SOCIOECONOMIC, ENVIRONMENTAL AND PERSONAL CORRELATES OF ASTHMA IN A COMMUNITY POPULATION OF MEN AND WOMEN

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ABSTRACT

Asthma is a multifactorial chronic disease that has shown a marked increase in prevalence over the past few decades, both in Canada and worldwide. Basic knowledge gaps remain about the pathways through which risk factors influence adult asthma. More adult women than men have asthma, and a growing body of research suggests that associations between certain risk factors and asthma may differ by sex. The aim of this thesis was to investigate the socioeconomic, environmental and personal correlates of asthma in men and women.

Data for this thesis were obtained from a cross-sectional study conducted in 2003 in the rural Canadian town of Humboldt, Saskatchewan. The survey response rate was 71% of the resident target population, with 1177 females and 913 males aged 18 to 79 participating in the study. Researchers collected objective data on atopy (skin prick test), and body mass index. Exposures and history of physician-diagnosed asthma in the past year (current asthma) and during the participant's lifetime (ever asthma) were self-reported. Multivariable logistic regression models adjusted for age, atopy, and parental asthma history were used to evaluate associations of correlates with asthma. The model building process was based on a conceptual framework of three categories: socioeconomic variables, home and work environment, and personal factors.

The prevalence of asthma was higher in women than men (ever asthma: 10.2% of women versus 5.8% of men; current asthma: 6.2% of women versus 2.8% of men). The logistic regression models for ever asthma and current asthma showed several sex differences. The sequential addition of each category of socioeconomic, environmental, and personal variables contributed significantly to model fit in women, but not in men. Living in a mobile, attached or multiple-family home, household dampness, and overweight/obesity were strong risk factors for female asthma, while farm living, occupational grain dust exposure, and regular alcohol use emerged as protective factors. Male models revealed a strong significant association between household dampness and current asthma. A significant interaction between home type and age was found only in females. Women living in homes other than single-family detached dwellings were more likely to have asthma, an association that decreased in strength with increasing age.

These results suggest that several risk factors for adult asthma may be sex-specific, therefore emphasizing the importance of considering sex as a potential effect modifier in future adult asthma epidemiology studies.

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INTRODUCTION

Asthma is a chronic inflammatory disorder of the airways that causes recurrent episodes of airflow limitation characterized by wheezing, breathlessness, chest tightness, and cough in susceptible individuals, and is spontaneously reversible or reversible on treatment.[1] The World Health Organization (WHO) estimates that 300 million people currently suffer from asthma,[2] resulting in a global loss of approximately 15 million disability-adjusted life years (DALYs) annually.[3] Over the past few decades, there has been a marked worldwide increase in asthma prevalence, incidence, morbidity and mortality, particularly in industrialized countries.

In Canada, although children and teens have higher asthma prevalence and hospitalization rates than adults, the absolute number of adults with asthma is higher than for the younger age groups.[4] The 2005 Canadian Community Health Survey of Canadians estimates the overall prevalence of self-reported physician-diagnosed asthma in adults 20 years and older at 7.8% (1.9 million).[5] Age-specific sex differences have also been observed across populations, as epidemiological studies of childhood asthma consistently report higher asthma incidence and hospital admissions for boys compared to girls, while most studies of adult asthma demonstrate a higher asthma burden in women compared to men.[6-8]

Between 1994 and 2005, asthma prevalence increased markedly in Canadian women 35 to 44 and 45 to 64 years of age (60% and 80% increases, respectively), and men 35 to 44 years of age (41% increase).[4] While hospitalization rates for asthma decreased for all age groups of both men and women over the same time period, hospitalization rates for women 25-64 years of age remained more than double the rates of their male peers.[4] Saskatchewan estimates illustrate the importance of asthma as a chronic public health condition at a provincial level, with 8.5% of the 2005 adult population reporting physician-diagnosed asthma.[5] In 2005, a higher proportion of females reported asthma compared to males (8.6% vs. 6.6%), which equates to approximately 22,000 men and 30,000 women in Saskatchewan who experienced negative health, social, and economic consequences as a result of asthma. In response to the increasing burden of asthma in

Canadian adults, the Public Health Agency of Canada has identified adult asthma as an important chronic health problem that requires more research.[4]

1.1 Study Rationale

Numerous epidemiological studies have investigated the associations of risk factors with subjective (i.e. questionnaire reported asthma or wheeze) and objective (i.e. lung function measures and bronchial provocation challenges) adult measures of respiratory health. Several interrelated factors, including genetics,[9] childhood exposures and respiratory symptoms,[10,11] allergic sensitization,[12,13] exposure to cigarette smoke,[14,15] obesity,[16-21] sex hormones,[7,22,23] indoor environmental factors,[24-28] outdoor air pollution,[29] and certain occupational exposures[30,31] have been identified as risk factors for adult asthma, with consistent associations found in multiple studies and settings. However, the pathways through which most of these risk factors act remain elusive. A variety of other risk factors (e.g. socioeconomic status,[32-34] pets,[35-37] and indoor combustion[38]) have shown conflicting or inconclusive results that require further clarification.[39] In addition, a growing body of epidemiological research suggests that associations between these established and prospective risk factors and respiratory conditions such as asthma may differ by sex,[40-46] with women often identified as more susceptible to the impacts of specific risk factors compared to men.[6]

Many investigations of adult asthma continue to control for sex in their analyses rather than explicitly examining similarities and differences in risk factor associations between and within men and women.[7,47-50] To better understand disease etiology, there is a need for more sex-comparative research that explores interrelated biological, social, environmental, and personal factors, and their associations with important adult health conditions such as asthma.[6,50-53] Therefore, this study will focus on identifying adult asthma correlates in a sex-specific manner.

1.2 Research Question and Study Objectives

The aim of this study is to investigate asthma and its associated factors in men and women residing in the rural Canadian town of Humboldt, Saskatchewan. This study addresses one main research question: What socioeconomic, environmental and personal factors are associated with asthma in men and women?

Asthma has been recognized as an important health problem in Canadian adults for which major basic knowledge gaps remain. Previous research on the Humboldt population has revealed

sex differences in associations of home dampness and obesity with certain respiratory outcomes and allergies, with some hypotheses postulated as to how specific factors might relate to sex and to each other.[16,41,54,55] Thus far, there has been little focus on considering asthma correlates within the context of the overall etiological processes and in particular, the potential role of socioeconomic status (SES) for adult asthma.

Public health researchers and clinicians have identified the need for more comprehensive, sex-specific explanations of how individual risk factors work together to impact chronic diseases such as asthma.[6,41-43,46] The current study adds to the knowledge base by using sex-specific analyses to consider associations of potential socioeconomic, environmental, and personal correlates with adult asthma.

LITERATURE REVIEW

This section begins with a general overview of asthma classification. Associations of selected demographic, biological, socioeconomic, environmental, and personal risk factors with adult asthma are then summarized, along with relevant sex-related associations that have been reported in the literature. For risk factors with limited research on associations with adult asthma, the review is supplemented with information from childhood investigations and other respiratory conditions such as wheeze and shortness of breath. The final section discusses the use of conceptual frameworks to examine interrelations of risk factors.

2.1 Asthma Classification

It is widely accepted that the term "asthma" does not describe a single disease, but is an 'umbrella term' for a heterogeneous group of obstructive respiratory disorders for which the complex pathogenesis remains unclear.[56] Despite ongoing intensive research efforts, there is still no established classification system for different asthma subtypes.[39] For this reason, the measurements and classification schemes used to define asthma and its subgroups are often debated, and differ between and among epidemiologists, pathologists, physiologists, clinicians and patients.[56-58] The Global Initiative for Asthma provides the following operational definition of asthma:[1]

> *Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. The chronic inflammation is associated with airway hyperresponsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, particularly at night or in the early morning. These episodes are usually associated with widespread, but variable, airflow obstruction within the lung that is often reversible either spontaneously or with treatment.*

Previous epidemiological studies in Canada have used a wide variety of classification systems for asthma including: asthma symptoms,[48,54,59-61] hospital or physician records,[62-69] self-reported ever, recent, or current asthma[61] *also* diagnosed by a health professional,[41,48,52,54,59,70,71]

lung function tests,[16] and combinations of results from survey questions about symptoms and previous diagnoses, skin prick tests, allergen-specific IgE antibody tests, and lung function tests.[72] There is no accepted "gold standard" for measuring asthma, so the choice of an appropriate operational definition depends on a combination of several factors including practicality, comparability, and the type of study and its aims.[57] As mentioned above, self reports of physician-diagnosed asthma have been widely used as an efficient method of measuring asthma. The potential for widely varying diagnostic criteria and patient recall error to influence this asthma measure has been discussed.[57] However, an analysis performed on previous Humboldt population data showed a high correlation between self reports of asthma and pulmonary test variables calculated from objective measures of forced expiratory flow and forced vital capacity.[73] In addition, a literature review that examined the validity of different questionnaire measures of asthma concluded that self report questions about physician-diagnosed asthma showed the highest levels of specificity (approximately 99%) regardless of whether they were validated against a clinical physiologic measure or a clinical asthma diagnosis.[74] High specificity is of particular importance in analytical epidemiology studies examining rare outcomes such as asthma, since even small increases in false positive outcomes can dilute estimates of measures of association.[74] Given the high specificity of self-reported measures of physician-diagnosed asthma, it is suitable to use these measures to determine asthma status in large population-based surveys.

2.2 Sex-Related Associations with Adult Asthma

Sex differences in asthma development and progression have been described in the literature, with asthma prevalence and incidence consistently higher in women than men.[6,7] A wide variety of overlapping factors work together during a person's lifespan to form a complex multifactorial causal web that influences adult asthma. Several risk factors have been reported to influence male and female respiratory health differently, including sex-specific genetic and hormonal differences, and sex-related personal factors, environmental exposures, and socioeconomic conditions.

Sex has been increasingly identified as an important factor in terms of its potential to act as an effect modifier of associations between certain risk factors and asthma. Table 2.1 summarizes the relevant findings from a review of epidemiological studies that reported sex-related associations of adult asthma or wheeze with specific socioeconomic, environmental, and

personal factors. With the exception of sex-specific asthma prevalence and incidence rates, only results from multivariate analyses that have been adjusted for potential confounding factors are summarized. Methodologically rigorous Canadian research of any study design and longitudinal studies from other Westernized countries are included in the table. Results from other relevant studies are limited to discussion in the text.

This scan of the adult asthma literature indicated that most research on sex-specific associations has shown an increased susceptibility of women to a variety of personal and environmental risk factors. Personal factors such as overweight/obesity and smoking status have shown stronger associations with asthma for women than men.[40,41,43,75,76] Limited evidence exists for similar sex-specific associations of asthma with environmental factors such as presence of dampness, pets and cooking gas in the household.[46,54] Few studies have investigated the potential for sex differences in associations between socioeconomic status and asthma.[77] The following sections of the literature review will discuss specific risk factors for asthma with particular attention to studies that examined sex-related associations.

2.2.1 Demographic/biological factors and sex

Associations between asthma and demographic and biological factors have been well-documented and are therefore not a main focus of this thesis. However, a basic understanding of how these factors relate to asthma in men and women is important in order to interpret their potential roles in the multifactorial etiology of adult asthma.

2.2.1.1 Age

Age-related sex differences in asthma have been well-documented, with young boys and adult women showing higher rates of asthma than young girls and adult men.[6-8] Classification by age is important because asthma has a different pathogenesis and clinical presentation for infants and young children, older children and adolescents, and adults.[1] Infants and young children often present with transient wheezing, while older children and adolescents usually have a moderate form of asthma that is mainly associated with atopy, and adults often experience a more severe form of persistent asthma that may be either atopic or nonatopic.[58] Age-specific sex differences have also been demonstrated between specific asthma subtypes, with a higher proportion of nonatopic asthmatics being female and older in comparison to atopic asthmatics.[78]

Changes in female sex hormones are strongly age-related, and there is accumulating evidence concerning the role of sex steroid hormones in female adult asthma. Severe

perimenstrual asthma is a recognized phenomenon, and fluctuations in sex hormones due to pregnancy and hormone replacement therapy have been linked to changes in asthma symptoms, although the mechanisms remain unknown.[22] Some studies have also suggested associations between early age at menarche and asthma severity,[42] and new-onset asthma after puberty.[23] However, these studies had limitations in their design and implementation, and a cohort study with a much higher follow-up rate did not find a similar association.[43] Age is also a well-recognized confounder for the associations of several risk factors with asthma. For these reasons, asthma epidemiology studies routinely focus on specific age groups and perform age-adjusted analyses.

2.2.1.2 Atopy

The World Allergy Organization defines atopy as "a personal and/or familial tendency, usually in childhood or adolescence, to become sensitised and produce IgE antibodies in response to ordinary exposure to allergens, usually proteins."[79] Although the precise mechanisms that link atopy and asthma remain unclear,[1] the proposed causal mechanism features the development of airway wall abnormalities from IgE-mediated inflammatory reactions that occur at mucosal surfaces when specific allergens are inhaled by sensitized atopic individuals.[57] The pathophysiology of nonatopic asthma remains a subject of debate, with several non-IgE mediators proposed in the literature.[80,81]

Atopic status can be documented by a positive skin prick test or the presence of specific serum IgE antibodies, with negative tests indicating "nonatopic" individuals who do not have circulating IgE to the allergens being examined. The panel of allergens tested varies according to research objectives and geographic location, usually featuring a range of the most common indoor and outdoor local allergens. Differentiating between atopic and nonatopic asthma in this manner is a common, practical and accepted practice. However, it is important to recognize the potential for misclassification due to false positive and false negative skin tests, true positive skin tests in asthmatics with allergies that are unrelated to the pathophysiology of their asthma symptoms,[56] and true negative skin tests in asthmatics who may have allergic reactions that are localized in their respiratory mucosa.[82] The use of elevated total serum IgE for the diagnosis of atopy has several well-known limitations including the influence of age, sex, genetics, hormones, smoking status, and conditions other than atopy (i.e. parasitic infections, immunodeficiencies,

and certain neoplasms).[12,83] Total IgE values also show considerable overlap between atopic and nonatopic individuals, resulting in a very limited predictive value.[83]

Atopy is widely accepted as one of the strongest individual risk factors for asthma in children, and appears to also be a strong risk factor for adult-onset asthma.[12,84] While the association between atopy and asthma has been well-established, the precise nature of this relationship is complex and remains an area of ongoing debate and investigation. Population-based studies have shown considerable variation in the proportion of adult asthma cases attributable to atopy, with population attributable risks ranging from 8 to 55 percent (weighted mean of 37 percent) when atopy was defined as "at least one positive skin test".[85] Accordingly, atopic status has shown poor sensitivity and specificity as a predictor of adult asthma, a finding which may be due to the large proportions of nonatopic adult asthmatics in many populations.

2.2.1.3 Parental history of asthma

Asthma has a strong familial predisposition, although the heritability of adult asthma is less clear than for childhood asthma. Recent reviews of asthma genetics show that the inheritance patterns for different asthma phenotypes remain a subject of intense research, with hundreds of genes influencing asthma and atopy through a variety of complex mechanisms involving inflammatory pathways, remodelling of airways, and altered susceptibility to environmental factors.[86,87] The scope of this study does not allow for the investigation of specific genetic influences on asthma. Instead, the effects of genetic heritability on asthma and atopy are crudely controlled for by using the asthma history of biological parents and the atopic status of participants (previously discussed), both measures with widespread use in asthma epidemiology research.

2.2.2 Socioeconomic factors and sex

Socioeconomic status (SES) is a major societal predictor of ill health in children and adults worldwide, with socioeconomic inequalities between and within countries consistently showing associations with a variety of health outcomes. A wide range of causal mechanisms have been suggested and a growing body of evidence suggests that socioeconomic inequality has important health effects that are independent from absolute poverty levels and living conditions.[88,89] A variety of measures have traditionally been used in epidemiology research to represent SES, including individual-level and area-based scales and categories based on occupation, income, education, and wealth.[90] However, these traditional SES measures may not

accurately reflect the socioeconomic experiences of women. Therefore, the investigation of additional SES indicators that could be more relevant to the SES-health causal pathways for women has been encouraged, with some researchers using variables such as marital status, maternal status, and housing tenure.[53]

Disentangling the role of SES from among other risk factors for adult asthma is a problematic task, as factors such as education and income do not directly affect respiratory health. Associations between SES and a wide variety of asthma-related factors including obesity, smoking status, and physical housing conditions have been reported, indicating that SES may influence respiratory health through its effects on intermediary risk factors which in turn impact asthma. In contrast to the substantial body of research on environmental and personal risk factors, few asthma epidemiology studies have focused on the more distal influence of SES, with even fewer considering potential sex differences in SES effects. In general, evidence from the limited adult research that has been conducted on the associations between SES and asthma is inconclusive due to conflicting results, potential biases, limited generalizability as a result of participant selection methods, and different measurements of SES, asthma and confounding factors.

A recent literature review highlighted the multilevel nature of the mechanisms through which the social environment may act to influence asthma.[34] While evidence supporting the association between low SES and increased asthma morbidity in previously diagnosed asthmatics was fairly strong, relationships between SES and newly developed asthma were less clear. The review did not examine sex differences, and the relevance of the review's findings to adult asthma is uncertain since the lack of adult studies on the topic forced the review to focus on childhood asthma.[34]

National Population Health Survey data from Canadians 12 years and older were used to examine sex-specific associations between self-reported asthma and low-, middle- and high-income adequacy categories that represented household income adjusted for the number of people living in the household.[77] Compared to middle-income survey participants, low-income participants were approximately 25 to 30% more likely to report having physician-diagnosed asthma, while high income participants were 20 to 25% less likely. These results were similar for both men and women. The trend of increasing asthma prevalence with decreasing household income adequacy is interesting, but the fact that almost one-quarter of the survey participants did

not provide income information means that the results must be interpreted with caution due to the potential for bias. No significant association was found between income adequacy and 2-year cumulative incidence of asthma for men or women in this study.[77] A nationally-representative U.S. survey showed a similar association between SES and asthma, with low SES adult participants approximately 25% more likely to report current physician-diagnosed asthma than adult participants who were not low SES.[91] Low SES participants were defined as those who had not completed Grade 12 and/or who had an annual household income less than $15,000, and the association between SES and asthma remained the same after adjusting for sex and several other demographic and behavioural factors.[91] In contrast to this suggestion of an association between low SES and asthma, a German study that measured SES with a composite score derived from household income, education, and occupation found that high SES parents were significantly more likely to report prevalent asthma than low SES parents (OR = 1.738, 95% CI = 1.078, 2.801).[92] However, these results were not sex-specific and were obtained from unadjusted analyses.[92]

Data from a cross-sectional study performed in California between 1964 and 1972 indicated the possibility of divergent relationships between SES and different adult asthma subtypes.[93] For both women and men, higher education levels were positively associated with asthma with hay fever, but negatively associated with asthma without hay fever.[93] With regards to sex differences, the strength of association between education levels and asthma did reveal minor variations between men and women when they were grouped according to hay fever status.[93] The positive gradient in hay fever participants was steeper among men, while the negative gradient in participants without hay fever was steeper among women.[93] The suggestion of an SES gradient that differs for allergic and non-allergic asthmatic adults is interesting, but the importance of these findings is uncertain since the data is old, hay fever status was determined by participant self-reports, and all study members were selected from a prepaid healthcare program.

Given the paucity of research that has examined SES effects on adult female and male asthma, it is also constructive to examine sex-specific findings from studies that examined other health outcomes. Many studies have highlighted sex differences in the relationship between SES and health, with men generally showing steeper and more consistent socioeconomic gradients in health than women.[94] In contrast, some studies have failed to find sex differences in the

associations between traditional SES variables and health.[95-97] A recent Canadian example of such research was a longitudinal analysis of middle-aged respondents to the Canadian National Population Health Survey (1994-2003) that used household income adequacy, education and employment variables to examine the impact of temporal changes in SES on general health outcomes for men and women.[97] Sex and changes in socioeconomic status were shown to independently influence chronic health conditions and psychological distress even after adjusting for covariates representing social structure, health-related behaviours and psychosocial factors.[97] Women had poorer health outcomes than men, with poorer health also experienced by participants who experienced a reduction in income adequacy.[97] However, no sex differences were found for the effect sizes of temporal SES changes on health outcomes, as interaction terms between sex and SES factors were not significant.[97]

Several authors have suggested that the inconsistent results for sex differences in socioeconomic health gradients may be due to the relationship varying according to several factors such as age, marital status, measurement of SES, and health outcomes examined.[98-100] Traditional SES measures such as income and education have also been criticized for the questionable assumption that they impact both men and women equally. As mentioned previously, additional variables have been proposed for use in SES measurement that appear to be more sex-specific, including marital status and housing factors.[32,53]

No studies were found that explicitly examined the relationship between marital status and adult asthma. However, several studies have explored the relationship between marital status and health, with a range of hypotheses about the different behavioural, financial, social, and physiological mechanisms through which marital status may impact male and female health.[99,101,102] In general, marriage has shown a protective health effect for both sexes, with the degree of protection usually markedly larger for men than women.[101] A Finnish study showed that sex differences in the socioeconomic mortality gradient existed only for married women, whereas single, divorced and widowed women showed a similar gradient to men.[99] Research findings have further suggested that mental and physical health outcomes are influenced by the complex interrelations of sex and marital status with a variety of other factors such as age, SES, parental status, work roles, health-related behaviours, and social factors such as community support.[102-105] Lone parents, the large majority of whom are women, have been singled out as a group that suffers disproportionately in terms of negative mental health outcomes and

socioeconomic status.[105,106] Given the increasing interest in the impacts of mental health[107] and SES on adult asthma, it is important to consider the potential role that marital status might play in shaping sex-specific associations between SES and health.

