Prevalence of ACO (Asthma COPD Overlap) and associated risk factors in Aboriginal People

by

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Abstract

Aboriginal peoples are at a higher risk of many chronic respiratory diseases compared to the general Canadian population. Gender differences in incidence, susceptibility and severity of chronic respiratory diseases have also been long recognized among Aboriginal Peoples. Patients with Asthma-COPD Overlap (ACO), a disease newly described in 2015, are associated with frequent exacerbations, rapid decline in lung function, poor quality of life, high mortality and disproportionate utilization of healthcare resources than patients with asthma and COPD alone. The aim of this analysis is to investigate the prevalence and risk factors of ACO in Aboriginal peoples and to assess their gender-specific risk factors.

The Aboriginal Peoples Survey 2012 (N=28,410) is the fourth cycle of a national cross-sectional survey representative of the First Nations living off reserve, Metis and Inuit. The ACO definition was based on the respondent giving positive responses to both of the following questions *"Do you/Does(name) have Asthma diagnosed by a health professional?"* and *"Do you/Does (name) have chronic bronchitis, emphysema or chronic pulmonary obstructive disease or COPD diagnosed by a health professional?"*

The prevalence of ACO was 1.65% and 3.53% in Aboriginal males and females respectively. Aboriginal peoples older than 45 years, having a total personal income below $20,000 were associated with a significant risk of ACO. Residing in Ontario and Quebec, living in a rented dwelling, dwelling in need of major repairs and working more than 40 hrs a week were also significantly associated with increased risk of ACO while female-specific risk factors significantly associated with increased risk of ACO included being widowed, separated or divorced, a current daily smoker and having a diagnosis of diabetes. The results from this study will offer useful evidence for future development of prevention and public health intervention programs in Aboriginal communities to reduce the burden of ACO.

Dedication

This dissertation is dedicated to my wonderful parents, Dr Adenrele Koleade and Mrs Roseline Koleade, for their support and encouragement throughout my Master's program.

Also to my brother, Babatomiwa Koleade, my sister, Tejumade Koleade, my best friend, Adeboye Olaoye for their support and help you have provided to me.

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List of Abbreviations

Asthma COPD Overlap	ACO
Chronic Obstructive Pulmonary Disease	COPD
Obstructive Airway Diseases	OADs
Medical Research Council	MRC
Chronic Bronchitis	CB
European Community for Coal and Steel	ECSC
American Thoracic Society and the Division of Lung Diseases	ATS-DLD-78
Tasmanian Asthma Survey	TAS
International Study of Asthma and Allergies in Childhood	ISAAC
Aboriginal Peoples Survey	APS
Behavioural Risk Factor Surveillance	BRFSS
Confidence Intervals	CI
Environmental Tobacco Smoke	ETS
Global Initiative for Obstructive Lung Disease	GOLD
Health Research Ethics Board	HREB
National Health Survey	NHS
National Longitudinal Survey of Youth	NLSY
Newfoundland and Labrador	NL
Odds Ratio	OR
Particulate Matter$_{2.5}$	$PM_{2.5}$
Quality of Life	QoL
Regional Health Authority	RHA
Socioeconomic Status	SES

Standard Deviation	SD
Statistical Analysis System	SAS
Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans	TCPS2

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CHAPTER 1

INTRODUCTION

1.1 Asthma-COPD Overlap (ACO)

Asthma-COPD Overlap (ACO) is clinically characterized by persistent airflow limitation with several features usually associated with asthma and several features usually associated with Chronic Obstructive Pulmonary Disease (COPD).[1,2] ACO is therefore identified by the features that it shares with both asthma and COPD. This is a new obstructive lung disease with its first treatment and management guidelines reported in 2015.[1]

1.2 Diagnosis of ACO

ACO is a disease that affects patients above 40 years of age but may have had symptoms in childhood or early adulthood. This is similar to patients with COPD who are usually diagnosed around the same age.[3,4] Patients with ACO report a history of physician-diagnosed asthma which could be current or previous, allergies, family history of asthma and exposure to noxious gases.[2-4] Respiratory symptoms for ACO may include persistent exertional dyspnea but variability may be prominent while asthma may be triggered by exercise, emotions, dust or exposure to allergens.[5-7] COPD is quite similar to ACO with continuous symptoms particular during exercise. Patients with ACO present with worse exacerbations compared to asthma and COPD which can be reduced considerably by treatment.[5,8] The presence of comorbidities is also common among patients with ACO which could also contribute significantly to impairment. Chest X-ray scans of patients with COPD are similar to those with ACO which include severe hyperinflation.

1.3 Survey Questionnaires

The use of questionnaires for assessing obstructive airway diseases (OADs) have been in practice for a long time. The first widely used questionnaire in respiratory epidemiology was

the Medical Research Council (MRC) of Great Britain. In the first version, from 1960, there were only a few questions about wheezing, but in later editions, more questions about asthma, Chronic Bronchitis (CB), which is a type of COPD and asthma-like symptoms were added.[9,10] The MRC questionnaire initiated the development of other questionnaires such as the European Community for Coal and Steel (ECSC) questionnaire of respiratory symptoms and the questionnaire from the American Thoracic Society and the Division of Lung Diseases (ATS-DLD-78).[10] In the 1960 version of the MRC questionnaire, there were only a few questions about wheezing and unspecified chest illnesses. In the 1966 version, this topic was expanded with questions about attacks of shortness of breath and wheezing. A specific question on bronchial asthma was also added. In the 1986 version, the questions about wheeze and episodic breathlessness also dealt with the occurrence within the last 12 months.[9-11]

In more recent years, large population-based surveys, often rely on questionnaires as they are relatively economical when compared to examination of each subject.[12,13] The Tasmanian Asthma Survey (TAS) and the International Study of Asthma and Allergies in Childhood (ISAAC) are more recent questionnaires to measure the prevalence of asthma in adults and children.[14] These two questionnaires showed high agreement with respiratory physician diagnosis with respect to asthma symptoms in the past 12 months. For the TAS questionnaire the positive and negative predictive values for physician diagnosis for adults were 0.89 and 0.94 respectively. The instrument was also sensitive 0.80 (0.58-0.93) and highly specific 0.97 (0.90-0.99).[12]

1.4 Aboriginal Peoples Survey 2012 (APS)

The APS 2012 is a national cross-sectional survey data collected by Statistics Canada from February to July 2012. This is the fourth cycle representative of the First Nations living off reserve, Metis and Inuit. The APS 2012 was reported to have a response rate of 76% and

respondents were chosen based on self-identification as being Aboriginal or having Aboriginal ancestry from the 2011 National Health Survey (NHS). It collected detailed information on Aboriginal identity, education, culture, income, health status, housing and family background. This study included only Aboriginal peoples aged ≥12 years to whom the information on the diagnosis of ACO was collected. A total of 28,410 Aboriginal peoples in the APS provide sufficient power for our statistical analysis

1.5 Outcome Variable

The outcome variable for this thesis, as mentioned earlier is ACO. This is a new disease described in 2015 and identified by the features that it shares with both asthma and COPD. The primary outcome variable ACO was based on the respondent giving positive responses to both of the following questions *"Do you/Does(name) have Asthma diagnosed by a health professional?"* and *"Do you/Does (name) have chronic bronchitis, emphysema or chronic pulmonary obstructive disease or COPD diagnosed by a health professional?"*.

1.6 Predictor Variables

The predictor variables selected for this thesis were based on literature review on the risk factors associated with asthma and COPD[15,16] and also the availability of variables in the survey data. We assessed the questions asked in the survey codebook putting into consideration missing values and valid answers to several questions. Several epidemiological studies show that demographic variables of Age, Sex and Marital Status have a significant association with OADs.[5,17,18] Environmental variables which include rural or urban, province, dwellings in need repairs, number of people in a household and number of rooms in a dwelling have also been associated with asthma, COPD and ACO.[19-21] In addition, socio-economic variables such as total personal income, number of paid hours per week and dwelling whether owned or rented have been reported to be associated with OADs.[22-24] Also, lifestyle variables which includes

smoking status and smoking in the home have been reported to be associated with COPD.[25] We considered a number of diseases in the APS survey data, however we either could not prove the relationship with respiratory diseases in the literature review or the variables had high missing values. Diabetes was the only disease that can be linked to respiratory diseases and also had a good number of values for analysis.[26-28]

1.7 Statement of the problem

Aboriginal peoples are at a higher risk of many chronic respiratory diseases compared to the general Canadian population.[29-31] A recent Canadian survey showed that approximately 15% of Aboriginal peoples had been diagnosed with at least one of the chronic respiratory diseases (COPD, CB, emphysema and asthma) compared to 10% for non-Aboriginal peoples in Canada.[32] Inequalities in health status often result from social, cultural, economic, environmental and political factors. Education level, occupation, income, rurality, accessibility to health care and possible interplays between these determinants of health can lead to disparities. A higher prevalence of chronic respiratory diseases in Aboriginal peoples has been associated with many factors including higher smoking rate, poor housing, poor schooling, low household income and lack of timely access to health care.[33]

OADs including asthma and COPD have been associated with social, economic and health impact on individuals, families and society in general.[34] In a US study, the prevalence of adult asthma was reported to be 7.7% in those aged 35-64 years, while the prevalence of COPD was between 6.6% to 9.2% across the age group of 45 to 64 years; and even higher from 11.6% to 12.1% across age 65 years and older.[35,36] Recently, a new obstructive airway disease, Asthma-COPD Overlap (ACO) was described, with its first treatment and management guidelines reported in 2015.[37] Patients with ACO experience a greater health burden including worse respiratory symptoms, poorer health-related quality of life (QOL), frequent

exacerbations leading to more emergency visits, comorbidities and higher doses of medications, as compared to asthma and COPD alone.[34,38-40]

Several studies on the incidence of ACO in the general population have been carried out in the US, UK, Poland, Finland, Spain and Latin American countries.[2,27,34] A recent study from Finland suggested that the prevalence of ACO was about 27% in asthma patients with a smoking history.[41] Another study suggested that about 10 to 20% of patients with COPD may have ACO.[2] A retrospective study reported that patients with ACO had a significantly higher prevalence of comorbidities, greater health care utilization rates and nearly doubled health care costs.[38] Another retrospective cohort also reported higher hospitalization rates in patients with ACO compared to the patients with COPD only (31.3% vs 13%, P = 0.0001).[42]However, there remains a gap in knowledge about the burden and risk factors of ACO in Aboriginal peoples.

Sex and gender differences in incidence, susceptibility and severity of many chronic respiratory diseases have been long recognized. Females generally experience more severe symptoms and a worse prognosis for asthma compared to males of the same age,[43]; while males are at higher risk for COPD than females.[44] Although the biological mechanisms of sex differences are not fully understood, recent evidence suggests the involvement of sex-related hormones. Epidemiological studies consistently show differences in many lung diseases before and after both puberty and menopause when sex hormones experience dramatic changes.[45-47] Macsali et al, 2012. observed that women who underwent early puberty had a lower lung function and more asthma in adulthood. Varying levels of the female sex hormones (oestrogen and progesterone) during the regular, pregnancy and late ovulatory cycles play a key role in chronic respiratory diseases.[48] Increased asthma exacerbation and lung functions changes have been reported during pregnancy and menstrual cycle phases respectively.[49-51]

Results from these studies have suggested that sex hormones play a significant role in many chronic lung diseases. Recent epidemiological studies consistently show that gender differences significantly affect the risk of lung diseases. Females in rural areas exposed to high levels of biomass smoke and other indoor air pollutants due to routine cooking are associated with higher levels of respiratory diseases compared to males, and about 50% of deaths in females were associated with COPD.[52]Another study reported that due to the recent increased rate of cigarette smoking among women, they may be more disposed to the development of severe COPD.[53]

1.8 Study objectives

The primary objective of this study is to investigate the prevalence and risk factors of this new disease ACO in Aboriginal people. The secondary objective is to assess the gender-specific risk factors associated with ACO in Aboriginal people. Data from the 2012 Aboriginal Peoples Survey (APS), a national survey with detailed information on the demographics, environmental, health and lifestyle status of Aboriginal people provided a unique platform to address these questions.

1.9 Thesis submitted for the partial fulfilment of MSc

This thesis consists of a comprehensive literature review on Aboriginal peoples, the prevalence of Asthma and COPD, Asthma COPD Overlap (ACO). It is followed by two studies designed to address each of the two specific objectives.

In Chapter 2, a detailed description of the prevalence and risk factors of ACO in Aboriginal people.

In Chapter 3, gender-specific risk factors associated with ACO in Aboriginal People were assessed.

A summary of the results of the two studies earlier mentioned is presented in Chapter 4. This chapter includes an overview of the thesis research, specific risk factors and gender specific risk factors associated with ACO in Aboriginal people, strength and limitations of the studies and plans for future research.

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CHAPTER 2

PREVALENCE AND RISK FACTORS OF ACO (ASTHMA COPD OVERLAP) IN ABORIGINAL PEOPLE

2.1 ABSTRACT

Aboriginal peoples are at a higher risk of many chronic respiratory diseases compared to the general Canadian population. Patients with Asthma-COPD Overlap (ACO), a disease newly described in 2015, are associated with frequent exacerbations, rapid decline in lung function, poor quality of life, high mortality and disproportionate utilization of healthcare resources than patients with asthma and COPD alone. The objective was to investigate the prevalence and risk factors of ACO in Aboriginal peoples. Data from the 2012 Aboriginal Peoples Survey (APS) was used for this study. The ACO definition was based on the respondent giving positive responses to both of the following questions *"Do you/Does(name) have Asthma diagnosed by a health professional?"* and *"Do you/Does (name) have chronic bronchitis, emphysema or chronic pulmonary obstructive disease or COPD diagnosed by a health professional?"*. Aboriginal peoples older than 45 years, female, widowed, separated or divorced, having a total personal income below $20,000 were associated with a significant risk of ACO. Residing in Ontario, being a daily smoker, living in a rented dwelling, dwelling in need of major repairs, having diabetes and working more than 40 hrs a week were also significantly associated with increased risk of ACO. The results from this study will provide information to aid the development of prevention and intervention strategies for Aboriginal communities.

