The Incidence, Prevalence and Mortality of Ischemic Heart Disease in Alberta

By

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Abstract

In 2008, cardiovascular disease accounted for 29% of all deaths in Canada. Yet information on the incidence, prevalence, and mortality of IHD (ischemic heart disease) over time in Canada or in Alberta has not been fully organized or modeled systematically. An overall picture of IHD in the population should give policy-makers, researchers, and clinicians a greater understanding of the pattern and magnitude of the disease. This knowledge can then be used to organize health care resources, to define health priorities for specific regions, and to develop research.

The two major questions were:

1) What has been reported on the incidence, prevalence and mortality of IHD in Canada and in the provinces of Canada?

2) Can existing publicly available Alberta data be organized and analyzed in a systematic fashion to provide policy makers insights on the incidence, prevalence, and mortality of IHD in Alberta?

To fulfill the first aim of the paper, a systematic review of literature was conducted to find existing information on IHD in Canada and Alberta. The research revealed that hospital data was used as a proxy for incidence rates and that incidence rates were decreasing from 1975 to 2002. Vital statistics were used to determine mortality rates by review articles that reported decreasing mortality rates after the mid-1970's. Prevalence of MI was reported to be higher in men than women by one study that used a self-administered survey in 2000/2001.

This project modeled IHD incidence, prevalence, and mortality in Alberta using publicly available surveillance data from the Alberta Health web site. The dataset included patients who were Alberta residents. The analysis used a logistic regression, four independent variables (year, age groups, sex, and geography) as well as interactions among these four independent variables. Overall, incidence and mortality probabilities have decreased over time while prevalence probabilities showed signs of stabilizing over time. Males have higher incidence and mortality probabilities than females. Both sexes exhibited increases in incidence and prevalence with age. These findings show that current preventative and treatment measures are indeed decreasing IHD incidence and mortality in Alberta. Despite the indication of effective IHD health care measures, the South zone shows a statistically lower

decline in mortality compared to other health zones. Further research might focus on the reasons behind this difference in mortality.

Preface

This thesis is an original work by Zing-Wae Wong. No part of this thesis has been previously published.

Acknowledgement

I would like to express my deepest appreciation to my committee chair, Professor Don Schopflocher, who continually provided support and guidance. His thoroughly planned curriculum led to a fulfilling thesis. Without his guidance and persistence help, this thesis would not have been possible. I could not imagine a better thesis advisor for my thesis.

I would like to thank my committee members, Professor Don Voaklander and Dr. Colleen Norris, whose work and teaching demonstrated the importance of surveillance epidemiology.

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Chapter 1: Introduction

The Public Health Agency of Canada gave a conservative estimate of 1.6 million Canadians living with heart disease or the effects of stroke in 2009. [1] In 2008, cardiovascular disease (CVD) accounted for 29% of all deaths in Canada. [2] In year 2000, CVDs were the second most costly contributor to the total health care cost in Canada accounting for $7.6 billion in direct costs. One of the largest components of CVD is ischemic heart disease (IHD). [1] In fact, Alberta Health cited IHD as one of the leading causes of death in Alberta, responsible for 112 deaths per 100,000 people in Alberta in 2004. [3]

Cardiovascular disease encompasses: atherosclerosis, hypertension, IHD, and stroke. Of the CVDs, IHD is the largest component of CVD. [4] Although all the CVDs are associated with common risk factors, the relative importance of risk factors such as smoking, hypertension, and hyperlipidemia differs among them. The relative improvements in treatments have also differed among these conditions in both acute in-hospital settings and in outpatient settings. [5] For these reasons, this thesis focused on IHD because it is one of the major components of CVDs.

Currently, information on the incidence, prevalence, and mortality of IHD over time in Canada or in Alberta has not been fully organized and or modeled systematically. An overall picture of disease in the population should give policy-makers, researchers, and clinicians a greater understanding of the pattern and magnitude of the disease. This knowledge can then be used to organize health care resources, to define health priorities for specific regions, and to develop research. [6]

1.1 Objectives

The goals of this project were to: 1) find what is known about the incidence, prevalence and mortality of IHD in Canada and in the provinces of Canada, and 2) organize and analyse existing publicly available Alberta data to provide insights to policy makers on the incidence, prevalence, and mortality of IHD in Alberta.

1.2 Significance

This is the first project in Alberta and Canada to use administrative data to estimate incidence, prevalence and mortality in Alberta organized by zones, age groups, sex, and year. While decision makers can call up IHD rates for any intersection of these variables by specifying a gender, an age grouping, a year and a geographic zone, aggregate patterns considering these variables simultaneously are not available because they are difficult to examine. An understanding of these broader patterns may be useful to better organize health care resources.

In the sections to follow I briefly described IHD, the way in which people with Ischemic Heart Disease are recorded, the process of health surveillance to track cases of IHD, and then briefly described what is known about rates of IHD in Canada and Alberta. The last two chapters are a systematic review of IHD rates in Canada and Alberta followed by the modelling of the administrative data from Alberta.

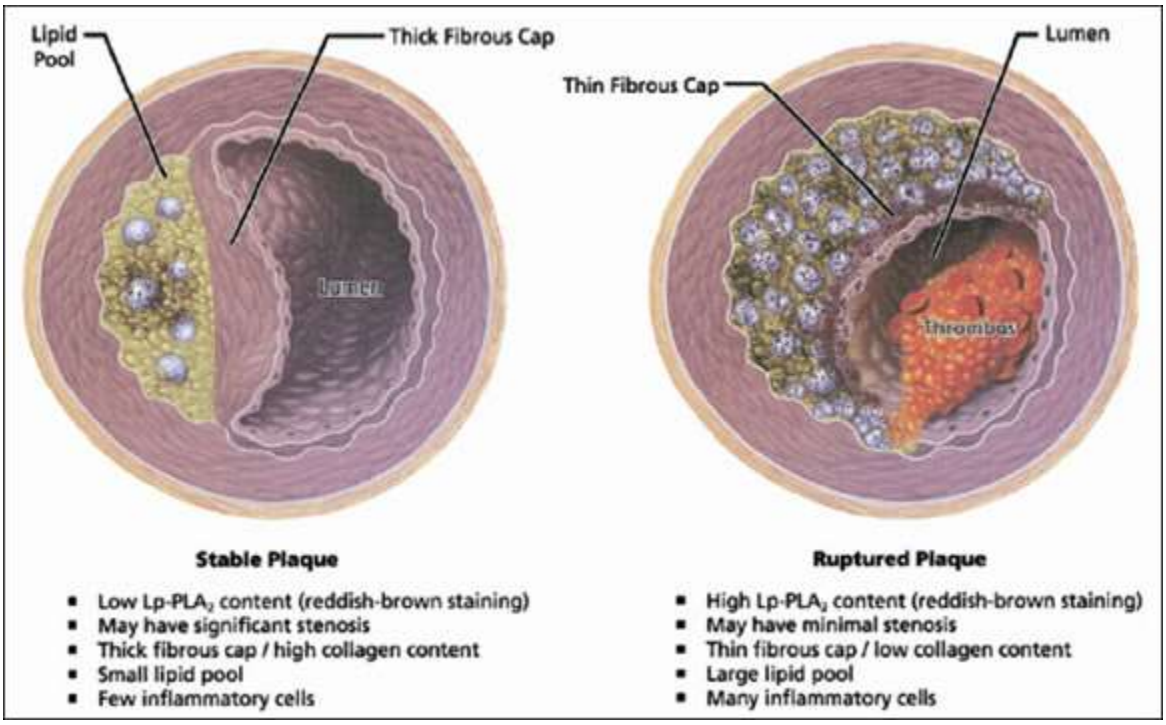
Chapter 2: Background

2.1 Ischemic Heart Disease

Ischemic heart disease (also known as coronary artery disease) occurs when the heart muscles work inefficiently due to the lack of blood supply (ischemia). Ischemia is caused by the hardening and narrowing of the arteries (atherosclerosis) from plaque buildup inside the vessels. Vessels can be blocked by plaque in the vessel (thrombus), or a thrombus that broke off in another part of the body and became an embolism (moving thrombus). The arteries that supply the heart muscles with blood are very small and can easily be clogged by arterial plaque, thrombus, and embolism. Once the coronary artery is clogged, the heart will not receive enough blood, which means there is not enough oxygen, and the heart cells supplied by the clogged artery may die (necrosis). [7] The arteries of the heart are able to compensate for up to 60% in narrowing of the arteries. A coronary artery block larger than 70% means reduced blood flow during exertion; a block larger than 90% means that the heart may not receive enough oxygen even during rest. [8]

Plaque is made of various proportions of lipids and or fibrous tissue. Depending on the composition, plaque can be classified into two main types: stable (lipid-poor, thick fibrous cap) to unstable (lipid-rich, thin fibrous cap). [7]

Figure 1 Stable plaque (left), unstable plaque (right). [9]



2.1.1 Endothelium dysfunction

Another factor that contributes to ischemia is endothelial cell dysfunction. The endothelial cells line the inside (lumen) of arteries and serve as a barrier between the blood and the muscles in the arteries. These endothelial cells release substances which control artery diameter and prevent blood clots. A dysfunction of the endothelial cells leads to artery diameters that are too narrow. When the oxygen demands are increased in the heart and the endothelial cells do not release the appropriate substances to dilate the arteries, the narrow vessels fail to bring the appropriate amount of oxygen to the heart causing ischemia. In addition to the artery diameter, endothelial cells release substances that prevent blood clotting (thrombosis) which prevent blood clots from

narrowing coronary arteries. The lack of anti-thrombotic factors increases the chances of blood clots forming and the chances ischemia in the heart. [8]

2.2 Epidemiology of IHD

Disease surveillance is defined by WHO as, "the ongoing systematic collection, analysis and interpretation of health-related data essential to the planning, implementation, and evaluation of public health practice, closely integrated with the timely dissemination of these data to those who need to know." [10,11] Disease surveillance uses measures of disease and causes of death to characterize the profile of disease burden within a population. Basic measures include incidence, prevalence, and mortality. Information of the IHD surveillance will provide the general picture about prevention and treatment in Alberta and guide future research questions.

2.2.1 Definitions of Incidence Prevalence and Mortality

This study defined incidence as the number of new cases in a defined group diagnosed in a year divided by the number of people at risk during the same year in that group. This represents the proportion of new cases of disease that appear within the year. Prevalence is defined as the number of existing cases in a defined group during the year divided by the number of people in the population (at risk for the disease and not at risk for the disease) during the same year in that group. Mortality is the number of people in a defined group who died of IHD during the year divided by the number of people in that group during the same year. [12] Groups can be defined by various characteristics, but will be defined by sex, age, and location of residence for this study.

2.2.2 Disease Monitoring

World-wide efforts in heart disease surveillance include the MONICA project. The MONICA project began in 1979. The study collected information on coronary event mortality, prevalence, and risk factors. This project trained epidemiologists from 21 different countries to screen and record data. Coronary events were systematically identified and recorded into a database. The data from the MONICA project database was available to researchers to test their own hypothesis-driven research. Although this database contains world-wide coronary event rates, this database is underused for research. [13] The data from MONICA project covers Halifax County, in Canada.

A Canadian effort in heart disease surveillance includes the CCORT (Canadian Cardiovascular Outcomes Research Team) Atlas. The first objective was to highlight regional variations in the burden of illness and quality of cardiac care across Canada. [14] This goal resulted in a study on the burden of cardiovascular disease using death rates, CCHS survey for prevalence, and health related quality of life measures to measure burden. [15] The Atlas demonstrated variation in the burden of disease using IHD mortality as the measure of burden across Canada.

Past Canadian research efforts used vital statistics, hospital separation rates, and CCHS data to measure the burden of IHD. Vital statistics, discharge databases and self-administered surveys only gave rough estimates of the mortality, incidence and prevalence of disease. Physician clinics can be the first point of patient contact for IHD. For this reason, administrative databases should be included in surveillance to provide a more refined measure of IHD in the population.

A more accurate measure of IHD in the population would give decision makers reliable information to make informed decisions about IHD.

Provincial efforts in heart disease surveillance in Alberta are limited at the government level as well as at the level of individual research groups. The chronic disease report from Alberta Health showed decreasing mortality from IHD over time; however, Alberta still has higher IHD mortality when compared to other Canadian provinces. [3] Another report from Alberta Health predicts a doubling in IHD prevalence in 2036 from 2006. [16] Other heart disease research groups are the Mazankowski and the APPROACH groups which focus on patient outcomes and clinical research instead of surveillance.

2.2.3 IHD in Alberta

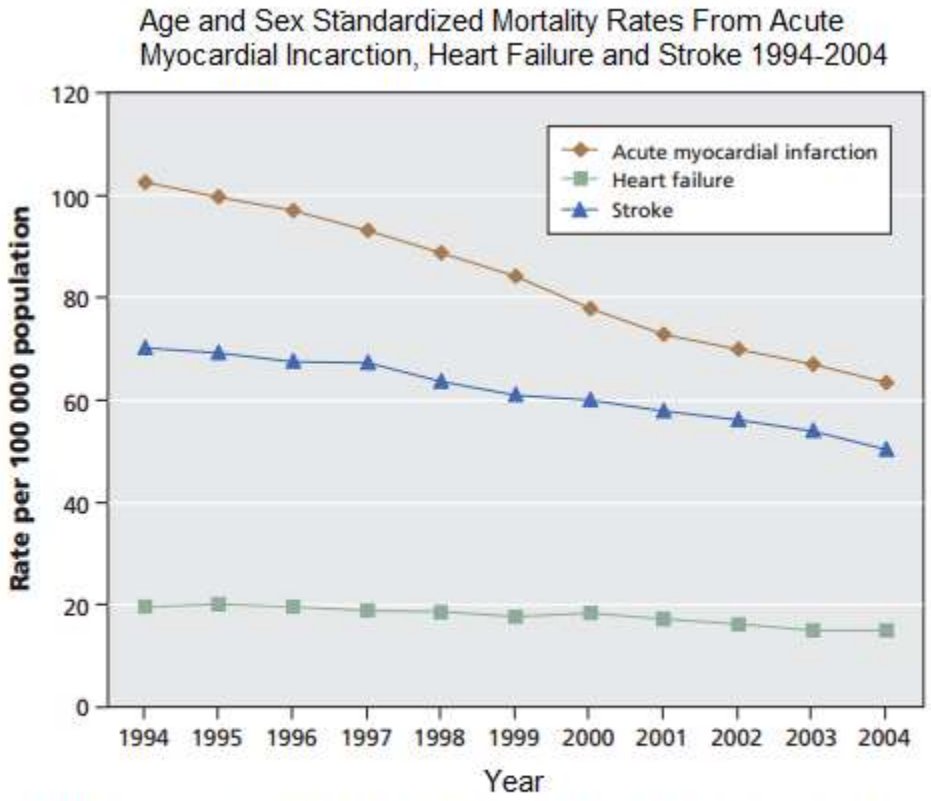
In 2004, 112 per 100,000 Albertans died from ischemic heart disease (IHD), it was one of the worst age standardized rates in the country. [3] On the other hand, the Atlas study reported a 3.5% heart disease prevalence rate during year 2000 in Alberta, which was the lowest rate in the country. [14] The discrepancy between the two statistics raised questions about the incidence and survival of IHD patients in Alberta. Which report was more accurate, and what was the age and sex standardized IHD rate in Alberta? In addition, Alberta Health projections showed that a higher proportion of Albertans will have ischemic heart disease in the future. [16] These figures underscore the need to develop a systematic picture of IHD incidence, prevalence, and mortality.

2.2.4 Prevalence and Incidence Trends and Information Sources

The declining mortality rate from CVD and the declining hospital visits for CVD in the last decade makes mortality and hospitalization rates poor estimates of CVD prevalence. The general

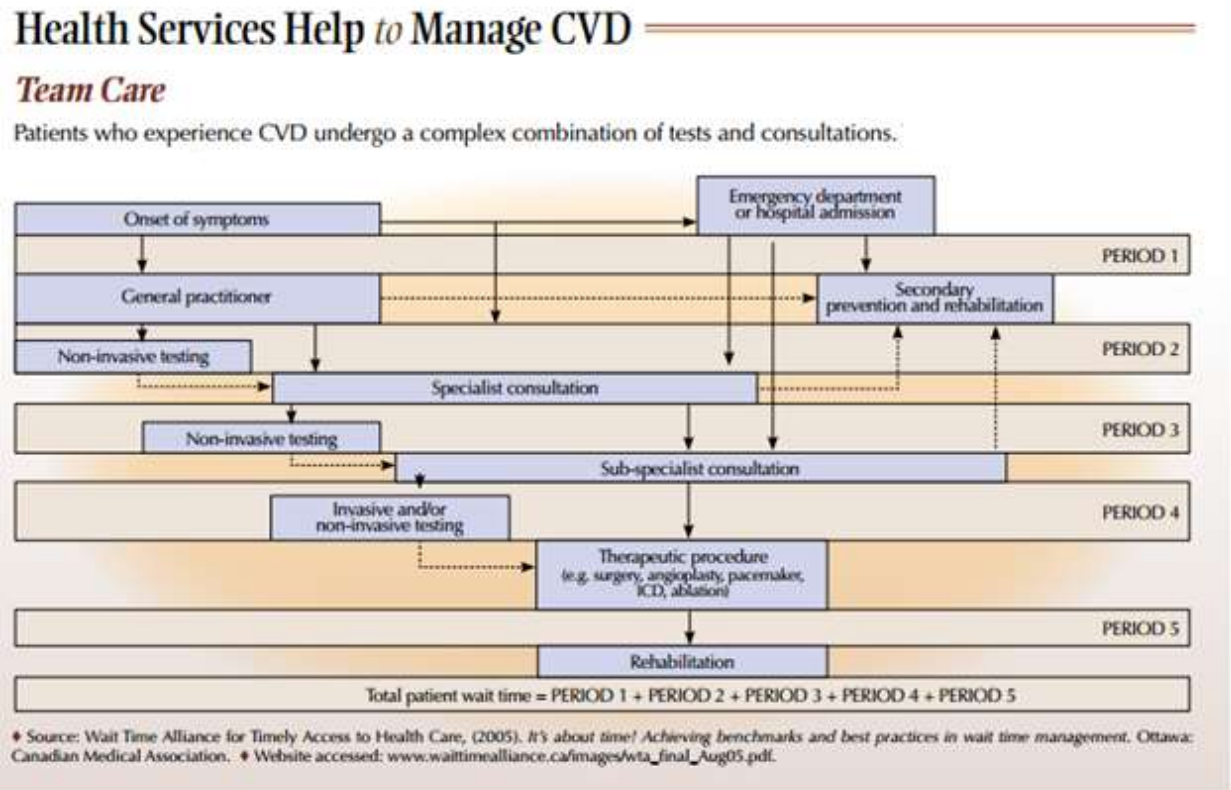
public has become more aware of CVDs and seek health services from primary care physicians as well as hospitals (Figure 3). In order to gather accurate CVD prevalence data, patient records are needed from hospitals as well as physician clinics. Using hospital visits as a proxy for prevalence may underestimate the CVD prevalence as fewer people may have gone to the hospital for CVDs.

Figure 2 Age and Sex Standardized Mortality Rates From AMI, Heart Failure and Stroke 1994-2004.