Participant reluctance to disclose personal details often limits the ability of researchers to obtain information about traditional socioeconomic variables such as income. Therefore, the use of housing-related factors to measure SES is an interesting and practical option. Study participants may be less hesitant to provide information about their housing situation compared to more personal income or wealth information. Furthermore, the connections of housing security and housing quality with health are plausible and intuitive. However, since housing-related factors can potentially influence health through overlapping pathways featuring both physical and psychological factors, the independent effects of housing on health can be difficult to measure and interpret. The multidimensional aspects of housing have resulted in researchers from a broad range of disciplines reviewing the role of housing as an important social determinant of health.[108-112]

The potential for associations between housing-related SES factors and adult respiratory health has not been thoroughly investigated, with most researchers simply adjusting for housing characteristics while analyzing the relationships between health outcomes and other specific exposures. An exploratory study of 533 adult residents of English public sector dwellings showed an association between higher numbers of self-reported respiratory symptoms and several SES housing factors including: increased age of housing, living in a 'bad' versus 'good' housing area, and living in an apartment versus a house.[113] The only sex-specific housing and respiratory health study located was a British cross-sectional population study of partnered parents with children under one year old.[32] This study found that self-reported crude prevalence of wheeze was significantly higher in both mothers ($p<0.001$) and fathers ($p<0.01$) who lived in council house/rented accommodation compared to those living in owner occupied/mortgaged accommodation, but the authors did not report specific prevalence values or effect sizes for comparisons.[32] For mothers, the effect of relative deprivation on wheeze was only partially mediated by paternal smoking, while for fathers the effect appeared to be independent of the social risk factors examined (i.e. poor housing conditions and parental smoking behaviour).[32]

In contrast to the previously-described respiratory study, a cross-sectional Canadian study that investigated self-reported general health outcomes did show sex differences in associations

between several housing-related factors and fair/poor self-rated health in adult residents of Vancouver.[114] Male and female multivariable logistic regression models were constructed in a sequential manner from blocks of variables (i.e. sociodemographic characteristics, housing characteristics, dwelling satisfaction, neighbourhood satisfaction, housing demand/control, meaningful housing dimensions, and social support and stress) using pre-specified criteria for variable inclusion.[114] The final sex-specific models showed that: the female model had higher explanatory power than the corresponding male model; fair/poor self-rated health was strongly and significantly associated with several socioeconomic-related housing factors in women (i.e. living in rental housing, higher levels of crowding, dissatisfaction with sunlight, and high levels of housework strain); and a significant association with fair/poor health in men was found for only a single housing factor in an unexpected direction (decreased crowding).[114]

Another Canadian cross-sectional study of Vancouver residents reported associations between several specific housing-related psychosocial factors (i.e. housing tenure, length of residence in neighbourhood, and hating to be at home) and self-reported general and mental health outcomes, but potential sex differences in these associations were not investigated.[115] Housing tenure was strongly and significantly associated with health, as renters were approximately twice as likely to report poor general or mental health compared to owner-occupiers, associations that remained after controlling for age, sex, education, household demand/control, and neighbours.[115] Social support may have partially mediated the health effects of housing tenure, as addition of social support factors to the fully adjusted models resulted in attenuation of the effect size and significance of housing tenure, particularly for self-reported mental health. The same research group conducted a Needs, Gaps and Opportunities Assessment (NGOA) that examined housing as a socioeconomic determinant of health in Canada.[116] The NGOA exposed the scarcity of research on the topic, emphasized the importance of investigating the multidimensional roles of housing in the health of vulnerable subgroups, and called for more research on the intersection of SES aspects of housing with the more well-known physical housing risk factors.[116]

Researchers who performed longitudinal analyses of a 1958 birth cohort study in Great Britain downplayed the possibility of a 'health selection' or reverse causality process accounting for associations between housing and health.[108] Instead, they concluded that several housing-related variables (e.g. non-self-contained accommodation and dissatisfaction with living

arrangements) increased the odds of poor health in 33-year-old cohort members, an effect that was independent from genetic, social, and behavioural factors. Their investigation of potential longitudinal housing deprivation 'pathways' further suggested that current housing and childhood housing were the most important influences on adult health, rather than a cumulative impact of housing conditions over the entire lifecourse.[108]

As illustrated by the studies described above, housing tenure (i.e. owner, renter, and/or public housing) has been commonly used by researchers as a crude proxy for the psychosocial dimension of housing. A literature review of the health impacts of housing summarized a wide variety of theories proposed by researchers to explain the association between housing tenure and health.[32] Some researchers regarded housing tenure as an indicator of social position to be used alongside income, education, and occupation measures, while others viewed housing as a health-enabling resource made accessible through the greater income earning potential of higher social positions. Similar theories exist for psychological characteristics, with arguments for psychological wellbeing both enabling and resulting from secure housing arrangements. In general, home ownership has been described as positively impacting health through a wide variety of complex psychosocial pathways including factors such as increased sense of pride, self-identity, security, control, permanence, and belonging.[117]

For studies without access to detailed information about housing tenure, housing stability, or housing/neighbourhood satisfaction, alternative housing measures have been used that were judged suitable to the local setting. For example, a study of U.S. asthmatic children investigated the associations of allergen concentrations with single family versus multiple family homes,[118] while an English study compared respiratory conditions in people living in 'bad' versus 'good' housing areas, and different apartment types versus houses.[113] A study of housing-related stressors and health in the United Kingdom confirmed a strong link between dwelling type and housing tenure by showing that the significantly greater amount of housing stressors reported by tenants versus owner-occupiers could be largely explained by the association between housing tenure and dwelling type (i.e. substantially higher proportions of owner-occupied houses and renter-occupied apartments/other dwelling types).[119] The same study supported the use of housing type as an independent health-related variable by demonstrating a persistent association between housing type and poor mental health outcomes even after controlling for the combined effects of housing tenure, housing stressors, income, neighbourhood, area assessment, and sex.[119]

2.2.3 Environmental factors and sex

Some studies have shown specific household environmental factors to have stronger associations with asthma in women compared to men. Several reasons for these sex differences have been suggested, including biological differences in susceptibility to allergens and irritants, and increased exposure as a result of sociocultural differences that lead to many women spending more time in the home environment than men.[7]

2.2.3.1 Home dampness

A recent review of the association between respiratory health and indoor dampness and mould included a meta-analysis of five studies of adult wheeze.[26] Although the magnitude of association was slightly lower than for children and the confidence intervals were wider (likely due to the limited sample size), adults reporting exposure to indoor dampness were estimated as being 40 percent more likely to experience wheezing than adults not exposed to indoor dampness (OR = 1.39, 95% CI: 1.04, 1.85).[26] The limited number of studies reporting sex-specific associations meant that this review was not able to perform sex-specific meta-analyses, instead combining data from both single and mixed-gender studies that met the study criteria.[26] Finally, although current asthma and ever asthma were also examined in this review, the limited number of adult asthma studies prohibited the calculation of adult-specific effect estimates.[26] Another review performed in 2001 presented age- and sex-stratified results from selected studies, with adult asthma and wheeze again showing strong associations with self-reported indoor dampness.[120] Adjusted odds ratios presented from the two studies that presented sex-stratified results indicated the potential for sex differences in the association between indoor dampness and asthma. However, both studies were relatively small cross-sectional surveys that could not rule out over-reporting of symptoms by occupants of damp homes or vice versa, particularly in the case of the pilot study that was prompted by home occupants' concerns about the health impacts of home dampness.[25,121]

One Canadian study analyzed questionnaire data from almost 15,000 parents of primary school children.[122] Although sex comparisons were limited by the fact that over 80% of the parents were female, the main conclusion was that self-reported home dampness and mould were significantly associated with lower respiratory symptoms of parents. Another Canadian study, performed in 1993 in the same population investigated by the current study (Humboldt, Saskatchewan), showed that women reporting damp housing were more likely to report

wheezing symptoms and respiratory allergies, while damp housing was not associated with male respiratory health.[54]

2.2.3.2 Farming

A substantial amount of research has examined the interrelationships between farming exposures, allergies, and respiratory health. For the purposes of this discussion, farming-related exposures that have been shown to impact atopy and asthma will be broadly divided into two categories: living on a farm, and occupational farm exposures.

Living on a farm. von Mutius and Radon (2008) have recently reviewed the international evidence for the effects of farm-living on asthma development and progression.[123] They found that children living on farms have consistently shown lower atopy and asthma prevalence than non-farm rural children, and similar protective associations for atopy have been demonstrated for both farm-dwelling adults and adults who lived on farms during childhood.[123] Suggestions for possible mechanisms include increased animal contact and consumption of unpasteurized milk, with the role of animal contact less convincing for adults than children.[123] Investigations into the role of farm living on adult asthma have yielded more variable results, with Canadian, New Zealand, and Norwegian studies showing significant protective associations between current farm living and adult asthma, while no such associations were found in a Danish study or in other European studies examining childhood farm exposure.[123]

Studies that examined temporal patterns of farm living have shown that childhood farm life may modify the effects of adult farm residence, with adults who live on a farm during both life stages showing markedly reduced risks of adult atopy.[123] As previously mentioned, similar associations between childhood/adulthood farm living and adult asthma have not been consistently demonstrated. However, the authors of the review suggest that this may be due to differences between atopic and nonatopic adult asthma subtypes since few studies stratify asthma by atopic status, and farming-related exposures (e.g. endotoxins) may act as risk factors for the development of nonatopic asthma but not atopic asthma.[123]

Sex-specific associations for farm residence and adult asthma have not been widely investigated in Canada. However, a rural Quebec cross-sectional study of farm and nonfarm adolescents (635 girls and 564 boys, 12 to 19 years old) suggested a potential sex difference for the association between farm living and current asthma (presence of both self-reported wheeze in past year and airway hyperresponsiveness on methacholine testing).[124] Rural girls raised on a

farm were significantly less likely to have asthma than rural girls not raised on farm (5.9% versus 11.4%, p = 0.01), whereas the difference between farm and nonfarm boys was not significant (4.3% versus 6.6%, p = 0.26).[124]

While contemplating these research results, one must be mindful of the immense variations in farm types and upbringings that occur on global, national, regional, and even local levels. Such contextual differences can result in highly variable exposures of farm dwellers to different types and intensities of farm-related asthma risk factors and protective agents, as illustrated by a rural Australian study that showed protection against atopy for children living in a town with mixed livestock and crop farms but no such association for children from a crop-only farming town.[125] Therefore, research results obtained from farm settings similar to the target population should be emphasized.

Working on a farm. In contrast to the beneficial allergic and respiratory health effects associated with farm residence, research on occupational exposure to farm environments has mainly focused on negative farm-related respiratory impacts. The impacts and potential pathophysiological mechanisms of a wide variety of agricultural respiratory hazards including bacterial endotoxins, dusts, and other substances have been widely investigated and are a field of active and ongoing research. Details about these specific substances and their respiratory effects are beyond the scope of this thesis and have been reviewed by Kirkhorn and Garry (2000).[30] von Mutius and Radon briefly reviewed the impact of occupational farm exposures on asthma, again noting the potential differences in risk factors for atopic and nonatopic adult asthma.[123] Although many studies did not stratify asthma by atopic subtypes, the combined evidence (mostly European research) suggested that occupational farm exposures might increase the risk of nonatopic asthma while being protective for atopic asthma.[123]

Farm work environments are not homogeneous, with crop and animal farmers exposed to very different work conditions and risk factors. Even within animal farmers, exposure to different types of livestock and rearing systems has been shown to impact adult asthma differently. A comprehensive multi-country European cross-sectional study in 20 to 44-year-old crop and animal farmers demonstrated the complexities involved in examining the multidimensional impacts of occupational farm exposures on respiratory health.[126] Considering only the asthma and asthma-like syndrome measures investigated by the study, farmers as a group were significantly less likely to report asthma symptoms than the general population,

while pig farmers reported a higher prevalence of work-related respiratory symptoms than poultry, cattle, and sheep farmers.[126] Further analyses showed a dose-response relationship with daily hours spent working inside swine confinement facilities associated with increased prevalence of respiratory symptoms, while all types of farmers showed fewer respiratory symptoms in facilities with better ventilation.[126]

Sex differences in the prevalence of work-related farm exposures are known to exist due to a markedly higher proportion of males than females working in most farming-related jobs. However, few studies have examined the potential for sex-specific associations between occupational farm exposures and respiratory health. A Canadian cross-sectional study performed in Saskatchewan examined female and male commercial swine workers and non-farming controls, and suggested the possibility of increased susceptibility of atopic females to work-related exposures.[127] Atopic female swine workers showed a significantly greater prevalence of asthma than nonatopic female swine workers ($p = 0.03$), a difference that was not seen in male swine workers or control groups of either sex.[127]

Previous analyses of the data used in this thesis (Humboldt 2003 adults) showed that grain and/or livestock farmers had a lower prevalence of atopy and asthma than non-farmers, although the adjusted association was only statistically significant for atopy (OR = 0.73, 95% CI = 0.58, 0.93).[128] Separate analyses for men and women, grain farmers versus non-grain farmers, and livestock farmers versus non-livestock farmers did not reveal any further patterns or associations. Research performed in the same geographical population over a decade earlier showed a significantly increased risk of asthma for grain farmers in men but not women.[129]

2.2.3.3 Household pets

Most of the epidemiological evidence for the association between pet exposure and asthma has arisen from studies on children, with a recent meta-analysis of case-control and cohort studies on the subject only finding four case-control studies that examined adult asthma.[130] Of these adult studies, only one reported a significant association between pets and asthma, with exposure to any furry pet increasing the risk of asthma by 70%.[130] A Canadian longitudinal study found that an increased risk of incident asthma was only present for female smokers who also had pets in their household, showing a 150% increased risk compared to female smokers without pets.[46] Interpretation of findings from cross-sectional studies that have

examined this topic is difficult due to the strong possibility of bias caused by asthmatics choosing not to have pets.

2.2.3.4 Gas cooking

A sex-related effect of gas cooking on wheezing symptoms has been inconsistently observed. Combined data from European Community Respiratory Health Survey centres that had adequate variation in cooking fuel to allow for analyses suggested that wheeze in females was positively associated with gas cooking.[131] Smoking status appeared to modify the association, as female non-smokers who used gas cooking were more likely to report wheeze than female smokers who cooked with gas.[131] These associations were not found for the United States centre or the other two non-European centres in the study, and no such associations were found for males.

2.2.4 Personal factors and sex

Overweight/obesity and smoking status are both well-known risk factors for adult respiratory health conditions including asthma and wheeze. However, the etiological pathways and interrelationships with other biological, personal, environmental and socioeconomic risk factors have yet to be determined. Investigations have examined whether sex differences exist for asthma associations with personal factors such as body weight and smoking, with some sex-related patterns emerging from the growing body of literature.

2.2.4.1 Overweight/obesity

Several studies with different study designs, methods of measuring participant body size, and asthma definitions, have reported that women who were classified as overweight/obese had a significantly higher risk of asthma than women who were not overweight, with adjusted odds ratios generally between 1.5 and 3.5.[19,40,41,43,75,76] Men from the same studies did not show an association between overweight/obesity and asthma. Body mass index (BMI) was the most commonly used measure of overweight status, with waist circumference and self-report of body silhouette size also demonstrating associations between larger body sizes and asthma in women. Findings from a European modified case-control study showed that the clinical severity of asthma significantly increased with BMI in women, with hormonal factors (age at menarche) modifying this association.[42] No association between BMI and asthma was seen in men.

Pathophysiological mechanisms for these sex-specific associations remain unclear, with suggestions that obesity may indirectly influence asthma through its impact on progesterone levels.[76] Several sources of bias could also influence study results, including diagnostic or reporting bias if exercised-induced dyspnea caused by obesity is more likely to be misinterpreted as asthma for females than males. Another potential source of bias that could impact this association is differential self-report of body condition by sex. However, this explanation is unlikely since associations reported by longitudinal and cross-sectional studies that used objective methods to measure body size[41,43] were of similar or greater magnitude to the studies that used subjective self-report methods.[19,40,76] Cross-sectional studies that find associations between overweight/obesity and prevalent asthma cases cannot exclude the possibility of reverse causation, since asthma may cause individuals to modify their exercise patterns and become overweight as a result. However, a New Zealand birth cohort study that showed an association between increased female BMI and asthma did not show an association between childhood asthma and adult obesity, therefore refuting the hypothesis that the association between BMI and asthma was mediated by reduced physical activity.[43]

2.2.4.2 Smoking status

Female smokers, but not male smokers, were shown to have an increased risk of asthma in some studies.[46,75,76] A Canadian cross-sectional study found that female smokers were 60% more likely to have physician-diagnosed asthma compared to female non-smokers.[76] As previously mentioned, the presence of household pets has been shown to modify the association between female smoking status and asthma, increasing the risk of asthma for female smokers but not for female non-smokers.[46] Smoking has also been shown to modify the effects of other environmental factors (e.g. gas cooking)[131] on asthma, suggesting that interactions between personal and environmental factors may play a role in some sex-related associations.

It remains unknown whether there are sex-specific pathophysiological differences that are responsible for an increased susceptibility to smoke in females. When evaluating alternative explanations for this association, sex-related diagnosis bias is particularly important to recognize, as females and males presenting to physicians with similar clinical histories and symptoms are more likely to be diagnosed as having asthma and chronic obstructive pulmonary disease, respectively.[132]

2.3 Summary

Asthma is a chronic inflammatory disorder of the airways that encompasses a heterogeneous group of respiratory disorders. The complex pathophysiological mechanisms of asthma and its different subtypes remain unclear despite intensive research efforts. Due to this uncertainty, there is no accepted "gold standard" for measuring asthma and epidemiology studies have used several different subjective and objective measures, including self-reported physician diagnosis of asthma.

Sex differences in asthma development, progression, and occurrence have been widely recognized. Sex-related associations of specific risk factors with adult asthma are a more recent area of investigation. The majority of adult asthma studies adjust for sex as a confounding factor without further investigation of potential sex-specific effects. Some studies indicate an increased susceptibility of women to personal and household risk factors, while few studies have examined the potential for sex-related associations between SES and adult asthma.

Associations of demographic and biological factors with asthma have been well-documented. Age-specific sex differences in asthma occurrence show boys with higher asthma rates than girls during childhood, while adult women have higher asthma rates than men. Atopy appears to be a strong risk factor for adult asthma. However, many questions remain about the mechanisms that link atopy and adult asthma, particularly with regards to potential pathophysiological differences and sex-related aspects of atopic versus nonatopic asthma. Asthma has a strong familial disposition which is less clear in adults than children, and gene-environmental interactions are being intensively examined with ongoing asthma genetics research.

Socioeconomic status has been shown to impact a wide range of physical and mental health outcomes in a wide variety of populations. Evidence from the few studies that have explicitly examined SES and adult asthma has been inconclusive due to conflicting results, the use of different SES and outcome measures, study designs with potential biases and limited generalizability, and inadequate control for confounding factors. Although studies have not consistently found interactions between SES and sex, SES has been repeatedly associated with sex-related risk factors such as obesity. Debate exists as to whether traditional SES measures such as income, education and occupation accurately reflect the sex-specific mechanisms through which adult asthma develops. Variables such as housing tenure and home type have

been proposed as important and practical SES factors that capture some of the psychosocial aspects of housing, thereby potentially representing more sex-specific SES effects. Connections between the psychosocial dimensions of housing and general/mental health have been demonstrated, but little is known about the potential for sex-specific associations. There is also a lack of research specifically investigating the relationship between psychosocial housing factors and adult respiratory health.

Several environmental factors in the household and workplace have been shown to impact adult asthma. Some researchers have suggested that certain household environmental factors have a larger impact on female asthma than male asthma, offering both biological and sociocultural explanations for these differences. Farm-related environmental exposures have also been the focus of much asthma research, with evidence suggesting a protective effect of farm residence. The roles of occupational farm exposures are less clear and could vary for atopic and nonatopic adult asthma subtypes. In general, intensive and prolonged exposures to many animal and crop farming environments have been reported to increase adult asthma symptoms. Recent Canadian research has suggested the possibility of a female-specific association between atopy, swine farming, and asthma susceptibility. However, since farm-related occupations usually have a markedly higher proportion of men than women, most studies have limited power to examine sex-specific associations between occupational farm exposures and respiratory health.

Research into personal asthma risk factors has revealed the most consistent sex-related patterns. Many studies have shown strong and significant associations between overweight/obesity and asthma in adult females, while similar associations have not been demonstrated for males. Several studies have also reported a sex-specific association for smoking and asthma, suggesting that females may be more susceptible to the negative respiratory effects of smoke.

Table 2.1: Summary of selected studies that examined sex-related associations with adult asthma or wheeze.

Refer-ence	Study year(s), location, and design	Adult Sample	Outcome measure(s)	Main Findings	Comments
Chen et al., 2007[128]	2003 Canada Cross-sectional	18 – 79 yrs Women n=1,175 Men n=906	**Ever-asthma**: Asthma that had ever been diagnosed by a physician during the patient's lifetime.	• For both sexes, farmers and non-farmers were equally likely to report ever-asthma.*	For both sexes, farmers were less likely to be atopic than non-farmers.
Chen et al., 2005[41]	2003 Canada Cross-sectional	18 – 79 yrs Women n=1,161 Men n=896	**Recent asthma**: "During the past 12 months, has a doctor ever said you had asthma?" **Ever-asthma**: Asthma that had ever been diagnosed by a physician during the patient's lifetime.	• Women had higher prevalence of ever-asthma and recent asthma (10.0% and 6.0%) than men (5.7% and 2.7%). • **Obese** women (measured BMI ≥ 30 kg/m^2) were more likely to report recent asthma (OR = 3.47, 95% CI: 1.64, 7.32) and ever-asthma (OR = 2.06, 95% CI: 1.42, 4.05) compared to women with a BMI of < 25 kg/m^2. **Overweight** women (BMI 25.0 to 29.9 kg/m^2) were more likely to report recent asthma (OR = 3.23, 95% CI: 1.57, 6.99) than women with a BMI of < 25 kg/m^2. † • Women with larger **waist circumferences** (WC ≥100 cm) were more likely to report recent asthma (OR = 1.95, 95% CI: 1.11, 3.43) and ever-asthma (OR = 1.87, 95% CI: 1.18, 2.98) than women with WC < 100cm. • Men did not show any significant associations between BMI or WC and asthma.	

* Analyses adjusted for age, sex, household size, number of bedrooms, pets at home, income, educational level, smoking status, alcohol use, and BMI.
† Analyses adjusted for age, household size, number of bedrooms, pets at home, respiratory allergy, income, educational level, smoking status, and alcohol use.

Refer-ence	Study year(s), location, and design	Adult Sample	Outcome measure(s)	Main Findings	Comments
Rennie et al., 2005 [54]	1993 Canada Cross-sectional	18 – 74 yrs Women n=1120 Men n=878	**Chronic wheeze**: "Does your chest ever sound wheezy or whistly most nights?" **Wheeze with SOB**: "Have you ever had an attack of wheezing that has made you feel short of breath?"	• Men had significantly higher prevalence of chronic wheeze than women (55.3% vs. 44.7%). • Women reporting **damp housing** were more likely to have chronic wheeze (OR = 3.04, 95% CI: 1.41, 6.60), and wheeze with shortness of breath (SOB) (OR = 1.85, 95% CI: 1.08, 3.17) than women who did not report damp housing. Although the association with recent asthma was not significant (OR = 2.61, 95% CI: 0.96, 7.09), the wide CI and the lower limit approaching 1.0 suggested that an association might have been found if the study power had been higher.* • Men did not show any significant associations between damp housing and wheeze.	Women reporting damp housing were also more likely to have a history of respiratory allergy.
Hancox et al., 2005[43]	1972 to 1998 Dunedin, New Zealand Longitudinal	26 year- old sample at 10th follow-up since birth (1998) Women n=481 Men n=499	**Current asthma**: Diagnosed asthma with symptoms within 12 months. **Asthma with airway hyperresponsiveness**: Current asthma and specified FEV_1 changes with methacholine or salbutamol. **Current wheeze**: More than two episodes of wheezing lasting more than 1hr in the previous year.	• Females had a lower prevalence of asthma than men from age 9 to 15, and a higher prevalence from age 18 to 26. • Females with higher measured **BMI** were more likely to have current asthma (OR = 1.14, 95% CI: 1.05, 1.23), asthma with airway hyperresponsiveness (OR = 1.20, 95%CI: 1.04, 1.39), and current wheeze (OR = 1.12, 95% CI: 1.07, 1.18).† • Separate data analyses at all ages showed that the female BMI-asthma association was only significant at age 26, but seemed to begin during the late teens. The BMI-wheeze association in females was significant from age 15 onward and was apparent at all ages. • Males did not show any significant associations between BMI and asthma or wheeze. • The authors reported that similar sex-specific associations between BMI and asthma were observed in the parents of study participants.	No evidence of reverse causation, as childhood asthma did not increase the risk of becoming overweight as an adult.

* Analyses adjusted for age, education, family history of asthma, smoking status, grain dust exposure, working status, and pets.
† Odds ratios represent the change in odds of asthma or wheeze for *each* kg/m^2 unit increase in BMI. Analyses were performed across 9-26 years, and adjusted for breastfeeding, birth order, parental asthma, personal smoking, family smoking, and maternal smoking during pregnancy.

Refer-ence	Study year(s), location, and design	Adult Sample	Outcome measure(s)	Main Findings	Comments
Romieu et al., 2003[19]	1990 to 1993 France Longitudinal	40 – 65 yrs at baseline Women only n=67,229	**Incident asthma case**: "Did you have an asthma attack?" Negative answer at baseline (*ever*), and affirmative answer during follow-up (*since baseline*).	• Women with a self-reported **BMI** of ≥27 and 24.62-26.99 had increased risks of incident asthma (OR = 2.02, 95% CI: 1.38, 2.98; and OR = 1.46, 95% CI: 1.01, 2.12, respectively) compared to women with a BMI of 20.2-21.4.[*] • Women with the largest (≥5) self-reported **body silhouettes** [represented by eight figure drawings] at baseline had increased risks of incident asthma (OR = 1.82, 95% CI: 1.28, 2.59) compared to women who chose the two smallest silhouette drawings.[†] • Women who reported gaining two or more body silhouette sizes between the age of 20 years and baseline had increased risks of incident asthma (OR = 1.89, 95% CI: 1.37, 2.60) compared to women with no silhouette change.[‡]	Limited generalizability: low response rate, participants all members of a national health insurance plan for teachers, and a higher proportion of women who were excluded from the analysis had allergies than those included.
Chen et al., 2002[40]	1994 to 1997 Canada Longitudinal	20 – 64 yrs at baseline Women n=4,883 Men n=4,266	**Incident asthma case**: "Do you have asthma diagnosed by a health professional?" Negative answer at baseline, and affirmative answer during follow-up.	• Women had a higher 2-year cumulative incidence of asthma than men (2.9% vs. 1.6%). • Women with a self-reported baseline **BMI** of ≥30.0 were more likely (OR = 1.92, 95% CI: 1.09, 3.41) to report incident asthma during the 2-year follow-up period than women with a BMI of 20.0-24.9.[§] • Men did not show any significant associations between BMI and asthma.	

[*] Analyses adjusted for age, total caloric intake, physical activity, smoking status, and menopausal status.
[†] Analyses adjusted for age, total caloric intake, physical activity, smoking status, menopausal status, and use of nutritional supplements.
[‡] Analyses adjusted for age, total caloric intake, physical activity, smoking status, menopausal status, use of nutritional supplements, and body silhouettes at age 20 years.
[§] Analyses adjusted for age, smoking, pet(s) at home, immigrant status, history of allergy, income adequacy, and alcohol drinking.

Refer-ence	Study year(s), location, and design	Adult Sample	Outcome measure(s)	Main Findings	Comments
Chen et al., 2002[46]	1994 to 1997 Canada Longitudinal	>20 yrs at baseline Women n=6,889 Men n=5,747	**Incident asthma case:** "Do you have asthma diagnosed by a health professional?" Negative answer at baseline, and affirmative answer during follow-up.	• The 2-year cumulative incidence of asthma was higher in women than men, with the most pronounced differences in the young and middle-aged (12 to 54 yrs). • In women, the presence of **household pets** acted as an effect modifier on the association between **smoking** and asthma.* -Among women *with* household pets, smokers were more likely to report incident asthma during the 2-year follow up period (OR = 2.50, 95% CI: 1.24, 5.05) than non-smokers. -For women *without* household pets, smokers did not have a significantly increased risk of asthma (OR = 0.95, 95% CI: 0.49, 1.85). • Men did not show any evidence of an effect of smoking, pets, or interaction of any other risk factors with smoking on asthma. • For both sexes, participants with a history of allergy had a greatly increased risk of asthma.	
Chen et al., 1999[76]	1994-1995 Canada Cross-sectional	≥12 yrs Women n=9,557 Men n=8,048	**Asthma:** "Do you have asthma diagnosed by a health professional?"	For participants 25 years and older: • Women with a self-reported **BMI** of ≥28 and 25.0-27.9 were more likely to have asthma (OR = 1.89, 95% CI = 1.33, 2.68; and OR = 1.81, 95% CI: 1.22, 2.68) compared to women with a BMI of 20.0-24.9.† • Women **smokers** were more likely to have asthma (OR = 1.61, 95% CI: 1.17, 2.21) than women non-smokers. • Men did not show evidence of an effect of BMI or smoking on asthma. • For both sexes, participants with allergies or low income adequacy were significantly more likely to report asthma than participants without allergies or with high income adequacy.	