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2.2 Introduction

Aboriginal peoples are at a higher risk of many chronic respiratory diseases compared to the general Canadian population.[1-3] A recent Canadian survey showed that approximately 15% of Aboriginal peoples had been diagnosed with at least one of the chronic respiratory diseases (chronic obstructive pulmonary disease [COPD], chronic bronchitis (CB), emphysema and asthma) compared to 10% for non-Aboriginal peoples in Canada.[4] Inequalities in health status often result from social, cultural, economic, environmental and political factors. Education level, occupation, income, rurality, accessibility to health care and possible interplays between these determinants of health can lead to disparities. A higher prevalence of chronic respiratory diseases in Aboriginal peoples has been associated with many factors including higher smoking rate, poor housing, poor schooling, low household income and lack of timely access to health care.[5]

Obstructive airway diseases including Asthma and COPD have been associated with social, economic and health impact on individuals, families and society in general.[6] In a US study, the prevalence of adult asthma was reported to be 7.7% in those aged 35-64 years, while the prevalence of COPD was between 6.6% to 9.2% across the age group of 45 to 64 years; and even higher from 11.6% to 12.1% across age 65 years and older.[7,8] Recently, a new obstructive airway disease, the Asthma-COPD Overlap (ACO) was described, with its first treatment and management guidelines reported in 2015.[9] However, little information is currently available including the prevalence of ACO and its associated risk factors. A recent study from Finland suggested that the prevalence of ACO was about 27% in asthma patients with a smoking history.[10] Another study suggested that about 10 to 20% of patients with COPD may have ACO.[11]

Patients with ACO experience a greater health burden including worse respiratory symptoms, poorer health-related quality of life (QOL), frequent exacerbations leading to more emergency visits, comorbidities and higher doses of medications, as compared to asthma and COPD alone.[6,12-14] Given that aboriginal peoples are at a higher risk of chronic respiratory diseases,[1,2,15] there is a need to study the prevalence and risk factors of this new disease (ACO) in Aboriginal people. Data from the 2012 Aboriginal Peoples Survey (APS), a national survey with detailed information on the demographics, environmental, health and lifestyle status of Aboriginal peoples provided a unique platform to address these questions.

2.3 Methods

2.3.1 Study design:

Data from the 2012 APS collected by Statistics Canada from February to July 2012 was used for this study. This is a national cross-sectional survey of First Nations living off reserve, Metis and Inuit. It collected detailed information on Aboriginal identity, education, culture, income, health status, housing and family background. The APS 2012 was reported to have a response rate of 76%. Respondents were chosen based on self-identification as being Aboriginal or having Aboriginal ancestry from the 2011 National Health Survey (NHS). This study included only Aboriginal peoples aged ≥12 years to whom the information on the diagnosis of COPD was collected.

2.3.2 Outcome variable and risk factors:

The primary outcome variable ACO was based on the respondent giving positive responses to both of the following questions *"Do you/Does(name) have Asthma diagnosed by a health professional?"* and *"Do you/Does (name) have chronic bronchitis, emphysema or chronic pulmonary obstructive disease or COPD diagnosed by a health professional?"*.

The variables of interest were categorized into demographics, environmental, socioeconomic, lifestyle variables and other diseases. Demographic variables consist of *Age, Sex* and *Marital Status*; Environmental variables consist of *Rural or Urban* (This is defined by the NHS Population Centre size), *Province, Dwelling - owned or rented, Dwelling – need repairs, Number of people in a household/Number of rooms in a dwelling*. Socio-economic variables consisted of *Total Personal Income, Employment – the number of paid hours per week.* Lifestyle variables consisted of *Smoking Status and Anybody smoking in the dwelling* and other diseases such *as Diabetes*. The ethics approval for this study has been approved by the Health Research Ethics Board (HREB) of Newfoundland and Labrador with reference protocol number: 20171751.

2.4 Statistical analysis:

Mean (standard deviation), and count (frequency) was calculated for continuous and categorical variables, respectively. Sampling weights were included in all statistical analyses. PROC SURVEYLOGISTIC was used to identify the significant risk factors for ACO in the univariate and multivariate analysis. Only clinically important factors and variables with a p-value lower than 0.20 in the univariate analysis were included in the multivariate analysis. To account for complex survey design of the APS, variances were estimated using 1,000 bootstrap weights with a Fay adjustment factor of 0.75**.** The level of significance α=0.05 was used for the multivariate logistic regression. Data analysis was conducted using SAS version 9.4.

2.5 Results

2.5.1 Descriptive statistics:

The distribution of the population is shown in Table 1. The prevalence of ACO in the Aboriginal population was (2.7%).

Examinations of demographic variables showed that almost half the population was between the age of *12 to 34 years* (45%) followed by those aged 3*5 to 44 years* (17%), *45 to 54 years* (18%), *55 to 64 years* (12%) and *65 years and over* (8%). Fifty-four percent of the sample were f*emales*. *Married and Living in common-law* represented the highest proportion of (48%) followed closely by *Single and never married* (38%) while the *Widowed, separated and divorced group* was (14%).

Examination of environmental variables showed that individuals from a *Large urban population centre* (100,000 or more) represented the highest proportion (43%), followed by *Rural area* which was (24%), *Small population centre* (1,000 to 29,999) was (21%) while the *Medium population centre* (30,000 to 99,999) had the least at 12%. Individuals by province showed that *Prairies (Alberta, Manitoba, Saskatchewan)* had the highest proportion (36%), followed by *Ontario* (25%), *British Columbia* (17%), *Quebec* (10%), *Atlantic Canada (Nova Scotia, Newfoundland and Labrador, Prince Edward Island and New Brunswick)* (8%) while the *Territories (Nunavut, Yukon, Northwest Territories)* (4%). *Dwellings that needed only regular maintenance* recorded the highest proportion (62%) while *dwellings that required major repairs* yielded a proportion of (12%). Most people living in a dwelling of *3 to 5 rooms* yielded (45%), *6 to 8 rooms* recorded (33%), *9 rooms and over* recorded (16%) while the least proportion was *0 to 2 rooms* with (6%).

Examination of social-economic status showed that individuals who earn *$20,000 to 49,999* per year had the highest proportion (32%), followed by those that earn between *$5,000 to 19,999* (28%). Individuals earning *$50,000 to $100,000 and over* were (23%) while the lowest proportion was *$5,000 or less* with (18%). About employment hours per week, individuals working above *80 hours and above* recorded the highest proportion (46%), *21 to 40 hours* (37%), *41 to 79 hours* per week and working part-time of *0 to 20 hours* yielded (9%)

and (8%) respectively. Individuals that *Owned a dwelling* had a higher proportion (58%) when compared to those that *Rent a dwelling* (42%).

Examination of lifestyle variables showed that individuals that smoked *Daily* had a proportion of (28%) while those that smoked *Occasionally* recorded a lower proportion (9%). Individuals that *Smoke at home* recorded a proportion of (64%) when compared to those that *do not smoke at home* (36%). Diabetes (type 1 and 2) was reported to be (9%) of the respondents.

2.5.2 Univariate Analysis

The results from the Univariate analysis are shown in Table 2. *Age* was significantly associated with ACO. In comparison to those aged *12-34 years*, individuals who were older than 45 years were about three times more likely to have ACO ($OR_{45\ to\ 54\ years}$ = 2.81; 95% CI = 1.71 - 4.61, p <0.0001; $OR_{55\ to\ 64\ years}$ = 2.80; 95% CI = 1.71 - 4.59, p <0.0001) and ($OR_{65\ years\ and\ over}$ = 3.20; 95% CI = 1.89 - 5.43, p <0.0001). *Females* were two times more likely to be associated with ACO than *Males* (OR = 2.18; 95% CI = 1.58 - 3.00, p <0.0001). In comparison to those *Married or Living in common-law*, individuals who were *Widowed, Separated and Divorced* (OR = 3.80; 95% CI = 2.48 - 5.84, p <0.0001) and *Single and never married* (OR = 1.42; 95% CI = 1.01 - 2.00, p <0.0001) were more likely to be associated with higher risks of ACO.

Individuals from the *Small population centre* were significantly less likely to be associated with ACO in comparison to individuals from a *Large urban population centre* (OR = 0.66; 95% CI = 0.45 - 0.98, p <0.0370). In comparison to Ontario, other provinces and regions were significantly less likely to be associated with ACO except for *Quebec*, (OR_{Quebec} = 1.72; 95% CI = 1.05 – 2.81, p <0.0320), ($OR_{Atlantic}$ = 0.32; 95% CI = 0.18 – 0.59, p <0.0002), ($OR_{Prairies}$ = 0.65; 95% CI = 0.42 – 1.00, p <0.0471), ($OR_{British\ Columbia}$ = 0.52; 95% CI = 0.32 – 0.86, p <0.0100), ($OR_{Territories}$ = 0.29; 95% CI = 0.17 - 0.51, p <.0001). Individuals residing in

a *dwelling in need of major repairs* were three times more likely to be associated with ACO compared to those that reside in a *dwelling that needs only regular maintenance*. (OR = 3.35; 95% CI = 2.19 - 5.13, p <0.0001). In comparison to those living in a dwelling of *0 to 2 rooms,* individuals living in a dwelling with *6 – 8 rooms* and *9 rooms – over* were significantly less likely to be associated with ACO, ($OR_{6-8\ rooms}$ = 0.32; 95% CI = 0.16 - 0.63, p <0.0010), ($OR_{9\ rooms+}$ = 0.21; 95% CI = 0.10 - 0.44, p <0.0001).

Among the socioeconomic variables, individuals who earn between *$5,000 or less* to *$100,000 and over* were significantly less likely to be associated with ACO in comparison to individuals who earn *$5,000 to 19,999* ($OR_{\$5,000\ or\ less}$ = 0.35; 95% CI = 0.22 – 0.55, p <0.0001), ($OR_{\$20,000\ to\ \$49,999}$ = 0.36; 95% CI = 0.25 – 0.53, p <0.0001), ($OR_{\$50,000\ to\ \$100,000\ and\ over}$ = 0.13; 95% CI = 0.07 – 0.24, p <0.0001). Individuals who worked *80 hours and over* were approximately four times more likely to be associated with increased risk for ACO when compared to *0 to 20 hours* of paid hours per week. (OR = 3.65; 95% CI = 1.82 - 7.32, p = 0.0003). Also, individuals *living in the rented dwelling* were three times more likely to be associated with ACO when compared to those *owning the dwelling* (OR = 2.69; 95% CI = 1.95 - 3.70, p <0.0001).

Among lifestyle variables, *Daily smoking* was more than two times more likely to be associated with ACO in comparison to individuals reporting *No smoking at all* (OR = 2.42; 95% CI = 1.78 - 3.32, p <0.0001). Furthermore, individuals with a report of *smoking at home* were two times more likely to be associated with ACO when compared to those with report *Not smoking at home* (OR = 2.04; 95% CI = 1.42 - 2.94, p <0.0001).

Individuals who report a diagnosis of *Diabetes type 1 and 2* were three times more likely to be associated with ACO compared to those without the *diagnosis of diabetes* (OR = 3.38; 95% CI = 2.34 - 4.90, p <0.0001).

2.5.3 Multivariate Analysis

As shown in Table 3, the results from the multivariate analysis showed the following demographic variables were significantly associated with ACO: Individuals aged between 45 to 54 years were two times more likely to be associated with ACO in comparison to individuals aged between *12-34 years* (OR = 2.43; 95% CI = 1.34 - 4.42, p = 0.0035). *Females* were approximately two times more likely to be associated with ACO compared to *Males* (OR = 1.74; 95% CI = 1.25 - 2.45, p = 0.0013) Also, individuals who were *widowed, separated or divorced* were two times more likely to be associated with ACO compared to individuals who were either *married or living in common-law* (OR = 1.97; 95% CI = 1.19 to 3.25, p = 0.0080).

In comparison to individuals from *Ontario*, individuals from *Atlantic regions*, *Territories* and *British Columbia* were significantly less likely to be associated with ACO. ($OR_{Atlantic\ Canada}$ = 0.31; 95% CI = 0.16 to 0.61, p = 0.0007), ($OR_{Territories}$ = 0.21; 95% CI = 0.21 - 0.39, p = <0.0001) and ($OR_{British\ Columbia}$ = 0.51; 95% CI = 0.30 to 0.88, p = 0.0158). Also, individuals *living in a dwelling in need of major repairs* were two times more likely to be associated with ACO compared to those living in a *dwelling* in *need of regular maintenance* (OR = 2.31; 95% CI = 1.46 - 3.65, p = 0.0004).

Among the socioeconomic variables, the following three variables were significantly associated with ACO: Individuals who earn between *$5,000 to $19,999* were three times more likely to be associated with ACO compared to those who earn *$50,000 to $100,000 and over*. (OR = 3.00; 95% CI = 1.44 to 6.23, p = 0.0033). Individuals working long hours of *41 to 80 hours* and *81 hours and over* were significantly associated with ACO compared to those working *0 to 20 hours per week.* ($OR_{41\ to\ 80\ hours}$ = 2.83; 95% CI = 1.12 to 7.14, p = 0.0273), ($OR_{81\ hours\ and\ over}$ = 2.85; 95% CI = 1.36 to 5.97, p = 0.0057). Also, individuals who live in a *rented dwelling* were approximately two times more likely to be associated with ACO than those *owning a dwelling* (OR = 1.76; 95% CI = 1.24 to 2.51, p = 0.0018).

Smoking was significantly associated with ACO: individuals who *smoke daily* were found to be about two times more likely to be associated with ACO compared to those that *do not smoke at all* (OR = 1.66; 95% CI = 1.14 - 2.41, p = 0.0084). Aboriginal people with diabetes (type 1 and 2) were also approximately two times more likely to develop ACO compared to those without the diagnosis of diabetes (OR = 1.68; 95% CI = 1.10 to 2.58, p = 0.0188).

2.6 Discussion

Using the APS dataset, our results suggest that Aboriginal peoples older than 45 years, female, widowed, separated or divorced, having a total personal income below $20,000 were associated with a significant risk of ACO. Residing in Ontario, being a daily smoker, living in a rented dwelling, dwelling in need of major repairs, having diabetes and working more than 40 hrs a week were also significantly associated with increased risk of ACO.

Individuals aged 45 to 54 years old are two times more likely to be associated with ACO when compared to the younger individuals aged 12 to 34 years. In a longitudinal population-based study in the Netherlands, the authors reported that the risk of being diagnosed with COPD increased with age. A male who was free of COPD at age 40, had an increased risk of being diagnosed with COPD from 0.8% to 12% with increasing years from 10 to 40 years; while a female of the same age, had increased risk from 0.8% to 8.3%.[16] In another population-based cohort study from Ontario, Canada, estimating trends in the prevalence and incidence of concurrent physician-diagnosed asthma and COPD, the authors reported that the standardized prevalence increased by 10.5% from 2002 to 2012 mainly in young adults.[17] Additionally, a cross-sectional study among Aboriginal people assessed the risk factors associated with COPD. It was reported that individuals aged 55 and older were significantly associated with the risk of COPD.[18] We could find no other studies that focused on Aboriginal peoples with ACO.

Chronic respiratory diseases, especially COPD have always been attributed to men older than 40 years. However, recent findings suggest that there is a growing increase in women diagnosed with COPD. In a study of 1,633 residents from Saskatchewan, Canada, it was reported that in females, the combined effect of grain farming and smoking history had a significant association with CB but not in males.[19] Another study assessing the prevalence of CB in Aboriginal peoples reported that females had a higher prevalence than males.[4] Additionally, females with more severe COPD have a higher risk of hospitalization and death due to respiratory failure and possible comorbidities when compared to males.[20] Our study which appears to be the first to assess the risk of ACO in Aboriginal peoples, suggests that Aboriginal females are approximately two times more likely to report ACO compared to males.

The association between obstructive airway diseases and marital status has been examined in many population studies. In a study, patients diagnosed with COPD were described and compared based on their nutritional status, gender, pulmonary function and marital status. The authors reported that individuals diagnosed with COPD who lived alone had a worse nutritional status.[21] A longitudinal study in the US focused on the psychological imbalance caused by bereavement and divorce in relation to COPD. It was reported that remarriage after bereavement or divorce was associated with a significantly decreased risk of COPD onset.[22] Our study showed that Widowed, Separated and Divorced Aboriginal peoples were found to be two times more likely to be associated with ACO compared to those married or living common-law.