Note: Rates are reported per 100,000, data included only patients aged 20 and over, rates standardized to the 1991 Canadian population.
Source: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2696549/pdf/180e118.pdf

Figure 3 Health Services for Patients with CVD. This figure illustrates the health services CVD patients can access and the patient records that need to be included to have accurate CVD rates.



Source: page 13 of "Tracking Heart Disease And Stroke In Canada"
http://www.phac-aspc.gc.ca/ publicat/2009/cvd-avc/pdf/cvd-avs-2009-eng.pdf

2.3 Risk Factors

Known risk factors for ischemic heart disease are: family history, male, smoking, diabetes, obesity, blood cholesterol, diet and hypertension. Hypertension, also known as high blood pressure, is a measure of the force of blood against the arteries. The higher the blood pressure, the more damage this pressure can cause to arteries. Damaged arteries then develop fatty plaque

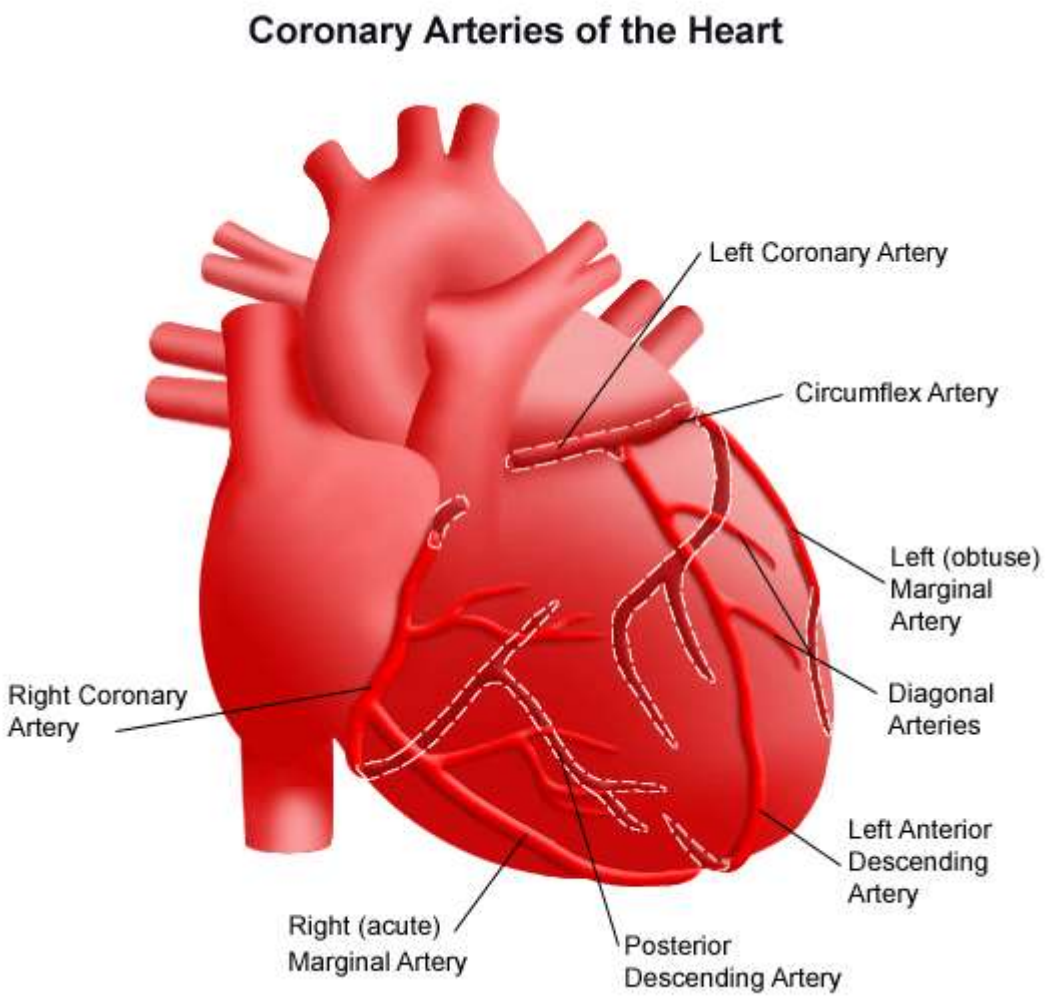
which narrows the arteries and increases the risk of IHD. Blood cholesterol is a fat in the blood that is used for normal functions. The two main types of cholesterol are low-density lipoprotein (LDL) and high-density lipoprotein (HDL). LDL is the cholesterol we would want to control as it promotes buildup of plaque on artery walls when present in high concentrations. HDL carries LDL away from the artery walls. High concentrations of LDL and low concentrations of HDL can lead to atherosclerosis and increase the risk of IHD. Diabetes patients have an increased risk of high blood pressure and atherosclerosis both of which can lead to IHD. Lifestyles that are conducive to high cholesterol and diabetes include physical inactivity, diets high in fats, and being overweight. Having diets high in LDL cholesterol, being physically inactive and being obese are all correlated. These factors are associated with higher fat levels in the body and hence a higher risk of plaque buildup in arteries. Smoking increases the risk of IHD by increasing the plaque buildup in arteries, increasing the risk of blood clots, reducing the oxygen in the blood, increasing the blood pressure, and making the heart work harder. [17]

Non-modifiable risk factors include age, family history, gender, and ethnicity. Older patients have higher risks of disease as most IHD occurs in people over the age of 65. [4] Men over the age of 55 and postmenopausal women are at greater risk of heart disease. The risk of heart disease can also be related to genetic factors. Having a first degree family member who has had heart disease, and being over a certain age are both correlated with higher risk of heart disease. First Nations people, those of African or those of south Asian descent are more likely to have heart disease because of higher rates of high blood pressure and diabetes in these populations compared to the general population. [17]

IHD consists of a few main types of heart problems: angina pectoris, acute coronary syndromes, myocardial infarction (heart attack), and complications from ischemia. The acute coronary syndromes and complications will be described along with the ICD codes. Angina pectoris is when the oxygen supply to the heart is insufficient due to higher demands for oxygen, such as exercise. [18] The vessel blockage reduces the blood flow to the heart vessel and the lack of oxygen is apparent during exertion because the artery is not completely blocked. Myocardial infarction occurs when the plaque completely blocks the heart vessel. The muscles that depend on the blocked vessel could die from the lack of oxygen. The dead muscle tissue becomes scar tissue which can cause chronic heart problems. [19]

Blood circulation in the heart, for the purposes of describing IHD, involves: 4 chambers, 3 layers of heart muscle/tissue on each wall, and coronary (heart) arteries. There are 2 chambers on the top and 2 larger chambers at the bottom of the heart. These chambers are surrounded by the heart wall which is made up of the inner tissue layer (endocardium), the middle muscle layer (myocardium), and the outer tissue layer (pericardium). The top and bottom chambers are separated by valves. The 4 chambers work together to collect deoxygenated blood from the body, re-oxygenate the blood through the lungs and circulate oxygenated blood through the body. [20] The coronary arteries supply the heart with blood. There are two main coronary arteries: the left and right coronary arteries. The left coronary arteries supply blood to the chambers on the left side of the heart; the right coronary arteries supply blood to the chambers on the right side of the heart.

Figure 4 Coronary Arteries. [21]



Note that the left coronary artery is located under another vessel in the anterior (front) part of the heart.

Describing the part of the heart affected by IHD, involves anatomy terminology briefly described below. When referring to the "right of left" side of the heart, the description refers to the patient's "right of left" side. In anatomy, anterior refers to parts of the organ that are closer to the front of the torso where the chest and belly button are located. Posterior refers to a location closer to the back/spine of the torso. Lateral aspects of the body are the sides, closer to the arms; when one talks about the lateral aspect of the heart, it is referring to the left and right sides of the

heart. Superior describes the place of one body part above another; for example, the heart is superior to the stomach. Inferior describes the opposite; for example, the stomach is inferior to the heart.

2.4 Treatment

Medical treatments for IHD include nitroglycerine and other drugs in the same class. Nitroglycerine causes dilation of veins in the body, leading to a lower blood flow to the heart, decreasing the volume of blood the heart needs to pump and hence decreasing the heart's oxygen demand. [8]

Atherosclerosis buildup causing the vessels to narrow can be treated with Percutaneous Coronary Intervention (PCI) or a Coronary Artery Bypass Graft (CABG). The PCI is a non-surgical procedure in which a catheter with a metal stent (tube) is inserted into the patient's vessel, guided by fluoroscopy. When the catheter reaches the narrowed arteries, the end of the catheter is expanded in turn expanding the stent to widen the artery. The catheter is then removed, leaving the stent to widen the vessel which was narrowed by plaque. A CABG is a procedure which can be performed with an "open heart" surgery or other non-invasive techniques. The idea is to use vessels from another part of the patient's body (graft), and connect one end of the graft above the clot and one end below the clot. The graft successfully bypasses the vessel clot by allowing blood to circulate around the clot.

Chapter 3: Systematic Review

3.1 Systematic Review Methods

A systematic review was conducted to show that modelling surveillance data on IHD would be useful as it has never been done for Alberta with administrative data.

3.1.1 Inclusion Criteria

In order for the study/report to be included in this systematic review, the study had to report data on incidence, prevalence, and or mortality of any cardiovascular disease in a Canadian population over time. The condition that was studied could have been CVD, all the IHD conditions or one of the heart conditions encompassed by IHD. The study can be of any type of study design. The source of the data had to be described in the article or described elsewhere. Information on how the data was obtained, the type of information obtained and (if rates were calculated then) the methods used to calculate rates needed to be available. Analysis of the study had to include the trends of heart disease incidence and or prevalence and or mortality over time. The study must have focused on adults or have some method to differentiate children from adult CVD cases as childhood cases of CVD are likely due to congenital problems.

3.1.2 Search Strategy

In order to locate studies characterizing IHD incidence, prevalence and/or mortality, a systematic review was performed using Medline and Embase. The search was conducted August 17, 2014 without restricting publication date. Using Medline, the following search terms were each searched separately using the "exploded" search in the text or subject heading: "myocardial ischemia or acute coronary syndrome," "prevalence," "incidence," "population surveillance,"

"public health surveillance," "sentinel surveillance," "Canada," "ischemic heart disease* or myocardial ischemia" A combination of search terms were then used, see Appendix 1 for the exact combinations. This search strategy was developed with the help of a librarian. After performing the review, 15 Medline articles met the inclusion criteria and were summarized in Appendix 1. Embase and Medline search engines cover similar North American journals; Embase searches European journals as well as North American journals. Embase was not searched using the Medline search terms because of the focus on Canadian data and the overlap in North American journals in these search engines. The titles of these 15 Medline articles were entered onto Embase to find articles which referenced the summarized articles. From the bibliographies of the summarized Medline articles, additional articles were discovered.

In order to search 'grey' literature, a GOOGLE meta-browser was used to find government reports on ischemic heart disease surveillance in Canada. The following search terms were used: "Canada incidence ischemic heart disease," "Canada prevalence ischemic heart disease," "Canada Mortality ischemic heart disease," "Canada surveillance ischemic heart disease," "Canada burden of disease ischemic heart disease." The search terms were then repeated replacing Canada with Alberta. A few initiatives on IHD surveillance were found: ICES from Ontario, CCORT cardiovascular disease atlas, MONICA project.

Table 1 Systematic Review Article Selection Table.

Step	Pulled Articles	Relevant Articles
Number of articles found in Medline search	15	7
Number of relevant articles citing the original 15 Medline articles	9	5
Number of relevant articles in bibliographies of the original 15 Medline articles	23	5
Grey Literature	4	2
Total number of articles in systematic review		19

Appendix 1 presents further technical details of the search terms (Table 1) and detailed listings of the studies located (Tables 2-4).

The findings of the systematic review are summarized in Appendix 1. The data sources are described along with the shortcomings of the study and the results of the existing studies.

3.2 Results of the Systematic Review

3.2.1 Results of the Systematic Review: Incidence

Five studies [22-26] used data from hospital discharge abstract databases and found a decrease in the hospitalization of IHD patients after 1975. [24] This decrease in hospitalization with IHD as the main cause for visit was used as a proxy to measure incidence in the population. The timeline was limited, but the studies collectively cover a period between 1950 and 2002. Most studies agreed with this trend of decreasing IHD incidence, and mortality after 1975. Only one of the

five studies [22-26] noted a decrease in CVD hospital separation in men but an increase in hospital separation rate in women between 1983 and 1993; [23] this finding may have be due to the timeline (1984-1993) or different patterns of CVD subtypes which were studied. For example, if AMIs decreased by 10 units and strokes increased by 20 units, the overall CVD rate would be higher even though IHD incidence rates decreased. [27]

From the studies that reported mortality and incidence changes over time, [26, 27, 28] a decrease in incidence and mortality was noted. One study noted an average annual decline in MI mortality of 3.9% from 1984-1993. [26] Another study used data from 1980-1991 and reported a 4% decrease in CHD mortality for both sex. [28] A study with an older dataset (1950-1977) reported an increase in age-standardized mortality in males by 0.5% annually from 1950 till 1975 where it decreased 1.7% annually. The same study noted female mortality rates were constant till 1950, decreased 0.4% annually after 1960, and decreased 2.4% annually after 1970. [27] One study noted an average annual change in male MI incidence rate of -3.25% (95% CI -4.4% to-2.0%) between 1984 and 1993. [26]

Other findings that should be mentioned are the age, geography and time correlations to IHD surveillance rates. The lack of change in the age curve over time for AMI incidence suggested that AMI age risk is independent of time. [25] We would expect to see only one coefficient for the continuous age group variable. The same study also discovered that the only statistically significant decline in incidence is in the 55-75 age group. [25] Another study noticed that the greatest decrease in incidence is among the 45-64 age group. [24] This may indicate that the middle-aged group was the cohort most affected by AMI and IHD thus the changes in rates

would be most prevalent in this age group. We would expect to see some "time by age" variable for the middle-aged patients in the incidence model.

Another finding of note is the elevated incidence risk of IHD in the Palliser Health Region compared to other health regions in Alberta. [16] Although this study did not use the same health regions, perhaps there are differences in the incidence rates between Albertan zones.

3.2.2 Results of the Systematic Review: Prevalence

Only one study examined prevalence of IHD in Canada from 1950 to 1999 using the CCHS for data. The study found that heart disease was more prevalent among men than women; that angina was equally prevalent among both sexes, and that MIs were more prevalent among males than females. The study also found that older age groups had more complex and sever CVD. [15]

3.2.3 Results of the Systematic Review: Mortality

The studies examining IHD mortality reported a general decline in IHD mortality rates over time after the mid-1970s adjusting for age and or sex. Some studies examined AMI and found a decrease in AMI over time [25,26,29,30] while other studies examined MI and also found a decrease in MI over time. [24,30,31] One study noted that the in-hospital fatality rate was higher in females than in males. [29]

Other findings of note were the differences in mortality rate between the age and sex variables. Two studies noted that male IHD mortality decreased faster than female IHD mortality rates even though male IHD mortality rates were still higher than female rates. [24,30] This would suggest that the mortality model would have a "sex by time" interaction. Another study noted that the

largest relative decrease in in-hospital mortality was observed in the <50 age group. [29] This finding may suggest that the mortality model would have a "time by age" interaction variable.

Another finding was made when one study showed the decrease in mortality from MI was not due to decreases in severity. In fact, MI severity has increased in hospitals. [32] This means the severity of the MIs, a component of IHD, is not confounding the pattern of decreasing MI mortality over time. Researchers cannot conclude that the decrease in IHD mortality is due to a decrease in IHD severity. It is possible that the decrease in IHD mortality is not influenced by an IHD severity.

3.4 Conclusions And Need for Empirical Research

None of the studies used multiple administrative databases and a case definition to measure IHD incidence, prevalence and mortality. The studies relied on either databases with voluntary reporting or self-reports to identify IHD cases. A database that does not have consistent reporting over time can underestimate IHD cases. Self reported data are unreliable because a physician or professional diagnosis may differ from self-diagnosis. As a result, the findings from previous studies could not be put into a meta-analysis due to the lack of consistent definition and the poor quality of the data. Without comparable numbers from a high quality dataset, one cannot make inferences about the burden of IHD. This high quality data is available in Alberta. Alberta Health has recently provided aggregated data to the public on the incidence, prevalence, and mortality from IHD using explicit case definitions and applying it to administrative databases. These data

allow for the systematic surveillance of IHD in Alberta using direct measures. Consequently, this study will focus on modelling the incidence, prevalence, and mortality from IHD in Alberta.

Chapter 4: Empirical Analysis of Ischemic Heart Disease In Alberta

4.1 Anticipated Model Findings

The findings from the systematic review suggested that incidence and mortality were expected to decrease over time in the Alberta data. The age by incidence curve created from the Alberta data was not expected to change over time; this means that the incidence model created from Alberta data was not expected to have an age by time variable and was expected to have only one coefficient for the continuous age variable.[24,25] At the same time, the incidence and mortality models created from the Alberta data were expected to have a "time by age" interaction due to the prediction that the middle-aged population would experience the largest decrease in incidence and mortality over time.[25] The model created from the Alberta data may have higher incidence rates in the South Zone (Palliser Health Region). [16] The mortality model created from Alberta data may also have a "sex by time" interaction as males are expected to have a steeper decline in mortality rates than females. The lack of existing prevalence data prevents meaningful predictions about the prevalence model created from Alberta data. [25,26,29,30, 15, 22-26]

Figure 5 Map of zones in Alberta [33]

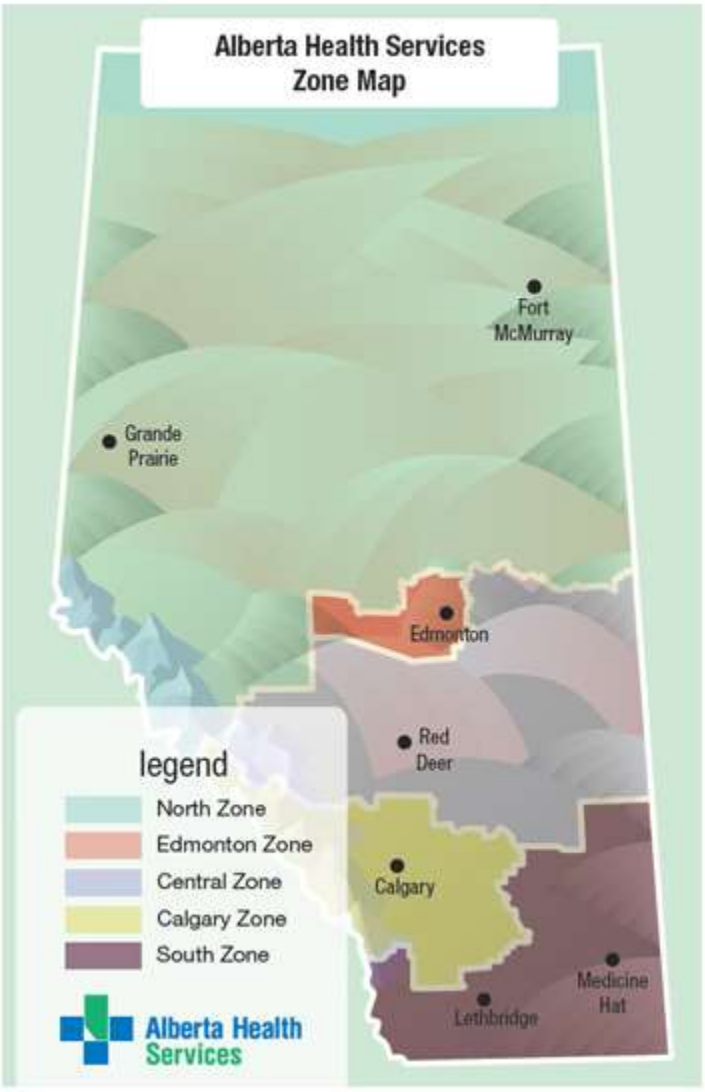


Table 2 Hospital and Physician Resources By Zone. [34]This table shows the number of hospitals and physicians in each zone, which can be used to diagnose IHD.