* Analyses adjusted for age, immigrant status, and history of allergy. Similar interactive effect when adjusted for income adequacy and baseline BMI.
† Analyses adjusted for age, immigrant status, history of allergy, income adequacy, BMI, and smoking status.

Refer-ence	Study year(s), location, and design	Adult Sample	Outcome measure(s)	Main Findings	Comments
Chen et al., 2002[77]	*Prevalence:* 1996-97 *Cumulative incidence:* 1994-95 & 1996-97 Canada Cross-sectional	≥12 yrs *Prevalence*: Women n=88,721 Men n=84,311 *Cumulative incidence*: Women n=6,889 Men n=5,747	**Prevalent asthma:** "Do you have asthma diagnosed by a health professional?" **Incident asthma:** Reported no asthma in 1994-95, but reported asthma in 1996-97.	• Women had higher prevalence of asthma (7.9%) than men (5.7%). • For both sexes, lower **income adequacy** was associated with higher prevalence of asthma. With middle income adequacy as the reference group, lower income men and women were 1.30 times (95% CI: 1.00, 1.68) and 1.26 times (95% CI: 1.08, 1.47) as likely to report current asthma, respectively. Higher income men and women were 26% and 21% less likely than middle income participants to report current asthma (male OR = 0.74, 95% CI: 0.63, 0.87; female OR = 0.79, 95% CI: 0.70, 0.91).* • No significant association between income adequacy and 2-year cumulative incidence of asthma for men or women.	Potential for bias: 23% of male and female study participants used in prevalent asthma analysis did *not* provide income adequacy information.
Beckett et al., 2001[75]	1985 to 1995 U.S.A. Longitudinal	18 – 30 yrs at baseline Women n=2,498 Men n=2,049	**Current asthma**: "(1) Subject taking medication typically used to treat asthma; failing this, (2) reporting at one examination taking a medication not typically used to treat asthma, but reporting at a later examination taking a medication typically used to treat asthma; failing this, (3) self-reported doctor or nurse diagnosis of asthma."	• Baseline prevalence was slightly higher in men compared to women, while 10-yr cumulative incidence was almost 1.5 times higher in women compared to men for both African American (10.5% vs. 6.7%) and white participants (9.7% vs. 5.4%). • **Active smoking** was significantly associated with asthma in women but not in men, and in African Americans but not whites. • **BMI** at year 10 and change of BMI (time period not specified in paper) were significantly associated with asthma in women but not in men.	Multivariable results for specific risk factors were *adjusted* for sex throughout the paper, with sex-stratified results mentioned in the text without ORs. Sex-specific results for physical activity were not mentioned.

* Analyses adjusted for age, allergic history, household size, and number of bedrooms.

METHODOLOGY

The data used in this study were previously collected in 2003 by a cross-sectional respiratory study performed in Humboldt, Saskatchewan, Canada. The study was supported by a grant from the Canadian Institutes of Health Research (MOP#57907). The original study was approved by the University of Saskatchewan Research Ethics Board (BMC#02-633), and written informed consent was completed by every study participant (see Appendix A).

3.1 Original Study

Details of the original study have been previously published.[41] The adult portion of the study targeted all 18 to 79 year old residents of the rural town of Humboldt. 2090 adults (71% of the target population) participated in the study, almost all of whom were Caucasian. Self-administered questionnaires (see Appendix B) were distributed to eligible adult residents, with canvassers contacting and requesting participation from adults living in town, while mail surveys were used to contact adults living in the rural municipality. Study participants returned completed surveys at their health screening visits in town, during which additional clinical information was collected (see Appendix C). Self-reported information included data on respiratory symptoms, family medical history, demographic factors, income, education, occupation, living environment, alcohol consumption, and smoking habits. Objective information was collected on lung function, atopic status by skin prick tests to specific allergens, height, and weight during the clinical examination that also included blood for genetic studies, measurement of waist circumference and blood pressure. The last three clinical measures were not examined in the present study.

3.2 Present Study

3.2.1 Study sample

This study is a secondary data analysis of the self-reported and clinical data obtained from the total adult study population of 2090 described above.

3.2.2 Dependent variables

Self-reported ever asthma and current asthma were investigated separately, with their respective comparison groups consisting of adults who did not meet the following definitions. *Current asthma* was defined as a positive response to the survey question, "During the past 12 months, has a doctor ever said you had asthma?". *Ever asthma* was asthma that had ever been diagnosed by a doctor during a patient's lifetime, determined by a positive response to the current asthma question and/or to the question, "Before the past 12 months, has a doctor ever said you had asthma?". Both asthma definitions were considered because misclassification of childhood asthma status due to poor recall by adults (i.e. false negatives for ever asthma) has been shown to be very common, particularly in women.[133] The use of current asthma (a subcategory of ever asthma) reduces the likelihood of such misclassification and also increases the possibility that current exposures such as house type and household dampness temporally preceded the development of asthma. Self-reported physician diagnosis of asthma has been used in previous studies of the Humboldt study population,[41,54,128,134] and has been widely used to define asthma in other epidemiological studies.[25,59,60,135,136] Self reports of asthma in the Humboldt population have also been shown to have a high level of validity when compared with pulmonary test variables calculated from objective measures of forced expiratory flow and forced vital capacity.[73]

3.2.3 Independent variables

Table 3.1 describes the demographic and biological factors, socioeconomic factors, environmental factors, and personal factors included in the analyses. All variables except height, weight and atopy were self reported by questionnaire. The definition of atopy was chosen to allow comparability of results between studies, and because use of this definition has been shown to result in a greater estimate of the population attributable risk due to atopy compared to definitions that require more than one positive skin prick test per person.[85] The four specific allergens were selected because sensitization is most common for these aeroallergens. Income data could not be used in this analysis to assess socioeconomic status because of the high proportion of participants who did not provide their income. Well-known physical housing risk factors such as dampness are included in the environmental factors category, while house type is considered as an overarching socioeconomic factor. The purpose of this simplistic categorization is to provide structure for the analyses and discussion, as the causal pathways for the impact of

different housing-related factors on health are almost certainly interdependent. Farming exposure was originally considered for use as an independent variable*: 'In the last 5 years have you grown or handled wheat, durham, oats, barley, flax, rapeseed, rye, mustard, alfalfa, or other grain, seeds, or legumes?*' or *'In the last 5 years have you worked at looking after cattle, hogs, sheep, poultry, horses, or other livestock animals?'*. However, the farming exposure and grain dust variables were found to be highly correlated ($r = 0.73$, $p<0.001$), so the decision was made to use the more specific grain dust variable for further analyses in order to avoid multicollinearity.[137]

Table 3.1: Definitions of independent variables examined in analyses.

Category	Factor	Definition
Demographic and biological factors (Potential confounders/ predetermined risk factors)	• Age	• Self-reported (years)
	• Atopy	• Positive skin prick test to one or more of the following common allergens: *Alternaria tenius*, *Dermatophagoides pteronyssinus* (house dust mite), Fel d (feline saliva allergen), or mixed grasses. Raised wheals to allergens were considered positive when they were ≥3 mm of the saline control.[138]
	• Parental asthma history	• 'Has (did) your biological father/mother had (have) asthma?'(Y/N)
Socioeconomic factors (Distal)	• Education	• 'What is the highest grade completed in school?' (Grade 12 completed or less; Postsecondary – attended or completed trade school/college)
	• Home type	• 'Which best describes the building in which you live?' (Standard – one-family house not attached to any other house; Other – mobile home, trailer, one-family house attached to other house(s), or building for two or more families)
	• Marital status	• 'What is your marital status?' (Married/Common law; Other – single, widowed, separated or divorced)

Category	Factor	Definition
Environmental factors (Intermediate)	*Home*	
	• Household dampness	• 'Does your house have any damage caused by dampness (e.g. wet spots on walls or floors)?' (Y/N)
	• Ever lived on a farm	• 'Have you ever lived on a farm?' (Y/N)
	• Household pets	• 'Have you ever had any pets [dogs, cats, birds] living inside your home?' (Y/N)
	• Passive smoking	• 'Except for you, does any family member smoke cigarettes regularly in your home at present?' (Y/N)
	Work	
	• Grain dust exposure	• 'Have you ever been exposed to grain dust in your work?' (Y/N)
Personal factors (Proximal)	• Body mass index	• Body mass index calculated from objective clinic measurements of height and weight (Normal weight < 25 kg/m^2; Overweight/Obese ≥ 25 kg/m^2)
	• Alcohol use	• 'Do you presently use alcohol beverages? If YES, is this as often as: 1, 2, or 3+ days per week?' (Regular drinker – reported drinking alcoholic beverages ≥ 1 day/week; Abstainer/Infrequent drinker – reported no drinking *or* < 1 day/week)
	• Smoking status	• Current smoker – smoked ≥ 20 packs of cigarettes during lifetime *and* reported smoking every day or almost every day at the time of the survey. Ex-smoker – had been a regular daily smoker, but had quit for at least 6 months at the time of the survey. Never smoker: smoked < 20 packs in lifetime.

3.2.4 Ethics approval

The University of Saskatchewan Behavioural Research Ethics Board approved this study (BMC#02-633). This 'Below Minimal Risk Protocol' study did not involve contact or interaction with the original study participants. The principal investigators of the *Exposure to Endotoxin and the Lung Study* (Dr. Dosman and Dr. Rennie) approved the secondary data analysis performed by this M.Sc. study and supplied de-identified data from the adult participants of the Humboldt portion of their study. Data confidentiality was maintained by locked storage and computer password-protection. This study did not involve access to the questionnaires, as all specific data

queries that required access to the original surveys were addressed by Dr. Rennie. The approval letter from the University of Saskatchewan Behavioural Research Ethics Board appears in Appendix A.

3.2.5 Sample size

Research question: **What socioeconomic, environmental and personal factors are associated with asthma in men and women?** A main objective of this study was to determine the sex-specific associations of specific factors with adult asthma. The analysis was carried out on data that had been previously collected from 1177 females and 913 males. Power calculations were performed in order to determine whether collected data from these study participants would provide enough statistical power to detect meaningful relationships between exposures and asthma.

The dichotomous exposure considered in these calculations was atopy, with a prevalence of atopy in skin-tested male and female study participants of 31% (n=271) and 29% (n=325), respectively (44 men and 46 women were not tested for atopy). The significance level was set at 0.05 ($\alpha = 0.05$), with a statistical power of approximately 0.80 ($\beta = 0.20$) considered a reasonable level. An odds ratio of 2.0 would indicate a clinically meaningful association between atopy and asthma. Stata's *sampsi* command was used to calculate power:

sampsi #1 #2, n1(#) n2(#) (3.1)

where: *#1* = proportion of unexposed (nonatopic) group with outcome

#2 = proportion of exposed (atopic) group with outcome

n1(#) = size of unexposed (nonatopic) group

n2(#) = size of exposed (atopic) group.

Ever asthma. *Females*: From participant data, it was known that 8.4% of nonatopic women reported ever asthma, 806 women were nonatopic, and 325 women were atopic.

In order to calculate whether there was sufficient power to detect an odds ratio of 2.0, the proportion of ever asthma in the exposed (atopic) group (P_1) was calculated:[139]

$$P_1=P(Y=1|x=1)\frac{2.0*0.084}{(1-0.084)+2.0*0.084}=\frac{0.168}{1.084}=0.155 \quad (3.2)$$

Substituting the numbers into Stata syntax (3.1):

sampsi 0.084 0.155, n1(806) n2(325); power = 0.91

suggests that there will be sufficient power to detect an odds ratio of 2.0.

Males: The same calculations and assumptions were used for males, with 271 atopic males and 598 nonatopic males (3.7% of whom reported ever asthma). Using equation (3.2) with OR=2.0, P_1=0.071.

sampsi 0.037 0.071, n1(598) n2(271); power = 0.52

This estimate suggests that, due to the lower prevalence of asthma in men and the smaller male sample size, there may not be sufficient power to detect this effect. If the power calculations are performed substituting an OR of 2.5, P_1=0.088:

sampsi 0.037 0.088, n1(598) n2(271); power = 0.80

This is an acceptable level of power. This suggests that, in males, analyses may not be able to detect significant effects between atopy and ever asthma if the odds ratio is less than 2.5.

Current asthma. *Females*: From participant data, it was known that 5.2% of nonatopic women had ever asthma, 806 women were nonatopic, and 325 women were atopic. Using equation (3.2) with OR=2.0, P_1=0.099.

Substituting these numbers into Stata syntax (3.1):

sampsi 0.052 0.099, n1(806) n2(325); power = 0.76

shows that the level of power is slightly less than 0.80, but may be sufficient to detect odds ratios greater than 2.0.

Males: There were 271 atopic males and 598 nonatopic males (2.0% of whom reported current asthma). Using equation (3.2) with OR=2.0, P_1=0.040:

sampsi 0.020 0.040, n1(598) n2(271); power = 0.34

This estimate suggests that, due to the lower prevalence of current asthma in men and the smaller male sample size, there will not be sufficient power to detect this effect. Repeated power calculations with increasing proportions of current asthma in exposed males showed that the power would only be adequate to detect markedly higher magnitudes of association (OR $\geq$ 3.5).

The results from the male calculations must also be interpreted with caution, since the small sample size and proportions mean that the normal approximation to the binomial is likely inaccurate.

Taken together, these calculations suggest that there is sufficient power to examine associations for ever asthma and current asthma in females. In males, there are limitations imposed by the male sample size and low asthma prevalence, especially for current asthma.

3.2.6 Data analysis

3.2.6.1 Asthma prevalence in the study population

The prevalence of self-reported ever asthma (during participant's lifetime) and current asthma (during 12 months prior to survey) in male and female study participants was calculated by age groups and overall. Chi-square (χ^2) tests for proportions or trend were used for formal statistical comparisons.

3.2.6.2 Comparisons of asthma risk factor distributions in men and women

Sex-specific descriptive statistics were calculated and presented for all independent variables. Sex comparisons of categorical variables were performed using χ^2 or Fisher's exact tests (if the expected cell frequency was less than five), while Student's t-test was used for the continuous age variable. Stratified comparisons of socioeconomic factors by broad age groups were used to further examine general patterns in the data.

3.2.6.3 Socioeconomic, environmental and personal factors associated with asthma in men and women

Univariable analyses. Unadjusted odds ratios and 95% confidence intervals were calculated for independent variables to evaluate the strength, direction, and significance of their statistical associations with ever asthma and current asthma. The continuous age variable was transformed (Age/10) so that estimates of the measure of association would represent more meaningful units (change in odds of asthma for every 10-year increase in age).

Multivariable logistic regression analyses and model-building strategy.

Conceptual framework. Analyses were based on a conceptual framework composed of three categories of adult asthma correlates (see Figure 3.1). These categories were based on modified groupings of selected population health determinants recognized by the Public Health Agency of Canada (i.e. income and social status, education and literacy, physical environments, and personal health practices and coping skills).[140] The importance of biology and genetic

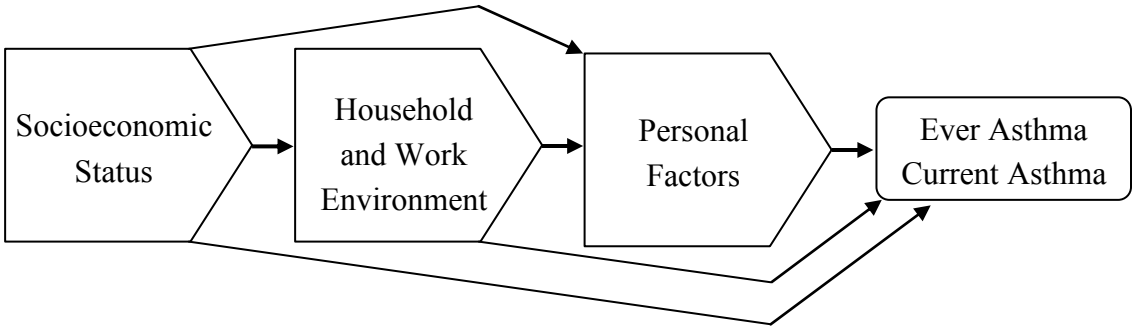

Figure 3.1: Conceptual framework for multivariable analyses of adult asthma correlates.

endowment as a key health determinant was also acknowledged by the adjustment of the logistic regression models for relevant biological and heritable covariates, while the role of gender was recognized by the sex-specific logistic regression models that were based on the conceptual framework. In order to guide the analyses in this study, the conceptual framework features only a few hypothetical etiological pathways, and should not be misinterpreted as a comprehensive attempt to represent the etiology of adult asthma.

This framework is based on the premise that adult asthma is impacted by multiple layers of interrelated factors. The distal category is comprised of socioeconomic factors (i.e. education, marital status, and home type), the intermediate category includes household and occupational environmental conditions (i.e. exposure to household dampness, pets, smoke, farm life, and grain dust), and the proximal category encompasses more immediate personal factors (i.e. body mass index, smoking status, and alcohol use). The arrows in the model represent the multiple routes through which the factors comprising the different categories are hypothesized to directly and indirectly impact adult asthma. The framework also explicitly demonstrates the assumption that some of the effects of socioeconomic factors on adult asthma are mediated through environmental and personal factors, with environmental factors mediated by personal factors. Several plausible causal pathways exist in which the more proximal factors mediate the effects of distal factors. For example, low socioeconomic status could contribute to increased household dampness which then impacts asthma, or low socioeconomic status could contribute to increased overweight/obesity which then impacts asthma.

Multivariable logistic regression models for current asthma and ever asthma were constructed using variables from each category of the proposed conceptual framework. Sex-specific models were constructed in order to investigate differences in associations between men and women. The model-building strategy used a well-defined and consistent approach based on a combination of methods proposed by Hosmer and Lemeshow (2000), Massons and Pastor (2006), and Victora *et al.* (1997).[137,139,141] The aim was to use the conceptual framework to build models for ever asthma and current asthma in men and women. All models were adjusted for age, parental history of asthma, and atopic status as well-known confounders and risk factors for adult asthma.

Variable selection. Variables were selected as candidates for the multivariable model based on their biological plausibility and previous findings from studies that examined socioeconomic, environmental and/or personal correlates of adult respiratory health. At each stage of the model-building process, likelihood ratio tests (LRTs) were used to assess nested models to determine whether a model with an additional variable or set of variables provided a significantly better fit than the constrained model. If the LRT indicated that the additional variable(s) did add significantly to the model, the variable was retained in the interest of best fit, while variables that did not contribute significantly were excluded from the model in the interest of parsimony. A significance level of $\alpha = 0.10$ was used for final variable selection in order to avoid excluding variables that were potentially important to the overall model. Variables were also retained if their presence/absence meaningfully changed the estimates of other variables in the model. Pairwise correlations between independent variables were used to reject the possibility of multicollinearity problems in the models ($r < 0.40$). The models were built according to the steps outlined below, with all variables considered in step one regardless of the significance of their univariable associations with asthma. Steps one through four were repeated separately for male and female ever asthma and current asthma models. The sequential steps of the variable selection process are summarized in Table 3.2.

Step one. Each variable was initially evaluated by comparing a logistic regression model that was adjusted for age, parental history of asthma, and atopy (base model) with a model that also included the additional variable. Variables with LRTs with p-values < 0.25 were retained for the next step.[139] The exception to this rule was the socioeconomic variable 'education', as this variable was forced into every model due to its overriding theoretical significance.

Table 3.2: Summary of variable selection process for multivariable logistic regression models.

	Selection process
Main effects model	
Demographic and biological factors	• Age forced into all models as an important pre-established confounder. • Atopy and parental asthma history included in all models as well-known risk factors for adult asthma.
Socioeconomic factors	• Education forced into all models due to its theoretical significance. • *Step one:* LRT p-value < 0.25 when variable added to base model (i.e. model that includes demographic and biological variables). • *Step two:* LRT p-value < 0.10 when variable added to category-specific model (i.e. model that includes all base model variables and other socioeconomic variables selected in step one).
Household and work environmental factors	• *Step one:* same as above. • *Step two:* same as above except with environmental variables in category-specific model.
Personal factors	• *Step one:* same as above. • *Step two:* same as above except with personal variables in category-specific model.
Preliminary final model	
Product terms ▪ Age × SES ▪ SES × Environment	• *Step three:* LRT p-value < 0.10 when product term added to the main effects model (i.e. model that includes all demographic and biological, socioeconomic, environmental and personal variables selected in previous steps).
Final model	
	• *Step four:* combined all variables and product terms that met the selection criteria for either female or male preliminary final models. This was performed separately for ever asthma and current asthma, resulting in a separate comprehensive set of variables and product terms for ever asthma and current asthma final models.

Step two. Remaining variables were then evaluated within category-specific models (i.e. models with only the socioeconomic variables, environmental variables, or personal variables selected in step one, and all models also adjusted for age, atopy and parental asthma history). The subset of variables with LRT p-values of < 0.10 within each category were retained along with 'education' to form the *preliminary main effects model*. Each excluded variable was then re-examined for the possibility of a previously unseen contribution to a better model fit that occurred only in the presence of variables from all categories. This was done by assessing each variable's re-entry into the preliminary main effects model for the impact on other model parameters and LRT significance. The variables remaining after this step formed the *main effects model*.

Step three. The potential for effect modification was assessed by individually entering product terms to the main effects model. Theoretically meaningful interactions that were chosen for assessment included the following product terms: age × all retained 'main effect' SES variables (i.e. age × education, age × home type), and all retained SES variables × all retained environmental variables. Interactions with LRT p-values of < 0.10 were retained. The combination of variables and interactions after this step formed the *preliminary final model*.

Step four. The variable selection process was performed separately for female and male study participants, resulting in different sets of variables in the preliminary final models for women and men. In order to operationalize the conceptual framework for both sexes and facilitate sex comparisons, all variables and interactions that had been chosen for either the male or female preliminary final models were combined for each asthma definition (i.e. ever asthma and current asthma). This resulted in two comprehensive sets of independent variables and product terms (a slightly different set for each asthma definition) to be used by both sexes as the *final models* for ever asthma and current asthma.

Model analysis. Models for current asthma and ever asthma were constructed separately for men and women. All base models included age, parental history of asthma, and atopy. Variables selected for the final models in the process outlined above were then entered in sets according to the predefined conceptual framework: (1) distal socioeconomic factors, (2) intermediate environmental factors, (3) proximal personal factors, and finally (4) product terms. The likelihood ratio test was used to compare the fit of each model to the previous model. Model fit was assessed and diagnostics were performed to evaluate the assumption of linearity for the

continuous variable (age), goodness of fit of the model, and potential for outliers or influential observations. LRT p-values were also calculated to determine the significance of individual variables and interaction terms within each model.

Product term analysis. The "moderator approach" described by Jaccard (2001)[142] was used to conceptualize and interpret the interactions found for current and ever asthma models. Significant product terms between a continuous and categorical variable (age and home type) were investigated through simple additive transformations to the continuous variable. These transformations involved the subtraction of a chosen number ('x') from the original age variable, and the creation of a new product term between the newly transformed age variable and home type. When the transformed variable and its product term were substituted into Model 4, the odds ratio and 95% confidence intervals obtained for home type reflected estimates that were specific to women aged 'x' years when fully adjusted for all other model variables. Models were identical aside from the transformed age variables and product terms, with estimates for all other variables and significance of the overall model consequently remaining unchanged in comparison to Model 4. This process was repeated to produce estimates of the association between home type and asthma at 10-year intervals between the ages of 20 and 70 years. Odds ratio and confidence interval estimates from these analyses were then plotted sequentially by age on a logarithmic scale. All analyses were performed with Intercooled Stata 9.2 (StataCorp, Texas).

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RESULTS

This chapter commences with a description of asthma prevalence in the study population. The distributions of demographic and biological, socioeconomic, environmental, and personal risk factors in males and females are then examined. This is followed by results from sex-specific univariable and multivariable logistic regression analyses for ever asthma and current asthma that form the major analyses addressing the study research question.

Of the total of 2090 adults aged 18 to 79 years who participated in the 2003 Humboldt study, 1177 (56.3%) were women and 913 (43.7%) were men. The response rate to the survey was 71% of the target population.

4.1 Asthma Prevalence in the Study Population

The overall prevalence of ever asthma and of current asthma in the study population was 8.3% and 4.7%, respectively. Compared to men, a significantly higher proportion of women (10.2% of women versus 5.8% of men) had been ever diagnosed with asthma and 6.2% of women versus 2.8% of men reported physician-diagnosed asthma during the past twelve months (see Figure 4.1). When age was categorized by approximately 20 year intervals, sex differences in asthma prevalence were present in all age groups, with greater proportions of women than men consistently reporting both ever asthma and current asthma (Figures 4.2 and 4.3). The variations in asthma prevalences ranged in magnitude from 1.6 times greater proportions of women than men reporting ever asthma in 40 to 59 year olds, to 2.5 times more women reporting current asthma than men in the 60 to 79 year age category.