We reported significant geographic variation in the prevalence of ACO with people in Ontario being at a significantly higher risk of ACO compared to people from other provinces or regions. A study in Ontario, Canada, assessed individuals with asthma and COPD to see if higher levels of exposure to air pollution will increase the risk for ACO.[23] The authors reported that individuals exposed to higher levels of air pollution had nearly three times the risk of

developing ACO.[23] The same group of researchers in a longitudinal cohort of women reported that the risk of COPD increased by more than 20% with each unit increase in exposure to $PM_{2.5.}$[24] The presence of industries and a huge population with automobiles Quebec and Ontario could play a role in the association between air pollution and ACO. The APS 2012 survey focused on aboriginal people living off reserve which could be interpreted that certain parts of these two provinces inhabited by aboriginal people might experience air pollution.

In our study, we reported that Aboriginal peoples living in dwellings in need of major repairs were two times more likely to develop ACO. A study examining the differences in hospitalization for respiratory tract infections among First Nations using the 2006 census reported that poor housing conditions and income were contributing factors in hospitalization.[25] Another study from Saskatchewan, Canada, which assessed the prevalence of CB in two Aboriginal communities, reported that houses with a musty smell of mould were positively associated with CB.[26] This is also consistent with a study from the United States, which reported that 15% of people who reported a musty smell in their dwelling also reported CB and asthma.[27]

Meanwhile, studies have shown that lower socioeconomic status is associated with respiratory diseases.[28,29] Total personal income and paid employment hours in our study suggested Aboriginal peoples working over 40 hours a week and earning a low annual income of $20,000 were more likely to develop ACO when compared to Aboriginal peoples earning an income of $50,000 or greater and working same or fewer hours. A large population-based study of 8, 028 individuals reported that low income and low quality of education were risk factors for asthma and COPD.[29] In a cross-sectional study that focused on the associated factors of COPD among Aboriginal peoples, the authors reported that Aboriginal peoples making less than the median income of $20,600 were at a higher risk to be associated with COPD.[18]

There is still conflicting information about the impact of work hours on chronic respiratory diseases. A longitudinal study that continued for a 32-year period made use of the National Longitudinal Survey of Youth (NLSY) 1979. It collected information on job histories and work hours in relation to chronic disease status. The authors reported that there were no significant findings for an association between long hours and asthma.[30] This was not consistent with the result of our study. This could be due to the homogeneity of the Aboriginal population used in our study compared to the general population used in this longitudinal study. In a study that focused on housing conditions, it was reported that homeownership was related to home quality.[31] Poorly maintained houses could also lead to the loss of vapour barrier, which allows areas of dampness that are prone to contamination with mould.[32] Owned dwellings tend to have their repairs fixed quicker than rented dwellings. Our results suggest that individuals renting a dwelling are also approximately three times more likely to develop ACO when compared to owning a house.

In our study, individuals who smoke daily were found to be about two times more likely to be associated with ACO compared to those that do not smoke. Even though cigarette smoking has decreased considerably over the past decades, there is still a significant link between positive smoking or the exposure to environmental tobacco and respiratory diseases.[10,33-35] Aboriginal peoples are observed to have higher smoking rates compared to the general Canadian population,[5] but there are not many studies that have focused on the association between smoking and ACO. Kiljander et al. investigated the prevalence of ACO among 190 asthmatic patients with a smoking history. These patients had no previous diagnosis of COPD but were either current or ex-smokers with a history of at least ten pack years. It was reported that 27% of the patients were found to have ACO.[10] Another study from Sweden examining the association between environmental tobacco smoke (ETS) and risk of COPD showed that ETS was independently associated with COPD. However, the association was

more significant with increased ETS exposure either at home, previous or current work or at the three mentioned locations.[33] In two Aboriginal studies that investigated the factors associated with the prevalence of CB and COPD, daily or current smokers were significant compared to never smokers.[4,18]

In our study, Aboriginal peoples a diagnosis of diabetes (either type 1 or type 2) were approximately two times more likely to develop ACO. Epidemiological studies have consistently reported that many socioeconomic and lifestyle factors such as smoking are significantly associated with both diabetes and chronic respiratory diseases.[36,37] Pleasants et al, made use of the Behavioural Risk Factor Surveillance System (BRFSS) to assess the relationships between COPD, asthma and co-morbidities such as diabetes. It was reported that adults with overlap syndrome had the highest prevalence of diabetes.[37]

In addition to the shared risk factors between chronic respiratory diseases and diabetes, the current medication for patients with asthma and COPD may also play a role. However, the results from different studies are not consistent. A nested case-control study from Quebec, Canada assessed whether the use and dose of inhaled corticosteroids increase the risk of diabetes onset and progression in patients treated for respiratory diseases. It was reported that current use of inhaled corticosteroids was associated with a 34% increase in diabetes onset and progression while risks were even more significant at higher doses for the treatment of COPD.[38] Another study from Poland reported that concomitant diseases were diagnosed in 85% of patients with ACO, with the prevalence of diabetes being approximately 20%.[39] In contrast, a retrospective study evaluated whether there was an increased risk of new onset of diabetes or hyperglycemia among patients with asthma or COPD treated with inhaled corticosteroids. It was reported that treatment with inhaled corticosteroids in patients with asthma and COPD was not associated with increased risk of diabetes or hyperglycemia.[40]

As mentioned above, it was reported that aboriginal females are 1.74 times more likely to be associated with ACO than aboriginal males. However, the possible risk factors associated with the increased risk of ACO in aboriginal females are yet to be investigated. This lead us to the main research question of the 2nd manuscript (Chapter 3), which is to identify these risk factors.

2.7 Limitations:

There were several limitations to this study. The APS is a cross-sectional survey in which the information collected was gathered at a one-time period. This could lead to self-reporting bias or misclassification. Individuals self-reported the presence of asthma and COPD which lacks clinical accuracy. All other answers in this survey were also self-reported which could underestimate the prevalence of some variables.

2.8 Conclusion

To our knowledge, this is the first study to evaluate the prevalence and risk factors associated with ACO among Aboriginal peoples. Our study highlights the increasing prevalence of respiratory diseases in Aboriginal females. Even though ACO is a relatively new disease, our study still highlights the significance of smoking, dwelling in a house in need of major repairs; factors already known to be linked with respiratory diseases. Our study also highlights the association between ACO and concomitant diseases such as diabetes in Aboriginal peoples. There is a need to better understand the burden and risk factors of ACO in Aboriginal peoples. The findings from this study will provide information to health care workers, patients and their families, Indigenous governments/organizations and government agencies.

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2.1 Table of Descriptive Statistics

Variables	Labels	% of the population
Age	12 to 34 35 to 44 45 to 54 55 to 64 65 and over	45% 17% 18% 12% 8%
Sex	Male Female	46% 54%
Marital Status	Married and Living common-law Widowed, Separated and Divorced Single, never married	48% 14% 38%
Rural or Urban	Rural area Small population centre Medium population centre Large urban population centre	24% 21% 12% 43%
Personal Income	$5000 or less income $5000 to $19,999 $20,000 to 49,999 $50,000 to $100,000 and over	18% 28% 32% 23%
Province	Atlantic* Quebec Ontario Prairies British Columbia Territories**	8% 10% 25% 36% 17% 4%
Smoking Status	Daily Occasionally Not at all	28% 9% 63%
Anybody smoking at home	Yes No	64% 36%
Dwelling (Owned/Rented)	Owned Rented	58% 42%
Dwelling in need of major repairs	Yes, major repairs are needed Yes, minor repairs are needed No, only regular maintenance is needed	12% 26% 62%

Diabetes	Diabetes type 1 and type 2 Gestational and no diagnosis of diabetes	9% 91%
How many rooms are there in a dwelling	0 and 2 rooms 3 and 5 rooms 6 and 8 rooms 9 rooms and over	6% 45% 33% 16%
Number of paid hours per week	0 to 20 hours 21 to 40 hours 41 to 79 hours 80 hours and over	8% 37% 9% 46%

*: including Nova Scotia, Newfoundland and Labrador, Prince Edward Island and New Brunswick

**: including Nunavut, Yukon, Northwest Territories

2.2 Table of Univariate analysis

Variables	Prevalence of ACO	Odds ratio (95% CI)	p-value
Age			
35 to 44	1.68	1.07 (0.62 - 1.84)	0.8045
45 to 54	4.31	2.81 (1.71 - 4.61)	<0.0001
55 to 64	4.28	2.80 (1.71 - 4.59)	<0.0001
65 and over	4.88	3.20 (1.89 - 5.43)	<0.0001
12 to 34	1.57	1	
Sex			
Female	3.53	2.18 (1.58 - 3.00)	<0.0001
Male	1.65	1	
Marital Status			
Widowed, Separated and Divorced	6.76	3.80 (2.48 - 5.84)	<0.0001
Single, never married	2.64	1.42 (1.01 - 2.00)	<0.0001
Married and Living common-law	1.87	1	
Rural or Urban			
Rural area	2.17	0.72 (0.48 - 1.06)	0.0953
Small population centre	2.00	0.66 (0.45 - 0.98)	0.0370
Medium population centre	3.63	1.22 (0.74 - 2.00)	0.4346
Large urban population centre	3.00	1	
Personal Income			
$5000 or less income	2.12	0.35 (0.22 – 0.55)	<.0001
$20,000 to 49,999	2.18	0.36 (0.25 – 0.53)	<.0001
$50,000 to $100,000 and over	0.81	0.13 (0.07 – 0.24)	<.0001
$5000 to $19,999	5.85	1	
Province			
Atlantic*	1.11	0.32 (0.18 - 0.59)	0.0002
Quebec	5.68	1.72 (1.05 - 2.81)	0.0320
Prairies	2.23	0.65 (0.42 - 1.00)	0.0471
British Columbia	1.81	0.52 (0.32 - 0.86)	0.0100
Territories**	1.01	0.29 (0.17 - 0.51)	<.0001
Ontario	3.41	1	
Type of Smoker			
Daily	4.47	2.42 (1.78 - 3.32)	<.0001
Occasionally	2.38	1.26 (0.72 - 2.20)	0.4112
Not at all	1.89	1	
Anybody smoking at home			
Yes	4.21	2.04 (1.42 - 2.94)	0.0001
No	2.38	1	

Dwelling (Owned/Rented)			
Rented	4.12	2.69 (1.95 - 3.70)	<0.0001
Owned	1.58	1	
Dwelling in need of major repairs			
Yes, major repairs are needed	6.44	3.35 (2.19 to 5.13)	<0.0001
Yes, minor repairs are needed	2.47	1.24 (0.86 to 1.78)	0.2525
No, only regular maintenance is needed	2.01	1	
Diabetes			
Diabetes type 1 and type 2	7.20	3.38 (2.34 to 4.90)	<0.0001
Gestational and no diagnosis of diabetes	2.24	1	
How many rooms are there in a dwelling			
3 and 5 rooms	3.70	0.65 (0.38 to 1.11)	0.1136
6 and 8 rooms	1.87	0.32 (0.16 to 0.63)	0.0010
9 rooms and over	1.23	0.21 (0.10 to 0.44)	<0.0001
0 and 2 rooms	5.58	1	
Number of paid hours per week			
21 to 40 hours	1.22	1.03 (0.50 to 2.11)	0.9402
41 to 80 hours	2.09	1.77 (0.75 to 4.17)	0.1887
80 hours and over	4.21	3.65 (1.82 to 7.32)	0.0003
0 to 20 hours	1.19	1	

*: including Nova Scotia, Newfoundland and Labrador, Prince Edward Island and New Brunswick

**: including Nunavut, Yukon, Northwest Territories

2.3 Table of Multivariate Analysis

Variables	Labels	Odds ratio (95% CI)	p-value
Age	35 to 44	1.01 (0.54 to 1.87)	0.9858
	45 to 54	2.43 (1.34 to 4.42)	0.0035
	55 to 64	2.00 (0.97 to 4.09)	0.0597
	65 and over	1.68 (0.71 to 3.99)	0.2406
	12 to 34	1	
Sex	Female	1.74 (1.25 to 2.45)	0.0013
	Male	1	
Marital Status	Widowed, Separated and Divorced	1.97 (1.19 to 3.25)	0.0080
	Single, never married	1.44 (0.94 to 2.20)	0.0908
	Married and Living common-law	1	
Personal Income	$5000 or less income	1.59 (0.71 to 3.54)	0.2559
	$5000 to $19,999	3.00 (1.44 to 6.23)	0.0033
	$20,000 to 49,999	1.80 (0.89 to 3.66)	0.1019
	$50,000 to $100,000 and over	1	
Province	Atlantic	0.31 (0.16 to 0.61)	0.0007
	Quebec	1.58 (0.94 to 2.64)	0.0834
	Prairies	0.73 (0.47 to1.14)	0.1660
	British Columbia	0.51 (0.30 to 0.88)	0.0158
	Territories	0.21 (0.12 to 0.39)	<0.0001
	Ontario	1	
Type of Smoker	Daily	1.66 (1.14 to 2.41)	0.0084
	Occasionally	1.10 (0.52 to 2.00)	0.9896
	Not at all	1	
Dwelling (Owned/Rented)	Rented	1.76 (1.24 to 2.51)	0.0018
	Owned	1	
Dwelling in need of major repairs	Yes, major repairs are needed	2.31 (1.46 to 3.65)	0.0004
	Yes, minor repairs are needed	1.15 (0.79 to 1.69)	
	No, only regular maintenance is needed	1	0.4579
Diabetes	Diabetes type 1 and type 2	1.68 (1.10 to 2.58)	0.0188
	Gestational and no diagnosis of diabetes	1	
Number of paid hours per week	21 to 40 hours	1.16 (0.55 to 2.44)	0.7004
	41 to 80 hours	2.83 (1.12 to 7.14)	0.0273
	80 hours and over	2.85 (1.36 to 5.97)	0.0057
	0 to 20 hours	1	

*: including Nova Scotia, Newfoundland and Labrador, Prince Edward Island and New Brunswick

**: including Nunavut, Yukon, Northwest Territories

CHAPTER 3

GENDER-SPECIFIC RISK FACTORS OF ACO (ASTHMA COPD OVERLAP) IN ABORIGINAL PEOPLE

3.1 Abstract

Gender differences in incidence, susceptibility and severity of many chronic respiratory diseases have been long recognized. Asthma-COPD Overlap (ACO), is a newly recognised disease with its management guidelines reported in 2015. The aim of this analysis is to assess the gender-specific risk factors associated with ACO in Aboriginal people. The Aboriginal Peoples Survey (APS) 2012 (N=28,410) is the fourth cycle of a national cross-sectional survey representative of the First Nations living off reserve, Metis and Inuit. The 2012 APS collected information on employment, education, health status, housing, family background and income. Survey Logistic Regression was used to identify the significant risk factors for ACO in the multivariate analysis. The prevalence of ACO was 1.65% and 3.53% in males and females respectively. The increased risk of ACO in both males and females was significantly associated with increased age, living in Quebec, longer hours of work per week, living in a rented dwelling and dwelling in need of major repairs while female-specific risk factors significantly associated with increased risk of ACO included being widowed, separated or divorced, a current daily smoker and having a diagnosis of diabetes. The results of our study will offer useful evidence for future development of prevention and public health intervention programs in aboriginal communities to reduce the burden of ACO.