Zone	Number of Hospitals	Physicians	Population
North	34	433	447,099
Edmonton	13	---	1,186,121
Central	31	801	453,469
Calgary	13	2,857	1,400,000
South	15	439	281,934

4.2 Methods

4.2.1 Study Design and Setting

This study was conducted in the Edmonton health region; the data covered the five geographic zones of Alberta. Although the political boundaries have changed during the time frame of the data set 1994-2005, zone geography (see figure 5) was used as it was the current health care region during the time of the study. The study analyzed IHD using incidence, prevalence and mortality as measures for surveillance for reasons mentioned before. The goal of this study was to use the data from passive surveillance and model the incidence, prevalence, and mortality of IHD over time.

4.2.2 Data Sources

The study used data from the Alberta Health web site from the Interactive Health Data Application (IHDA).[35] The IHDA data is a database with information on IHD incidence, prevalence and mortality based on administrative data. This freely available information allows researchers to be more efficient in the research by eliminating the need for each research group to recompile and pay for administrative data. As such, the methodology used in this study mirrors the methodology used to obtain the administrative data. Appendix 2 presents further technical details on the location of the administrative health data from the IHDA along with screen shots. Data from the administrative database covers Alberta residents -- those eligible for coverage of publicly funded and universally available health care. The populations not covered are: Armed Forces, Royal Canadian Mounted Police, inmates in Federal Penitentiaries, those who opted out of AHCIP, and Aboriginals.[36-38] The AHCIP covers 99% of the Albertan population. At its peak opt-out year, between 2007 to 2008, only 292 opted out.[39,40]

Incidence data from the IHDA were gathered from:

1) Alberta Health Care Insurance Plan (AHCIP) Physicians Claims Data
2) Alberta Health Care Insurance Plan Quarterly Population Registry Files
3) Alberta Health Hospital Inpatient Database

Prevalence data from the IHDA were gathered from:

1) Alberta Health Care Insurance Plan Physicians Claims Data
2) Alberta Health Care Insurance Plan Quarterly Population Registry Files
3) Alberta Health Hospital Inpatient Database

4) Alberta Health and Wellness Postal Code translation File

Mortality data from the IHDA were gathered from:

1) Alberta Vital Statistics Death File
2) Alberta Health Care Insurance Plan Quarterly Population Registry Files

4.2.3 IHD Case Definition

The data from Alberta Health, the dataset for this project, used the following definition for IHD:

1) two physician billings within a 1-year period with ICD-9 code 410 to 414 in any of the three diagnosis positions. At least one of the physician billings had to be from a physician (GP or specialist) in a hospital or emergency setting.

or

2) hospital discharge with a IHD diagnosis (ICD-9 = 410-414 or ICD-10 = I20 to I25) in any diagnosis position.

or

3) Procedure/Intervention code for IHD treatments PCI or CAPG (ICD-9 procedure codes = 36.01, 36.02, 36.05, 36.10-36.19)

The third criteria for IHD case definition was the treatment of IHD using PCI or CABG which were described before. Although ambulatory care was not included in these rates, this type of surveillance provided a better prevalence estimate of IHD as it includes physician (GP or specialist) IHD visits instead of just considering hospital discharges or specialist visits for IHD prevalence. An electrocardiogram can be used to diagnose IHD, however not all patients with IHD will get ECG or other diagnostic tests to confirm IHD. Thus the case definition included

only confirmed diagnoses of IHD and or patients who received treatment for IHD. Although the case numbers may underestimate IHD as some patients may not verify their diagnoses, the goal is to obtain the relative numbers so an underestimate in all categories will give appropriate relative IHD probabilities.

The databases covered most of the population (except for Canadian Armed Forces, RCMP, those who opted out, and inmates in Federal penitentiaries) and allowed for an estimate of the incidence, prevalence, and mortality of IHD in Alberta in an ecological manner.

Physician billing allowed for a maximum of three diagnosis positions while the hospital discharge allowed a maximum of 25 diagnosis positions. The first two diagnostic criteria use all the diagnosis positions in the administrative databases to find IHD cases. The criteria allowed for the collection of all the possible IHD cases recorded in the administrative database. [36-38]

4.2.4 IHD Calculations

Due to the small population in Alberta, we examined IHD as a whole. Separating IHD by ICD codes (410, 411,…, 414) and or severity would render the case count of some subtypes too unstable for age, sex and geographic analysis.

The rules that determined geography, age, sex, and calculate rates are outlined in this paragraph. The patient's postal code at the mid-year population registry was used to assign the zone as of June 30 each year. The postal code was linked to the postal code translation file to obtain the zone. [36-38] A person's age and sex were calculated from the mid-year population registry file as of

June 30 of the given year. [36-38] The people at risk were defined as those who were not prevalent cases as of June 30 of that year. Prevalent cases were defined as those who met the criteria described above on or before June 30 of that year. The incidence cases were those who met the criteria during the calendar year. [38] Incident cases were then divided by the total population in each age-sex cohort. The prevalence rate was calculated using prevalent cases divided by the total population in each age-sex cohort. Prevalent cases were defined as those who met the criteria on or before June 30 of that year x. [37] The mortality rate was calculated using mortality cases divided by the total population in each age-sex cohort. Age and sex were calculated as of June 30 in each year for those in the denominator. [36-38]

4.3 Analysis

4.3.1 Data Organization

The data from Alberta Health IHDA [35] were downloaded into a text file readable directly by Excel. [41] This spreadsheet was organized with variables in the columns, and data related to a specific group in each row. The variables needed for the analyses which follow were: age (from 0 to 85+ or 0 to 90+ by 5 year groupings), sex (male, female), geography (Zone), year, number of cases, and total population.

Additional codes were included (e.g. ages combined, sex combined, zones combined) but discarded prior to analysis. (Additional variables were included but also discarded prior to analysis: rate, standard error of rate, and standard score of rate). Appendix 3 presents an example dataset.

Separate datasets were downloaded for mortality, incidence, and prevalence. Table 3 shows the organization of the intermediate datasets.

Table 3 Data Variables and Values

Variable	Type	Values	Notes
Year	Scale	1993-2012	Year of IHD rate
Integer Year	Scale	1 to 20	Year subtract 1992 (for smaller coefficients)
Integer Age	Ordinal	1 to 21	5 year age groups from birth till 85+ or 90+ and "all ages"
Sex	Nominal	1,2	1 for females, 2 for males
Zone	Nominal	1 to 5	Number corresponds to the zone
Cases	Scale	n/a	Number of cases in the population
Population at risk	Scale	n/a	Total number of people at risk during the year

4.3.2 Data Preparation

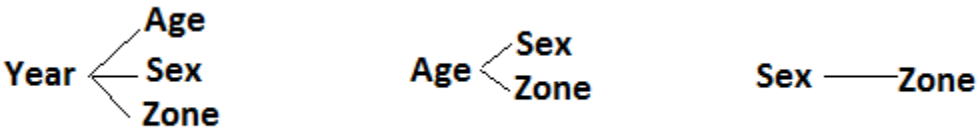
The data from Alberta health were then rearranged in order to suit the logistic regression analysis in SPSS. The variables which were used to create the logistic regression dataset were: geography (zones), sex (male or female), age (5 year age groups), year, numerator and denominator. The age, sex, geography, and time variables and their interactions were used to predict the probability that an individual would be in the IHD category. (Appendix 3)

4.3.3 Modeling Strategy

For each of incidence, prevalence, and mortality models, the dependent variable (incidence, mortality, prevalence) was fitted using four independent variables: year, age, sex, and zone. Age, sex, and zone were fitted into a regression with years individually, which created three separate regressions for incidence, prevalence and mortality. Predicted probabilities were generated for the model. Year and age were modeled initially as continuous variables, whereas sex and geography were binomial variables. The predicted values were plotted against the original data from the Albertan population. The model was refined to improve the fit. This process involved creating additional variables to improve the fit. The improvement of fit required the creation of non-linear variables that allowed a more complex fit or variables that coded interactions between the independent variables (e.g. to fit a different curve to each geography). After the three regressions (age by year, sex by year, zone by year) had the two-variable interaction terms, the three regressions were combined into one model. The model was plotted against the original data and new variables were created till the fit was deemed sufficient. A model was deemed sufficient when any new variables added were insignificant. The final model was then presented and interpreted.

The first and last data points are removed as outliers where, the deviation can be due to errors in mortality counts or errors in the population counts in the denominator. If the population counts stayed similar in all zones across time, then the population file is most likely accurate. Then there would be no need to adjust the population file. If the mortality counts jump over time in all zones, then there is most likely a systematic counting error which cannot be changed using statistical software.

Interaction terms were added to the single variable regression using a nominal significance level of <0.05 as a general guideline. Two-variable interaction terms (for example, year by zone) were added if the regression showed the term to be significant. The terms which were shown to be insignificant were taken out of the regression for the next iteration. To ensure all two-unit interactions were tested for significance, the following permutations were regressed:



Year by age, year by sex, and year by zone interactions were tried first, then the next three interactions shown in the above diagram. Any significant two-variable interaction needed to be hierarchically well formulated so the variables making up the two-unit interaction were included into the regression whether or not the single variables were significant. When the two-variable interactions were significant, three-unit interactions were regressed for significance; however, if the two-unit interactions were non-significant the three-unit interactions were not added to the equation.

A plot of the actual and predicted IHD rates showed if any predicted values which differed from the actual values. Points that lay outside a linear plot at 45 degrees showed that the model under or overestimated data points. Another way to determine model fit was the use of delta. Delta was defined as the difference between the actual IHD rate and the predicted IHD rate. A graph of delta and the predicted values should have been as close as possible to a horizontal line at zero

delta. Graphs were used to identify variables in which values were over or underestimated, new variables were added to the model to determine significance and improve model fit.

When the model was sufficient, any new variables added to the regression would not make a large difference to the delta graph and the graph with predicted versus actual probabilities. A change in delta was large when the slope of the line of best fit changed by 0.1 or more. Appendix 4 (available on request from the author in electronic form) provides a comprehensive example of the entire iterative process of developing a model. These analyses were performed using logistic regressions [42] with SPSS statistical software [43].

4.4 Results

4.4.1 Mortality Model

Table 4 below shows the equation for the final logistic regression model for mortality.

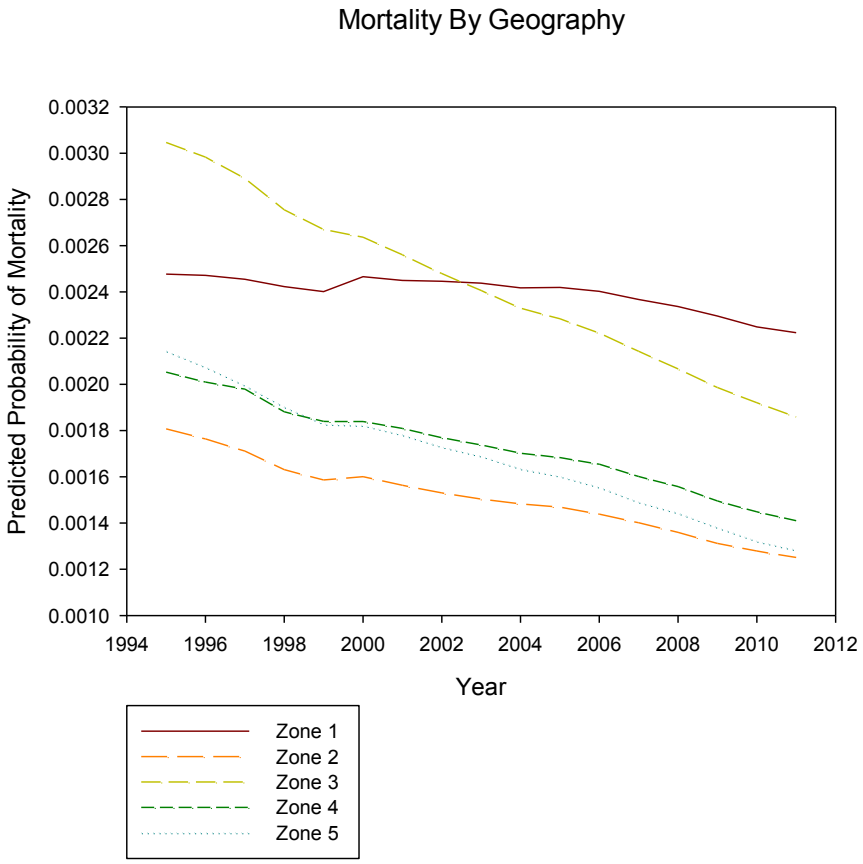
Table 4 Logistic Regression Model for Mortality.

Variable	B	Sig.	Exp(B)
Integer year	-0.0400	0.0000	0.9610
Zone		0.0000	
Zone 1 compared to Zone 5	-0.3260	0.0000	0.7220
Zone 2 compared to Zone 5	-0.1460	0.0000	0.8640
Zone 3 compared to Zone 5	-0.0370	0.0200	0.9640
Zone 4 compared to Zone 5	-0.1170	0.0000	0.8890
Integer age group	0.5160	0.0000	1.6760
Sex (female compared to male)	-3.3430	0.0000	0.0350
Zone 1 X year	0.0210	0.0000	1.0220
Age less than 45	-4.1300	0.0000	0.0160
Age less than 45 X integer age	0.3770	0.0000	1.4570
Age less than 45 X sex(1)	0.4980	0.0000	1.6450
Age 90 plus	0.0840	0.0000	1.0880
Age 90 plus X Zone 1or2	0.2400	0.0000	1.2710
Age 90 plus X Zone 1or2 X year before 2000	-0.0950	0.0450	0.9090
Age 90 plus X year before 2000	-0.1080	0.0010	0.8970
Integer age X sex	0.1550	0.0000	1.1680

Constant	-12.7370	0.0000	0.0000

The model has main effects for Year (year), Zone (igeo with 4 binary factors igeo1 to igeo4), Age (iage), and Sex (isex). It also has interactions and additional variables to capture nonlinear changes. The South Zone (Igeo1) has a stabilized probability over the years while other zones exhibited a decrease in probability over the years (igeo1 by iyear) as is ploted in figure 6, which gives the model predicted IHD mortality probabilities by geography and year.

Figure 6 Model predicted IHD mortality probabilities by geography and year.

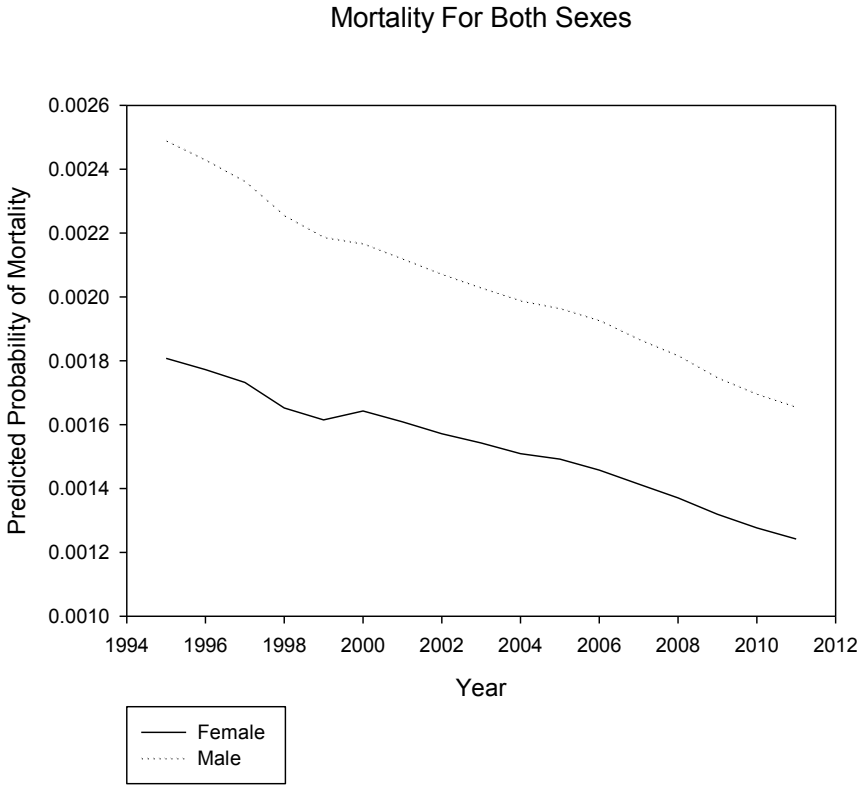


The age relationship has a number of complexities including discontinuities below age 45 (agelt45) and at age 90 plus (age90plus) as well as a different slope below age 45 (agelt45xiage). The sexes also have a differential mortality rate (iage by isex, agelt45 by isex). These relationships are shown in figure 7.

Figure 7 Model predicted IHD mortality probabilities by age and sex.

Finally figure 8 presents the trend across time for the two sexes. The figure shows a main effect for both year and for sex, but shows that the rate of decline does not differ between the sexes (ie there is no interaction).

Figure 8 Model predicted IHD mortality probabilities by year and sex.



It should also be noted that fitting the model for individuals over the age of 90 required additional interaction terms, This may be due in part to the fact that over age 90 is an open-ended age category therefore differing dramatically from the other age groupings which are only 5 years wide.

In summary, the model has four main features. The first feature is the marked sex difference with males having higher mortality rates than females. The second feature is the dramatic mortality probability increase with age, more dramatically for males than females. There is a marked general decline in mortality rates through time. Lastly, the South zone stands out because its decline is much less marked than the decline over time in other regions.

4.4.2 Incidence Model

Table 5 below shows the equation for the final logistic regression model for incidence.

