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The Utility of Administrative Data for Surveillance of Children With Chronic High Risk Medical Conditions (CHRMC) That Places Them at Risk for Influenza-related Complications.

by

Donatus Rutajama Mutasingwa

A THESIS

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Abstract

Background: Children with chronic high risks medical conditions (CHRMC) are more likely to develop severe influenza-related complications than those without CHRMC. As a result, prevention and control policies continue to target these risk groups. However, identifying these risk groups remains a challenge. Healthcare administrative data (HAD) have the potential to provide population-based data on children with CHRMC. However, there is lack of studies that have examined comprehensively the utility of HAD for this purpose.

Objectives: a) To develop a population based method for using HAD to identify children with CHRMC and b) to determine the correlates of CHRMC incidence and prevalence.

Methods: A retrospective cohort design was used. Two birth cohorts of children born in Alberta during fiscal years 1984/85 (n=41171) and 1994/95 (n=39864) were followed from birth to a maximum of eight years. CHRMC visits were identified from physicians' claims by using ICD-9 codes. A child was classified as having CHRMC using either of the two criteria: criterion A: primary care (≥ 1 paediatrician or ≥ 2 family physician visits only) or consultant (≥ 1 paediatrician and ≥ 2 family physician visits) or ≥ 2 emergency room visits or ≥1 hospitalization; criterion B: two or more of the components of criterion A. The validity of the case definition was determined by: a) determining the positive predictive value (PPV) in terms of the proportion of children with CHRMC who made ≥ 1 subsequent visits post-classification (i.e. evidence of continued healthcare use post-classification); b) examining the consistency of epidemiological patterns of children with CHRMC between the two cohorts, case definitions and previous studies. The correlates of incidence and prevalence were determined through multivariate regression models.

Results: Both case definitions had the highest PPV when children were followed continuously for at least two years post-classification. The maximum PPV of criterion A for identifying children with CHRMC was 88.7%, while that of Criterion B was 94.6%. Although there were differences in the prevalence and incidence rates between the two cohorts, there was consistency in the epidemiological pattern of CHRMC as follows: males had higher CHRMC incidence and prevalence rates than females; First Nations had the highest CHRMC prevalence and incidence rates; children in rural areas had the highest CHRMC prevalence and incidence rates. **Conclusions:** HAD can be used to identify children with CHRMC. The consistency of results between the two cohorts coupled with case definitions with high PPV, provide preliminary evidence that the approach used is valid. These findings are relevant to those who need a practical way to identify target groups for influenza vaccination.

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Dedication

I would like to dedicate this dissertation to:

-my father: The late George Mutasingwa

-my mother: Winifrida Mutasingwa

-my wife: Milembe

-my Daughters: Maxine and Danica

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List of Abbreviations

ACIP=Advisory Committee on Immunization Practices

AHCIP=Alberta Health Care Insurance Plan

AHIPR=Alberta Health Care Insurance Plan Registry

CDC=Centers for Diseases Control

CHREB=Conjoint Health Research Ethics Board

CHRMC= Chronic High Risk Medical Conditions

COPD=Chronic Obstructive pulmonary Disease

HUF=Healthcare Utilization File

ICD-9 CM =International Classification of Diseases 9th Revision-Clinical Modification

IRR=Incidence Rate Ratio

NACI=National Advisory Committee on Immunization

PHN=Personal Health Number

PRR=Prevalence Rate Ratio

SDF=Social-demographic File

SES=social economic status

CHAPTER ONE: INTRODUCTION

This chapter provides background information on the purpose, the research problem and the rationale for this study. This chapter also outlines the organization of the dissertation.

1.1 Purpose

The purpose of this study was to develop a method of using large healthcare administrative databases to determine the incidence and prevalence of chronic high-risk medical conditions (CHRMC) that place children at high risk of influenza-related complications. Incidence and prevalence of CHRMC are necessary indicators for population-based surveillance of influenza immunization rates among children with CHRMC.

1.2 Objectives

The objectives of this study were as follows:

a. To develop case definitions of CHRMC that can be used to identify target groups for influenza vaccination from healthcare administrative data.
b. To estimate the prevalence and incidence of CHRMC from administrative data.

1.3 Research Questions

Specifically, the research questions were the following:

1. Can we use Alberta Health and Wellness (AHW) databases to identify children with CHRMC in Alberta?
2. What is the construct validity of CHRMC case definitions developed from administrative database?
3. Using the developed CHRMC case definitions, what is the incidence rate of CHRMC among children in Alberta?
4. Using the CHRMC case definitions, what is the prevalence of CHRMC among children in Alberta?
5. What are the socio-demographic correlates (age, sex, social economic status and residence) of prevalence and incidence rate of CHRMC in Alberta?
6. What is the proportion of children with multiple CHRMC (i.e. more than one CHRMC)?

1.4 The Research Problem

Influenza is a common disease in childhood and is associated with substantial social-economic burden. In addition to healthcare utilization costs, influenza causes loss in productivity due to work absenteeism of parents who must take care of their sick children (1). Although all children are vulnerable to influenza infection, children with CHRMC such as chronic cardiovascular and respiratory conditions are more likely to develop influenza related complications than children without CHRMC (2). To reduce the impact of influenza, vaccination specifically targeting children with CHRMC remains one of the most effective way of reducing the burden of influenza (3,4).

Vaccine coverage provides a reasonable measure of vaccine program performance (except when there is vaccine failure or an antigen mismatch) (5-7). Vaccine coverage can also provide an indicator for determining if there is a problem with immunization delivery (8) for a particular target group. An increasing number of studies have dealt with mechanisms for improving vaccine coverage (9-11), however, few have focused on the need for improved methods of surveillance of vaccination of target groups such as children with CHRMC (12-17). A key challenge facing influenza immunization programs therefore is the lack of reliable and regular information on the prevalence or incidence of CHRMC. These are key indicators for surveillance of children with CHRMC.

The lack of data on incidence and prevalence of CHRMC impedes efforts to monitor and subsequently improve influenza vaccination coverage rates for children with underlying CHRMC (18). In addition, the comparison of vaccination coverage for this target group between and within regions is impossible due to the lack of data on the total population at risk (19-21).

The World Health Organisation (WHO) has identified the assessment of national and local influenza vaccination rates within target groups as top priority activities that are critical to reducing morbidity and mortality from influenza (22). This study attempts to address this problem by developing a method of using healthcare administrative databases to estimate incidence and prevalence of children with CHRMC.

1.5 Rationale for Using Administrative Data to Determine Prevalence and Incidence of Chronic Diseases

Healthcare administrative databases are increasingly being used for various research purposes in many developed countries (23). Basically these databases are available in electronic format and are created to track records for administrative purposes of hospital discharge summaries, physician billing claims, claims for prescription drugs and other health related data (24). Improvement in computers and information technology has made the storage and retrieval of information contained in these databases much easier and therefore has expanded opportunities for population-based epidemiological studies (23, 25).

Healthcare administrative databases possess features that make them potentially suitable for various surveillance purposes, including timeliness, population coverage and flexibility (23, 24, 26). Healthcare administrative databases can be available in a timely manner because they are already in electronic format, therefore retrieval and analysis would be relatively easier than a comparable effort needed for primary data collection.

Healthcare administrative databases often have information of the whole population who receive health services from a particular geographical location. Because the whole population is likely to be included in the databases, establishing a surveillance system from

healthcare administrative databases would likely provide population-based data that is representative of the whole population. Population coverage is probably one of the most important features of healthcare administrative databases, something that would be costly if a survey of similar magnitude would be undertaken. Unlike surveys, healthcare administrative databases can be used to assess the health status of the entire population repeatedly over time (27).

In addition, healthcare administrative databases can be manipulated to provide flexible surveillance tool to adapt to changing needs without necessarily having to go through complete primary data collection. Because of these reasons, large computerized healthcare administrative databases have the potential to provide a powerful surveillance tool for children with CHRMC, and therefore enable an efficient way of monitoring influenza vaccination coverage among children with chronic diseases.

Monitoring of vaccination coverage among children with CHRMC is paramount for reduction of influenza-associated morbidity and mortality. Through monitoring of vaccine coverage, "pockets of under-immunization" can be identified to enable appropriate interventions for increasing vaccination coverage in the target groups (28-29).

1.6 Organisation of the Dissertation

This dissertation is organised into eight chapters as follows. Chapter 2 describes the background information about influenza diseases in children as well the relevant literature review. This includes aetiology, clinical feature, burden and control of influenza. It also includes a literature review of previous studies that have used healthcare administrative data to identify individuals with chronic diseases, limitations of those studies and gaps in knowledge. Chapter 3 outlines the methods used to answer the research questions. This includes the study population, the development of case definition used to identify children from administrative data, the validation of the case definitions and the approach used to determine the correlates of prevalence and incidence of CHRMC.

The results of this study are organized into four chapters: chapter 4, 5, 6 and 7. Chapter 4 includes the description of the social demographic characteristics of the study population. Chapter 5 has the results of the validation of case definition. Chapter 6 includes results on the analysis of correlates of incidence and prevalence. In chapter 7, a sensitivity analysis of the findings is done by restricting the analysis of to individuals who had chronic Obstructive Pulmonary Diseases (COPD), which constituted over 75 percent of all CHRMC-related visits. Finally, chapter 8 includes the discussion of findings from chapter 4 to 7, in the light of the existing literature (chapter 3). The Strengths and limitations of the methods employed in this study are also discussed in chapter 8. Chapter 8 also outlines the practical application of the research findings.

CHAPTER TWO: LITERATURE REVIEW

2.1 Introduction

This chapter provides the background information on influenza disease in children including the aetiology, clinical features, risk factors, burden, control and prevention methods. The chapter also summarises the previous literature on existing methods of surveillance of children with CHRMC. Finally, a review of literature on various methodological approaches used to identify individuals with chronic diseases other than CHRMC from healthcare administrative data is presented.

2.2 Epidemiology of Influenza in Children

2.2.1 Aetiology, Transmission, Clinical Features

Influenza, also known as flu, is an ancient disease that has caused great human sufferings since year 412 BC (30). It is caused by influenza viruses that belong to a family of virus called orthomyxoviridae (31). Their genera are known as type A, B and C. Influenza type A and B are the most common human type. Influenza type C cause mild respiratory illness and are not thought to cause epidemics.

Unlike other viruses that cause respiratory illnesses in children, influenza viruses are unique in that they constantly undergo antigenic changes (30). The antigenic changes results from continuous and sequential evolution of genetic materials that involve Ribonucleic acid (RNA) segments coding for surface glycoprotein known as haemaglutinin or neuraminidase. The changes are known as antigenic drift if there are minor changes in surface antigens, or antigenic shift if there are major structural changes. Antigenic drift is responsible for annual epidemics, which are associated with variable attack rates. The

annual epidemics are common because individuals lack immunity or have partial immunity to the constantly changing virus. Antigenic shift can cause pandemics, which are associated with high attack rates with widespread epidemics and deaths.

Influenza is transmitted through virus-laden respiratory secretions via droplets expelled during coughing and sneezing. Viral shedding occurs one to two days before and five to seven days after the onset of symptoms and can be prolonged in young children and immuno-compromised hosts (32).

Influenza exhibits well-defined seasonality patterns. In northern temperate zones, the peak influenza activity occurs during winter from November through March. Sporadic cases may occur during summer. In southern temperate zones, peak activity occurs between April and September. In tropical zones, the pattern is less well described but is thought to increase during rainy seasons (33).

2.2.2 Clinical presentation of influenza

Clinical symptoms of influenza vary with age. In adults and adolescents, influenza presents with abrupt onset of fever and chills accompanied by symptoms of muscle aches (mylagia), headache and a non-productive cough. Infants and young children can present with a fever or with respiratory illness such as croup, bronchiolitis or bronchitis (34). These symptoms are not unique to influenza, they overlap greatly with symptoms caused by other respiratory viruses such as respiratory syncitial virus (RSV) or Para influenza viruses. It is therefore difficult to diagnose influenza on clinical grounds alone especially in children.

Influenza is usually associated with a U-shaped epidemic curve. Attack rates are generally highest in young children, whereas mortality is generally highest in the elderly (33). Each year, the attack rates in children are variable. Attack rates of up to 19 percent have been reported during mild influenza seasons (35).

Influenza is normally a self-limiting disease, but it can be associated with other complications, mostly respiratory in nature (e.g. pneumonia). In children, non-respiratory complications include middle ear infection (acute otitis media), myositis (inflammation of voluntary muscles), Guillain Barre Syndrome, and Reye syndrome (acute encephalopathy with cerebral oedema) (36-39).

2.2.3 Chronic Diseases as a Risk Factor for Serious Influenza-related Complications

The relationship between infectious diseases and chronic diseases is well known (40). A number of chronic diseases predispose individuals to certain infectious diseases. For example, children with chronic cardiovascular and respiratory conditions are at a risk for severe influenza-related complications similar to the risk in the elderly aged over 65 years (31, 41-43).

Chronic diseases that are currently regarded as CHRMC include chronic pulmonary or cardiovascular conditions such as asthma, bronchopulmonary dysplasia and cystic fibrosis. Other CHRMCs include: chronic metabolic disease (e.g. diabetes), chronic kidney diseases, hemoglobinopathies, immunosuppression caused by medication or disease (e.g. HIV, cancer), rheumatoid arthritis and other inflammatory polyarthropathies and polyarteritis nodosa (3-4).

Several studies have shown that children with CHRMC are at a higher risk of various types of influenza related complications than those without CHRMC. For example, children with CHRMC are between two and twenty times more likely to be hospitalised for acute respiratory disease than children without CHRMC (2, 44-49).

2.2.4 Burden of influenza in children

Generally, estimating the burden of influenza is very challenging due to the overlap of symptoms with other viruses such as RSV. Children with influenza present with non-specific symptoms that are similar to other viruses (e.g. RSV) (46;50-53). Therefore, it is difficult to distinguish disease caused by influenza from those caused by RSV on clinical grounds alone (54). Virological confirmation is therefore needed to differentiate between

RSV and influenza illness. However, virological confirmation is not routinely done. Because of these reasons, this section provides an overview of the burden of influenza in children derived from influenza like illness, with or without virological confirmation.

Influenza is a unique disease in that it is associated with recurrent winter morbidity (45-46, 53, 55-58). The burden of influenza in children resulting from morbidity can be divided into healthcare utilization costs (e.g. hospitalization, physician office visits and emergency room visits), absenteeism (school and work) and intangibles (such as general malaise and impaired function) (58).

It is estimated that between 9 and 20 percent of children will seek health care annually for influenza-related illness (53). There is a wide variation in the influenza-associated hospitalization rates in children depending on the season and the concept used (example excess versus cumulative). Excess hospitalization rate can be estimated from the difference between the baseline and the observed hospitalization rate. For example, among children under the age of 16 years, the excess hospitalization is estimated to be from 53 per 100,000 children to 2800 per 100,000 children per year (46, 51-53, 59-60). Among children with chronic lung diseases, hospitalization rates are estimated to be between 200 per 100,000 and 1900 per 100,000 children per year (50). There is paucity of data on the burden of influenza in tropics or subtropics, however one study estimated that for the period between 1997 and 1999, influenza related hospitalization was responsible for five to eight percent of all annual paediatric bed days (51).

Influenza can result in complications, some of which necessitate the use of antibiotics for treatment. Examples of these influenza-related complications include middle ear infection (i.e. acute otitis media) and secondary bacterial pneumonia. In

children, influenza is known to cause Eustachian tube dysfunction, which predisposes some children to invasion of the middle ear by respiratory bacteria thereby causing middle ear infections (61). In one study, middle ear infections were the most common complication affecting one out of five children aged younger than 13 years old (62). In another study children with influenza were up to three times as likely to get middle ear infections compared to children without influenza (49). Other investigators estimated that up to five percent of middle ear infections among children under the age of two years are directly attributable to influenza (53).

Depending on the severity of the influenza season, excess use of antibiotics attributable to influenza has been estimated to be between 140 prescriptions per 1000 children to 1080 prescriptions per 1000 children (50). Children who suffer from influenza-related complications are more likely to require multiple health visits than those with uncomplicated influenza. In one study (63), 30 percent to 50 percent of children younger than 14 years with complications required three or more doctors visits compared to only five to seven percent of children without complications. Because of these additional visits to doctors, the average direct influenza-related costs was three times higher among children with complications compared to those without complications (63).

In addition to direct healthcare-related costs, influenza also causes considerable economic burden due to work absenteeism of parents who have to take care of their sick children (1). Influenza is associated with one to four lost work days that are used by parents to take care of their sick children (1, 62, 64, 65).

Compared to adults aged 65 years or older, influenza-associated mortality in children is low (66-68). One study estimated that the influenza-related mortality was 7.7

per 10,000,000 children (46). However, a more recent study has shown a higher rate of deaths than the previous study, with a rate of 21 per 10,000,000 (69). The variation in the death rates is not surprising because mortality due to influenza depends on the virulence of the virus, the vaccination coverage of the population studied as well as the degree of matching between the vaccination and the circulating influenza virus. To sum up, considering both the direct and indirect effects of influenza, the overall socioeconomic burden of influenza in children is substantial to the society as a whole.

2.2.5 Control and Prevention of Influenza

2.2.5.1 Influenza Vaccine

Children with CHRMC are at greatest risk for severe complications from influenza as a result, prevention and control policies continue to target these risk groups (70). The Canadian National Advisory Committee on Immunization (NACI) (3), the American Advisory Committee on Immunization practice (ACIP) (4) and the Committee on Infectious Diseases of the American Academy of Paediatrics' (71) acknowledge that increasing vaccination coverage among persons with CHRMC is among the top priorities for expanding influenza vaccine use, because the strategies can reduce the serious effects of influenza.

The efficacy of influenza vaccine depends on several factors such as degree of match between the vaccine antigen and the circulating virus and types of outcomes assessed (e.g. hospitalization or culture positive infection). For example, in children aged one to fifteen years, the inactivated influenza vaccine has efficacy rates of between 64 percent and 98 percent in preventing laboratory-confirmed influenza when there is a good match between the vaccine antigens and the circulating virus (72).

The efficacy of the influenza vaccine in reducing the occurrence of otitis media or acute respiratory infections has been estimated to be between 20 percent and 70 percent (73-76). However, one recent study did not show any difference in the rates of acute otitis media for children aged younger than two years who were vaccinated with the inactivated influenza vaccine compared to those who received placebo (77).

The effectiveness of influenza vaccine in children with chronic diseases remains uncertain. For example, recent systematic reviews concluded that despite good serological response, the effectiveness of influenza vaccine in preventing exacerbation of asthma or preventing lung function deterioration in children with cystic fibrosis remains uncertain (78-80).

2.2.5.2 Antiviral Drugs

Antiviral drugs are used as an adjunct to influenza vaccine. Two major classes of drugs are now available: adamantines (amantadine and rimantadine) and neuraminidase inhibitors (zanamavir and oseltamivir). None of these drugs have been shown to be effective in preventing serious influenza related complications among children with CHRMC (81). Moreover even in healthy children, these drugs have not been evaluated among children under one year old and therefore they are not used in that age group (82-83). In healthy children aged over one year old, the neuraminidase inhibitors have been shown to reduce the duration of influenza illness by up to 26 percent (i.e. between 1.25 and 1.5 days) (81, 84).

2.3 Surveillance of CHRMC

Several definitions of surveillance have been proposed (85-86). The common elements among these definitions are collection, analysis, interpretation and most importantly the actual use of the data for public health action. Immunization surveillance is closely linked to the ability to know the target populations for vaccination. Therefore, a critical component of influenza immunization surveillance is the ability of the surveillance system to identify relevant target groups for influenza vaccination. For this particular study, surveillance of CHRMC is crucial for influenza vaccination programs that need data to be able to monitor the vaccination coverage among subgroups. This section provides a review of relevant literature on studies that have employed deferent types of methodologies for surveillance of CHRMC or other relevant chronic diseases in children.

2.3.1 Survey as a Method for CHRMC Surveillance

Survey is one of the most common methods for surveillance of various conditions in a population (87). Prevalence and incidence obtained from surveys can be used to enumerate the target populations for vaccination. However, the validity of incidence or prevalence estimates from surveys depends on many factors such as the sampling strategy (that ensures representativeness) and the accuracy of self-report.

Few surveys have provided prevalence estimates of people with CHRMC. Table 2.1 summarises studies that have specifically focused on estimating the prevalence or incidence of CHRMC. One study (15) provided estimates for persons younger than 65 years (including children). This study estimated that up to 36 percent persons aged younger than 65 years had at least one indication for influenza vaccination. However, in

this study, the age-specific rates of CHRMC were not provided, to enable prevalence estimates among children aged younger than 18 years. Secondly, the number of children included in this study was very small.

Another study was conducted in Canada (17) and was based on secondary data analysis of the 1996 General Social Survey (GSS). This study had a very good response rate of 80.1 percent and a large representative sample size. According to this study, the prevalence of CHRMC was between 8.6 percent and 29.4 percent of the study population, with some gender differences. However, this study did not include children younger than 15 years old. The study also excluded First Nations and some CHRMC (e.g. kidney diseases).

Other US investigators (88) estimated that in the US, between seven and fourteen percent of children aged six months to seventeen years had one or more CHRMC. However, this study included only the following CHRMCs: diabetes, asthma, cystic fibrosis, sickle cell anaemia and congenital heart disease or another heart conditions. Therefore, this study will likely underestimate the true burden of CHRMC in that particular population.

In Italy, 5.4 percent of children who attended one emergency room had CHRMC (89). However, this study was based on only children attending emergency room on selected days. In addition, the catchment area of the emergency room was not described. Therefore, it is likely that the observed prevalence (5.4%) is probably an underestimate due to the potential selection bias inherent in the design of this study. Additional studies provided prevalence of various chronic diseases, however the majority of chronic diseases included in those studies are not regarded as CHRMC (90-95).

Table 2.1 Examples of Surveys That Have Estimated the Prevalence of CHRMC

Study	Country	Target population	Prevalence of CHRMC	Main limitation(s)
MacIntyre C.R *et al* 1993 (15)	Australia	Under 65 yrs	36%	1) small number of children, 2) no age-specific prevalence rate
Russell M.L 1996 (17)	Canada	15 to 64 years	8.6% to 29%	1) excluded <15 children 2) a few CHRMC not included
Erhart LM *et al* 2004 (88)	USA	6 month to 17 years	7.4-14.2%	1) did not include all CHRMC
Esposito S *et al* (89)	Italy	<14 years	5.4%	Based on children attending Milan University Emergency room on selected days. Selection bias likely.

2.3.2 Administrative Data as a Tool for Surveillance of CHRMC

This section provides an overview of published studies that have used administrative data to determine incidence or prevalence of CHRMC or for the purpose of surveillance of CHRMC relevant for influenza control programs. Table 2.2 summarises studies that have specifically used administrative data to identify children with CHRMC from administrative data.

One study by Daley *et al* (96) provides estimates of the prevalence of children aged up to six years with one or more CHRMC. Investigators estimated that the overall prevalence of CHRMC was 12 percent. However, this study was conducted in four private clinics that may not be representative of the general population. In another study, the prevalence of CHRMC was estimated to be 9.7 percent (2). This study was conducted among children under 18 years old who were enrolled in Northern California Kaiser Permanente and Group Co-operative managed care organizations (2). However, in this study children who did not make any healthcare contact during the one year prior to the study period could be misclassified as healthy.

Neuzil *et al* (45) studied children of low income enrolled in the Tennessee Medicaid program. The prevalence of CHRMC among this population was 8.7 percent. However, this study only focused on children who came from low-income families within one Medicaid program, therefore the results were unlikely to be applicable to groups of other socio-economic status.

Two additional studies that were conducted in the Netherlands (16, 97) examined the utility of administrative data for surveillance of CHRMC for adults and children aged under 65 years. The prevalence of CHRMC among the population studied was between 11

percent and 12 percent. However, these studies did not provide age-specific CHRMC prevalence rates to enable application to children younger than 18 years.

Several other studies have used administrative data to identify target groups for influenza vaccination without providing the prevalence or incidence of CHRMC. For example, three studies were identified that used pharmacy databases for identification of persons on medication for one or more CHRMC (16, 98-99). None of these studies provided prevalence estimates of CHRMC. One additional study used healthcare administrative data for identification of persons with CHRMC (12). Similarly, the study did not provide prevalence estimates.

Table 2.2: Studies That Have Used Administrative Data for Surveillance of CHRMC.

Study	Country	Target group	Case definition	Prevalence of CHRMC	Limitation(s)
Alexander D.L 1999 (12)	Canada	<65 and ≥ 65 yrs	≥ 1 Diagnosis codes from billing claims	Not provided	No prevalence
Daley M.F. *et al* 2004 (96)	U.S.A	6 month-6yrs	≥ 1 CHRMC related visit per from billing data	12%	Limited to four private clinics
Grabenstein J.D. *et al* 1990 (98)	Germany	All age groups	Use of specific prescription drugs	Not Provided	No prevalence Based on one small hospital
Hak E.*et al* 1998 (97)	The Netherlands	≥ 65 and < 65 (including children)	Any CHRMC related diagnoses or prescription	11%	No age-specific rates. Limited to six

Study	Country	Target group	Case definition	Prevalence of CHRMC	Limitation(s)
					family practices
Izurieta H.S. *et al* 2000 (2)	U.S.A	<18	≥ 1 CHRMC related physician visit (inpatient or outpatient) during the previous year	9.7%	Potential misclassification of nonusers of health services
Neuzil K.M. *et al* 2000 (45)	U.S.A	< 15	≥ 1 Diagnosis or prescription drug	8.7%	Limited to children from low income families
Pearson D.C *et al* 1998 (99)	U.S.A	All age groups	a) prescription drugs indicated for CHRMCs	Not provided	No prevalence

Study	Country	Target group	Case definition	Prevalence of CHRMC	Limitation(s)
			b) other disease registries (Diabetes and Heart disease) d) recent receipt of a pneumoccocal vaccine		
Perenboom R.J. *et al* 1996 (16)	The Netherlands	All age groups	≥ 1 Diagnosis or prescription drug	12%	No age-specific prevalence. select group of general practitioners

2.3.3 Identification of Chronic Diseases from Administrative Data

The utility of administrative data for surveillance of chronic diseases is partly dependent on the process used to identify the chronic diseases of interest. Several published studies have described comprehensively the processes used to identify various chronic diseases from administrative data. The processes include case definitions and appropriate timeframe required to maximise case identification. Other pertinent processes include the order of diagnosis in case of multiple diagnosis fields, the validity of case definitions and the denominator used to calculate rates. Although some of the previous studies did not focus on CHRMC, the processes used to identify children or adults with chronic diseases from administrative are relevant for this study. Therefore, this section provides the review of literature of pertinent processes for identification of individuals with chronic diseases from healthcare administrative data.

2.3.3.1 Case definitions

Table 2.3 summarizes the various types of case definitions used in the previous studies for identification of individuals with chronic diseases. Several published studies across different countries have addressed the various methods used to identify chronic diseases from healthcare administrative data. The majority of these studies have used billing data (also known as physicians' claims or reimbursement data). The most common approach for defining chronic diseases involves counting the number of disease-specific physician visits. The majority of studies shown in Table 2.3 included a combination of both inpatient and outpatient visits. For example, as shown in Table 2.3, the most common case definition used

two or more outpatient visits or one or more inpatient visit. However, some studies have shown that identifying individuals with chronic diseases by using one outpatient visit as opposed to two outpatient visits resulted in higher sensitivity but low specificity (100). In contrast, other investigators did not find any additional benefit of using more than one diagnosis to define a case (101). Lastly, almost none of the studies listed in Table 2.3 took into account the physicians' speciality.