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3.2 Introduction

Asthma-COPD Overlap (ACO), is a newly recognised disease with its management guidelines reported in 2015.[1] Several studies on the incidence of ACO in the general population have been carried out in the US, UK, Poland, Finland, Spain and Latin American countries.[2-4] Aboriginal people are at a higher risk of many chronic respiratory diseases.[5,6] However, there remains a gap in knowledge about the burden and risk factors of ACO in Aboriginal peoples. Patients with ACO have a significantly higher prevalence of comorbidities, greater health care utilization rates and nearly doubled health care costs.[7,8]

Sex and Gender differences in incidence, susceptibility and severity of many chronic respiratory diseases have been long recognized. Females generally experience more severe symptoms and a worse prognosis for asthma compared to males of the same age;[9] while historically, males are at higher risk for COPD than females.[10] Although the biological mechanisms of sex differences are not fully understood, recent evidence suggests the involvement of sex-related hormones. Epidemiological studies consistently show differences in many lung diseases before and after both puberty and menopause when sex hormones experience dramatic changes.[11-13]

In addition to sex hormones, many epidemiological studies also report many environmental and lifestyle risk factors for chronic respiratory diseases including COPD. Females in rural areas exposed to high levels of biomass smoke and other indoor air pollutants due to routine cooking are associated with higher levels of respiratory diseases compared to males, and about 50% of deaths in females were associated with COPD.[14] Another study reported that due to the recent increased rate of cigarette smoking among women, they may be more disposed to the development of severe COPD.[15] The aim of this analysis is to assess the

gender-specific risk factors associated with ACO in Aboriginal people using data from the 2012 Aboriginal Peoples Survey (APS).

3.3 Methods

3.3.1 Study design:

The APS 2012 was collected by Statistics Canada from February to July 2012. This is the fourth cycle of a national cross-sectional survey representative of the First Nations living off reserve, Metis and Inuit. The APS 2012 was reported to have a response rate of 76%. Respondents were chosen based on self-identification as being Aboriginal or having Aboriginal ancestry from the 2011 National Health Survey (NHS). A total of 28,410 Aboriginal peoples in the APS provide sufficient power for our statistical analysis

3.3.2 Outcome variable:

The primary outcome variable ACO was based on the respondent giving positive responses to both of the following questions *"Do you/Does(name) have Asthma diagnosed by a health professional?"* and *"Do you/Does (name) have chronic bronchitis, emphysema or chronic pulmonary obstructive disease or COPD diagnosed by a health professional?"*

3.3.3 Predictor Variables:

Demographic variables consist of *Age, Sex* and *Marital Status*; Environmental variables include *Rural or Urban* (This is defined by the NHS Population Centre size), *Province, Dwelling – need repairs, Number of people in a household/Number of rooms in a dwelling*. Socio-economic variables consist of *Total Personal Income, Employment – the number of paid hours per week* and *Dwelling - owned or rented.* Lifestyle variables consisted of *Smoking Status and Smoking in the home,* and other diseases such *as Diabetes.* This ethics approval for this study has been approved by the Health Research Ethics Board (HREB) of Newfoundland and Labrador with reference protocol number: 20171751.

3.4 Statistical analysis:

Data analysis was conducted using SAS version 9.4. Mean/SD and count/percent were used to summarize the study population. The differences in the continuous and categorical variables between males and females were examined by t-test and chi-square tests, respectively. Survey Logistic Regression was used to identify the significant risk factors for ACO in the univariate and multivariate analysis. Clinically important variables with p-value<0.20 in the univariate analysis were included in the multivariate analysis. To identify gender-specific risk factors for ACO, the multivariate analysis was stratified into a male and female domain statement. Sampling weights were included in all statistical analyses. Variances were estimated using 1,000 bootstrap weights to account for complex survey design of the APS**.**

3.5 Results

3.5.1 Descriptive statistics:

As shown in Table 1, female aboriginal people have a significantly higher prevalence of ACO than males (3.53% vs 1.65%, p <0.0001).

Demographic variables represented by *Age* shows that there are no significant differences in the age distribution between males and females (47%) for males and (44%) for females (p = 0.3214). However, *Marital Status* shows a significantly higher proportion of males reporting *Married and Living in common-law* (51%) vs females (45%) (p <0.0001).

Environmental variables shows a significant difference in proportion of people living in *rural or urban* between males and females (26% vs 23%, p = 0.0055). Individuals by *province of residence* did not show any significant differences. Females were also more likely to report living in *Dwellings in need of major repairs* (14% vs 9%, p <0.0001). On average, males live in a dwelling with more rooms than females (21% vs 18%, p = 0.0308).

Socio-economic variables highlight that males had a higher proportion of individuals earning *$40,000 and over* per year (32% vs 19%, p <0.0001). 49% of males were reported to work above *80 hours and above* in comparison to 46% of females (p<0.0001). Males were less likely to live in *Owned Dwellings* than females, (40% vs 45%, p<0.0001). There were no significant differences in the distributions of *Smoking status* and *Smoking at home* between males and females.

3.5.2 Univariate Analysis

The results from the Univariate analysis are shown in Table 2. *Age* was significantly associated with ACO. Compared to males aged *12-34 years*, males aged more than 45 years were more likely to be associated with ACO. ($OR_{45\ to\ 54\ years}$ = 2.21; $OR_{55\ to\ 64\ years}$ = 4.71; $OR_{65\ years\ and\ over}$ = 5.22). Similar associations were observed in females. In comparison to those *Married or Living in common-law*, Aboriginal males and females who were *Widowed, Separated and Divorced* were more likely to be associated with higher risks of ACO. (OR_{Males} = 3.61; $OR_{Females}$ = 3.36).

Among males, in comparison to Aboriginal people *living in Quebec*, other provinces and regions of residence were significantly less likely to be associated with ACO ($OR_{Atlantic\ and\ Territories}$ = 0.17; $OR_{Ontario}$ = 0.38; $OR_{Prairies}$ = 0.29; $OR_{British\ Columbia}$ = 0.24). Similar associations were also observed in females. Aboriginal males and females residing in a *dwelling in need of major repairs* were three times more likely to be associated with ACO compared to those that reside in a *dwelling that needs only regular maintenance*. (OR_{Males} = 2.56; $OR_{Females}$ = 3.31). In comparison to those living in a dwelling with *0 to 5 rooms*, males living in a dwelling with *6 – 8 rooms* were significantly less likely to be associated with ACO ($OR_{6-8\ rooms}$ = 0.39) while females living in a dwelling with *6 – 8 rooms or 9 rooms and over* were also significantly less likely to associated with ACO ($OR_{6-8\ rooms}$ = 0.51; $OR_{9\ rooms\ +}$ = 0.19).

Among the socio-economic variables, males with annual income between *$5,000 to 19,999* and *$20,000 to $39,999* were three times more likely to be associated with ACO in comparison to males who earn *$40,000 and over* ($OR_{\$5,000\ to\ \$19,999}$ = 2.94; $OR_{\$20,000\ to\ \$39,999}$ = 2.65). Females with an annual income between *$5,000 or less income* to *$20,000 to $39,999* were also significantly more likely to be associated with ACO in comparison to females who earn *$40,000 and over* ($OR_{\$5,000\ or\ less\ income}$ = 1.86; $OR_{\$5,000\ to\ \$19,999}$ = 3.81; $OR_{\$20,000\ to\ \$39,999}$ = 3.08).

Aboriginal males who work *80 hours and over* were approximately three times more likely to be associated with increased risk for ACO when compared to *0 to 40 hours* of paid hours per week ($OR_{80\ hours\ and\ over}$ = 2.48) while females who worked *41 to 80 hours* to *80 hours and over* were significantly associated with increased risk for ACO with the same comparison ($OR_{41\ to\ 80\ hours}$ = 2.73; $OR_{80\ hours\ and\ over}$ = 4.21). Aboriginal males and females *living in rented dwellings* were three times more likely to be associated with ACO when compared to those *owning the dwelling*. (OR_{Male} = 2.59; OR_{Female} = 2.60).

Among lifestyle variables, *Daily smoking* was associated with increased risk of ACO in comparison to those reporting *No smoking at all* for both gender. (OR_{Males} = 2.00; $OR_{Females}$ = 2.60). Furthermore, males who report *smoking at home* were less likely to be associated with ACO (OR_{males} = 0.77) while females who report *smoking at home* were three times more likely to be associated with ACO ($OR_{Females}$ = 2.78)

Aboriginal people, of both genders, with a diagnosis of *Diabetes type 1 and 2* were three times more likely to be associated with ACO compared to those without the *diagnosis of diabetes* (OR_{Males} = 3.81; $OR_{Females}$ = 3.26).

3.5.3 Multivariate Analysis

The results from the multivariate analysis are shown in Table 3. In males, in comparison to those aged 12-34 years, males in all age groups above 45 years were increasingly associated with ACO while only females between 45 to 54 years were associated with ACO, Males ($OR_{45 \text{ to } 54 \text{ years}}$ = 2.30, 95% CI = 1.09 - 4.85; $OR_{55 \text{ to } 64 \text{ years}}$ = 4.42, 95% CI = 1.89 – 10.35; $OR_{65 \text{ and over}}$ = 4.99, 95% CI = 1.98 – 12.59), Females ($OR_{45 \text{ to } 54 \text{ years}}$ = 2.39, 95% CI = 1.18 - 4.85). A linear relationship between the risk of ACO and age was observed in males (trend test: $p<0.0001$) but not in females (trend test: $p = 0.3226$). Aboriginal females who are *widowed, separated or divorced* are more than two times more likely to be associated with ACO compared to those who were either *married or living in common-law* (OR = 2.20, 95% CI = 1.17 - 4.16), no such associations was observed in males in terms of the p-value however the adjusted OR was 1.96.

In comparison to those from *Quebec*, males from *Atlantic and Territories region and British Columbia*, females from *Atlantic and Territories region, Prairies and British Columbia* were significantly less likely to be associated with ACO. Males ($OR_{Atlantic \text{ and } Territories}$= 0.23, 95% CI = 0.09 - 0.56; $OR_{British \ Columbia}$ = 0.36, 95% CI = 0.14 - 0.90), Females ($OR_{Atlantic \text{ and } Territories}$ = 0.15, 95% CI = 0.07 - 0.31; $OR_{Prairies}$= 0.41, 95% CI = 0.23 - 0.69; $OR_{British \ Columbia}$ = 0.34, 95% CI = 0.18 - 0.66). Aboriginal males and females living in a *dwelling in need of major repairs* were more than two times more likely to be associated with ACO compared to those living in a *dwelling* in *need of regular maintenance.* (OR_{Males} = 2.66, 95% CI = 1.37 – 5.15; ($OR_{Females}$ = 2.59, 95% CI = 1.49 – 4.52).

Among the socio-economic variables, males working *80 hours and over* and females working *40 hours and over* were significantly associated with increased risk of ACO when compared to those working *0 to 40 hours* per week. Males ($OR_{81 \text{ hours and over}}$ = 1.89, 95% CI = 1.05 - 3.41), Females ($OR_{41 \text{ hours to } 80 \text{ hours}}$ = 3.11, 95% CI = 1.29 - 7.45; $OR_{81 \text{ hours and over}}$ = 4.11, 95% CI = 2.52 - 6.36). Males and females who live in a *rented dwelling* are approximately two

times more likely to be associated with ACO than those *owning a dwelling* (OR_{Males} = 2.27, 95% CI = 1.33 - 3.89; $OR_{Females}$ = 1.70, 95% CI = 1.13 - 2.58).

ln females, individuals who smoked *daily* were two times more likely to be associated with ACO compared to those that *do not smoke at all* (OR = 1.83, 95% CI = 1.16 - 2.90); while males did not show any statistical significance. In females, individuals with a diagnosis of diabetes (type 1 and 2) were also approximately three times more likely to be associated with ACO compared to those without the diagnosis of diabetes, (OR = 2.46, 95% CI = 1.52 to 3.99); no such association was observed in males.

3.6 Discussion

This study identified the risk factors associated with increased risk of ACO in both males and females which include increased age, living in Quebec, longer hours of work per week, living in a rented dwelling and dwelling in need of major repairs. In addition, we also identified the following female-specific risk factors associated with increased risk of ACO: being widowed, separated or divorced, a current daily smoker and having a diagnosis of diabetes.

Epidemiological studies have consistently observed the association between age and the risk of chronic respiratory diseases.[16,17] A large cross-sectional study of Aboriginal people in Canada reported that individuals above 50 years of age were significantly associated with higher risks of COPD.[16] Similar results were also reported in another large cross-sectional study showing that older individuals above 55 years of age had a higher likelihood of Chronic Bronchitis (CB).[17] The results from our study support the conclusions from these studies that increased age is associated with increased risk of ACO. In addition, we observed a linear relationship between increased age and a higher risk of ACO in males, not in females. In our analysis, a higher risk of ACO was also observed among aboriginal males and females living

in Quebec than other provinces of residence in Canada. A study from the US found distinct geographic variations in COPD hospitalization rates across the country which could be attributed to various environmental factors such as socioeconomic status, high-regionalized population rates and occupational exposures.[18] Another study from the US concluded that the observed differences in rates of COPD exacerbation across the US could be due many reasons such as regional variation in provider care, environmental factors and climatic differences.[19]

Furthermore, our study found that both males and females living in rented dwellings or dwelling in need of major repairs are associated with increased risks of ACO. There are various exposures that have been associated with many chronic respiratory diseases that affects the quality of dwellings such as physical, biological, chemical risks.[20-25] A study in the US showed that indoor mildew odour or musty smell in dwellings were associated with risk of CB and asthmatic attacks.[21] Efforts to improve dwelling conditions through intervention such as elimination of moisture intrusion have also helped reduce the effects of chronic respiratory diseases.[25,26]

Lastly, the relationship between long work hours and chronic respiratory diseases could be due to low socioeconomic status (SES) which is also a known risk factor for chronic respiratory diseases.[27-29] In our study, we found that both males and females working longer hours have an increased risk of ACO. Many studies have consistently reported an increased risk of COPD associated with low SES status.[28,30] In a population-based study, it was reported that low SES measured by income and educational levels are independent risk factors for asthma and COPD respectively.[31] In a study which made use of population from Finland, Sweden and Estonia (FinEsS Study), it was reported that female workers who are inclined to work longer hours were associated with increased risk for chronic respiratory symptoms such as CB compared to men.[32]

In our study, daily smoking is one of the female-specific risk factors associated with ACO. Females who reported daily smoking are approximately two times more likely to be associated with ACO, however this association was not observed in males. Smoking has been a well-known risk factor for many chronic respiratory diseases and females are more predisposed to the negative influence of smoking than males.[33-35] A population-based study reported that among individuals who smoked ≥ 10 years, the prevalence of ACO was significantly higher in women than men.[33] Another study from Denmark found a significant association between the risk of COPD and cigarette pack years in females only and not males.[34] Similar association between smoking pack-years and the risk of CB in females only was also reported in a study of two First Nations communities in Saskatchewan, Canada.[35]

Increased risk of Diabetes has been associated with chronic respiratory diseases in many population studies.[36-39] However, current literature provides inconsistent conclusion regarding the sex-specific association between diabetes and ACO. A cross-sectional study of patients hospitalized for COPD exacerbation in Spain reported that female COPD patients had a higher prevalence of diabetes when compared to their male counterparts.[36] Although, another population study from Sweden reported males aged 45 years and above have an increased risk of diabetes type 2 than females,[37] females might be more predisposed to diabetes type 1 than males.[38] A prospective cohort study of important chronic comorbid diseases associated with COPD showed that males with the severe form of COPD (GOLD stage 3 or 4) had a higher prevalence of diabetes and hospitalization compared to females.[39] The inconsistent results from different studies could be due to differences in study design, study population and disease severity. Our study supported the conclusion of significant association between increased risk of ACO and diagnosis of diabetes in females but not in males.