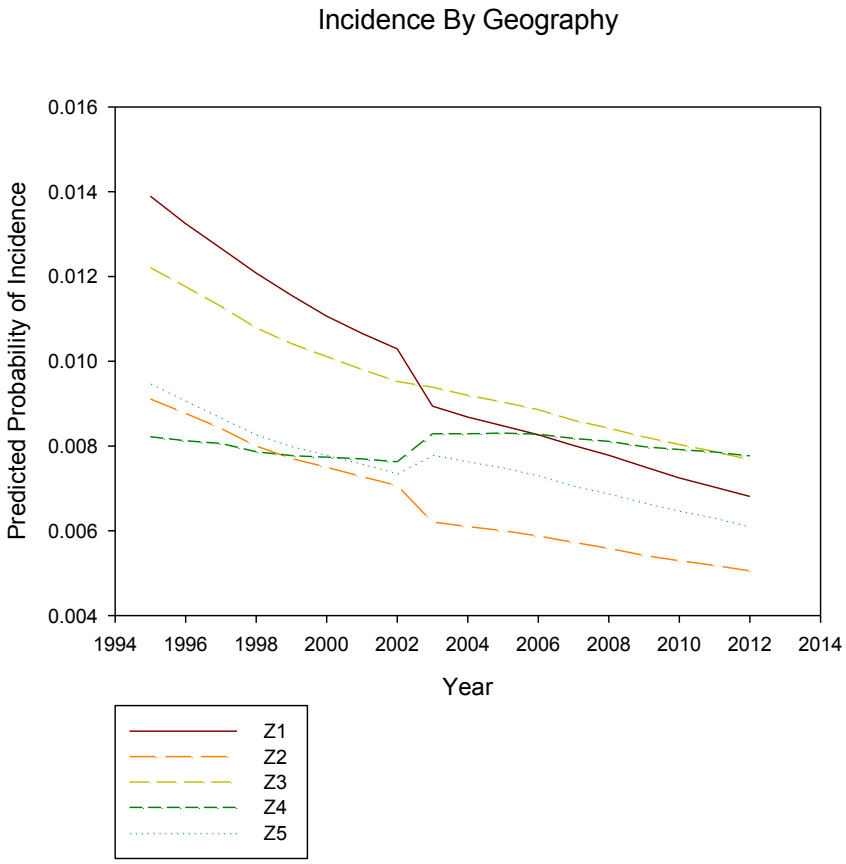
Table 5 Logistic Regression Model for Incidence

Variable	B	Sig.	Exp(B)
Integer year	0.0350	0.0000	1.0360
Sex (female compared to male)	-1.2510	0.0000	0.2860
Zone		0.0000	
Zone 1 compared to Zone 5	-0.3270	0.0000	0.7210
Zone 2 compared to Zone 5	-0.4120	0.0000	0.6620
Zone 3 compared to Zone 5	-0.3220	0.0000	0.7250
Zone 4 compared to Zone 5	-0.2640	0.0000	0.7680
Year less than 2003	0.1340	0.0000	1.1440
Age less than 45	-4.6240	0.0000	0.0100
Integer year X year less than 2003	-0.0060	0.0000	0.9940
Age less than 45 X integer age group	0.4150	0.0000	1.5150
Integer age group	0.3580	0.0000	1.4310
Integer age group X sex	0.0470	0.0000	1.0480
Zone 4 X integer age group	0.0160	0.0000	1.0160
Zone 2 X sex	-0.0590	0.0000	0.9430
Integer age group X integer year	-0.0040	0.0000	0.9960
Zone 4 X year less than 2003	-0.1640	0.0000	0.8490

Zone 4 X integer year	0.0200	0.0000	1.0200
Zone 5 X year less than 2003	-0.1430	0.0000	0.8670
Age 85 plus X sex	-0.1080	0.0000	0.8980
Constant	-8.6270	0.0000	0.0000

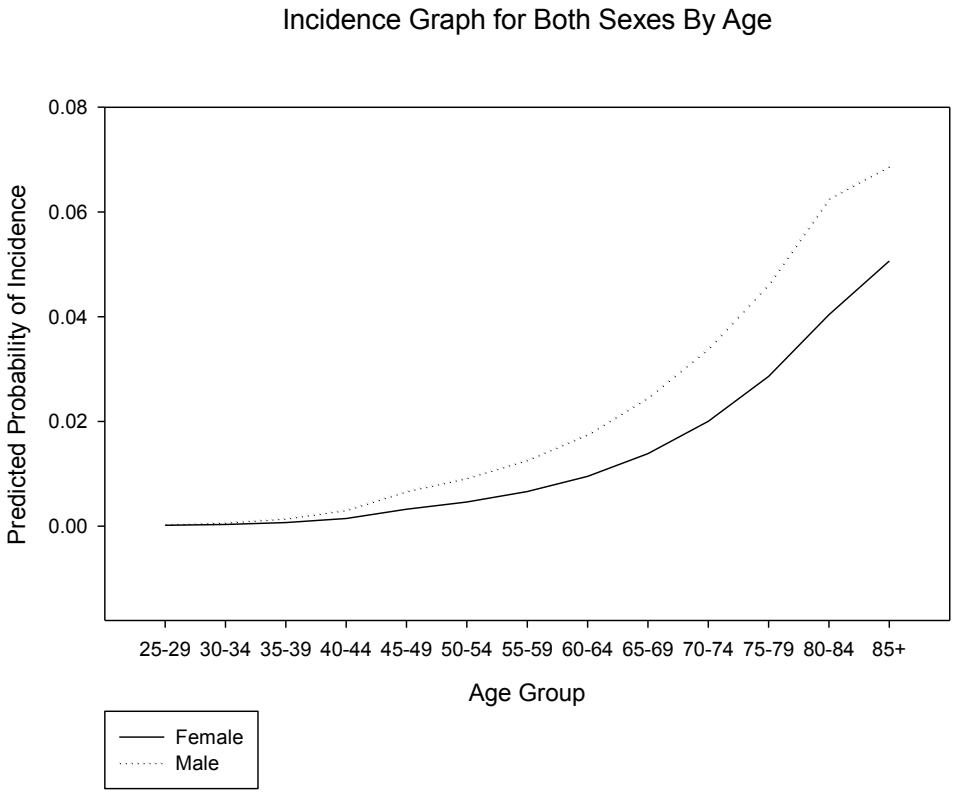
The model contains main effects for Year (year), Zone (igeo with 4 binary factors igeo1 to igeo4), Age (iage), and Sex (isex). It also contains interactions and additional variables to capture nonlinear changes. The pattern of incidence was discontinued before 2003 and after 2003 as shown by figure 9 which gives the incidence per year by geography. Zones 4 and 5 seem to have different slopes before and after 2003 (geo4 by year less than 2003, and geo5 by year less than 2003).

Figure 9 Model predicted IHD incidence probabilities by year and geography



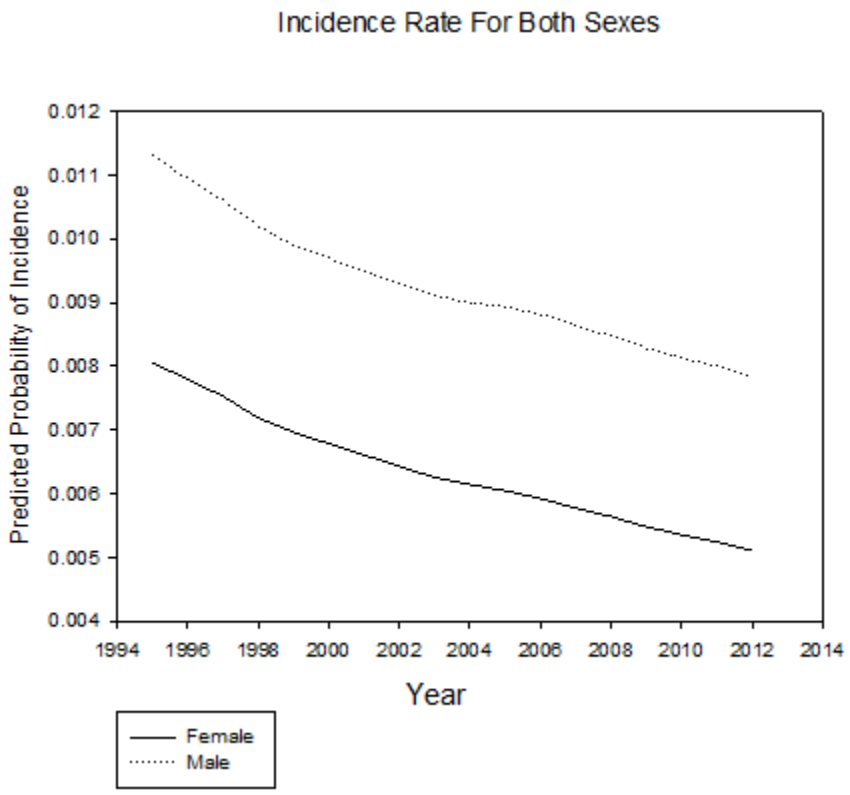
The age relationship has a number of complexities including discontinuities below age 45 (agelt45) and at age 85 plus (age85plus) as well as a different slope below age 45 (agelt45xiage). Zone 2 has a different curve for the sexes compared to other zones (geo2 by sex). Zone 4 demonstrates a different slope for age (geo4 by iage).

Figure 10 Model predicted IHD incidence probabilities by age and sex



Finally figure11 presents the trend across time for the two sexes. The figure shows a main effect for both year and for sex, but shows that the rate of decline does not differ between the sexes (ie there is no interaction).

Figure 11 Model predicted IHD incidence probabilities by year and sex



It should also be noted that fitting the model for individuals over the age of 85 required additional interaction terms, This may be due in part to the fact that over age 85 is an open-ended age category therefore differing dramatically from the other age groupings which are only 5 years wide.

In summary, there were five main features of this model. The first feature is the marked sex difference where males had higher incidence probabilities than females. The second feature was the dramatic incidence in probabilities with age, which was more dramatically for males than females.

There was a marked general decline in incidence probabilities through time for both sexes. Zones 4 and 5 had significantly different slopes from the other zones because the incidence

probabilities rose between 2002 and 2003 while the other zones exhibited a decrease in incidence probabilities during this time. Lastly, there was a significant change in the incidence probabilities in three age groups (less than 45, 45 to 74, 75+).

4.4.3 Prevalence Model

Table 6 below shows the equation for the final logistic regression model for prevalence.

Table 6 Logistic Regression Model for Prevalence

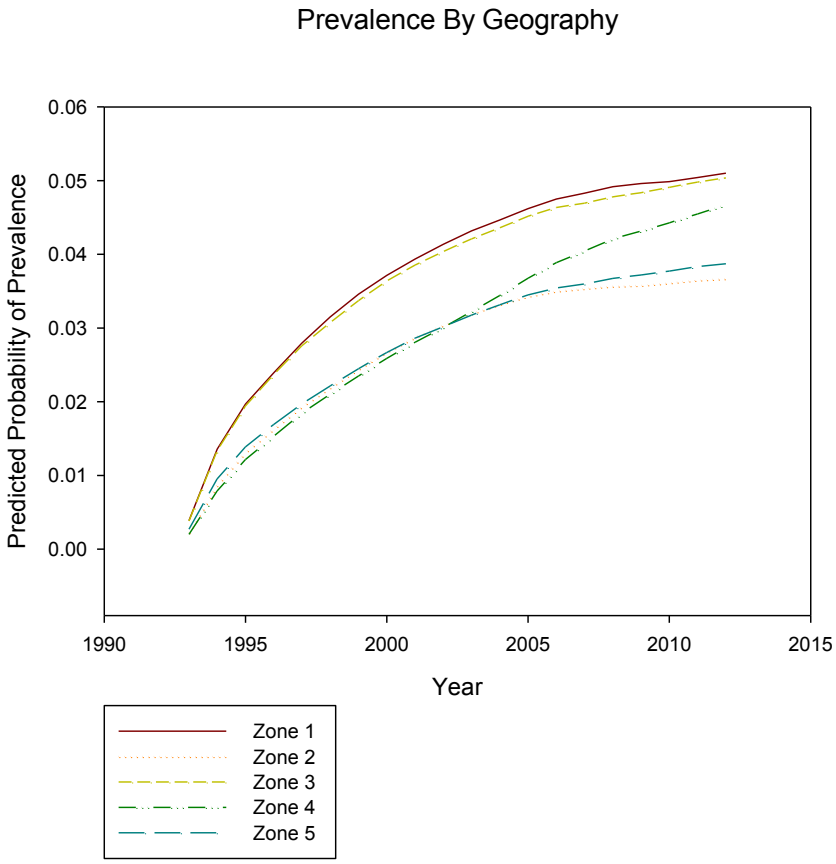
Variable	B	Sig.	Exp(B)
Zone		0.0000	
Zone 1 compared to Zone 5	-0.0090	0.0240	0.9910
Zone 2 compared to Zone 5	-0.5480	0.0000	0.5780
Zone 3 compared to Zone 5	-0.0950	0.0000	0.9090
Zone 4 compared to Zone 5	-0.6040	0.0000	0.5460
Sex	0.3530	0.0000	1.4240
Year	4.2470	0.0000	69.8820
Integer age group	0.7010	0.0000	2.0150
Integer year squared	-1.3150	0.0000	0.2690
Integer year cubed	0.1430	0.0000	1.1540
Knot 1	-0.1420	0.0000	0.8670
Knot 2	-0.0010	0.0000	0.9990
Knot 3	0.0000	0.7560	1.0000
Age greater than 75	-2.8430	0.0000	0.0580
Age between 45 and 74	-3.1860	0.0000	0.0410

Integer age group X sex	-0.1110	0.0000	0.8950
Age greater than 85 X sex	1.4840	0.0000	4.4100
Integer age group X age greater than 85	-0.2860	0.0000	0.7510
Integer age group X age between 45 and 84	-0.2610	0.0000	0.7700
Age between 45 and 84 X sex	-1.5210	0.0000	0.2190
Integer age group X age between 45 and 84 X sex	0.1490	0.0000	1.1600
Zone 2 X integer year	0.3380	0.0080	1.4020
Zone 2 X integer year squared	-0.1110	0.0130	0.8950
Zone 2 X integer year cubed	0.0130	0.0130	1.0130
Zone 2 knot 1	-0.0130	0.0130	0.9870
Zone 2 knot 2	0.0000	0.0150	1.0000
Zone 2 knot 3	-0.0010	0.4400	0.9990
Zone 4 X integer year	0.1900	0.1460	1.2090
Zone 4 X integer year squared	-0.0530	0.2520	0.9490
Zone 4 X integer year cubed	0.0050	0.2950	1.0050
Zone 4 knot 1	-0.0050	0.3290	0.9950
Zone 4 knot 2	-0.0010	0.0000	0.9990
Zone 4 knot 3	0.0010	0.0830	1.0010
Zone 2 or 4 X sex	-0.0990	0.0000	0.9050
Zone 1 or 3 X sex	-0.0300	0.0000	0.9700
Zone 2 or 3 or 4 X integer age	0.0050	0.0000	1.0050

groups			
Constant	-8470.4490	0.0000	0.0000

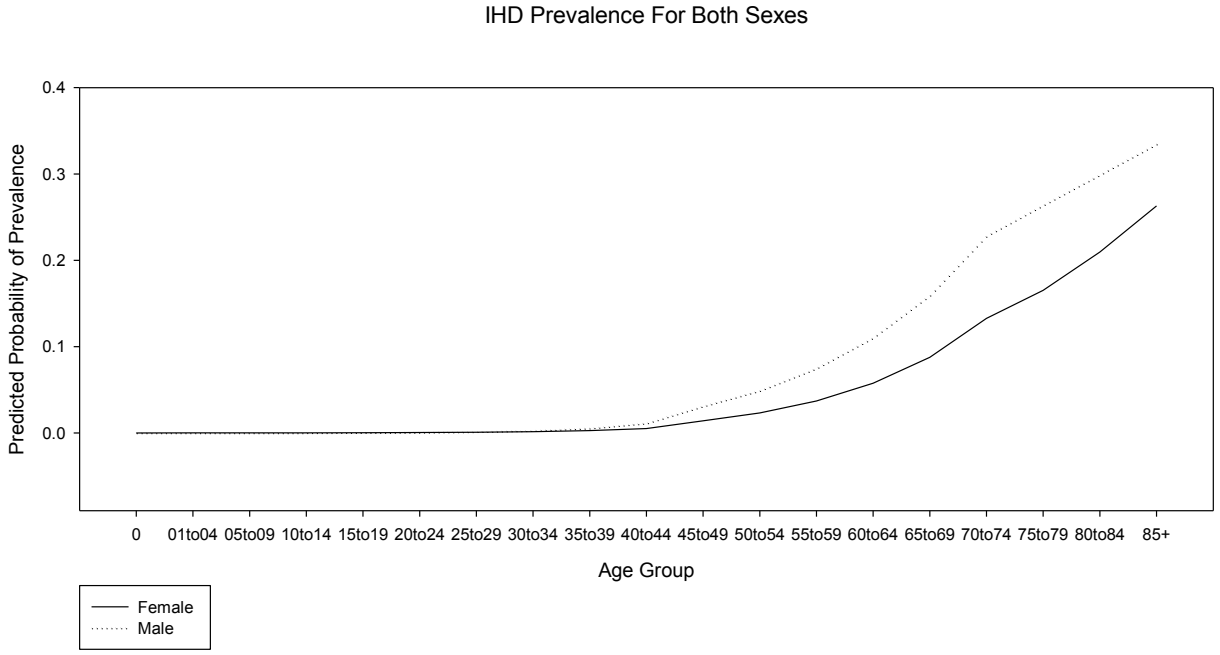
The model contains main effects for Year (year), Zone (igeo with 4 binary factors igeo1 to igeo4), Age (iage), and Sex (isex). The model contains a square and cubed year variable for the cubic spline. It also contains interactions and additional variables to capture changes that were different from the cubic spline. Geographies 2 and 4 seemed to have a different slope (g4sk1-3, g2sk1-3) of which zone 2 were visually different as shown by figure 12, which gave the predicted prevalence by year and geography.

Figure 12 Model predicted IHD prevalence probabilities by year and geography



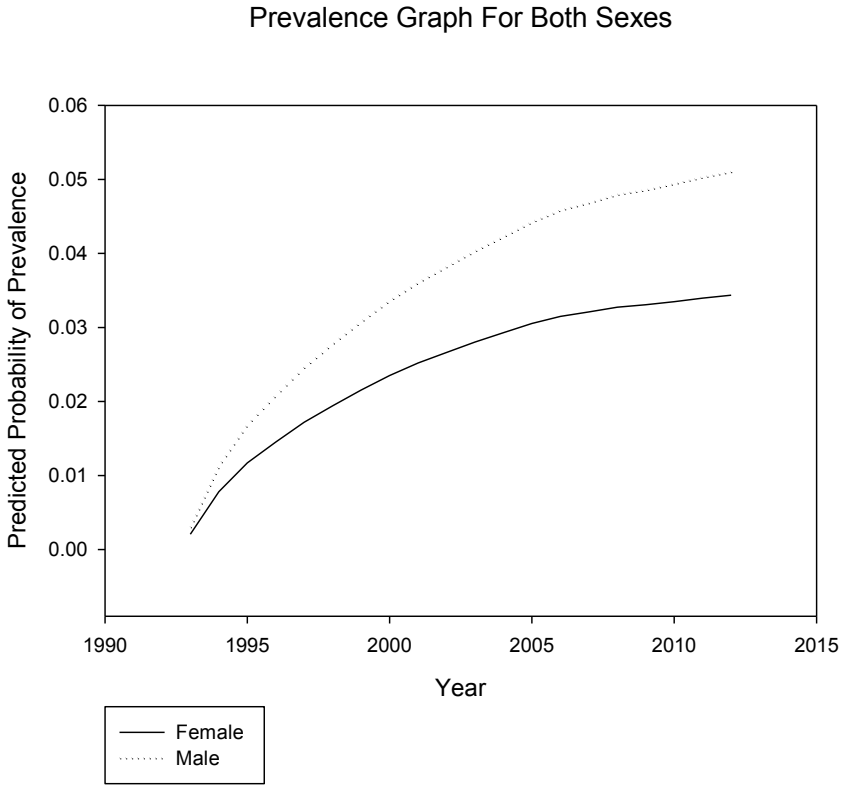
The age relationship has a number of complexities including discontinuities below age 45 (agelt45) and at age 85 plus (age85plus) as well as a different slope below age 45 (agelt45xiage). The sexes also have a differential prevalence rate for the oldest age group and the middle age group (iage by isex, agegt75 by isex, agegt75 by iage, agegt75 by isex by iage, iagebt45and74 by isex, iage by iagebt45and74 by isex). These relationships are shown in figure 13.