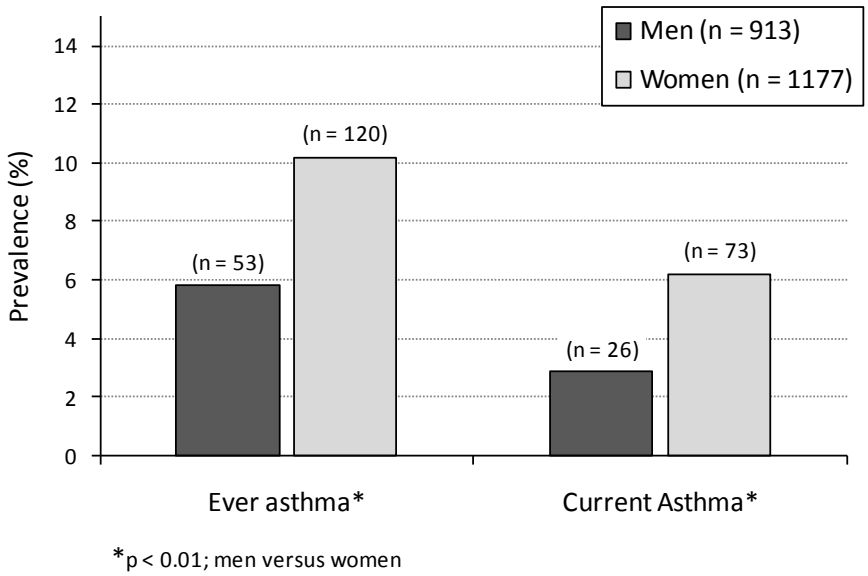


Figure 4.1: Prevalence of ever asthma and current asthma in men and women.

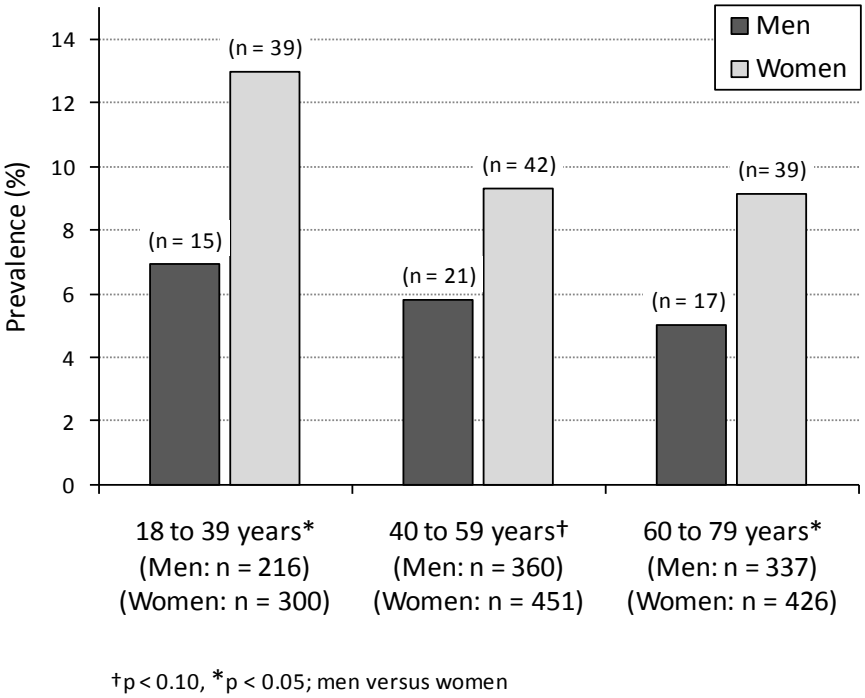
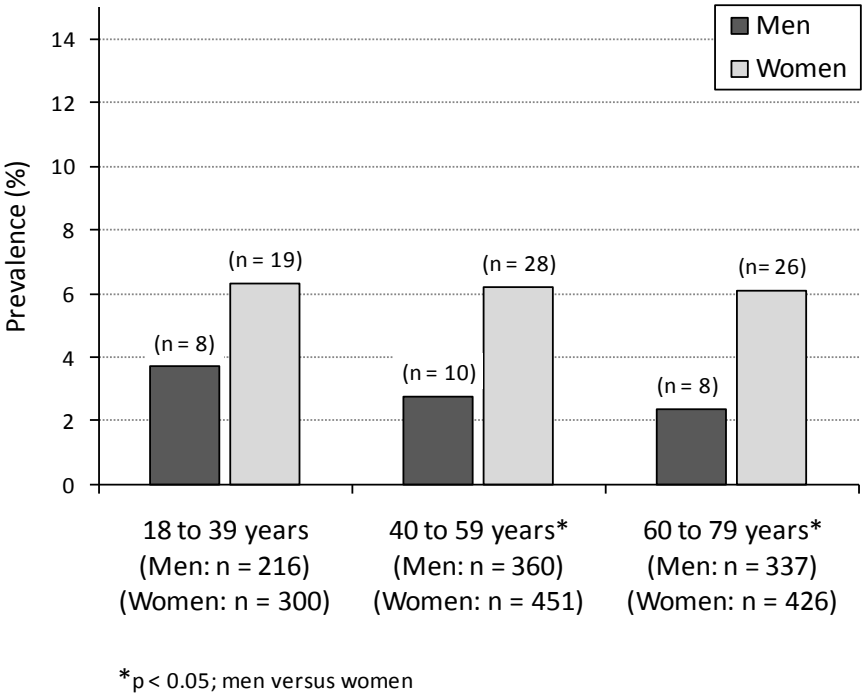


Figure 4.2: Prevalence of ever asthma in men and women by age group.



*p < 0.05; men versus women

Figure 4.3: Prevalence of current asthma in men and women by age group.

4.2 Characterization of the Study Population

A comparison of the demographic and biological factors, socioeconomic factors, environmental factors, and personal factors by sex are presented in Tables 4.1 to 4.5.

Demographic and biological factors. The sex-specific and overall distributions of age, parental history of asthma, and atopy in the study population are presented in Table 4.1. Age distributions were similar for females and males, with study participants of both sexes ranging from age 18 to 79 years, similar mean ages and standard deviations for women (51.5 ± 16.0 years) and men (52.4 ± 15.6 years), and median ages of 51 and 52 years, respectively. Parental history of asthma and atopy skin prick test results were also similar for men and women, with fewer than ten percent reporting a family history of asthma and approximately one-third testing positive for atopy.

Table 4.1: Comparison of demographic and biological factors by sex.

	Men (n=913)		Women (n=1177)		Total (n=2090)	
	mean	*(sd)*	*mean*	*(sd)*	*mean*	*(sd)*
Age, years	52.4	(15.6)	51.5	(16.0)	51.9	(15.8)
Parental history of asthma	*n*	*(%)*	*n*	*(%)*	*n*	*(%)*
no	840	(92.0)	1063	(90.3)	1903	(91.1)
yes	73	(8.0)	114	(9.7)	187	(8.9)
Atopy						
no	598	(65.5)	806	(68.5)	1404	(67.2)
yes	271	(29.7)	325	(27.6)	596	(28.5)
not tested	44	(4.8)	46	(3.9)	90	(4.3)

Socioeconomic factors. As shown in Table 4.2, the distributions of all three socioeconomic factors differed significantly by sex. A higher percentage of women (48.4%) than men (40.0%) reported some postsecondary education. The majority of male and female study participants lived in standard single family detached houses. However, women were significantly more likely than men (12.1% versus 8.7%) to live in mobile homes, trailers, attached houses or

multi-family dwellings. A significantly greater proportion of women (26.3%) were single, separated, divorced, or widowed compared with men (14.9%).

Table 4.2: Comparison of socioeconomic factors by sex.

	Men (n=913)		Women (n=1177)		Total (n=2090)	
	n	*(%)*	*n*	*(%)*‡	*n*	*(%)*
Education						
grade 12 or less	548	(60.0)	607	(51.6)***	1155	(55.3)
postsecondary	365	(40.0)	570	(48.4)	935	(44.7)
Marital status						
married/common law	777	(85.1)	868	(73.7)***	1645	(78.7)
other (single/separated/divorced/widowed)	136	(14.9)	309	(26.3)	445	(21.3)
Home type						
standard (1-family detached house)	834	(91.3)	1034	(87.9)*	1868	(89.4)
other (mobile/attached/multi-family)	79	(8.7)	143	(12.1)	222	(10.6)

‡ p-values for sex differences calculated with χ^2 tests.

* $p < 0.05$, *** $p < 0.001$

Stratification of data by broad age groups (18 to 39 years, 40 to 59 years, and 60 to 79 years) revealed a significant trend for reduced education levels in older age groups for both men and women (χ^2 tests for trend across age groups: $p < 0.001$). Significant sex differences in education were present for the youngest and oldest age groups, with higher proportions of women reporting postsecondary education (Table 4.3). Women and men aged 18 to 39 years were equally likely to be married/common law, with progressively lower proportions of women in married/common law relationships in the higher age groups. A significant sex difference in the frequency distribution of home type within age groups was present only for the oldest age group, with 16.4% of women versus 9.5% of men aged 60 to 79 years living in non-standard housing.

Table 4.3: Comparison of socioeconomic factors by sex and age group, n (%).

	18 to 39 years‡		40 to 59 years‡		60 to 79 years‡	
	Men (n=216)	Women (n=300)	Men (n=360)	Women (n=451)	Men (n=337)	Women (n=426)
Education						
grade 12 or less	98 (45.4)	107 (35.7)*	185 (51.4)	201 (44.6)	265 (78.6)	299 (70.2)***
postsecondary	118 (54.6)	193 (64.3)	175 (48.6)	250 (55.4)	72 (21.4)	127 (29.8)
Marital status						
married/common law	149 (69.0)	212 (70.7)	326 (90.6)	379 (84.0)**	302 (89.6)	277 (65.0)***
other	67 (31.0)	88 (29.3)	34 (9.4)	72 (16.0)	35 (10.4)	149 (35.0)
Home type						
standard	189 (87.5)	260 (86.7)	340 (94.4)	418 (92.7)	305 (90.5)	356 (83.6)**
other	27 (12.5)	40 (13.3)	20 (5.6)	33 (7.3)	32 (9.5)	70 (16.4)

‡ p-values for sex differences within age categories calculated with χ^2 tests.

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Environmental factors. The workplace environment showed the only significant environmental sex difference, with men more than twice as likely to report a history of exposure to grain dust at work compared with women (Table 4.4). With respect to household environmental exposures, a higher percentage of women (14.2%) reported household dampness compared with men (11.5%). Similar proportions of men and women reported ever living on a farm, ever having a pet inside their home, and currently having a family member smoking cigarettes regularly in their home (approximately 70%, 50% and 12%, respectively).

Table 4.4: Comparison of environmental factors by sex.

	Men (n=913)		Women (n=1177)		Total (n=2090)	
	n	*(%)*	*n*	*(%)* ‡	*n*	*(%)*
Household dampness						
no	808	(88.5)	1010	(85.8) †	1818	(87.0)
yes	105	(11.5)	167	(14.2)	272	(13.0)
Ever exposed to grain dust at work						
no	372	(40.7)	905	(76.9) ***	1277	(61.1)
yes	541	(59.3)	272	(23.1)	813	(38.9)
Ever lived on a farm						
no	266	(29.1)	348	(29.6)	614	(29.4)
yes	647	(70.9)	829	(70.4)	1476	(70.6)
Ever pet in home						
no	467	(51.2)	566	(48.1)	1033	(49.4)
yes	446	(48.8)	611	(51.9)	1057	(50.6)
Passive smoking						
no	809	(88.6)	1030	(87.5)	1839	(88.0)
yes	104	(11.4)	147	(12.5)	251	(12.0)

‡ p-values for sex differences calculated with χ^2 tests.

† $p < 0.10$, *** $p < 0.001$

Personal factors. All personal factors showed significant differences in their distributions for men and women (Table 4.5). Men were significantly more likely to report regular use of alcohol than women, with 61.3% of men drinking on more than one day per week versus 35.6% of women. Objective measurements of body mass index showed that more than seventy percent of all study participants were overweight or obese, with a significantly greater proportion of men (81.7%) overweight/obese compared to women (65.7%). A higher proportion of women were non-smokers, while more men were ex-smokers or current smokers.

Table 4.5: Comparison of personal factors by sex.

	Men (n=913)		Women (n=1177)		Total (n=2090)	
	n	*(%)*	*n*	*(%)*[‡]	*n*	*(%)*
Smoking status						
non-smoker	420	(46.0)	693	(58.9)***	1113	(53.3)
ex-smoker	368	(40.3)	350	(29.7)	718	(34.4)
smoker	125	(13.7)	134	(11.4)	259	(12.4)
Alcohol use						
abstainer/infrequent drinker	353	(38.7)	758	(64.4)***	1111	(53.2)
regular drinker (≥ 1 day/week)	560	(61.3)	419	(35.6)	979	(46.8)
Body mass index						
normal (< 25 kg/m^2)	160	(17.5)	392	(33.3)***	552	(26.4)
overweight/obese (≥ 25 kg/m^2)	746	(81.7)	773	(65.7)	1519	(72.7)
not measured	7	(0.8)	12	(1.0)	19	(0.9)

[‡] p-values for sex differences calculated with χ^2 or Fisher's exact tests.

*** $p < 0.001$

4.3 Research Question: What Socioeconomic, Environmental and Personal Factors are Associated with Asthma in Men and Women?

Ever asthma and current asthma were rare outcomes in male and female study participants, with the highest prevalence reaching 10.2% for ever asthma in women.

4.3.1 Univariable analyses for ever asthma and current asthma

Tables 4.6 – 4.13 present results from the univariable logistic regression analyses for independent variables from each category (demographic and biological, socioeconomic, environmental, and personal factors). The odds ratios and confidence intervals were obtained from unadjusted logistic regression analyses that were performed separately for each sex and each independent variable. The strength and significance of many associations varied by sex and by asthma definition.

4.3.1.1 Demographic and biological factors

Atopy was strongly and significantly associated with ever asthma in both men and women. The odds of ever asthma in atopic men was 2.78 times greater than nonatopic men,

while atopic women were 1.84 times as likely to report ever asthma than nonatopic women (Table 4.6). The relationship between atopy and current asthma was weaker and less certain for both men and women, with wider confidence intervals resulting in an estimate that lacked significance in men and was only of borderline significance in women (Table 4.7). Adults of both sexes were more than 2.5 times as likely to report ever asthma or current asthma if they had one or more biological parent with a history of asthma compared to those with no parental history of asthma, an association that was statistically significant in all cases. Age appeared to be mostly unrelated to asthma, with most confidence intervals spanning the null value. The only significant estimate suggested the presence of a protective effect in women with an estimated 12 percent decrease in odds of ever asthma for every 10-year increase in age, but this estimate must be interpreted with caution given its upper confidence limit of 0.99.

Table 4.6: Ever asthma: unadjusted odds ratios (OR) and 95% confidence intervals (95% CI) for demographic and biological factors in men and women.

	Men (n=913)	Women (n=1177)
	OR (95% CI)	OR (95% CI)
Age[†]	0.93 (0.78, 1.11)	**0.88 (0.79, 0.99)**
Atopy[‡]		
Nonatopic	1.00	1.00
Atopic	**2.78 (1.55, 5.00)**	**1.84 (1.23, 2.73)**
Parental history of asthma		
No	1.00	1.00
Yes	**2.94 (1.41, 6.13)**	**2.52 (1.52, 4.16)**

[†]Estimate represents the change in odds of ever asthma for every 10-year age increase.
[‡]Sample size was 869 for men and 1131 for women (excluded untested study participants).

Table 4.7: Current asthma: unadjusted odds ratios (OR) and 95% confidence intervals (95% CI) for demographic and biological factors in men and women.

	Men (n=913)	Women (n=1177)
	OR (95% CI)	OR (95% CI)
Age[†]	0.93 (0.72, 1.19)	0.95 (0.82, 1.10)
Atopy[‡]		
Nonatopic	1.00	1.00
Atopic	2.07 (0.90, 4.74)	**1.72 (1.04, 2.82)**
Parental history of asthma		
No	1.00	1.00
Yes	**2.87 (1.05, 7.84)**	**2.63 (1.44, 4.80)**

[†]Estimate represents the change in odds of current asthma for every 10-year age increase.
[‡]Sample size was 869 for men and 1131 for women (excluded untested study participants).

4.3.1.2 Socioeconomic factors

The main finding for the univariable associations between socioeconomic factors and asthma was the significant relationship between home type and asthma in women (Tables 4.8 and 4.9). Compared to women who lived in a standard one-family detached house, women who lived in other non-standard types of homes (i.e. trailers, mobile homes, attached houses or multiple-family houses) were 2.78 times as likely and 1.97 times as likely to report current asthma and ever asthma, respectively. Although the odds ratio estimates for men also indicated the potential for an increased risk of asthma with non-standard home types, these associations were not significant.

Education was not significantly related to asthma, with the exception of ever asthma in women. Women with postsecondary education were 50% more likely than women with grade 12 or less to report ever asthma. Marital status was not associated with asthma in either sex.

Table 4.8: Ever asthma: unadjusted odds ratios (OR) and 95% confidence intervals (95% CI) for socioeconomic factors in men and women.

	Men (n=913)	Women (n=1177)
	OR (95% CI)	OR (95% CI)
Education		
Grade 12 or less	1.00	1.00
Postsecondary	0.70 (0.38, 1.26)	**1.50 (1.03, 2.20)**
Marital status		
Married/common law	1.00	1.00
Other (single/separated/divorced/widowed)	1.02 (0.47, 2.21)	1.18 (0.78, 1.79)
Home type		
Standard (1-family detached)	1.00	1.00
Other (mobile, attached or multiple family)	1.67 (0.73, 3.82)	**1.97 (1.21, 3.21)**

Table 4.9: Current asthma: unadjusted odds ratios (OR) and 95% confidence intervals (95% CI) for socioeconomic factors in men and women.

	Men (n=913)	Women (n=1177)
	OR (95% CI)	OR (95% CI)
Education		
Grade 12 or less	1.00	1.00
Postsecondary	0.44 (0.18, 1.11)	1.31 (0.82, 2.11)
Marital status		
Married/common law	1.00	1.00
Other (single/separated/divorced/widowed)	1.37 (0.51, 3.71)	1.32 (0.79, 2.20)
Home type		
Standard (1-family detached)	1.00	1.00
Other (mobile, attached or multiple family)	2.62 (0.96, 7.14)	**2.78 (1.60, 4.85)**

4.3.1.3 Environmental factors

The environmental factor that showed the most consistent and strongest associations with asthma was household dampness (Tables 4.10 and 4.11). Study participants of both sexes had significantly higher odds of current asthma if their homes had damage caused by dampness compared to those who lived in homes without moisture damage (ORs = 2.97 and 2.46 for men and women, respectively). Although a similar association was present for women and ever asthma, there was not a significant association between household dampness and ever asthma in men.

No other environmental variables were associated with asthma in men, while a history of living on a farm showed a significant protective association with ever asthma in women. Women who had ever lived on a farm were 47% less likely to report ever asthma than women who had never lived on a farm. A comparatively weaker protective effect was also found for current asthma in women, with a confidence interval that included the possibility of no association.

Table 4.10: Ever asthma: unadjusted odds ratios (OR) and 95% confidence intervals (95% CI) for environmental factors in men and women.

	Men (n=913)	Women (n=1177)
	OR (95% CI)	OR (95% CI)
Household dampness		
No	1.00	1.00
Yes	1.63 (0.77, 3.44)	**2.36 (1.51, 3.69)**
Ever exposed to grain dust at work		
No	1.00	1.00
Yes	1.14 (0.65, 2.03)	0.73 (0.45, 1.18)
Ever lived on a farm		
No	1.00	1.00
Yes	0.86 (0.48, 1.57)	**0.53 (0.36, 0.78)**
Ever pet in home		
No	1.00	1.00
Yes	0.79 (0.45, 1.39)	1.07 (0.73, 1.56)
Passive smoking		
No	1.00	1.00
Yes	0.80 (0.31, 2.06)	1.47 (0.88, 2.45)

Table 4.11: Current asthma: unadjusted odds ratios (OR) and 95% confidence intervals (95% CI) for environmental factors in men and women.

	Men (n=913)	Women (n=1177)
	OR (95% CI)	OR (95% CI)
Household dampness		
No	1.00	1.00
Yes	**2.97 (1.22, 7.24)**	**2.46 (1.43, 4.23)**
Ever exposed to grain dust at work		
No	1.00	1.00
Yes	0.94 (0.43, 2.06)	0.57 (0.30, 1.10)
Ever lived on a farm		
No	1.00	1.00
Yes	0.77 (0.34, 1.75)	0.62 (0.38, 1.00)
Ever pet in home		
No	1.00	1.00
Yes	0.76 (0.35, 1.68)	1.07 (0.66, 1.72)
Passive smoking		
No	1.00	1.00
Yes	1.02 (0.30, 3.44)	1.73 (0.94, 3.19)

4.3.1.4 Personal factors

Personal factors showed the largest sex differences in univariable associations. Tables 4.12 and 4.13 show that body mass index (BMI) and alcohol use were strongly and significantly associated with ever asthma and current asthma in women, while significant associations were not found for men.

Overweight/obese women were almost twice as likely to report ever asthma and more than three times as likely to report current asthma compared to women with normal BMIs. On the other hand, women who reported drinking alcohol regularly (at least one day per week) were almost half as likely to have ever asthma or current asthma compared to female non-drinkers or women who drank alcohol less often than one day per week.

Table 4.12: Ever asthma: unadjusted odds ratios (OR) and 95% confidence intervals (95% CI) for personal factors in men and women.

	Men (n=913)	Women (n=1177)
	OR (95% CI)	OR (95% CI)
Body mass index[†]		
Normal (< 25 kg/m^2)	1.00	1.00
Overweight/obese (≥ 25 kg/m^2)	0.77 (0.39, 1.53)	**1.93 (1.22, 3.03)**
Smoking status		
Non-smoker	1.00	1.00
Ex-smoker	0.79 (0.43, 1.45)	0.94 (0.61, 1.45)
Smoker	0.86 (0.37, 2.03)	1.10 (0.61, 1.99)
Alcohol use		
Abstainer/infrequent drinker	1.00	1.00
Regular drinker (≥ 1 day/week)	0.96 (0.54, 1.69)	**0.55 (0.35, 0.84)**

[†]Sample size was 906 for men and 1165 for women (excluded unmeasured study participants).

Table 4.13: Current asthma: unadjusted odds ratios (OR) and 95% confidence intervals (95% CI) for personal factors in men and women.

	Men (n=913)	Women (n=1177)
	OR (95% CI)	OR (95% CI)
Body mass index[†]		
Normal (< 25 kg/m^2)	1.00	1.00
Overweight/obese (≥ 25 kg/m^2)	0.64 (0.25, 1.63)	**3.33 (1.69, 6.57)**
Smoking status		
Non-smoker	1.00	1.00
Ex-smoker	0.95 (0.41, 2.23)	0.67 (0.38, 1.18)
Smoker	1.12 (0.36, 3.55)	0.72 (0.32, 1.64)
Alcohol use		
Abstainer/infrequent drinker	1.00	1.00
Regular drinker (≥ 1 day/week)	0.86 (0.39, 1.89)	**0.49 (0.28, 0.86)**

[†]Sample size was 906 for men and 1165 for women (excluded unmeasured study participants).

4.3.1.5 Effect modification by sex

Simple logistic regression models for ever and current asthma were run separately for each independent variable. These models included sex, the independent variable being examined, and the product term between sex and the independent variable. Results from these models showed significant interactions between sex and numerous independent variables ($p<0.05$; data not shown). Given that sex acted as an effect modifier for associations between asthma and several variables, all multivariable analyses were stratified by sex.

4.3.2 Multivariable analyses

Sex-specific multivariable logistic regression models were constructed for ever asthma and current asthma, resulting in a total of four final models. As previously described in the methodology chapter, each model was built in a sequential manner with female and male models using the same set of variables and interaction terms for each asthma definition. Study participants who were not tested for atopy and/or did not have their body mass indices measured (53 women and 49 men) were excluded from the multivariable analyses due to their missing data.

The strength and statistical significance of the associations found for the variables included in the ever asthma and current asthma models differed markedly by sex. Female multivariable models showed significant associations for socioeconomic, environmental and personal factors with both asthma definitions. In addition to the main effects found for women, a significant multiplicative interaction between home type and age was found in both the ever asthma and current asthma models. Conversely, aside from atopy and parental asthma history, almost every variable and interaction appeared to be unrelated to male asthma. Only a single environmental factor, household dampness, emerged as a significant association in the final male multivariable model of current asthma. Aside from the expected influence of parental asthma history on asthma, the main congruence between sexes was the significant association between household dampness and current asthma in both female and male multivariable models.

Each multivariable model was constructed in a sequential manner with selected variables entered in categorical sets. This sequential process was followed in order to assess the changes in effect estimates due to confounding and/or the influence of mediating variables from other categories. No meaningful changes in odds ratio estimates of socioeconomic, environmental or personal factors were detected through the sequential model construction process for the male or

female multivariable models of ever asthma or current asthma (see Tables 4.14 to 4.17). The only sequential trend observed was for atopy in women, where a slight reduction in the magnitude of odds ratios was seen across models. Odds ratio estimates decreased from 1.69 to 1.41 for ever asthma and 1.60 to 1.22 for current asthma, but the importance of this trend is questionable since most of the estimates were not significant.