There are fewer studies investigating the female-specific association between marital status and chronic respiratory diseases. A study from the US concluded that female subjects

who remained divorced or separated had a significantly increased risk of COPD.[40] To our knowledge, our study is the first paper to investigate the effects of marital status and a new disease, ACO, among Aboriginal people. Our results suggest that Aboriginal females who are widowed, separated or divorced are two times more likely to be associated with ACO, and this was not observed in males.

3.7 Limitations

This study was based on self-reported questionnaires without any objective measurements which are subject to misclassification. However, questionnaires using self-reported health conditions diagnosed by a health professional have been widely used in many large population surveys with reasonable sensitivity and specificity.[16,32]

3.8 Conclusion

This study has identified many risk factors for ACO for both males and females, which include age, province, long hours at work, living in rented dwelling and dwelling in need of major repairs. It also highlights female-specific risk factors for ACO, which includes smoking status, marital status and diabetes. The results of our study will provide useful information for future development of prevention and public health intervention programs in aboriginal communities to reduce the burden of ACO.

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3.1 **Table of Descriptive Analysis of Gender-specific risk factors**

Variables	Labels	Males (%) (n = 393,000)	Females (%) (n = 459,160)	p value
ACO	Yes	1.65%	3.53%	<0.0001
Age	12 to 34 years	47%	44%	0.3214
	35 to 44years	17%	18%	
	45 to 54 years	17%	18%	
	55 to 64 years	12%	12%	
	65 years and over	7%	8%	
Marital Status	Married and Living in common-law	51%	45%	<0.0001
	Widowed, Separated and Divorced	8%	18%	
	Single, never married	41%	37%	
Rural or Urban	Rural area	26%	23%	0.0055
	Small population centre	21%	21%	
	Medium population centre	11%	12%	
	Large urban population centre	42%	44%	
Total Personal Income	$5,000 or less income	27%	24%	<0.0001
	$5,001 to $19,999	19%	29%	
	$20,000 to $39,999	22%	28%	
	$40,000 and over	32%	19%	
Province of residence	Atlantic and Territories*	11%	11%	0.3862
	Quebec	11%	10%	
	Ontario	24%	25%	
	Prairies	37%	37%	
	British Columbia	17%	17%	
Smoking Status	Daily	27%	28%	0.6987
	Occasionally	9%	9%	
	Not at all	64%	63%	

Anybody smoking at home	Yes No	19% 81%	20% 80%	0.3089
Dwelling (Owned/Rented)	Owned Rented	40% 60%	45% 55%	<0.0001
Dwelling in need of major repairs	Yes, major repairs are needed Yes, minor repairs are needed No, only regular maintenance is needed	9% 26% 65%	14% 26% 60%	<0.0001
Diabetes	Diabetes type 1 and type 2 Gestational and no diagnosis of diabetes	9% 91%	9% 91%	0.8780
How many rooms are there in a dwelling	0 and 5 rooms 6 and 8 rooms 9 rooms and over	48% 31% 21%	50% 32% 18%	0.0308
Number of paid hours per week	0 to 40 hours 41 to 79 hours 80 hours and over	47% 4% 49%	39% 15% 46%	<0.0001

*: including Nova Scotia, Newfoundland and Labrador, Prince Edward Island, New Brunswick Nunavut, Yukon, Northwest Territories

3.2 **Table of Univariate Analysis of Gender-specific risk factors**

Variables	Males			Females		
	% of ACO	Odds Ratio (95% CI)	p-value	% of ACO	Odds Ratio (95% CI)	p-value
Age						
35 to 44 years	0.79	0.94 (0.32 – 2.76)	0.9051	2.39	1.07 (0.57 – 2.02)	0.8316
45 to 54 years	1.87	2.21 (1.07 – 4.53)	0.0311	6.25	2.93 (1.59 – 5.38)	0.0006
55 to 64 years	3.90	4.71 (2.32 – 9.58)	<0.0001	4.61	2.12 (1.16 – 3.89)	0.0152
65 years and over	4.30	5.22 (2.66 – 10.25)	<0.0001	5.36	2.48 (1.23 – 5.01)	0.0114
12 to 34 years	0.85	1		2.23	1	
Marital Status						
Widowed, Separated and Divorced	4.62	3.61 (1.75 – 7.44)	0.0005	7.59	3.36 (2.00 – 5.64)	<0.0001
Single, never married	1.79	1.36 (0.77 – 2.41)	0.2918	3.41	1.45 (0.95 – 2.21)	0.0849
Married and Living common-law	1.32	1		2.39	1	
Rural or Urban						
Rural area	1.71	0.98 (0.53 – 1.79)	0.9388	2.62	0.64 (0.38 – 1.07)	0.0877
Small population centre	1.15	0.66 (0.32 – 1.36)	0.2556	2.73	0.67 (0.42 – 1.06)	0.0876
Medium population centre	2.18	1.25 (0.55 – 2.85)	0.5922	4.69	1.16 (0.64 – 2.12)	0.6180
Large urban population centre	1.74	1		4.05	1	
Total Personal Income						
$5,000 or less income	1.16	1.26 (0.56 – 2.87)	0.5783	2.57	1.86 (1.04 – 3.33)	0.0378
$5,000 to $19,999	2.66	2.94 (1.33 – 6.45)	0.0075	5.15	3.81 (2.28 – 6.36)	<0.0001
$20,000 to $39,999	2.41	2.65 (1.23 – 5.74)	0.0131	4.21	3.08 (1.59 – 5.94)	0.0008
$40,000 and over	0.92	1		1.41	1	
Province of residence						
Atlantic and Territories**	0.79	0.17 (0.07 – 0.41)	<0.0001	1.31	0.18 (0.11 – 0.34)	<0.0001
Ontario	1.72	0.38 (0.18 – 0.81)	0.0125	4.78	0.68 (0.37 – 1.25)	0.2094
Prairies	1.32	0.29 (0.14 – 0.62)	0.0014	2.99	0.42 (0.24 – 0.72)	0.0019
British Columbia	1.12	0.24 (0.11 – 0.57)	0.0011	2.38	0.33 (0.18 – 0.61)	0.0005
Quebec	4.38	1		6.89	1	

Type of Smoker						
Daily	2.46	2.00 (1.16 – 3.44)	0.0122	6.12	2.60 (1.75 – 3.87)	<0.0001
Occasionally	1.46	1.19 (0.46 – 3.08)	0.7285	3.15	1.30 (0.67 – 2.55)	0.4415
Not at all	1.24	1		2.45	1	
Anybody smoking at home						
Yes	1.13	0.77 (0.43 – 1.40)	0.3968	6.51	2.78 (1.80 – 4.29)	<0.0001
No	1.46	1		2.44	1	
Dwelling (Owned/Rented)						
Rented	2.53	2.59 (1.55 – 4.33)	0.0003	5.32	2.60 (1.76- 3.85)	<0.0001
Owned	0.99	1		2.11	1	
Dwelling in need of major repairs						
Yes, major repairs are needed	3.31	2.56 (1.40 – 4.68)	0.0022	8.24	3.31 (1.96 – 5.56)	<0.0001
Yes, minor repairs are needed	1.71	1.30 (0.72 – 2.38)	0.3870	3.11	1.18 (0.76 – 1.82)	0.4563
No, only regular maintenance is needed	1.31	1		2.65	1	
Diabetes						
Diabetes type 1 and type 2	4.93	3.81 (2.07 – 6.95)	<0.0001	9.17	3.26 (2.04 – 5.21)	<0.0001
Gestational and no diagnosis of diabetes	1.34	1		3.01	1	
How many rooms are there in a dwelling						
6 and 8 rooms	1.03	0.39 (0.21 – 0.79)	0.0081	2.59	0.51 (0.26 – 0.95)	0.0353
9 rooms and over	2.59	0.57 (0.23 – 1.38)	0.2112	0.98	0.19 (0.09 – 0.38)	<0.0001
0 and 5 rooms	2.56	1		5.06	1	
Number of paid hours per week						
41 to 80 hours	1.58	1.67 (0.69 – 4.03)	0.2568	3.74	2.73 (1.18 – 6.31)	0.0188
80 hours and over	2.33	2.48 (1.41 – 4.36)	0.0016	5.67	4.21 (2.79 – 6.37)	<0.0001
0 to 40 hours	0.95	1		1.41	1	

*: including Nova Scotia, Newfoundland and Labrador, Prince Edward Island, New Brunswick, Nunavut, Yukon, Northwest Territories

3.3 Table of Multivariate Analysis

Variables	Male		Female	
	Odds Ratio (95% CI)	p-value	Odds Ratio (95% CI)	p-value
Age				
35 to 44	1.07 (0.38 – 3.01)	0.8989	0.94 (0.48 – 1.83)	0.8446
45 to 54	2.30 (1.09 – 4.85)	0.0286	2.39 (1.18 – 4.85)	0.0162
55 to 64	4.42 (1.89 – 10.35)	0.0006	1.15 (0.46 – 2.86)	0.7657
65 and over	4.99 (1.98 – 12.59)	0.0007	0.98 (0.34 – 2.84)	0.9729
12 to 34	1		1	
Marital Status				
Widowed, Separated and Divorced	1.95 (0.91 – 4.23)	0.0917	2.20 (1.17 – 4.16)	0.0151
Single, never married	1.96 (0.97 – 3.97)	0.0603	1.46 (0.92 – 2.32)	0.1098
Married and Living common-law	1		1	
Province of residence				
Atlantic and Territories*	0.23 (0.09 – 0.56)	0.0014	0.15 (0.07 – 0.31)	<0.0001
Ontario	0.58 (0.25 – 1.37)	0.2156	0.62 (0.34 – 1.12)	0.1140
Prairies	0.49 (0.21 – 1.13)	0.0929	0.41 (0.23 – 0.69)	0.0011
British Columbia	0.36 (0.14 – 0.90)	0.0291	0.34 (0.18 – 0.66)	0.0014
Quebec	1		1	
Type of Smoker				
Daily	1.36 (0.74 – 2.50)	0.3211	1.83 (1.16 – 2.90)	0.0101
Occasionally	1.11 (0.41 – 3.08)	0.8462	0.81 (0.35 – 1.84)	0.6070
Not at all	1		1	
Dwelling (Owned/Rented)				
Rented	2.27 (1.33 – 3.89)	0.0029	1.70 (1.13 – 2.58)	0.0118
Owned	1		1	
Dwelling in need of major repairs				
Yes, major repairs are needed	2.66 (1.37 – 5.15)	0.0037	2.59 (1.49 – 4.52)	0.0008
Yes, minor repairs are needed	1.09 (0.56 – 2.10)	0.8462	1.31 (0.85 – 2.02)	0.2191
No, only regular maintenance is needed	1		1	

Diabetes				
Diabetes type 1 and type 2	1.56 (0.79 – 3.07)	0.2027	2.46 (1.52 -3.99)	0.0003
Gestational and no diagnosis of diabetes	1		1	
Number of paid hours per week				
41 to 80 hours	1.94 (0.79 – 4.77)	0.1486	3.11 (1.29 – 7.45)	0.0112
81 hours and over	1.89 (1.05 – 3.41)	0.0353	4.11 (2.52 – 6.36)	<0.0001
0 to 40 hours	1		1	

*: including Nova Scotia, Newfoundland and Labrador, Prince Edward Island, New Brunswick, Nunavut, Yukon, Northwest Territories

CHAPTER 4
GENERAL DISCUSSION AND CONCLUSIONS

4.1 Summary of Research

The main goal of the research studies in this thesis were to assess the prevalence and gender specific risk factors associated with ACO in Aboriginal peoples. The first study found out that Aboriginal peoples older than 45 years, female, widowed, separated or divorced, having a total personal income below $20,000 were associated with a significant risk of ACO. Residing in Ontario, being a daily smoker, living in a rented dwelling, dwelling in need of major repairs, having diabetes and working more than 40 hrs a week were also significantly associated with increased risk of ACO. The second study, identified the risk factors associated with increased risk of ACO in both males and females included increased age, living in Quebec, longer hours of work per week, living in a rented dwelling and dwelling in need of major repairs. In addition, we also identified the following female-specific risk factors associated with increased risk of ACO: being widowed, separated or divorced, a current daily smoker and having a diagnosis of diabetes.

4.2 Summary of Results

There are several risk facors associated with ACO in the general Aboriginal population. Our results showed that individuals aged between 45 to 54 years were two times more likely to be associated with ACO in comparison to individuals aged between 12-34 years. Aboriginal females were approximately two times more likely to be associated with ACO compared to Males. Similarly, individuals who were widowed, separated or divorced were two times more likely to be associated with ACO compared to individuals who were either married or living in common-law. In comparison to individuals from Ontario, individuals from Atlantic regions, Territories and British Columbia were significantly less likely to be associated with ACO. Also,

individuals living in dwellings in need of major repairs were two times more likely to be associated with ACO compared to those living in a dwelling in need of regular maintenance.

Among the socioeconomic variables Individuals who earn between $5,000 to $19,999 were three times more likely to be associated with ACO compared to those who earn $50,000 to $100,000 and over. Individuals working long hours of 41 to 80 hours and 81 hours and over were significantly associated with ACO compared to those working 0 to 20 hours per week. Also, individuals who live in a rented dwelling were approximately two times more likely to be associated with ACO than those owning a dwelling.

Individuals who smoke daily were found to be about two times more likely to be associated with ACO compared to those that do not smoke at all. Aboriginal people with diabetes (type 1 and 2) were also approximately two times more likely to develop ACO compared to those without the diagnosis of diabetes.

4.3 Study Limitations

There were several limitations to this study. The APS is a cross-sectional study, it suffers from all the disadvantages of a cross-sectional study, such as no casual association and being susceptible to recall bias since the information was collected at a specific time point. This study was based on self-reported questionnaires without any objective measurements which are subject to misclassification. Individuals self-reported the presence of asthma and COPD which lacks clinical accuracy. All other answers in this survey were also self-reported which could underestimate the prevalence of some variables. The lack of spirometry and presence of confounding diseases in this population was also a limitation.