Figure 13 Model predicted IHD prevalence probabilities by age and sex



Finally figure 14 presents the trend across time for the two sexes. The figure shows a main effect for both year and for sex, but shows that the prevalence has reached a plateau for both sexes while male prevalence probability is higher than female prevalence probability. (i.e. there is an interaction).

Figure 14 Model predicted IHD prevalence probabilities by year and sex



In summary, there were four main features of the model. The first feature is a marked sex difference with males having higher prevalence probabilities than females. The second feature was the dramatic increase in prevalence probabilities with age, more dramatically for males than females. The prevalence probability seemed to be heading toward a plateau except for zone 4. There was a significant change in the incidence probabilities in three age groups (less than 45, 45 to 74, 75+).

Chapter 5: Discussion

5.1 Discussion

Some of the results from the models for incidence, prevalence and mortality of IHD in Alberta present were what would have been expected given the findings of the systematic review. The first expected result was the increase in probability of mortality and incidence for older age groups. The second expected result was the decrease in incidence and mortality probabilities over time.

There were also certain unexpected relationships involving differences between geographies. Edmonton zone portrayed an increase in IHD incidence in 2003 and decreasing mortality rate over time, resulting in an increasing prevalence as opposed to a plateau. The increase in incidence contributed to a linear pattern in prevalence because prevalence patterns are reflected by the difference in the incidence and mortality probabilities.

Despite the high mortality probabilities in South and Central zones, the prevalence of IHD in these two zones were still the highest in the province. This pattern may be because the difference between the incidence and mortality rate were higher in the South and Central zones than that of the Edmonton and North zones. South zone had a higher incidence probability and lower mortality probability than the Central zone until 2003 where the reverse is true. Nevertheless, the prevalence rates for South and Central zones were very similar. The difference in the incidence probabilities between South and Central zones were similar in 1994 and 2012; the same can be said about the difference in mortality rate between the South and Central zones comparing 1994 to 2012. This similarity caused the prevalence rate to remain stable despite the change in

incidence and mortality. Calgary and North zones also had similar prevalence probabilities despite the divergent incidence probability change after 2003 for the same reason outlined beforehand.

From the models, we saw prevalence reaching equilibrium and unexpected differences IHD probabilities among different geographies. Zone 5 (North zone) was expected to have high probabilities but after controlling for age and sex, North zone was an area which had one of the lower prevalence of IHD. This may be because the North zone has many men working in the oil industry, resulting in a higher number of IHD patients but when the model controlled for sex the probabilities of IHD were lower among these physically active men.

The models used for incidence and mortality has certain implications for prevalence. Thus there were several possibilities for the nature of the prevalence relationships through time: prevalence could be increasing through time if incidence is greater than mortality, or prevalence might be decreasing if mortality is greater than incidence, or prevalence might be unchanging if incidence and mortality were equal. A population was considered to be in equilibrium in this third case. The results from the analysis suggested that Alberta is approaching an equilibrium state where the total incidence equals the total mortality leading to a stable prevalence probability. It should be noted that this does not mean that the absolute number of individuals with IHD remains the same however, since changes in population size have been eliminated from the modelled data. It does suggest that population change, perhaps primarily through migration, will be a major contributor to the number of individuals with IHD in Alberta in the future. These suggestions must be viewed as speculative, of course, but may point to interesting research possibilities.

5.2 Strengths

This project was possible due to publicly available data the Alberta government provided. The data was aggregated so public access did not infringe on the privacy of the patients. Publicly available data tools such as the Interactive Health Data Application [35] allowed for quick and unencumbered access to data for surveillance purposes. The systematic case definition used combined administrative data sets to give a more accurate incidence and prevalence rate than previous studies. The data also covered more than 99% of the Alberta population and thus applicable to the population without sampling bias. From the analysis, we were able to produce diagrams which allowed easy visualizations of the findings for use in communicating to both researchers and policy makers. The models gave numerical estimates and clear potential for projections into the future.

5.3 Limitations

5.3.1 Limitations of The Systematic Review

The Canadian research was performed using data from a few sources: 1) the CCHS, 2) the hospital discharge abstract database (or the equivalent), or 3) the Statistics Canada mortality database. Details of each database are outlined in Appendix 1. Each of these data sources has drawbacks. Since the CCHS is a standalone self-report survey, self-reported rates cannot be verified with clinical diagnoses. Prevalence rates based upon hospitalization data will not include cases managed in physician clinics that have not resulted in hospitalization. Mortality rates, the primary rates used to study IHD, underestimated IHD in the population because improved treatments allow patients to survive after an IHD incident.

The database (along with inclusion and exclusion criteria) used in the study may have affected the results. Some studies recorded cases of heart disease (or any one of the conditions encompassed by IHD) only when it was the primary reason for the hospital visit. While other studies included cases if heart disease was used as the primary and secondary reason for visit. Including a case only if heart disease was the primary cause for hospital visit would underestimate the prevalence of heart disease. While including a case if any one of 16 diagnosis positions had heart disease might over-estimate heart disease as the 16th diagnosis may be an underlying condition. Alberta Health considered a case if IHD appears in the first three diagnosis positions. This case definition would consider a higher IHD event rate than if only the first diagnostic position was used to define cases.

Many Canadian studies did not verify the diagnosis of physicians using third party reviewers and medical records like the MONICA study. This would mean that the independent IHD diagnoses in studies using DAD were not subject to the same systematic diagnostic criteria as the cases in the MONICA project. Due to the limited amount of information in DAD, unless a chart review was performed, the systematic diagnostic criteria used in the MONICA project would not be feasible in Alberta. The most efficient IHD identification in Alberta is through physician diagnosis obtained from administrative databases.

Surveillance for IHD was typically episodic, limited in time, and limited in IHD subtype analysis. Only a few studies used data from a time frame greater than 10 years studying IHD. [27,30,31] The rest of the studies took an average of 5 year separation rates, took a sample of two years or took data for 10-years. Longitudinal analyses on IHD or CVD prevalence and incidence

in Canada or any Canadian province was limited due to the lack of systematic collection, analysis and interpretation of IHD data.

The purpose of the review was not to provide a meta-analysis but to show that there has not been consistent IHD surveillance. The systematic review could have been improved if an independent reviewer also went through the articles so that inclusion criteria could have been checked and administered systematically.

5.3.2 Limitations of The Model

The case definition was applied consistently throughout the dataset but because of the nature of the data, different definitions could not be used to test the robustness of our results. The aggregated nature of the data restricts the types of variables available for the model although it is also clear that there may not be other variables which are available on every member of the population. One obvious limitation is the inability to calculate rate based on aggregated data because the individual follow-up times were not available. One concern about applying this model to project future IHD patterns is the lack of information on immigration and emigration that is needed to predict IHD cases in the future. Other limitations arose from the lack of information on: IHD severity, changes in IHD treatments, and the change in cases that arose from the updated ICD codes.

5.4 Conclusions

From the systematic review, incidence and mortality were predicted to decrease over time. Mortality was expected to decrease around 4% annually [28] while incidence was expected to decrease around 3% annually [26] due to findings from studies which examined the MI subtype of

IHD. The incidence model was expected to have a "time by age" variable. The mortality model was expected to have "sex by time" and "time by age" variables.

As expected, the mortality probability decreased by 4% each year, according to the logistic regression output. Even though the annual incidence probability is not readily discernible from the odds ratio, the overall pattern is a decrease in incidence over the 1994-2012 time frame. The incidence model did have a "year by age" variable while the mortality model had an "age by sex variable" and an "age90plus by zone by year before 2000" variable instead of the predicted "sex by time" and "time by age" variables.

IHD incidence and mortality probabilities decreased in both genders according to the models. One study mentioned a more pronounced decrease in the mortality among males than females [5] which was not supported by data in Alberta (figure 8). The models showed that incidence and mortality probabilities increased with age in an exponential manner which was not explored by the articles in the systematic review. The incidence and mortality models both have variables separating the three main age groups (less than 45, 45-last age group, and the last age group 85+ or 90+). This showed that there was a significant difference in the incidence and mortality between these age groups. The last age group may have been different because of the small population or the open ended age category. A few cases of IHD (numerator) would have a large effect on the probability of IHD if the population (denominator) was small. If the population had been larger in the last age category, the model may not have needed to fit the last age category using a separate variable. The last age category may have been fit using a "45+ age category."

The prevalence probability of IHD in Alberta seemed to indicate a plateau in the future. The plateau indicates that the difference between the incidence and mortality is stabilizing. As a result, the prevalence of IHD in the population is coming to equilibrium. The systematic review did not yield results on IHD prevalence over time.

Publicly available data from Alberta health can be used for surveillance epidemiology as demonstrated by the results presented above. Despite the clear pattern of the data, definite conclusions about the number of individuals with IHD in Alberta now or in the future cannot be drawn without information on immigration and emigration in Alberta.

5.4.1 Summary

The first chapter outlined the rationale and objectives of this project. The second chapter presented background information on IHD while the third chapter outlined the results from the systematic review. The fourth chapter presented the steps in the empirical analysis as well as the models resulting from the analysis. The following chapter summarizes the results and implications of this thesis. The literature suggests that previous efforts to examine IHD have a limited sample size, have narrow non-systematic IHD case identification, and have focused mainly on incidence and mortality. The systematic review revealed a general decline in IHD incidence and mortality rates as well as a "time by age" variable in the incidence and mortality models. The review also suggested that the mortality model would have a "time by sex" interaction term. The model demonstrated a mortality probability decrease with time. The South zone had the smallest decrease in mortality probability over time. The mortality probability was higher among men than women and increased with age more dramatically among men than

women. Mortality probabilities were significantly different for those between the 25 to 45 age group, the 46 to 89 age group, and the 90+ age group. Incidence probabilities in the incidence model declined through time for both sexes. Incidence probability in males was higher than females and increased with age more dramatically among males than females. Edmonton and North zones exhibited an increase in incidence probabilities between 2002 and 2003 while other zones exhibited a decrease in incidence probabilities. Incidence probabilities were significantly different for three age groups (25 to 45, 45 to 84, 85+). Overall, the South zone did not experience a decrease in incidence probabilities to the same extent as the rest of the province. The prevalence model showed the probabilities heading to a plateau with significantly higher prevalence probabilities among males compared to females. Prevalence probabilities increased more dramatically with age in males than females. There was a significant change in incidence probabilities for three age groups (less than 45, 45 to 84, 85+). These findings demonstrate a different pattern of IHD before and after the age of 45, higher probabilities of IHD in males, and perhaps South zone's need for preventative programs to decrease incidence probabilities.

5.5 Future Directions

Future research needs to address the effect of migration on IHD probabilities. Migration between zones can affect probabilities and must be addressed to increase confidence in conclusions about IHD patterns between zones. Another question that should be addressed is the effect of ICD code changes on the probabilities. Differentiating between real changes in probabilities and changes due to coding will clarify the pattern of IHD in Alberta. The rates of zones should be recalculated using various borders to ensure that rates are not solely dependent on the borders of geographic zones. As mentioned before, multiple IHD case definition should be tested to determine the robustness of the results. Together, these steps will give a better picture of IHD in Alberta and

identify zones with poorer IHD rates which may need more IHD initiatives to improve IHD health in the area.

List of Figures

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List of Acronyms

CVD	Cardiovascular Disease
IHD	Ischemic Heart Disease
PCI	Percutaneous Coronary Intervention
CABG	Coronary Artery Bypass Graft
LDL	Low-Density Lipoprotein
HDL	HIgh-Density Lipoprotein
ICD	International Classification of Disease
ICS	Intermediate Coronary Syndrome
AMI	Acute Myocardial Infarction
MI	Myocardial Infarction
WHO	World Health Organization
MONICA	Multinational MONItoring of trends and determinants in CArdiovascular disease
CCORT	Canadian Cardiovascular Outcomes Research
CCHS	Canadian Community Health Survey
APPROACH	Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease
ICES	Institute for Clinical Evaluation Sciences

Appendix 1 –Systematic Review Flow Chart, Search Strategy and Article Selection

PRISMA flow chart

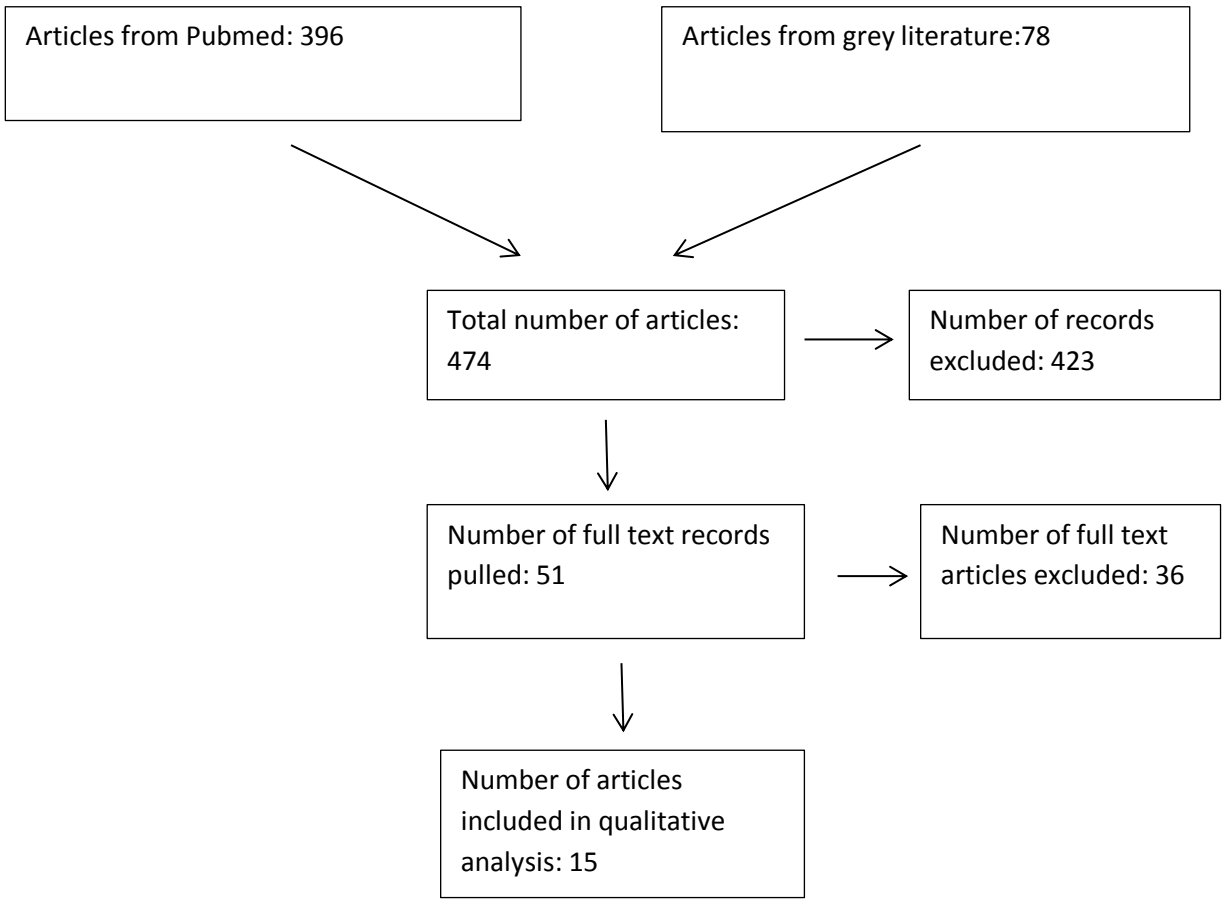


Table 7 Search terms for systematic review of IHD studies in Canada and Alberta

Combination	Number of Articles Found	Relevant Articles φ
"myocardial ischemia or acute coronary syndrome" and " population surveillance" and "Canada"	7	1
"myocardial ischemia or acute coronary syndrome" and " sentinel surveillance" and "Canada"	0	0
"myocardial ischemia or acute coronary syndrome" and "prevalence" and "Canada"	17	0
"myocardial ischemia or acute coronary syndrome" and "incidence" and "Canada"	33	4
"myocardial ischemia or acute coronary syndrome" and "Mortality" and "Canada"	89	6
{"myocardial ischemia or acute coronary syndrome" or "ischemic heart disease* or myocardial ischemia"} and "population surveillance" and "Canada"	14	1
{"myocardial ischemia or acute coronary syndrome" or "ischemic heart disease* or myocardial ischemia"} and "public health surveillance" and "Canada"	0	0
{"myocardial ischemia or acute coronary syndrome" or "ischemic heart disease* or myocardial ischemia"} and "sentinel surveillance" and "Canada"	0	0
{"myocardial ischemia or acute coronary syndrome" or "ischemic heart disease* or myocardial ischemia"} and "prevalence" and "Canada"	33	0
{"myocardial ischemia or acute coronary syndrome" or "ischemic heart disease* or myocardial ischemia"} and "incidence" and "Canada"	45	6
{"myocardial ischemia or acute coronary syndrome" or "ischemic heart disease* or myocardial ischemia"} and "mortality" and "Canada"	158	8
	Total number of articles	26
	Number of distinct articles	15

ϕArticles chosen after reading the abstract if abstract was available

Table 8 Summary of Articles from the PubMed Search Meeting Inclusion Criteria

Source Article	Location/Time/Study Type	Database	IHD Case Definition	Calculations	Rates and Conclusions
Trends in the Incidence of Acute MI Between 1984 and 1993—The Halifax County MONICA Project [26]	-Halifax -1984-1993 (10 years) -prospective study	-Data from: discharge database from the cardiac ward of hospitals, hospital discharge lists, Canada Mortality Database, obituary checked for missed cases	-ICD-9: 250,410-414, 427,798-799 -Patients aged 25-74 -MONICA study diagnostic criteria [44]	-MI events and incident cases modelled as Poisson processes -Covariates: sex, age, and year of occurrence -Trends estimated from loglinear models	-Average annual decline in MI mortality rate 3.9% (1.9%-5.8%) -There was an interaction between sex and time, trends were evaluated by sex - MI age and sex standardized incidence in women increased for the 25-44age group (statistically significant) as well as the 55-64 age group (statistically insignificant) between 1984 and 1993 -Male annual change in MI event rate was independent of age with an average value of -3.25% (95% CI -4.4% to-2.0%) between 1984 and 1993
Trends in incidence and mortality from acute myocardial infarction in Nova Scotia and Saskatchewan 1974 to 1985 [25]	-Nova Scotia and Saskatchewan -Incidences in 1977, 1981, 1985 (4 year scanning period to eliminate previous AMI)	-Hospital discharge records (DAD) were linked to the Canadian mortality database, generalized iterative record linkage system operated by	-ICD 410 and 411-414 -Patients 25-74 with primary or secondary discharge of AMI (5 year age groups) -MONICA study diagnostic criteria	-Study Reported Rates -Statistical test not reported	-Age standardized incidence rate per 100,000 decreased in both provinces (no analysis) -no statistical difference in the age-specific incidence among the incidence curves within each province -Incidence rates for MI increases with increasing age -No significant differences in the age-specific incidence

