrimination. A greater proportion of men than women indicated exercising, being employed, and having a high school education or more. Conversely, a higher percentage of women than men reported financial strain, being overweight/obese, and a depression diagnosis. No statistically significant sex differences were reported for age, marital status, income, needed housing repairs, home dampness, mold, pets, smoking status, alcohol use, comorbidity, and racial discrimination.

Table 4.1. Distribution of study variables for the total sample and by sex

	Total n=956 (%)	**Women n=465 (%)**	**Men n=491 (%)**	**p-value**
Age				
18-39 years	616 (64.4)	292 (62.8)	324(66.0)	0.30
40 years and older	340 (35.6)	173 (37.2)	167 (34.0)	
Marital status				
Single	573 (61.1)	266 (58.1)	307 (63.9)	0.07
Partnered	365 (38.9)	192 (41.9)	173 (36.1)	
Educational attainment				
High school or greater	458 (48.0)	182 (39.2)	276 (56.3)	**<0.001****
Less than high school	496 (52.0)	282 (60.8)	214 (43.7)	
Employment				
Employed	482 (51.0)	196 (42.5)	286 (59.1)	**<0.001****
Unemployed	463 (49.0)	265 (57.5)	198 (40.9)	
Household income (annual)				
$<20,000	343 (38.1)	167 (37.4)	176 (38.9)	0.56
$≥20,000	267 (29.7)	140 (31.3)	127 (28.0)	
Refused/don't know	290 (32.2)	140 (31.3)	150 (33.1)	
Financial strain				
No	508 (53.6)	229 (49.7)	279 (57.3)	**0.02***
Yes	440 (46.4)	232 (50.3)	208 (42.7)	
Exercise				
No	285 (29.9)	178 (38.4)	107 (21.9)	**<0.001****
Yes	668 (70.1)	286 (61.6)	382 (78.1)	
Exercise duration				
<15 minutes	369 (38.8)	222 (47.9)	147 (30.1)	**<0.001****
≥15 minutes	582 (61.2)	241 (52.1)	341 (69.9)	
Alcohol				
Never drinker	179 (18.8)	92 (19.8)	87 (17.8)	0.41
Ever drinker	775 (81.2)	372 (80.2)	403 (82.2)	
Smoking status				
Non -smoker	221 (23.1)	115 (24.8)	106 (21.6)	0.24
Current smoker	734 (76.9)	349 (75.2)	385 (78.4)	

	Total n=956 (%)	Women n=465 (%)	Men n=491 (%)	p-value
BMI				
Normal/ underweight	498 (52.2)	207 (44.7)	291 (59.3)	**<0.001****
Overweight/obese	456 (47.8)	256 (55.3)	200 (40.7)	
Housing in need of repairs				
No, regular maintenance	252 (27.5)	118 (26.0)	134 (29.0)	0.31
Yes, repairs need	664 (72.5)	336 (74.0)	328 (71.0)	
Home dampness past 12 months				
No	351 (38.3)	173 (38.1)	178 (38.4)	0.92
Yes	566 (61.7)	281 (61.9)	285 (61.6)	
Signs of mold or mildew in home				
No	455 (49.6)	222 (48.8)	233 (50.4)	0.62
Yes	462(50.4)	233 (51.2)	229 (49.6)	
Pet in home				
No	581 (63.5)	283 (62.5)	298 (64.5)	0.52
Yes	334 (36.5)	170 (37.5)	164 (35.5)	
Depression diagnosis	767 (80.6)	346 (74.7)	421 (86.1)	**<0.001****
No	185 (19.4)	117 (25.3)	68 (13.9)	
Yes				
Comorbidity				
No	507 (53.0)	245 (52.7)	262 (53.4)	0.84
Yes	449 (47.0)	220 (47.3)	229 (46.6)	
Racial discrimination				
No situation	313 (32.7)	146 (31.4)	167 (34.0)	0.62
1 or 2 situations	278 (29.1)	135 (29.0)	143 (29.1)	
3 or more situations	365 (38.2)	184 (39.6)	181 (36.9)	

Bold p-values indicate statistical significance *p < 0.05; **p<0.01

*** Due to missing values of variables, frequency may not add up to totals

Overall, 15.6% of respondents reported asthma, with non-atopic asthma (11.0%) more common than atopic asthma (4.6%). Table 4.2 shows that asthma phenotype prevalence did not differ by

sex or age. Table 4.3 shows sex-specific asthma prevalences stratified by age with no statistically significant differences observed.

Table 4.2. Prevalence of asthma phenotype by sex and age

	Sex			**Age**		
	Women n=465 (%)	**Men n=491 (%)**	**p-value**	**18-39 yrs. n=465 (%)**	**≥ 40 yrs. n=491 (%)**	**p-value**
No asthma	393 (84.5)	414 (84.3)	0.61	516 (83.8)	291 (85.6)	0.65
Atopic asthma	24 (5.2)	20 (4.1)		31 (5.0)	13 (3.8)	
Non-atopic asthma	48 (10.3)	57 (11.6)		69 (11.2)	36 (10.6)	

Table 4.3. Sex-specific asthma phenotype prevalence by age

	18-39 years of age			**40+ years of age**		
	Women n=292 (%)	**Men n=324 (%)**	**p-value**	**Women n=173 (%)**	**Men n=167 (%)**	**p-value**
No asthma	250 (85.6)	266 (82.1)	0.22	143 (82.7)	148 (88.7)	0.29
Atopic asthma	16 (5.5)	15 (4.6)		8 (4.6)	5 (3.0)	
Non-atopic asthma	26 (8.9)	43 (13.3)		22 (12.7)	14 (8.3)	

Associations between asthma phenotype and each independent variable are shown in Table 4.4 (total sample), Table 4.5 (women) and Table 4.6 (men). Regarding the total sample (Table 4.4), a greater proportion of those with atopic asthma than non-atopic or no asthma indicated the presence of home dampness and a depression diagnosis. Conversely, a higher percentage of those with non-atopic asthma compared to atopic asthma or no asthma reported ever alcohol use and comorbidity. When stratified by sex, women (Table 4.5) and men (Table 4.6) with atopic or non-atopic asthma were significantly more likely to report home dampness and depression compared to those without asthma.