APPENDIX A: ETHICS APPROVAL FOR THE STUDY FROM THE NEWFOUNDLAND AND LABRADOR HEALTH ETHICS RESEARCH ETHICS BOARD

Ethics Office Suite 200, Eastern Trust Building 95 Bonaventure Avenue St. John's, NL A1B 2X5

February 15, 2018

Suite 4M130, Medical Education Building Memorial University, 300 Prince Phillip Drive St. John's, NL A1B 3V6

Dear Mr. Koleade:

Researcher Portal File # 20171751 Reference # 2017.047

RE: "Prevalence and risk factors of chronic respiratory diseases including asthma and COPD in adult Aboriginal people"

Your application received a delegated review by a sub-committee of the Health Research Ethics Board (HREB). Full approval of this research study is granted for one year effective February 15, 2018.

This is your ethics approval only. Organizational approval may also be required. It is your responsibility to seek the necessary organizational approval from the Regional Health Authority (RHA) or other organization as appropriate. You can refer to the HREA website for further guidance on organizational approvals.

This is to confirm that the HREB reviewed and approved or acknowledged the following documents (as indicated):

• Application, approved

• Research Proposal, approved

• List of Variables, approved

• Letter of request, approved

• Letter of support Nunatsiavut, acknowledged

• Budget, approved

MARK THE DATE

This approval will lapse on February 15, 2019 . It is your responsibility to ensure that the Ethics

Renewal form is submitted prior to the renewal date; you may not receive a reminder. The Ethics Renewal form can be found on the Researcher Portal as an Event form.

If you do not return the completed Ethics Renewal form prior to date of renewal:

- ***You will no longer have ethics approval***
- *You will be required to stop research activity immediately*
- *You may not be permitted to restart the study until you reapply for and receive approval to undertake the study again*
- ***Lapse in ethics approval may result in interruption or termination of funding***

You are solely responsible for providing a copy of this letter, along with your approved HREB application form; to Research Grant and Contract Services should your research depend on funding administered through that office.

Modifications of the protocol/consent are not permitted without prior approval from the HREB. Implementing changes without HREB approval may result in your ethics approval being revoked, meaning your research must stop. Request for modification to the protocol/consent must be outlined on an amendment form (available on the Researcher Portal website as an Event form) and submitted to the HREB for review.

The HREB operates according to the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS2), the Health Research Ethics Authority Act (HREA Act) and applicable laws and regulations.

You are responsible for the ethical conduct of this research, notwithstanding the approval of the HREB.

We wish you every success with your study.

Sincerely,

Ms. Patricia Grainger (Chair, Non-Clinical Trials Health Research Ethics Board) Dr. Joy Maddigan (Vice-Chair, Non-Clinical Trials Health Research Ethics Board)

CC: Dr. Zhiwei Gao

APPENDIX B: SAS OUTPUTS

UNIVARIATE ANALYSIS

AGE

The SURVEYLOGISTIC Procedure

Type 3 Analysis of Effects

Effect	F Value	Num DF	Den DF	Pr > F
acos_age	**10.14**	**4**	**1000**	**<.0001**

Analysis of Maximum Likelihood Estimates

Parameter		Estimate	Standard Error	t Value	Pr > |t|
Intercept		-4.1342	0.1954	-21.16	<.0001
acos_age	1	0.0683	0.2758	0.25	0.8045
acos_age	2	1.0338	0.2521	4.10	<.0001
acos_age	3	1.0284	0.2522	4.08	<.0001
acos_age	4	1.1641	0.2698	4.31	<.0001
acos_age	0	0	.	.	.

NOTE: The degrees of freedom for the t tests is 1000.

Odds Ratio Estimates

Effect	Point Estimate	95% Confidence Limits	
acos_age 1 vs 0	1.071	0.623	1.840
acos_age 2 vs 0	2.812	1.715	4.611
acos_age 3 vs 0	2.797	1.705	4.587
acos_age 4 vs 0	3.203	1.886	5.439

SEX

Type 3 Analysis of Effects

Effect	F Value	Num DF	Den DF	Pr > F
sex_male	**22.80**	**1**	**1000**	**<.0001**

Analysis of Maximum Likelihood Estimates

Parameter		Estimate	Standard Error	t Value	Pr > |t|
Intercept		-4.0873	0.1261	-32.42	<.0001
sex_male	0	0.7783	0.1630	4.77	<.0001
sex_male	1	0	.	.	.

NOTE: The degrees of freedom for the t tests is 1000.

Odds Ratio Estimates

Effect	Point Estimate	95% Confidence Limits	
sex_male 0 vs 1	2.178	1.582	2.999

MARITAL STATUS

The SURVEYLOGISTIC Procedure

Type 3 Analysis of Effects

Effect	F Value	Num DF	Den DF	Pr > F
Mar_status	**18.89**	**2**	**1000**	**<.0001**

Analysis of Maximum Likelihood Estimates

Parameter	Estimate	Standard Error	t Value	Pr > |t|
Intercept	-3.9602	0.1187	-33.36	<.0001
Mar_status 2	1.3357	0.2189	6.10	<.0001
Mar_status 3	0.3516	0.1721	2.04	0.0413
Mar_status 1	0	.	.	.

NOTE: The degrees of freedom for the t tests is 1000.

Odds Ratio Estimates

Effect	Point Estimate	95% Confidence Limits	
Mar_status 2 vs 1	3.803	2.475	5.843
Mar_status 3 vs 1	1.421	1.014	1.992

RURAL OR URBAN

The SURVEYLOGISTIC Procedure

Type 3 Analysis of Effects

Effect	F Value	Num DF	Den DF	Pr > F
rural_urb	**2.61**	**3**	**1000**	**0.0500**

Analysis of Maximum Likelihood Estimates

Parameter	Estimate	Standard Error	t Value	Pr > |t|
Intercept	-3.4747	0.1216	-28.57	<.0001

rural_urb 1	-0.3334	0.1996	-1.67	0.0953
rural_urb 2	-0.4176	0.2000	-2.09	0.0370
rural_urb 3	0.1964	0.2513	0.78	0.4346
rural_urb 4	0	.	.	.

NOTE: The degrees of freedom for the t tests is 1000.

Odds Ratio Estimates

Effect	Point Estimate	95% Confidence Limits	
rural_urb 1 vs 4	0.717	0.484	1.060
rural_urb 2 vs 4	0.659	0.445	0.975
rural_urb 3 vs 4	1.217	0.743	1.993

PROVINCE OF RESIDENCE

Type 3 Analysis of Effects

Effect	F Value	Num DF	Den DF	Pr > F
prov_new2	**10.20**	**5**	**1000**	**<.0001**

Analysis of Maximum Likelihood Estimates

Parameter	Estimate	Standard Error	t Value	Pr > |t|
Intercept	-4.4843	0.2321	-19.32	<.0001
prov_new2 2	1.6754	0.3009	5.57	<.0001
prov_new2 3	1.1362	0.3060	3.71	0.0002
prov_new2 4	0.7049	0.2682	2.63	0.0087
prov_new2 5	0.4828	0.2841	1.70	0.0895
prov_new2 6	-0.1029	0.3139	-0.33	0.7430
prov_new2 1	0	.	.	.

Odds Ratio Estimates

Effect	Point Estimate	95% Confidence Limits	
prov_new2 2 vs 1	5.341	2.960	9.639
prov_new2 3 vs 1	3.115	1.709	5.678
prov_new2 4 vs 1	2.024	1.195	3.426
prov_new2 5 vs 1	1.621	0.928	2.830
prov_new2 6 vs 1	0.902	0.487	1.670

NOTE: The degrees of freedom in computing the confidence limits is 1000.

TOTAL PERSONAL INCOME

The SURVEYLOGISTIC Procedure

Type 3 Analysis of Effects

Effect	F Value	Num DF	Den DF	Pr > F
total_harmzed	**21.06**	**3**	**1000**	**<.0001**

Analysis of Maximum Likelihood Estimates

Parameter	Estimate	Standard Error	t Value	Pr > |t|
Intercept	-2.7776	0.1282	-21.67	<.0001
total_harmzed 1	-1.0560	0.2365	-4.46	<.0001
total_harmzed 3	-1.0265	0.1947	-5.27	<.0001
total_harmzed 4	-2.0353	0.3028	-6.72	<.0001
total_harmzed 2	0	.	.	.

NOTE: The degrees of freedom for the t tests is 1000.

Odds Ratio Estimates

Effect	Point Estimate	95% Confidence Limits	
total_harmzed 1 vs 2	0.348	0.219	0.553
total_harmzed 3 vs 2	0.358	0.245	0.525
total_harmzed 4 vs 2	0.131	0.072	0.237

SMOKING STATUS

The SURVEYLOGISTIC Procedure

Type 3 Analysis of Effects

Effect	F Value	Num DF	Den DF	Pr > F
smk_typ	**15.99**	**2**	**1000**	**<.0001**

Analysis of Maximum Likelihood Estimates

Parameter	Estimate	Standard Error	t Value	Pr > |t|
Intercept	-3.9487	0.1208	-32.68	<.0001
smk_typ 1	0.8874	0.1587	5.59	<.0001
smk_typ 2	0.2324	0.2827	0.82	0.4112
smk_typ 0	0	.	.	.

NOTE: The degrees of freedom for the t tests is 1000.

Odds Ratio Estimates

Effect	Point Estimate	95% Confidence Limits	
smk_typ 1 vs 0	2.429	1.779	3.316
smk_typ 2 vs 0	1.262	0.724	2.197

ANYBODY SMOKING AT HOME

The SURVEYLOGISTIC Procedure

Type 3 Analysis of Effects

Effect	F Value	Num DF	Den DF	Pr > F
smk_hom	**14.89**	**1**	**1000**	**0.0001**

Analysis of Maximum Likelihood Estimates

Parameter		Estimate	Standard Error	t Value	Pr > |t|
Intercept		-3.8961	0.1081	-36.04	<.0001
smk_hom	1	0.7144	0.1851	3.86	0.0001
smk_hom	0	0	.	.	.

NOTE: The degrees of freedom for the t tests is 1000.

Odds Ratio Estimates

Effect	Point Estimate	95% Confidence Limits	
smk_hom 1 vs 0	2.043	1.421	2.938

DWELLING (OWNED/RENTED)

The SURVEYLOGISTIC Procedure

Type 3 Analysis of Effects

Effect	F Value	Num DF	Den DF	Pr > F
hou_owned	**37.00**	**1**	**1000**	**<.0001**

Analysis of Maximum Likelihood Estimates

Parameter		Estimate	Standard Error	t Value	Pr > |t|
Intercept		-4.1349	0.1124	-36.78	<.0001
hou_owned	0	0.9883	0.1625	6.08	<.0001
hou_owned	1	0	.	.	.

NOTE: The degrees of freedom for the t tests is 1000.

Odds Ratio Estimates

Effect	Point Estimate	95% Confidence Limits	
hou_owned 0 vs 1	2.687	1.953	3.695

DWELLING IN NEED OF MAJOR REPAIRS

The SURVEYLOGISTIC Procedure

Type 3 Analysis of Effects

Effect	F Value	Num DF	Den DF	Pr > F
hou_rep	**16.55**	**2**	**1000**	**<.0001**

Analysis of Maximum Likelihood Estimates

Parameter		Estimate	Standard Error	t Value	Pr > |t|
Intercept		-3.8872	0.1125	-34.54	<.0001
hou_rep	1	1.2101	0.2170	5.58	<.0001
hou_rep	2	0.2117	0.1849	1.14	0.2525
hou_rep	0	0	.	.	.

NOTE: The degrees of freedom for the t tests is 1000.

Odds Ratio Estimates

Effect	Point Estimate	95% Confidence Limits	
hou_rep 1 vs 0	3.354	2.191	5.134
hou_rep 2 vs 0	1.236	0.860	1.776

DIABETES

The SURVEYLOGISTIC Procedure

Type 3 Analysis of Effects

Effect	F Value	Num DF	Den DF	Pr > F
diab_type12	**41.61**	**1**	**1000**	**<.0001**

Analysis of Maximum Likelihood Estimates

Parameter		Estimate	Standard Error	t Value	Pr > |t|
Intercept		-3.7747	0.0967	-39.02	<.0001
diab_type12	1	1.2188	0.1889	6.45	<.0001
diab_type12	0	0	.	.	.

NOTE: The degrees of freedom for the t tests is 1000.

Odds Ratio Estimates

Effect	Point Estimate	95% Confidence Limits	
diab_type12 1 vs 0	3.383	2.335	4.901

HOW MANY ROOMS ARE THERE IN A DWELLING

The SURVEYLOGISTIC Procedure

Type 3 Analysis of Effects

Effect	F Value	Num DF	Den DF	Pr > F
hous_rms	**8.71**	**3**	**1000**	**<.0001**

Analysis of Maximum Likelihood Estimates

Parameter		Estimate	Standard Error	t Value	Pr > |t|
Intercept		-2.8297	0.2436	-11.62	<.0001
hous_rms	2	-0.4290	0.2709	-1.58	0.1136
hous_rms	3	-1.1308	0.3439	-3.29	0.0010
hous_rms	4	-1.5568	0.3715	-4.19	<.0001
hous_rms	1	0	.	.	.

NOTE: The degrees of freedom for the t tests is 1000.

Odds Ratio Estimates

Effect	Point Estimate	95% Confidence Limits	
hous_rms 2 vs 1	0.651	0.383	1.108
hous_rms 3 vs 1	0.323	0.164	0.634
hous_rms 4 vs 1	0.211	0.102	0.437

NUMBER OF PAID HOURS PER WEEK

The SURVEYLOGISTIC Procedure

Type 3 Analysis of Effects

Effect	F Value	Num DF	Den DF	Pr > F
hrs_wrk	**19.92**	**3**	**1000**	**<.0001**

Analysis of Maximum Likelihood Estimates

Parameter	Estimate	Standard Error	t Value	Pr > |t|

Intercept		-4.4195	0.3415	-12.94	<.0001
hrs_wrk	2	0.0274	0.3653	0.08	0.9402
hrs_wrk	3	0.5734	0.4359	1.32	0.1887
hrs_wrk	4	1.2936	0.3553	3.64	0.0003
hrs_wrk	1	0	.	.	.