	- Retrospective	Statistics Canada[44] -No previous MI in previous 4 years to qualify as first case of AMI -all AMIs within 28 day period is considered one episode. -Fatal episodes classified as: in-hospital (record of death and AMI hospitalization) or before hospitalization (no record of hospitalization with ICD-410 found 28 days prior to and including date of death).			curves between 1977,1981 or 1985 for both sexes- Statistically significant decline in the age-standardized incidence rate in the 55-74 age group for males and females within each province between 1977 and 1981 and between 1977 and 1985 for both sexes -AMI mortality and case fatality decreased for both genders (no statistical analysis). This study reported a 49% decrease in standardized AMI mortality for Nova Scotia males, 29% decrease for Nova Scotia females, 24% decrease for Saskatchewan males, and 22% decrease for Saskatchewan females.
The epidemiology of acute Myocardial Infarction and ischemic heart disease in Canada: Data from 1976 to 1991[24]	-Canada -1976-1991	-mortality and hospital separation data (DAD) from Statistics Canada in the annual reports of vital statistics catalogue (84-206 [1970 and 1981),	-ICD 410, 410-414 -age groups: <45, 45-64,65+	-For each period, sex-specific death rates are reported for MI and IHD by 5-year intervals. -Age adjusted to 1971 Canadian population.	-Age-adjusted mortality rate from AMI and IHD showed both male and female decreasing, male decreasing more than females but male rate still higher than female rate -Age-adjusted separation rate decreased for all age groups but decreased the most for the

		catalogue 84-206 [1986] and catalogue 84-209 [1991].			45-64 age group; 65+ age group has the largest numerical increase in hospital separation rate -Most of the coronary artery diseases mortality occur in the 65+ age group for men and women -Females exhibit a lower mortality rate than males for ages 36-64 and 65+ but when all ages are taken into account, male and female rates seem to be similar till 1960 when female death rates are consistently lower than male death rates -For ages 65+, both genders show an increase in mortality till 1960 then decline. Male rates are higher than female rates
Trends in mortality from ischemic heart disease in Canada, 1986-2000. [45]	-Canada -1986-2000 - Retrospective	-Annual mortality files from Statistics Canada containing: age, sex, province, county -Patients aged 35+ -3 geographic levels: province/territory,	-ICD codes 410-414	-Age-standardized mortality rates calculated using 1991 population -Poisson model applied to age-standardized rates after logarithmic transformation	-Substantial decrease in Canadian mortality rates -Age-standardized mortality rates (ASMR) were plotted for age groups, with the rate increasing with increasing age groups and the mortality rate sharply increasing for the 75+ age group and highest for the 85+ age group -ASMR decreased with each

		Canada, county			consecutive time period
Avoidable mortality across Canada from 1975 to 1999 [31]	-Canada -(1975–1979, 1980–1985, 1985–1989, 1990–1994, and 1995–1999 -Retrospective	-Canada Mortality Database	-"The data analyses were restricted to deaths under 65 years of age, since health care can have the greatest impact on preventing deaths in this group"	- Age-standardized mortality rates (ASMRs) were derived using the direct method with Canada 1991 as the reference population.	-Age-standardized mortality from IHD is decreasing in constantly over the study period.
The epidemiology of acute myocardial infarction and ischemic heart disease in Canada: data from 1976 to 1991. [24]	-Canada -1931-1990	-Statistics Canada Mortality Database			-already have this
Cardiovascular disease mortality trends and related risk factors in Canada. [30]	-Canada -1976-1991 (1976-1981, 1986,1991)	-Statistics Canada mortality and hospital separation data from the annual reports of vital statistics	-Unspecified	-Sex specific death rates by 5-year intervals were reported for AMI and IHD -Direct standardization to 1971 population -Hospital separation data was divided into ages <45, 45-64, 65+	-Age and sex adjusted rates showed a decrease in mortality from IHD/AMI for both sexes but the decrease was larger in males -Hospital separation rates decreased for all ages and both sexes; decrease in separation rates was more pronounced in the middle aged (25% less) than the elderly (6% less) -The decline in IHD mortality

					was mostly due to the decline in AMI deaths -Men had higher rates of mortality from IHD and AMI
Cardiovascular disease mortality in Canada.[27]	-Canada -1950-1977	-Population mortality data from Statistics Canada	-ICDA-8 codes were used to identify the diagnosis	-Age standardized rates were done with direct method with the 1971 Canadian populations standard	-Age standardized mortality rate for IHD in males increased 0.5% annually from1950 until 1975 where it decreased 1.7% annually. IHD rates for females were constant till 1950s but declined after 1960 0.4% annually with larger changes in the 1970s at 2.4% decline annually. -Rate of decline for various components of IHD differed. AMI decreased persistently among all age groups and both sexes after 1969. After 1969, chronic and subacute forms of IHD increased among women aged 35 to 54 and men aged 35-64. Authors are unsure of whether sex differences in the survival of IHD (subacute/chronic) in 1974-76 were due to actual changes in survival or separate disease entities with different incidence rates. [-First period 1950-1968, second period 1969-1977]

					-Mortality for males aged <35 increased in the first period, then showed decline in the second period. All age groups of females showed decline in both periods with a greater decline in the second period. The largest average annual relative changes occurred in the first period for ages <35 - 1.5% for males and -2.4% for females.

Table 9 Summary of Articles from the PubMed Search Excluded from Review

Source Article	Location/Time/Study Type	Database	IHD Case Definition	Calculations	Rates and Conclusions
Regional variation in cardiovascular mortality [46]	-Canada -1995-1997	-Age standardized mortality rates obtained from Statistics Canada	-Causes of death that qualified were ICD codes 390-459 and 410-414 -Cardiac risk factors and some social determinants measures were taken from the CCHS 2000/2001	-Mortality rates were calculated from death counts and population size estimates by province	-excluded because the main objective was to find relationships between the regional characteristics and regional mortality rates. -Newfoundland and Labrador had the highest CVD and IHD mortality rates while Nunavut and the Northwest Territories had the lowest CVD and IHD mortality rates. -smoking and unemployment were the most important factors associated with CVD

					and IHD
Unstable angina report from Canadian expert roundtable [47]	-Canada				-excluded article as it only describes angina patterns without analytical proof
Living with heart disease: the 2001 Annual Report Card on the Health of Canadians [48]	-Canada -1984-1997	-source for data not stated			-excluded because data source unknown and focus was on survival more than surveillance -number of heart attack deaths has decreased 21%, percentage of hospitalized patients who survive heart attacks increased 10%, number of recurrent heart attacks decreased 6% over the 13 year time frame.
Regional variations in cardiovascular mortality in Canada. [49]	-Canada -1995 to 1997	-Statistics Canada age standardized mortality rates	-"Health region characteristics were taken from the 2000/2001 Canadian Community Health Survey, and the 1996 Canadian Census and the Labour Force Survey."	-"Linear regression analyses and analyses of variance were employed to identify relationships between these health region characteristics and CVD and IHD mortality rates."	-excluded because of the focus on risk factors
Decline in ischemic heart disease					-excluded-this was a letter to the editor

mortality. [50]					
Living with heart disease: the 2001 Annual Report Card on the Health of Canadians. [48]					-excluded-this was not based on data from a database
Mortality from ischemic heart disease. Changes in middle-aged men since 1900. Anderson TW. JAMA. 224(3):336-8, 1973 Apr 16.					-excluded-because it used American data

Table 10 Summary of Relevant Articles Citing PubMed Articles

Source Article	Location/Time/Study Type	Database	IHD Case Definition	Calculations	Rates and Conclusions
The burden of cardiovascular disease in Canada [23]	-Canada -1983-1993	-Data from Health Canada, Laboratory Centre for Disease control (Ref 18, which no longer exists), and Statistics Canada		-Age standardized rate	-Age standardized hospital separation rate slightly decreasing for men -Age standardized separation rate slightly increasing for women -IHD responsible for the most hospital separation rates out of CVDs

		-All the sources from this article state "Statistics Canada" as a source, the data is likely to be the DAD and the Vital Statistics databases			
Trends in the event rate and case fatality of patients hospitalized with myocardial infarction between 1984 and 2001 [22]	-Halifax/Nova Scotia -1984-1993/1998-2002	-Hospitalization records taken till 2001 to obtain 28-day survival -Used data from 2 different studies: MONICA (1984-1993) project and ICONS study (1998-2002).	-Patients between the ages 25 and 74 -Case definition is the discharge diagnosis by the attending physician as the primary problem. This study only included patients who reached the hospital and received a diagnosis. -Case fatality was defined as death from any cause occurring within 28 days of symptom onset that led to admission. Death date and time	-Age and sex standardized hospitalization rate and 28 day mortality rate -Cochrane Armitage Trend Test	-MI hospitalization and 28 day mortality rate decreased from 1984 to1993 and from 1998 to 2002 -AMI event rate decreased from 1984-1989, no trend afterwards

			obtained from Vital statistics or Province of Nova Scotia.		
National trends in rates of death and hospital admissions related to acute myocardial infarction, heart failure and stroke, 1994-2004 [5]	- Canada -Jan 1 1994 to Dec 31 2004.	-Data: Canadian Mortality database with CVD as most responsible cause of death (AMI, heart failure and stroke), and DAD -Hospital admission from April 1 1994 to March 31 2004 with MI, heart failure and stroke as most responsible diagnosis for stay.	-Cases were aged 20+ -Same day transfer=same event	-Calculation: 1991 Canadian standard population -Age and sex standardized rates compared	-Historically CVD mortality was higher among men but by 2000, more women than men had died of stroke in hospital. And more women than men had been admitted to the hospital for stroke and heart failure. -The overall age and sex standardized rate of death from all cardiovascular disease declined 18.2% (95% CI 17.8%-18.6%); the overall age and sex standardized in-hospital case-fatality rate decreased 20.2% (95% CI 19.1-22.2)
Chapter 3: Burden of Cardiovascular disease In Canada [15]	-Canada -1950-1999	-Prevalence data from CCHS	-Respondents who reported heart disease were asked whether it was heart attack, angina and or heart failure.	-calculation: percentages	-Men reported living with heart disease more than women (5.4% and 4.6%) -Angina prevalence similar (1.8% men 1.9% women) -Disease prevalence for

			-Mortality was defined by the most responsible underlying condition on the death certificate using ICD8 and 9 codes.		reported previous heart attack was lower form women (1.5% vs 2.7% men) -25% of people aged 80 and over reported having this heart disease -Heart disease becomes increasingly complex and severe with increasing age -In the 40-49 age group, 19% of people with heart disease reported to have at least 2 of: angina, previous heart attack, congestive heart failure. For people aged 80+, the same proportion increased to 35%
Trends in even rate and case fatality of patients hospitalized with myocardial infarction between 1984 and 2001 [22]					-Already included

Table 11 Excluded articles from the Embase Search

Source Article	Location/Time/Study Type	Database	IHD Case Definition	Calculations	Rates and Conclusions

Patterns and costs of hospital care for coronary heart disease related and not related to diabetes [51]	-South Glamorgan, Wales -1991/2 to 1994/5	-hospital data -ages 35+	-CHD= ICD9 codes 410-414, 425-429, 440 as the primary or subsidiary reason for visit	-excluded this article because the study population is not Canadian
Thirty-Year trends in incidence rates, clinical features, treatment practices, and short term outcomes of patients <55 years of age hospitalized with an initial acute MI [52]	-Worcester			-excluded this article because the study population is not Canadian
Recent trends in acute coronary heart disease--mortality, morbidity, medical care, and risk factors. The Minnesota Heart Survey	Minneapolis-St.Paul, Minnesota			-excluded this article because the study population is not Canadian

Investigators. [53]		
How many people have had a myocardial infarction? Prevalence estimated using historical hospital data [54]		-excluded because the study only studied prevalence for one year not over time -in 2004 the prevalence was 2.03% (95% CI: 2.01%-2.05%) -CCHS self-reported heart attack yielded different rates than administrative data

After identifying relevant articles, the bibliographies of all articles were scanned for potentially relevant articles. The following articles were found:

Table 12 Summary of Relevant Articles from Bibliographies of PubMed Articles

Source Article	Location/Time/Study Type	Database	IHD Case Definition	Calculations	Rates and Conclusions
The epidemiology of acute myocardial infarction and IHD in Canada: data from 1976 to 1991 [24]					-Already summarized above
Contribution of trends in survival and coronary-	-Halifax, Canada -1980's-1991 -Prospective study	-MONICA project [44]		-Event rate for ages 35-64 were standardized by 5-year age groups	-Official CHD mortality rates based on death certificates decreased in men by -4% (-10.8% to 3.2%)

events rates to changes in coronary heart disease mortality: 10 year results from 37 WHO MONICA project populations [28]				to World Standard Population. Authors used the relation between the Poisson and chi squared distribution to derive 95% CIs for weighted sums of Poisson parameters. The trends were calculated using a log-linear model where t is the year, e is the error : log r,=a+bt+e,.	and in women by -4% (-15.7% to 3%). Changes in the rate of non-fatal coronary events were smaller; men had a decrease of -2.1% (-6.9% to 2.8%) women had a decrease of -0.6% (1.4% to 3.1%) -In Halifax, the official CHD mortality decreased -4% with se(standard error) of 2.1%. The MONICA CHD mortality rate decreased -4.1% se 1.8%. The MONICA non-fatal event rate increased 2.9% se 1.1%.
Population-wide mortality trends among patients hospitalized for acute myocardial infarction: the Ontario experience [29]	-Ontario, Canada -1981-1991	-Ontario discharge abstracts from DAD	- Only primary diagnoses as AMI were included (ICD-9 code 410). Records were excluded if they met one of the following: 1) patients were >105 or <20 years old 2) record had missing gender 3) the patient signed himself of herself out of hospital 4)	-Chi squared tests were done for categorical variables and analysis of variance tests done for continuous variables.	-Crude and age-sex adjusted hospital fatality rates decreased over time. In the adjusted rate, there was a significant decline from 1985 to 1991 and a slight decrease between 1981 and 1985. -The largest relative decrease for the in-hospital case fatality rate was in the <50 age group -The In-hospital case fatality is higher in females than males across the age

			the patient had been previously discharged from any hospital with the same primary diagnosis within 3 months of current admission that fiscal year (prevent double counting one incident).		categories. This difference is greater in the <70 age group
Trends in incidence and mortality form acute myocardial infarction in Nova Scotia and Saskatchewan 1974-1985 [25]					-already included this article in Pubmed search
Population-wide mortality trends among patients hospitalized for acute myocardial infarction[53]					-already excluded previously

Table 13 Summary of Articles from The Bibliographies of PubMed Excluded from Review

Source Article	Location/Time/Study Type	Database	IHD Case Definition	Calculations	Rates and Conclusions

The World Health Organization MONICA project (MONItoring of trends and determinants in Cardiovascular disease): a major international collaboration [55]		-Study relationships between: 1) 10 year trends in serum cholesterol, blood pressure and cigarette consumption and 10 year trends in coronary heart disease incidence rates 2) 10 year trends in 28 day case fatality rates and 10 year trends in acute coronary care	-excluded this study because it explains the reasons for the project and the algorithm to determine an IHD case, IHD probably case, or not IHD case.
Myocardial Infarction and coronary deaths in the World Health Organization MONICA Project [56]	-Halifax, Canada	-MONICA project	-excluded, this provides a description of procedures used in the MONICA project database.
Decreasing mortality from acute myocardial infarctions: effect	-Halifax, Canada	-Halifax County MONICA project	-excluded because of the focus on severity -mortality from MI decrease not due to decrease in

of attack rates and case severity [32]			severity. Severity has increased over the 1984-1993 time frame
Recent trends in acute coronary heart disease-mortality, morbidity, medical care and risk factors [57]	Minneapolis–St. Paul, Minnesota		-excluded because of the use of non-Canadian data
Trends in the incidence of myocardial infarction and in mortality due to coronary heart disease [58]	-United States		-excluded because of the use of non-Canadian data
Death rates from coronary disease-progress and puzzling paradox [59]	-United States		-excluded because of the use of non-Canadian data
Sex and time trends in cardiovascular disease incidence and mortality [60]	-Framingham, Massachusetts	-Framingham Study	- excluded because of the use of non-Canadian data

21 year trends in incidence of myocardial infarction and mortality from coronary disease in middle-age [61]	-Turku, Finland			- excluded because of the use of non-Canadian data
Myocardial infarction patients in the 1990s-their risk factors, stratification and survival in Canada: the Canadian assessment of myocardial infarction (CAMI) study [62]	-Canada -1990-1992	-9 Canadian hospitals		-excluded because the study objective was to examine post-discharge mortality
Outcomes of acute myocardial infarction in Canada [63]	-All Canadian provinces -1997/98 and 1999/2000	-Canadian mortality database, discharge abstract database and the CCHS	-A cohort of new AMI hospitalization cases was identified between 1997/98 and 1999/2000, No data from Yukon, or Northwest Territories and Nunavut. Patients	-excluded because of focus on outcomes post AMI instead if IHD trends

			were excluded if less than 20 years old or over 105 years old, if AMI was coded as complication of condition, if invalid health card number, if total length of stay is less than 3 days, if previous AMI within the previous year.	
Temporal changes in outcomes of acute myocardial infarction in Ontario, 1992-1996 [64]	-Ontario -1997-2002	-DAD-Ontario Myocardial Infarction Database project	-Data from DAD for all patients discharged from an acute care hospital in Ontario with most responsible diagnosis as AMI ICD-9 code 410. Between April 1 2002 to March 31 1997. -DAD hospitalization was linked to OHIP numbers and linked to physician claims data in the Ontario health care system. The Ontario	-excluded this study as the information focuses on 30-day and 1-year mortality -The study found that there were modest improvements of 300-day and 1 year survival after AMI during this period primarily in younger and male patients. Virtually all improvements were in the 30 days of AMI with little change observed beyond that time.