Table 4.4. Distribution of study variables by asthma phenotypes for total sample

	No asthma n = 807 (%)	**Atopic asthma n = 44 (%)**	**Non-atopic asthma n = 105 (%)**	**p-value**
Age				
18-39 years	516 (63.9)	31 (70.4)	69 (65.7)	0.65
40 years and older	291 (36.1)	13 (29.6)	36 (34.3)	
Sex				
Women	393 (48.7)	24 (54.5)	48 (45.7)	0.61
Men	414 (51.3)	20 (45.5)	57 (54.3)	
Marital status				
Single	485 (61.2)	28 (66.7)	60 (58.3)	0.64
Partnered	308 (38.8)	14 (33.3)	43 (41.8)	
Educational attainment				
High school or greater	385 (47.8)	17 (38.6)	56 (53.3)	0.25
Less than high school	420 (52.2)	27 (61.4)	49 (47.7)	
Employment				
Employed	398 (49.9)	26 (61.9)	58 (55.2)	0.21
Unemployed	400 (50.1)	16 (38.1)	47 (44.8)	
Household income				
$<20,000	284 (37.4)	18 (42.7))	41 (41.8)	0.85
$≥20,000	227 (29.9)	11 (26.2)	29 (29.6)	
Refused/don't know	249 (32.8)	13 (31.1)	28 (28.6)	
Financial strain				
No	434 (54.3)	20 (46.5)	54 (51.4)	0.55
Yes	366 (45.8)	23 (53.5)	51 (48.6)	
Exercise				
No	236 (29.3)	13 (30.2)	36 (34.3)	0.58
Yes	569 (70.7)	30 (69.8)	69 (65.7)	
Exercise duration				
<15 minutes	314 (39.1)	15 (35.7)	40 (38.1)	0.90
≥15 minutes	390 (60.9)	27 (64.3)	65 (61.9)	

	No asthma n = 807 (%)	Atopic asthma n = 44 (%)	Non-atopic asthma n = 105 (%)	p-value
Alcohol				
Never drinker	162 (20.1)	7 (15.9)	10 (9.5)	**0.03***
Ever drinker	643 (79.9)	37 (84.1)	95 (90.5)	
Smoking status				
Non -smoker	181 (22.4)	12 (27.9)	28 (26.7)	0.47
Current smoker	626 (77.6)	31 (72.1)	77 (73.3)	
BMI				
Normal/Underweight	431 (53.5)	16 (36.4)	51 (49.0)	0.07
Overweight/Obese	375 (46.5)	28 (63.4)	53 (51.0)	
Housing in need of repairs				
No, regular maintenance				
Yes, repairs need	219 (28.4)	6 (14.6)	27 (26.2)	0.15
	553 (71.6)	35 (85.4)	76 (73.9)	
Home dampness past 12 months				
No				
Yes	315 (40.8)	9 (21.9)	27 (26.2)	**0.002****
	458 (59.2)	32 (78.1)	76 (73.8)	
Signs of mold or mildew in home				
No	393 (50.8)	16 (29.0)	46 (44.7)	0.19
Yes	380 (49.2)	25 (61.0)	57 (55.3)	
Pet in home				
No	494 (63.7)	25 (61.0)	62 (62.6)	0.921
Yes	281 (36.3)	16 (39.0)	37 (37.4)	
Depression diagnosis				
No	663 (82.5)	27 (62.8)	77 (73.33)	**0.001****
Yes	141 (17.5)	16 (37.2)	28 (26.7)	
Comorbidity				
No	443 (54.9)	22 (50.0)	42 (40.0)	**0.02***
Yes	364 (45.1)	22 (50.0)	63 (60.0)	
Racial discrimination				
No situation	270 (33.5)	12 (27.3)	31 (29.5)	0.65
1 or 2 situations	235 (29.1)	15 (34.1)	28 (26.7)	
3 or more situations	302 (37.4)	17 (38.6)	46 (43.8)	

Bold p-values indicate statistical significance *p < 0.05; **p<0.01

*** Due to missing values, frequencies may not add up to totals.

Table 4.5. Distribution of study variables by asthma phenotype for women

	No asthma n = 393 n (%)	**Atopic asthma n = 24 n (%)**	**Non-atopic asthma n = 48 n (%)**	**p-value**
Age				
18-39 years	250 (63.6)	16 (66.7)	26 (54.2)	0.41
40 years and older	143 (36.4)	8 (33.3)	22 (45.8)	
Marital status				
Single	226 (58.4)	13 (56.5)	27 (56.3)	0.95
Partnered	161 (41.6)	10 (43.5)	21 (43.7)	
Education				
Less than high school	154 (39.3)	7 (29.2)	21(43.7)	0.49
High school or greater	238 (60.7)	17 (70.8)	27 (56.3)	
Household income (annual)				
$<20,000	138 (36.5)	9 (39.2)	20 (43.5)	0.90
$≥20,000	119 (31.5)	7 (30.4)	14 (30.4)	
Refused/don't know	121 (32.0)	7 (30.4)	12 (26.1)	
Employment status				
Employed	165 (42.2)	11 (50.0)	20 (41.7)	0.77
Unemployed	226 (57.8)	11 (50.0)	28 (58.3)	
Financial strain				
No	201 (51.5)	10 (43.5)	18 (37.5)	0.15
Yes	189 (48.5)	13 (56.5)	30 (62.5)	
Housing in need of repairs				
No, regular maintenance	104 (27.1)	3 (13.6)	11 (22.9)	0.36[±]
Yes, repairs need	280 (72.9)	19 (86.4)	37 (77.1)	
Home dampness past 12 months				
No	156 (40.6)	6 (27.3)	11 (22.9)	**0.03***
Yes	228 (59.4)	16 (72.7)	37 (77.1)	
Signs of mold or mildew in home				
No	192 (49.9)	9 (40.9)	21 (43.7)	0.55
Yes	193 (50.1)	13 (59.1)	27 (56.3)	
Pet in home				
No	243 (63.1)	14 (63.6)	26 (56.5)	0.68
Yes	142 (36.9)	8 (36.4)	20 (43.5)	

	No asthma n = 393 n (%)	**Atopic asthma n = 24 n (%)**	**Non-atopic asthma n = 48 n (%)**	**p-value**
Smoking status				
Non -smoker	96 (24.4)	6 (26.1)	13 (27.1)	0.91
Current smoker	297 (75.6)	17 (73.9)	35 (72.9)	
Alcohol				
Never drinker	85 (21.7)	3 (12.5)	4 (8.3)	0.06±
Ever drinker	307 (78.3)	21 (87.5)	44 (91.7)	
BMI				
Normal/Underweight	181 (46.1)	6 (25.0)	20 (42.5)	0.12
Overweight/obese	211 (53.8)	18 (75.0)	27 (57.5)	
Exercise				
No	148 (37.7)	8 (34.8)	22 (45.8)	0.51
Yes	245 (62.3)	15 (65.2)	26 (54.2)	
Exercise duration				
<15 minutes	188 (48.0)	10 (43.5)	24 (50.0)	0.88
≥15 minutes	204 (52.0)	13 (56.5)	24 (50.0)	
Depression diagnosis				
No	301 (76.8)	12 (52.2)	33 (68.8)	**0.02***
Yes	91 (23.2)	11 (47.8)	15 (31.2)	
Comorbidity				
No	214 (54.5)	12 (50.0)	19 (39.6)	0.15
Yes	179 (45.5)	12 (50.0)	29 (60.4)	
Racial discrimination				
No situation	127 (32.3)	7 (29.2)	12 (25.0)	0.61
1 or 2 situations	115 (29.3)	8 (33.3)	12 (25.0)	
3 or more situations	153 (38.4)	9 (37.5)	24 (50.0)	