In addition to using physicians visits only, a combination of physician visits and prescription drugs data is also common (2, 97-98,102). However, this approach has been of limited value because some drugs have multiple indications to other diseases that may not be of interest.

Table 2.3: Examples of Case Definitions Used to Identify Various Chronic Diseases From Healthcare Administrative Data			
Study	**Country, province**	**Chronic disease(s)**	**Case definition**
Alexander D.L 1999 (12)	Canada, Ontario	CHRMC	≥ 1 Diagnosis codes from billing claims
Coffin C.S. *et al* 2005 (103)	Canada, Calgary	Chronic diseases eligible for pneumococcal vaccination	≥ 1 hospitalization
Svenson L.W. *et al* 1993 (104)	Canada, Alberta	asthma	a) ≥ 1 claim b) ≥ 3 claims
Daley M.F. *et al* 2004 (96)	U.S.A	CHRMC	≥ 1 visit to a paediatrician
Fultz S.L. *et al* 2006 (102)	U.S.A	HIV/AIDS	a) ≥ 1 inpatient or outpatient b) ≥ 1 inpatient c) HIV prescription drug
Grabenstein J.D. *et al* 1990 (98)	Germany	CHRMC	≥ 1 prescription drug(s)
Hak E *et al* (97)	Netherlands	CHRMC	≥ 1 visit or specific prescription drug(s)
Hux J.E et al 2002 (100)	Canada, Ontario	diabetes	≥ 2 physician claim or ≥ 1 hospitalization; within 2 years
Izurieta H.S. *et al* 2000 (2)	U.S.A	CHRMC	≥ 1 hospitalization or ≥ 2 outpatient visits or ≥ 1 prescription during the previous year
James R.C. *et al* 2004 (105)	Canada, Saskatchewan, Alberta, Manitoba	diabetes	≥ 1 hospitalization or ≥ 2 outpatient visits within two year period
Lix L *et al* 2006 (106)	Canada, Manitoba	Arthritis Asthma Diabetes	Maximum validity: Arthritis-≥ 1 hospitalization or ≥ 2 outpatient visits or ≥ 2 prescription drug within five years.

Table 2.3: Examples of Case Definitions Used to Identify Various Chronic Diseases From Healthcare Administrative Data			
Study	**Country, province**	**Chronic disease(s)**	**Case definition**
			Asthma-≥ 1 hospitalization or ≥ 2 outpatient visits or ≥ 2 prescription drug in five years. Diabetes- -≥ 1 hospitalization or ≥ 2 outpatient visits or ≥ 1 prescription drug in two years.
Neff J.M. *et al* 2006 (107)	USA	All chronic diseases	Identification by using proprietary software Clinical Risk Grouping (CRG) no details on case definitions
Negoita S *et al* 2001 id 2849(108)	U.S.A &Canada	Thyroid disease, asthma diabetes, osteoarthritis	Any mention of relevant ICD-9 code(s)
Neuzil 2000 (45)	U.S.A	asthma, other lung disease, other chronic diseases	Asthma: ≥ 2 prescription drugs in the previous year. Other diseases: ≥ 1 hospitalization.
NordStrom D.L. *et al* 1994 (109)	U.S.A	Various Chronic diseases (some are CHRMC)	≥ 1 medical diagnosis from computerised medical records
Paul I.M. *et al* 2006 (110)	U.S.A a single paediatric practice	asthma	≥ 1 visit within a year
Pearson D.C. *et a*l 1998 (99)	U.S.A	CHRMC	a) ≥ 1 specific prescription drugs. b) ≥ 1diagnosis from Clinical Registries c) recent receipt of a pneumoccocal vaccine
Perenboom R.J *et al* 1996 (16)	The Netherlands	CHRMC	≥ 1 specific prescription drug or >=1 visit to a general practitioner
Powell K.E *et al* 2003 (111)	U.S.A.	arthritis	Any mention of arthritis related ICD-9 code

Table 2.3: Examples of Case Definitions Used to Identify Various Chronic Diseases From Healthcare Administrative Data			
Study	**Country, province**	**Chronic disease(s)**	**Case definition**
Solberg L.I. *et al* 2006 (112)	U.S.A	Diabetes Mellitus, coronary heart disease& depression	≥ 2 outpatient or ≥ 1 inpatient or prescription in a year
To T *et al* 2006 (113)	Canada, Ontario	Asthma, Asthma related respiratory conditions Non asthma condition	≥ 1 outpatient visits
Erzen D. *et al* 1997 (114)	Canada, Manitoba	Asthma, COPD bronchitis	a) Asthma (≥ 1 diagnosis of asthma or bronchitis (490) or COPD (491,492,496) b) COPD (≥ 1 diagnosis of COPD none for asthma , none for bronchitis) c) (≥ 1 diagnoses of bronchitis ,none for a bronchitis study
Robinson J.R *et al* 1997 (101)	Canada, Manitoba	Diabetes Hypertension, other heart disease, elevated cholesterol, stroke, Myocardial infarction	≥ 1 visit over three years

2.3.3.2 Timeframe

The timeframe required to generate sufficient number of healthcare visits is also important for improving case identification (115). However, the optimal timeframe needed for identification of patients with chronic diseases varies by the type of chronic disease. A two to three years timeframe has been suggested as sufficient especially for chronic diseases with relatively structured visiting behaviour such as diabetes and hypertension (101, 116). It has been shown that the errors of prevalence estimates decreases with increasing follow up time (101, 116). Up to five years may be required for conditions that are difficult to diagnose such as asthma (104, 106). Other investigators (111), have suggested that for a given population, five years (rather than one year) of data for diseases such as arthritis may be sufficient to provide more accurate prevalence estimate. For diseases like arthritis, the number of service utilization decreases with time due to improvement with time, slow progression or low expectation for improvement (111). In other circumstances, using a period longer than two years may be impractical for ongoing surveillance system (100). Other investigators have used a short timeframe of two years primarily because the purpose of their investigations was mostly to identify rather than to estimate the burden of disease (12, 103).

In summary, there is no consensus on the optimal search period or timeframe required to identify chronic diseases. The timeframe required to identify individuals with chronic diseases from administrative data is variable and depends on the chronic disease, the data source and the purpose of identification.

2.3.3.3 Order of Diagnosis

Most administrative databases have one or more fields for diagnosis. The main diagnosis may not necessarily be the most responsible reason for a specific healthcare visit. Therefore, investigators using administrative data with more than one diagnosis field have suggested ignoring the order of diagnosis in order to maximise case identification (117). For example, in one study, investigators showed that if only the primary diagnosis is used for identification, only one fifth (20%) of asthma cases could be identified (118). In the US, the importance of the order of diagnosis depends on the data source and jurisdictions. For example, in Medicaid database the first diagnosis listed corresponds to the relative importance of the diagnosis for a specified healthcare visit (111). However, data from other health plans (e.g. Kaiser Permanente Georgia) the order of diagnosis is not related to the primary reasons of the visit (111).

2.3.3.4 Enrolment Period

When using administrative data for the purpose of surveillance, it is important to be able to identify all at-risk population. One reason that may account for the inability to identify specific groups is the fact that some individuals may not be identified in a specific database because of the inactive enrolment status. Knowledge of the appropriate at risk population is important for several reasons. Individuals with inactive enrolment status are likely to be misclassified as healthy because of lack of healthcare visit for the disease of interest. However, if these individuals sought the disease-specific healthcare visit elsewhere, some administrative data will not capture those visits.

The definition of enrolment period also affects the number of individuals that will be included in both the numerator and denominator for the purpose of calculation of various rates. For example, Powell *et al* (111) conducted a sensitivity analysis on various types of enrolment definitions and how they affected the denominator and the numerator used in the calculation of arthritis prevalence. In that study, investigators found that the least number of arthritis cases was among those who were continuously enrolled compared to those who were not. In the previous literature, the definition of enrolment period was variable from a minimum of three months to over one year (2;45;111;112). For the purpose of calculating prevalence in a defined population, other investigators (119) have excluded individuals with discontinuous enrolment or those with multiple insurance coverage.

The most appropriate type of enrolment period (denominator) to be used for calculating various rates will depend on the context. External census-based denominators have been recommended as most appropriate in case of jurisdictions with client list that do not accurately reflect the population structure (105). In summary, the enrolment period necessary to obtain accurate denominators is variable depending on the data source and the purpose of a study.

2.3.3.5 Validity of Case Definition and Identification Algorithm

The validity of a case definition or an identification algorithm can be defined as the degree to which the case definition/identification algorithm identifies a target group that it purports to identify from healthcare administrative data (120). There are two major types of validity. Internal validity refers to the accurate

identification of target groups from healthcare administrative data apart from random errors (121). External validity refers to application of study findings beyond the subjects in the study (120). Internal validity is a prerequisite for external validity (121).

The validity of a case definition varies depending on the objective, diseases and jurisdictions. For example, Canadian databases differ substantially from those of the U.S.A in that historically, financial incentives for recording inaccurate diagnosis have been minimal compared those of US (115). Even within Canadian provinces the validity of administrative data varies by Province and diseases condition (115). Therefore, the validity of case definitions for identifying chronic diseases developed in US may not necessarily be applicable to Canada. Even within Canada, the validity of case definitions derived from one province may not necessarily be applicable to other provinces.

There is quite extensive literature on the validity of administrative databases. This section provides an example of studies that have validated case definitions for the purpose of identification of chronic diseases. Table 2.4 provides examples of studies that have validated various case definitions.

In one study (96), by using a case definition of one or more visits to a pediatrician, the case definition identified more than 70 percent of children with CHRMC, giving a positive predictive value of between 72 percent to 95 percent. In another study done in adults (122) hospital discharge files had a positive predictive value for correctly identifying cancer patients of between 86 percent and 94 percent. Solberg *et al* (112) showed that the PPV for diabetes mellitus, coronary

heart disease or depression increased significantly when cases were identified on the basis of two outpatients ICD-9 codes or one inpatient code rather than only code (e.g. from 0.20 to 0.95 for diabetes, 0.6 to 0.95 for coronary heart disease).

Theoretically, sensitivity and specificity should remain constant regardless of populations. However, in practice they do change with patient mix (123). Comparing the positive predictive value for identification of CHRMC from one setting to another is also difficult because of the underlying characteristics of the healthcare administrative database and the prevalence of the disease condition of interest (123). For example, in one study (122) data from certified cancer hospitals had a higher positive predictive for identifying cancer cases compared to data from non-certified cancer programs. The differences in the PPV may possibly be due to higher cancer prevalence in the certified cancer hospitals than in non-certified hospitals.

Hux *et al* (100) illustrated that when using two physicians' claims over two years for diagnosis of diabetes, the sensitivity was lower than when using only 1 diagnosis of diabetes (90 percent versus 85 percent respectively). Increasing the number of claims required for case definition increased sensitivity but reduced the specificity of the algorithm in identifying cases. In contrast, Robinson *et al* (101), did not find any meaningful gain in sensitivity by increasing the number of diagnosis while holding timeframe constant.

As shown Table 2.4, the selected examples of case definitions show that the specificity of the case definitions in identifying individuals with chronic diseases across various jurisdictions was generally higher than the sensitivity. This indicates

that individuals without a chronic disease are less likely to be misclassified by most case definitions (i.e. lower false negative rate). The lower sensitivity of most case definitions compared to specificity also indicates that there is higher probability of misclassification among those identified to have chronic diseases (i.e. higher false negative rate).

In summary, most previous studies have used similar case definitions that required one or more diagnoses for a particular chronic disease with or without use of prescription drugs. Several studies have examined the validity of case definitions. These studies were conducted across various jurisdictions and focused on different types of chronic diseases. The outcome of these studies was variable sensitivity, specificity and PPV, depending on the chronic disease studied and the jurisdiction. The gold standard used to validate the case definitions has been mostly medical charts and occasionally surveys. Using chart review is expensive and may not be practical for those who want to use administrative data for population based surveillance purposes. Cheaper, practical and alternate ways to examine the validity of administrative data for ongoing surveillance purposes are therefore warranted given the gap in literature review.

Table 2.4: Validity of Various Case Definitions from Previous Studies.					
Study	**Country/context Age, province**	**Chronic disease (s)**	**Case definition**	**Gold standard**	**Validity**
Alexander DL 1999 (12)	Canada ,Ontario	CHRMC	One Diagnosis codes from billing claims	medical charts	(<65years),Sensitivity 72.2%,specificity 92.3% (≥ 65 years) Sensitivity 87.5%, 99.9%
Coffin C.R *et al* 2005 (103)	Canada, Calgary	Chronic diseases eligible for pneumoccocal vaccination	>=1 Hospitalization during 1 calendar year	Medical charts	Sensitivity 83%, Specificity 78% PPV 87% NPV 72%
Daley M.F. *et a*l 2004 (96)	U.S.A	CHRMC	>=1 visit to a paediatrician in previous 2 years	Medical charts	Sensitivity 72%, specificity 95%, overall accuracy 90%
Fultz S.L. *et al* 2006 (102)	U.S.A	HIV/AIDS	a) >=1 diagnoses. b) >=2 outpatient visits or 1 inpatient & prescription drug	a)Immunology Case Registry , b)laboratory data, c)pharmacy database	Algorithm 1 (≥ 1 outpatient code)=sensitivity 93.0%,specificity 99.8%, PPV 69.1% NPV 100.0%, Algorithm 2 (>=2 codes): sensitivity 90.4%, specificity 99.9%, PPV 87.9%, NPV 99.9%
Grabenstein J.D. *et al* 1990 (98)	Germany	Reception of infection-risk-indicating drugs in a pharmacy database	Specific Prescription Drug(s)	Medical charts	Variation of PPV by type of drug (0-100%). overall PPV was 82%

Table 2.4: Validity of Various Case Definitions from Previous Studies.					
Study	**Country/context Age, province**	**Chronic disease (s)**	**Case definition**	**Gold standard**	**Validity**
Hux J.E. *et al* 2002 (100)	Canada	diabetes	>=2 physician claim or >= 1 hospitalization; within 2 years	a) prescription drug data b) National Population Health Survey (NPHS) c) chart review	a) Prescription drug data: Sensitivity 94% for 1 claim, and 91% for two claims. b) NPHS: sensitivity 90% for 1 claim and 85% for 2 claims; PPV 44% for 1 claim and 64% for 2 claims. c) Chart review sensitivity 90.7% for 1 claim, 86.1% for 2 claims. Specificity: 93.4% (1-claims) 97.1 (2 claims). PPV 61.3% (1 claim) 79.8% (2 claims)
Lix L *et al* 2006 (106)	Canada, Manitoba	Arthritis Asthma Diabetes	Maximum validity: Arthritis-≥ 1 hospitalization or ≥ 2 outpatient visits or ≥ 2 prescription drug within five years. Asthma-≥ 1 hospitalization or ≥ 2 outpatient visits or ≥ 2 prescription drug in five years.	Survey: self-report chronic diseases from the Canadian Community Health Survey cycle 1.1	Arthritis: sensitivity 51.7%, specificity 84.9% Asthma: sensitivity 75.4%, specificity 94.2%. PPV-64.4% Diabetes: sensitivity 86.1%, specificity 99.2%, PPV-

Table 2.4: Validity of Various Case Definitions from Previous Studies.					
Study	**Country/context Age, province**	**Chronic disease (s)**	**Case definition**	**Gold standard**	**Validity**
			Diabetes- ≥ 1 hospitalization or ≥ 2 outpatient visits or ≥ 1 prescription drug in two years.		
Penberthy L *et al* 2003 (124)	U.S.A	Cancer	≥ 1 Hospitalization	Virginia Cancer Registry	PPV 84%-98%
Perenboom R.J. *et al* 1996 (16)	The Netherlands Involved 56 general practitioners	CHRMC	a) usage of specific drugs b) ≥ 1 visits to a general practitioner	Physicians review	Medicine list had a PPV of 62%
Robinson J.R. *et al* 1997 (101)	Canada, Manitoba	Diabetes, Hypertension ,Other heart disease, elevated cholesterol, stroke, myocardial infarction	≥ 1 visit within 3 years	survey	Agreement :kappa values: Diabetes (0.72), Hypertension (0.59) Other Heart Disease (0.38), Elevated cholesterol (0.40), Stroke (0.44) Myocardial infarction (0.40)
Solberg L.I. *et al* 2006 (112)	U.S.A	Diabetes Mellitus, coronary heart disease& depression	≥ 2 outpatient or ≥ 1 inpatient ICD-9 code or prescription in a year	Medical charts	PPV Diabetes :PPV 0.97-1 Coronary heart disease 0.95 Depression 0.65-0.99

Table 2.4: Validity of Various Case Definitions from Previous Studies.					
Study	**Country/context Age, province**	**Chronic disease (s)**	**Case definition**	**Gold standard**	**Validity**
To T *et al* (113)	Canada Ontario Province, using billing records from 21 Primary care practitioners	Asthma, Asthma related respiratory conditions Non asthma condition	≥ 1 outpatient visit	Medical charts	Agreement rates: 84.8% (overall), 60.2% (asthma) 94.8(asthma-related) 99.5% (non-asthma related). Sensitivity 91.4% (asthma) 82.9 %((asthma-related).

2.3.4 Summary of Literature Review

Influenza is a disease of public health importance in children because it is associated with substantial social economic burden. Children with CHRMC are at a higher risk of influenza-related complication than those without CHRMC. Influenza vaccine remains the only primary method of control. Influenza vaccination surveillance among target group is important. Large healthcare administrative databases provide a promising tool that can be used to supplement existing methods of surveillance of children with CHRMC to aid in the planning of influenza vaccination programs.

There are limited data on how administrative data can be optimally used for the purpose of population-based surveillance of children with CHRMC. Studies that have used administrative databases were not population based and were limited to surveillance of one or multiple chronic conditions most of which are not relevant to influenza programs. Besides, the methods for validation of case definitions have mostly been chart review, which may not be practical for population-based surveillance purposes, that requires ongoing and relatively cheaper and inexpensive alternatives.

The majority of previous studies have used two or more outpatient diagnoses or one or more inpatient diagnoses to define various chronic diseases. A few studies have also used a single diagnosis to define certain chronic disease with high specificity and sensitivity. Almost none of the case definitions that have used office visits have taken into consideration the physicians' speciality. This may misclassify visits that are valid but do not reach the number required to satisfy a case definition. This is a gap in that this present study will address by developing case definitions that incorporate the role of primary care

physicians versus consultant physicians as well as hospitalizations and emergency room visits.

Because there are no systematic, population-based studies that have examined comprehensively the method of maximizing healthcare administrative databases for surveillance of persons with CHRMC, a significant gap of knowledge exists in that aspect and seriously limits how control efforts for influenza are being monitored among children with CHRMC. The proposed study will address the following gaps in the existing literature:

- Systematically and comprehensively, study how to maximize the utilization of healthcare administrative databases for the purpose of surveillance of children with CHRMC relevant for influenza prevention programs. This includes a comprehensive description of the process needed to make the best use of administrative data for surveillance of children with CHRMC.
- Provide population-based rates (incidence and prevalence) of CHRMCs that are necessary for public health surveillance of children with CHRMC.

CHAPTER THREE: METHODS

3.1 Introduction

This chapter outlines the methodology used to answer the research questions. The chapter includes the description of design, study populations, data sources, methods used to manipulate the data, descriptive analysis as well as multivariate analysis. The chapter also outlines methods used to validate case definitions.

3.2 Design

The study design was a retrospective cohort. Two cohorts were retrospectively followed from birth to a maximum of eight years. Cohort 1 included children born during the fiscal year 1984/85 i.e. those born between April 1st 1984 and March 31st 1985. Cohort 2 included children who were born during the fiscal year 1994/95 i.e. those born between April 1st 1994 and March 31st 1995. The year 1984/85 was chosen as the beginning of cohort 1 based on data availability. The year 1994 was chosen as the beginning of follow up period for cohort 2 because most Alberta Health and Wellness (AHW) databases underwent significant improvement that year. For example prior to 1994, only one diagnosis field was available in physicians' claims file while after 1994, 2 additional fields were added (125). Both cohorts were followed for a maximum of eight years. Therefore, cohort 1 was followed from fiscal years 1984/85 to fiscal year 1991/92, while cohort 2 was followed from 1994/95 to fiscal year 2001/02.

Two cohorts were necessary to account for period effects such as changes in healthcare organisation, changes in the database maintenance or other historical artefacts.

These changes may affect utilization patterns of healthcare services or data quality and therefore affect incidence or prevalence estimates derived from healthcare utilization patterns.

3.3 Study population

The study population consisted of two birth cohorts. The first cohort (referred to as Cohort 1) consisted of children born during the fiscal year 1984/85 (i.e. between April 1st 1984 and March 31st 1985). The second cohort (referred to as cohort 2) consisted of children born during the fiscal year 1994/95 (i.e. between April 1st 1994 and March 31st 1995). Children in both cohorts were enrolled with the Alberta Health Care Insurance Plan.

3.4 Data Sources

Alberta Health and Wellness (AHW) supplied data for this study. Data from two databases were used for this study. In the next sections, I briefly describe these databases.

3.4.1 Alberta Healthcare Insurance Plan Registry (AHCIPR)

The Alberta Healthcare Insurance Plan Registry (AHCIPR) includes over 99% of Alberta residents. The following persons are not included in AHCIPR: members of the Armed Forces, Royal Canadian Mounted Police (RCMP), inmates at federal penitentiaries and individuals from other provinces during their first three months in Alberta. Other persons not included in the AHCIPR are those who have not registered for eligibility for example visitors with alternative insurance coverage as well as those who opt out of the coverage (125).

Alberta is one of two provinces in Canada that charges insurance premiums for essential healthcare services. Therefore, AHCIPR database has information on the proxy

indicators of socio-economic status of enrolees depending on the ability to pay the insurance premiums. The ability to pay the premiums was regarded as a proxy for social economic status (SES). The SES proxy can identify individuals' SES with moderate accuracy and has high specificity when compared with self reported income (126).

Four levels of SES status were available based on the ability to pay healthcare premiums. First, residents earning less than 14,000 dollars per year as determined through income tax returns are eligible for partial healthcare insurance premium assistance. The provincial government reduces or waves their premiums. These are referred to as *subsidy status*. Families classified under this group may be regarded as "working poor".

First Nations registered by the Indian Northern Affairs Canada are also eligible for premium assistance. The Canadian Federal Government pays the premiums of First Nations. First Nations individuals generally have lower income than the general Canadian population (127). Alberta Human Resources Department and Employment Department pays the healthcare premiums of individuals requiring social assistance. These individuals are referred to as being on *social welfare*. Finally, Alberta residents who have sufficient come pay their own healthcare premiums. These are referred to as *not on subsidy*.

The AHCIPR file also has information on date of birth, death or cessation of enrolment. The dates of birth and death are updated regularly from Alberta Vital Statistics. The date of birth, death or cessation of enrolment was used to calculate duration of follow up.

3.4.2 Alberta Health Care Insurance Plan Payment (AHCIP) File

The Alberta Health Care Insurance Plan Payment (AHCIP) file has data on physician claims submitted for service reimbursement. Services provided may be in Alberta or outside Alberta if the recipient of service is still enrolled with AHW. About 98% of physicians in Alberta were paid under fee for service system during the study years (128). This database was used to identify children who made CHRMC-related visits and those who did not.

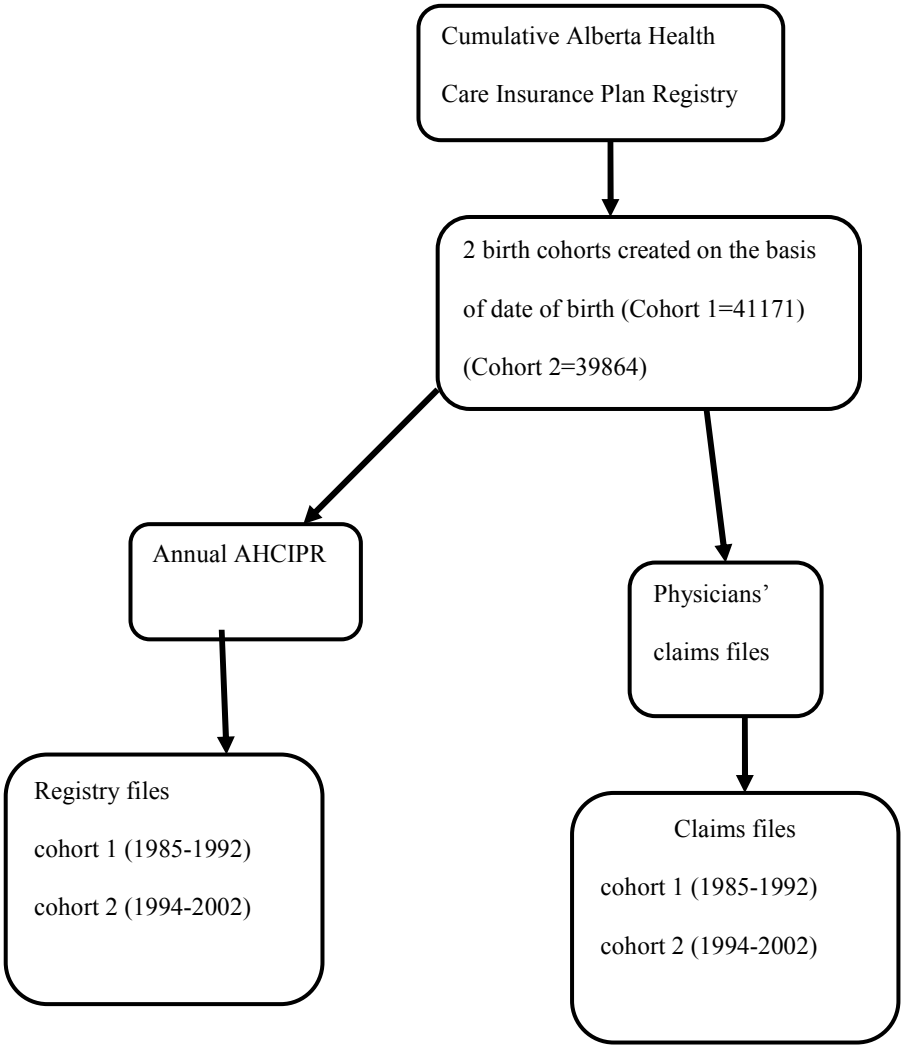
Because of different fee codes for physician encounters, AHCIP file has a feature that helps to identify emergency room visits as well as hospitalizations different from regular physicians' office visits. Therefore, data on hospitalizations and emergency room visits were also obtained from this file.

3.5 Preliminary Database linkage

The process of combining information available in two or more datasets is known as linkage (120, 129). Two types of linkages are commonly used in administrative data: deterministic and probabilistic linkages. Deterministic linkage involves the linkage of two or more files based on exact agreement of unique identifiers such as personal health number or other types of unique identifiers (130). Unlike deterministic linkage, probabilistic linkage involve combining information from two databases that are believed to relate to the same individual based on non unique identifiers such as age, gender, last name, postal code etc. (131). A correct match is based on the pre-specified level of agreement between the data sources.

The AHW files have unique identifiers known as Personal Health Number (PHN). Using the PHNs, deterministic linkage of the data was possible. Figure 3-1 illustrates how the preliminary database linkage was conducted.