Odds Ratio Estimates

Effect	Point Estimate	95% Confidence Limits	
hrs_wrk 2 vs 1	1.028	0.502	2.105
hrs_wrk 3 vs 1	1.774	0.754	4.173
hrs_wrk 4 vs 1	3.646	1.816	7.322

FINAL MODEL: MULTIVARIATE ANALYSIS

The SURVEYLOGISTIC Procedure

Type 3 Analysis of Effects

Effect	F Value	Num DF	Den DF	Pr > F
acos_age	3.65	4	1000	0.0058
sex_male	10.47	1	1000	0.0013
Mar_status	4.80	2	1000	0.0084
total_harmzed	4.43	3	1000	0.0042
prov_new2	9.71	5	1000	<.0001
smk_typ	4.24	2	1000	0.0147
hou_owned	9.82	1	1000	0.0018
hou_rep	6.54	2	1000	0.0015
diab_type12	5.54	1	1000	0.0188
hrs_wrk	7.56	3	1000	<.0001

The SURVEYLOGISTIC Procedure

Analysis of Maximum Likelihood Estimates

Parameter		Estimate	Standard Error	t Value	Pr > |t|
Intercept		-6.5037	0.5152	-12.62	<.0001
acos_age	1	0.00561	0.3153	0.02	0.9858
acos_age	2	0.8894	0.3037	2.93	0.0035
acos_age	3	0.6903	0.3663	1.88	0.0597
acos_age	4	0.5175	0.4408	1.17	0.2406
acos_age	0	0	.	.	.
sex_male	0	0.5564	0.1720	3.23	0.0013
sex_male	1	0	.	.	.
Mar_status	2	0.6774	0.2547	2.66	0.0080
Mar_status	3	0.3647	0.2154	1.69	0.0908
Mar_status	1	0	.	.	.
total_harmzed	1	0.4637	0.4079	1.14	0.2559
total_harmzed	2	1.0983	0.3723	2.95	0.0033
total_harmzed	3	0.5896	0.3601	1.64	0.1019
total_harmzed	4	0	.	.	.

prov_new2	1	-1.1592	0.3399	-3.41	0.0007
prov_new2	2	0.4549	0.2625	1.73	0.0834
prov_new2	4	-0.3150	0.2272	-1.39	0.1660
prov_new2	5	-0.6659	0.2754	-2.42	0.0158
prov_new2	6	-1.5462	0.3116	-4.96	<.0001
prov_new2	3	0	.	.	.
smk_typ	1	0.5046	0.1911	2.64	0.0084
smk_typ	2	-0.00438	0.3348	-0.01	0.9896
smk_typ	0	0	.	.	.
hou_owned	0	0.5660	0.1806	3.13	0.0018
hou_owned	1	0	.	.	.
hou_rep	1	0.8353	0.2347	3.56	0.0004
hou_rep	2	0.1441	0.1941	0.74	0.4579
hou_rep	0	0	.	.	.
diab_type12	1	0.5171	0.2197	2.35	0.0188
diab_type12	0	0	.	.	.
hrs_wrk	2	0.1460	0.3794	0.38	0.7004
hrs_wrk	3	1.0414	0.4711	2.21	0.0273
hrs_wrk	4	1.0455	0.3776	2.77	0.0057
hrs_wrk	1	0	.	.	.

NOTE: The degrees of freedom for the t tests is 1000.

Odds Ratio Estimates

Effect		Point Estimate	95% Confidence Limits	
acos_age	1 vs 0	1.006	0.542	1.867
acos_age	2 vs 0	2.434	1.341	4.417
acos_age	3 vs 0	1.994	0.972	4.092
acos_age	4 vs 0	1.678	0.706	3.985
sex_male	0 vs 1	1.744	1.245	2.445
Mar_status	2 vs 1	1.969	1.194	3.245
Mar_status	3 vs 1	1.440	0.944	2.198
total_harmzed	1 vs 4	1.590	0.714	3.540
total_harmzed	2 vs 4	2.999	1.444	6.227
total_harmzed	3 vs 4	1.803	0.890	3.656
prov_new2	1 vs 3	0.314	0.161	0.611
prov_new2	2 vs 3	1.576	0.942	2.638
prov_new2	4 vs 3	0.730	0.467	1.140
prov_new2	5 vs 3	0.514	0.299	0.882
prov_new2	6 vs 3	0.213	0.116	0.393
smk_typ	1 vs 0	1.656	1.138	2.410
smk_typ	2 vs 0	0.996	0.516	1.921
hou_owned	0 vs 1	1.761	1.236	2.510
hou_rep	1 vs 0	2.306	1.455	3.654
hou_rep	2 vs 0	1.155	0.789	1.690
diab_type12	1 vs 0	1.677	1.090	2.581
hrs_wrk	2 vs 1	1.157	0.550	2.437
hrs_wrk	3 vs 1	2.833	1.124	7.140
hrs_wrk	4 vs 1	2.845	1.356	5.968

UNIVARIATE ANALYSIS FOR GENDER-SPECIFIC ANALYSIS

AGE

Male

Domain Analysis for domain sex_male=1

Type 3 Analysis of Effects

Effect	F Value	Num DF	Den DF	Pr > F
acos_age	**8.85**	**4**	**1000**	**<.0001**

Analysis of Maximum Likelihood Estimates

Parameter		Estimate	Standard Error	t Value	Pr > |t|
Intercept		-4.7556	0.2293	-20.74	<.0001
acos_age	1	-0.0657	0.5506	-0.12	0.9051
acos_age	2	0.7910	0.3665	2.16	0.0311
acos_age	3	1.5504	0.3616	4.29	<.0001
acos_age	4	1.6525	0.3439	4.81	<.0001
acos_age	0	0	.	.	.

NOTE: The degrees of freedom for the t tests is 1000.

Odds Ratio Estimates

Effect	Point Estimate	95% Confidence Limits	
acos_age 1 vs 0	0.936	0.318	2.759
acos_age 2 vs 0	2.206	1.074	4.527
acos_age 3 vs 0	4.713	2.318	9.583
acos_age 4 vs 0	5.220	2.658	10.251

Female

Domain Analysis for domain sex_male=0

Type 3 Analysis of Effects

Effect	F Value	Num DF	Den DF	Pr > F
acos_age	**5.21**	**4**	**1000**	**0.0004**

Analysis of Maximum Likelihood Estimates

Parameter		Estimate	Standard Error	t Value	Pr > |t|
Intercept		-3.7804	0.2460	-15.37	<.0001
acos_age	1	0.0687	0.3230	0.21	0.8316

acos_age	2	1.0735	0.3108	3.45	0.0006
acos_age	3	0.7517	0.3090	2.43	0.0152
acos_age	4	0.9084	0.3586	2.53	0.0114
acos_age	0	0	.	.	.

Odds Ratio Estimates

Effect	Point Estimate	95% Confidence Limits	
acos_age 1 vs 0	1.071	0.568	2.019
acos_age 2 vs 0	2.925	1.590	5.383
acos_age 3 vs 0	2.121	1.156	3.889
acos_age 4 vs 0	2.480	1.227	5.013

MARITAL STATUS

Male

Domain Analysis for domain sex_male=1

Type 3 Analysis of Effects

Effect	F Value	Num DF	Den DF	Pr > F
Mar_status	**6.05**	**2**	**1000**	**0.0025**

Analysis of Maximum Likelihood Estimates

Parameter	Estimate	Standard Error	t Value	Pr > |t|
Intercept	-4.3113	0.1929	-22.35	<.0001
Mar_status 2	1.2826	0.3690	3.48	0.0005
Mar_status 3	0.3072	0.2913	1.05	0.2918
Mar_status 1	0	.	.	.

Odds Ratio Estimates

Effect	Point Estimate	95% Confidence Limits	
Mar_status 2 vs 1	3.606	1.748	7.439
Mar_status 3 vs 1	1.360	0.768	2.408

Female

Domain Analysis for domain sex_male=0

Type 3 Analysis of Effects

Effect	F Value	Num DF	Den DF	Pr > F
Mar_status	**10.66**	**2**	**1000**	**<.0001**

Analysis of Maximum Likelihood Estimates

Parameter	Estimate	Standard Error	t Value	Pr > |t|
Intercept	-3.7125	0.1557	-23.84	<.0001
Mar_status 2	1.2122	0.2639	4.59	<.0001
Mar_status 3	0.3699	0.2145	1.72	0.0849
Mar_status 1	0	.	.	.

Odds Ratio Estimates

Effect	Point Estimate	95% Confidence Limits	
Mar_status 2 vs 1	3.361	2.002	5.641
Mar_status 3 vs 1	1.448	0.950	2.205

RURAL OR URBAN

Male

Domain Analysis for domain sex_male=1

Type 3 Analysis of Effects

Effect	F Value	Num DF	Den DF	Pr > F
rural_urb	**0.65**	**3**	**1000**	**0.5803**

Analysis of Maximum Likelihood Estimates

Parameter	Estimate	Standard Error	t Value	Pr > |t|
Intercept	-4.0326	0.1959	-20.58	<.0001
rural_urb 1	-0.0237	0.3080	-0.08	0.9388
rural_urb 2	-0.4225	0.3714	-1.14	0.2556
rural_urb 3	0.2243	0.4187	0.54	0.5922
rural_urb 4	0	.	.	.

Odds Ratio Estimates

Effect	Point Estimate	95% Confidence Limits	
rural_urb 1 vs 4	0.977	0.534	1.787
rural_urb 2 vs 4	0.655	0.316	1.358
rural_urb 3 vs 4	1.252	0.550	2.846

Female

Domain Analysis for domain sex_male=0

Type 3 Analysis of Effects

Effect	F Value	Num DF	Den DF	Pr > F
rural_urb	**1.98**	**3**	**1000**	**0.1146**

Analysis of Maximum Likelihood Estimates

Parameter	Estimate	Standard Error	t Value	Pr > |t|
Intercept	-3.1654	0.1509	-20.98	<.0001
rural_urb 1	-0.4509	0.2638	-1.71	0.0877
rural_urb 2	-0.4070	0.2380	-1.71	0.0876
rural_urb 3	0.1519	0.3045	0.50	0.6180
rural_urb 4	0	.	.	.

Odds Ratio Estimates

Effect	Point Estimate	95% Confidence Limits	
rural_urb 1 vs 4	0.637	0.380	1.069
rural_urb 2 vs 4	0.666	0.417	1.062
rural_urb 3 vs 4	1.164	0.640	2.116

PROVINCE OF RESIDENCE

Male

Domain Analysis for domain sex_male=1

Type 3 Analysis of Effects

Effect	F Value	Num DF	Den DF	Pr > F
prov_new2	**4.74**	**4**	**1000**	**0.0009**

Analysis of Maximum Likelihood Estimates

Parameter	Estimate	Standard Error	t Value	Pr > |t|
Intercept	-3.0803	0.3073	-10.03	<.0001
prov_new2 1	-1.7535	0.4342	-4.04	<.0001
prov_new2 3	-0.9656	0.3859	-2.50	0.0125
prov_new2 4	-1.2337	0.3860	-3.20	0.0014
prov_new2 5	-1.4003	0.4281	-3.27	0.0011
prov_new2 2	0	.	.	.

Odds Ratio Estimates

	Point	95% Confidence

Effect	Estimate	Limits	
prov_new2 1 vs 2	0.173	0.074	0.406
prov_new2 3 vs 2	0.381	0.179	0.812
prov_new2 4 vs 2	0.291	0.137	0.621
prov_new2 5 vs 2	0.247	0.106	0.571

Female

Domain Analysis for domain sex_male=0

Type 3 Analysis of Effects

Effect	F Value	Num DF	Den DF	Pr > F
prov_new2	**7.98**	**4**	**1000**	**<.0001**

Analysis of Maximum Likelihood Estimates

Parameter	Estimate	Standard Error	t Value	Pr > |t|
Intercept	-2.6015	0.2326	-11.19	<.0001
prov_new2 1	-1.7131	0.3216	-5.33	<.0001
prov_new2 3	-0.3897	0.3103	-1.26	0.2094
prov_new2 4	-0.8756	0.2810	-3.12	0.0019
prov_new2 5	-1.1097	0.3166	-3.51	0.0005
prov_new2 2	0	.	.	.

NOTE: The degrees of freedom for the t tests is 1000.

Odds Ratio Estimates

Effect	Point Estimate	95% Confidence Limits	
prov_new2 1 vs 2	0.180	0.096	0.339
prov_new2 3 vs 2	0.677	0.368	1.245
prov_new2 4 vs 2	0.417	0.240	0.723
prov_new2 5 vs 2	0.330	0.177	0.614

TOTAL PERSONAL INCOME

Male

Domain Analysis for domain sex_male=1

Type 3 Analysis of Effects

Effect	F Value	Num DF	Den DF	Pr > F
tot_inc	**3.61**	**3**	**1000**	**0.0130**

Analysis of Maximum Likelihood Estimates

Parameter	Estimate	Standard Error	t Value	Pr > |t|

Intercept		-4.6779	0.3106	-15.06	<.0001
tot_inc	1	0.2325	0.4182	0.56	0.5783
tot_inc	2	1.0770	0.4018	2.68	0.0075
tot_inc	3	0.9761	0.3929	2.48	0.0131
tot_inc	4	0	.	.	.

Odds Ratio Estimates

Effect	Point Estimate	95% Confidence Limits	
tot_inc 1 vs 4	1.262	0.555	2.867
tot_inc 2 vs 4	2.936	1.334	6.459
tot_inc 3 vs 4	2.654	1.228	5.738

Female

Domain Analysis for domain sex_male=0

Type 3 Analysis of Effects

Effect	F Value	Num DF	Den DF	Pr > F
tot_inc	**9.88**	**3**	**1000**	**<.0001**

Analysis of Maximum Likelihood Estimates

Parameter		Estimate	Standard Error	t Value	Pr > |t|
Intercept		-4.2523	0.2236	-19.01	<.0001
tot_inc	1	0.6186	0.2974	2.08	0.0378
tot_inc	2	1.3380	0.2609	5.13	<.0001
tot_inc	3	1.1243	0.3355	3.35	0.0008
tot_inc	4	0	.	.	.

Odds Ratio Estimates

Effect	Point Estimate	95% Confidence Limits	
tot_inc 1 vs 4	1.856	1.036	3.328
tot_inc 2 vs 4	3.811	2.284	6.360
tot_inc 3 vs 4	3.078	1.594	5.946

SMOKING STATUS

Male

Domain Analysis for domain sex_male=1

Type 3 Analysis of Effects

Effect	F Value	Num DF	Den DF	Pr > F
smk_typ	**3.21**	**2**	**1000**	**0.0407**

Analysis of Maximum Likelihood Estimates

Parameter		Estimate	Standard Error	t Value	Pr > |t|
Intercept		-4.3753	0.1806	-24.22	<.0001
smk_typ	1	0.6928	0.2758	2.51	0.0122
smk_typ	2	0.1695	0.4880	0.35	0.7285
smk_typ	0	0	.	.	.

Odds Ratio Estimates

Effect	Point Estimate	95% Confidence Limits	
smk_typ 1 vs 0	1.999	1.164	3.435
smk_typ 2 vs 0	1.185	0.455	3.087

Females

Domain Analysis for domain sex_male=0

Type 3 Analysis of Effects

Effect	F Value	Num DF	Den DF	Pr > F
smk_typ	**11.28**	**2**	**1000**	**<.0001**

Analysis of Maximum Likelihood Estimates

Parameter		Estimate	Standard Error	t Value	Pr > |t|
Intercept		-3.6856	0.1574	-23.41	<.0001
smk_typ	1	0.9552	0.2032	4.70	<.0001
smk_typ	2	0.2640	0.3429	0.77	0.4415
smk_typ	0	0	.	.	.

ANYBODY SMOKING AT HOME

Male

Domain Analysis for domain sex_male=1

Type 3 Analysis of Effects

Effect	F Value	Num DF	Den DF	Pr > F
smk_hom	**0.72**	**1**	**1000**	**0.3968**

Analysis of Maximum Likelihood Estimates

Parameter		Estimate	Standard Error	t Value	Pr > |t|
Intercept		-4.2141	0.1606	-26.25	<.0001
smk_hom	1	-0.2580	0.3044	-0.85	0.3968
smk_hom	0	0	.	.	.