±Fisher's Exact test

Bold p-values indicate statistical significance *p < 0.05

*** Due to missing values, frequencies may not add up to totals.

Table 4.6. Distribution of study variables by asthma phenotype for men

	No asthma n = 414 n (%)	**Atopic asthma n = 20 n (%)**	**Non-atopic asthma n = 57 n (%)**	**p-value**
Age				
18-39 years	266 (64.3)	15 75.0)	43 (75.4)	0.17
40 years and older	148 (35.7)	5 (25.0)	14 (24.6)	
Marital status				
Single	259 (63.8)	15 (78.9)	33 (60.0)	0.35±
Partnered	147 (36.2)	4 (21.1)	22 (40.0)	
Education				
Less than high school	231 (55.9)	10 (50.0)	35 (61.4)	0.62
High school or greater	182 (85.1)	10 (50.0)	22 (38.6)	
Household income				
$<20,000	146 (38.2)	9 (47.4)	21 (40.4)	0.94±
$≥20,000	108 (28.3)	4 (21.0)	15 (28.8)	
Refused/don't know	128 (33.5)	6 (31.6)	16 (30.8)	
Employment status				
Employed	233 (57.2)	15 (75.0)	38 (66.7)	0.13
Unemployed	174 (42.8)	5 (25.0)	19 (33.3)	
Financial strain				
No	233 (56.8)	10 (50.0)	36 (63.2)	0.53
Yes	177 (43.2)	10 (50.0)	21 (36.8)	
Housing in need of repairs				
No	115 (29.6)	3 (15.8)	16 (29.1)	0.50±
Yes, major repairs	273 (70.4)	16 (84.2)	29 (70.9)	
Home dampness past 12 months				
No	159 (40.9)	3 (15.8)	16 (29.0)	**0.03**±*
Yes	230 (59.1)	16 (84.2)	39 (70.9)	
Signs of mold or mildew in home				
No	201 (51.8)	7(36.8)	25 (45.4)	0.33
Yes	187 (48.2)	12 (63.2)	30 (54.6)	
Pet in home				
No	251 (64.4)	11 (57.9)	36 (67.9)	0.73
Yes	139 (35.6)	8 (42.1)	17 (32.1)	

	No asthma n = 414 n (%)	Atopic asthma n = 20 n (%)	Non-atopic asthma n = 57 n (%)	p-value
Smoking status				
Non-smoker	85 (20.5)	6 (30.0)	15 (26.3)	0.39
Current smoker	329 (79.5)	14 (70.0)	42 (73.7)	
Alcohol				
Never drinker	77 (18.6)	4 (20.0)	6 (10.5)	0.30±
Ever drinker	336 (81.4)	16 (80.0)	51 (89.5)	
BMI				
Normal/underweight	250 (60.4)	10 (50.0)	31 (54.4)	0.48
Overweight/obese	164 (39.6)	10 (50.0)	26 (45.6)	
Exercise				
No	88 (21.4)	5 (25.0)	14 (24.6)	0.81
Yes	324 (78.6)	15 (75.0)	43 (75.4)	
Exercise duration				
<15 minutes	126 (30.6)	5 (26.3)	16 (28.1)	0.87
≥15 minutes	286 (69.4)	14 (73.7)	41 (71.9)	
Depression diagnosis				
No	362 (87.9)	15 (75.0)	44 (77.2)	**0.03***
Yes	50 (12.1)	5 (25.0)	13 (22.8)	
Comorbidity				
Absent	229 (55.3)	10 (50.0)	23 (40.3)	0.10
Present	185 (44.7)	10 (50.0)	34 (59.7)	
Racial discrimination				
No situation	143 (34.5)	5 (25.0)	19 (33.3)	0.93
1 or 2 situations	120 (29.0)	7 (35.0)	16 (28.1)	
3 or more situations	151 (36.5)	8 (40.0)	22 (38.6)	

±Fisher's Exact test

Bold p-values indicate statistical significance *p < 0.05

*** Due to missing values of variables, frequency may not add up to totals.

4.2 Multivariable analyses

Table 4.7 displays the results of the univariable multinomial logistic regression analyses for the total sample, with the goal of identifying those variables eligible for multivariable modelling. The following variables met the statistical criterion ($p<0.25$) for inclusion in relation to atopic and/or non-atopic asthma: education, employment status, housing in need of repairs, damp housing, signs of mold/mildew in the home, BMI, alcohol use, depression, and comorbidity. Though they failed to meet the statistical cut-off, age, financial strain and racial discrimination were also included in the multivariable analyses due to their biological and/or theoretical importance. Several of the variables also met the conventional standard for statistical significance ($p<0.05$): home dampness and depression were associated with an increased odds of both atopic and non-atopic asthma, whereas body mass index was associated with an elevated odds of atopic asthma and ever alcohol use and comorbidity were associated with an elevated odds of non-atopic asthma (Table 4.7).

Table 4.7. Results of univariable multinomial logistic regression analyses assessing risk factors for atopic and non-atopic asthma (referent: no asthma) for total sample

	Atopic asthma n = 44 OR_{unadj} (95% CI)	**p-value**	**Non-atopic asthma n = 105 OR_{unadj} (95% CI)**	**p-value**
Age (18-39 years) 40 years and older	ref 0. 74 (0.38,1.44)	0.38	ref 0.93 (0.60, 1.42)	0.72
Sex (Men) Women	ref 1.3 (0.69, 2.32)	0.45	ref 0.89 (0.59, 1.33)	0.57
Marital status (Single) Partnered	ref 0.79 (041, 1.52)	0.48	ref 1.13 (0.74, 1.71)	0.57
Education (High school or greater) Less than high school	ref 1.46 (0.78, 2.71)	0.23	ref 0.80 (0.53, 1.21)	0.29
Household income ($<20,000) $≥20,000 Refused/don't know	ref 0.76 (0.35, 1.65) 0.82 (0.40, 1.72)	 0.49 0.60	ref 0.88 (0.53, 1.47) 0.78 (0.10, 1.30)	 0.64 0.34