Figure 3-1: Schematic Presentation of Database Linkages



3.6 Data Cleaning and Creation of the Analytical Datasets

Once the preliminary data linkage was completed, the raw data were examined for duplicate entries or any other inconsistencies. Claims filed by non-physicians (18% of total claims) were removed. Non-physicians'' claims those submitted by chiropractors, physiotherapists and others. Non-physicians' claims were removed because most previous studies that have used claims data have used physicians' claims and therefore it would be possible to compare findings from this study with the previous one.

After data cleaning, two analytical databases were created: the healthcare utilization file (HUF) and the socio-demographic file (SDF). The HUF was created from AHCIP. The HUF had the following variables: the age at visit (calculated as the difference between date of birth and the date of service); the type of provider, which is an indicator variable to identify whether the service was provided at physician office, at a hospital, or emergency room. Physicians' office visits were further categorised according to the physician speciality: family physician, paediatrician or other specialists. The HUF also has primary and secondary diagnoses responsible for a particular visit.

The SDF was constructed from AHCIPR file and had the following variables: duration of enrolment, area of residence and socio-economic status marker. The duration of follow up was defined as the total time (in years) that a child was continuously enrolled with AHW. This duration was calculated as the difference between date of birth and the first recorded date of loss of insurance coverage due to death or out-migration. The geographical location was the census division of residence. The socio-economic status marker was as described previously had four levels not on subsidy, subsidy, First Nation and social welfare. Table 3.1 summarizes the analytical datasets, data sources and

variables. All data manipulations and handling were done using SAS version 8.2 for Windows (132) and STATA (133).

Table 3.1: A List of Analytical Datasets.

Analytical Dataset	**Source Database**	**Variables**
Health Utilization File (HUF).	Claims files	1)Unique identifier 2) Age at visit 3) Diagnoses, primary and secondary (CHRMC vs. non-CHRMC) 4) Indicator variable for the provider/setting (family physicians, paediatricians, other specialists, emergency room visits and hospitalization)
Socio-demographic file (SDF)	Alberta Health Care Insurance Plan registry (Annual and cumulative files)	1) Unique identifier 2) Duration of enrolment (years) with Alberta Health and Wellness 3) Census Division 4) Socio economic status marker

3.6.1 Description of Variables and How They Were Created

Healthcare administrative files contains data that was collected for other purposes than for this particular study. Therefore, a substantial amount of time was devoted to defining and creating relevant variables. This section outlines the methods used to create the various types of variables.

3.6.1.1 Chronic High Risk Medical Conditions (CHRMC)

The CHRMC were identified from claims file by using International Classification of Diseases-9th edition-Clinical Modification (ICD-9-CM) codes. The ICD-9 codes for CHRMC were obtained from literature (101, 13, 134-135) and a textbook of ICD-9CM codes (136). The CHRMC diseases groups were developed in accordance with the recommendations from the Canadian (83) and United States (82) Advisory Committees on Immunizations. A complete list of relevant conditions that were classified as CHRMC is attached in Appendix. The CHRMC disease groups were initially divided into 31 major groups. These 31 groups were then collapsed into five major groups: cardiovascular, pulmonary, metabolic, immunodeficiency/cancer and others.

3.6.1.2 Preliminary Case definitions

Preliminary case definitions (Table 3.2) were derived from the literature (137). The assumptions underlying the preliminary case definitions (Table 3.2) were as follows:

- **Validity**: the degree of validity increases from family physicians based case definitions to hospitalization based case definition.
- **Severity**: there is underlying assumption of increasing CHRMC severity across the case definition (Table 3.2). For example, a child who is hospitalised is more likely to be sicker than a child only seen by a family physician.
- **Specificity and sensitivity**: family physician-based case definition would have high sensitivity but low specificity. However, hospitalization-based case definition would likely have high specificity but low sensitivity.

Table 3.2: Preliminary Case Definition for CHRMCs

Case Definitions
1. Two or more family physician's visits
2. One or more Specialist (paediatrician or other specialists) visits
3. Two or more Emergency Room visits
4. One or more hospitalization(s)
5.. Any two of no. 1-4 above (criterion B)
6. Any of no. 1-4 above (Criterion A) # 1-4

3.6.1.3 Refined Case Definitions

After preliminary analysis and consultation with clinical experts, it was evident that some assumptions listed above, may not be valid. This was the case for specialist based case definition (Table 3.2), that assumes that all children satisfying this definition would see a paediatrician as a consultant rather than a primary provider. The data indicated that this assumption was not true. Therefore, the decision was made to develop the refined case definitions shown in Table 3.3. All subsequent analyses are therefore based on the refined case definitions (Table 3.3).

Table 3.3: Refined Case Definition for CHRMC

Type and Number of CHRMC[1]-related Physician Claims
1. Claims from primary care providers: two or more claims from a family physician or one or more claim from a paediatrician
2. Claims from consultants: a combination of two or more family physicians claims and one or more specialist claims
3. Two or more emergency room visits
4. One or more hospitalization
5. Any two of the above, i.e. no. 1-4 (referred to as criterion B)
6. Any of the above i.e. no 1-4 (referred to as criterion A)

[1] CHRMC –chronic high risk medical conditions

3.6.1.4 Time to event

The time to event in this study is defined as the time from birth to when one could be classified as a case. Depending on a case definition, the time to event was calculated differently. The following sections outline methods used to calculate the time to event for each case definition (listed in Table 3.3). In both cohorts, non-CHRMC cases had a maximum follow up time equivalent to the maximum duration of enrolment with AHW (i.e. eight years).

a) Primary Care Provider Case definition (>=2 Family Physician Visits or >=1 Paediatrician Visits)

The time to event was calculated as the earliest time from birth to time when a child made a second visit to a family doctor or the first visit to a paediatrician, whichever was applicable.

b) Consultant Case definition (>=2 Family Physician Visits and >=1 Paediatrician Visits)

The time to event was calculated by using the maximum time from birth to when both conditions (i.e. 2 visits to a family doctor and first visits to a paediatrician/specialist) were satisfied. For example, if it took one year to see a family physician and two years to see a paediatrician then the appropriate time to event was two years.

c) Emergency Room and Hospitalization Case Definitions

The time to event was calculated from date of birth to the date when a particular emergency room or hospital visit qualified a child to be a case. Because the emergency room case definitions requires two or more visits, the time from birth to the second emergency room visit was as the appropriate time to event. For children with at least one

hospitalization, the time to event was calculated as the duration from birth to the first hospitalization.

d) Criterion A

Criterion A includes one or more component case definitions (i.e. primary care, consultant, emergency room or hospitalization case definitions). The time to event was calculated by using the minimum time required to satisfy any of the component case definitions. For example, if a child was classified as having CHRMC using all component case definitions, then the corresponding time to event would be the earliest time taken to satisfy any of the four component case definitions. Let say a child saw a primary care provider at 6 months of age, was hospitalised at 1 year, visited emergency room at 2 years and was hospitalised at 8 years, the time to event in this scenario would be 6 months.

e) Criterion B

Criterion B includes two or more of the component case definitions. Two methods were used to calculate time to event depending on how many case definitions were satisfied. First, if child satisfied three or more of the component case definitions, then the time to event was the average time taken to satisfy the 3 (or 4) component case definitions. Secondly, if a child satisfied two case definitions, then the corresponding time to event was the minimum time needed to satisfy both case definitions. For example if a child was hospitalised at the age 2 years and then visited a family physician at the age 3 years, then appropriate time to event would be 2 years.

3.6.1.5 Residence

The area of residence was based on census divisions. The residential postcodes were mapped to the corresponding census divisions units. In Alberta, there are 19 census

divisions. For analysis purposes, these 19 census divisions were grouped into the three main groups. Table 3.4. shows the three main residential area categories. The grouping of area of residence was based on the assumption that differential healthcare resources are available in these areas. The differential availability of healthcare resources may affect healthcare utilization and therefore prevalence or incidence of CHRMC in those areas. Unlike Regional Health Authorities, there have been no changes in the census divisions' boundaries during the study period.

Table 3.4: Area of Residence Classification by Census Division

Residence Category	**Corresponding Cities**	**Census Divisions Numbers**
Urban (extensive health services available)	Edmonton and Calgary	6,11
Small urban (extensive health services available but not all inclusive)	Medicine Hat, Lethbridge, Red Deer, Fort McMurray, Grand Prairie	1,2,8,16,19
Rural (limited availability of health services)	Fort McLeod, Hanna, Drumheller, Stetler, Rock Mountain House, Camrose-Llyodminster, St.Paul, Athabasca, Edson, Banff, Slave Lake, Grande Cache	3,4,5,7,9,10,12,13,14,15, 17,18

3.6.1.6 Gender

No manipulation was done on the gender variable. This variable was obtained directly from the AHIPR file. Gender was coded as follows: 1 for males and 0 for females.

3.6.1.7 Social Economic Status (SES)

The SES categories are described in section 3.4.1. Baseline SES categories at birth were used for this analysis. The only exception was children classified as First Nations. A child classified as First Nations any time during the study period was classified as First Nations. This modification was necessary because of the legislative changes of the *Indian Act* of Canada, which occurred in 1985 and led to the introduction of Bill C31 (138). Prior to 1985 marrying a person without a First Nations' Treaty Status led to loss of First Nations Status. No children born of such union had First Nations status.

3.7 Data analysis

3.7.1 Theoretical Framework Underlying Data Analysis

This study derived prevalence and incidence of CHRMC from diagnoses recorded on administrative data, which are dependent on healthcare utilizations patterns. Because prevalence and incidence was dependent of utilization patterns, a model that described various factors that could contribute to various patterns of healthcare utilization was used to help discern different, alternate explanation for the observed healthcare utilization patterns. Andersen Behavioural Model of health services utilization (139-140) provided the appropriate conceptual framework.

The Andersen model which was originally proposed in the 1960s, states that people's use of health services is a function of their predisposition to use services, factors which enable or impede use and their need for care. The model classifies explanatory variables of healthcare utilization into three main groups: predisposing, enabling and need. Predisposing factors are factors that are inherently present within an individual that increase one's propensity to seek health care regardless of the need. These factors include age, sex, and race. Enabling factors are a set of conditions that would make the actual use of heath care to be possible. These factors include availability and access to health care as well as social economic factors. Need factors included those factors related to the reason that people have that make them use the health services. Additional distinction is made between the perceived and the actual need. An example of perceived (subjective) need is self-reported health status. An actual (objective) need refers to the number of chronic conditions or other diseases as evaluated by physicians.

The Andersen model has been used extensively to examine the predictive factors for utilization of various types of health services (141-144). Not all factors as suggested by the model are routinely recorded in AHW database however, data analysis was based on available variables that were considered as proxies of factors as described in the Andersen Model. Table 3. summarises the proxy operational variables used in accordance with the model.

Table 3.5: Operational Definitions of Variables According to the Andersen Model of Healthcare Utilization.

Variable category According to Andersen Model	variable	Operational definition
predisposing	Age	age
	Sex	sex
Enabling	Access*	Usual source of care (defined visited same GP throughout the year).
	Social economic status	Ability to pay health insurance premium as a proxy for social economic status (categorised as no subsidy, subsidy, First nations and Welfare)
Need*	visit intensity	Number of CHRMC-related visits.

*Not assessed in the current analysis but can be assessed when using other designs

3.7.2 Validation of the Case Definition

No external standard was employed to assess the validity of the case, however the longitudinal nature of the study design provided a unique opportunity to examine the validity of diagnoses using the approaches that are discussed in this section.

3.7.2.1 Consistence of CHRMC Diagnoses over Time

CHRMC are chronic diseases that are more likely to result into repeated healthcare contacts. Therefore, children with only one isolated diagnosis of CHRMC throughout the eight-year follow up period were considered to be of questionable validity compared to children with repeated healthcare contacts. The positive predictive value (PPV) of a case definition could be calculated among those who were classified as having CHRMC, by using additional visit post-classification as a gold standard. In this study, the PPV of a case definition refers to the proportion of children who were classified as being cases using the case definition who made subsequent CHRMC-related visit post- classification. The PPV analyses were restricted to children who were still enrolled with AHW for at least one or two years after the date they were classified as being a case.

3.7.2.2 Consistence of CHRMC Diagnoses From More Than One Physician or Across Multiple Settings

Analyses were done to determine whether children got the same diagnoses from more than one type of provider or setting which provides an increased confidence in the case definition. Children receiving a CHRMC diagnosis from more than one physician or setting were considered more likely to have the CHRMC than those who have not. The CHRMC incidence and prevalence were therefore calculated by using two case definitions,

one that combines any of the component case definition (criterion A) and another that combines two or more component case definitions (criterion B).

3.7.2.3 The Similarity of Trends or Epidemiological Patterns of CHRMC Incidence and Prevalence Between the Two Cohorts.

Unless there are known historical reasons such as changes in reporting or disease incidence or prevalence, it was expected that rates should be similar for cohort 1 and 2 or at least show the same trend or epidemiological patterns across the two cohorts. Therefore, additional analyses were done to compare the CHRMC incidence and prevalence rates between two cohorts. Furthermore, the correlates of CHRMC incidence and prevalence were also compared between the two cohorts.

3.7.3 Descriptive analysis

The descriptive analyses included tabulation of frequency distributions of the baseline characteristics of children in each cohort in terms of age, gender, area of residence and SES status. The age-specific CHRMC incidence rate was calculated by gender and cohort. The number of children that could be classified as cases using various case definitions was tabulated by cohort, age, sex and residence. Fisher's exact test and 95% Confidence Intervals were used to compare proportions among subgroups. A two-sided p-value of less than 0.05 was considered statistically significant.

3.7.4 Loss to follow up

Loss to follow up is a common problem with cohort studies (145) and can cause selection bias if study participants who remain in the study are systematically different from those who are lost with respect to the outcome of interest. Causes and percentage of loss to follow up were examined across age groups, sex, residence, and cohort.

3.7.5 Incidence of CHRMC

The CHRMC incidence rate was calculated by using either criterion A or B (Table 3.3) These two case definitions provide a overall incidence using the broadest possible combinations (Criterion A) and a more restrictive criterion (Criterion B). The crude incidence rate was calculated as follows:

Equation 1: Incidence rate

$$\text{Incidence Density} = \frac{number\ of\ children\ who\ satisfy\ specific\ case\ definition}{sum\ of\ total\ children\ years} X 10{,}000$$

The numerator was the number of children who satisfied a particular case definition during a specified time period and the denominator was the total number of children years (CY). The CY was defined as the sum of individual years from birth to death or loss of insurance coverage with Alberta Health and Wellness, whichever applicable.

3.7.5.1 Survival Analysis

The preliminary survival analysis involved plotting of Kaplan Meier Survival curves for covariates, in order to understand incidence rate patterns by subgroups. The correlates for the CHRMC incidence rate were examined by using Cox proportional hazard model. The dependent variable was time to event (i.e. time from birth to when one was classified as a CHRMC case). Independent variables included: variables that may affect healthcare utilization patterns in accordance with Andersen Model, these were as follows: predisposing factors (e.g. age, sex), enabling: subsidy status (proxy for Social Economic Status), area of residence and cohort. The resulting hazard ratio between covariates can be interpreted as incidence rate ratio (146).

Two interaction terms were included in the Cox Proportional hazard model. These were the interaction between the cohort and SES and secondly, the interaction between the cohort and area of residence. The interaction terms were chosen to reflect the potential influence exerted by the cohort on different levels of SES. For example, during the period from the year 1995 to 2002, there were changes in the number of First Nations because of the legislative amendment of the *Indian Act* of Canada that led to the introduction of Bill C-31. The interaction between the cohort and area of residence was also chosen because there may be different resource allocation during the two cohorts in different geographical areas that in turn may affect healthcare utilization.

3.7.5.1.1 **Assessing Proportional Hazard Assumptions of the Cox Proportional Hazard Model**

The Cox Proportional Hazard model requires an assumption that the hazard ratio of the hazard functions of subgroups (e.g. sex) is constant (i.e. proportional) throughout the entire follow up time (147). The most common method used to assess the proportionality assumption is by using "log log plots" (146, 148). The "Log log plot" is a plot of minus the natural logarithm of the logarithm of survival function versus the log of follow up time. For a given covariate (e.g. sex), the plotted graphs must be parallel. In some of the analyses, the proportionality of hazard assumption was violated.

3.7.5.2 Piecewise Cox Regression Model

Given, the violation of proportionality assumptions, piecewise Cox regression analysis was conducted (149). In piecewise Cox regression modeling, a stratification of time at risk is done to account for the time varying nature of the covariates. This approach has been used previously in similar studies (150). Children who did not become a case ("fail") during the preceding interval were carried forward to the next interval, while children who became cases during the preceding interval or those who out-migrated were censored and therefore did not contribute to person years calculations of subsequent intervals.

3.7.5.3 Cox Proportional Hazard Model building

Starting with a univariate analysis, variables that were significantly associated with the outcome were entered into the model. Using a backward elimination approach, non significant covariates ($p>0.05$) were removed one after another from the model. Assessment of adequacy of the reduced model was assessed by using likelihood ratio test. A non-significant likelihood ratio test (i.e. $p> 0.05$) indicated a good model fit.

Qualitative assessment of the impact of the removed covariate was also assessed to rule out confounding. Confounding was present if a variable that was non significant by likelihood ratio test, caused a change in the estimated hazard rates of 15% or higher (151).

3.7.5.4 Censoring

The analysis of incidence rates required the total follow-up time, which was calculated from birth to when one of the following events occurred a) death, b) out-migration, c) loss of insurance coverage due to other reasons or d) March 31st 1992 for cohort 1 or March 31st 2002 for those in cohort 2. In this study, individuals who died, out-migrated or lost their insurance coverage before they were classified as a CHRMC case were censored from the analysis.

3.7.6 Eight Year Period Prevalence of CHRMC

The eight-year period prevalence of CHRMC was determined as follows:

Equation 2:

$$\textbf{Prevalence} = \frac{number\ of\ children\ who\ satisfy\ case\ definition}{total\ no.\ of\ children\ \text{Continuously}\ enrolled\ for\ eight\ years}$$

The numerator was the number of children who satisfied criterion A or B. The denominator was the number of children who were continuously enrolled with AHW for eight years. This type of denominator has been used in similar studies(111, 152) This includes all new cases within a particular year and all the prevalent cases from previous years who had neither died nor left the province. This allows prevalence estimation based on the "living population" during the eight-year period.

3.7.6.1 Binomial Regression model

Correlates for the eight-year period prevalence were examined by using binomial multivariate regression. The binomial regression model rather than logistic regression model is appropriate for this design because CHRMC is a frequent event. Therefore using logistic regression which produces odds ratio can strongly overestimate the prevalence ratio (153). Odds ratio provides unbiased risk ratio estimates if an outcome of interest is uncommon in a study population (i.e. less than five percent) (154).

The dependent variable was having CHRMC (coded as 1=yes, 0=no) by using Criterion A or B. Independent variables were age, gender (coded as 0=females 1=male);

SES (coded as 0=no subsidy, 1=Subsidy, 2=First Nations, 3=Welfare); area of residence (coded as 0=Urban, 1=Small Urban, 3=Rural) and cohort (coded as 0=cohort 1, 1=cohort 2). In addition, two interaction terms were included in the model, these were: interaction between cohort and SES economic marker; secondly, interaction between cohort and area of residence.

3.7.6.2 Calculating the Adjusted Prevalence

The adjusted prevalence was derived from the final binomial regression model. For each criterion, the adjusted prevalence was calculated by using the mean of covariate method (155). In this method, the mean values of covariates are substituted into the binomial regression equation. For example, when calculating the adjusted CHRMC prevalence among children in rural areas, an average value of gender is inserted into the regression equation to reflect the composition by gender of children in the rural area.

3.8 Supplementary Analyses: Incidence and Prevalence of Chronic Obstructive Pulmonary Disease (COPD)

Additional analyses were done to determine the correlates of prevalence and incidence of Chronic Obstructive Pulmonary Disease (COPD) (ICD 490-496). These analyses were necessary because, in both cohorts, 75 percent of CHRMC related visits were due to COPD. Results from such analyses would therefore help us better understand the overall results. The type and methods of analyses used are as described in Section 3.7.

3.9 Ethical Considerations

The University of Calgary Conjoint Health Research Ethics Board (CHREB) and Research Resource Team of Research and Evidence Branch (Alberta Health and Wellness) approved the research protocol. A number of ethical principles guided the research project. First, the authorised AHW personnel did the preliminary data linkages and created the two birth cohorts. Secondly, data released was on the "need to know basis". This means that only the information needed to answer the project research questions was obtained from AHW. This minimised the risk of access to personal information not required for this particular project.

Additional database linkage and creation of analytical datasets with unidentifiable information was done within AHW premise, which has strict data security protocol and a secure network server. No information was allowed outside AHW premises at this stage. The final data included completely de-identified information i.e. Personal Health Numbers were scrambled. One authorised AHW personnel scrambled the PHN such that only that person could link back to the true PHNs. In addition, all relevant variables were released in aggregate form. For example, diagnoses were in major diseases categories (e.g. ICD 490-496) rather than individual disease categories. Area of residence was also released in the form of Census Divisions (CD) rather than postal codes. The date of birth and death were not released. Instead, the duration of continuous enrolment-this was calculated from date of birth to the date of death or out-migration. It would be very difficult to determine the date of birth from this information. Finally, the data was taken outside AHW premise after signing confidentiality agreements with AHW.

CHAPTER FOUR: RESULTS 1-DESCRIPTION OF STUDY POPULATION

4.1 Introduction

This chapter describes the social-demographic characteristics of children in the two study cohorts. The description includes age and sex distributions, socioeconomic status, area of residence, duration of follow-up and healthcare utilization patterns.

4.2 Study Populations

The final study population included two birth cohorts of children born in Alberta Province, Canada during the fiscal years 1984/85 (Cohort 1) and 1994/1995 (cohort 2). The total number of children in cohort 1 and 2 was 41,171 and 39,864 respectively.

4.3 Socio-demographics

Table 4.1 shows the distribution of socio-demographic characteristics of children in the study cohorts. Overall, both cohorts had similar proportions of males (51.2% in cohort 1 and 51.5% in cohort 2, p=0.339). There were no statistically significant differences in the distribution of area of residence by cohort (p=0.055). Almost two thirds of the children in each cohort resided in urban areas (i.e. Calgary or Edmonton census divisions). Most children (88%) did not change their area of residence during the study period (Table 4.2). This means that 88 percent of children lived in urban area only, small urban area only or rural areas only throughout the study period.

The two cohorts differed significantly in the frequency distribution of children in various SES categories. Cohort 1 had a smaller proportion of children classified as First Nations (4.7%) than cohort 2 did (6.9%). In addition, cohort 1 had statistically significantly smaller proportion of children from families receiving health premium subsidies (cohort 1:

9.1 percent versus cohort 2: 14.8 percent) and on welfare (cohort 1: 4.7 percent versus cohort 2: 6.9 percent). Sixty seven percent (67%) of children in cohort 1 and 60 percent in cohort 2 came from families that did not receive any subsidy during the eight years of follow-up.

About five percent of children in each cohort were classified across the three SES categories during that same period. Only a few children (0.1 percent in cohort 1 and 0.7 percent in cohort 2) came from families on welfare throughout the study period. Three quarters of children (74.5%) in cohort 1 and 71.5 percent of children in cohort 2 did not change their SES status during the eight-year follow up period (Table 4.3).

Table 4.1: Baseline Socio-Demographic Characteristics of the Study Population

Attribute	Cohort 1 (n=41171)	Cohort 2 (n=39864)	P-value two sided
Gender			
Males n (%)	21062 (51.2)	20528(51.5)	0.339
Social Economic Status			
1-no subsidy n (%)	35347 (85.9)	28846 (72.4)	
2-subsidy n (%)	3748 (9.1)	5883 (14.8)	
3-First Nations n (%)	1933 (4.7)	2768 (6.9)	<0.0001
4. Social Welfare n (%)	143 (0.4)	2367 (5.9)	
Residence[γ]			
Urban n (%)	25933 (63.4)	25484 (64.2)	
Small urban n (%)	6900 (16.9)	6562 (16.5)	0.055
Rural n (%)	8043 (19.7)	7647 (19.3)	

[γ] Derived from Census Divisions, further classified according to health services availability.
Urban (Calgary and Edmonton, expected to have all services); Small urban (Fort Mc Murray, Grand Prairies. Lethbridge, Medicine Hat and Red Deer-extensive but not all inclusive services); Rural (the rest of the province-limited health services).

Table 4.2: Longitudinal Migration Patterns

	Cohort 1		Cohort 2	
Area of Residence	**N**	**%**	**N**	**%**
Urban, small urban and rural	362	0.9	221	0.6
Urban and small urban	1473	3.6	1241	3.1
Urban and rural	2161	5.3	1952	4.9
Small urban and rural	949	2.3	873	2.2
Urban only	24027	58.8	23701	59.7
Small urban only	5571	13.6	5500	13.9
Rural only	6344	15.5	6207	15.6

Table 4.3: Frequency Distributions of the Longitudinal Changes in the Socioeconomic Status

	Cohort 1 (Born in Fiscal yr. 1984/85)		Cohort 2 (Born in Fiscal yr. 1994/95)	
Socio-economic status categories	**N**	**%**	**n**	**%**
First Nations[1]	1933	4.7	2768	6.9
No subsidy, subsidy and welfare	2038	5.0	1945	4.9
No subsidy and subsidy	6064	14.7	7495	18.8
No subsidy and welfare	2253	5.5	1374	3.4
Subsidy and welfare	176	0.4	525	1.3
No subsidy only	27936	67.9	24106	60.5
Subsidy only	722	1.8	1370	3.4
Welfare only	49	0.1	281	0.7

[1] First Nations group includes all children who were "ever" recorded as First Nations during the study period.

4.4 Loss to follow-up

During the eight years of follow up (i.e. between the fiscal year 1984/85 and fiscal year 1991/92) cohort 1 had 197 children who died and 7508 who lost their insurance coverage due to out-migration or other reasons. Therefore, the overall loss to follow up in cohort 1 during this period was 18.7 percent. For the same duration of follow up but at a different period (i.e. between fiscal year 1994/95 and fiscal year 2001/02), cohort 2 had 205 children who died and 8001 children who lost their healthcare insurance coverage due to out-migration or other reasons. Therefore, the overall loss to follow up in cohort 2 was 20.1 percent.

Figure 4-1 illustrates the loss to follow-up comparison between children in cohort 1 and those in cohort 2. There were no observable differences in the survival curves (loss to follow up rates) during the first year of follow-up. However, from age one to six years, the loss to follow-up rate was higher among children in cohort 1 than that of cohort 2. In addition, from age six to eight years the loss to follow-up occurred earlier among children in cohort 2 than those in cohort 1. Overall, the survival functions for cohort 1 and 2 were statistically significant different from each other (log rank test, $p=0.001$). Of those who were lost to follow up, 9.9 percent in cohort 1 and 8.3 percent were lost after they were classified as cases by either criterion A or B.

Table 4.4 summarizes the characteristics of children who were lost to follow-up and those who were not. There were no statistically significant in the gender composition, between those who were and those who were not lost to follow-up. In both cohorts, the distribution of area of residence was similar to those of children who remained in the cohorts, but with different proportions. Majority of children who were lost to follow-up

resided in urban areas (67.4 percent in cohort 1, and 63.9 percent in cohort 2). The second largest proportion of children who were lost to follow-up resided in rural areas (20.4 percent in cohort 1 and 19.6 percent in cohort 2). Lastly, the least proportion of children who were lost to follow-up resided in small urban areas (cohort 1: 17.2 percent; cohort 2: 16.6 percent).