4.3.2.1 Ever asthma in women and men

Tables 4.14 and 4.15 show how the significant associations in the final multivariable models for ever asthma in both women and men paralleled those that were seen in the unadjusted univariable analyses. As demonstrated in Table 4.14, when the socioeconomic factors, environmental factors, personal factors, and product term were sequentially added during the model building process for women, likelihood ratio tests comparing each new model with the previous model revealed that each new set of variables contributed significantly to the model fit ($p \leq 0.01$). In direct contrast, although the demographic and biological base model for men had a significantly better fit than a model with only a constant ($p < 0.001$), none of the subsequent variable additions contributed significantly to the base model (Table 4.15).

Examination of the demographic and biological factors (included in all models regardless of statistical significance) showed that biological factors remained strongly and significantly related to ever asthma in men in the final model. Atopic men and men with a parental history of asthma were more than three times as likely to report ever asthma compared to men without atopy and men with no parental history of asthma (ORs = 3.03 and 3.36, respectively). Parental history of asthma was also significant in females with an odds ratio of 2.40, while atopic status was no longer significant after adjusting for all other factors in the final model. Since socioeconomic status was a critical component of the conceptual framework, education level was forced into the model.

Although education was not a statistically significant variable in the male or female ever asthma models, women with more education tended to have a higher risk of ever asthma when all other factors were controlled for (OR = 1.47; 95% CI: 0.97, 2.24), an association that approached statistical significance ($p = 0.07$).

Table 4.14: Multivariable logistic regression models for ever asthma in women (n = 1124).

	Base Model	Model 1	Model 2	Model 3	Model 4
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Demographic and biological factors (referent)					
Age (10-year intervals)	0.91 (0.81, 1.03)	0.93 (0.82, 1.06)	1.01 (0.88, 1.15)	0.95 (0.83, 1.09)	1.04 (0.89, 1.22)
Atopic (nonatopic)	**1.69*** (1.13, 2.54)	**1.63*** (1.08, 2.45)	1.51 (0.99, 2.28)	1.41 (0.92, 2.14)	1.41 (0.92, 2.15)
Parental history of asthma (no history)	**2.64***** (1.58, 4.42)	**2.55***** (1.51, 4.29)	**2.52**** (1.49, 4.27)	**2.37**** (1.39, 4.05)	**2.40**** (1.40, 4.10)
Socioeconomic factors (referent)					
Postsecondary education (grade 12 or less)†		1.41 (0.93, 2.13)	1.40 (0.92, 2.12)	1.45 (0.95, 2.20)	1.47 (0.97, 2.24)
Other home type (standard)		**2.06**** (1.23, 3.44)	**1.93*** (1.15, 3.26)	**1.94*** (1.15, 3.29)	**12.06***** (2.79, 52.16)
Environmental factors (referent)					
Household dampness (no dampness)			**2.05**** (1.26, 3.34)	**2.02**** (1.23, 3.30)	**1.92*** (1.16, 3.17)
Ever lived on farm (never lived on farm)			**0.59*** (0.39, 0.90)	**0.59*** (0.39, 0.91)	**0.60*** (0.39, 0.93)

	Base Model	Model 1	Model 2	Model 3	Model 4
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Personal factors (referent)					
Overweight/obese (normal BMI)				**2.06**** (1.27, 3.37)	**2.10**** (1.28, 3.44)
Regular drinker (abstainer/infrequent drinker)				**0.54**** (0.34, 0.85)	**0.53**** (0.33, 0.85)
Product term					
Home type × Age (10-year intervals)					**0.68**** (0.51, 0.92)
Log likelihood	-357.47	-352.93	-346.15	-337.68	-334.30
p-value (compared with previous model)	< 0.001	0.011	0.001	< 0.001	0.009

Significant variables: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

[†]Education variable forced into model due to theoretical significance.

Table 4.15: Multivariable logistic regression models for ever asthma in men (n = 864).

	Base Model	Model 1	Model 2	Model 3	Model 4
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Demographic and biological factors (referent)					
Age (10-year intervals)	0.98 (0.80, 1.20)	0.95 (0.78, 1.16)	0.98 (0.79, 1.22)	0.99 (0.80, 1.23)	0.99 (0.79, 1.26)
Atopic (nonatopic)	**2.99*** ** (1.62, 5.51)	**3.03*** ** (1.64, 5.60)	**3.03*** ** (1.63, 5.60)	**3.03*** ** (1.64, 5.62)	**3.03*** ** (1.64, 5.62)
Parental history of asthma (no history)	**3.38** ** (1.58, 7.22)	**3.38** ** (1.58, 7.25)	**3.39** ** (1.57, 7.30)	**3.36** ** (1.56, 7.26)	**3.36** ** (1.56, 7.25)
Socioeconomic factors (referent)					
Postsecondary education (grade 12 or less)†		0.65 (0.33, 1.26)	0.65 (0.33, 1.26)	0.64 (0.33, 1.26)	0.64 (0.33, 1.26)
Other home type (standard)		1.36 (0.51, 3.61)	1.36 (0.51, 3.61)	1.42 (0.53, 3.80)	1.57 (0.09, 26.19)
Environmental factors (referent)					
Household dampness (no dampness)			1.59 (0.68, 3.70)	1.58 (0.68, 3.68)	1.58 (0.68, 3.68)
Ever lived on farm (never lived on farm)			0.94 (0.47, 1.88)	0.95 (0.47, 1.89)	0.95 (0.47, 1.89)

	Base Model	Model 1	Model 2	Model 3	Model 4
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Personal factors (referent)					
Overweight/obese (normal BMI)				0.87 (0.40, 1.88)	0.87 (0.40, 1.88)
Regular drinker (abstainer/infrequent drinker)				1.20 (0.63, 2.29)	1.20 (0.63, 2.29)
Product term					
Home type × Age (10-year intervals)					0.98 (0.58, 1.67)
Log likelihood	-168.99	-167.97	-167.38	-167.17	-167.16
p-value (compared with previous model)	< 0.001	0.358	0.556	0.809	0.940

Significant variables: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

[†]Education variable forced into model due to theoretical significance.

When adjusted for all other variables in the final model (Model 4, Table 4.14), women who reported household dampness were approximately twice as likely to have a history of asthma than women who did not report dampness ($p < 0.05$). An association of similar magnitude and direction was also seen for overweight/obese women versus women of normal weight ($p < 0.01$). Significant protective associations with environmental and personal factors were found for ever asthma in women. Women who had lived on a farm at some point in their lives were 40% less likely to report ever asthma than women who had never lived on a farm, and regular drinkers were approximately 50% less likely to report ever asthma compared to abstainers/infrequent drinkers.

In females, a significant product term emerged between age and home type in Model 4, indicating the presence of effect modification on a multiplicative scale. This prevented direct interpretation of the odds ratios for the main effects of either of these variables as the association between home type and ever asthma differed according to a woman's age. In an attempt to further characterize the relationship between home type and age, the "moderator approach" for conceptualization and interpretation of interactions was followed.[142] The association of home type with ever asthma was the primary association of interest, with age acting as the moderator variable. The full female multivariable model (Table 4.14, Model 4) was used to calculate multiple age-specific odds ratios and 95% confidence intervals (see methodology section for a description of estimate calculation methods). Estimates were then plotted on a logarithmic scale to compare the odds of ever asthma in women who lived in 'other' housing with women who lived in standard housing. Figure 4.4 illustrates how the association of home type with ever asthma in women varied in magnitude, direction, and precision according to age.

The age-specific odds ratio estimates for home type and ever asthma show that living in 'other' homes versus standard homes was significantly associated with ever asthma for adult women younger than 50 years old. The magnitude of this association was largest for the youngest adults, with 20-year-olds in 'other' homes 5.6 times as likely as 20-year-olds in standard homes to report ever asthma. Although this estimate was statistically significant, the wide confidence interval for the odds ratio in this age group indicated a large degree of imprecision, with the true increase in odds due to home type likely to fall somewhere between 2.19 and 14.34. The magnitude of association decreased as age increased, with odds ratios of 30- and 40-year-old women estimated at 3.82 and 2.60, respectively. Odds ratio estimates decreased

by approximately one-third for every 10-year increase in age, a multiplicative factor of 0.68. The 95% confidence interval widths indicated a greater degree of estimate precision for women in the middle age groups (40 and 50 years old), with increasing uncertainty as the youngest and oldest ages were approached. The lower limit of the confidence interval for women aged 50 years was scarcely above one (95% $CI_{50\ yrs} = 1.01, 3.14$). Odds ratio estimates for women older than 50 years were not significant since all their 95% confidence intervals spanned the null value of one, therefore including the possibility of home type having no association with ever asthma, or acting as either a protective factor or a risk factor in women of these ages.

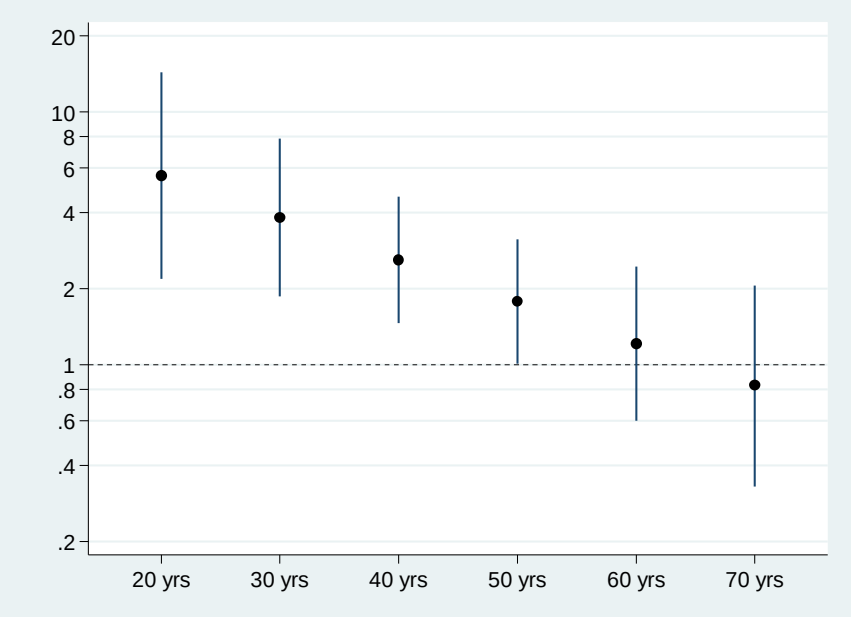


Figure 4.4: Ever asthma: fully adjusted odds ratio estimates and 95% confidence intervals for 'other' home type versus standard home type in women of different ages.

4.3.2.2 Current asthma in women and men

The variable selection process for current asthma multivariable logistic regression models resulted in an identical model to that of ever asthma with the exception of the variable 'ever exposed to grain dust at work' replacing 'ever lived on a farm'.

Multivariable logistic regression models for current asthma (Tables 4.16 and 4.17) showed many similarities with the ever asthma models. As observed for ever asthma, the additional variables in each sequential female current asthma model contributed significantly to model fit (Models 1-3: $p < 0.01$; Model 4: $p < 0.05$), while the male models revealed that only the base model was statistically significant in terms of contributing to a better model fit ($p = 0.028$). In contrast to male ever asthma where none of the sequential variable additions approached significance ($p > 0.35$ for Models 1 to 4), the addition of socioeconomic factors to the current asthma base model verged on contributing significantly to model fit ($p = 0.052$), with the subsequent addition of environmental factors showing a p-value of 0.128.

Female odds ratio estimates for atopy, parental history of asthma, education, alcohol use, and home dampness for current asthma did not differ notably from the values in the ever asthma model. Women who reported ever having been exposed to grain dust at work were 62% less likely to have current asthma compared to women who had not been similarly exposed (OR = 0.38; CI: 0.17, 0.82), similar in direction and magnitude to the association between ever living on a farm and ever asthma. Also, women who were obese/overweight were 3.72 times as likely to have reported current asthma compared to women of normal weight.

Most of the variables assessed in the final multivariable models for ever and current asthma in males were not significant. In contrast to male ever asthma, a strong and significant association between household dampness and male current asthma emerged, with men who reported home dampness more than three times as likely to have current asthma compared to men who did not have household dampness problems ($p < 0.05$). The associations of atopy and parental asthma history with current asthma were reasonably consistent in magnitude with those seen with ever asthma, although at a reduced level of significance ($p < 0.05$).

Table 4.16: Multivariable logistic regression models for current asthma in women (n = 1124).

	Base Model	Model 1	Model 2	Model 3	Model 4
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Demographic and biological factors (referent)					
Age (10-year intervals)	1.01 (0.86, 1.17)	1.02 (0.87, 1.20)	1.09 (0.93, 1.29)	1.01 (0.85, 1.19)	1.14 (0.93, 1.40)
Atopic (nonatopic)	1.60 (0.96, 2.66)	1.51 (0.90, 2.54)	1.38 (0.82, 2.33)	1.24 (0.73, 2.11)	1.22 (0.71, 2.09)
Parental history of asthma (no history)	**2.81**** (1.52, 5.20)	**2.64**** (1.41, 4.93)	**2.87**** (1.52, 5.40)	**2.61**** (1.37, 4.96)	**2.64**** (1.38, 5.04)
Socioeconomic factors (referent)					
Postsecondary education (grade 12 or less)†		1.42 (0.84, 2.39)	1.43 (0.85, 2.41)	1.48 (0.87, 2.51)	1.50 (0.88, 2.56)
Other home type (standard)		**2.83***** (1.57, 5.07)	**2.72***** (1.51, 4.89)	**2.77***** (1.52, 5.05)	**19.43***** (3.36, 112.25)
Environmental factors (referent)					
Household dampness (no dampness)			**2.39**** (1.30, 4.38)	**2.39**** (1.29, 4.43)	**2.28*** (1.21, 4.26)
Ever exposed to grain dust at work (not exposed)			**0.40*** (0.19, 0.86)	**0.37**** (0.17, 0.80)	**0.38**** (0.17, 0.82)

	Base Model	Model 1	Model 2	Model 3	Model 4
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Personal factors (referent)					
Overweight/obese (normal BMI)				**3.64*** ** (1.75, 7.59)	**3.72*** ** (1.77, 7.82)
Regular drinker (abstainer/infrequent drinker)				**0.47** ** (0.25, 0.86)	**0.46** ** (0.25, 0.84)
Product term					
Home type × Age (10-year intervals)					**0.68*** (0.48, 0.95)
Log likelihood	-252.84	-246.95	-240.53	-229.59	-226.96
p-value (compared with previous model)	0.004	0.003	0.002	< 0.001	0.022

Significant variables: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

[†]Education variable forced into model due to theoretical significance.

Table 4.17: Multivariable logistic regression models for current asthma in men (n = 864).

	Base Model	Model 1	Model 2	Model 3	Model 4
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Demographic and biological factors (referent)					
Age (10-year intervals)	0.91 (0.68, 1.21)	0.86 (0.65, 1.14)	0.92 (0.69, 1.24)	0.95 (0.70, 1.28)	0.89 (0.64, 1.25)
Atopic (nonatopic)	2.32 (0.96, 5.60)	**2.44*** (1.01, 5.91)	**2.47*** (1.01, 6.02)	**2.49*** (1.02, 6.10)	**2.48*** (1.01, 6.05)
Parental history of asthma (no history)	**3.59*** (1.27, 10.16)	**3.67*** (1.28, 10.55)	**3.67*** (1.26, 10.64)	**3.58*** (1.23, 10.46)	**3.64*** (1.24, 10.62)
Socioeconomic factors (referent)					
Postsecondary education (grade 12 or less)†		0.40 (0.14, 1.13)	0.39 (0.13, 1.13)	0.38 (0.13, 1.11)	0.39 (0.13, 1.14)
Other home type (standard)		2.70 (0.86, 8.42)	2.81 (0.89, 8.87)	3.04 (0.95, 9.76)	0.87 (0.03, 27.75)
Environmental factors (referent)					
Household dampness (no dampness)			**3.14*** (1.11, 8.90)	**3.15*** (1.11, 8.89)	**3.25*** (1.14, 9.21)
Ever exposed to grain dust at work (not exposed)			1.12 (0.45, 2.81)	1.13 (0.45, 2.82)	1.10 (0.44, 2.76)

	Base Model	Model 1	Model 2	Model 3	Model 4
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Personal factors (referent)					
Overweight/obese (normal BMI)				0.69 (0.24, 1.99)	0.69 (0.24, 2.00)
Regular drinker (abstainer/infrequent drinker)				1.38 (0.53, 3.60)	1.36 (0.52, 3.54)
Product term					
Home type × Age (10-year intervals)					1.28 (0.69, 2.39)
Log likelihood	-94.24	-91.29	-89.23	-88.79	-88.49
p-value (compared with previous model)	0.028	0.052	0.128	0.645	0.434

Significant variables: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

[†]Education variable forced into model due to theoretical significance.

A significant product term between age and home type emerged for current asthma in females but not for males, similar to the situation in ever asthma. Fully adjusted age-specific odds ratios for the odds of current asthma in women living in 'other' housing versus standard housing are plotted in Figure 4.5. The age trend was identical to ever asthma, with the highest odds ratios seen with the younger age groups, and a decrease in odds ratios for home type of about one-third for every 10-year age increase (a multiplicative factor of 0.68). The decreased estimate precision for the older and younger age groups was also similar to ever asthma. While these overall trends were similar, the association of home type with current asthma was stronger than for ever asthma, with age-specific odds ratios more than 1.5 times larger. As seen in ever asthma, confidence intervals for odds ratios for persons aged 60 years and over included the null value.

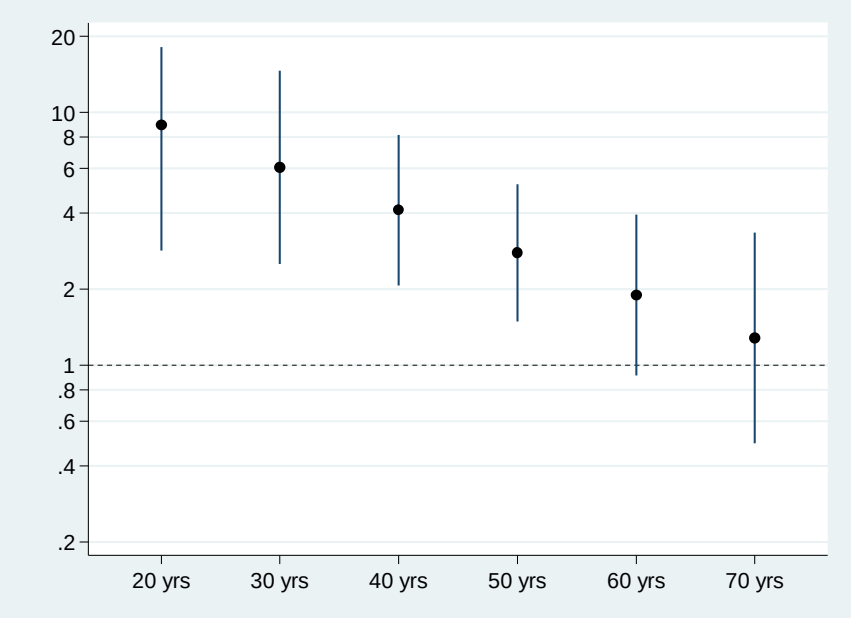


Figure 4.5: Current asthma: fully adjusted odds ratio estimates and 95% confidence intervals for 'other' home type versus standard home type in women of different ages.

4.4 Summary

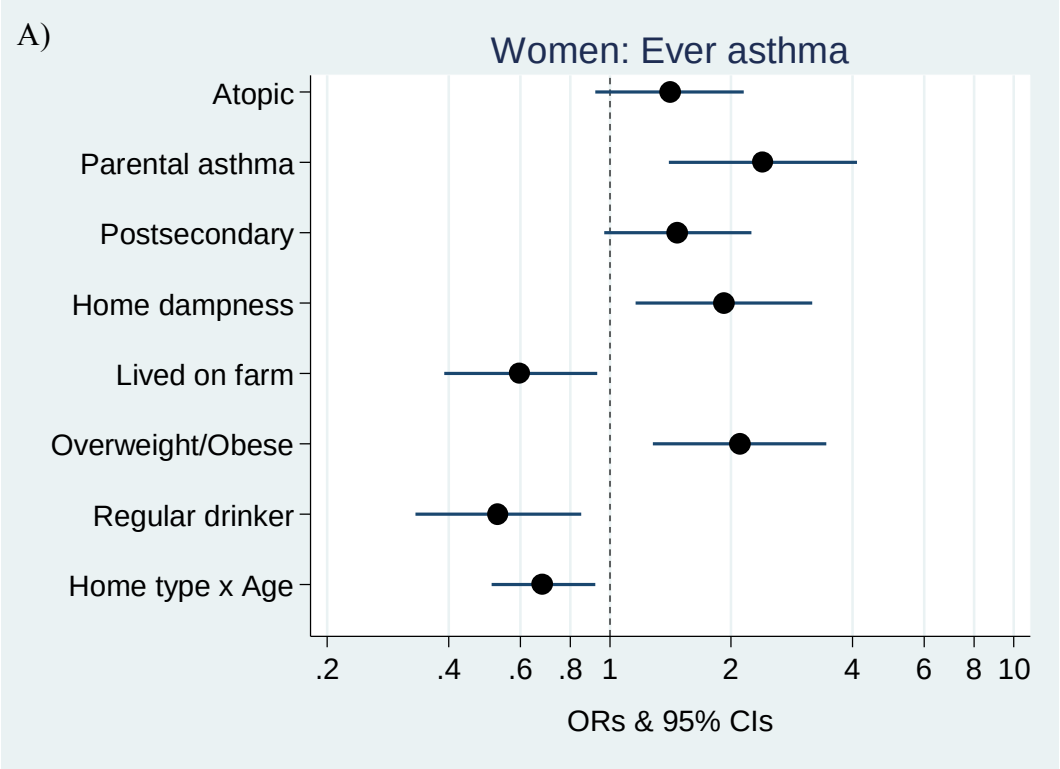
- Compared to men, a significantly higher proportion of women reported ever asthma (10.2% of women versus 5.8% of men) and current asthma (6.2% of women versus 2.8% of men).
- The distributions of all SES factors differed significantly by sex, with greater proportions of women than men reporting some postsecondary education, and living in mobile homes, trailers, attached houses or multi-family dwellings. The only significant difference for environmental factors was occupational exposure to grain dust, with men more than twice as likely as women to have been exposed. There were also significant sex differences in distributions of all personal factors, with higher percentages of men than women overweight/obese, and drinking alcohol regularly (see Table 4.18).
- Univariable analyses of ever asthma showed significant associations with atopy and parental asthma history in both men and women. Ever asthma was also significantly associated with age, education, home type, household dampness, farm living, BMI, and alcohol use in women, whereas no other associations were found in men. Current asthma results were similar aside from household dampness showing a strong and significant association in both men and women, and a few variables no longer showing significant associations (i.e. age and education in women, and atopy in men).
- Multivariable logistic regression models for ever asthma and current asthma showed marked sex differences (see Figures 4.6 and 4.7). Fully-adjusted female multivariable models showed strong significant associations for demographic and biological, socioeconomic, environmental and personal factors (i.e. parental history of asthma, 'other' home type, household dampness, ever lived on farm, ever exposed to grain dust at work, overweight/obese, and drinking alcohol). In direct contrast to women, atopy was strongly associated with both ever asthma and current asthma in the male multivariable models, whereas no associations were found for any socioeconomic or personal factors. Some sex similarities did emerge, with male models also revealing a strong association of parental asthma history with both ever asthma and current asthma, and household dampness showing a strong association with current asthma in men.

- In females, a significant product term was found between age and 'other' home type for both ever asthma and current asthma. The magnitude of the association between home type and asthma decreased as age increased. Odds ratio estimates decreased by approximately one-third for every 10-year increase in age, with estimates no longer statistically significant in older age groups.
- For both ever asthma and current asthma, the addition of each category of variables (i.e. socioeconomic, environmental, and personal factors) during the sequential multivariable model-building process contributed significantly to the model fit for women. In contrast, although the base models for male ever asthma and current asthma fit significantly better than models with only a constant, none of the sequential variable additions contributed to significantly better model fits.

Table 4.18: Ever asthma and current asthma: summary of significant univariable associations for demographic and personal factors, socioeconomic factors, environmental factors and personal factors in men and women.