	Atopic asthma n = 44 OR_{unadj} (95% CI)	**p-value**	**Non-atopic asthma n = 105 OR_{unadj} (95% CI)**	**p-value**
Employment (Employed) Unemployed	ref 0.61 (0.32, 1.16)	0.13	ref 0.81 (0.54, 1.21)	0.30
Financial strain (No) Yes	ref 1.36 (0.74, 2.52)	0.32	ref 1.12 (0.75, 1.68)	0.59
Housing in need of repairs (No) Yes, repairs need	ref 2.31 (0.96, 5.57)	0.06	ref 1.11(0.70, 1.78)	0.64
Home dampness past 12 months (No) Yes	ref 2.44 (1.15, 5.19)	**0.02***	ref 1.94 (1.22, 3.07)	**0.01***
Signs of mold or mildew in home (No) Yes	ref 1.62 (0.85, 3.07)	0.14	ref 1.28 (0.84, 1.94)	0.24
Pet in home (No) Yes	ref 1.13 (0.59, 2.14)	0.72	Ref 1.05 (0.96, 0.16)	0.83
Smoking status (Non-smoker) Current smoker	ref 0.75 (0.37, 1.48)	0.41	Ref 0.80 (0.50, 1.26)	0.33
Alcohol (Never drinker) Ever Drinker	ref 1.33 (0.58, 3.04)	0.50	Ref 2.39 (1.22, 4.70)	**0.01***
BMI (normal/underweight) Overweight/Obese	ref 2.01 (1.07, 3.77)	**0.03***	Ref 1.19 (0.79, 1.79)	0.39
Exercise (No) Yes	ref 0.96 (0.49, 1.87)	0.90	Ref 0.79 (0.52, 1.22)	0.30
Exercise duration (<15 minutes) ≥15 minutes	ref 1.15 (0.60, 2.20)	0.66	Ref 1.04 (0.693, 1.58)	0.85
Depression diagnosis (No) Yes	ref 2.79 (1.46, 5.31)	**0.002****	Ref 1.71 (1.07, 2.73)	**0.03***
Comorbidity (No) Yes	ref 1.22 (0.66, 2.23)	0.53	Ref 1.83 (1.21, 2.76)	**0.004****

	Atopic asthma n = 44 OR_{unadj} (95% CI)	**p-value**	**Non-atopic asthma n = 105 OR_{unadj} (95% CI)**	**p-value**
Racial discrimination (No situation)	ref		Ref	
1 or 2 situations	1.44 (0.66, 3.13)	0.36	1.04 (0.60, 1.78)	0.89
3 or more situations	1.27 (0.59, 2.70)	0.54	1.33 (0.82, 2.15)	0.25

Bold p-values indicate statistical significance *p < 0.05; **p<0.01

Subsequent to an evaluation of the assumption of independence of irrelevant alternatives , which was satisfied, relevant variables were entered simultaneously into the multinomial logistic regression, followed by an examination of all two-way interactions with sex. Table 4.8 shows the final multinomial logistic regression model. There was only one variable associated with atopic asthma: those with depression had 2.9 times higher odds of atopic asthma compared to those without depression (95%CI: 1.38, 6.20). Statistically significantly associated with an elevated odds of non-atopic asthma were home dampness (OR=1.83, 95%CI: 1.08-3.11), ever alcohol use (OR=2.21, 95%CI: 1.09-4.48) and the presence of comorbidity (OR=1.77, 95% CI: 1.17, 2.68).

Table 4.8. Results (final model) of multivariable multinomial logistic regression assessing risk factors for atopic and non-atopic asthma (referent: no asthma) for the total sample

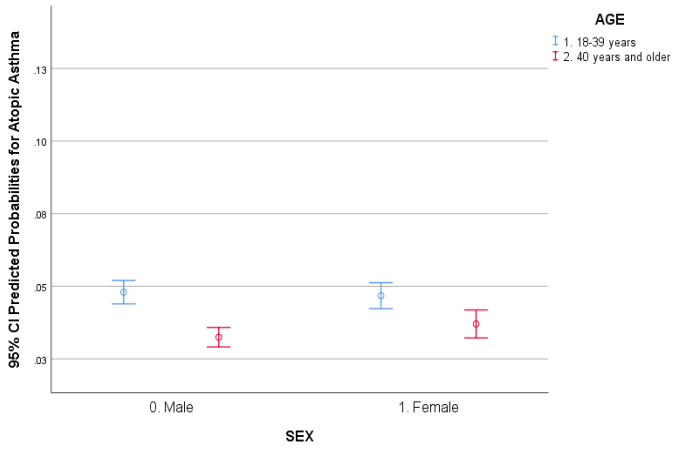
	Atopic asthma n = 44 OR_{adj} (95% CI)	**Non-atopic asthma n = 105 OR_{adj} (95% CI)**
Age (18-39 years)	ref	ref
40 years and older	0.58 (0.20,1.71)	**0.49 (0.25, 0.94) ***
Sex (Men)	ref	ref
Women	0.52 (0.17, 1.58)	**0.38 (0.19, 0.76) ****
Education (High school or higher)	ref	ref
Less than high school	1.41 (0.72, 2.79)	0.77 (0.51, 1.18)

	Atopic asthma n = 44 OR_{adj} (95% CI)	**Non-atopic asthma n = 105 OR_{adj} (95% CI)**
Employment (Employed) Unemployed	ref 0.69 (0.36, 1.33)	ref 0.84 (0.52, 1.34)
Financial strain (No) Yes	ref 1.05 (0.44, 2.50)	ref 0.70 (0.38, 1.30)
Housing in need of repairs (No) Yes, need repairs	ref 1.46 (0.54, 3.96)	ref 0.95 (0.56, 1.61)
Home dampness past 12 months (No) Yes	ref 2.06 (0.85, 4.99)	ref **1.83 (1.08, 3.11) ***
Signs of mold or mildew in home (No) Yes	ref 0.89 (0.37, 2.09)	Ref 0.98 (0.62, 1.55)
Alcohol (Never drinker) Ever Drinker	ref 1.24 (0.52, 2.92)	ref **2.21 (1.09, 4.48) ***
BMI (Normal/Underweight) Overweight/Obese	ref 1.57 (0.82, 3.01)	ref 1.24 (0.79, 1.95)
Depression diagnosis (No) Yes	ref **2.92 (1.38, 6.20) ****	ref 1.57 (0.94, 2.64)
Comorbidity (No) Yes	ref 1.06 (0.53, 2.14)	ref **1.77 (1.17, 2.68) ****
Racial discrimination (No situation) 1 or 2 situations 3 or more situations	ref 0.99 (0.39, 2.53) 0.97 (0.44, 2.13)	ref 0.96 (0.55, 1. 66) 1.19 (0.70, 2.02)
Sex*Financial strain (Male *No) Female*Yes	ref 1.82 (0.48, 6.88)	ref **2.52 (1.08, 5.88) ***
Sex*Age (Male *18-39 years) Female*40 years and older	ref 1.21 (0.25, 5.79)	ref **2.50 (1.02, 6.13) ***