There were statistically significant differences in SES between children who were lost to follow-up and those who were not. In cohort 1, there were significant differences between the proportion of First Nations children who dropped from the cohort and those who remained (4.9 percent versus 3.7 percent). There were also significant differences in the proportion of children on welfare (0.2 percent lost, 1 percent remained) (Table 4.4). In cohort 2, the differences between those who were lost to follow up and those who remained in the cohort were as follows: a) more children who did not receive subsidy (74 percent lost, 65.8 percent remained); b) less proportion of children who were on subsidy (14.0 percent lost, 17.6 percent remained); c) similar proportions of First Nations children that were lost to follow-up and those who were not (6.8 percent remained 6.9 percent lost) and d) fewer children on welfare were lost to follow up (4.5 percent lost, 9.8 percent remained) (Table 4.4).

The proportion of children with two or more out-migrations during the eight-year follow-up period was 0.9 percent (n=357) in cohort 1 and 1.7 percent (n=676) in cohort 2. These children had between two and five different loss of insurance coverage dates. However, the date when these children regained their insurance coverage was not available. Therefore, the maximum follow-up time was calculated from the date of birth to the first date when a child lost his or her insurance coverage.

Figure 4-1: Comparison of Loss to Follow-up Rates by Cohort

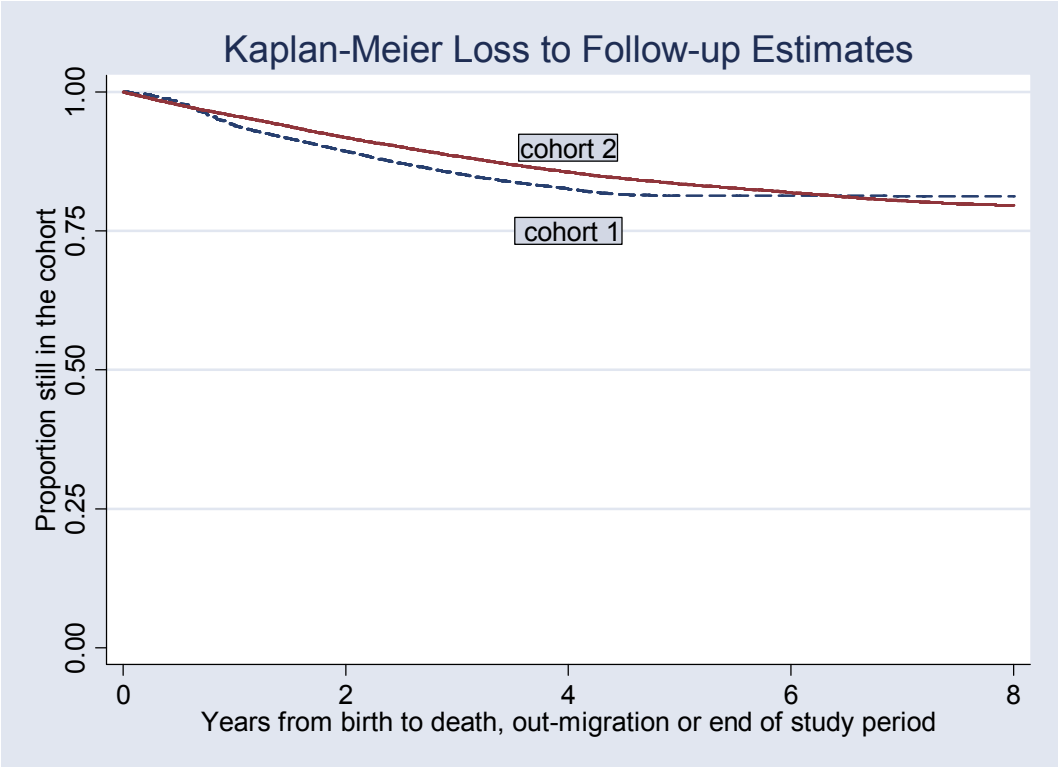


Table 4.4: Characteristics of Children Who Were Enrolled With Alberta Health and Wellness

	Cohort 1			Cohort 2		
Characteristic	Continuously enrolled for up to 8 years N=33466	Lost to follow-up N=7705	p-values	Continuously enrolled for up to 8 years N=31863	Lost to follow-up N=8001	p-value two sided
Male %	51.03	51.2	0.810	51.3	51.4	0.707
Residence at birth (%)						
Urban	62.5	67.4	<0.001	65.6	63.9	0.004
Small urban	15.7	17.2	0.003	16.3	16.6	0.575
Rural	16.9	20.4	<0.001	18.1	19.6	0.003
Social economic status (SES) (%)						
No Subsidy	86.5	85.7	0.079	65.8	74.01	<0.001
Subsidy	8.8	9.2	0.292	17.6	14.04	<0.001
First Nations	3.7	4.9	<0.001	6.8	6.99	0.499
Welfare	1	0.2	<0.001	9.8	4.49	<0.001

4.5 Overall Healthcare Utilization Patterns

Table 4.5 shows the overall healthcare utilization patterns among children in cohort 1 and 2. A larger proportion of children in cohort 2 than those in cohort 1, made visits to family doctors (58 percent in cohort 2 versus 51 percent in cohort 1), paediatricians (18 percent versus 9.5 percent) and emergency rooms (13.7 percent versus 8.5 percent). In contrast, a larger proportion of children in cohort 1 compared to those in cohort 2 made visits to other specialists (25.3 percent versus 6.9 percent) and visits to hospitals (5.5 percent in cohort 1 versus 3.1 percent in cohort 2).

During the eight years of follow-up, the total number of physician claims for any reason was greater in cohort 1 than in cohort 2 (Table 4.5). Of those visits (i.e. total number of visits), only 4.3 percent in cohort 1 and 5.6 percent in cohort 2 were CHRMC-related. Children in the two cohorts had statistically significant differences in healthcare utilization intensity. Cohort 1 had larger proportion of children who made more than 14 visits per year (9.8%) compared to cohort 2 (3.1%).

Table 4.5: Description of Healthcare Utilization Patterns among Children in Cohort 1 and 2 during the Eight Years of Follow-up.

Description of Healthcare Visits	**Cohort 1 (Born in Fiscal Year 1984/85) N (%)**	**Cohort 2 (Born in Fiscal year 1994/95) N (%)**	**p-values two sided**
Total Number of Visits-all diagnoses	2041786 (100)	1197443 (100)	n/a
Number of CHRMC-related visits n (%)	84288 (4.1)	68376 (5.7)	n/a
Visits to a family physician n (%)	1047098 (51.3)	694130 (58.0)	n/a
Visits to a paediatrician n (%)	193043 (9.5)	218859 (18.3)	n/a
Visits to other specialists n (%)	516064 (25.3)	82528 (6.9)	n/a
Visits to emergency room n (%)	172882 (8.5)	164194 (13.7)	n/a
Hospitalizations n (%)	112699 (5.5)	37732 (3.1)	n/a
No. of visits per year for any diagnosis n (%) <7 8-14 >=15	24234 (58.9) 12889 (31.3) 4050 (9.8)	32069 (80.5) 6576 (16.5) 1219 (3.1)	<0.001

n/a=not applicable: visits not independent events therefore highly correlated

4.6 Healthcare Utilizations Patterns by Disease Groups

Table 4.6 summarises the healthcare utilization patterns of children with CHRMC by cohort and CHRMC disease groups. Chronic pulmonary diseases were responsible for the majority of CHRMC-related physician visits accounting for 82 percent and 79 percent of the visits in cohort 1 and 2 respectively (Table 4.6). The proportions of CHRMC-related visits contributed by other disease categories include: chronic cardiovascular diseases (6.6 percent in cohort 1 and 6.3 percent in cohort 2); chronic disease due to immunodeficiency or immune suppression (4.1 percent in cohort 1 and 6.1 percent in cohort 2) and disorders of haemoglobin (hemoglobinopathies) (3.4 percent in cohort 1 and 2.8 percent in cohort 2) (Table 4.6).

Figure 4-2 provides the breakdown of visits by the type of provider or setting and cohort. In both cohorts, family doctors submitted over 50 percent of chronic pulmonary diseases claims (Graph A in Figure 4-2). In addition, family doctors also submitted more than 50 percent of non-CHRMC related claims (Graph F in Figure 4-2). In contrast, paediatricians submitted the majority of chronic cardiovascular disease claims (i.e. 40 percent in cohort 1 and 49 percent in cohort 2) (Graph B in Figure 4-2). Paediatricians in cohort 2 submitted a larger proportion of claims across all disease groups of CHRMC than paediatricians in cohort 1 (Graph A-F in Figure 4-2). The proportion of emergency room visits was larger in cohort 2 than cohort 1 across the following CHRMC disease groups: pulmonary (Graph A, Figure 4-2), metabolic (Graph C, Figure 4-2), immunodeficiency (Graph E, Figure 4-2), other CHRMC (Graph D, Figure 4-2) and non-CHRMC (Graph F, Figure 4-2).

The proportion of hospitalizations was higher among children in cohort 1 than in cohort 2, across all CHRMC groups and non-CHRMC diseases (Figure 4-2). In both cohorts, 66 percent of children visited one type of provider or setting for a CHRMC-related reason. Thirty four percent (34%) of children in both cohorts visited more than one type of provider or setting for a CHRMC-related reason.

Table 4.6: Frequency Distributions of Physicians Claims for Each CHRMC Disease Category.

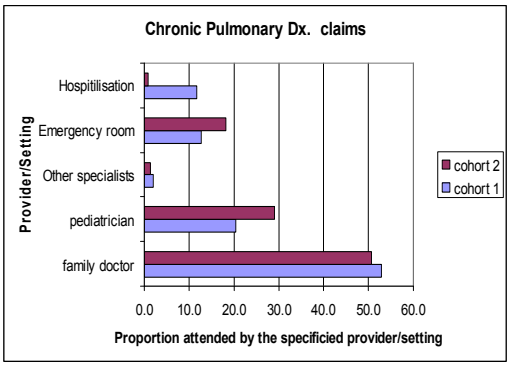
Chronic Disease Category	ICD-9 CM Codes	Cohort 1 N (%)	Cohort 2 N (%)	Examples
Pulmonary Diseases	490-496, 510-519, 010-012,018,135	71707 (82.6)	54173 (79.2)	Chronic obstructive diseases and allied conditions (e.g. chronic bronchitis, emphysema, asthma, bronchiectasis, extrinsic allergic alveolitis), other diseases of respiratory tract e.g. empyema, lung or mediastinal abscess and pulmonary tuberculosis.
Cardiovascular	393-398, 410-414, 745-747,416, 424-438,342,440-447	5730 (6.6)	4330 (6.3)	Congenital heart diseases, chronic rheumatic heart disease, ischemic heart disease, chronic pulmonary heart disease, other heart diseases, cerebral vascular diseases, diseases of arteries, arterioles and capillaries
Immunosuppression/ Immunodeficiency	042-044,710,714.0,714.1, 715,555-556	3553 (4.1)	4198 (6.1)	Congenital disorders of immunity (e.g. deficiency of humoral immunity, cell mediated immunity, T cell-defect, complement deficiency or dysfunction and combined immunity deficiency), HIV/AIDS, high levels of corticosteroid use to control conditions such as: rheumatoid arthritis, endocrine disorders, severe psoriasis, systemic lupus erythyromatosis, Crohn's diseases, ulcerative colitis and sarcoidosis
Hemoglobinopathies	282,286-289	2982 (3.4)	1923 (2.8)	Hereditary haemolytic anaemia e.g. sickle cell disease, coagulation defects, purpura and other hemorraghic conditions
Central Nervous System (CNS)	330-337,340-344,290	1363 (1.6)	1968 (2.9)	Hereditary and degenerative disease of Central Nervous System (CNS),other disorders of CNS (e.g. multiple sclerosis, other demylinating disease of CNS, hemiplegia and hemiparesis, infantile cerebral palsy), other paralytic syndromes, hereditary and degenerative disease of CNS.,

Table 4.6: Frequency Distributions of Physicians Claims for Each CHRMC Disease Category.

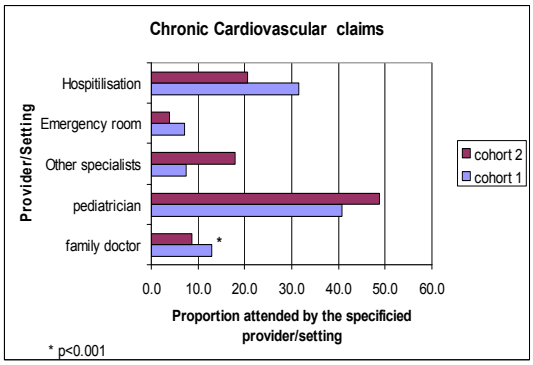
Metabolic Diseases	250-251	818 (0.9)	972 (1.4)	Diabetes Mellitus, other disorders of pancreatic internal secretion
Cancer	140-208	608 (0.7)	812 (1.2)	Malignant neoplasm of lip, oral cavity , pharynx, digestive organs and peritoneum, respiratory and intra-thoracic organs, bone connective tissue, skin and breast, genitourinary organs, lymphatic and haematopoietic tissue
Total		86761 (100)	68376 (100)	

Figure 4-2: Percent Distributions of Physician Claims with CHRMC and Non-CHRMC Diagnosis by Physician Speciality or Healthcare Setting.

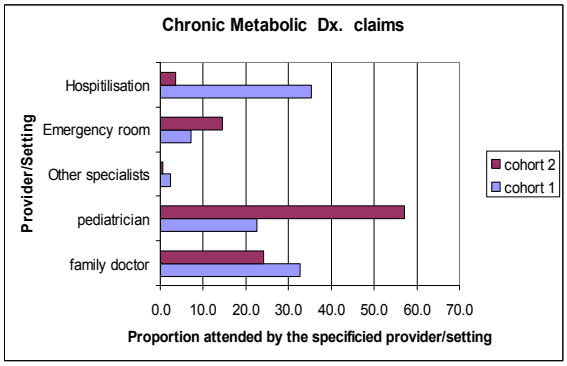
Graph A: Chronic pulmonary diseases



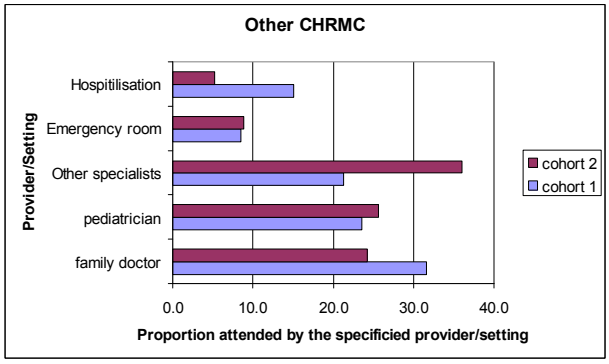
Graph B: chronic cardiovascular disease



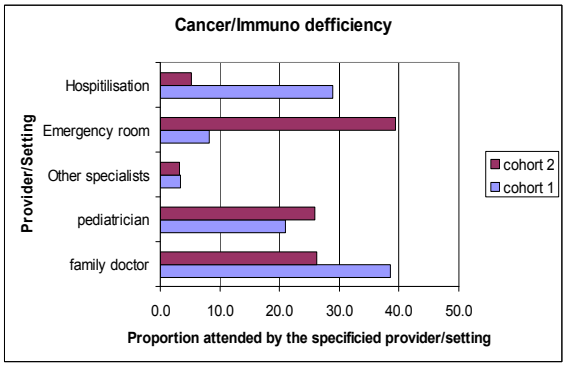
Graph C: chronic metabolic Disease



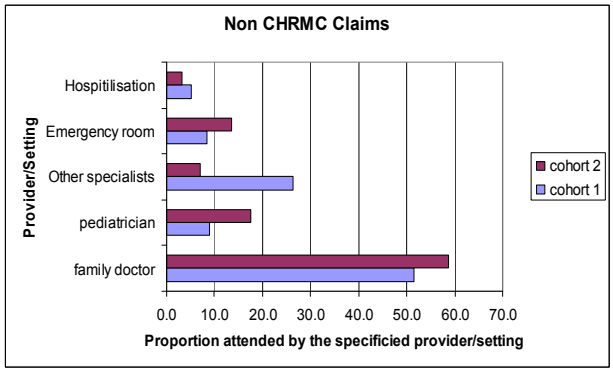
Graph D: other CHRMC



Graph E: Cancer or immunodefficiency



Graph F: non-CHRMC



CHAPTER FIVE: RESULTS 2 DESCRIPTION OF CASE DEFINITION AND THE VALIDATION OF THE CASE DEFINITIONS

5.1 Introduction

This chapter outlines the frequency distributions of children that were classified by using each component case definitions as well as Criterion A and B. The component case definitions are: primary care providers (≥ 2 family doctor visits or ≥ 1 paediatrician visits), consultants (≥ 2 visits to family doctor visits AND ≥ 1 visits to a specialist/paediatrician); emergency room (≥ 2 visits to emergency room) and hospitalizations (≥ 1 hospitalization). Criteria A and B are summary case definitions derived from one or more component case definitions. Criterion A includes any of the four component case definitions while criterion B combines two or more of the four component case definitions. This chapter also provides the quantitative assessment of the validity of Criterion A and B by examining the proportion of children with CHRMC who made one or more visits after they were classified as having CHRMC. This is referred to as the positive predictive value (PPV) of the case definition.

5.2 Frequency Distribution of children identified by using component case definitions

Table 5.1 provides the frequency distribution of children identified by each component case definition as well as those identified by criterion A and B. In both cohorts, the majority of children were identified by primary care provider case definition (cohort 1: 13.9 percent versus cohort 2: 9.6 percent). Cohort 1 had statistically significant larger proportion of children with CHRMC than cohort 2 by using the following case definitions:

primary care providers (cohort 1: 13.9 percent versus cohort 2 9.6 percent, $p<0.001$); consultants (cohort 1: 5.1 percent versus cohort 2: 4.3 percent, $p<0.001$) and hospitalizations (cohort 1: 7.8 percent versus cohort 2: 1.1 percent, $p<0.001$) (Table 5.1). However, cohort 1 had statistically significant less children classified based on emergency room visits than cohort 2 (cohort 1:4 percent versus cohort 2: 4 percent, $p<0.001$). Cohort 1 had a statistically significant larger proportion of children with CHRMC by criterion A than among children in cohort 2 (cohort 1: 22.6 percent versus cohort 2: 16.8 percent cohort 2). In addition, cohort 1 had a larger proportion of children with CHRMC by criterion B than those in cohort 2 (cohort 1: 4.4 percent versus cohort 2: 2 percent) (Table 5.1).

Table 5.1: Frequency Distributions of Children Classified by Various Case Definitions[1]

	Cohort 1 (n=41171)		Cohort 2 (n=39864)	
Case definition	%	95% Confidence Interval	%	95% Confidence Interval
1. Primary Care Physician (≥ 2 family doctor visits or ≥ primary care paediatrician)	13.1	12.8-13.4	9.6	9.3-9.9
2. Consultants (≥ 2 family doctor visits and ≥ 1 paediatrician visits or ≥ 1 other specialists visits)	5.1	4.9-5.3	4.3	4.1-4.5
3. Emergency room (≥ 2 visits)	4.0	3.8-4.2	5.6	5.4-5.8
4. Hospitalizations (≥ 1 visits)	7.8	7.5-8.0	1.1	0.9-1.2
5. Criterion A (any of the component case definitions, no. 1 to 4 above)	22.6	22.2-23.0	16.8	16.4-17.1
6. Criterion B (≥ 2 component case definitions, no.1 to 4 above)	4.4	4.2-4.6	2.0	1.8-2.1

[1] Notes: primary care and consultant case definitions are mutually exclusive.

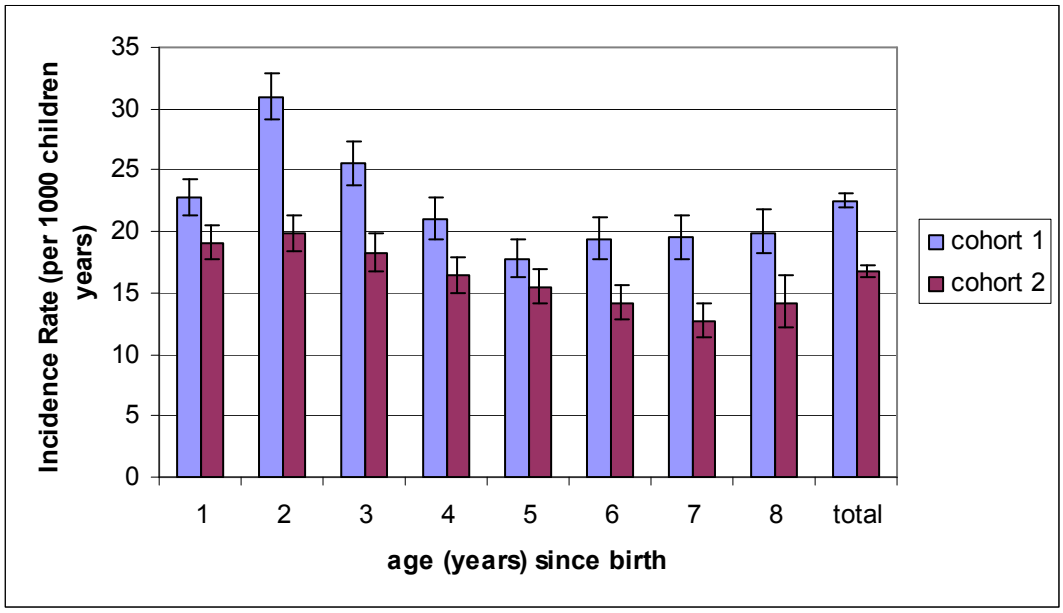
5.3 Incidence Rate Comparisons by Using Component Case Definitions

This section presents the age-specific CHRMC incidence rates by each component case definition (i.e. primary care, consultant, emergency room and hospitalization-based case definitions.).

5.3.1 Incidence Rate Estimates By Using a Primary Care Case Definition

Figure 5-1 shows the variability of the age-specific CHRMC incidence rate by cohort and age. The primary care case definition was defined based on two or more visits to a family physician or one or more visits to a primary care paediatrician. Children who saw both the family physician and the paediatrician are not included in this case definition. By using the primary care providers case definition, cohort 1 had significantly higher age specific incidence rates than cohort 2 across all ages except for children aged five year old (Figure 5-1). In both cohorts, the age-specific CHRMC incidence rate was highest among two year olds (cohort 1: 31 per 1000 children years (CY) 95% CI: 29.2-32.9; cohort 2 19.1 per 1000 CY, 95% CI 18.4-21.3). However, the incidence rate was lowest for children aged five years in cohort 1 (rate 17.7 per 1000 CY , 95% CI 16.2-19.4 per1000 CY) and those aged seven years in cohort 2 (rate 12.7 per 1000 CY, 95% CI 11.4-4.2per 1000 CY**).**

Figure 5-1: Age-specific CHRMC Incidence Rate -Primary Care Case Definition

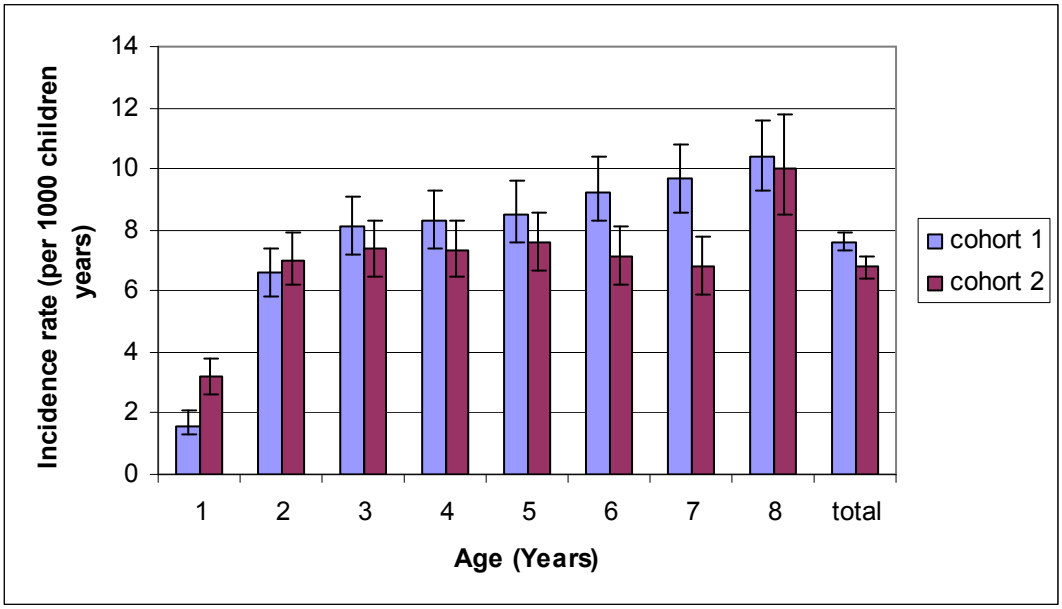


5.3.2 Incidence Rate Estimates By Using the Consultant Case Definition

Figure 5-2 shows the CHRMC age-specific incidence rates defined by using the consultant case definition. The consultant case definition included claims that indicate a specialist (e.g. a paediatrician) saw a child as a consultant rather than primary care provider (Section 5.3.1). Therefore, a child could satisfy this case definition if he/she makes two or more visits to a family physician and one or more visits to a paediatrician or other specialists for the condition.

There were no statistically significant differences in the age-specific CHRMC incidence rates between cohort 1 and 2 for children aged two to five years, as well as those aged eight years (Figure 5-2). Children in cohort 1 had higher age-specific incidence rates than cohort 2 for children aged six years (rate: cohort 19.2 per 1000 CY; 95% CI 8.3-10.4; cohort 2: 7.1 per 1000 CY; 95% CI 6.2-8.1) and those aged 7 years (rate cohort 1: 9.7 per 1000 CY '95 % CI 8.6-10.8; cohort 2: 6.8 95% CI 5.9-7.8). However, children in cohort 1 had lower CHRMC age-specific incidence rate than cohort 2, for children aged one old (rate cohort 1:1.6 per 1000CY, 95% CI 1.3-2.1; cohort 2: 3.2 per 1000 CY, 95% CI 2.6-3.8). In both cohorts, the highest age specific CHRMC incidence rate was found for children aged eight years. The lowest age-specific CHRMC incidence rate was among one-year-old children.