Odds Ratio Estimates

Effect	Point Estimate	95% Confidence Limits	
smk_hom 1 vs 0	0.773	0.425	1.404

Female

Domain Analysis for domain sex_male=0

Type 3 Analysis of Effects

Effect	F Value	Num DF	Den DF	Pr > F
smk_hom	**21.48**	**1**	**1000**	**<.0001**

Analysis of Maximum Likelihood Estimates

Parameter		Estimate	Standard Error	t Value	Pr > |t|
Intercept		-3.6891	0.1395	-26.44	<.0001
smk_hom	1	1.0238	0.2209	4.63	<.0001
smk_hom	0	0	.	.	.

Odds Ratio Estimates

Effect	Point Estimate	95% Confidence Limits	
smk_hom 1 vs 0	2.784	1.804	4.294

DWELLING (OWNED/RENTED)

Male

Domain Analysis for domain sex_male=1

Type 3 Analysis of Effects

Effect	F Value	Num DF	Den DF	Pr > F
hou_owned	**13.10**	**1**	**1000**	**0.0003**

Analysis of Maximum Likelihood Estimates

Parameter	Estimate	Standard Error	t Value	Pr > |t|
Intercept	-4.6035	0.1890	-24.35	<.0001
hou_owned 0	0.9500	0.2624	3.62	0.0003
hou_owned 1	0	.	.	.

Odds Ratio Estimates

Effect	Point Estimate	95% Confidence Limits	
hou_owned 0 vs 1	2.586	1.545	4.328

Female

Domain Analysis for domain sex_male=0

Type 3 Analysis of Effects

Effect	F Value	Num DF	Den DF	Pr > F
hou_owned	**22.90**	**1**	**1000**	**<.0001**

Analysis of Maximum Likelihood Estimates

Parameter	Estimate	Standard Error	t Value	Pr > |t|
Intercept	-3.8358	0.1428	-26.87	<.0001
hou_owned 0	0.9570	0.2000	4.79	<.0001
hou_owned 1	0	.	.	.

DWELLING IN NEED OF REPAIRS

Male

Domain Analysis for domain sex_male=1

Type 3 Analysis of Effects

Effect	F Value	Num DF	Den DF	Pr > F
hou_rep	**4.72**	**2**	**1000**	**0.0091**

Analysis of Maximum Likelihood Estimates

Parameter		Estimate	Standard Error	t Value	Pr > |t|
Intercept		-4.3209	0.1828	-23.64	<.0001
hou_rep	1	0.9405	0.3069	3.07	0.0022
hou_rep	2	0.2647	0.3059	0.87	0.3870
hou_rep	0	0	.	.	.

Odds Ratio Estimates

Effect	Point Estimate	95% Confidence Limits	
hou_rep 1 vs 0	2.561	1.403	4.677
hou_rep 2 vs 0	1.303	0.715	2.375

Female

Domain Analysis for domain sex_male=0

Type 3 Analysis of Effects

Effect	F Value	Num DF	Den DF	Pr > F
hou_rep	**10.75**	**2**	**1000**	**<.0001**

Analysis of Maximum Likelihood Estimates

Parameter		Estimate	Standard Error	t Value	Pr > |t|
Intercept		-3.6042	0.1341	-26.88	<.0001
hou_rep	1	1.1938	0.2662	4.49	<.0001
hou_rep	2	0.1651	0.2215	0.75	0.4563
hou_rep	0	0	.	.	.

DIABETES

Male

Domain Analysis for domain sex_male=1

Type 3 Analysis of Effects

Effect	F Value	Num DF	Den DF	Pr > F
diab_type12	**18.68**	**1**	**1000**	**<.0001**

Analysis of Maximum Likelihood Estimates

Parameter	Estimate	Standard Error	t Value	Pr > |t|
Intercept	-4.2957	0.1460	-29.42	<.0001
diab_type12 1	1.3336	0.3085	4.32	<.0001
diab_type12 0	0	.	.	.

Odds Ratio Estimates

Effect	Point Estimate	95% Confidence Limits	
diab_type12 1 vs 0	3.795	2.071	6.952

Female

Domain Analysis for domain sex_male=0

Type 3 Analysis of Effects

Effect	F Value	Num DF	Den DF	Pr > F
diab_type12	**24.46**	**1**	**1000**	**<.0001**

Analysis of Maximum Likelihood Estimates

Parameter	Estimate	Standard Error	t Value	Pr > |t|
Intercept	-3.4742	0.1215	-28.60	<.0001
diab_type12 1	1.1818	0.2389	4.95	<.0001
diab_type12 0	0	.	.	.

Odds Ratio Estimates

Effect	Point Estimate	95% Confidence Limits	
diab_type12 1 vs 0	3.260	2.040	5.211

HOW MANY ROOMS ARE THERE IN A BUILDING

Male

Domain Analysis for domain sex_male=1

Type 3 Analysis of Effects

Effect	F Value	Num DF	Den DF	Pr > F
hous_rms	**3.77**	**2**	**1000**	**0.0233**

Analysis of Maximum Likelihood Estimates

Parameter		Estimate	Standard Error	t Value	Pr > |t|
Intercept		-3.6396	0.1810	-20.11	<.0001
hous_rms	3	-0.9305	0.3510	-2.65	0.0081
hous_rms	4	-0.5657	0.4522	-1.25	0.2112
hous_rms	1	0	.	.	.

Odds Ratio Estimates

Effect	Point Estimate	95% Confidence Limits	
hous_rms 3 vs 1	0.394	0.198	0.785
hous_rms 4 vs 1	0.568	0.234	1.379

Female

Domain Analysis for domain sex_male=0

Type 3 Analysis of Effects

Effect	F Value	Num DF	Den DF	Pr > F
hous_rms	**11.94**	**2**	**1000**	**<.0001**

Analysis of Maximum Likelihood Estimates

Parameter		Estimate	Standard Error	t Value	Pr > |t|
Intercept		-2.9309	0.1325	-22.12	<.0001
hous_rms	3	-0.6991	0.3317	-2.11	0.0353
hous_rms	4	-1.6858	0.3647	-4.62	<.0001
hous_rms	1	0	.	.	.

Odds Ratio Estimates

Effect	Point Estimate	95% Confidence Limits	
hous_rms 3 vs 1	0.497	0.259	0.953
hous_rms 4 vs 1	0.185	0.091	0.379

NUMBER OF PAID HOURS PER WEEK

Male

Domain Analysis for domain sex_male=1

Type 3 Analysis of Effects

Effect	F Value	Num DF	Den DF	Pr > F
hrs_wrk	**5.03**	**2**	**1000**	**0.0067**

Analysis of Maximum Likelihood Estimates

Parameter		Estimate	Standard Error	t Value	Pr > |t|
Intercept		-4.6434	0.2313	-20.08	<.0001
hrs_wrk	3	0.5105	0.4499	1.13	0.2568
hrs_wrk	4	0.9090	0.2871	3.17	0.0016
hrs_wrk	1	0	.	.	.

Odds Ratio Estimates

Effect	Point Estimate	95% Confidence Limits	
hrs_wrk 3 vs 1	1.666	0.689	4.028
hrs_wrk 4 vs 1	2.482	1.413	4.359

Female

Domain Analysis for domain sex_male=0

Type 3 Analysis of Effects

Effect	F Value	Num DF	Den DF	Pr > F
hrs_wrk	**23.27**	**2**	**1000**	**<.0001**

Analysis of Maximum Likelihood Estimates

Parameter		Estimate	Standard Error	t Value	Pr > |t|
Intercept		-4.2497	0.1660	-25.60	<.0001
hrs_wrk	3	1.0045	0.4268	2.35	0.0188
hrs_wrk	4	1.4381	0.2109	6.82	<.0001
hrs_wrk	1	0	.	.	.

Odds Ratio Estimates

Effect	Point Estimate	95% Confidence Limits	
hrs_wrk 3 vs 1	2.730	1.182	6.309
hrs_wrk 4 vs 1	4.213	2.785	6.372

FINAL MODEL: MULTIVARIATE ANALYSIS

Male

Domain Analysis for domain sex_male=1

Type 3 Analysis of Effects

Effect	F Value	Num DF	Den DF	Pr > F
acos_age	4.16	4	1000	0.0024
Mar_status	2.66	2	1000	0.0707
prov_new3	3.09	4	1000	0.0152
smk_typ	0.51	2	1000	0.6020
hou_owned	8.94	1	1000	0.0029
hou_rep	4.51	2	1000	0.0112
diab_type12	1.62	1	1000	0.2027
hrs_wrk	2.45	2	1000	0.0872

Analysis of Maximum Likelihood Estimates

Parameter		Estimate	Standard Error	t Value	Pr > |t|
Intercept		-5.5983	0.5458	-10.26	<.0001
acos_age	1	0.0669	0.5266	0.13	0.8989
acos_age	2	0.8336	0.3803	2.19	0.0286
acos_age	3	1.4851	0.4339	3.42	0.0006
acos_age	4	1.6077	0.4715	3.41	0.0007
acos_age	0	0	.	.	.
Mar_status	2	0.6671	0.3952	1.69	0.0917
Mar_status	3	0.6744	0.3586	1.88	0.0603
Mar_status	1	0	.	.	.
prov_new3	1	-1.4764	0.4600	-3.21	0.0014
prov_new3	3	-0.5403	0.4360	-1.24	0.2156
prov_new3	4	-0.7223	0.4294	-1.68	0.0929
prov_new3	5	-1.0303	0.4715	-2.18	0.0291
prov_new3	2	0	.	.	.
smk_typ	1	0.3080	0.3102	0.99	0.3211
smk_typ	2	0.1013	0.5220	0.19	0.8462
smk_typ	0	0	.	.	.
hou_owned	0	0.8201	0.2743	2.99	0.0029
hou_owned	1	0	.	.	.
hou_rep	1	0.9786	0.3367	2.91	0.0037
hou_rep	2	0.0832	0.3366	0.25	0.8048
hou_rep	0	0	.	.	.
diab_type12	1	0.4423	0.3469	1.27	0.2027
diab_type12	0	0	.	.	.
hrs_wrk	3	0.6628	0.4585	1.45	0.1486
hrs_wrk	4	0.6353	0.3014	2.11	0.0353
hrs_wrk	1	0	.	.	.

NOTE: The degrees of freedom for the t tests is 1000.

Domain Analysis for domain sex_male=1

Odds Ratio Estimates

Effect		Point Estimate	95% Confidence Limits	
acos_age	1 vs 0	1.069	0.380	3.005
acos_age	2 vs 0	2.302	1.091	4.854
acos_age	3 vs 0	4.415	1.885	10.346
acos_age	4 vs 0	4.991	1.979	12.590
Mar_status	2 vs 1	1.949	0.897	4.232
Mar_status	3 vs 1	1.963	0.971	3.967
prov_new3	1 vs 2	0.228	0.093	0.563
prov_new3	3 vs 2	0.583	0.248	1.371
prov_new3	4 vs 2	0.486	0.209	1.128
prov_new3	5 vs 2	0.357	0.141	0.900
smk_typ	1 vs 0	1.361	0.740	2.501
smk_typ	2 vs 0	1.107	0.397	3.082
hou_owned	0 vs 1	2.271	1.326	3.890
hou_rep	1 vs 0	2.661	1.374	5.152
hou_rep	2 vs 0	1.087	0.561	2.104
diab_type12	1 vs 0	1.556	0.788	3.074
hrs_wrk	3 vs 1	1.940	0.789	4.770
hrs_wrk	4 vs 1	1.888	1.045	3.410

Female

Domain Analysis for domain sex_male=0

Type 3 Analysis of Effects

Effect	F Value	Num DF	Den DF	Pr > F
acos_age	3.23	4	1000	0.0120
Mar_status	3.91	2	1000	0.0204
prov_new3	7.84	4	1000	<.0001
smk_typ	4.89	2	1000	0.0077
hou_owned	6.36	1	1000	0.0118
hou_rep	5.65	2	1000	0.0036
diab_type12	13.39	1	1000	0.0003
hrs_wrk	17.81	2	1000	<.0001

Analysis of Maximum Likelihood Estimates

Parameter		Estimate	Standard Error	t Value	Pr > |t|
Intercept		-4.8860	0.3647	-13.40	<.0001
acos_age	1	-0.0671	0.3422	-0.20	0.8446
acos_age	2	0.8705	0.3614	2.41	0.0162
acos_age	3	0.1386	0.4651	0.30	0.7657
acos_age	4	-0.0184	0.5419	-0.03	0.9729
acos_age	0	0	.	.	.
Mar_status	2	0.7892	0.3244	2.43	0.0151
Mar_status	3	0.3781	0.2362	1.60	0.1098
Mar_status	1	0	.	.	.
prov_new3	1	-1.9082	0.3523	-5.42	<.0001
prov_new3	3	-0.4814	0.3043	-1.58	0.1140
prov_new3	4	-0.9215	0.2824	-3.26	0.0011

prov_new3	5	-1.0631	0.3310	-3.21	0.0014
prov_new3	2	0	.	.	.
smk_typ	1	0.6049	0.2346	2.58	0.0101
smk_typ	2	-0.2161	0.4200	-0.51	0.6070
smk_typ	0	0	.	.	.
hou_owned	0	0.5319	0.2109	2.52	0.0118
hou_owned	1	0	.	.	.
hou_rep	1	0.9520	0.2831	3.36	0.0008
hou_rep	2	0.2710	0.2204	1.23	0.2191
hou_rep	0	0	.	.	.
diab_type12	1	0.9007	0.2461	3.66	0.0003
diab_type12	0	0	.	.	.
hrs_wrk	3	1.1329	0.4460	2.54	0.0112
hrs_wrk	4	1.3862	0.2360	5.87	<.0001
hrs_wrk	1	0	.	.	.

Domain Analysis for domain sex_male=0

Odds Ratio Estimates

Effect		Point Estimate	95% Confidence Limits	
acos_age	1 vs 0	0.935	0.478	1.830
acos_age	2 vs 0	2.388	1.175	4.853
acos_age	3 vs 0	1.149	0.461	2.861
acos_age	4 vs 0	0.982	0.339	2.844
Mar_status	2 vs 1	2.202	1.165	4.161
Mar_status	3 vs 1	1.459	0.918	2.320
prov_new3	1 vs 2	0.148	0.074	0.296
prov_new3	3 vs 2	0.618	0.340	1.123
prov_new3	4 vs 2	0.398	0.229	0.693
prov_new3	5 vs 2	0.345	0.180	0.661
smk_typ	1 vs 0	1.831	1.155	2.902
smk_typ	2 vs 0	0.806	0.353	1.837
hou_owned	0 vs 1	1.702	1.125	2.575
hou_rep	1 vs 0	2.591	1.486	4.516
hou_rep	2 vs 0	1.311	0.851	2.021
diab_type12	1 vs 0	2.461	1.518	3.990
hrs_wrk	3 vs 1	3.105	1.294	7.449
hrs_wrk	4 vs 1	3.999	2.517	6.355