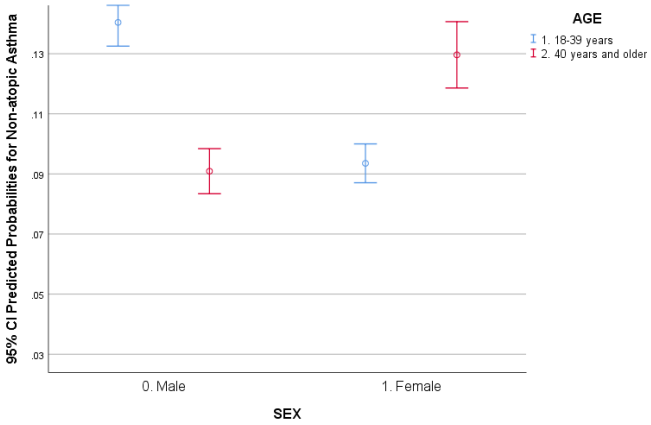
Bold p-values indicate statistical significance *$p < 0.05$; **$p < 0.01$

Sex significantly interacted with age (Fig 4.1) and financial strain (Fig 4.2) in relation to non-atopic asthma. As shown in Figure 4.1, while the relationship between age and atopic asthma was

similar for both sexes (4.1a), for non-atopic asthma, older age was associated with an increased likelihood of asthma for women but a lower likelihood of asthma for men (4.1b). The relationship between financial strain and atopic asthma was similar for women and men (4.2a), whereas for non-atopic asthma, the presence of financial strain was associated with a greater probability of asthma for women but a lower probability for men (4.2b).

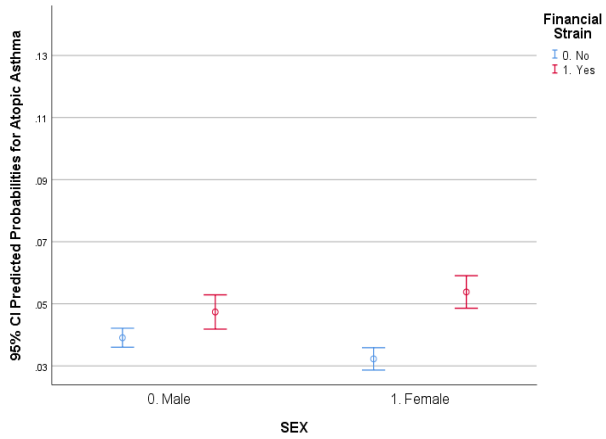


(a)

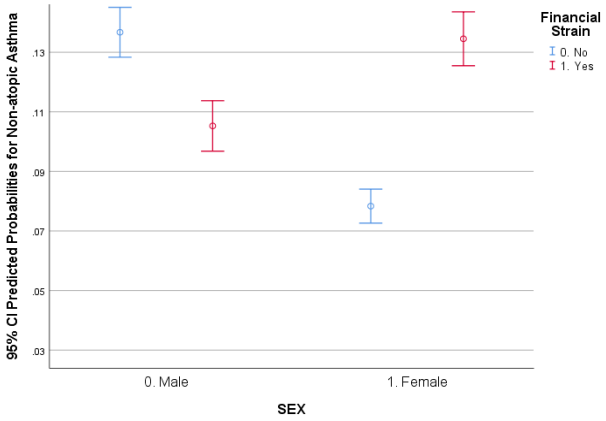


(b)

Figure 4.1 (a, b): Interaction between sex and age for (a) atopic asthma and (b) non-atopic asthma



(a)



(b)

Figure 4.2 (a, b): Interaction between sex and financial strain for (a) atopic asthma and (b) non-atopic asthma.

Chapter 5

Discussion

This cross-sectional study determined the prevalence and risk factors associated with asthma phenotype among Saskatchewan reserve-dwelling First Nations women and men. The overall prevalence of asthma was 15.6%, with non-atopic asthma (11.0%) more prevalent than atopic (4.6%). There were no significant sex differences in the prevalence of asthma (overall or by phenotype) in crude or age-stratified estimates; however, the results of the multivariable analysis indicated a significantly higher occurrence of non-atopic asthma in women 40 years of age and older compared to same age men. Depression was associated with an increased odds of atopic asthma, as was damp housing, alcohol use, and co-morbidities in relation to non-atopic asthma. Financial strain was related to an increased odds of non-atopic asthma in women and decreased odds in men.

While the absence of previous work documenting the prevalence of asthma phenotype by sex in adult Indigenous populations makes it difficult to compare these results with other research directly, some comparisons can be made. Relative to an asthma prevalence of approximately 8.6% in the general Canadian adult population (16), the overall asthma prevalence of 15.6% observed in this First Nations sample is higher, consistent with previous research indicating elevated asthma rates among Indigenous than non-Indigenous populations (176). However, the results of this study contrast with previous research showing a higher asthma prevalence in adult Indigenous women than men (20,24,180–183). As shown in Table 5.1, while the female-specific asthma prevalence in this study is not that dissimilar from previous research, the male-specific prevalence obtained here is consistently higher than in other studies, with the exception of Karunanayake et al. (179), which focused on a sample of 12–19-year-old Indigenous youth. Variation in estimates may have arisen due to differences in the populations sampled in terms of Indigenous identity, country, degree of urbanization, and other demographic characteristics, such as age. The presence of bias also cannot be ruled out and will be discussed in the limitations section below.

Table 5.1 Comparison of sex-specific asthma prevalence (%) in the present study to other research on Indigenous people

	Women	**Men**
Present study	**15.5**	**15.7**
Karunanayake et al. (179)	15.3	16.8
Chang et al. (20)	16.2	11.2
Orell et al. (181)	12.5	9.5
Crighton et al.(24)	13.6	8.5
Janz et al. (183)	17.2	11.0
Loveland et al. (182)	14.0	6.7
Dixon et al. (180)	8.2	3.2

Regarding asthma phenotypes, this study's higher prevalence of non-atopic than atopic asthma is consistent with previous research with adult general population samples. A significant proportion of adult asthma patients (up to 40%) are non-atopic (194,195), and after the age of 40 years, most new cases of asthma are non-atopic (36). One study demonstrated that, compared to asthmatic subjects ≤40 years, older subjects with asthma had lower odds of atopic and eosinophilic phenotypes and higher odds of irreversible airflow obstruction and severe asthma phenotypes (196). Approximately 5% of women go through menopause between 40 and 45 years of age (197), and women reach menopause at an average age of 51 years, although it can occur as early as age 40 to as late as the early 60s (198). Given research showing that menopause has an impact on asthma (199–201), in combination with the age pattern of menopause onset described above, age in this study was categorized into two groups: 18-39 years and ≥ 40 years; unfortunately, sample size limitations, particularly in the older age groups, prevented more nuanced age stratification.

Based on multivariable analyses, a higher rate of non-atopic asthma was observed among women than men aged 40 years and older. Consistent with these results, previous research has demonstrated that women have a higher risk of developing non-atopic asthma (48,49) and that because of allergies, hormone-related events play an important role in the development and severity of adult-onset asthma in women (199). One study reported a history of nasal polypectomy, female sex, an FEV_1 < 80% predicted, and greater age to be positively associated with non-allergic asthma (42). Menopause can coincide with the onset of asthma; epidemiological studies suggest a peak in the frequency of asthma beginning in women around 50 years of age (200). A study from

northern Europe reported that women were more prone to new-onset asthma during transitional times in early postmenopausal and late postmenopausal periods (201). In a prospective cohort study, the incidence of non-atopic asthma was higher in women than in men throughout the reproductive years, whereas no sex difference was observed for the incidence of atopic asthma (202). Non-atopic asthma is associated with more severe asthma and lower responsiveness to standard therapy (203).