	Ever Asthma		Current Asthma	
	Men	Women	Men	Women
Demographic and biological factors				
Age		*		
Atopy	*	*		*
Parental history of asthma	*	*	*	*
Socioeconomic factors				
Education		*		
Marital status				
Home type		*		*
Environmental factors				
Household dampness		*	*	*
Ever exposed to grain dust at work				
Ever lived on farm		*		
Ever pet in home				
Passive smoking				
Personal factors				
Body mass index		*		*
Smoking status				
Alcohol use		*		*

*Significant association ($p < 0.05$)



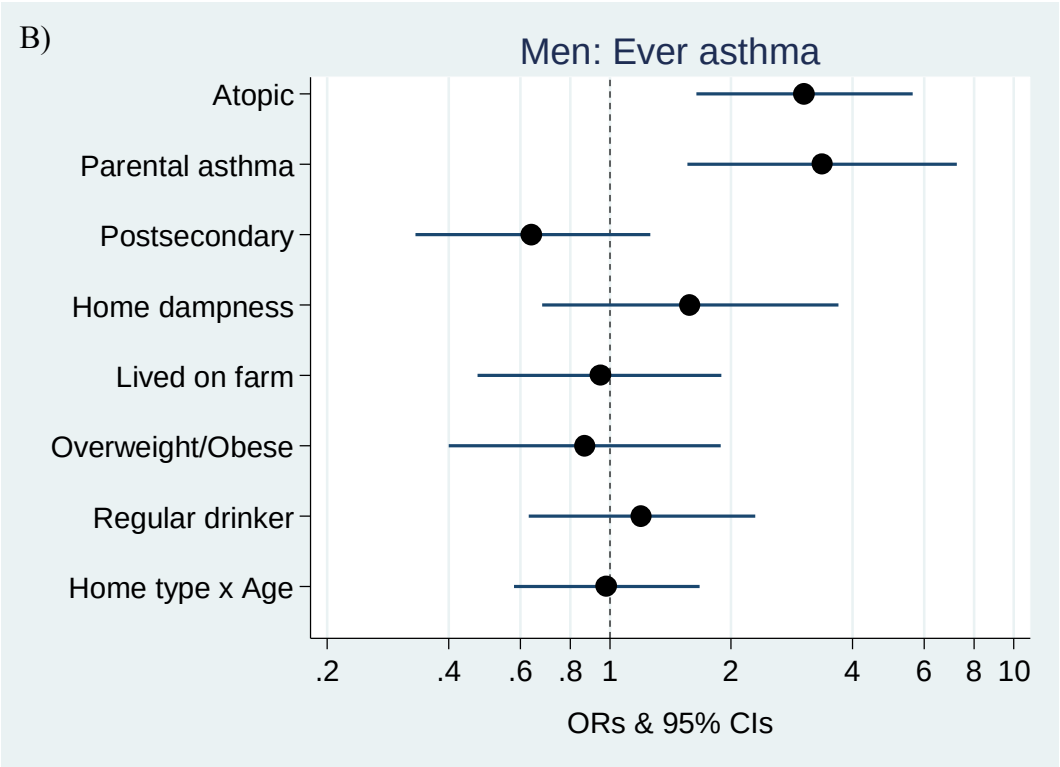
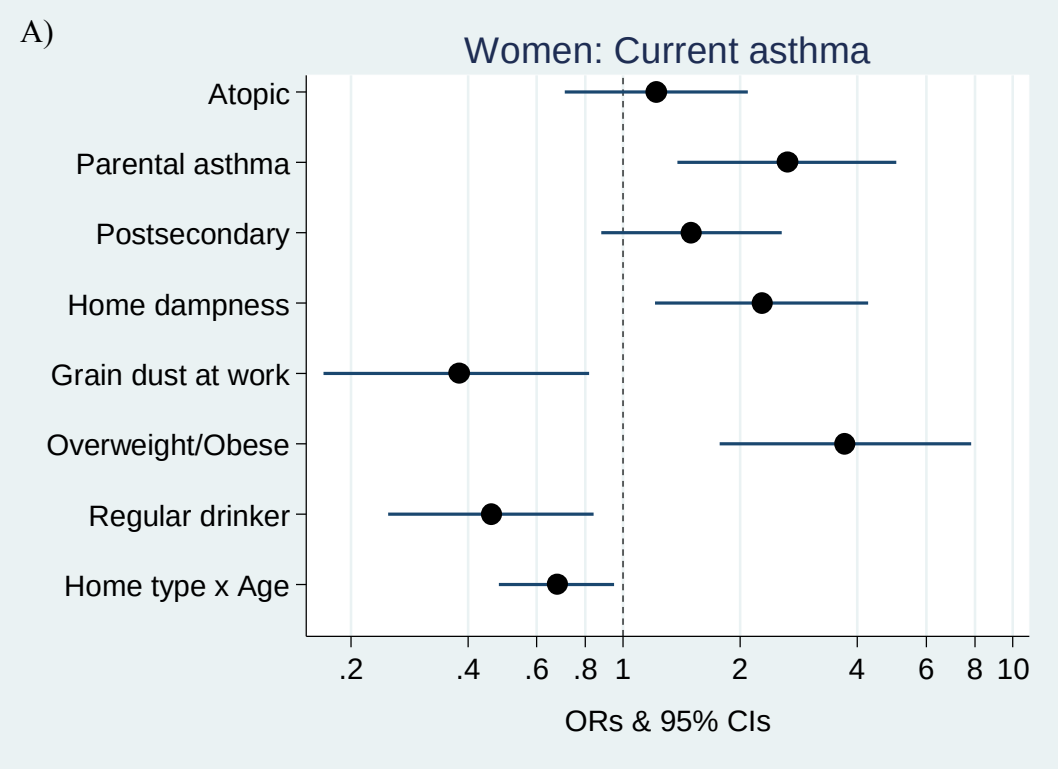


Figure 4.6: Ever asthma: summary of fully adjusted odds ratios and 95% confidence intervals for women (A) and men (B). Estimates from Tables 4.14 and 4.15; Model 4.



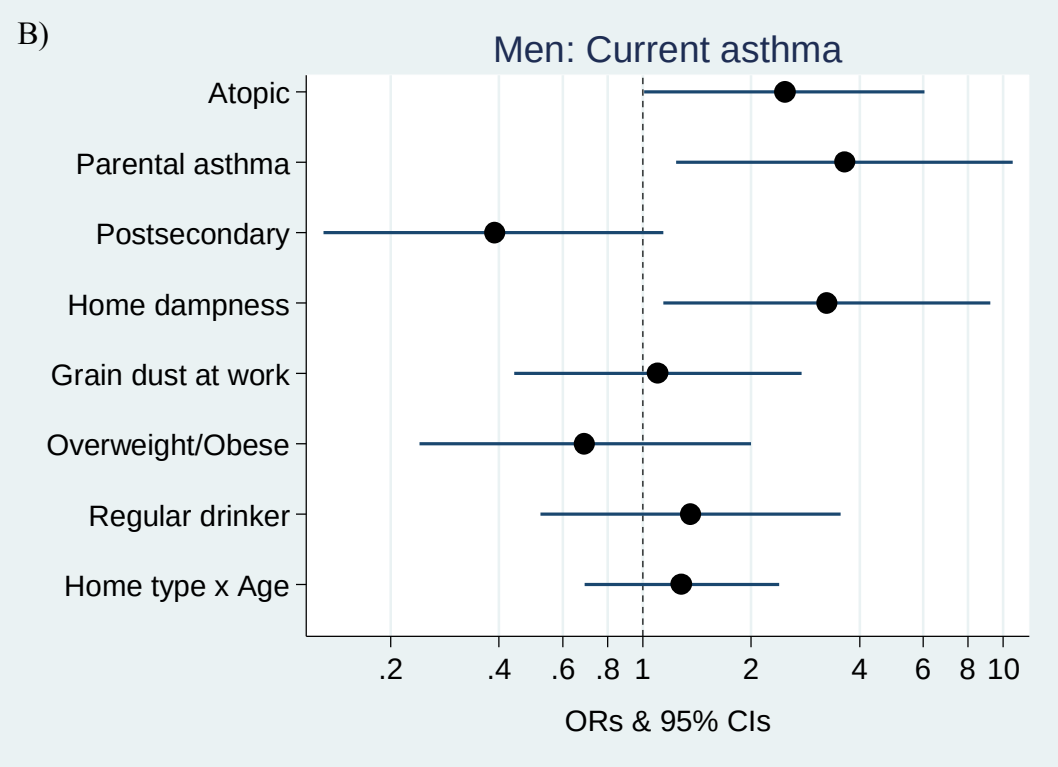


Figure 4.7: Current asthma: summary of fully adjusted odds ratios and 95% confidence intervals for women (A) and men (B). Estimates from Tables 4.16 and 4.17; Model 4.

DISCUSSION

Data used in this thesis were from a cross-sectional study that assessed the prevalence of current asthma, ever asthma, and a variety of exposures in adults of Humboldt, Saskatchewan. This secondary data analysis used a sex-specific approach to examine the prevalence of asthma, distribution of socioeconomic, environmental and personal correlates, and associations of asthma with these correlates in the study population. The chapter begins with a discussion of the main findings of the study. This is followed by an examination of the study's strengths and limitations, and concludes with a consideration of the unanswered questions and suggestions for future research.

5.1 Asthma Prevalence in the Study Population

Significant sex differences in self-reported prevalences of both current asthma and ever asthma prevalence were observed in the Humboldt adult study population. The current study showed that higher proportions of women than men reported doctor-diagnosed asthma during the year prior to the survey (6.2% versus 2.8%), and during their lifetime (10.2% versus 5.8%). This finding was expected, as analyses from the same study population have previously shown sex differences in the prevalences of a variety of respiratory health outcomes including asthma.[41] Numerous other asthma epidemiology studies and surveillance systems have also shown higher asthma prevalence and incidence in adult females compared to adult males, despite widely varying methodologies, asthma definitions, and geographical locations.[5,40,43,46,75]

Comparisons of asthma prevalence estimates with Canadian estimates from other data sources must be interpreted with caution due to the aforementioned study and population differences. The 2005 Canadian Community Health Survey (CCHS) results for Saskatchewan showed that 8.6% of female and 6.6% of male adults 20 years and older reported doctor-diagnosed asthma, while 9.4% and 6.2% of all Canadian female and male adults 20 years and older reported doctor-diagnosed asthma.[5] These CCHS female asthma prevalence estimates are broadly similar to the Humboldt data, while the male asthma prevalence estimates are slightly higher. These CCHS provincial and national statistics support the pattern of sex differences found in the Humboldt population, but the ratio between female and male asthma prevalence is of a smaller magnitude than that found in the current study. These are qualitative comparisons

only, as the estimates are not directly comparable for several reasons. The Humboldt study and CCHS both asked about doctor-diagnosed asthma, but the CCHS survey question also specified that they were interested in current "long-term conditions" which were expected to last or have already lasted six months or more, which may have elicited different responses.[143] Humboldt study asthma prevalence estimates were slightly elevated due to the comparatively lower age category limits for adulthood, with asthma prevalence estimates decreasing slightly for both women and men when 18- and 19-year-olds were excluded from the dataset. The Humboldt adult study population also has a more mature population structure compared to the total Saskatchewan adult population, with a lower proportion of 20 to 34 year-olds in Humboldt adult study participants compared to Saskatchewan adult residents (14.3% versus 25.8% of adults over 20 years old, respectively) and a conversely higher proportion of senior (65+ years) Humboldt study participants than Saskatchewan (28.3% versus 19.7% of adults, respectively).[5] Therefore, comparing estimates from the current study and the CCHS that have not been age-standardized means that the lower prevalence of asthma in older age groups will result in lower unadjusted Humboldt prevalence estimates simply due to the mature age structure of the population.

Examination of asthma prevalence across broad age categories showed consistent sex differences within all age groups for both current and ever asthma. No significant trends across age groups were apparent. However, the prevalence of ever asthma showed a tendency to decrease with age in both men and women, while the prevalence of current asthma remained more stable across age groups. The ever asthma prevalence pattern was similar to that found by the CCHS, with the highest asthma prevalence in the youngest age category (20 to 34 years) of male and female adults.[5] For current asthma, prevalence differences between men and women were larger and more significant with increasing age categories. The potential impacts of health selection on these prevalence measures in the older age groups must be considered. Selective survival of the fittest elderly men and women means that the oldest age groups may not accurately represent their birth cohorts in terms of past and current health status, and the well-documented higher mortality rates of men compared to women further distorts the ability to interpret sex differences in health outcomes at different ages. The potential for age and cohort effects to distort prevalence measures obtained from cross-sectional data has been widely recognized.[144]

5.2 Characterization of the Study Population

Women and men showed similar distributions of demographic and biological confounders and risk factors (i.e. age, parental history of asthma, and atopy). Conversely, significant sex differences were found in the distributions of all socioeconomic and personal asthma risk factors.

Compared to men, a significantly higher proportion of women in the current study were single, had higher education levels, and lived in housing other than standard one-family detached houses. Several population-based surveys that have investigated socioeconomic determinants in adult women and men have shown similar sex-specific patterns of SES risk factors, with widespread agreement that women are generally over-represented in most low-SES indicators. Analysis of the 2000 Canadian Community Health Survey (CCHS) revealed higher proportions of partnered men than women, and more older men than women living in detached dwellings.[145] A Statistics Canada report (using 2001 data) also supported these sex-specific patterns, further illustrating how the marital status discrepancies between sexes increase with age and that women are also more likely than men to be single parents regardless of age group.[146] Although the Statistics Canada report did not investigate specific dwelling types, it did show that females were more likely to have housing affordability problems and had consistently lower incomes than their male peers.[146] In contrast to the current study population, 2001 Statistics Canada figures suggest that the educational advantage of women over men occurred mainly in younger adults, with the trend reversing for adults over 45 years old.[146]

The only significant difference for environmental factors between men and women in the current study was for exposure to grain dust at work, with male study participants more than twice as likely to report grain dust exposure compared with women. This finding was not surprising, given that most agricultural occupations have traditionally been male-dominated. This trend has not shown any recent signs of changing, with women comprising approximately one-quarter of all Canadian farm operators in 2001.[146]

Sex differences were also present in the distributions of all personal factors. Compared to women, a significantly higher proportion of men were overweight/obese, ex-smokers or current smokers, and regular alcohol users. The 1994/95 Canadian National Population Health Survey supported all of these sex differences, also finding that men were significantly more likely to be overweight, smoke, and drink more alcohol than women.[147] Statistics Canada data (2003)

confirmed that, despite women reporting less physical activity than men in their leisure time, adult females were generally less likely than their male peers to be overweight/obese.[146]

5.3 Research Question: What Socioeconomic, Environmental and Personal Factors are Associated with Asthma in Men and Women?

This study found several significant associations of socioeconomic, environmental and personal correlates with current asthma and ever asthma for women, while only a single significant environmental correlate was found for current asthma in men. A significant interaction between home type and age was also present in multivariable analyses for females but not for males. These sex-specific results are discussed in more detail below.

Ever asthma and current asthma. The odds ratios for all associations were similar in direction and general magnitude for current asthma and ever asthma, a finding that was expected since current asthma is a subcategory of ever asthma. In women, stronger associations for variables of all categories were found for current asthma compared to ever asthma. In men, the association between atopy and ever asthma was stronger and more significant than for current asthma. This finding supports the well-described role of atopy as a major risk factor for asthma in young males, with many 'growing out of' their asthmatic condition with age.[148] The degree of uncertainty surrounding most odds ratio estimates for men precluded informative comparisons of estimates for current asthma versus ever asthma, aside from home dampness showing a stronger association with current asthma than ever asthma. Given the similarities between the results for ever asthma and current asthma and the generally stronger magnitudes of association seen for current asthma, the majority of the discussion will focus on the findings for current asthma except in cases where there are important divergences.

Demographic and biological factors. These factors were not a major focus of this study, with their effects controlled for rather than forming part of the main investigation. However, given the important roles of age, atopy, and parental asthma history in adult asthma development, their results will be briefly considered. The main findings from fully-adjusted multivariable models that included these factors confirmed the importance of adjusting for and examining their associations in the analyses: 1) a strong and significant association of atopy with asthma in men, but not in women; 2) a strong and significant association of parental asthma history with asthma in both men and women; and 3) a significant interaction between age and a socioeconomic factor (home type) for women. The first finding of a male-specific association

between atopy and adult asthma is consistent with the fact that, in comparison to atopic asthma, a higher proportion of nonatopic asthmatics are older females who experience a later onset of symptoms.[78] It has been shown that a larger proportion of non-eosinophilic asthmatics are nonatopic, while eosinophilic asthma is more closely linked with atopy.[149] Therefore, although the specific immune mechanisms behind these distinct phenotypes remain unclear, one possible explanation for the male-specific association between atopy and adult asthma is that a higher proportion of female asthma is non-eosinophilic whereas male asthma is largely eosinophilic. The second finding was expected due to the strong associations between parental asthma history and asthma consistently reported by most asthma research,[150,151] with many adult asthma studies choosing to control for this widely accepted risk factor in their multivariable analyses rather than to investigate and report it.[43,54] The final finding of a sex-specific interaction between age and home type will be discussed in the 'Socioeconomic factors' section.

5.3.1 Socioeconomic factors

The current study showed different associations between socioeconomic factors and asthma for men and women. 'Other' home type (i.e. living in housing other than a standard one-family detached home) was associated with asthma in women, an association that was modified by age in the multivariable analysis. Univariable analyses also showed a crude association between postsecondary education and ever asthma in women, but this association was no longer present after controlling for demographic and biological factors. In contrast, none of the socioeconomic factors examined were associated with asthma in men.

A key finding from this study was the association of 'other' home type (i.e. lower SES) with both ever and current asthma for women, but not for men. Age modified this relationship, with the youngest women showing the strongest association between home type and asthma and the magnitude of association steadily decreasing with increasing age until approximately 50 to 60 years old when the association was no longer statistically significant. The analyses performed in the current study do not provide an etiological explanation for these sex and age differences. However, it seems reasonable to surmise that women in this study population may be uniquely susceptible to the health impacts of home type in an age-dependent manner.

Potential explanations for this sex- and age-specific association extend beyond the traditional biomedical model, as housing is a health determinant that can potentially impact asthma and other health outcomes through a wide variety of physical and social pathways.[109,115]

The use of home type as a socioeconomic variable in the current study was supported by the fact that the proportion of study participants in standard one-family detached homes consistently increased with higher self-reported gross family income, a trend that appeared for both men and women across the four income categories (p-value for trend < 0.0001). While this trend supports a relationship between home type and SES in the Humboldt population, it could be biased due to the large proportion of study participants who chose not to provide income information (24.6% of women and 21.7% of men). Statistics Canada has reported that mobile home residents have lower education and income levels compared to residents of single-family detached homes, further supporting the presence of an association between home type and SES in Canada.[152] Sex differences in income by home type were also apparent in the Humboldt population. Higher proportions of women than men living in 'other' homes reported incomes under $25,000 (62.4% versus 48.4%, respectively), while lower proportions of women than men living in 'other' homes reported incomes over $50,000 (6.9% versus 21.0%, respectively). Therefore, the closer association between 'other' home type and low household income in adult women compared to men suggests that home type may be related to SES in a sex-specific manner in this study population.

One possible explanation for the association between home type and asthma is that different environmental exposures present in lower versus higher SES home types could be related to asthma. Several studies have examined the health impacts of the physical housing environment, demonstrating how disadvantaged housing circumstances can lead to suboptimal living conditions that impact a variety of health conditions.[28,119,153,154] In the current study, the proportion of participants who were exposed to home environmental risk factors (i.e. household dampness, pets in home and passive smoking) did not differ significantly by home type for either men or women. However, we can not rule out associations with other household environmental factors that were not directly assessed in this study (e.g. endotoxin, moulds).

A causal pathway that features the psychosocial impacts of SES on asthma seems a plausible explanation for the association between disadvantaged housing circumstances and asthma. Raphael *et al.* (2005) describe psychosocial pathways as "explanations related to either the experience of belonging to a particular social class or the experiences of stress associated with differing levels of income and how these come to be related to health".[155] Multiple biological pathways linking low-SES circumstances to asthma through stress and immunological

responses have been proposed, but these mechanisms have yet to be explicitly tested.[111,156] Another possibility is that psychosocial stress may cause people to engage in unhealthy behaviours such as smoking or overeating, thereby increasing the risk of asthma. Few Canadian researchers have considered the potential role of psychosocial pathways in explaining relationships between income and health,[155] perhaps because they are more difficult to quantify than pathways mediated by environmental and behavioural risk factors. However, Canadian research has shown that social structural and psychosocial health determinants seem to be more important for adult women than men,[147] which provides support for the sex-specific association between 'other' home type and female asthma seen in the current study.

The general association between lower SES and higher adult asthma prevalence has been supported by several large cross-sectional studies,[77,91,93,157,158] while other studies have shown a contrasting relationship (higher SES associated with higher adult asthma prevalence).[92,93] Few studies have examined whether the SES-asthma association differs for men and women.[77,93] The odds ratios for 'other' home type and female adult asthma in the current study were of a greater magnitude than those reported for traditional SES measures in the adult asthma epidemiology literature to date. It is unclear whether this discrepancy is attributable to a truly stronger relationship between SES and asthma in the Humboldt adult population, the use of different SES measures, differences in study methodologies, or a combination of these factors. A U.S. national survey showed that low SES adults (i.e. less than grade 12 education or annual household income less than $15,000) were 1.36 times more likely to report current physician-diagnosed asthma than adults in other SES categories after adjustment for confounders.[91] A multi-country cross-sectional study showed that young adults of lower occupational classes and with less education were more likely to report current asthma symptoms, with adjusted odds ratios ranging from 1.18 to 1.51 for participants in the lower SES categories compared to those in the highest SES reference groups.[157] These studies controlled for sex and age in their analyses, but did not examine the potential for sex or age to modify the relationship between SES and adult asthma.

Very little research has investigated the possibility of sex-specific associations between socioeconomic factors and adult asthma. The general component of the Canadian 1996/97 National Population Health Survey (NPHS) suggested a trend of increasing asthma prevalence with decreasing SES (i.e. household income adequacy), a finding that is consistent with the current study.[77] However, in contrast to the findings of the current study, the NPHS study did not

support the presence of sex-specific associations between SES and asthma, as the magnitude and significance of the SES-asthma association was similar for both males and females.[77] Sex differences were similarly lacking in a British cohort study of young adults that examined asthma and other health outcomes for social inequalities by occupational class and educational attainment.[98] On the other hand, subtle sex differences in the association between education and adult asthma were found in a California study, with the positive gradient between education and asthma in hay fever participants steeper among men and the negative gradient between education and asthma in participants without hay fever steeper among women.[93] One possible explanation for these contrasting findings is the fact that most adult asthma studies have examined traditional SES factors such as income, occupation, and education in their analyses, and these factors (particularly income and occupation) have been shown by some studies to be more strongly associated with male than female morbidity and mortality outcomes.[100,159] This suggests that these common SES factors may not adequately represent SES-related health pathways that are more relevant to women such as the psychological impacts of their housing and social environments. Sex differences in the magnitude and direction of social inequalities have also been shown to vary widely by age group and measurement of health outcome.[98]

Research has consistently shown that housing deprivation can influence a variety of general and mental adult health outcomes through pathways that are not entirely mediated by physical housing characteristics.[108,113,115,119] However, no studies were found that examined the sex-specific associations of home type or other housing-related SES risk factors with adult asthma. The limited evidence that exists in this area for other health outcomes suggests that the associations between relatively deprived housing circumstances and health may be stronger for women than men.[32] Canadian research into general health outcomes has also provided support for a sex difference, with an analysis of 2000 CCHS data showing that women living in semi-detached houses or townhouses were significantly more likely than women living in detached houses to report both poor health and chronic conditions.[145] This finding is congruent with the current study results, which show a strong relationship between house type and asthma for women but not for men. Sex-specific health impacts of SES may be due to biological and physiological mechanisms that are unique or more vulnerable in women, and/or risk factor pathways that are influenced by gender roles (i.e. increased exposure of women to the social and

physical impacts of SES factors such as home type due to their roles within the household and community).

As illustrated by the previous discussion, results from the current study provide only a general starting point from which to form hypotheses about the etiological relationship between home type and asthma. Therefore, etiological explanations of the interaction between home type and age are also speculative and assume that the interpretation of home type as an SES risk factor for adult asthma in women is correct. Most adult asthma studies control for age as a confounding factor without considering the potential role of age as an important effect modifier for the impacts of asthma risk factors. No studies were found that examined age-specific associations of housing factors with adult asthma. In the current study, the decreasing magnitude of the association between 'other' home type and asthma with increasing age in women has several possible explanations. One possibility is that home type represents different things for women during different life stages. During their child-bearing and child-rearing years, women who live in detached homes may experience higher income levels, increased access to resources, healthier neighbourhoods, increased residential stability, and/or increased social status compared to their peers who live in 'other' types of housing during the same life stage. In contrast, women in later life stages may choose to move out of detached homes for reasons entirely unrelated to their resources and social position. For example, single/widowed senior women may shift from their standard one-family homes to housing that would be classified as 'other' due to their reduced need for space or for health reasons during this later stage of life.[117,160] Shifting between the 'standard' and 'other' housing categories could include downsizing into some type of apartment or attached dwelling, moving into a multiple-generation home (i.e. with their adult children), or institutional housing. This means that the use of home type to represent SES may become less accurate as women age, which would result in a weakening of the association between home type and asthma with increasing age even if a relationship between SES and asthma still existed. Another possible explanation is a selective survival effect, in that low-SES (i.e. 'other' housing) women may have reduced longevity compared to high-SES (i.e. single-family detached housing) women. Over time, the surviving low-SES women would become increasingly unrepresentative of their original low-SES cohort, as they would be healthier and potentially less likely to have asthma than those who had died. This possibility could not be examined by the current cross-sectional study. However, a higher mortality rate among

disadvantaged women could plausibly be caused by more low-SES women suffering from comorbid conditions, or having decreased access to healthcare and social support. In the current study, such a selective survival effect would result in a weakening association between 'other' home type and asthma with increasing age. Overall, given the well-documented complexities of health selection and SES measurement in studies of health inequalities that include elderly people,[161] the lifecourse effects of SES on health,[162] and the fact that this study examines current and ever asthma rather than incident cases, it is unlikely that the effect modification by age represents a true weakening of the impact of SES on asthma as women age.