	Registered Persons Database contains information on the vital status of Ontario residents. (Deaths after hospitalization searched to obtain deaths associated with subsequent hospital admission.)	
Acute myocardial outcomes in Canada		-excluded because the PDF format is not available
Ten year trends of myocardial infarction rates, measure by MONICA and by hospital discharge diagnosis [65]		-excluded because it is a presentation abstract
Weekly Epidemiological Record: World Health Organization, Geneva [66]		-excluded because this article talks about heart disease and does not analyse data

Burden of cardiovascular disease in Canada [15]					-excluded because the study estimates the CVD mortality rates
The recent decrease in CHD mortality [67]					-excluded because of the use of only American data
The recent decline in ischemic heart disease mortality [68]					- excluded because of the use of only American data

Table 14 Summary of Relevant Articles from Grey Literature

Source Article	Location/Time/Study Type	Database	IHD Case Definition	Calculations	Rates and Conclusions
Tracking heart disease and stroke In Canada 2009 [1]	-Canada -1971-2005	-Data from Hospital Morbidity Database	-IHD as condition most responsible for hospital stay	-raw numbers, or rates standardized to 1991 population	-"In 2005/06, there were 160,323 hospitalizations with ischemic heart disease as the condition most responsible for staying in hospital" -Mortality from IHD rose from 1950-1970, then started declining -Age standardized

					hospitalization rates for IHD have decreased -As age increases, hospitalizations for IHD also increases (2005/6 data) -During this time period age standardized CVD hospitalization rate decreased for both sexes -Rate of CVD death increases with increasing age
Chronic disease projections 2006 to 2035: ischemic heart disease [16]	-Alberta -1990-2035, prediction from 2006-2035	-Source: Alberta health care insurance stakeholder registration, Alberta vital statistics, Alberta health care insurance claims.	-Case definition, one of the following: • had three encounters with a physician with a diagnosis code for IHD (ICD9 code between 410 and 414) • was hospitalized with a diagnosis of IHD • had a heart attack (ICD9 code equal to 410)	-Incidence risk modeled using Lee-Carter method and singular value decomposition -Vectors for males and females: Age vs year, health region versus age, in-migrants,	-There were ~82000 prevalent cases in 2005 -Age groups 40-54 and 85+ had increasing risk over time -Female and males in the Palliser Health Region showed elevated incidence risk at most ages. (No other vectors for males or females showed consistent regional difference over time) -Decreasing death rates for all ages except at the "younger ages" where more variation exists -Between 2005 and 2036, number of prevalent cases expected to double

					-Death rates expected to decrease

Table 15 Summary of Articles from Grey Literature Excluded from Review

Source Article	Location/Time/Study Type	Database	IHD Case Definition	Calculations	Rates and Conclusions
Chronic disease and injury [3]	-Alberta -2004	-IHD Mortality rate from Alberta Vital Statistics, Death File 2006 edition			-excluded because this study does not look at rates over time -112/100,000 deaths in Alberta, 2004 from IHD
Archived-cardiovascular disease Morbidity surveillance information [69]	-Canada -1989-1993 average of 5 years	-Data source-Laboratory Centre for Disease Control, 1996 using Statistics Canada Data -Hospital Separation Rate- ICD9 410-414, 429.2	- ICD9 410-414, 429.2	-1991 standard population	-excluded because this study does not look at rates over time -Morbidity 600/100,000-Canada 580/100,000-Alberta

Database Information

DAD and HMDB

Many Canadian studies in the systematic review have used the Discharge Abstract Database (DAD) of the Hospital Morbidity Database (HMDB). The HMDB is created from the DAD data. Both of these databases contain patient demographic data from inpatient separations and day surgeries from 1979-2013. Day surgeries have not been a mandatory field for reporting consistently across provinces over time; when the reporting was not mandatory, there were low report rates. Thus, this lack of information renders DAD and HMDB incomplete sources for information on day surgery in Canada. The DAD has been used to collect information on other hospital activities but the reporting is inconsistent as these were not mandatory fields. The DAD database covers all provinces and territories except Quebec. Quebec's ministry of health submits their acute care data directly to HMDB. The DAD covers 75% of inpatient separations, while HMDB covers all reported inpatient separations. Each separation is a single entry; a separation is defined as: discharge, death, sign-out, or transfer. Each entry is a separation, so patients who transferred five times would have five entries. This type of information would be inaccurate if it is used to calculate the number of patients from the number of entries/separations. Patient health card information is included so multiple transfers by one individual can be matched to a single person to prevent overestimating the number of patients.

Provinces determine which institutions are eligible to report to DAD and these institutions are given Institution Numbers. From these institutions, each separation entry contains data on: coded diagnostic, intervention, patient demographic and administrative information. Diagnosis is inputted using ICD-9 or ICD-10 codes. A full list of mandatory fields is available from the CIHI

web site for years 2011 and later. [70] Full postal codes of patients are not released; researchers can access the first three digits of the postal code, the forward sortation area. The forward sortation area allows researchers to link the patient separation to an area of residence. [70]

The HMDB is based on DAD data, but instead of using all entries it is a survey with a cross-sectional design. HMDB can contain data on inpatient hospitalizations in Canada that occur in general, convalescent, rehabilitation and chronic hospitals. The database contains data from 1960-2013 upon request. The database excludes hospitalizations in psychiatric hospitals and hospitalizations in federal facilities (for example, military hospitals, prisons and Indian reserves.) Error detection is done at the provincial level first then another time at Statistics Canada. At Statistics Canada, error detection is done using two edits:

1) Validity edits checked that all elements were present.
2) Correlation edits checked that the reported diagnoses and procedures were consistent with the reported age and sex.

Missing items were imputed according to a module based on past experience. An annual average of 1% of records had an error detected during the validation and correlation edits. Only 1.2% of records have uncorrected missing data or invalid data. Re-abstraction studies were performed to verify consistency in coding and adherence to rules and guidelines. [71]

PHAC

The PHAC report on Ischemic heart disease [69] used information from the Laboratory Centre for Disease Control in 1996 which used data from Statistics Canada. However, government reports

on hospital separation data was not found for the years before 2010. Since the Laboratory Centre for Disease Control no longer exists, this data would be hard to find. One can only infer that the data for this archived report was based on DAD and HMDB data.

Alberta Health

Physician's claims data from Alberta is available from January 1, 1994 to the present. This database was created from the Fee for Service claims physicians and other providers who were compensated for their health services. The entries contain recipient, provider and service data. ICD-9CM and the Schedule of Medical Benefits was used to code disease and procedures. The database is updated weekly but the completeness of the claims improves as the time from the date of service increased. Data from 1983-1993 is limited. [72]

The Alberta Inpatient database is the Alberta's version of the DAD, it is available from 1993 to the present. The Alberta Inpatient Database contains the recipient, service, diagnosis and procedures/interventions for people who have been discharged from an inpatient bed. The database used ICD-9-CM (till 2002) and ICD-10-CA/CCI (from 2002) to denote diagnosis. This database is updated annually. [72]

Canadian Mortality Database

The Canadian Mortality Database assembled and maintained by Statistics Canada is an administrative database that has demographic information and cause of death information on the deceased. All provinces and territories have registries that report to Statistics Canada annually. The database includes deaths of Canadian residents in Canada. From 2010 onwards, Canadian

residents who die in the American states are no longer collected. The cause of death is recorded according to the World Health Organization's ICD codes. [73]

Canadian Community Health Survey (CCHS)

The CCHS is a cross-sectional self-report survey conducted by Statistics Canada [71,73] which collects information on health status, health care utilization and health determinants in the population. The CCHS samples the whole Canadian population aged 12 and over living in the ten provinces and 3 territories. People excluded from the survey include: persons living on reserves, Aboriginal settlements, full time members of Canadian Forces, institutionalized population and persons living in Quebec health regions of Region du Nunavik and Region Terres-Cries-de-la-Baie-James. These exclusions represent less than 3% of the population. Response to the survey is voluntary. In the systematic review, one study [49] used data from the CCHS where data collection began September 2000 and the total sample size was 131,535 household respondents with a 84.7% response rate. The authors noted that CCHS utilized planned sampling of one respondent per household, but planned over-sampling of youth resulted in a second member of some households to be interviewed. Respondents who reported heart disease were asked whether it was heart attack, angina and or heart failure. [49]

MONICA

MONICA was a world-wide heart disease project spearheaded by the World Health Organization (WHO) with the goal of monitoring trends and determinants in cardiovascular disease. The study involved 37 populations from around the world, and used administrative or census-based data to

monitor heart disease around the world over time. Halifax was one of the 37 populations, and the only Canadian population to participate in the study. Hospital discharge data was used in the Halifax population. As long as patients were Halifax residents between the ages of 25 and 74, data on the following fields were abstracted: health history at admission, symptoms and onset, cardiac enzyme data, ECG, investigations and procedures performed during hospital stay, discharge diagnosis, medication before during and after hospital stay, autopsy data, and vital status 28 days after symptom onset. This data was applied to an algorithm to determine definite MI, possible I, ischemic arrest, no MI or insufficient data for diagnosis. Applying the same algorithm throughout, allowed for consistent diagnosis and comparable rates across Halifax County. [44]

Alberta Vital Statistics

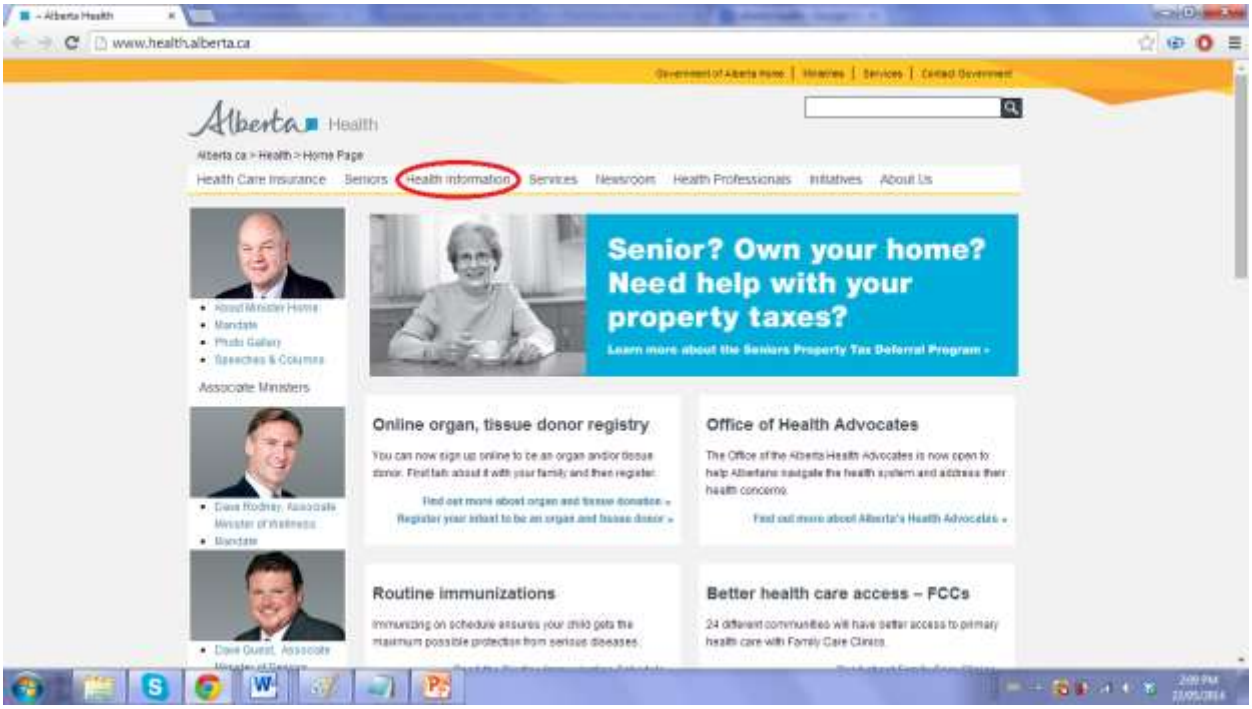
Alberta Vital Statistics records births, deaths, marriages and legal name changes. Alberta health and Wellness receives the vital data for births and deaths each year. Vital Statistics only contains births and deaths of Alberta residents occurring within province. The result is a slight underestimate of mortality and birth in the province. [72]

Appendix 2 – Accessing Administrative Health Data from the Alberta IHDA

The administrative data was accessed through these steps:

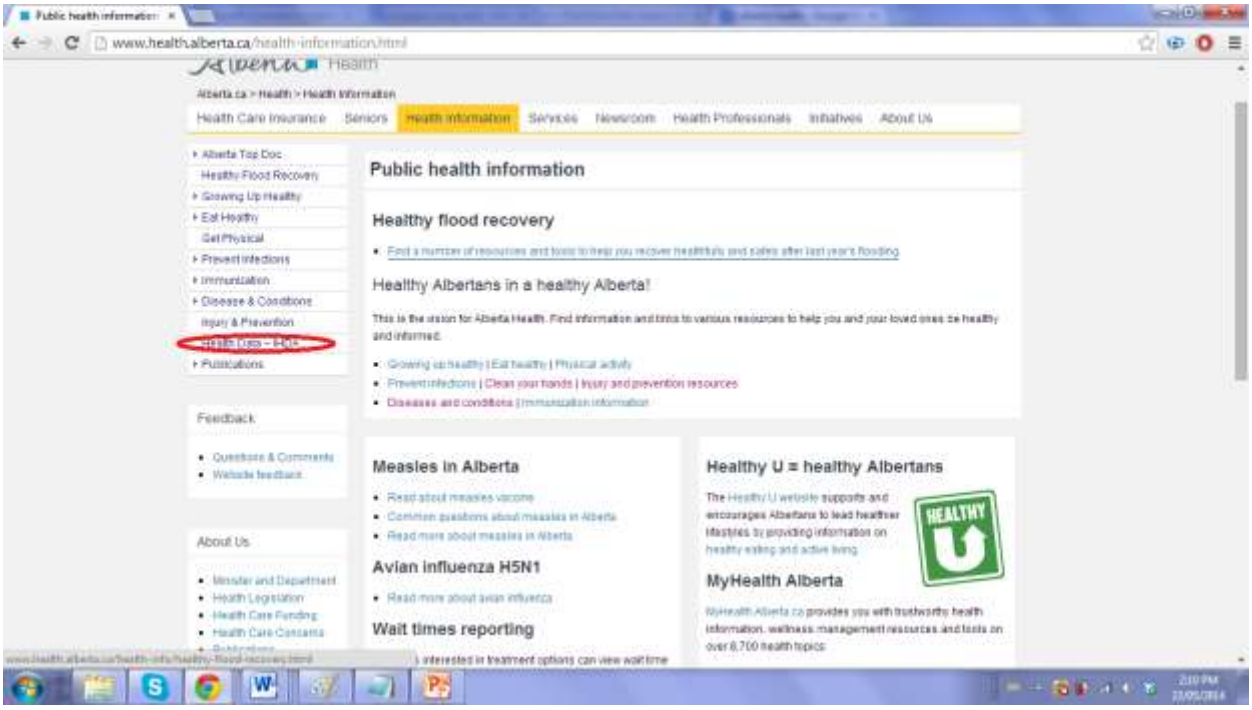
1) Click on the Health Information link on the tool bar on the top. (http://www.health.alberta.ca/)

Figure 15 Screen Shot of The Alberta Health Web Site



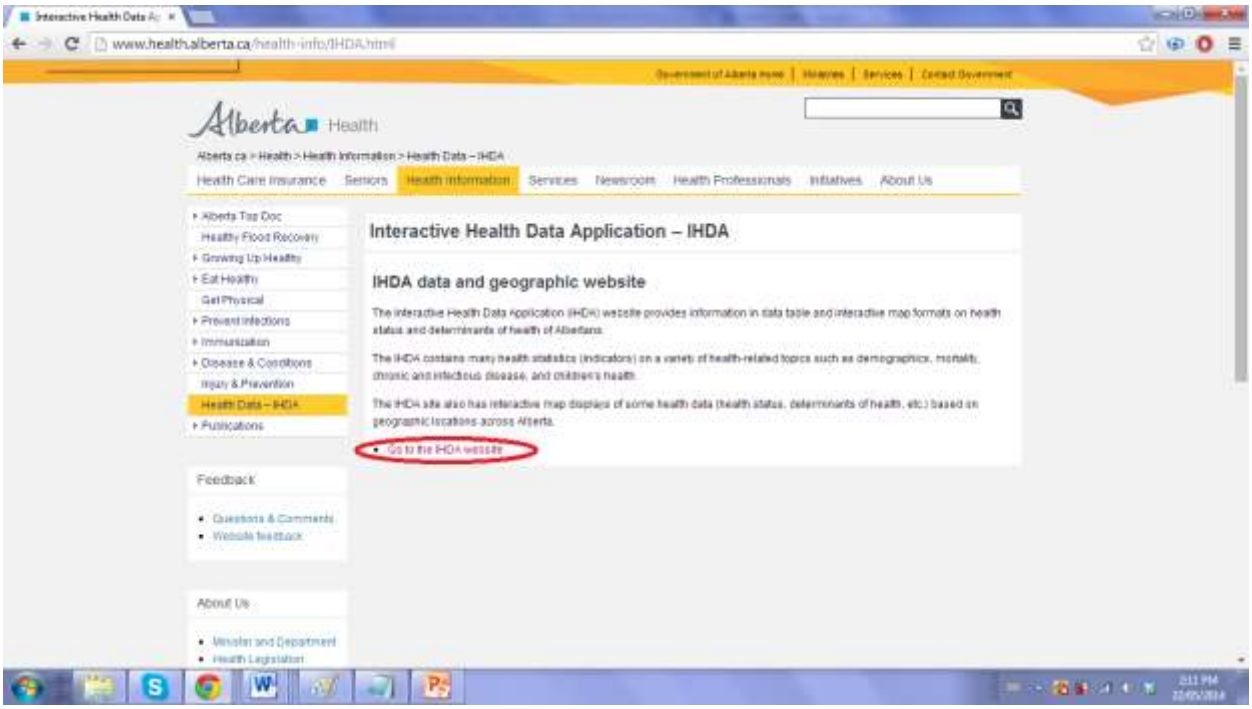
2) Click on the IHDA tool on the side bar to the left