In this study, approximately 60% of participants reported exposure to damp housing, which was associated with an increased odds of non-atopic asthma. Previous research has similarly reported a relationship between damp housing and asthma prevalence in the general adult population (77,204,205), and a narrative, systematic review of 43 studies with children concluded that damp housing was consistently associated with non-atopic asthma (206). In contrast, a recent study of Danish adults found self-reported household moisture damage to be associated with an increased occurrence of asthma in atopic individuals (207); however, the authors acknowledged that the low prevalence of dampness in the homes of non-atopic participants, with the possibility of reporting bias among those with atopy, prevented drawing any definitive conclusions (207). Similar to the Danish study, other research using data from the FNLHP has reported a relationship between dampness and atopic asthma in children (22) and adults (25). In contrast to this study which combined baseline and follow-up FNLHP data, these two studies (28,31) used only baseline data, and one (28) did not include adults. Inconsistent results may also have arisen due to differences in confounder control, assessment of effect modification, and the inclusion of particular exposures in multivariable modelling. In the present study, while dampness was associated with both atopic and non-atopic asthma in unadjusted analysis, in adjusted analyses, statistical significance was only maintained for non-atopic asthma. In a further exploratory analysis, alternating variables were included in the multivariable model, and the impact on the relationship between dampness and atopic/non-atopic asthma was noted. Regardless of the other variables included, a statistically significant relationship between dampness and non-atopic asthma remained, though, in some models, dampness also became associated with atopic asthma. Relatively few studies on asthma and dampness have differentiated by phenotype; still, several reviews have concluded that dampness can be related to respiratory symptoms in non-atopic as well as atopic

individuals (185,204). Additional research is clearly needed to provide clarification regarding the relationship between household dampness to atopic and non-atopic asthma.

Depression was associated with an increased odds of atopic asthma in the present study, which is consistent with previous research using general population samples. For example, the results of recent meta-analyses of prospective studies have found strong evidence of a link between depression and adult-onset asthma (208), including atopic asthma (209). While evidence to date is more suggestive of depression and other psychosocial factors being risk factors for the development of asthma rather than vice versa (210), evidence of a reciprocal relationship has also been reported (209). Depression and asthma are believed to be connected by psychological, behavioural and/or physiological pathways. Irrespective of the exact nature of the association, considerable evidence suggests that people with asthma who also experience depression have poorer outcomes, such as greater health care utilization, lower levels of general well-being, and poorer management of symptoms (211). Regarding Indigenous populations, although no studies specifically on asthma and depression could be located, compromised mental health has been observed in some studies of Indigenous people, often linked to colonization and intergenerational trauma (212). Evidence is mixed, however, regarding whether rates of common mental disorders are elevated in some Indigenous groups compared to non-Indigenous people (213,214).

The presence of one or more other co-morbidities, which included cancer, diabetes and/or a variety of respiratory ailments, was also associated with elevated odds of non-atopic asthma in the current study. Previous research has reported a link between respiratory infections and non-atopic asthma (22,206). The prevalence of obstructive sleep apnea (215), tuberculosis (216), type 2 diabetes (217), emphysema (218), and bronchitis (218) has been found to be more common in asthmatic compared with non-asthmatic individuals. One study reported that women with adult-onset asthma experienced a 2-fold increase in incident CHD and stroke, independent of other risk factors, including smoking, body mass index, and physical activity (219). Patients with asthma experienced an 81% higher likelihood of heart disease when compared to those without asthma in another study (220), and those with non-atopic asthma may have a greater risk of cancer than those with atopic asthma (221). Etiologic relations between asthma and various co-morbid conditions are undoubtedly complex, even more so when one considers asthma a complex syndrome in and of

itself. Regardless of causal relationships, individuals with asthma and co-morbidities are more likely to report poorer asthma control, lower quality of life, and greater health care utilization (222).

In this study, every use of alcohol was also associated with an increase in non-atopic asthma. Previous research examining the relationship between alcohol and many chronic health conditions, including asthma (223), suggests a complex relationship with few established facts. Regarding asthma, protective (224), benign (225), u-shaped (226), and harmful (227) effects of alcohol have been reported. Regarding the latter, alcohol contains antihistamines and sulphites, and these compounds can trigger asthma (228). Wine is the most common alcohol to cause an asthma exacerbation due to the level of sulphites, although beer, cider, and hard alcohol can also act as triggers (228). Alcohol consumption increases the level of serum total IgE, even if consumed in lower quantities (229–231). Vidal et al. found a significant association between alcohol consumption and increased IgE values which were more evident in those who were non-atopic (231). In one experimental study, after ethanol ingestion, about one-half of asthmatic individuals developed bronchoconstriction with concomitant increases in blood acetaldehyde and histamine (232).

Financial strain in this study was linked with an increased odds of non-atopic asthma for women (but not for men). In a recent Swedish study, the economic strain was associated with asthma diagnosis in women and men (249), whereas other research reported no relationship (233). High-stress levels, from a variety of sources, have been associated with an elevated incidence of asthma in several longitudinal studies (234–237). Women may be more vulnerable to strains associated with domestic environments, such as finances, caregiving and interpersonal family relationships (238). Stress has been shown to modulate and activate several biological that may be involved in asthma pathophysiology (239). Stress activates the hypothalamic–pituitary–adrenal axis, with subsequent production of cortisol and adrenalin, and also shifts the immune response from an antibacterial T-helper (Th)1 response toward a (Th)2 response and alters the psychological, immunological and endocrine systems, which contribute to the onset of asthma (240).

However, it is important to note that no associations in this study were found between asthma and other indicators of SES, namely income and education. While considerable research suggests that lower SES, measured in a variety of ways, is related to increased asthma risk (140–145), some research indicates, similar to the present study, more complex associations, dependent not only on sex but also asthma phenotype and SES indicator (241). Schyllert (241) found that lower income was associated with increased atopic asthma in women but not in men, whereas lower educational attainment was related to increased non-atopic asthma but was protective for atopic asthma. The relationship between SES and asthma may be even more complex when Indigeneity is considered. As reviewed previously, indicators of SES have been inconsistently associated with asthma prevalence in Indigenous samples, with some showing a positive association (24,182) and others no association (27,28). Inconsistent findings may be due to methodological issues, such as the constrained variability of SES measures in some populations (242). Others have pointed to the idea of diminishing health returns which holds that some social groups may not benefit to the same degree as others from the health-enhancing resources that typically accompany higher SES due to harmful exposures, such as systemic racism (243).