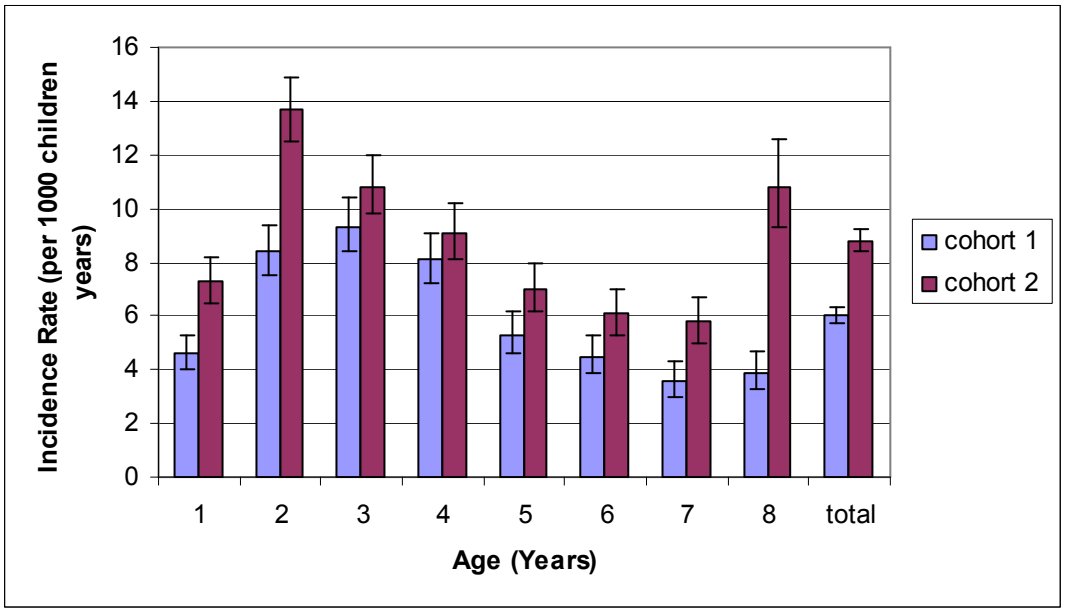
Figure 5-2: Age-specific Incidence Rate of CHRMC-Consultant Case Definition



5.3.3 Incidence Rate Estimates by Using Emergency Room Case Definition

Figure 5-3 shows the CHRMC age-specific incidence rates defined by using emergency room case definition. A child satisfied this case definition if he or she made two or more visits to the emergency room during the study period for a CHRMC related reason. As shown in Figure 5-3, the age-specific CHRMC incidence rates as defined by the emergency room case definition, were statistically significant higher among children in cohort 2 than those in cohort 1 for children aged one, two, six and seven years. There were no statistically significant differences in the age-specific CHRMC incidence rates between the two cohorts for children aged three, four and five years. The largest discrepancies in the age-specific CHRMC incidence rates between the two cohorts were for children aged two years (corresponding to fiscal year 1985/86 for cohort 1 and 1995/96 for cohort 2) and for children aged 8 years (fiscal years 1991/92 for cohort 1 and 2001/02 for 2).

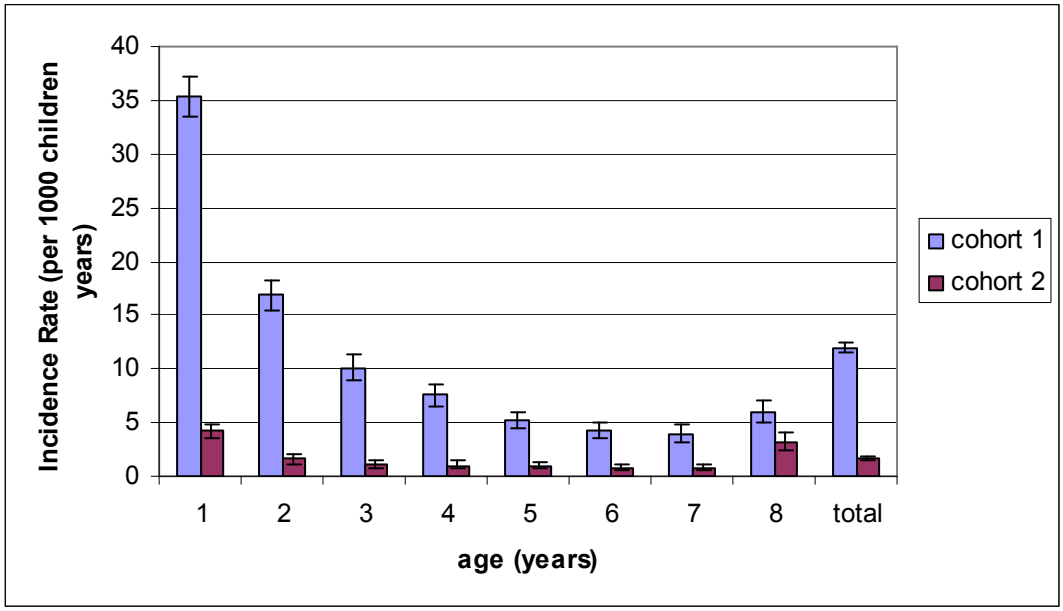
Figure 5-3: Age-specific Incidence Rate of CHRMC-Emergency Rooms Case Definition



5.3.4 Incidence Rate Estimates by Using Hospitalization Case Definition

Figure 5-3 shows the CHRMC age-specific incidence rates defined by the hospitalization case definition. A child satisfied this case definition if he or she was hospitalized for at least once during the study period for a CHRMC-related reason. Using the hospitalization case definition, children in cohort 1 had statistically significantly higher age-specific CHRMC incidence rate than those in cohort 2 throughout the study period (Figure 5-4). In both cohorts, the peak CHRMC incidence rate was among one year olds. In addition, the age-specific incidence rate of CHRMC decreased with increasing age.

Figure 5-4: Age-specific Incidence Rate of CHRMC-Hospitalization Case Definition



5.3.4 Summary of Incidence Rate Estimates by Various Case Definitions

Table 5.2 shows a summary of age-specific CHRMC incidence rate comparison between cohort 1 and 2 by each component case definition. With the exception of emergency room case definition, children in cohort 1 had higher age-specific CHRMC incidence rates than those in cohort 2 when using primary care, consultant or hospitalizations case definitions. The distribution of CHRMC incidence rate was different for each component case definition, although there were similarity of incidence rate patterns between the two cohorts.

Table 5.2: A Summary Age Specific Incidence Rate Findings by Component Case Definitions

Component Case Definition	Age specific CHRMC incidence rate comparison			Figure
	Cohort 1> cohort 2	Cohort 1< cohort 2	No Difference	
Primary care	Age: 1,2,3,4,6,7	Age: 5	-	Figure 5-1
Consultant	Age 6,7	Age: 1	Age 2,3,4,5,8	Figure 5-2
Emergency Room	-	Age : 1,2,6 and 7	3,4,5	Figure 5-3
Hospitalization	Age 1-8	-	-	Figure 5-4

5.4 Proportions of Children with Multiple CHRMC

The proportion of cohort 1 children with two or more CHRMC was 2.1 percent when using criterion A and 0.24 percent when using criterion B. Similarly, the proportion of cohort 2 children with multiple CHRMC was 1.3 percent when using criterion A and 0.2 percent when using criterion B.

5.5 CHRMC Case Validation

5.5.1 Introduction

This section outlines the process used for internal validation of CHRMC case definitions. This section therefore presents the proportion of children classified as having CHRMC who made one or more CHRMC-related visits during any time after they were classified as having CHRMC by using Criterion A or B. The underlying assumption for this approach is that once a child is diagnosed with CHRMC, he or she will continue to seek care for CHRMC-related reasons and these contacts will be captured through physicians' claims.

5.5.2 Internal Validation of CHRMC Cases Identified by Criterion A

Table 5.3 shows the proportion of children classified as having CHRMC by criterion A who made one or more subsequent visit post-classification. Eighty four percent (84.1 percent) of children with CHRMC by criterion A in cohort 1 and 82 percent of children in cohort 2 made 1 or subsequent CHRMC related visits (Table 5.3). In both cohorts, over 40 percent of children made 3 or more subsequent visits post-classification.

When the analysis was restricted to only those cases that were continuously enrolled with AHW for at least one year post-classification, the proportion of children who made at least one CHMRC related visits was 87.4 percent and 87.1 percent for cohort 1 and 2 respectively (Table 5.3). Furthermore, if the analysis was restricted to at least two years of continuous enrolment, the proportion of children making one or more visits increased from 87.4 percent to 88.7 percent for cohort 1 and from 87.1 percent to 88.1 percent for cohort 2 (Table 5.3).

Table 5.3: The Proportion of Children who had CHRMC-related Visits Post-Classification by Criterion A

	Period (years) of continuous enrolment with Alberta Health and Wellness					
	No restriction on continuous enrolment period to a maximum of 8 years		**At least 1 year of continuous enrolment post-classification to a maximum of 8 years**		**At least 2 years of continuous enrolment post-classification to a maximum of 8 years**	
Number of visits	**Cohort 1 N=9295 n (%)**	**Cohort 2 N=6695 N (%)**	**Cohort 1 N=8286 N (%)**	**Cohort 2 N=5799 n (%)**	**Cohort 1 N=7346 n (%)**	**Cohort 2 N=5102 n (%)**
0	1481 (15.9)	1203 (18.0)	1045 (12.6)	749 (12.9)	830 (11.3)	607 (11.9)
1	2012 (21.7)	1428 (21.3)	1714 (20.7)	1173 (20.2)	1418 (19.3)	942 (18.5)
2	1336 (14.4)	932 (13.9)	1234 (14.9)	845 (14.6)	1094 (14.9)	718 (14.1)
≥ 3	4466 (48.1)	3132 (46.8)	4293 (51.8)	3032 (52.3)	4004 (54.5)	2835 (55.6)
≥ 1	7814 (84.1)	5492 (82)	7241 (87.4)	5050 (87.1)	6516 (88.7)	4495 (88.1)

5.5.3 Internal Validation of CHRMC Cases Identified by Criterion B

Table 5.4 shows the proportion of children classified as having CHRMC by criterion B who made one or more subsequent visits post-classification. Almost eighty nine percent (88.5 %) of children in cohort 1 and 83.6 percent in cohort 2 had 1 or more CHRMC-related visits, post-classification. When the analysis was restricted to only those children who were continuously enrolled with AHW for at least 1 year post-classification, the proportion of children with one or more CHRMC related visits was 93.2 percent for cohort 1 and 93.1 percent for cohort 2 (Table 5.4). When enrolment period was increased from one to two years post-classification, there was a slight increase in the proportion of children who made 1 or more visits. The proportion increased from 93.2 percent to 94.6 percent for cohort 1 and from 93.1 percent to 94.2 percent for cohort 2 (Table 5.4). Increasing the period of continuous enrolment from one to two years also resulted in the increase of the proportion of children who made three or more subsequent visits i.e. from 72.3 percent to 75 percent among children cohort 1 and from 64.8 percent to 70.4 percent among those in cohort 2.

Table 5.4: The Proportion of Children who had CHRMC-related Visits Post-Classification by Criterion B

	Period (years) of continuous enrolment with Alberta Health and Wellness					
	No restriction on enrolment period to a maximum of 8 years		At least 1 year of continuous enrolment with AHW post diagnosis to a maximum of 8 years		At least 2 years of enrolment post diagnosis to a maximum of 8 years	
Number of visits	**Cohort 1 N=1807 n (%)**	**Cohort 2 N=787 n (%)**	**Cohort 1 N=1612 n (%)**	**Cohort 2 N=622 n (%)**	**Cohort 1 N=1451 n (%)**	**Cohort 2 N=497 n (%)**
0	207 (11.5)	128 (16.4)	110 (6.8)	43 (6.9)	78 (5.4)	29 (5.8)
1	238 (13.2)	114 (14.6)	199 (12.3)	77 (12.4)	165 (11.4)	43 (8.7)
2	158 (8.7)	109 (14.0)	138 (8.6)	99 (15.9)	120 (8.3)	75 (15.1)
≥ 3	1204 (66.6)	428 (54.9)	1165 (72.3)	403 (64.8)	1088 (75.0)	350 (70.42)
≥ 1	1600 (88.5)	659 (83.6)	1502 (93.2)	579 (93.1)	1373 (94.6)	468 (94.2)

CHAPTER SIX: RESULTS 3: CORRELATES OF CHRMC INCIDENCE AND PREVALENCE RATES

6.1 Introduction

This chapter provides the descriptive, univariate and multivariate analyses to determine correlates of CHRMC incidence and prevalence rates as defined by using criterion A (one or more component case definitions) and criterion B (two or more the component case definitions).

6.2 CHRMC Incidence Rates

6.2.1 Descriptive Analysis by using Criterion A.

Descriptive analysis is a very crucial step that helps our understanding of the more complex relationship among the covariates derived from multivariate analysis. Table 6.1 provides the demographic characteristics of children with CHRMC by criterion A and those without CHRMC. In both cohorts, males formed a larger proportion of CHRMC cases than females (cohort 1: 56.6 percent; cohort 2: 58.7 percent) (Table 6.1).

Compared to cohort 1, the majority of children with CHRMC in cohort 2 resided in urban areas (cohort 1: 57.1 percent versus cohort 2: 64.2 percent versus). In contrast, cohort 1 had a larger proportion of CHRMC cases who resided in rural areas as compared to cohort 2 (cohort 1: 24.9 percent; cohort 2 18.7 percent). Finally, in both cohorts children with CHRMC who resided in small urban areas formed the smallest of all residential categories (cohort 1: 18 percent; cohort 2:17.1 percent).

First Nations children formed a higher proportion of children with CHRMC in cohort 2 than those in cohort 1 (11.4 percent in Cohort 2 versus 8.5 percent in cohort 1). In

addition, the proportion of children with CHRMC who were on social welfare was 0.2 percent among cohort 1 children and 7 percent among those in cohort 2 (Table 6.1).

In both cohorts, children with CHRMC and those without CHRMC had similar median follow-up times of eight years among those in cohort 1 and 7.5 years among those in cohort 2 (Table 6.1). The median age at diagnosis (classification by using criterion A) was 2.4 years among children in cohort 1 and 2.7 years among those in cohort 2.

Table 6.1: Demographic Characteristics of Children with and Without CHRMC by Criterion A

Characteristic	Cohort 1 (N=41171)		Cohort 2 (N=39864)	
	CHRMC n=9295 % (95% CI[1])	**Non-CHRMC n=31876 % (95% CI)**	**CHRMC n=6695 % (95% CI)**	**Non-CHRMC n=33169 % (95% CI)**
Gender, male%	56.6 (55.5-57.6)	49.6 (49.0-50.1)	58.7 (57.5-59.9)	50.0 (49.5-50.6)
Residence				
Urban %	57.1 (56.1-58.1)	65.2 (64.7-65.6)	64.2 (63.7-64.7)	64.2 (63.0-65.3)
Small urban %	18.0 (17.2-18.8)	16.6 (16.2-17.0)	17.1 (16.7-17.5)	13.9 (13.0-14.7)
Rural %	24.9 (24.0-25.8)	18.2 (17.8-18.6)	18.7 (18.3-19.1)	22.0 (21.0-23.0)
SES marker at birth				
No premium asst. %	82.2 (81.4-82.9)	86.9 (86.6-87.3)	67.6 (66.5-68.7)	73.3 (72.8-73.8)
Premium assistance %	9.2 (8.6-9.8)	9.1 (8.8-9.4)	14.0 (13.2-14.8)	14.9 (14.5-15.3)
First Nations %	8.5 (7.9-9.1)	3.6 (3.4-3.8)	11.4 (10.7-12.2)	6.0 (5.8-6.3)
Social welfare %	0.2 (0.1-0.30	0.4 (0.3-0.5)	7.0 (6.4-7.6)	5.7 (5.5-6.0)
Follow up				
median -years	8	8	7.4	7.3
range years	0.13-8	0.003-8	0.003-7.99	0.003-8
Age at diagnosis (classification)-years				
Median	2.4	Not applicable	2.7	Not applicable
Range	0.003-8		0.003-7.99	

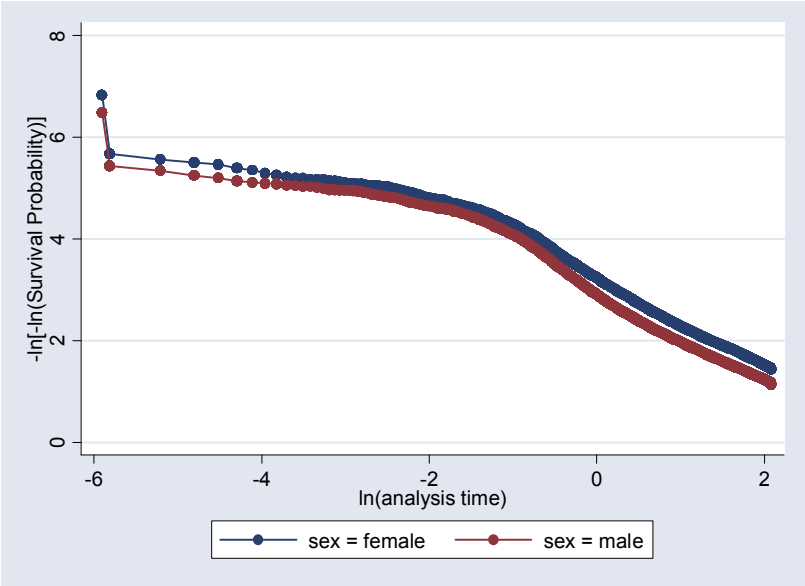
[1] CI-confidence interval

6.2.2 Assessment of the Proportional Hazard Assumptions

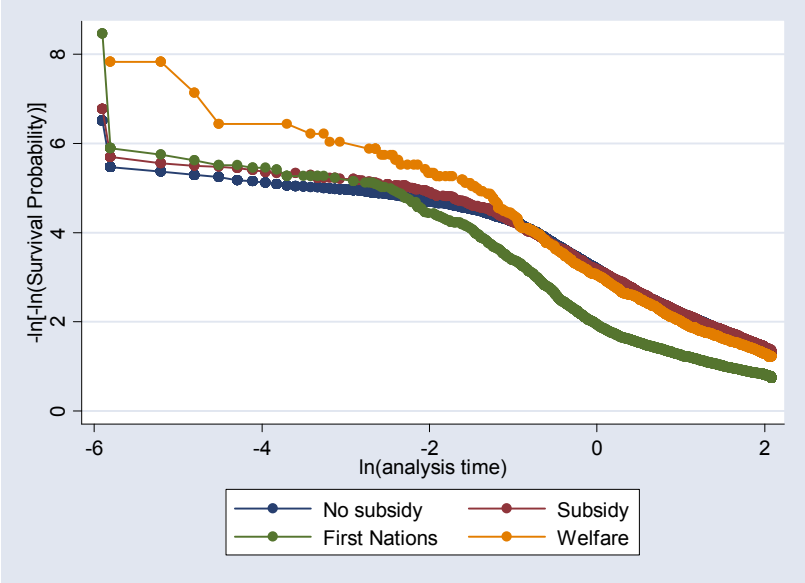
As described on section 3.7.5.1.1, (pg. 61), a graphical approach was used to assess the proportional hazard assumption by comparing the log-log survival curves for various subgroups. Figure 6-1 shows the log-log plots by gender and SES. Graph A (in Figure 6-1) shows the log-log plot for males and females. The relative hazard (incidence rates) of males and females is constant throughout the duration of follow-up. In contrast, Graph B in Figure 6-1 shows that the incidence rates among the three SES strata is not constant. This is evidenced by the non-parallel curves that intersect and cross with each other. This is a serious violation of the proportional hazard assumptions.

Figure 6-1: Examination of the proportional Hazards assumption: Log-log Curves

Graph A: Proportional hazard assumptions: gender as covariate



Graph B: Proportional hazard assumption socio-economic status as a covariate



6.2.3 Multivariate Survival Analysis-Criterion A

6.2.3.1 Introduction

Given the violation of the proportional hazard assumptions described in the previous section (section 6.2.2, pg. 101), the piecewise Cox regression modelling approach was used. This entailed stratifying the time to event into four categories: age 0-2 years (model 1), 3-4 years (model 2), 5-6 years (model 3) and 7-8 years (model 4). The following sections provide the univariate and multivariate results for each of the four models.

6.2.3.2 Correlates of Incidence Rate Ratio (IRR)-Main Effects

Table 6.2 and Table 6.3 show the results of survival analysis using Cox Proportional hazard models (model 1-4). Table 6.2 shows the main effects models correlates while Table 6.3 shows joint effect modification of cohort and SES or cohort and residence on incidence rate ratio (IRR).

Males had higher CHRMC incidence rate than females regardless of other covariates across models 1-4 (i.e. age groups: 0-2, 3-4, 5-6 and 7-8). The incidence rate of CHRMC among males was 30 to 40 percent higher than that of females (Table 6.2). The CHRMC incidence rates of First Nations' children aged younger or equal to six years (Model 1-3, Table 6.2) was between 1.2 and 2.8 times higher than those of children from families not receiving any subsidy. There were no difference in the CHRMC incidence rate between FN and the reference group among those aged between 7 and 8 years. Children aged 0-2 years (model 1, Table 6.2) from families on welfare had CHRMC incidence rates that were 1.5 times higher than those of children from no subsidy families. There were no statistically significant differences between the rates of children on welfare and those not on subsidy group in all other age groups (model 2 age 3-4, Table 6.2).

6.2.3.3 Correlates of CHRMC Incidence-Joint Effect Modification

Table 6.3 provides the results of joint effect modification of cohort and residence as well as cohort and SES on the CHRMC incidence rates. Across all models (i.e. for age groups: 0-2, 3-4, 5-6 and 7-8 years), there were statistically significant two-way interactions between cohort and residence or cohort and SES. Among children aged 0-2 years (model 1, Table 6.3), the incidence rate of CHRMC was jointly modified by cohort and area of residence. The CHRMC incidence rate among children residing in small urban was 1.2 times higher than that of children in cohort 1 residing in urban (the reference group), while the CHRMC incidence rate of children in cohort 2 residing in small urban was two times higher than that of the reference group ($p<0.001$). The CHRMC incidence rate among children residing in rural areas was 1.5 times higher than that of children in cohort 1 residing in urban (the reference group), while the CHRMC incidence rate of cohort 2 children residing in rural areas was 1.2 times higher than that of the reference group ($p<0.001$).

Among children aged 3-4 years (model 2, Table 6.3), the incidence rate of CHRMC was also jointly modified by the cohort and area of residence as well cohort and SES. Compared to cohort 1 children residing in urban areas (the referent group), the CHRMC incidence rate among children aged 3-4 years in cohort 1 residing in rural areas was 1.27 higher, while the rate of those cohort 2 children in rural areas was 0.9 times that of the reference group (model 2, Table 6.3).

The CHRMC incidence rate of children in cohort 1 residing in small urban areas was 1.1 times higher than that of children in cohort 1 residing in urban areas. In contrast, the

incidence rate of children in cohort 2 residing in small urban areas was 0.78 times that of the reference group (Model 2, age 3-4, Table 6.3).

The adjusted ratio between the CHRMC incidence rate of children in cohort 1 who were on welfare and the incidence rate of children in cohort 1 not on subsidy was 0.43 (Model 2, age 3-4, Table 6.3). Comparatively, the adjusted ratio of the CHRMC incidence rate of children in cohort 2 who were on welfare and the incidence rate of children in cohort 1 who were not on subsidy (the referent group), was 1.47. This means that compared to the reference group, children in cohort 1 who were on welfare, had incidence rate that was 67 percent lower (i.e. IRR 0.43). Unlike those in cohort 1, children in cohort 2 had CHRMC incidence rate that was 47 percent higher (i.e. IRR of 1.47) than the reference group.

The cohort and place of residence also jointly modified the CHRMC incidence rate among children aged 5-6 years (Model 3, age 5-6,Table 6.3). Cohort 1 children who resided in small urban areas had lower incidence rates than children of the same age group and cohort residing in urban areas (IRR 0.98). Similarly, cohort 2 children who resided in small urban areas had a lower CHRMC incidence rate than cohort 1 children in urban areas (IRR 0.67). This means that compared to the reference group (cohort 1 children in urban areas), the CHRMC incidence rate among cohort 1 children in small urban was 2 percent lower, while cohort 2 children in small urban areas had the incidence rate that was 33 percent lower than the reference group.

Finally, the CHRMC incidence rate among children aged 7-8 years was also jointly modified by the cohort and SES status or the cohort and area of residence (Model 4, Age 7-8,Table 6.3). Compared to the reference group (cohort1 children not on subsidy), cohort 1

children on subsidy had lower CHRMC incidence rate (IRR 0.9), while cohort 2 children on subsidy had higher CHRMC incidence rates (IRR 1.2). This means that compared to the reference group, the incidence rate among cohort 1 children on subsidy was 9 percent lower, while the incidence rate among cohort 2 children was 20 percent higher.

Cohort 1 children residing in small urban areas had the CHRMC incidence rate that was 4 percent (IRR of 1.04) higher than the reference group (i.e. cohort 1 children, urban) (Model 4, age 7-8, Table 6.3). In contrast, cohort 2 children in urban areas had the CHRMC incidence rate that was 31 percent lower (i.e. IRR of 0.69) than the reference group.

Table 6.2: Cox Proportional Hazard Models When Using Criterion A

Model 1: Age 0-2	Univariate Analysis		Multivariate Analysis[2]	
Variable	Incidence rate Ratio	95% Confidence interval	Incidence Rate Ratio	95% Confidence interval
Females	Referent			
Males	1.40	1.33-1.47	1.40	1.33-1.47
No subsidy	Referent			
Subsidy	1.00	0.92-1.08		
First Nations	2.89	2.70-3.10	2.80	2.61-3.01
Welfare	1.13	0.99-1.30	1.51	1.32-1.74
Model 2: Age 3-4				
Females	Ref.			
Males	1.30	1.22-1.38	1.30	1.22-1.38
No subsidy				
Subsidy	1.00	0.90-1.10		
First Nations	1.55	1.38-1.75	1.57	1.39-1.76
Model 3: Age 5-6				
Females	Ref.			
Males	1.36	1.26-1.46	1.36	1.26-1.47
No subsidy				
Subsidy	0.95	0.84-1.07		
First Nations	1.20	1.03-1.40	1.22	1.04-1.42
Welfare	1.04	0.83-1.30		
Urban				
Rural	1.04	0.95-1.14		
Model 4: Age 7-8				
Females	Ref.			
Males	1.26	1.16-1.37	1.26	1.16-1.37
no subsidy	Ref.			
First Nations	0.96	0.79-1.17		
Welfare	1.06	0.80-1.40		
Urban	Ref.			
Rural	0.88	0.79-0.98	0.88	0.79-0.98

[2] The final model includes significant interaction terms shown in Table 6.3

Table 6.3: Joint Effect Modification of Cohort and Area of Residence or Socioeconomic Status on the CHRMC Incidence Rates

Interaction Terms	Multivariate IRR*	p-value
Model 1: Age 0-2		
Cohort 1, urban	Referent	
Cohort 1, Small urban	1.23	<0.001
Cohort 2, Small urban	2.0	<0.001
Cohort 1, Rural	1.52	<0.001
Cohort 2, Rural	1.22	<0.001
Model 2: Age 3-4		
Cohort 1, Urban	Referent	
Cohort 1, Rural	1.27	<0.001
Cohort 2, Rural	0.90	<0.001
Cohort 1, Small urban	1.12	<0.001
Cohort 2, Small urban	0.78	<0.001
Cohort 1, No subsidy	Referent	
Cohort 1, welfare	0.43	<0.001
Cohort 2, welfare	1.47	<0.001
Model 3: Age 5-6		
Cohort 1, urban	Reference	
Cohort 1, Small urban	0.98	<0.001
Cohort2, Small urban	0.67	<0.001
Model 4: Age 7-8		
Cohort 1, No subsidy	Referent.	
Cohort 1, subsidy	0.91	0.037
Cohort 2, subsidy	1.20	0.037
Cohort 1, Urban	Referent	
Cohort 1, Small urban	1.04	0.001
Cohort 2, Small urban	0.69	0.001

* IRR-Incidence rate ratio was adjusted for sex, area of residence or social economic status

6.2.4 Descriptive Analysis-Criterion B

Table 6.4 shows the demographic characteristics of children with CHRMC by criterion B and those who were not. In both cohorts, male was the predominant gender among children with CHRMC (64.1 percent in cohort 1 and 61.5 percent in cohort 2). In both cohorts, the proportion of children residing in urban areas was larger among children without CHRMC compared to children with CHRMC (cohort1: 64.1 percent versus 47.4; cohort 2: 64.5 percent versus 51.7 percent) (Table 6.4). In addition, the proportion of children residing in small urban areas was larger for children with CHRMC than children without CHRMC (Cohort 1 20.9 percent versus 16.7 percent; cohort 2: 18.4 percent versus 16.5 percent). Finally, a larger proportion of children with CHRMC resided in rural areas compared to the proportion of children without CHRMC (cohort 1: 31.7 percent versus 19.2 percent; cohort 2: 29.2 percent versus 19.1 percent).