5.3.2 Environmental factors

The current study showed that household dampness was a significant risk factor for current asthma in both men and women. Both univariable and multivariable analyses revealed consistently strong associations between home dampness and current asthma, with adjusted odds ratios of 2.28 for women and 3.25 for men. A similar association with household dampness was seen for ever asthma in women, while no such association was found in men. Results for the farm-related environmental exposures showed a sex-specific pattern, with significant protective effects found only in women for living on a farm and occupational grain dust exposure (with ever asthma and current asthma, respectively).

Published reviews have confirmed building dampness as a significant risk factor for adult asthma and related respiratory symptoms, with reported adjusted odds ratios ranging widely from 1.2 to 4.2, and stronger associations for current asthma than ever asthma.[26,120] The current study found that damp housing was a strong risk factor for asthma in both adult women and men. Few other investigations were located that had examined sex-specific associations between indoor dampness and adult asthma. The overwhelming majority of studies chose to control for sex as a confounding factor rather than stratify their analyses by sex, thereby obscuring potential sex similarities or differences. Furthermore, some of the relevant adult asthma studies were based on data collected from mostly female parents of children who were participants of a pre-existing study,[25,122] were potentially biased due to pre-existing participant beliefs about the relationship between dampness and asthma,[121] or had inadequate power to detect potential sex differences. The only comparable sex-specific investigation located in the literature was performed in 1993 in the same town as that investigated by the current study, and the researchers did not find an association between damp housing and asthma for either sex.[54] However, the association

between household dampness and wheezing symptoms was stronger in women than men and was only statistically significant for women.[54] This result contrasts with the findings of the current study, as it suggests that sex may modify the relationship between exposure to damp housing and some respiratory symptoms.

The current study does not contribute towards an etiological explanation for the association between self-reported indoor dampness and adult asthma, as no measurements of potential causative agents were taken. One widely postulated causal mechanism for the association between indoor dampness and asthma is increased mould growth that causes sensitization and hypersensitivity reactions to airborne allergenic mould proteins.[24,163,164] A recent review has presented a substantial body of evidence for an association between damp-related indoor microbial exposures and asthma-like symptoms in adults, thereby providing further support for this mechanism.[164] Other probable mechanisms include exposure to dust mite and other insect allergens, with the role of bacterial endotoxins, organic chemicals, and respiratory viruses also under investigation.[24,165] The current study results are consistent with a causal mechanism that impacts both men and women to an equal degree. The degree of exposure to the damp indoor environment was not quantified for participants in the current study, potential causative agents (i.e. dust mites, fungi, and bacteria) were not measured, and biological mechanisms have yet to be determined. There is a lack of information in the literature about sex similarities and differences with regards to inhalation, absorption, and activation of immunological and inflammatory responses by these potential causative agents. These unknown factors mean it is not possible to hypothesize whether sex similarities or differences in the association between indoor dampness exposure and asthma would be expected.

A highly protective association between ever living on a farm and ever asthma (adjusted OR = 0.60) was found only for women. A recent review on this topic showed that the magnitude and direction of this finding is generally consistent with previous cross-sectional Canadian, New Zealand, and Norwegian studies that demonstrated protective associations between current farm living and adult asthma, while a Danish study showed no significant association.[123] In contrast to the current study findings, four European studies examining the impact of childhood farm exposure on adult asthma did not show any statistically significant associations, although the odds ratio point estimates all indicated a potential protective effect.[123] Since the 'ever' farm exposure variable used in the current study does not differentiate between current and childhood

farm living, it is not possible to determine whether the timing of farm exposure was consistent with the above findings or whether the temporal pattern of exposure differed by sex. The temporal sequence of the farm exposure and ever asthma association in the current study is further obscured by the fact that both childhood and adult asthma recalled by study participants would be classified as ever asthma. Specific comparisons between the current study and the research included in the review are also complicated by the heterogeneity of the studies with regards to participant ages, measurement of asthma, definitions of farm exposure, selection of comparison groups, and analytical methods.

There are even fewer studies with which to compare the sex-specificity of the current study findings for farm living, as most studies on this topic have not stratified their analyses by sex. Findings from a cross-sectional rural Quebec study do provide some support for a female-specific protective effect of living on a farm, although the study methods differed from the current study with the study population consisting of secondary school students rather than adults and current asthma defined as the presence of both airway hyperresponsiveness on methacholine testing and self-reported wheeze in past year.[124] The researchers showed that farm girls were significantly less likely to have current asthma than nonfarm girls (5.9% versus 11.4%, $p = 0.01$), whereas the difference between farm and nonfarm boys was not significant (4.3% versus 6.6%, $p = 0.26$).[124] A similar sex-specific pattern was seen for atopy, with 35.7% of farm girls and 53.3% of nonfarm girls showing at least one positive skin prick test ($p = 0.001$), whereas 46.0% of farm boys and 53.6% of nonfarm boys were atopic ($p = 0.10$).[124] This study did not stratify the multivariable analyses by sex, but it did show an overall significant protective association of farm living (OR = 0.71, 95% CI: 0.37, 0.98; adjusted for sex, current smoking, and number of siblings) which was similar in magnitude to that found for adult women in the current study.[124]

Several etiological hypotheses for the protective effects of farm living on asthma have been suggested in the literature, although they do not help to explain the sex-specificity found in the current analysis. Much emphasis has been placed on the possibility that higher levels of microbial exposures (e.g. bacterial endotoxins and fungal spores) may result in decreased atopic sensitization and protect against the development of atopic asthma, especially when the exposure occurs during childhood and involves contact with livestock.[123] Indeed, several studies that have stratified asthma by atopic status have shown that farm life appears to be selectively protective for atopic asthma but not nonatopic asthma.[123] This causal theory is compatible with the highly

consistent and cumulative protective effect of farm exposure against allergic sensitization that has been shown to occur across the lifecourse.[123]

The female-specific protective association between 'ever exposed to grain dust at work' and current asthma was not expected, as most research has focused on the negative impact of grain dust exposure on asthma and lung function measures.[166] Interpretation of this finding is complicated by similar issues as for the farm living variable, including the fact that the current study did not have information on the initiation, duration, or intensity of grain dust exposure. There are limited studies with which to compare the sex differences found in the current study, as the markedly higher proportion of male agriculture workers means that most respiratory studies examining farm work exposures have not stratified their analyses by sex. Previous research in the same rural location as the current study found that grain farming was a risk factor for asthma in men but not women.[167] In contrast, a Canadian study of swine workers suggested that occupational exposure may be a risk factor for asthma in atopic female but not atopic male swine workers.[127] A literature review examining studies with a variety of farming exposures and respiratory outcomes also found contradictory results as to the existence and direction of sex differences for associations between farm-related occupational exposures and respiratory health.[166]

In contrast to the protective effects thought to be conferred by the microbial exposures of farm life, continued exposure of farm workers to bacterial endotoxins through inhalation of grain dust has been widely implicated as a strong risk factor for the development of nonatopic asthma.[30,123] The reduced risk of asthma in women with an occupational history of grain dust exposure in the current study contrasts directly with this accepted role of grain dust as an asthma risk factor. The paradoxical protective association found in this study may be due to the "healthy worker effect", or the fact that employed people are likely to have lower morbidity and mortality rates than the general population to which they are being compared.[168] The potential for this effect to bias estimates of associations in asthma studies that examine occupational exposures has been recognized, with the problem of self-selection or employer selection at hire emphasized.[169] In the current cross-sectional study, this raises the possibility that the protective association between occupational grain dust exposure and asthma may be partially due to reverse causation, in that asthmatic women in the study population might not have been hired or chosen to work in occupations which exposed them to respiratory irritants such as grain dust. This

unexpected finding may also be partly attributable to the fact that many women in farm-related jobs could be simultaneously exposed to protective factors related to farm life. In theory, sex differences in the association of occupational grain dust exposure with asthma could also be due to physical and physiological differences between men and women, or sex-related differences in tasks or shifts resulting in different intensities and types of inhalation exposures despite working in broadly similar environments.[170]

Given the suggestion that similar microbial exposures encountered in farm life and occupational grain dust exposure may be protective against atopic asthma while acting as risk factors for nonatopic asthma, sex-specific associations may have also been influenced by sex differences in atopic versus nonatopic asthma subtypes. The current study was unable to examine this possibility due to insufficient power for stratification of asthma by both atopic status and sex.

5.3.3 Personal factors

Sex differences were found for asthma associations with body mass index and alcohol use in the current study. The body mass index of women was significantly associated with current and ever asthma in both univariable and multivariable analyses, while no association was found for men. A significant protective association between regular alcohol use and asthma was also found exclusively in women.

The association between female body mass index and asthma remained strong even after adjustment for all other factors in the full multivariable model, with overweight/obese women 2.10 and 3.72 times more likely than women with normal BMIs to report ever and current asthma, respectively. Numerous other studies with a variety of study designs, study populations, body size assessment methods, and asthma definitions have reported associations of similar magnitudes between female overweight/obesity and asthma, with adjusted odds ratios ranging from 1.5 to 3.5.[19,40,41,43,75,76] Reverse causation is a possible explanation for this association, as asthmatics may gain weight as a result of asthma-related activity limitations. The current study could not rule out this possibility due to its cross-sectional design. However, a New Zealand longitudinal study excluded reverse causation as a potential explanation for the association between BMI and female adult asthma by demonstrating that there was no association between childhood asthma and overweight/obesity in adulthood.[43] A large longitudinal study of female nurses aged 26 to 46 years in the United States has also demonstrated a strong association

between BMI and subsequent onset of adult asthma.[171] Higher baseline BMIs and weight gain since age 18 both showed a dose-response relationship with an increased risk of incident asthma during a four-year follow-up period, therefore providing further evidence for excess body fat temporally preceding the development of adult asthma.[171]

The sex-specificity found in this study has been widely reported in the literature, with most of the aforementioned research failing to find an association between BMI and asthma in adult men.[40,41,43,75,76] These investigations include analyses of the Canadian National Population Health Survey that showed sex differences in relationship of obesity with both prevalent[76] and incident[40] self-reported physician-diagnosed adult asthma. After controlling for several confounders including age, smoking status, allergic history, immigrant status, and income adequacy, both studies found that women in the highest BMI categories were almost twice as likely to report current asthma[76] or to develop asthma in the subsequent two-year period[40] compared to women with normal BMIs. Both studies also showed that the corresponding odds ratios for high versus normal BMI men were not significant for either prevalent (OR = 0.93, 95% CI: 0.62, 1.38) or incident (OR = 1.1, 95% CI: 0.3, 3.6) asthma.[40,76] A large birth cohort study in New Zealand analyzed longitudinal data on BMI, asthma, and several confounding factors from participants from age 9 through 26 years.[43] Sex differences were again observed, with only females showing a significant association between measured BMI and both asthma outcomes (i.e. current asthma and asthma with objectively-measured airway hyperresponsiveness).[43] While many epidemiological studies of both prevalent and incident asthma have provided support for the sex-specific findings of the current study, a meta-analysis of longitudinal studies that examined the obesity-asthma association did not find sex differences in the effect of increased body weight on incident asthma in one year.[172] Once data from multiple longitudinal studies were combined, the summary ORs for overweight/obese versus normal-weight adults and incident asthma were of a similar magnitude and significant for both men and women (Male OR = 1.46, 95% CI: 1.05, 2.02; Female OR = 1.68, 95% CI: 1.45, 1.94).[172] However, separate sex-specific summary ORs calculated for obese versus normal BMI (Female OR = 2.30; Male OR = 1.63), and obese versus overweight participants (Female OR = 1.58; Male OR = 1.17) resulted in OR estimates that were notably stronger and only significant in women, suggesting that uncertainty remains about the potential role of sex as an effect-modifier in the BMI-asthma relationship.[172]

Despite the widespread reports of a relationship between BMI and asthma in adult women, a clear explanation for the potential sex-specificity of the association has not yet been established. Several biological theories for a sex-specific relationship between obesity and asthma have been proposed, including the influence of obesity on female sex steroid hormones such as estrogen and progesterone, and the physiological impacts of different fat distribution patterns.[21,42] High male and female BMIs could also plausibly result in different exposure levels to environmental risk factors, as heavier women may be more likely than men to alter their activity patterns to spend more time inside the home thereby increasing their exposure to household asthma risk factors. Several non-causal explanations for the association have also been suggested, including the possibility of information bias due to female-specific misdiagnosis or misreporting of exercise-induced dyspnea as asthma, or differential self-reporting of body size by sex. Even if such biases were present, given the consistently large magnitude of association it seems unlikely that bias could be entirely responsible for the association. Furthermore, the current study and other studies have objectively measured the BMI of study participants, therefore eliminating the possibility of sex-specific differences in self-reported body weight.[41,43] The association could be confounded by factors that are related to both obesity and asthma such as physical activity and diet, although analyses that adjusted for total caloric intake and physical activity have continued to show a significant association between BMI and adult asthma.[19] Even if such confounding were present in the current study, it is difficult to understand how these factors could be responsible for sex differences in the association.

A protective association between regular alcohol use and asthma in women has not been found by previous studies. The reasons for this sex-specific association in the current study are not known, but there is no plausible etiological pathway through which alcohol intake might impact adult asthma. It seems reasonable to attribute this protective association to the assumption that adults with chronic disease conditions such as asthma may be less likely to drink, although it is unclear why this would occur only in females.

5.3.4 Conceptual framework

Multivariable analyses in the current study were based on a predefined conceptual framework that organized multiple asthma risk factors into categorical sets of socioeconomic, environmental and personal variables. These categories were ordered from distal to proximal influences on asthma (see Figure 3.1), and were sequentially added to the multivariable logistic

regression models in this order. For women, the addition of each category of variables significantly improved the fit of current asthma and ever asthma multivariable models, whereas in men only the demographic and biological factors made significant contributions to a better model fit. All three categories contained at least one variable that was significantly related to female adult asthma, whereas in men only a single significant environmental variable was found.

The conceptual framework was useful for contextualizing the asthma risk factors examined in this study and organizing the analytical approach. The framework also provided a logical structure upon which to base discussion and interpretation of the sex-specific study results. Several other conceptual frameworks have been proposed with a similar aim of helping to conceptualize the combined impact of multiple risk factors on respiratory health.[6,32,106,111,112,173] However, most of these conceptual frameworks are not comparable with the framework used in the current study, since they were based mainly on theory (i.e. their fit with research data had not yet been examined). No quantitative adult asthma epidemiological studies were found that based their analyses on an explicit conceptual framework. However, two cross-sectional childhood respiratory health studies have used analytical conceptual frameworks to clarify the interrelationships between risk factors, with one of these studies also investigating the social etiology of wheeze in parents.[32,106] In both of these studies and the current study, definite causal inferences could not be made as a cross-sectional study design was employed (please see strengths and limitations of study).

5.4 Study Strengths

Since this study was a secondary data analysis, the strong points of the original study (2003 Humboldt Study) from which the data were obtained also apply to the current study. The Humboldt Study collected information from study participants on a broad range of variables. Some variables used in the current study analysis were measured objectively (i.e. atopy and body mass index), therefore reducing the potential for measurement error. The study population consisted of adult residents in a rural town. The focus on adult asthma is an important strength of the study, as a large majority of asthma epidemiological research has focused on children. The rural location of the study is also valuable, given the widespread interest in the complex question of how asthma is impacted by rural environments and the relative paucity of asthma research in rural areas.[174] The current study also has several methodological strengths that merit recognition:

1) Risk factors for adult asthma were examined in a sex-specific manner rather than simply controlling for sex in analyses. Sex-comparative research is critical for achieving a better understanding of how adult asthma associations may differ by sex.
2) This study used asthma definitions that were consistent with several previous Canadian adult asthma epidemiology studies,[41,46,76,77,128] therefore facilitating comparisons of results.
3) The current study included men and women from older age groups, with study participants up to 79 years old. Public health epidemiology research often features study populations that are restricted in age, and research into health inequalities has been identified as a particular area that requires more attention directed towards elderly men and women.[161] This study contributes to this identified need by including older study participants, and by carefully examining the interaction between age and SES.
4) Multiple SES variables were considered for inclusion in the multivariable models, resulting in the use of both home type and education variables. The importance of examining as many material and social SES measures as possible in public health epidemiological studies has been repeatedly emphasized in the literature.[100,158,175] In addition, avoiding the exclusive use of traditional, male-oriented SES measures (e.g. employment status) is of particular importance in studies that aim to evaluate SES effects in both women and men.[100]
5) The investigation of home type as a component of SES was a strength of this study. Most asthma epidemiology studies have restricted their investigations to examinations of quantifiable physical housing-related characteristics such as dampness, allergens, and crowding. Many studies that have considered the potential impacts of dwelling type in a broader sense simply used different house types or housing tenure as control variables that were adjusted for in multivariable analyses rather than specifically investigated. The current study contributes to the scarce research on the potential for housing to impact asthma through its dual roles, as both an SES variable and a structure in which exposure to specific environmental risk factors can occur.
6) The association between SES and asthma was examined for different sexes and ages. This has been advocated as an essential approach for examining inequalities in morbidity,

since routine age and sex standardization often results in a lack of attention to important demographic influences.[176]

7) Variable selection and multivariable analyses in the current study were based on a predefined conceptual framework of the interrelationships between SES, environmental factors, and personal factors. Instead of treating all risk factors as if they only influenced asthma through individual direct pathways, the conceptual framework acknowledged that the effects of distal factors might also be mediated through more proximal factors. Basing data analyses on conceptual frameworks has been advocated as a useful method for examining disease determinants, particularly for conditions such as asthma for which there is widespread agreement that a complex network of risk factors work together to influence health.[141] This study also contributes towards a recently highlighted need for more Canadian income-health studies to explicitly conceptualize causal pathways and to examine the interrelationships between multiple health determinants.[155]

5.5 Study Limitations

A number of limitations must be taken into account when considering the risk estimates presented by the current study. Limitations which have been previously discussed in Section 5.3 will be mentioned only briefly in the points below.

1) The cross-sectional design of this study means that it is not possible to make definitive causal inferences from the study results. Since the presence or absence of exposures and asthma were determined simultaneously for each study participant, the temporal relationship between most of the exposures and asthma onset cannot be determined. In the absence of information on the temporal sequence of associations, the potential for reverse causation or another factor causing both the exposure and asthma cannot be ruled out for the current study. Despite this limitation, the use of pre-existing data from a cross-sectional study provided a practical, expedient, and economical method for performing analyses on which further hypotheses and future research plans could be based. In addition, relevant findings from previous longitudinal studies that examined temporal relationships between similar exposures and incident asthma were taken into account during the construction of the conceptual framework and interpretation of the current study's results.[19,40,43,46,75]

2) The classifications of current asthma and ever asthma in this study do not provide information about the timing of asthma onset or resolution during the lifetime of a study participant. Interpretations involving these temporally ambiguous outcomes are further complicated by the use of both lifetime exposures (e.g. ever lived on a farm, ever exposed to grain dust at work) and current exposures (e.g. home type, household dampness) that also lack detail in terms of commencement and duration of exposure. While this limitation is acknowledged, plausible assumptions about temporal differences between the two asthma measures and for lifetime versus current exposures can be made that allow for sensible interpretations of results from the current study. The weaker associations for ever asthma compared to current asthma were unsurprising, since many of the variables examined in the analysis were current exposures (i.e. current home type, home dampness, body mass index, and alcohol intake). Conversely, ever asthma diagnoses could have been made at any point during the study participants' child or adult lives, so asthma was no longer a current medical issue for approximately 40% of the women (n = 27) and 50% of the men (n = 47) who reported ever asthma at the time the survey was implemented. Consequently, one would expect a high degree of misclassification for variables measuring current socioeconomic, environmental, and personal factors in terms of their inaccurate representation of the exposure that was present in the relevant period before asthma development. If this misclassification was non-differential, associations of current variables with ever asthma would weaken as they would be biased towards the null value of one.[177] The degree of misclassification may be smaller for current asthma compared to ever asthma due to the increased possibility that the current exposures would also represent the conditions that preceded current asthma development.

3) The original study recruited all study participants from a single community, thereby limiting the generalizability of the current study findings. The community was rural and almost exclusively Caucasian, bringing into question the applicability of these findings to the urban and ethnically diverse communities that are also present in Canada.

4) Several potential sources of bias in the current study have already been discussed, including: the use of self-reported asthma; potential for an artificial strengthening of the relationship between home dampness and asthma due to asthmatic participants' increased

awareness of home dampness compared to non-asthmatic participants; potential for a "healthy worker effect" to account for the paradoxical protective association identified between occupational grain dust exposure and asthma; and the possibility of sex-specific misdiagnoses of exercise-induced dyspnea as asthma. Researchers have also suggested several other potential sources of bias that may partially explain sex differences in asthma prevalence or risk factor associations. There is potential for gender bias in physician diagnoses of asthma, with one study demonstrating that female and male smokers with similar clinical respiratory problems were more likely to be diagnosed with asthma and chronic obstructive pulmonary disease, respectively.[132] Increased willingness of women to visit a doctor, or sex-specific differential misreporting of important risk factors such as obesity have been suggested as further possibilities.[7,41] However, the current study and several others have circumvented the possibility of the latter source of bias by objectively measuring participant BMI.[41,43] In the original study from which the data for the current study were obtained, 71% of the target population chose to participate in the study. Therefore, selection bias is a possibility if the participants and non-participants differed according to their exposures and asthma status in some systematic way.

5) The current study attempted to minimize the possibility of residual confounding by controlling for a wide variety of factors in the multivariable analyses. However, as in all epidemiological research, the original study had practical and economic limitations on the data collection methods used and the amount of data collected for each participant. This means that residual confounding by factors that were imperfectly measured, misclassified, or not available for inclusion in the analysis could have impacted the magnitude of some of the associations found in the current study.[177] The associations between BMI and asthma may have been confounded by unmeasured factors such as participant diet, physical activity, and genetics. SES-asthma associations may have been similarly confounded by unmeasured occupational exposures. Since this study was performed in a small rural community at a single point in time, ambient environmental exposures and climatic conditions were not likely to act as confounding factors as they might in other more geographically widespread studies.

6) The current study also had several statistical limitations. The investigation of a small community population meant that the findings had a higher degree of variability than

would be expected with a larger sample size. Multiple statistical tests were performed which may have resulted in some spurious associations between exposures and asthma. The original plan to stratify analyses by both sex and atopic status had to be abandoned due to insufficient power. Given the sex differences found for the association of atopy with asthma, this would have been an informative addition to the analyses performed by the current study. Male odds ratio estimates also had wider confidence intervals than female estimates, which was not unexpected due to the smaller number of male participants and lower male asthma prevalence. Despite this reduced precision in the male estimates, strong and significant associations with asthma were found for atopy, parental history of asthma, and household dampness. *A priori* power calculations for atopy indicated that power limitations meant the male analyses may not be able to detect associations with asthma unless they were of a substantial magnitude (see Section 3.2.5). This brings into question whether some of the differences between other male and female asthma associations may have been due to insufficient power for the male analyses. In order to examine this possibility, a *post hoc* power analysis was performed for the association between grain dust exposure and male asthma. Grain dust exposure was not significant for males or females in the univariable analyses, and showed a female-specific association in the multivariable analysis. The *post hoc* power analysis showed that the male sample in the current study had sufficient power (>0.80) to detect grain dust exposure odds ratios greater than 2.2 and 2.7 for ever asthma and current asthma, respectively. Therefore, the current study had a higher level of statistical power for examining grain dust associations with asthma than for the atopy-asthma associations that were found in males.

5.6 Unanswered Questions and Future Research

The current study examined risk factors for self-reported physician-diagnosed asthma in male and female adults from a rural community population. Significant socioeconomic, environmental, and personal correlates were identified for women, whereas only a single environmental factor was significant for men. These results suggest that several risk factors for adult asthma may act in a sex-specific manner, while other risk factors are common to both men and women. Given the limited amount of previous research on sex-specific associations with

adult asthma, many of the results found by the current study were novel, while previous research provides some support for the sex-specificity of asthma associations with farm living and BMI.

More studies on adult asthma risk factors are needed to corroborate the sex differences and similarities suggested by this study. It should also be recognized that the identification of these sex differences for asthma is an initial step towards gaining a better understanding of the complexity and underlying mechanisms of 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.[51] Future studies should therefore aim to investigate the potential differences in both the biological and sociocultural pathways between risk factors and adult asthma in women and men. For example, research into male/female differences in associations between housing and asthma could examine the potential for biological sex differences (e.g. immunological responses to indoor exposures such as mould and fungi), while also considering the health implications of gender roles and identities in terms of men and women experiencing differential exposures to potential allergens and irritants (e.g. during home maintenance activities such as mowing the lawn, sweeping and vacuuming), and differential vulnerability to psychosocial factors (e.g. meaningful dimensions of housing such as dwelling and neighbourhood pride and comfort, housing demands such as domestic labour strain, and housing satisfaction with respect to factors such as sunlight, space and safety[114]).