5.1. Strengths

There were quite a few strengths to the present study. The FNLHP adopted a community-based, participatory research model, which encouraged meaningful involvement of communities in all aspects of research, including the identification of focal health issues and determinants. The present study was able to examine a broad array of risk factors for asthma, both traditional and novel, such as racial discrimination. Some variables used in the current study analysis were measured objectively (e.g., atopy, BMI), reducing the potential for measurement error. The focus on adult asthma was another strength, as the majority of research has centred on children. Further, rather than controlling for sex, which is common in research of this type, results were examined in a sex-specific manner, and the role of sex as a potential effect modifier was thoroughly explored. Finally, the differentiation of asthma by phenotype was an advance over much previous research with adult First Nations people, which allowed for a more nuanced estimate of prevalence and identification of risk factors.

5.2. Limitations

Study limitations were also present regarding both measurement and design. All the independent variables were self-reported, as was a component of the dependent variable, which may lead to some measurement error. Research suggests that self-reported asthma may result in an underestimation of prevalence, particularly among those with less severe respiratory symptoms (244,245). Conversely, one study reported that 30–35% of physician diagnosed asthma in children and adults may not have current asthma, suggesting issues of overdiagnosis (245). Recently, asthma guidelines combining clinical and economic evidence with sensitivity and specificity of diagnostic procedures was developed aimed at reducing overdiagnosis of asthma (246). In the present study, only participants who completed clinical testing were included in the sample; those who reported a history of anaphylactic reaction and/or severe eczema were excluded, potentially contributing to an underestimation of prevalence. In addition, only non-food allergens were used to measure atopy status, perhaps further contributing to an underestimation of atopic asthma in this study. Some potentially important exposures, such as the family history of asthma and atopy, were not measured. The study was cross-sectional, thus limiting the analysis to the assessment of prevalence and correlates of prevalence; thus, causal statements cannot be made based on these results. The communities were combined into one sample to enhance the sample size, which may mask important health and exposure differences between the two communities. Compared to the First Nations population of Saskatchewan, participants in this study tended to be older, which may limit generalizability, as did the sampling of only two of many First Nations communities in the province. Further, response rates in the original baseline study were 53.9 % for community A and 89.9 % for community B; therefore, selection bias is possible if the participants and non-participants differed according to their exposures and asthma status in some systematic way. Statistical limitations were also present. The consideration of asthma phenotype in this study resulted in smaller cell sizes, which may have reduced study power and increased the likelihood of type 2 errors, particularly when examining effect modification. Multiple statistical tests were performed, which may have resulted in some spurious associations between exposures and asthma phenotypes.

5.3. Future Research

The current study examined the prevalence and correlates of asthma phenotypes in First Nations adult women and men in rural Saskatchewan. These results suggest that asthma correlates may depend on phenotype in a sex-specific manner. Given the limited amount of previous research, many of the results reported in this study were novel. Additional studies on adult Indigenous asthma phenotypes and risk factors are needed to corroborate or refute the associations suggested by this study. It should also be recognized that the identification of these sex differences for asthma is an initial step toward gaining a better understanding of the complexity and underlying mechanisms of Indigenous adult asthma. Health Canada's "Gender-based Analysis Policy" describes the importance of investigating the interacting roles of sex (i.e. biological differences) and gender (i.e. socially and culturally constructed roles, relationships, attitudes, values, relative power and influence) in health research (247). Therefore, future studies should investigate the potential differences in biological and sociocultural pathways between risk factors and asthma phenotypes in Indigenous women and men. The current cross-sectional study can only hypothesize about temporal relationships between the purported exposures and asthma phenotypes. Additional sex-comparative longitudinal studies are needed to consider the timing of asthma-related exposures. Where study resources permit, future work in this field should strive to better understand the impact of modifiable risk factors on Indigenous adult asthma through more comprehensive exposure measurement methods.

5.4. Conclusions

The results from this study suggest the possibility of intriguing differences in the correlates of asthma by phenotype and sex. Future research incorporating a longitudinal design and enhanced measurement is required to advance understanding of the complex interrelationships between sex, asthma phenotype, and various risk factors in First Nations adults.

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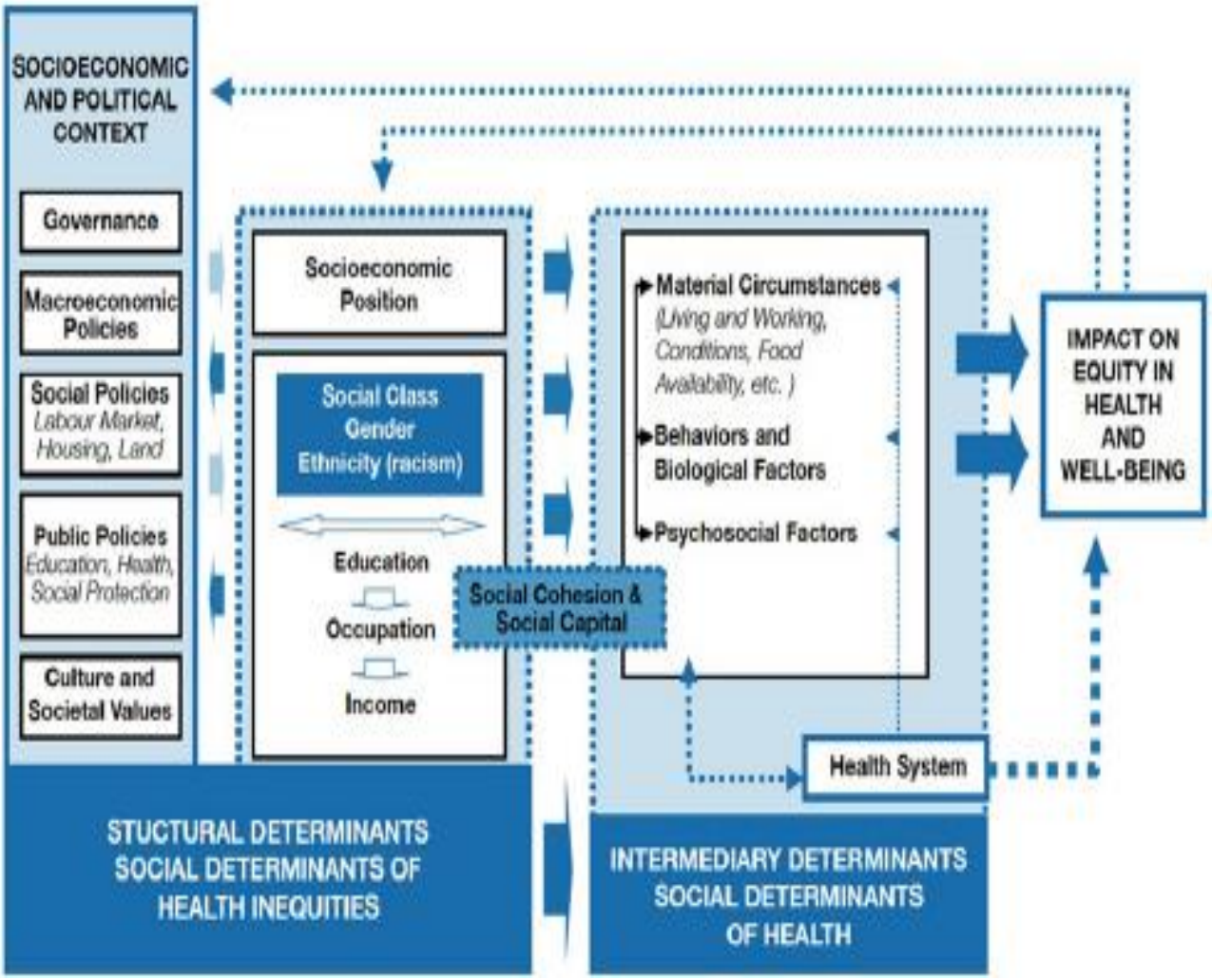
Appendix A