The comparison of SES of children with and without CHRMC is also shown in Table 6.4. The majority of children with CHRMC as defined by criterion B did not receive any subsidy (77.2 percent in cohort 1 and 62.5 percent cohort 2). Similar proportions of children with CHRMC and those without CHRMC, received subsidy in both cohorts. However, there were a larger proportion of First Nations children among those with CHRMC than those without CHRMC (cohort 1 13.3 percent with CHRMC versus 4.3 percent without CHRMC; cohort 2:16.4 percent with CHRMC versus 6.8 percent without CHRMC). Overall, there were fewer children on welfare in cohort 1 than cohort 2. Children on welfare formed 0.06 percent of children with CHRMC in cohort 1, while they formed 7.8 percent of children with CHRMC in cohort 2.

In both cohorts, children with CHRMC and those without CHRMC had similar median follow up times, i.e. 8 years among those in cohort 1, and 7.5 years among those in cohort 2 (Table 6.4). The median age at which children were classified as having CHRMC by criterion B was 3.02 years among children in cohort 1 and 3.7 years among those in cohort 2.

Table 6.4: Demographic Characteristics of Children with and those without CHRMC by Criterion B

Characteristic	Cohort 1 (n=41171)		Cohort 2 (n=39864)	
	CHRMC n =1807	Non-CHRMC n=39364	CHRMC n=779	Non-CHRMC n=39085
Gender, male %	64.1	50.6	61.5	51.3
Area of Residence at birth %				
Urban	47.4	64.1	51.7	64.5
Small urban	20.9	16.7	18.4	16.5
Rural	31.7	19.2	29.9	19.1
SES marker at birth %				
No Subsidy	77.2	86.2	62.5	72.6
Subsidy	9.2	9.1	13.2	14.8
First Nations	13.3	4.3	16.4	6.8
Social welfare	0.06	0.36	7.8	5.9
Follow up time (years)				
Median	8	8	7.5	7.3
Range	0.5-8	0.1-8	0.003-7.9	0.003-8.0
Age at diagnosis -years				-
Median	3.02	-	3.7	-
range	0.01-8	-	0.003-7.9	

6.2.5 Multivariate Survival Analysis -Criterion B

As in the previous analysis using criterion A (section 6.2.2-page 101), the Cox proportional hazard assumptions using criterion B were also violated. Therefore, the multivariate analysis described below involved fitting four separate Cox models for age groups 0-2, 3-4, 5-6 and 7-8 years.

Table 6.5 presents multivariate survival analysis by using the Cox proportional hazard model to determine the correlates of CHRMC incidence rates by criterion B. Males had higher CHRMC incidence rates than females across all age groups with IRR ranging from 1.4 to 1.8 (Model 1-4, Table 6.5), after adjusting for other confounders. There were no statistically significant differences in CHRMC incidence rates of children on subsidy versus children not on subsidy across all age groups. The CHRMC incidence rate among First Nations children were between 1.8 and 2.8 times higher than those of children from families not receiving any subsidy (Table 6.5). The highest incidence rates among First Nations children were found in the age group 0-2 years where the CHRMC incidence rate was 2.8 times higher than the reference group (children not on subsidy) after adjusting for sex and area of residence (Model 1, Table 6.5).

The cohort and area of residence jointly modified the CHRMC incidence among children aged 0-2 years (Table 6.6). The incidence rate of cohort 1 children in small urban areas was 1.96 times higher than that of cohort 1 children in urban areas. However, the CHRMC incidence rate of cohort 2 children in small urban areas was 1.18 times that of cohort 1 children in urban areas. In addition, the CHRMC incidence rate of cohort 1 children in rural areas was 2.2 times that of the reference group, while the CHRMC

incidence rate among cohort 2 children in rural areas was double that of the reference group, after adjusting for other covariates.

Children in the age groups 2-4 and 5-6 years old in cohort 2, were less likely to be classified as CHRMC by criterion B, regardless of sex, area of residence and SES marker. Their incidence rate ratio were one third (0.3) to one-half (0.5) times the rate of children in cohort 1 (Table 6.5). Children aged 2-4, 5-6 and 7-8 years who resided in small urban areas had CHRMC incidence rates that were between 1.4 and 1.7 times higher than that of cohort 1 children residing in rural areas.

The CHRMC incidence rates of children aged 3-4, 5-6 and 7-8 years in rural areas was between 1.6 and 1.9 times higher than the CHRMC incidence rates of children in the reference group (i.e. cohort 1 children in urban areas). The CHRMC incidence rate of children aged 3-4 years who came from families on welfare was 1.5 times higher than the rates of the reference group (cohort 1 children not on subsidy).

Table 6.5: Cox Proportional Hazard Model When Using Criterion B

	Univariate Analysis		Multivariate Analysis	
Model 1: Age 0-2	**Incidence Rate Ratio (IRR)**	**95% Confidence interval**	**Incidence rate Ratio (IRR)**	**95% Confidence interval**
Males	1.57	1.36-1.83	1.40	1.33-1.47
Subsidy	1.11	0.88-1.41		
First Nations	4.48	3.74-5.37	2.80	2.61-3.01
Welfare	0.91	0.56-1.48	1.51	1.32-1.74
Model 2: Age 3-4				
cohort 2	0.30	0.26-0.35	0.27	0.23-0.32
Females				
Males	1.68	1.46-1.93	1.69	1.47-1.94
Subsidy	0.95	0.76-1.18		
First Nations	2.32	1.89-2.85	2.25	1.82-2.77
Welfare	1.23	0.85-1.78	2.77	1.88-4.08
Small urban	1.36	1.13-1.63	1.36	1.13-1.63
Rural	2.04	1.75-2.37	1.84	1.57-2.15
Model 3: Age 5-6				
cohort 2	0.59	0.50-0.70	0.58	0.49-0.69
Males	1.64	1.38-1.95	1.65	1.39-1.96
no subsidy	Ref.		Ref.	
Subsidy	0.75	0.55-1.00		
First Nations	1.81	1.37-2.39	1.76	1.33-2.34
Welfare	0.74	0.41-1.35		
Small Urban	1.65	1.33-2.03	1.64	1.33-2.03
Rural	1.76	1.45-2.15	1.64	1.34-2.00
Model 4: Age 7-8				
cohort 2	0.59	0.50-0.70		
Females	Referent			
Males	1.64	1.38-1.95	1.78	1.45-2.17
Subsidy	0.75	0.55-1.00		

Table 6.6: Joint Effect Modification of Cohort and Residence on CHRMC Incidence Rate by Criterion B

Interaction Terms	Multivariate Incidence Rate ratio (IRR)[3]	p-value
Model 1 :age 0-2 years		
Cohort 1, urban	Referent	
Cohort 1, small urban	1.96	0.023
Cohort 2, small urban	1.18	0.023
Cohort 1, rural	2.20	0.002
Cohort 2, rural	1.20	0.002

[3] Incidence rate ratio was adjusted for sex, area of residence or social economic status

6.3 Prevalence of Chronic High Risk Medical Conditions (CHRMC)

6.3.1 Introduction

This section provides results of the analyses to determine the correlates of CHRMC prevalence defined using criterion A and B. These analyses included the multivariate binomial regression modelling (as described in section 3.7.6.1). The crude and adjusted eight-year period prevalence rates are also provided. The adjusted prevalence rate is the prevalence of CHRMC calculated after taking into account all other covariates that were included in the final multivariate binomial regression model.

6.3.2 Correlates of CHRMC Prevalence Criterion A

Table 6.7 shows the univariate and multivariate results of the binomial regression. The eight-year period prevalence rates were significantly associated with gender, cohort, residence and social economic status. In addition there was a statistically significant two-way interactions between the cohort and welfare status as well as cohort and small urban.

The prevalence rate of CHRMC among males was 27 percent higher than females regardless of other covariates (i.e. Prevalence rate ratio (PRR) of 1.27) (Table 6.7). There was no statistically significant difference in the prevalence rates of children on subsidy and those not on subsidies. The CHRMC prevalence among First Nations children was 64 percent (i.e. PRR of 1.64) higher than that of children not on subsidy, after taking into consideration of all other covariates.

The CHRMC prevalence was jointly modified by the cohort and welfare as well as the cohort and residence (small urban). The calculated PRR using these interaction terms are shown in Table 6.8. Cohort 1 children who were on welfare had the CHRMC

prevalence that was 26 percent (i.e. PRR was 0.74) lower than the prevalence of children in cohort who were not receiving subsidy. However, cohort 2 children on welfare had CHRMC prevalence rate that was 32 percent (PRR 1.32) higher than that of the reference group (i.e. cohort 1, no subsidy) (Table 6.8).

Finally, cohort 1 children who resided in small urban areas had the prevalence rate that was 12 percent higher than that of the reference group (cohort 1, urban) (Table 6.8). Unlike cohort 1 children, cohort 2 children who resided in small urban areas had lower prevalence rates (PRR 0.84) than that of the reference group (Table 6.8).

Table 6.7: Univariate and Multivariate Binomial Regression Models for Correlates of CHRMC Prevalence by Criterion A

	Univariate Analysis		**Multivariate Analysis**	
Covariate	**Prevalence Rate Ratio (PRR)**	**95% Confidence Interval**	**Prevalence Rate Ratio (PRR)**	**95% Confidence Interval**
Cohort 1	Referent		referent	
Cohort 2	0.71	0.69-0.73	0.73	0.70-0.75
Females	Referent		referent	
Males	1.28	1.24-1.31	1.27	1.23-1.31
No subsidy	Referent		referent	
Subsidy	0.99	0.95-1.04	-	
First Nations	1.68	1.60-1.75	1.64	1.57-1.72
Welfare	1.06	0.97-1.16	0.74	0.44-1.27
Small Urban	1.00	0.96-1.05	1.12	1.06-1.17
Rural	1.26	1.22-1.31	1.19	1.15-1.23
Cohort & Welfare			1.77	1.03-3.06
cohort& Small Urban			0.75	0.69-0.82

Table 6.8: Joint Effect Modification of Cohort and Residence or Socioeconomic Status on CHRMC Prevalence by Criterion A

Interaction terms	Multivariate Prevalence rate ratio (PRR)	p-value
Cohort 1, no subsidy	Referent	
Cohort 1, welfare	0.74	0.04
Cohort 2, Welfare	1.32	0.04
Cohort 1, urban	Referent	
Cohort 1, small urban	1.12	<0.001
Cohort 2, small urban	0.84	<0.001

6.3.3 Crude and Adjusted Eight-Years Period Prevalence of CHRMC Defined By Using Criterion A

Table 6.9 shows the crude and adjusted prevalence of CHRMC by gender, SES and residence. In both cohorts, males had higher adjusted prevalence of CHRMC than females (Cohort 1: 28.7 percent males versus 23.3 percent females; cohort 2: 20.3 percent males versus 16.3 percent females). Males in cohort 1 had higher adjusted prevalence than males in cohort 2. Similarly, females in cohort 1 had higher prevalence than females in cohort 2 (Table 6.9).

In terms of SES, children not receiving subsidies had the lowest CHRMC prevalence in both cohort 1 and 2 (25.1 percent in cohort 1 and 17.3 percent in cohort 2). Children on subsidy had a slightly higher adjusted prevalence than those not on subsidies (Table 6.9). First Nations children had the highest CHRMC prevalence in both cohort 1 and 2 (41 percent in cohort 1 and 29.1 percent in cohort 2). Finally, children on welfare had the lowest prevalence in cohort 1 (18.6 percent), while they had the second highest in cohort 2 (23.4 percent).

The adjusted CHRMC prevalence was different across various areas of residence. In cohort 1 the prevalence increased steadily from urban to rural areas (21.0 percent in urban, 27.1 percent in small urban and 28.8 percent in rural areas). However, the CHRMC prevalence patterns by area of residence were somewhat different among children in cohort 2. Cohort 2 children who resided in small urban areas had the lowest prevalence (15 percent) followed by children in urban areas (17.8 percent). Children residing in rural areas had the highest adjusted CHRMC prevalence (21.2 percent) (Table 6.9).

Table 6.9: Crude and Adjusted[1] Eight-years Period Prevalence of CHRMC Defined by Criterion A

		Cohort 1			Cohort 2			
Covariate	**N**	**n with CHRMC**	**crude prevalence**	**adjusted prevalence**	**n**	**n with CHRMC**	**crude prevalence**	**adjusted prevalence**
Gender								
Male	16431	4727	28.8	28.7	16423	3487	21.23	20.6
Female	15606	3639	23.3	22.6	15440	2447	15.85	16.3
Socio-economic status								
no subsidy	27442	6881	25.1	21.0	23582	4086	17.3	17.4
Subsidy	2917	754	25.9	25.9	4472	821	18.4	18.4
First Nations	1618	720	44.5	41.0	2227	665	29.9	29.1
Welfare	60	11	18.3	18.6	1582	362	22.9	23.4
Residence								
Urban	19872	4738	23.8	21.0	20342	3809	18.7	17.8
small urban	5514	1501	27.2	27.1	5282	804	15.2	15.0
Rural	6556	2107	32.1	28.8	6229	1320	21.2	21.2

[1] Adjusted for place of residence, social economic status, interaction between cohort and residence, cohort and social economic status.

6.3.4 Correlates of Chronic High Risk Medical Conditions (CHRMC) Prevalence Defined by Using Criterion B

Table 6.10 shows the univariate and multivariate binomial regression analyses of CHRMC prevalence by using criterion B. Cohort 2 had a lower prevalence than cohort 1 did, after taking into consideration of gender, SES and place of residence. The Prevalence rate ratio (PRR) was not very much different in univariate compared to multivariate analysis (0.42 versus 0.40) indicating that it was not confounded by other variables included in the model.

The eight-year period prevalence of CHRMC among males was 1.6 times higher than the prevalence of females regardless of cohort, residence and socio economic status. Among First Nations, the CHRMC prevalence was 2.4 times the rates of children not receiving subsidy. The prevalence of children on welfare was also higher when compared to children not receiving any subsidy (PRR 1.51). Children residing in small urban areas had prevalence that was 56 percent (PRR of 1.56) higher than that of children residing in urban areas after taking into consideration of cohort and SES. Similarly, the prevalence of CHRMC among children residing in rural areas was 84 percent higher than that of children residing in urban areas, regardless of other covariates (Table 6.10). The interaction terms between the cohort and area of residence or SES were not statistically significant.

Table 6.10: Univariate and Multivariate Binomial Regression Models for Correlates of Prevalence Defined by Using Criterion B

	Univariate Analysis		**Multivariate analysis**	
Covariate	**Prevalence Rate Ratio**	**95% Confidence Interval**	**Prevalence Rate Ratio**	**95% Confidence Interval**
cohort 1	Referent		referent	
cohort2	0.42	0.38-0.45	0.40	0.36-0.44
Females	Referent		referent	
Males	1.64	1.51-1.78	1.64	1.5-1.78
No subsidy	Referent		referent	
Subsidy	0.98	0.86-1.12	-	-
First Nations	2.60	2.32-2.91	2.38	2.12-2.67
Welfare	0.86	0.65-1.14	1.51	1.13-2.02
Urban	Referent			-
Small Urban	1.57	1.41-1.74	1.56	1.40-1.73
Rural	2.12	1.93-2.32	1.84	1.67-2.02

6.3.5 Crude and Adjusted CHRMC Prevalence using Criterion B

Table 6.11 provides crude and adjusted CHRMC prevalence as defined by Criterion B by cohort, gender, SES and residence. In both cohorts, male had higher adjusted CHRMC prevalence than females (Cohort 1: 6 percent among males versus 3.7 percent among females; cohort 2: 2.4 percent males versus 1.5 percent females). Males in cohort 1 had higher adjusted prevalence than males in cohort 2 (cohort 1: 6.4 percent versus cohort 2: 2.4 percent). Similarly, females in cohort 1 had higher prevalence than females in cohort 2 (Table 6.11).

There was a distinct pattern of increasing CHRMC prevalence across the SES strata. Children not receiving subsidies had the lowest CHRMC prevalence in both cohorts (3.2 percent in cohort 1 and 1.6 percent in cohort 2). Children on subsidy had a slightly higher adjusted prevalence than children not on subsidy (cohort 1 5.18 percent, cohort 2: 2.03 percent) (Table 6.11). Children on welfare ranked third in the CHRMC prevalence after the no subsidy and subsidy groups. These children had CHRMC prevalence of 6.7 percent among children in cohort 1 and 2.7 percent among those in cohort 2. First Nations children had the highest CHRMC prevalence in both cohorts (10.5 percent in cohort 1 and 4.2 percent in cohort 2). The adjusted CHRMC prevalence was also different across the areas of residence. In both cohorts, the adjusted CHRMC prevalence increased steadily from urban areas to rural areas. Children residing in urban areas had the lowest CHRMC prevalence (3.9 percent in cohort 1 and 1.5 percent in cohort 2). Children living in small urban areas had slightly higher prevalence than those in urban areas (6 percent in cohort 1 and 2.4 percent in cohort 2). Children in rural areas had the highest CHRMC prevalence (7.1 percent in cohort 1, 2.8 percent in cohort 2) (Table 6.11).

Table 6.11: Crude and Adjusted[1] Eight-Year Period Prevalence of CHRMC by Criterion B

		Cohort 1			Cohort 2			
Covariate	**n**	**n with CHRMC**	**crude prevalence**	**adjusted prevalence**	**n**	**n with CHRMC**	**crude prevalence**	**adjusted prevalence**
Gender								
Male	16,431	1,058	6.44	6.0	16,423	416	2.53	2.4
Female	15,606	585	3.75	3.7	15,440	264	1.71	1.5
Socioeconomic Status								
No subsidy	27,442	1,264	4.61	3.2	23,582	437	1.85	1.6
Subsidy	2,917	151	5.18	5.18	4,472	91	2.03	2.03
First Nations	1,618	227	14.03	10.5	2,227	106	4.76	4.2
Welfare	60	1	1.7	6.7	1582	46	2.9	2.7
Residence								
Urban	19,872	766	3.85	2.8	20342	341.0	1.68	1.5
Small urban	5,514	339	6.15	6.0	5,282	127	2.4	2.4
Rural	6,556	534	8.15	7.1	6,229	211	3.39	2.8

[1] Adjusted for place of residence, social economic status, interaction between cohort and residence, cohort and social economic status.

CHAPTER SEVEN: RESULTS 4: CHRONIC OBSTRUCTIVE PULMONARY DISEASES (COPD) AND ALLIED CONDITIONS

7.1 Introduction

This chapter focuses on Chronic Obstructive Pulmonary Diseases (COPD). These supplementary analyses were done exclusively for COPD (ICD-9 code 490-496) for two major reasons. First, this disease group contributed to 75 percent of all CHRMC-related visits. Secondly, the COPD disease group is composed of a set of more homogenous diseases compared to the entire CHRMC group. Therefore, analysis focusing on COPD would help to a better understanding of the overall CHRMC results. This chapter provides three types of results. First, a descriptive analysis of the characteristics of children classified as having COPD. Secondly, the correlates of COPD incidence rates are provided through univariate and multivariate analysis. Finally, the chapter provides analysis of internal validation of the COPD case definitions.

7.2 Descriptive analyses

Table 7.1 shows the distribution of children with COPD in each cohort by case definition. In both cohorts, the majority of COPD cases were identified through the primary care physician case definition. With the exception of emergency room case definition, cohort 1 had statistically significant greater proportion of children across all component case definitions than cohort 2. The discrepancy between cohort 1 and 2 was largest for hospitalization case definition, where the proportion of children with CHRMC in cohort 1 was 49 times greater than the proportion of children with COPD in cohort 2.

By using criterion A, 17.8 percent of children in cohort 1 and 13.5 percent of children in cohort 2 had COPD. In contrast, when using criterion B, 6.5 percent of children in

cohort 1 and 5.1 percent in cohort 2 had COPD. The observed differences in the proportion of children with COPD was statistically significant different between cohort 1 and 2 across all case definitions (Table 7.1).

Table 7.1: Frequency Distributions of Children with COPD By Various Case Definitions

Type of case definition	Proportion (%) of children who were classified as having COPD by the case definition		p-value (two sided)
	Cohort 1 (n=41171) n (%)	Cohort 2 (n=39864) n (%)	p-values (two sided)
Primary care physicians	4449 (10.8)	3177 (8.0)	<0.001
Consultants	1774 (4.3)	1598 (4.01)	0.033
Emergency room	1401 (3.4)	1633 (4.1)	<0.001
Hospitalization	1996 (4.9)	57 (0.1)	<0.001
Criterion B	2682 (6.5)	2049 (5.1)	<0.001
Criterion A	7310 (17.8)	5396 (13.5)	<0.001

7.2.1 Age-specific COPD Incidence Rates

Figure 7-1 shows the age-specific COPD incidence rates for children identified by using criterion A. Children in cohort 1 had statistically significant higher COPD incidence rates than those in cohort 2 across the age from one to three years and from six to eight years. There were no statistically significant differences between the two cohorts for children aged four and five years. In both cohorts, the highest age-specific incidence rate was among two year-olds.

Figure 7-2 shows age specific incidence rate of COPD for children identified by using criterion B. With the exception of age four and five years, the age-specific COPD incidence rates of children in cohort 1 were significantly higher than those of children in cohort 2 across all other age groups. There was no statistically significant difference in the COPD age-specific incidence rate between the two cohorts for children aged four and five years. In both cohorts, the highest age-specific COPD incidence rate was at the age of eight years.

Figure 7-1: Age-specific COPD Incidence Rate by Criterion A

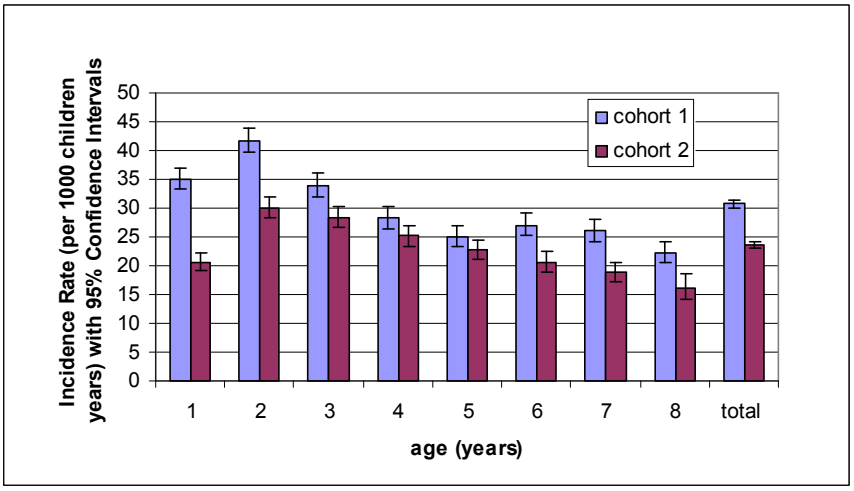
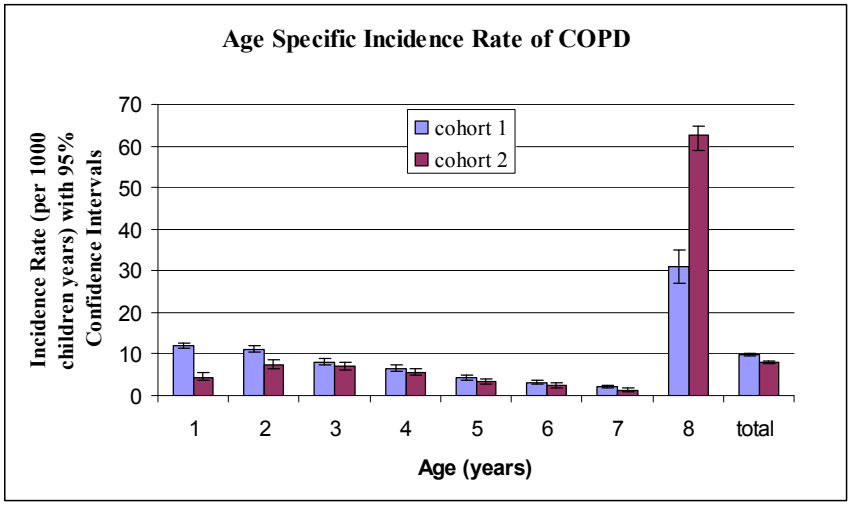


Figure 7-2: Age-specific COPD Incidence Rate by Criterion B



7.3 Correlates of Incidence Rates COPD by Criterion A

7.3.1 Demographic Characteristics of Children with COPD by Criterion A

Table 7.2 provides the demographic characteristics of children with and those without COPD as defined by criterion A. In both cohorts, males formed a larger proportion of COPD cases than females (cohort 1: 57.6 percent; cohort 2: 60.3 percent).

The majority of children (cohort 1: 55.2 percent; cohort 2: 64.6 percent) with COPD by criterion A, resided in urban areas (Table 7.2). The next largest proportion of children classified as having COPD by criterion A resided in rural areas (cohort 1: 25.9 percent; cohort 2: 21.67 percent). Children residing in small urban areas formed the smallest proportion of children with COPD by criterion A (cohort 1: 18.9 percent; cohort 2:13.9 percent).

The majority of children (cohort 1: 88.8 percent; cohort 2: 67.4 percent) with COPD by criterion A, came from families that did not receive any health premium subsidy (Table 7.2). The proportion of First Nations children with COPD by criterion A was 8.9 percent in cohort 1 and 11.6 percent in cohort 2. In addition, the proportion of children with COPD who were on social welfare was 0.2 percent and 7 percent in cohort 1 and 2 respectively.

In both cohorts, children with COPD and those without COPD had similar median follow-up times, i.e. 8 years among those in cohort 1, and 7.5 years among those in cohort 2 (Table 7.2). The median age from birth to the time when a child was classified as having COPD by criterion A, was 2.7 years among children in cohort 1 and 2.9 years among those in cohort 2.