The current cross-sectional study can only hypothesize about the temporal relationships between the risk factors examined and asthma. In order to disentangle the direction of effects, additional sex-comparative longitudinal studies are needed that consider the timing of exposures in relation to asthma occurrence. Ideally, longitudinal studies would examine incident asthma in order to exclude the possibility that associations indicate relationships between exposures and survival after asthma rather than the development of asthma, an issue of particular importance in the older age groups. Due to the low incidence of asthma, such a study would require a large sample size and long follow-up period in order to provide enough statistical power to detect associations. It would also be valuable to perform similar studies in other rural and urban communities, and with more ethnically diverse study populations in order to assess the generalizability of the current study findings.

Where study resources permit, future work in this field should strive to achieve a better understanding of the impact of risk factors on adult asthma through more comprehensive exposure measurement methods. This study found a strong association between self-reported household dampness and asthma in both men and women. Objective measurements of home dampness in future studies would help to address the concern that bias caused by participant awareness about the respiratory health effects of dampness could be responsible for this association. The current study also found a strong female-specific association between SES (i.e. current home type) and asthma that was modified by age. Given the inconsistent findings reported for the association between SES and adult asthma in the literature, the SES measurement methods used by future studies merit particular consideration. The dichotomous home type variable used in this study was an oversimplification of a complex SES factor, but was necessary due to the restricted housing data available. Future studies that examine SES as a risk factor for adult asthma should collect more detailed information on home type, and on other factors that could potentially contribute to the physical and psychosocial causal pathways between home type and asthma (e.g. home-related psychosocial factors, amount of time spent in home per day, and objective measurements of allergens and microbial exposures). In order to facilitate comparisons with results from other studies, future investigations should also strive to examine asthma associations with traditional SES factors (i.e. employment and income). These factors could not be examined by the current study due to lack of data and, in the case of income, high participant nonresponse rates. SES status is dynamic over a person's lifetime and there is widespread agreement that childhood SES and adult SES are likely to impact many adult health outcomes independently.[155,178] Indeed, a lag time of up to 15 years between income inequality and adult health status has been suggested.[162] Therefore, longitudinal studies that examine the effects of housing and other SES factors across the lifecourse would also provide valuable information. Studies which broaden their analyses beyond individual-level SES factors are needed, as it has been suggested that asthma disparities are also influenced by contextual SES factors (i.e. social and physical environments of neighbourhoods and communities).[174]

This study controlled for the influence of well-known demographic and biological risk factors while examining the associations of asthma with a variety of socioeconomic, environmental and personal factors. An important challenge for future studies will be to integrate genetic factors and their complex interactions with multifactorial analyses.[86] Additionally,

although not a main focus of the current study, the identification of a strong male-specific association between atopy and asthma suggests that different etiological mechanisms may exist for male and female adult asthma. In support of this hypothesis, some childhood asthma studies have shown atopic and nonatopic asthmatics to have different sets of risk factors, with home environmental factors such as mould/dampness and maternal smoking increasing the risk of only nonatopic asthma.[179,180] In order to examine this possibility in adults, future studies with sufficient statistical power should stratify their analyses by both atopic status and gender. Finally, the conceptual framework used to guide the multivariable analyses in the current study included direct impacts of all risk factors on adult asthma, and also showed how the impact of distal factors could be mediated by more proximal factors. The use of similar contextualized analyses by future studies could play a valuable role in clarifying multifactorial sex-specific pathways that impact adult asthma.

5.7 Conclusions

This study used a sex-comparative approach to identify factors associated with adult asthma in a rural community population. Female-specific associations with adult asthma were found for socioeconomic, environmental, and personal factors, while no male-specific associations with factors from these three categories were identified. A single environmental factor was significantly associated with asthma in both men and women. The analyses in the current study were performed with data from a cross-sectional study, so sex-specific etiological conclusions are not possible due to the uncertainty surrounding the temporal associations between exposures and asthma development. However, the results from this study do confirm the existence of intriguing differences between men and women that would have been obscured if sex had simply been controlled for as a confounding factor in the multivariable analyses. The value of sex-comparative health research and the reporting of sex-specific results has been increasingly recognized,[147,181] with cardiovascular disease research in particular directing considerable effort towards a better understanding of sex-specific biological, psychological, social, environmental, personal and behavioural risk factors.[182-185] Recent reviews have highlighted a similar need for more sex-specific asthma research into the contributions of a wide variety of asthma risk factors in order to develop more effective preventive measures and treatments.[6,50] Nonetheless, many adult asthma studies continue to statistically control for sex in their multivariable analyses, with sex comparisons often limited to measures of asthma incidence

or prevalence. The multiple sex differences found in the current study underscore the necessity of considering the role of sex as an effect modifier when attempting to advance the understanding of the complex interrelationships amongst risk factors and adult asthma.

The simple conceptual framework that was used to guide the multivariable analyses in the current study contextualized the risk factors by organizing them into interrelated categories. To date, few adult asthma studies have used an explicit conceptual framework to demonstrate their etiological hypotheses and the assumptions upon which their research approaches have been based. While the quantity of asthma risk factors identified in the research literature has consistently increased, there has not been a corresponding increase in comprehension of the interrelated causal pathways through which most of these risk factors act. The use of conceptual frameworks by future research for framing study design, analyses, and interpretation of results could be a positive step towards increased clarity in the complex, multifactorial field of adult asthma epidemiology.

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APPENDIX A: Ethical Approval of Study

UNIVERSITY OF SASKATCHEWAN

Biomedical Research Ethics Board (Bio-REB)

Certificate of Approval

PRINCIPAL INVESTIGATOR	DEPARTMENT	Bio #
Donna Rennie	Institute of Agricultural Rural and Environmental Health	09-83

INSTITUTION(S) WHERE RESEARCH WILL BE CARRIED OUT
University of Saskatchewan
Canadian Centre for Health and Safety in Agriculture (CCHSA)
Saskatoon SK S7N 0W8

STUDENT RESEARCHERS
Robyn Kydd

SPONSORING AGENCIES
CANADIAN INSTITUTES OF HEALTH RESEARCH (CIHR)

TITLE
Gender-Related Associations with Associations with Asthma in a Community Population of Adults

ORIGINAL REVIEW DATE	APPROVED ON	APPROVAL OF	EXPIRY DATE
21-April-2009	23-April-2009	Protocol as submitted	20-April-2010

Expedited Review: ☒ Full Board Meeting: ☐

CERTIFICATION
The study is acceptable on scientific and ethical grounds. The Bio-REB considered the requirements of section 29 under the Health Information Protection Act (HIPA) and is satisfied that this study meets the privacy considerations outlined therein. The principal investigator has the responsibility for any other administrative or regulatory approvals that may pertain to this research study, and for ensuring that the authorized research is carried out according to governing law. This approval is valid for the specified period provided there is no change to the approved protocol or consent process.

FIRST TIME REVIEW AND CONTINUING APPROVAL
The University of Saskatchewan Biomedical Research Ethics Board reviews above minimal studies at a full-board (face-to-face) meeting. 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. For more information visit http://www.usask.ca/research/ethics review/.

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 Division 5 of the Food and Drug Regulations and carries out its functions in a manner consistent with Good Clinical Practices. This approval and the views of this REB have been documented in writing. The University of Saskatchewan Biomedical Research Ethics Board has been approved by the Minister of Health, Province of Saskatchewan, to serve as a Research Ethics Board (REB) for research projects involving human subjects under section 29 of The Health Information Protection Act (HIPA).

Michel Desautels, Ph.D., Chair
University of Saskatchewan
Biomedical Research Ethics Board

Please send all correspondence to:
Research Ethics Office
University of Saskatchewan
Box 5000 RPO University
1607 - 110 Gymnasium Place
Saskatoon, SK Canada S7N 4J8

UNIVERSITY OF SASKATCHEWAN

Biomedical Research Ethics Board (Bio-REB)

Certificate of Re-Approval

PRINCIPAL INVESTIGATOR	DEPARTMENT	BMC #
James A Dosman	Institute of Agricultural Rural and Environmental Health	02-663

INSTITUTION (S) WHERE RESEARCH WILL BE CARRIED OUT

University of Saskatchewan
Saskatoon SK

SPONSORING AGENCIES

CANADIAN INSTITUTES OF HEALTH RESEARCH (CIHR)

TITLE

Exposure to Endotoxin and the Lung

RE-APPROVED ON	EXPIRY DATE
10-Dec-2008	09-Dec-2009

Full Board Meeting ☐

Delegated Review ☑

CERTIFICATION

The study 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 research study, and for ensuring that the authorized research is carried out according to governing law. This re-approval is valid for the specified period provided there is no change to the approved protocol or consent process.

FIRST TIME REVIEW AND CONTINUING APPROVAL

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REB ATTESTATION

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Michel Desaulels, Ph.D., Chair
University of Saskatchewan
Biomedical Research Ethics Board

Please send all correspondence to:

Ethics Office
University of Saskatchewan
Room 302 Kirk Hall, 117 Science Place
Saskatoon, SK S7N 5C8
Phone: (306) 966-2975 Fax: (306) 966-2069

UNIVERSITY OF SASKATCHEWAN

Biomedical Research Ethics Board (Bio-REB)

Certificate of Re-Approval

PRINCIPAL INVESTIGATOR	DEPARTMENT	BMC #
James A. Dosman	Institute of Agricultural Rural and Environmental Health	02-663a

INSTITUTION (S) WHERE RESEARCH WILL BE CARRIED OUT

Horizon School District (northwest Humboldt SK	Humboldt Humboldt SK

SPONSORING AGENCIES

CANADIAN INSTITUTES OF HEALTH RESEARCH (CIHR)

TITLE:

PART II: Exposure to Endotoxin and Lung Function

(Exposure to Endotoxin and the Lung (Bio-REB 02-663)

RE-APPROVED ON	EXPIRY DATE
10-Dec-2008	09-Dec-2009

Full Board Meeting ☐

Delegated Review ☑

CERTIFICATION

The study 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 research study, and for ensuring that the authorized research is carried out according to governing law. This re-approval is valid for the specified period provided there is no change to the approved protocol or consent process.

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UNIVERSITY OF SASKATCHEWAN Biomedical Research Ethics Board (Bio-REB)

Certificate of Re-Approval

PRINCIPAL INVESTIGATOR	DEPARTMENT	Bio #
Donna Rennie	Canadian Centre for Health and Safety in Agriculture	09-83

INSTITUTION (S) WHERE RESEARCH WILL BE CARRIED OUT

University of Saskatchewan
Saskatoon SK

STUDENT RESEARCHER(S)

Robyn Kydd

SPONSORING AGENCIES

CANADIAN INSTITUTES OF HEALTH RESEARCH (CIHR)

TITLE:

Gender-Related Associations with Associations with Asthma in a Community Population of Adults

RE-APPROVED ON	EXPIRY DATE
19-Apr-2010	20-Apr-2011

Full Board Meeting ☐

Delegated Review ☑

CERTIFICATION

The study 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 research study, and for ensuring that the authorized research is carried out according to governing law. This re-approval is valid for the specified period provided there is no change to the approved protocol or consent process.

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APPENDIX B: Study Questionnaire

Questionnaire for the Fourth Humboldt Survey 2003

(For Adults Aged 18 to 79 Years)

The questionnaire can be answered by checking the best answer or by filling in a blank with a number or word(s).

Example 1:

Do you usually have a cough? No ___ Yes ___

Example 2:

How long have you lived in your current residence?
___ Years

* * *

Name:

_____ _____
Last First

Telephone No.: _____

Street address: _____

Spouse's name:

_____ _____
Last First

Spouse address: _____
(if different)

If you have any **biological (natural)** children who are **aged 6 to 17 years** and presently living in Humboldt, list their names and ages:

1. _____ age___
2. _____ age___
3. _____ age___
4. _____ age___
5. _____ age___

Have you participated in a previous Humboldt Study?

In the 1977 survey? Yes ___ No ___

In the 1983 survey? Yes ___ No ___

In the 1993 survey? Yes ___ No ___

FOR OFFICE USE:

Personal I.D.: _____

Family I.D.: _____

CONFIDENTIAL WHEN COMPLETED

* * *

1

Personal ID: _____

COUGH

A. Do you usually have a cough? No ___ Yes ___

B. Do you usually cough at all on getting up, or first thing in the morning? No ___ Yes ___

C. Do you usually cough at all during the rest of the day? No ___ Yes ___
Or at night? No ___ Yes ___

If **YES** to A, B, or C, answer D and E:

D. Do you usually cough like this on most days for 3 consecutive months or more during the year? No ___ Yes ___

E. For how many years have you had this cough? Number of years ___

PHLEGM

A. Do you usually bring up phlegm from your chest? No ___ Yes ___

B. Do you usually bring up phlegm at all on getting up, or first thing in the morning? No ___ Yes ___

C. Do you usually bring up phlegm at all during the rest of the day? No ___ Yes ___
or at night? No ___ Yes ___

If **YES** to A, B, OR C, answer D, E and F:

D. Do you bring up phlegm like this on most days for 3 consecutive months or more during the year? No ___ Yes ___

E. For how many years have you had trouble with phlegm? Number of years ___

F. Have you had periods or episodes of (increased) cough and phlegm lasting for 3 weeks or more each year?
No ___
Yes, last 3 years only ___
Yes, more than 3 years ___

WHEEZING

A. Does your chest ever sound wheezy or whistling:

1. When you have a cold? No ___ Yes ___

2. Occasionally apart from colds? No ___ Yes ___

3. Most days No ___ Yes ___

Or nights? No ___ Yes ___

If **YES** to 1, 2, OR 3, for how many years has this been present? Number of years ___

B. Have you ever had an attack of wheezing that has made you feel short of breath? No ___ Yes ___

If **YES**, have you ever required medicine or treatment for the(se) attack(s)? No ___ Yes ___

BREATHLESSNESS

If disabled from walking by any condition other than heart or lung disease, please describe and do not answer the following questions (A-E)

_____

A. Are you troubled by shortness of breath when hurrying on the level or walking up a slight hill? No ___ Yes ___

If **YES** to A, answer B to E:

B. Do you have to walk slower than people of your age because of breathlessness? No ___ Yes ___

C. Do you ever have to stop for breath when walking at your own pace on the level? No ___ Yes ___

D. Do you ever have to stop for breath after walking about 100 yards(or after a few minutes) on the level? No ___ Yes ___

E. Are you too breathless to leave the house or breathless on dressing or undressing? No ___ Yes ___

CHEST ILLNESSES

A. **During the past twelve months**, has a doctor ever said you had any of the following chest illnesses:

1. Asthma	No ___ Yes ___
2. Attack of bronchitis	No ___ Yes ___
3. Pneumonia	No ___ Yes ___
4. Hay fever	No ___ Yes ___
5. Sinus trouble	No ___ Yes ___
6. Chronic bronchitis	No ___ Yes ___
7. Emphysema	No ___ Yes ___
8. Other chest illness (including chest operations and injuries)	No ___ Yes ___

Specify _____

If **YES** to asthma, at what age were you diagnosed?
Age_____

If **YES** to asthma, how many times have you required services for asthma from the following places during the past twelve months? Emergency room ___
Doctor's office ___

B. **Before the past twelve months**, has a doctor ever said you had any of the following chest illnesses:

1. Asthma	No ___ Yes ___
If yes, at what age were you diagnosed?	Age_____
2. Attack of bronchitis	No ___ Yes ___
3. Pneumonia	No ___ Yes ___
4. Hay fever	No ___ Yes ___
5. Sinus trouble	No ___ Yes ___
6. Pulmonary tuberculosis	No ___ Yes ___
7. Chronic bronchitis	No ___ Yes ___
8. Emphysema	No ___ Yes ___
9. Other chest illness (including chest operations and injuries)	No ___ Yes ___

Specify _____

C. Which of the following statements best describes your asthma medication use **in the past 12 months**:

Never in the past 12 months ___
At least once in the past 12 months ___
At least once per month ___
At least once per week ___
Every day ___

PAST ILLNESSES - GENERAL

A. During the past twelve months, were you **seen** by a doctor for stomach acidity or reflux?
No ___ Yes ___

B. **During the past twelve months,** were you seen by a doctor for an injury?
No ___ Yes ___

C. **During the past twelve months,** were you seen by a doctor for an ear infection?
No ___ Yes ___

D. Has a doctor ever said you had:

1. Diabetes	No ___ Yes ___
2. Heart disease	No ___ Yes ___
3. High blood pressure	No ___ Yes ___
4. Cystic fibrosis	No ___ Yes ___
5. Heart defect	No ___ Yes ___

If **YES**, do you currently have any treatment for it?

1. Diabetes	No ___ Yes ___
2. Heart disease	No ___ Yes ___
3. High blood pressure	No ___ Yes ___
4. Cystic fibrosis	No ___ Yes ___
5. Heart defect	No ___ Yes ___

E. **During the past twelve months**, were you kept overnight in the hospital for any illness?

No ___ Yes ___

If **YES**, how many times? Times ___

Please specify:

	Diagnosis	length of stay (days)
1.	_____	_____
2.	_____	_____
3.	_____	_____

FAMILY HISTORY

A. Has (did) your **biological** father had (have):

1. Chronic bronchitis, emphysema, or chronic obstructive lung disease No ___ Yes ___ Don't know ___
2. Asthma No ___ Yes ___ Don't know ___
3. Diabetes No ___ Yes ___ Don't know ___
4. Heart disease or defect No ___ Yes ___ Don't know ___
5. High blood pressure No ___ Yes ___ Don't know ___

B. Has (did) your **biological** mother had (have):

1. Chronic bronchitis, emphysema, or chronic obstructive lung disease No ___ Yes ___ Don't know ___
2. Asthma No ___ Yes ___ Don't know ___
3. Diabetes No ___ Yes ___ Don't know ___
4. Heart disease or defect No ___ Yes ___ Don't know ___
5. High blood pressure No ___ Yes ___ Don't know ___

C. What is the total number of brothers and sisters (exclude half-brothers and half-sisters) you have?

Number___

D. How many of your brothers and sisters have had the following disorders?

1. Chronic bronchitis, emphysema, or chronic obstructive lung disease Number___
2. Asthma Number___
3. Diabetes Number___
4. Heart disease or defect Number___
5. High blood pressure Number___

OCCUPATIONAL HISTORY

A. In the last 5 years, have you grown or handled wheat durham, oats, barley, flax, canola, rye, mustard, alfalfa, o other grain, seeds, or legumes?

No ___ Yes ___

If **YES**, how many years? Years ___

B. In the last 5 years have you worked at looking after cattle hogs, sheep, poultry, horses, or other livestock animals?

No ___ Yes ___

If **YES**, how many years? Years ___

C. Have you ever worked for more than six months in any o the following: Mining No ___ Yes ___

Lumber No ___ Yes ___

Welding No ___ Yes ___

Grain elevator No ___ Yes ___

Feed mill No ___ Yes ___

Autobody No ___ Yes ___

Other No ___ Yes ___

If other, specify _____

D. Have you ever been exposed to grain dust in your work? No ___ Yes ___

Total years worked ___

Was dust exposure: Mild ___ Moderate ___ or Severe ___

E. Have you ever lived on a farm? No___ Yes___

If **YES**, at what ages? age _____to age_____

F. Have you had a farm-related injury **in the past 1 months?**

No ___ Yes ___

If **YES**, briefly describe below how and what happened.

_____

_____

_____

_____

AND

If **YES**, did you see a doctor or other health care worker?

No ___ Yes ___

CIGARETTE SMOKING

A. Have you ever smoked cigarettes? (If you have smoked less than 20 packs of cigarettes in your lifetime, answer no).

No ___ Yes ___

If **YES** to A, answer B to F:

B. Do you now smoke cigarettes? No ___ Yes ___

C. How old were you when you first started regular cigarette smoking? Age in years ___

D. How many cigarettes do you smoke per day now? Cigarettes/day ___

E. On the average of the entire time you smoked, how many cigarettes did you smoke per day?

Cigarettes/day ___

F. If you have stopped smoking cigarettes completely, how old were you when you stopped?

Age stopped ___

G. If there have been periods when you abstained from smoking, indicate total years of abstinence from smoking.

Years ___

PIPES AND CIGARS

A. Have you ever smoked a pipe regularly? (Yes means more than 12 oz of tobacco in a life-time.)

No ___ Yes ___

B. Have you ever smoked cigars regularly? (Yes means more than 1 cigar a week for a year.)

No ___ Yes ___

C. Do you smoke a pipe or cigars regularly at present?

No ___ Yes ___

PASSIVE SMOKING

A. **Except for you**, does any family member smoke cigarettes regularly in your home at present?

No ___ Yes ___

If **YES**, how many persons smoke cigarettes?

Number ___

How many cigarettes do they smoke per day in total?

Cigarettes/day ___

How many cigarettes do they smoke per day at home?

Cigarettes/day ___

B. **Except for you**, does any family member smoke a pipe or cigars regularly in your home at present?

No ___ Yes ___

If **YES**, how many persons smoke a pipe or cigars?

Number ___

DRINKING

A. Do you presently use alcoholic beverages?

No ___ Yes ___

If **YES**, is this as often as:

1 day per week? No ___ Yes ___

2 days per week? No ___ Yes ___

3 or more days per week? No ___ Yes ___

B. How many cups of coffee do you drink a day?

Cups ___

C. How many glasses of soft drink do you drink a day?

Glasses ___

ALLERGIES

A. Have you ever had an allergic reaction to things that:

1. Are eaten or ingested (e.g. food or medicine)?
No ___ Yes ___

2. Are inhaled (e.g. pollen, dust, animal fur or smoke)?
No ___ Yes ___

3. Come in contact with the skin (e.g. detergents, wool or metals)?
No ___ Yes ___

4. Others

Specify _____

WEIGHT

A. Do you consider yourself to be: Underweight? ___

Just about right weight? ___

Overweight? ___

B. Have you ever tried to lose weight?
No ___ Yes ___

C. Are you presently trying to lose weight, gain weight or neither?

Lose weight ___

Gain weight ___

Neither ___

D. If you are presently trying to lose weight, which of the following are you doing to lose weight?

Dieting No ___ Yes ___

Exercising No ___ Yes ___

Skipping meals No ___ Yes ___

Smoking No ___ Yes ___

Taking diet pills No ___ Yes ___

Attending programs No ___ Yes ___

Other, specify _____

LIVING ENVIRONMENT

A. How long have you lived in your current home?
Years ___

B. Which best describes the building in which you live?
A mobile home or trailer ___

A one-family house not attached to any other house ___

A one-family house attached to other house(s) ___

A building for 2 families ___

A building for 3 or more families ___

Other, specify _____

C. About which year was this building originally built?
Before 1980 ___ After 1980 ___ Don't know ___

D. How many bedrooms are there in your home?
Rooms ___

E. How many people live in your home? Number ___

F. How is your home heated in winter?
Gas furnace No ___ Yes ___

Electricity No ___ Yes ___

Steam or hot water No ___ Yes ___

Other, specify _____

G. What is usually used for cooking in your home?
Gas No ___ Yes ___

Electricity No ___ Yes ___

Other, specify _____

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

Air conditioners No ___ Yes ___

Air filter No ___ Yes ___

Humidifier No ___ Yes ___

Dehumidifier No ___ Yes ___

Fireplace No ___ Yes ___

(Living Environment, cont'd)

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

J. Do you have any pets living **inside** your home?
Dog(s) No ___ Yes ___
Cat(s) No ___ Yes ___
Bird(s) No ___ Yes ___

Other, specify _____

K. Have you ever had a pet living **inside** your home?
Dog(s) No ___ Yes ___
Cat(s) No ___ Yes ___
Bird(s) No ___ Yes ___

PERSONAL INFORMATION

A: Sex: Male ___ Female ___

B: Date of Birth: _____ _____ _____
Mo. Day Yr.

C: Age: _____

D: Place of Birth: _____

E: What is your race?
Caucasian ___
Aboriginal ___

Other (specify) _____

F: What is your marital status?
Single ___
Married/Common law ___
Widowed ___
Separated/Divorced ___

G: What is the highest grade completed in school?
Grade school not completed ___
Grade school completed ___
High school completed ___
Trade school or only attended college ___
College graduate/postgraduate ___

H: What is the range of your total, gross family income last year?
Under $12,000 ___
$12,000 to $24,999 ___
$25,000 to $49,999 ___
$50,000 and over ___

I: What is the national origin of your grandparents?
Paternal grandfather _____
Paternal grandmother _____
Maternal grandfather _____
Maternal grandmother _____

REMARKS:

APPENDIX C: Information Collected During Clinic Visit

For Office Use Only

ID# _____

HUMBOLDT FOURTH LUNG STUDY

Height _____ (cm) Weight _____ (kg) Girth Measurement _____

NOTE: Has this person taken a bronchodilator in the past 6 hours? Yes _____ No _____

If yes, rebook.

	1	2
Systolic BP (mmhg)	_____	_____
Diastolic BP (mmhg)	_____	_____

Lung Function Testing: (check) Station A _____ Station B _____

Done _____ Not Done _____

Reason why:
1. Subject could not perform the test _____
2. Refused _____
3. Other, specify _____

Room Temperature _____

Today's Date: _____ Tester's Initials: _____

Blood Test for Genetic Testing: Yes _____ No _____

COMMENTS: _____

Skin Testing
Antihistamine or cold preparation in the last 72 hours: No _____ Yes _____
NOTE: If yes, rebook.

Allergy Tests

Neg Control	_____	Cat	_____
Alternaria	_____	Grass Mix	_____
HDM	_____	Histamine	_____

Not Done _____

Reason why:
1. Subject could not perform the test _____
2. Refused _____
3. Other, specify _____