Commission on Social Determinants of Health (CSDH) Framework on health inequities (57).



Appendix B

UNIVERSITY OF SASKATCHEWAN

Biomedical Research Ethics Board (Bio-REB) 09-Sep-2021

Certificate of Approval

Application ID: 2942

Principal Investigator: Bonnie Janzen

Department: Department of Community Health and Epidemiology

Locations Where Research Activities are Conducted: Data collection is complete. This proposal is for secondary data analysis. Data will be analyzed at the University of Saskatchewan, Saskatoon SK., Canada

Student(s): Naima Afzal

Funder(s):

Sponsor: College of Medicine

Title: Asthma in First Nation's Adults: Prevalence and Associated Factors

Protocol Number:

Approved On: 07-Sep-2021

Expiry Date: 07-Sep-2022

Approval Of:

* Revised Ethics Application (Bio 2942 NER)
* Data Variables

Acknowledgment Of:

* Notice of Ethical Review Response
* TCPS2 Core Tutorial Certificate of Completion for Naima Afzal
* McMaster Chart Review Tutorial Certificate of Completion for Naima Afzal
* Reviewed with COVID-19 safety considerations in mind

Review Type: Delegated Review

IRB Registration Number: Not Applicable

1 / 2

CERTIFICATION

The University of Saskatchewan Biomedical Research Ethics Board (Bio-REB) has reviewed the above-named project. The project is acceptable on scientific and ethical grounds. The principal investigator has the responsibility for any other administrative or regulatory approvals that may pertain to this project, and for ensuring that the authorized project is carried out according to governing law. This approval is valid for the specified period provided there is no change to the approved project.

FIRST TIME REVIEW AND CONTINUING APPROVAL

The University of Saskatchewan Research Ethics Boards review above minimal risk projects at a full-board (face-to-face) meeting. If a project has been reviewed at a full board meeting, a subsequent project of the same protocol may be reviewed through the delegated review process. Any research classified as minimal risk is reviewed through the delegated (subcommittee) review process. The initial Certificate of Approval includes the approval period the REB has assigned to a study. The Status Report form must be submitted within one month prior to the assigned expiry date. The researcher shall indicate to the REB any specific requirements of the sponsoring organizations (e.g. requirement for full-board review and approval) for the continuing review process deemed necessary for that project.

REB ATTESTATION

In respect to clinical trials, the University of Saskatchewan Research Ethics Board complies with the membership requirements for Research Ethics Boards defined in Part 4 of the Natural Health Products Regulations and Part C Division 5 of the Food and Drug Regulations and carries out its functions in a manner consistent with Good Clinical Practices. Members of the Bio-REB who are named as investigators, do not participate in the discussion related to, nor vote on such studies when presented to the Bio-REB. This approval and the views of this REB have been documented in writing. The University of Saskatchewan Biomedical Research Ethics Board is constituted and operates in accordance with the current version of the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS 2 2018).

Digitally Approved by Dr. Gordon McKay, Ph.D.
Chair, Biomedical Research Ethics Board
University of Saskatchewan

UNIVERSITY OF SASKATCHEWAN

Biomedical Research Ethics Board (Bio-REB) 07-Sep-2022

Certificate of Re-Approval

Application ID: 2942

Principal Investigator: Bonnie Janzen

Department: Department of Community Health and Epidemiology

Locations Where Research Activities are Conducted: Data collection is complete. This proposal is for secondary data analysis. Data will be analyzed at the University of Saskatchewan, Saskatoon SK., Canada

Student(s): Naima Afzal

Funder(s):

Sponsor: College of Medicine

Title: Asthma in First Nation's Adults: Prevalence and Associated Factors

Approval Effective Date: 07-Sep-2022

Expiry Date: 07-Sep-2023

Acknowledgment Of:

* Certificate of completion for The TCPS 2 Tutorial Course on Research Ethics (CORE)
* McMaster University Chart Review Tutorial.

Review Type: Delegated Review

IRB Registration Number: Not Applicable

* This study, inclusive of all previously approved documents, has been re-approved until the expiry date noted above

CERTIFICATION

The University of Saskatchewan Biomedical Research Ethics Board (Bio-REB) has reviewed the above-named project. The project was found to be acceptable on scientific and ethical grounds. The principal investigator is responsible for obtaining any other administrative or regulatory approvals that may pertain to this project, and for ensuring that the authorized project is carried out according to governing law. This approval is valid for the specified period, provided there is no change to the approved project.

FIRST TIME REVIEW AND CONTINUING APPROVAL

The University of Saskatchewan Research Ethics Boards review above minimal risk projects at full-board meetings. If a project is reviewed at a full-board meeting, any subsequent projects being added with the same protocol may be reviewed through the delegated review process. Research classified as minimal risk is reviewed through the delegated review process. The initial Certificate of Approval indicates the approval period the REB has assigned to a study.

To remain in compliance, the REB must receive a status report form (renewal or closure) prior to the assigned expiry date each year. Any specific requirements of the sponsoring organizations deemed necessary for continuing ethics review (e.g., requirement for full-board review and approval) should be indicated by the researcher to the REB. Any change to the approved project must be reported to the Chair of the Bio-REB for consideration in advance of its implementation through the amendment process.

REB ATTESTATION

In respect to clinical trials, the University of Saskatchewan Bio-REB complies with the membership requirements for Research Ethics Boards defined in Part 4 of the Natural Health Products Regulations and Part C Division 5 of the Food and Drug Regulations, and carries out its functions in a manner consistent with Good Clinical Practices. The University of Saskatchewan is constituted and operates in accordance with the current version of the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans - TCPS 2 (2018). If a member of the REB is named as an investigator on a project under review, the member is absent from REB deliberations and decisions regarding the project. This approval and the views of the Bio-REB have been documented in writing.

Digitally Approved on behalf of the Chair
Biomedical Research Ethics Board
University of Saskatchewan