Table 7.2: Demographic Characteristics of with COPD and those Without COPD by Criterion A

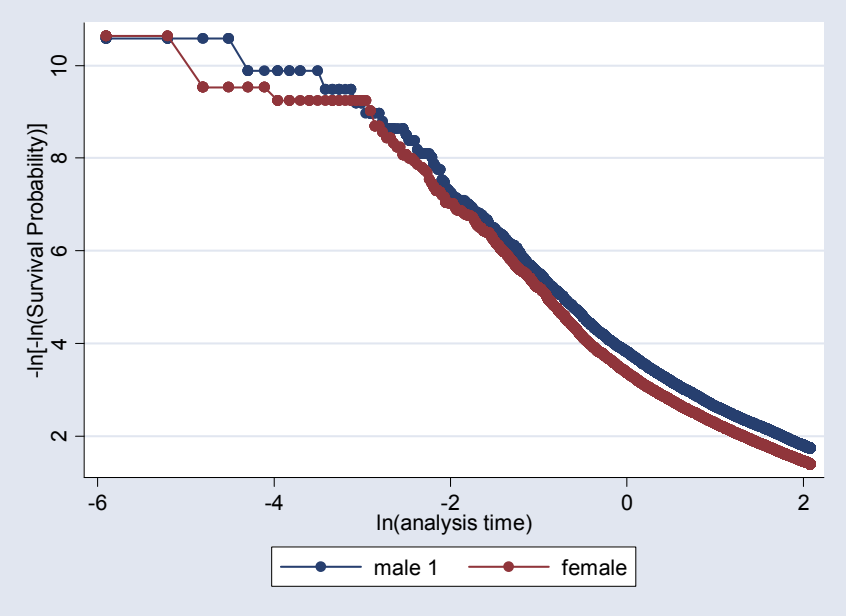
Characteristic	**Cohort 1 (N=41171)**		**Cohort 2 (N=39864)**	
	COPD n=7310	**Non-COPD n=33861**	**COPD n=5396**	**Non-COPD n=34468**
Gender, male%	57.6	49.8	60.3	50.1
Residence				
Urban %	55.2	65.2	64.6	64.2
Small Urban %	18.9	16.5	13.9	17.0
Rural %	25.9	18.4	21.6	18.9
Socio economic status (SES)				
No Subsidy %	81.8	86.7	67.4	73.1
Subsidy %	9.1	9.1	13.8	14.9
First Nations %	8.9	3.8	11.6	6.2
Social welfare %	0.2	0.4	7.2	5.7
Follow up				
Median (years)	8	8	7.5	7.3
Range (years)	0.9-8	0.01-8	1.6-8	0.001-8
Age at Diagnosis				
median -years	2.7	n/a	2.9	n/a
range years	0.003-8		0.08-8.00	

7.3.2 Assessment of the Proportional Hazard Assumptions

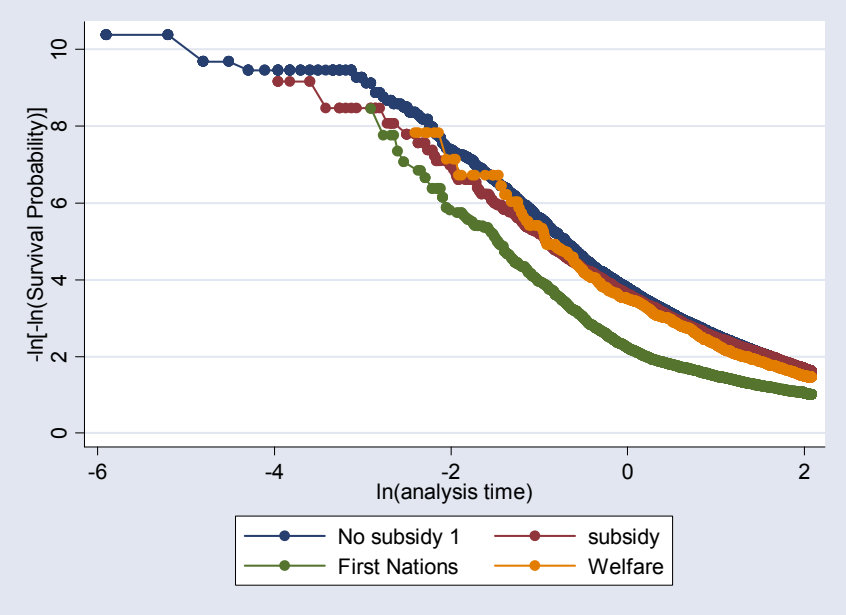
As described in section 3.7.5.1.1 (pg. 61), a graphical approach was used to assess the proportional hazard assumption by comparing log-log survival curves for various subgroups. Figure 7-3 shows the results of the assessment of the proportional hazard model assumptions. Graph A (in Figure 7-3) shows the log-log plot for males and females. The relative hazard (incidence rate) of males and females is constant throughout the duration of follow-up. Unlike the pattern observed for CHRMC (Figure 6-1), where there was serious violation of the proportional hazard assumptions, there is no serious violation in this case as shown in Graph B (in Figure 7-3). For a large part the curves are parallel and do not cross with each other. Therefore, the traditional Cox proportional hazard model was used to determine the correlates of COPD incidence rate. The results of the Cox Proportional hazard modelling are provided in the next sections.

Figure 7-3: Examination of the Proportional Hazards Assumption: Log-log Curves for Correlates of COPD incidence

Graph A: gender



Graph B Socio-economic Status



7.3.3 Multivariate Survival Analysis - Criterion A

Table 7.3 shows results of the univariate and multivariate analysis to determine correlates of COPD by using criterion A. Compared to children in cohort 1, children in cohort 2 had COPD incidence rate that was 16 percent (i.e. IRR 0.84) lower than that of children in cohort 1, regardless of other covariates. Males had COPD incidence rate that were 1.4 times higher than that of females regardless of other covariates. The COPD incidence rate among First Nations was double (i.e. IRR = 2) that of children not receiving subsidy.

There were statistically significant two-way interactions between cohort and welfare status and between cohort and place of residence. Table 7.4 shows the joint effect modification (interaction) of cohort and welfare as well as cohort and place of residence on the COPD incidence rate. Cohort 1 children who resided in small urban areas had CHRMC incidence rate that was 1.96 times higher than the reference group (i.e. cohort 1, urban). In contrast, cohort 2 children who resided in small urban areas had incidence rates that were 1.3 times higher than the incidence rate of the reference group (Table 7.4). In other words, this means that the incidence rate of CHRMC among cohort 1 children residing in small urban areas was 96 percent (IRR 1.96) higher than that of the reference group; while the CHRMC incidence rate of cohort 2 children residing in small urban areas was 26 percent higher (IRR of 1.26) than that of the reference group.

Cohort 1 children who resided in rural areas had incidence rate that was 1.99 times higher than that of children residing in urban areas. Comparatively, cohort 2 children who resided in rural areas had incidence rates that were 0.7 times that of cohort 1 children in urban areas (Table 7.4). Finally, cohort 1 children on welfare had incidence rate that was

4.3 times that of the reference group (i.e. cohort 1 children not on subsidy), while cohort 2 children on welfare had rates that were 1.5 times that of the reference group (Table 7.4).

Table 7.3: Cox Proportional Hazard Model for Children With COPD by Criterion A

	Univariate Analysis		**Multivariate Analysis**	
Variable	**Incidence Rate Ratio (IRR)**	**95% Conf. Interval**	**Incidence Rate Ratio (IRR)**	**95% Conf. Interval**
Cohort 1	Referent		Referent	
Cohort 2	0.75	0.73-0.78	0.84	0.80-0.88
Female	Referent			
Males	1.41	1.37-1.47	1.42	1.37-1.47
No subsidy	Referent			
Subsidy	0.99	0.94-1.05		
First Nations	2.01	1.90-2.14	2.0	1.89-2.13
Welfare	1.19	1.08-1.32	0.32	0.1-0.99
Urban	Referent			
Small Urban	1.04	0.99-1.10	1.96	1.70-2.27
Rural	1.31	1.25-1.36	1.99	1.75-2.26
Cohort and Welfare			2.14	1.2-3.8
Cohort and Small urban			0.64	0.59-0.71
Cohort and rural			0.70	0.65-0.77

Table 7.4: Joint Effect Modification of Cohort and Residence or Socioeconomic Status on COPD Incidence Rates by Criterion A

Interaction Terms	Multivariate Incidence Rate Ratio (IRR)[1]	P-value
Cohort 1, urban	Referent	
Cohort 1, small urban	1.96	<0.001
Cohort 2, small urban	1.26	<0.001
Cohort 1, rural	1.99	<0.001
Cohort 2, rural	0.70	<0.001
Cohort 1, no subsidy	Referent	
Cohort 1, welfare	4.32	0.01
Cohort 2, welfare	1.48	0.01

[1] Incidence rate ratio was adjusted for sex, area of residence or social economic status

7.4 Correlates of the COPD Incidence Rate Criterion B

7.4.1 Descriptive Analysis COPD by Criterion B

Table 7.5 shows the demographic characteristics of children with COPD defined by criterion B and those without COPD. In both cohorts, males formed the majority of COPD cases (cohort 1: 63.2 percent; cohort 2: 65.2 percent). The majority of children with COPD resided in urban areas (cohort 1: 59.6 percent; cohort 2: 70.7 percent). Twenty four percent (24 %) of children with COPD in cohort 1and 16.3 percent of children in cohort 2 resided in rural areas. Children residing in small urban areas formed the smallest proportion of children with COPD as defined by criterion B (cohort 1: 16.3 percent; cohort 2:13 percent).

The majority of children with COPD by criterion B (cohort 1: 81.6 percent; cohort 2: 69.5 percent), came from families that did not receive any health premium subsidy (Table 7.5). The proportion of First Nations children with COPD by criterion B was similar in both cohorts (i.e. 9.8 percent). The proportion of COPD cases that were on social welfare was 0.1 percent among cohort 1 children and 7.3 percent among those in cohort 2 (Table 7.5).

In both cohorts, children with COPD and those without COPD had similar median follow-up times, i.e. 8 years among those in cohort 1, and 7.5 years among those in cohort 2 (Table 7.5). The median age from birth to the time when a child was classified as having COPD by criterion B, was 3.7 years among children in cohort 1 and 5.4 years among those in cohort 2.

Table 7.5: Demographic Characteristics of Children with and without COPD by Criterion B

Characteristic	Cohort 1 (N=41171)		Cohort 2 (N=39864)	
	COPD N=2682	Non-COPD n=38489	COPD n=2049	Non-COPD n=37815
Gender, male%	63.2	50.3	65.2	50.8
Residence				
Urban %	59.6	63.7	70.7	63.9
Small urban %	16.3	16.9	13.0	16.7
Rural %	24.1	19.4	16.3	19.4
Social Economic Status (SES)				
No Subsidy %	81.6	86.2	69.5	72.5
Subsidy %	8.5	9.2	13.5	14.8
First Nations %	9.8	4.3	9.8	6.8
Social welfare %	0.1	0.4	7.3	5.9
Follow up				
Median (years)	8	8	7.5	7.3
Range (years)	0.9-8	0.01-8	1.6-8	0.001-8
Age at diagnosis (years)				
Median	3.7	n/a	5.4	n/a
Range	0.05-8		0.1-8	

7.4.2 Multivariate Survival Analysis to Determine Correlates of Chronic Obstructive Pulmonary Diseases (COPD) by Using Criterion B

Table 7.6 shows the univariate and multivariate analyses to determine the correlates of COPD incidence rates defined by using Criterion B. Table 7.7 shows the joint effect modification of cohort and SES as well as the cohort and area of residence on the COPD incidence rate.

The incidence rate of males was 1.7 times those of females, after taking into consideration of other covariates. There were no statistically significant differences between children on subsidy and children not on subsidy. Children on welfare had higher COPD incidence rate than children not on subsidy (IRR 1.31) (Table 7.6). The cohort and SES as well as the cohort and area of residence, jointly modified the COPD incidence rate (Table 7.7). First Nations children in cohort 1 had incidence rate that was 2.84 times that of the reference group (i.e. cohort 1 children, not on subsidy) (Table 7.7). However, cohort 2 First Nations had the COPD incidence rate that was only 1.3 times higher than the reference group (Table 7.7).

Cohort 1 children who resided in small urban areas had COPD rate that was 1.4 times that of the reference group (i.e. cohort 1 children, urban) (Table 7.7). In contrast, cohort 2 children who resided in small urban areas had incidence rates only that was almost similar (IRR=1.02) to that of the reference group (Table 7.7). Finally, cohort 1 children who resided in rural areas had COPD incidence rate that was 96 percent (IRR 1.96) higher than that of the reference group (Table 7.7). Unlike cohort 1 children, cohort 2 children who resided in rural areas had COPD incidence rate that was only 20 percent higher than that of the reference group (i.e. of 1.2) (Table 7.7).

Table 7.6: Cox Proportional Hazard Model to Determine the Correlates of Chronic Obstructive Disease (COPD) by Criterion B

	Univariate Analysis		**Multivariate Analysis**	
Variable	**Incidence Rate Ratio (IRR)**	**95% Conf. Interval**	**Incidence Rate Ratio (IRR)**	**95% Conf. Interval**
Cohort 2	Referent		Referent	
Cohort 1	1.51	1.42-1.62	1.74	1.61-1.90
Females	referent		Referent	
Males	1.72	1.62-1.83	1.72	1.62-1.82
No subsidy	Referent		Referent	
Subsidy	1.03	0.94-1.13	-	
First Nations	1.96	1.78-2.16	2.84	2.1-3.86
Welfare	1.62	1.38-1.91	1.31	1.11-1.55
Urban	Referent		Referent	
Small urban	0.87	0.80-0.94	1.47	1.15-1.89
Rural	1.04	0.97-1.12	1.96	1.57-2.45
Cohort and First Nations			0.76	0.62-0.93
Cohort and small urban			0.69	0.59-0.82
Cohort and Rural			0.60	0.52-0.70

Table 7.7: Joint Effect Modification of Cohort and Social Economic Status or Area of Residence on COPD Incidence Rates by Criterion B

Interaction Terms	Multivariate Incidence rate Ratio (IRR)	p-value
Cohort 1, no subsidy	referent	
Cohort 1, First Nations	2.84	<0.001
Cohort 2, First Nations	1.3	<0.001
Cohort 1, urban	referent	
Cohort 1, small urban	1.4	0.007
Cohort 2, small urban	1.02	0.007
Cohort 1, rural	1.96	<0.001
Cohort 2, rural	1.2	<0.001

7.5 .Internal COPD Case Validation

7.5.1 Introduction

This section outlines the internal validation process of COPD case definitions. Because of the chronic nature of COPD, it is plausible that once a child is diagnosed with COPD the child will continue to make healthcare visits for COPD-related reasons. Therefore, the validity of criterion A and B was determined (internally) by determining the proportions of children classified as having COPD who made one or more subsequent COPD-related visits during any time after they were classified as having COPD.

7.5.2 Internal Validation of COPD Cases Identified by Using Criterion A

Table 7.8 shows the proportion of children with COPD by criterion A, who made one or more subsequent visit post-classification (i.e. after they were classified as having COPD). Almost seventy percent (69.9%) of children in cohort 1 made one or more COPD related visits, while 67.7 percent of children in cohort 2 made one or more COPD-related visits after they were classified by using Criterion A (Table 7.8). When the analysis was restricted to only children who were continuously enrolled with Alberta Health and Wellness for at least 1 year post-classification, the proportion of children making 1 or more CHRMC related visits post diagnosis increased from 69.9 percent to 73 percent among cohort 1 children; and from 67.7 percent to 72 percent among children in cohort 2 (Table 7.8). When the same analysis repeated for only those who were continuously enrolled for at least 2 years after the COPD diagnosis, the proportion of children who made 1 or more visits further increased from 73 percent to 75.6 percent among cohort 1 children with COPD and from 72 percent to 74.6 percent among cohort 2 children (Table 7.8).

Table 7.8 : Proportions of Children who made COPD Related Visits Post-classification by Criterion A

	Period (years) of continuous enrolment with Alberta Health and Wellness					
	No restriction on continuous enrolment period to a maximum of 8 years		**At least 1 year of continuous enrolment post-classification to a maximum of 8 years**		**At least 2 years of continuous enrolment post-classification to a maximum of 8 years**	
Number of visits	**Cohort 1 N=7310 n (%)**	**Cohort 2 N=5396 N (%)**	**Cohort 1 N=6631 N (%)**	**Cohort 2 N=4819 n (%)**	**Cohort 1 N=5823 n (%)**	**Cohort 2 N=4196 n (%)**
0	2201 (30.11)	1743 (32.3)	1788 (26.96)	1350 (28.01)	1424 (24.45)	1066 (25.41)
1	1337 (18.29)	900 (16.68)	1209 (18.23)	795 (16.50)	1050 (18.03)	658 (15.68)
2	845 (11.56)	579 (10.73)	789 (11.90)	539 (11.18)	709 (12.18)	465 (11.08)
≥ 3	2927 (40.04)	2174 (40.29)	2845 (42.9)	2135 (44.30)	2640 (45.34)	2007 (47.83)
≥ 1	5109 (69.89)	3653 (67.7)	4843 (73.04)	3469 (71.99)	4399 (75.55)	3130 (74.59)

7.5.3 Internal Validation of COPD Cases Identified by Criterion B

The proportion of children making at least one visit post COPD classification by criterion B was 63.3 percent for cohort 1 and 51.2 percent (cohort 2) (without restriction on the period of continuous enrolment) (Table 7.9). When the analysis was restricted to only those children who were continuously enrolled with AHW for at least one year post-classification, the proportion of children who made at least one COPD visit was 99.9 percent and 100 percent for cohort 1 and 2 respectively (Table 7.9). With at least 2 years of continuous enrolment post diagnosis, the proportion of children making 1 or more visits was 99.96 percent for cohort 1 and 100 percent for cohort 2 (Table 7.9). With one or two years of continuous enrolment, the proportion of children with COPD by criterion B who made 3 or more visits was over 90 percent in both cohorts (Table 7.9).

Table 7.9: Proportion of children with COPD-related visits Post-classification by Criterion B

	Period (years) of continuous enrolment with Alberta Health and Wellness					
	No restriction on continuous enrolment period to a maximum of 8 years		At least 1 year of continuous enrolment post-classification to a maximum of 8 years		At least 2 years of continuous enrolment post-classification to a maximum of 8 years	
Number of visits	**Cohort 1 N=2682 n (%)**	**Cohort 2 N=2049 N (%)**	**Cohort 1 N=1654 N (%)**	**Cohort 2 N=1023 n (%)**	**Cohort 1 N=1568 n (%)**	**Cohort 2 N=965 n (%)**
0	984 (36.69)	1000 (48.80)	2 (0.07)	0 (0)	1 (0.04)	0(0)
1	51 (1.9)	36 (1.76)	45 (2.72)	29 (2.83)	41 (2.61)	23 (2.38)
2	120 (4.47)	61 (2.98)	113 (6.83)	56 (5.47)	108 (6.89)	50 (5.18)
≥ 3	1527 (56.94)	952 (46.46)	1494 (90.33)	938 (91.69)	1418 (90.43)	892 (92.44)
≥ 1	1155 (63.31)	1049 (51.2)	16529 (99.93)	1023 (100)	1567 (99.96)	965 (100)

CHAPTER EIGHT: DISCUSSION

8.1 Introduction

The purpose of this study was to develop case definitions for identifying children with chronic high-risk medical conditions (CHRMC) that place them at high risk for influenza - related complications from healthcare administrative data. Using those case definitions, the correlates of the prevalence and incidence of CHRMC were also determined. Therefore the objectives of this chapter are: a) to discuss pertinent findings as they relate to these objectives in the context of previous studies; b) to discuss the strength and limitation of the study, c) to discuss the practical applications of the study findings; d) to provide suggestions for areas for future research; and, e) to provide the conclusions.

8.2 Discussion of Study Findings

8.2.1 Case Definitions

The case definitions used in this study were a modification of the previously proposed case definition constructed based on the "hierarchy of accuracy" (137). Unlike most previous studies, discussed earlier on page 23, the case definitions used in this study incorporated the physician role when counting the number of physician office visits. This approach is unique in that different types of visits were assigned different weights depending on the role of the physician and therefore added a degree of certainty to the case definition. In addition to the degree of certainty, there is some hierarchy of severity graded from less severe (e.g. those who see only primary care physicians) to most severe (those who are hospitalised). The final case definitions included two distinct types: Criterion A: any of the component case definition of primary physician, consultant, emergency room or

hospitalization visits. Criterion B included any two of the component case definitions from criterion A.

There was a remarkable difference in the number of children identified by these criteria. In cohort 1, Criterion A identified five times more children with CHRMC than those identified by using criterion B. In cohort 2, criterion A produced 8 times more CHRMC cases than those identified by using criterion B. These differences are not surprising because criterion B requires more visits than criterion A and is therefore more stringent than A. Previous studies have shown that adding the number of visits may result in improved specificity but with loss of sensitivity (100, 112). Therefore, it is plausible that criterion A has high sensitivity but low specificity, while criterion B has a high specificity but low sensitivity, therefore accounting for the differential number of cases identified by the two case definitions.

Both of these case definitions may be useful for various purposes. In the context of influenza programs, these case definitions may be used to provide the minimum possible to the maximum possible number of cases. Criterion A is less stringent (likely higher sensitivity) therefore will likely produce the maximum possible number of children with CHRMC, while criterion B is more stringent (likely lower sensitivity) therefore will produce lowest number of children with CHRMC. In absence of additional sources of data, this information can help planners to incorporate the best-case and worst-case scenarios in their planning.

It is difficult to develop a perfect case definition for a group of chronic diseases that are not similar in terms of morbidity and healthcare utilization patterns. A recent study demonstrated that for each of the chronic disease studied i.e. asthma, coronary heart

disease, diabetes, hypertension and stroke, the best case definition was different in terms of number of visits required and the time frame required for a maximum yield in specificity sensitivity or kappa values (106). However, the case definitions developed in this study that are built on the hierarchy of accuracy, are likely to capture all CHRMC cases with an acceptable degree of accuracy, even though each disease within CHRMC is different.

8.2.2 Internal Validation of Case Definitions

The validation approach used in this study was unique in that it was based on the logical premise that once a child develops a chronic condition, he or she is expected to have the condition over a long term. With longitudinal data, it was therefore possible to validate the developed case definition using a new approach that requires evidence of continued healthcare use after a child is classified as having CHRMC.

Using this approach, the positive predictive values (PPV) could be calculated among those who were classified as having CHRMC, by using additional visit post-classification as a gold standard. The PPV in this context therefore refers to the proportion of children who were classified as being cases who made subsequent CHRMC-related visit post-classification. Using this approach, the maximum validity in terms of positive predictive values (PPV) was obtained when one or more visit was required for at least two years of continuous enrolment post-classification.

There was congruence in the PPV between the two cohorts when using both criterion A and B, in that the maximum PPV was obtained with at least 2 years of data post-classification. In both cohorts, criterion B had higher PPV than criterion A for identifying children with CHRMC. In cohort 1, the PPV of criterion A for identifying children with

CHRMC was 88.7 percent while that of criterion B was 94.6 percent. In cohort 2, the PPV of criterion A for identifying children with CHRMC was 88.1 percent, while the PPV for criterion B was 94.2 percent. A comparison of PPV from this study with previous studies that have examined the PPV of administrative data to identify children with CHRMC reveals mixed findings. Both high PPV 80-90 percent (96) and low PPV of 62 percent (16) have been previously reported. The differences in the observed PPV in this study with those observed in previous studies is not surprising because of the differences in data sources used, the definition of CHRMC and potential differences in the prevalence of CHRMC in this population and populations included in previous studies.

When a sensitivity analysis on PPV was done by restricting the analysis to COPD cases only, the maximum PPV was lower than those observed for the entire CHRMC. For COPD, the PPV were as follows: criterion A (PPV 75.6 percent, cohort 1, 74.6 percent cohort 2), while for criterion B the PPV were higher than those observed for CHRMC (i.e. cohort 1 94.96, cohort 2 100 percent). Once again, there were congruence in the PPV between the two cohorts with higher PPV observed for criterion B than criterion A and maximum PPV for those children with at least two years of enrolment post-classification.

Asthma is the most common chronic disease of childhood (156). Assuming that the majority of children with COPD have asthma, it is possible to compare the findings of this study with those of previous studies that have examined the validity of administrative data to identify individuals with asthma. Several studies have shown that the PPV of administrative data for identifying children with asthma was reasonably high, in order of 84 percent (106, 113). In this study, the PPV of administrative data for identifying children with COPD was 75%, which was lower than the previous studies. However, by using

criterion B, the PPV was higher than the previously reported on (>90%). However, the case definitions used in the previous studies were different from the one used in the present study.

The utility of this longitudinal approach to validate data is contingent upon the assumption that chronic diseases in children are more likely to be persistent. Therefore, this approach may have limitations in case of those chronic conditions in children which show improvement over time and therefore lower healthcare utilization. For example, one study showed that almost three quarters children with chronic conditions had status improvement over the 4-year period (107). Kozyrskyj *et al* (157) showed that only select group of children with asthma were more likely to have persistent asthma requiring continued use of healthcare over a two year period. Dombkowski *et al* (119) showed that by using Medicaid data there was moderate year-to-year agreement in children with asthma. The improvement or lack of year-to-year stability in healthcare utilization among children with chronic diseases may partly explain the low PPV values (<80 percent), especially among children who were identified by using criterion A, which is likely to capture both mild and severe cases of CHRMC.

8.2.3 Methodology Used to Determine CHRMC Incidence Rates

To determine incidence from administrative data, previous studies have applied a clearance period (also known washout period) of two to three years, in order to remove prevalent cases from the study population (158). The application of a washout period is necessary otherwise, prevalent cases may be erroneously misclassified as incident cases and therefore lead to an overestimate of incident cases. Applying the clearance period is reasonably accurate but may result in the loss of information from the early years of

observation and is dependent on the best duration of the clearance period. Therefore, the strength of the approach used in this study is that it did not require a washout period because children were followed from birth to the occurrence of the event. However, this approach may be more appropriate in examining the incidence of diseases in children, which may require up to 18 years of data. However, in adults using such an approach requires more than 18 years of data. Longitudinal data that spans from birth to more than 18 years may not be available, or if available may be fraught with high loss to follow up.

8.2.4 The Correlates of Incidence and Prevalence Rates

8.2.4.1 Gender

Regardless of the criterion used, males had higher CHRMC incidence rate than females. The incidence rates of males were between 30 and 40 percent higher than those of females when using criterion A. The CHRMC incidence rates were also higher in males than females when using criterion B (rates 40 percent to 70 percent higher in males than females). Therefore, there was congruence in the role of gender on prevalence or incidence between criterion A and B. When the analysis was restricted to COPD only, males still had higher incidence rate than females. When using criterion A, the COPD incidence rate among males was 78 percent higher that that of females, while by using criterion B the rate among males was 40 percent higher. The higher rates of chronic respiratory diseases such as asthma or COPD among males than females are consistent with other studies (159).

8.2.4.2 Residence

In this study the prevalence and incidence varied by the area of residence. With few exceptions, children in rural areas had higher incidence or prevalence rates of CHRMC than those residing in urban areas. In some circumstances, the variation of incidence or prevalence of CHRMC by area of residence was jointly modified by the cohort or age of the study participants. However, in the majority of cases, children in rural areas had higher CHRMC incidence rate (i.e. Incidence Rate ratio >1) or higher CHRMC prevalence rates (i.e. Prevalence Rate Ratio >1) than children residing in urban areas. These findings were replicated when the analysis was restricted to only those children with COPD.

The variation of incidence or prevalence of CHRMC by rural area is in contrast with other studies that have found that rural areas were associated with better health status than urban areas among people with asthma, or other chronic respiratory conditions (160). To the contrary, a recent study showed higher mortality from respiratory diseases among those in rural compared to those in urban areas (161). The inconsistencies may partly be because there is no universal definition of rurality (162).

The comparison of prevalence or incidence of CHRMC between children residing in small urban areas versus those in urban areas was less clear-cut than that of rural-urban one. The inconsistency was remarkable for incidence or prevalence defined by using criterion A. For example, children residing in small urban areas had higher incidence rate than those in urban areas among children aged 0-2 and 3-4 years regardless of other covariates. However, children aged 3-4 and 7-8 years residing in small urban had lower CHRMC incidence or prevalence than those residing in urban areas but only in cohort 2 (criterion A). When using criterion B to define CHRMC, the prevalence or incidence was

consistently higher among children residing in small urban areas than those in urban areas. The same finding of higher COPD prevalence or incidence in small urban children than those of urban areas was observed when the analysis was restricted to COPD only.

8.2.4.3 Social Economic Status

In this study, the ability to pay healthcare insurance premiums was used as a proxy for social economic status. The four groups of social economic status were as follows (in order from high to low SES): no subsidy, subsidy, First Nations and welfare. With minor exceptions, the incidence and prevalence of CHRMC did not differ significantly between children on subsidy compared to those not on subsidies, regardless of the criterion used to define CHRMC and other covariates. The same findings were observed when the analysis was restricted to children with COPD.

First Nations had higher CHRMC incidence and prevalence rates than children not on subsidy regardless of cohort, age, residence and the criterion used to define CHRMC. Similarly, First Nations children had higher COPD incidence and prevalence than children who did not receive subsidy regardless of the criterion used, residence and age. The finding of higher prevalence or incidence rate of CHRMC among First Nations compared to other is consistent with previous studies. Previous studies have shown higher rates of office or emergency room visit (163) or hospitalization (164, 165) for chronic diseases such as asthma or COPD. Higher rates of healthcare utilization for chronic diseases are suggestive of higher prevalence rates of these chronic conditions in First Nations compared to non First Nations. It is also well known that First Nations have disproportionate burden of chronic disease than the rest of the population (166) .

Finally, the incidence and prevalence rate of children on welfare compared to children not on subsidy was variable depending on the criterion, age and cohort. The comparison of incidence or prevalence of CHRMC among children on welfare was not consistent across criterion A or B. The CHRMC incidence and prevalence rates were higher, lower or same as those of children not on subsidy. However, when the analysis was restricted to COPD, children on welfare had consistently higher incidence and prevalence of COPD regardless of cohort, criterion and residence. For a large part those on welfare had higher CHRMC prevalence and incidence than those not on subsidies. Previous studies have shown that people of low SES (e.g. those with no income) tend to be heavy users of healthcare (167), therefore likely to be defined as a case. In one European study, respiratory diseases were more prevalent on those with low SES (defined by education level or social class) than those of higher SES level (168). Roos *et al* (169) showed that physician visits and hospitalization for all chronic diseases were higher among residents of low-income neighbourhoods than among their intermediate and high-income counterparts.

In summary with few exceptions, children coming from either welfare or First Nations families had higher incidence and prevalence of CHRMC than those not receiving subsidy. This was consistent with previous literature that shows higher burden of chronic diseases among individuals who are poor than those with a higher socioeconomic status.

8.2.5 Impact of Historical Events on CHRMC Prevalence and Incidence Rates

This study employed a unique approach of using two birth cohorts to allow detection of disease patterns that may be attributable to changes in organisation rather than the true changes in disease prevalence or incidence. The two study cohorts were longitudinally followed during the period when there were known changes in the organisation of Alberta

Health and Wellness Databases. Three main historical events occurred during the study period that may potentially affect healthcare utilization patterns therefore the prevalence or incidence estimates. These were: a) introduction of Bill C-31 b) regionalization of the healthcare system and c) organization changes within AHW. The implication of these changes on the healthcare utilization and therefore prevalence are discussed.

8.2.5.1 Introduction of Bill C-31

As described earlier, the legislative amendment to the *Indian Act of Canada* was adopted in 1985. This amendment led to the introduction of Bill C-31 that specifically affected First Nations. Prior to 1985 marrying a person without a First Nations' Treaty Status led to the loss of First Nations Status. No children born of such union got the First Nations status either. Because of the introduction of Bill C-31, in Canada, there was an increase in the population of registered or Status Indian by over 100,000 people during the period between 1985 and 2001 (170). Such changes were evident in this study. Cohort 1 was composed of a smaller proportion of children who were First Nations (4.7 percent) than cohort 2 (6.9 percent). However, these changes did not affect the overall prevalence or incidence of CHRMC. Cohort 1 still had higher incidence rate than cohort 2. In addition, the prevalence of CHRMC was higher among First Nations of cohort 1 than those of cohort 2 (cohort 1 41 percent, cohort 2 29.1 percent). The discrepancy between the CHRMC prevalence of children in cohort 1 may be due to improvement on living conditions over time, artefact of recording First Nations status or both. For example, analysis of the Aboriginals' living standards in terms of employment, education, income, showed an overall trend in improvement over twenty years from 1981-2001 (170).

8.2.5.2 Regionalization

In 1994, Alberta Health announced changes in the way healthcare in Alberta was managed. This included establishment of 17 Regional Health Authorities as well as large reductions in acute care spending (171). The 17 Regional Health Authorities replaced over 200 separate boards and other administration units (172). Many changes resulted from the regionalization of healthcare. Of relevance to this study, was a significant cut in acute care spending that resulted in fewer acute care beds being available. For example, for the period prior to and after the regionalization, there was a 25.6 percent fall in age standardized hospital separation rates in Alberta (171). These changes were also evident in this study where the comparison of age specific incidence rates of CHRMC on the basis of hospitalization (a component of criterion A and B), showed significantly higher CHRMC-related hospitalization rates in cohort 1 than cohort 2 (Figure 5-4). The regionalization process may also explain the observed significantly higher rates in emergency room visits in cohort 2 than cohort 1 (Figure 5-3). It is likely that children who prior to regionalization would have been hospitalized, they were not due to acute bed shortage. Therefore, the higher emergency room visits likely compensated for the lower hospitalization rates among children in cohort 2. Therefore, higher CHRMC prevalence among children in cohort 1 than those in cohort 2 cannot be entirely explained by the regionalization process.

8.2.5.3 Data Organization Changes in Alberta Health and Wellness

Prior to 1994, the physician claims file had a single diagnosis field coded using three-digit ICD-9 CM codes. After that year, the claims file had three diagnosis fields available using four digits ICD-9 CM codes (173). Therefore intuitively, one would expect more CHRMC related visits in cohort 2 (born in 1994/95) than cohort 1 (born 1984/85), because

the additional fields would capture relevant diagnoses even though they were not the main reason for the visit. In this study, 3522 additional CHRMC-related visits were identified from the additional diagnostic field. However, children in cohort 1 made more CHRMC-related visits than children in cohort 2. Therefore, these additional visits did affect prevalence of CHRMC in cohort 2, but was not enough to make children in cohort 2 to have higher prevalence than those in cohort 1 (cohort 1: 86,761 visits versus cohort 2: 68,376 visits).

8.3 Strengths

8.3.1 Population Coverage

One of the main advantages of healthcare administrative data for surveillance purposes is that of population coverage (23). Population coverage refers to inclusion of the entire population. The total number of children in cohort 1 and 2 was 41171 and 39864 respectively. These numbers were consistent with the Alberta Government Services published number of children born in the respective years (174). The similarity between the numbers from this birth cohort with those published by the Alberta Government Department responsible for maintaining vital statistics events, provides evidence of the population coverage of the two study cohorts. However, a large sample size may be problematic because the standard error of any observed differences decreases with increasing sample size, therefore a small difference that is clinically unimportant appears statistically significant (175). To mitigate this problem, comparison of rates were done by using the 95 percent confidence intervals rather than relying on p-values only.

8.3.2 Congruence of Epidemiological Patterns of CHRMC

By using two cohorts, the consistency (congruence) of epidemiological patterns can be assessed. Other investigators (176) have recommended that when epidemiological patterns of diseases are consistent (congruent) across data sources or periods, the observed healthcare use is likely to reflect the population's underlying prevalence or incidence of diseases. Therefore, by using two cohorts a decade apart, helped to discern congruence of prevalence or incidence or CHRMC while taking into consideration other socio-economic variables, as well as other contextual or historical artefacts that may affect healthcare utilization.

8.3.3 Alternate Approach to Data Validation

To assess the validity of administrative data, clinical charts are often used as "the gold standard" (23, 115, 177). Using this approach, a definite diagnosis is assigned to individuals with a specified number of healthcare visits for a particular disease during a specified period with a demonstrated diagnosis in the chart. However, charts have been shown to be unsuitable gold standards in a setting where patients are attended by more than one primary care physician (100). In such settings, using a chart from one physician alone may provide erroneous picture of patients' health care utilization profile, due to missing records on episodes of care recorded at a different physician's office. For example, in a recent study, verification of asthma diagnosis from charts by physician experts in Ontario was hampered by lack of documentation in the charts, leading to misclassification of asthma cases (113). The accuracy of charts also depends on how completely clinicians records their findings in sufficient details to enable a chart reviewer to make unequivocal judgement on presence or absence of a disease (178).

Alternatively, self-reports from surveys have also been used to validate information from administrative data (106, 179). However, this approach is dependent upon the availability of data on the disease of interest. This may not often be the case especially for rare diseases.

Given problems associated with charts or lack of relevant surveys coupled with the lack of true gold standard for validating administrative data, it was necessary to explore an alternative validation approach suitable for situations where chart review may not be feasible. Recently, a panel of experts on the use of administrative data has called for studies to explore alternative to chart reviews, i.e. establishing 'truer' gold standards (180).

The panel of experts also called for research on "internal consistency algorithms" as a method of validation. In this study, the internal consistency of data was established through the longitudinal follow-up of the study participants, comparing epidemiological patterns of CHRMC incidence and prevalence between the two cohorts, comparing the epidemiological patterns of this study with those from previous studies and by comparing the patterns between two case definitions.

In summary, the validation approach used in this study was logical and provides assurance on the validity of cases identified because of several reasons. First, previous studies have shown that the likelihood of physician contact was higher in children with poor health or chronic medical problems than those without chronic diseases (181). Secondly, up to 99 percent of the Alberta population is covered by the Alberta Healthcare Insurance Plan. This universal coverage minimises barriers to health care access, which would result in selection bias. Therefore, although utilization patterns are subject to external factors, it is unlikely to be due to affordability. Thirdly, AHW collects premiums; therefore, the list of enrolees and their corresponding address is updated on a regular basis. This allowed for more accurate estimations of time when an individual was insured with AHW, and when one lost their insurance coverage. Most physicians in Alberta are paid through fee for service arrangement whereby a fee is paid whenever the physician provides a medically insured service (182). This payment arrangement provides a mechanism for tracking most patient-physician encounters in Alberta, or elsewhere if one is still insured by AHW. Finally, given the fact that the healthcare system is publicly funded, there are no financial disincentives for obtaining medical care. Therefore, it is very likely that children

with chronic disease will seek healthcare. The more the healthcare contacts, the more the likelihood of capturing cases from healthcare administrative data.

8.4 Limitations

8.4.1 Using Secondary Data for Research

Secondary data such as healthcare administrative data are created for other purposes than the objective of this study. Therefore, the study is limited just like any other study that uses secondary data for research purpose. One of the key limitations inherent in using secondary data is the failure to adjust of other potential confounders. For example, only few variables as suggested by the Andersen model of healthcare utilization were available. For example, having a regular source of care has been shown to encourage the use of health services (183). Other important variables that were not available but are important determinants of healthcare utilization include maternal characteristics such as education and healthcare use that have also been shown to be related to the volume of healthcare used by children (184).

The Anderson model outlines enabling factors as also important when considering healthcare utilization. For example, one of the key enabling factors is physician supply, an ecological measure also known as physician per population ratio. This study did not examine the impact of physician per population ratio. However, it is likely that its exclusion is not a serious problem because other studies elsewhere in Canada have shown that access to physician as measured by the proportion of residents who contact a physician at least once over a year is uniform regardless of the physician to population to ratio (27). In addition the ratio may be inaccurate if does not distinguish physicians who engage in clinical activities from those who do not (162, 185). Moreover, there is evidence of a

decrease in the hours physician work that cannot be accounted when using a simple physician to population ratio (186).

8.4.2 Loss to Follow-Up

The loss to follow up was 18.7 percent for children in cohort 1 and 20 percent for those in cohort 2. This high loss to follow-up may be partly due to the fact that Alberta experienced a net out-migration (i.e. more people leaving the province than coming in) between 1985 and 1995 (172). One study conducted over a period of five years (between 1984-1989), reported an average loss to follow up of 6 percent per year amounting an overall loss to follow up of 25 percent over five years (104). In Manitoba, among children aged 0-14 the loss to follow-up in one year was 2.7 percent (137). It is likely that the observed differences in the loss to follow-up within and between provinces might be related to the characteristics of the study population as well as other historical artefacts such as economic downturns, which might have lead to the net provincial out-migration.

In survival analysis, individuals lost to follow-up are censored at the last date known to be in the cohort. The loss to follow-up can lead to selection bias in the CHRMC incidence if the censorship is related to the outcome. This is also known as informative or dependent censoring. Informative censoring occurs when the probability of being censored is dependent of on the subjects' prognosis for failure (187-189). In this study, informative censoring would have occurred if those who were censored had a high probability of being classified as having CHRMC. This is unlikely because of several reasons. First, the proportion of children who were lost to follow up versus those who remained in the cohort was qualitatively similar in terms of gender, residence and social economic status (Table 4.4, page 74). In addition the majority of those who were lost to follow-up (cohort 1: 96.9

percent , cohort 2 97.4 percent) were lost due to out-migration, rather than death. Therefore, the observed loss to follow up is likely random and likely unrelated to a higher probability of being classified as having CHRMC.

Censoring of individuals may also bias the incidence by increasing the time at risk if the date of loss of insurance coverage or death is inaccurate or greater than actual date (150). This may result in lower incidence rate than the actual incidence, because of the larger denominator in terms of person years. The accuracy of dates was not verified. However, it is likely that this is not a serious problem because Alberta Health and Wellness collects healthcare insurance premiums, therefore the list of enrolees and their corresponding social demographic information are updated on a regular basis.

A small proportion of children in both cohorts (cohort 1: 0.9 percent and cohort 2: 1.7 percent) had multiple dates when they lost their insurance coverage. This means that these individuals had their insurance coverage interrupted by leaving and coming back into Alberta more than once during the study period. The dates of return to the province were not available, therefore the duration of follow up was based on the first recorded date of loss of insurance coverage. Similar problems have been reported elsewhere in Canada. In Manitoba, one study estimated that during one year of follow up, 1 percent of the population cancelled their insurance coverage but the dates of cancellation were unknown (137). Using the first date of loss of coverage for those individuals with unknown dates of cancellation underestimates the total duration of follow-up. Therefore, the resulting incidence rates are likely an overestimate because of the smaller denominator, which combines the number of individuals at risk as well as the total duration of follow-up.

8.4.3 Misclassification Bias of the Correlates

One of the objectives of this study was to determine the correlates of incidence and prevalence of CHRMC. With the exception of gender, study participants could be potentially misclassified in terms of residence or social economic status. In the next paragraphs, I therefore discuss the potential implication such misclassifications on the prevalence or incidence of CHRMC.

8.4.3.1 Residence

The area of residence was based on census divisions that were developed by Statistics Canada for census purposes. Based on availability of healthcare sentences, the 19 census divisions that were divided into three major residential groups: rural, small urban and rural. Those classified as urban would be expected to have unlimited healthcare services while those in rural areas would be expected to have limited healthcare services. During the eight years of follow-up, 12.1 percent of children in cohort 1 and 10.8 percent of those in cohort 2, resided in more than residential category. This study did not examine the impact of such migration between residential categories. However, it is likely that the impact of such migration is minimal given that the majority were of children did not change their residence (87.9 percent cohort 1, 89.2 percent cohort 2). Future studies should examine the changing nature of residence on the incidence.

8.4.3.2 Social Economic Status

Four levels of social economic status (SES) were available based on the ability to pay healthcare premiums. The levels were welfare (limited income), First Nations (poor), on subsidy (working poor) and no subsidy (higher SES status). As expected, children changed their SES status, moving from one stratum to another. Specifically 25.5 percent of

children in cohort 1 and 28.5 percent in cohort 2 changed their social economic status during the eight years of follow up. The study used only the baseline SES and did not examine the impact of changes in SES status during the study period.

8.5 Applications of Research Findings

This section outlines the potential applications of the study findings.

8.5.1 Immunization Surveillance

Immunization surveillance involves the monitoring of vaccination coverage rates on a regular and timely fashion to allow for public health interventions in target groups such as children with CHRMC. Data on the incidence and prevalence of CHRMC are some of the key surveillance indicators for diseases (86). These indicators are most relevant to public health officials and program planners, who need flexible and timely information to evaluate annual influenza vaccination coverage.

Analysis of administrative data using the method proposed in this study would require yearly analysis to generate the most current list of children with CHRMC. Then using criterion A, which is likely to have maximum sensitivity children with CHRMC can be identified for supplying denominator for immunization monitoring, or for generating a list of eligible target groups who are active within a specified population.

8.5.2 Reminder and Recall Systems

Among the strategies needed to improve vaccination coverage levels include the use of reminder and recall systems and standing orders of vaccination for eligible groups (190). A reminder system reminds clients of upcoming immunization visits while recall systems reminds clients of overdue vaccinations. Examples of reminder/recall systems include letter, postcard, telephone autodialer or in person. A standing order is a reminder to

healthcare workers to vaccinate individuals whose medical records have been flagged as being eligible for vaccination. A recent meta-analysis that examined the effectiveness of recall/reminder systems, found that these systems resulted in improvements of childhood influenza of more than 20 percentage points compared to control (190). However, recall and reminder systems have not been widely adopted. Some of the reasons for lack of wide adoption may be reluctance of physician to adopt such systems due to the lack of easy way for identifying eligible, target groups (191). The programmatic challenges of identifying at risk target groups has been echoed elsewhere (16). The methodology used in this study offers a simple and practical way for identifying at risk target groups for vaccination.

This methodology can also be used to determine real time vaccine coverage. However, such a system would work best in those jurisdictions where billing records can be used to determine both the eligible population as well as vaccine receipt (110).

8.5.3 Immunization Registries

Methods used to identify persons with CHRMC can provide a starting point for establishment of an influenza immunization registry. If immunization registries are already in existence, methods developed in this study can be used to enhance the existing immunization registries.

8.5.4 Pandemic Planning

Influenza viruses can cause widespread epidemics (known as pandemics). Pandemics occur when a novel influenza virus emerges against which the vast majority of the world population has no immunity (192). Therefore, during a pandemic vaccine shortages are very likely because of inadequate production or increased demand. Distribution of vaccine during a pandemic will most likely be prioritised according to priority groups such as

children or adults with CHRMC (193-195). Methods developed in this study, therefore can be used to support pandemic planning activities. For example, prevalence and incidence of CHRMC can be used by pandemic planners to estimate logistic needs during a pandemic such as vaccine supply to the population segment at highest risk of morbidity and mortality from influenza infection.

8.6 Suggestions for Future Studies

Given the limitations stated above, future studies should examine the implications of the limitations stated. First, future studies should examine the impact of the longitudinal changing nature of social economic status and area of residence and its impact on classification algorithms for chronic diseases from administrative data. Secondly, using a triangulation of data sources the methods developed in this study should be further refined by determining the sensitivity and specificity of the case definitions. This study could not determine those validity indices because of the lack of external data sources. Finally, future studies should also focus on using this approach in adults, who more likely to have stable and well-defined chronic diseases compared to children who are likely to have chronic diseases that improve with time.

8.7 Conclusions

The validation of individuals with CHRMC through longitudinal data analysis and by examining coherence within similar cohorts provides a new practical way for identifying and validating case definition for identifying children with chronic diseases. This approach is simple and practical and has high positive predictive value compared to previous studies. This approach can be applicable to influenza surveillance in children and beyond and provides a sample of children with CHRMC with reasonable accuracy. Although this study focused on influenza programs, the findings from this study can be easily adopted for other chronic conditions.

This study advances the methodology for identifying individuals from administrative in several important ways. First, the case definitions were constructed by incorporating speciality of the physician, which adds a degree of accuracy to the identification algorithm. Secondly, the study introduces a practical way of validating the case definition by examining consistence (congruence or coherence) of epidemiological patterns within the data and across the two cohorts, as well as consistency with previous studies. Lastly, the study provides two case definition at the opposite end of the spectrum: one with possibly highest sensitivity and another with possibly highest specificity to enable users of the data to have all possible range of outcomes when trying to plan based on best-worst case scenario. Future studies should test and refine this methodology to children older than eight years, and adults with chronic diseases.

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APPENDICES

Table A.1: A List of Chronic High Risk Medical Conditions (CHRMC)

#	Description	ICD-9-CM
A: Chronic disorders of the cardiovascular system		
1.	Chronic rheumatic heart disease	393-398
2.	Ischaemic heart disease	410-414
1.	Congenital heart disease (especially cyanotic heart diseases)	745-747
2.	Chronic pulmonary heart diseases	416
3.	Other heart diseases (e.g. cardiomyopathy, dysrthmias, heart failure)	424-429
4.	Cerebral vascular diseases stroke, hemiplegia	430-438,342
5.	Diseases of arteries, arterioles and capillaries	440-447
B: Chronic pulmonary disorders		
6.	Chronic obstructive pulmonary diseases (COPD) and allied conditions (chronic bronchitis, emphysema, asthma, bronchiectasis, extrinsic allergic alveolitis and COPD not elsewhere classified	490-496
7.	Other diseases of respiratory tract e.g. empyema, lung or mediastinum abscess	510-519
8.	Pulmonary Tuberculosis	010, 011 012, 018
9.	Sarcoidosis	135
C: Chronic metabolic conditions		
10.	Diabetes Mellitus	250
11.	Other disorders of pancreatic internal secretion	251
12.	Other metabolic disorders and immunity disorders e.g. Congenital disorders of immune (Deficiency humoral immunity, cell mediated immunity, T-defect, single complement deficiency or dysfunction, combined immunity deficiency respectively to the coded listed on the right column. Mechanism	270-279
D: Hemoglobinopathies		
13.	Hereditary haemolytic anaemia e.g. Sickle cell disease, coagulation defects, purpura other haemorrghic conditions	282,286-289
E: Immunosuppression due underlying disease or therapy		
14.	HIV/AIDS	042-044
15.	High levels of corticosteroid to control conditions such as: RA, endocrine disorders, severe psoriasis, systemic lupus Erythromatosis (SLE)	710, 714.0,714.1, 715
16.	Crohn diseases, ulcerative colitis	555-556

#	Description	ICD-9-CM
	F: Malignant neoplasms	
17.	Malignant neoplasm of lip, oral cavity and pharynx	140-149
18.	Malignant neoplasm of digestive organs and peritoneum	150-159
19.	Malignant neoplasm of respiratory and intrathoracic organs	160-165
20.	Malignant neoplasm of bone connective tissue, skin and breast	170-176
21.	Malignant neoplasm of genitourinary organs	179-189
22.	Malignant neoplasm of other and unspecified sites	190-199
23.	Malignant neoplasm of lymphatic and haematopoietic tissue	200-208
24.	Hereditary and degenerative disease of central nervous system (CNS)	330-337
25.	Other disorders of CNS e.g. multiple sclerosis, other demylinating disease of CNS, hemiplegia, hemiparesis, infantile cerebral palsy, other paralytic syndromes	340-344, 290
	G: Chronic Renal diseases	
26.	Chronic glomerulonephritis	582
27.	Other chronic renal diseases e.g. chronic renal failure, renal failure unspecified, renal sclerosis, disorders of impaired renal function.	585-588

The Letter of Ethics Approval

JUN-15-2004 19:22 U OF C OFF. MED BIOETHICS 403 283 8524 P.01/01

FACULTY OF MEDICINE | UNIVERSITY OF CALGARY

2004-06-15

OFFICE OF MEDICAL BIOETHICS
Room 93, Heritage Medical Research Bldg
3330 Hospital Drive NW
Calgary, AB, Canada T2N 4N1
Telephone: (403) 220-7990
Fax: (403) 283-8524
Email: omb@ucalgary.ca

Dr. E.A. Henderson
Community Health Sciences
HMRB
Calgary, Alberta

Dear Dr. Henderson:

RE: The Utility of Administrative Data for Surveillance of Children with Chronic High Risk Medical Conditions (CHRMC) That Places Them at Risk for Influenza Related Complications

Grant-ID: 1781

The above-noted thesis proposal (dated May 2004) has been submitted for Committee review and found to be ethically acceptable.

Please note that this approval is subject to the following conditions:

(1) consent for access to personal identified health information in retrospective chart review is not required on grounds considered under Section X of the Health Information Act,

(2) a copy of the informed consent form must have been given to each research subject, if required for this study;

(3) a Progress Report must be submitted by 2005-06-11, containing the following information:
- i) the number of subjects recruited;
- ii) a description of any protocol modification;
- iii) any unusual and/or severe complications, adverse events or unanticipated problems involving risks to subjects or others, withdrawal of subjects from the research, or complaints about the research;
- iv) a summary of any recent literature, finding, or other relevant information, especially information about risks associated with the research;
- v) a copy of the current informed consent form;
- vi) the expected date of termination of this project.

(4) a Final Report must be submitted at the termination of the project.

Please note that you have been named as a principal collaborator on this study because students are not permitted to serve as principal investigators. Please accept the Board's best wishes for success in your research.

Yours sincerely,

Christopher J. Doig, MD, MSc, FRCPC

Chair, Conjoint Health Research Ethics Board

CJD/
c.c. Child Health Research Committee
Office of Information & Privacy Commissioner
Dr. T. Noseworthy (information)
Research Services

Source of Funding

07/07/2004 12:25 403-291-2571 PLC INFECTION CNTRL PAGE 02/07

Alberta Children's Hospital
1820 Richmond Road SW
Calgary, Alberta, Canada T2T 5C7
website www.calgaryhealthregion.ca

Child Health Research Office
Telephone: (403) 943-7241
Fax: (403) 543-9111
E.Mail: marilyn.ellergodt@calgaryhealthregion.ca

calgary health region
Alberta Children's Hospital

28 June 2004

Dr. Elizabeth Henderson
Department of Infectious Disease
Health Sciences Center
The University of Calgary

Dear Dr. Henderson:

Re: The Utility of Administrative Data for Surveillance of Children with Chronic High Risk Medical Conditions (CHRMC) That Places Them at Risk for Influenza Related Complications - $13,084

The above grant has been reviewed on behalf of the Alberta Children's Hospital Foundation by the Child Health Scientific Review Committee and the Child Health Research Executive Committee. I am happy to inform you that this project has been funded in the amount specified above.

Funding will be available upon receipt of approval from the Conjoint Health Research Ethics Board. This award is contingent on your not accepting overlapping funds to do this same project, although cost-sharing amongst funding agencies is quite acceptable. It is our understanding that you want these funds administered through The University of Calgary. Would you please contact Marilyn Ellergodt, Child Health Research Office, to activate these funds.

Within six months after you have completed this project, the Child Health Research Executive Committee would like to receive a short one-page summary of the progress made. As the purpose of these grants is to provide seed money in establishing research programs, we would be particularly interested in how the ACH Foundation might have helped towards obtaining funds from other sources.

For your information, please find attached a copy of the reviewers' comments. Congratulations and best wishes for a successful scientific endeavour.

Yours sincerely,

James D. Kellner, MD, MSc, FRCPC
Chair
Child Health Scientific Review Committee

Marilyn Ellergodt
Child Health Research Administrator

cc Calgary Health Region Finance
Fund Accounting, U of C