Figure 16 Screen Shot of The IHDA Link



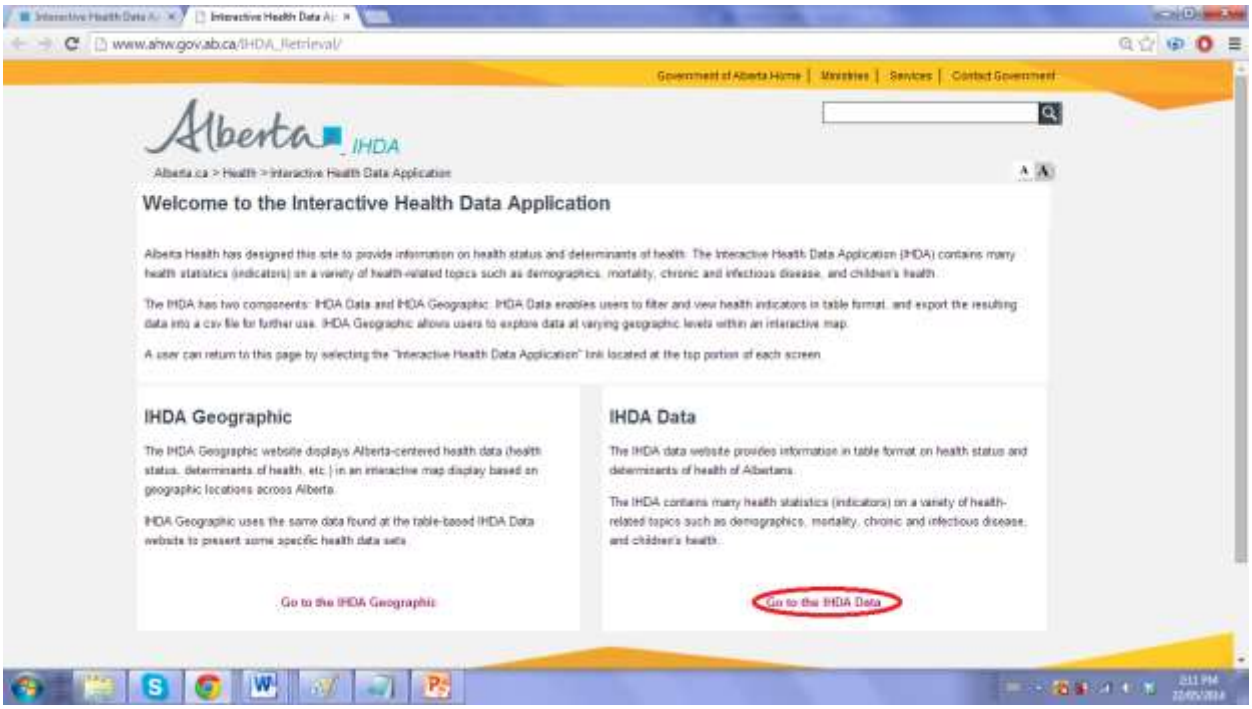
3) Click on the IHDA link

Figure 17 Screen Shot of The IHDA Link



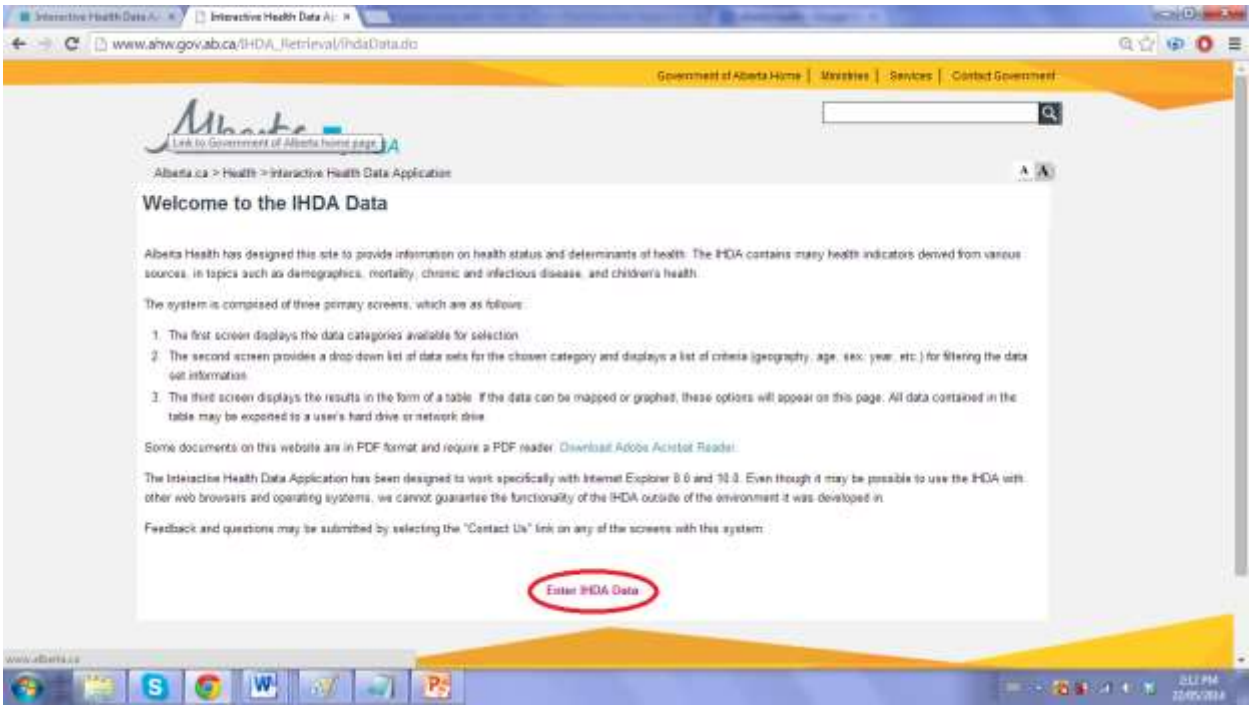
4) Click on the “go to IHDA data” link

Figure 18 Screen Shot of The Link To The IHDA Tool



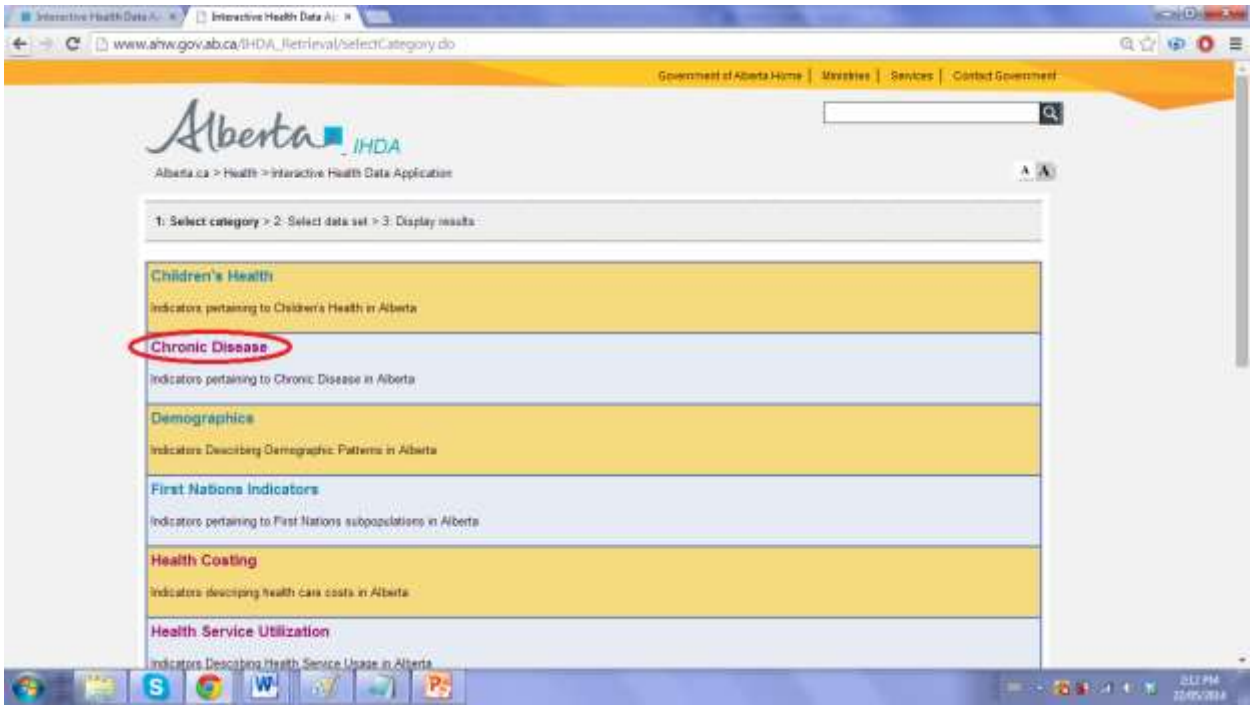
5) Click “Enter IHDA Data”

Figure 19 Screen Shot of The Link To The IHDA Tool



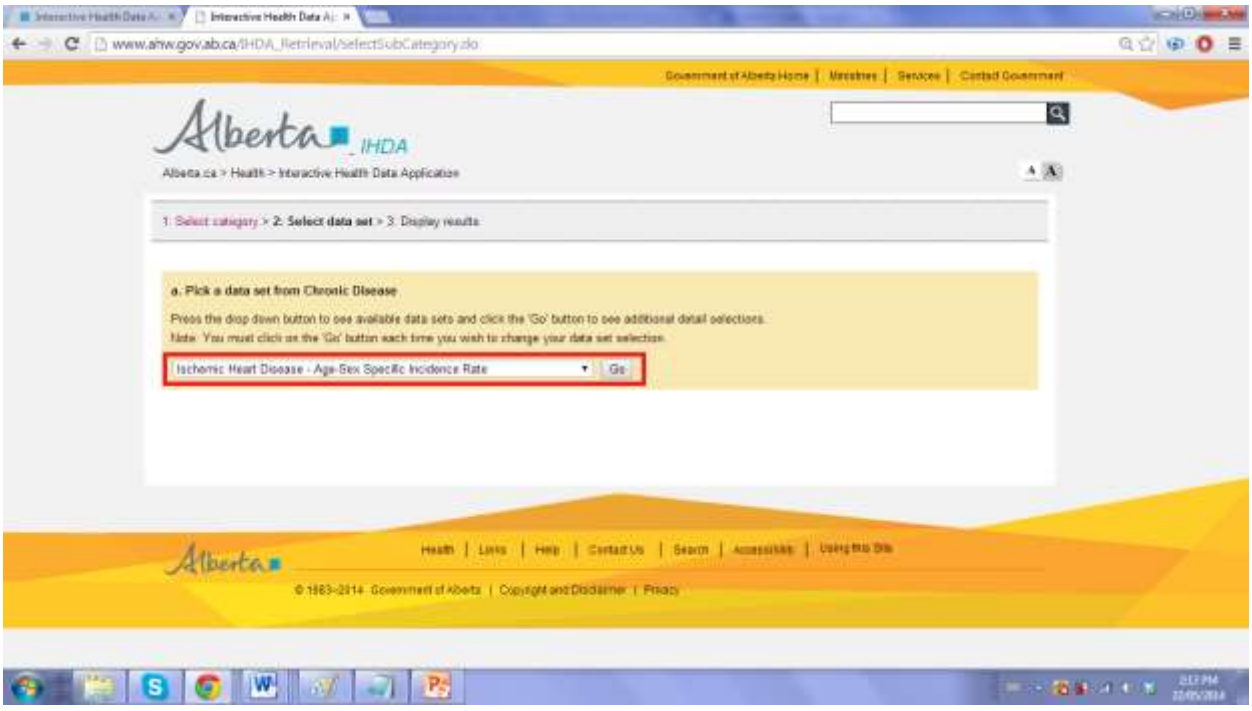
6) Click on the “Chronic Disease” link

Figure 20 Screen Shot of The Link To Chronic Diseases Data



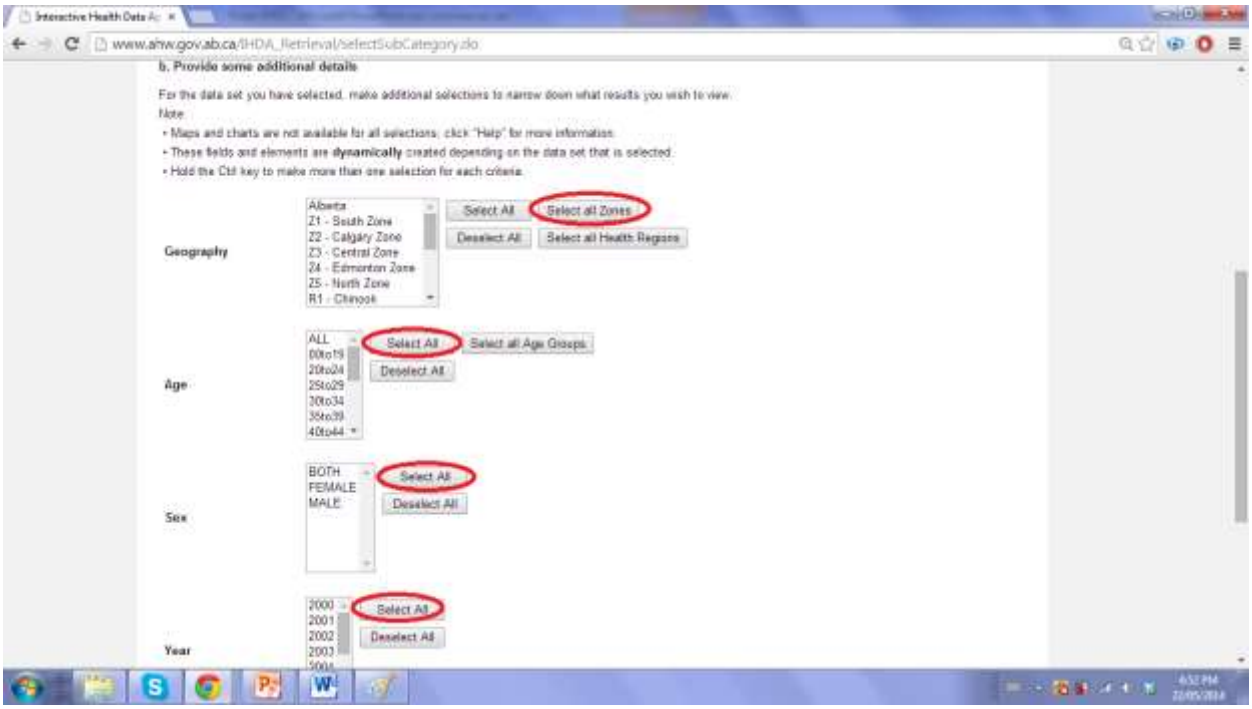
7) Click on the scroll down menu for “Ischemic Heart Disease- Age Sex specific Incidence/Prevalence” and click on the “Go” button

Figure 21 Screen Shot of The Link To IHD Data



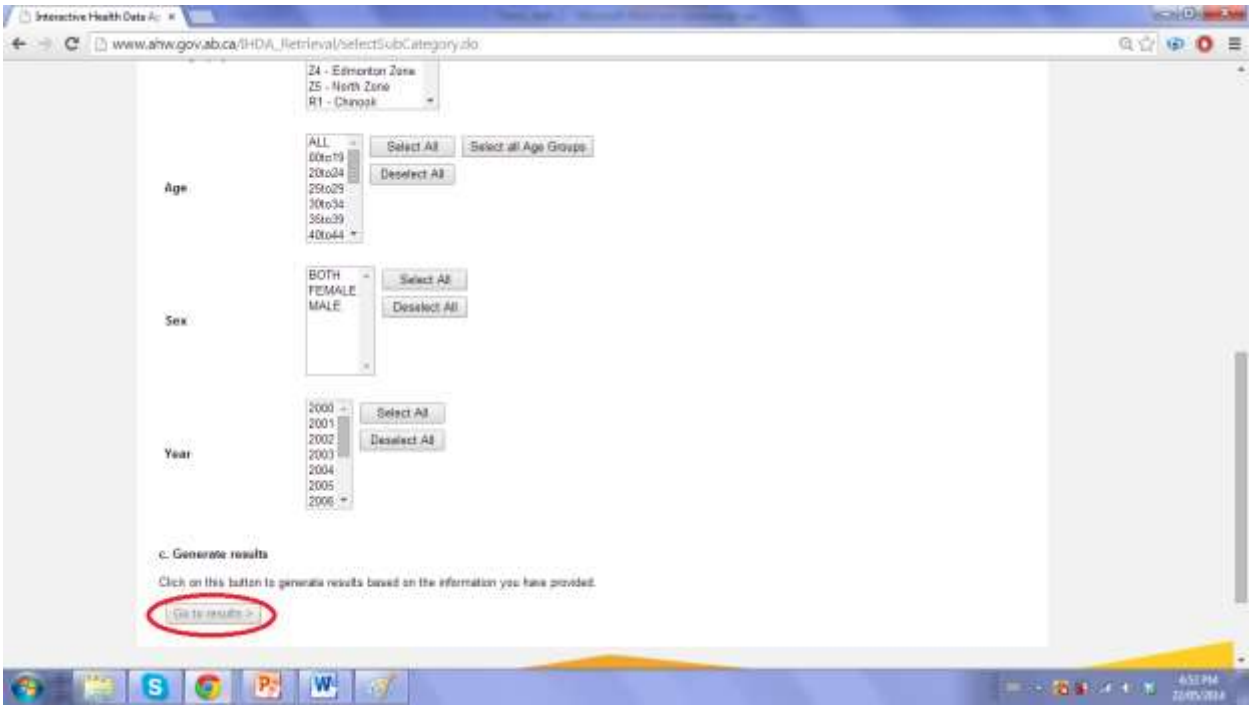
8) After clicking the “Go” button, scroll down to section b and “Select All” for the age groups, sex, and year

Figure 22 Screen Shot of Input Values for IHD Data



9) Scroll Down further on the page and click "Go to results"

Figure 23 Screen Shot of The Link To IHD Data



10) The data can be downloaded using the “Export Data” link
Figure 24 Screen Shot of The Link To Download Data

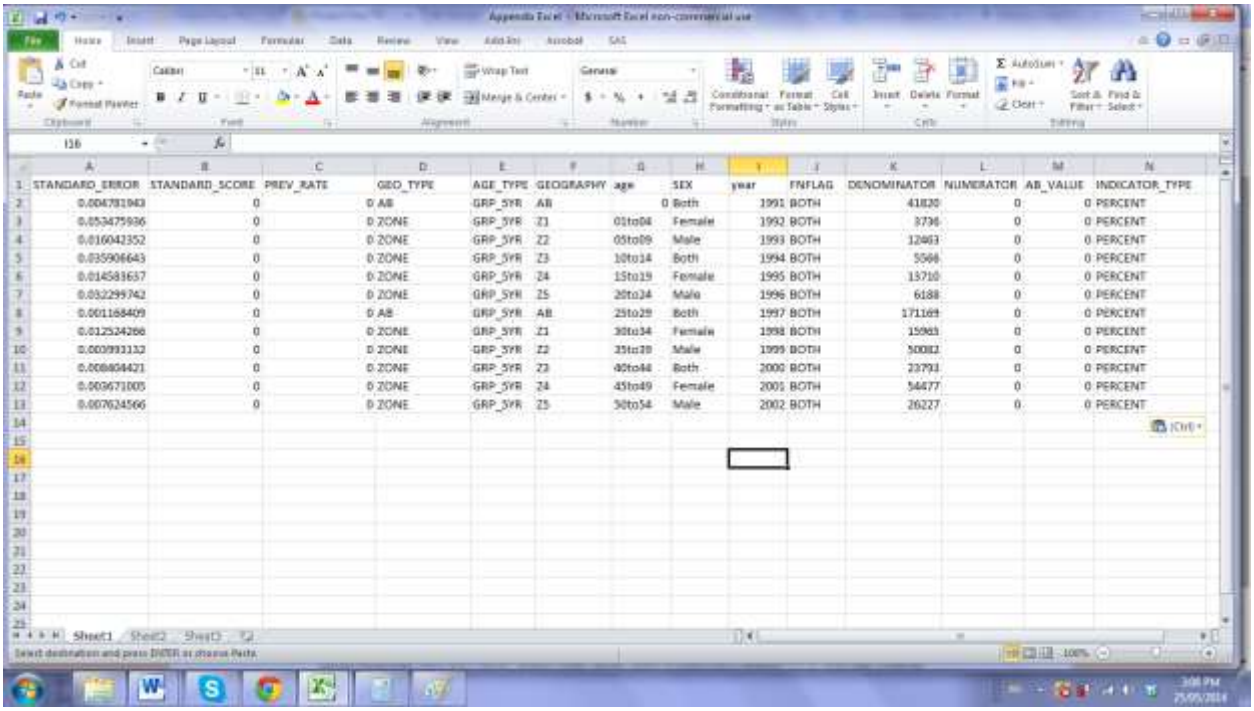
11) Data notes are on the bottom of the page at the “View Data Notes” link

Figure 25 Screen Shot of The Link To Obtain Data Methodology

Appendix 3 – An example to illustrate Management of administrative health data from IHDA Excel Screen shots

1) Screen shot of example data

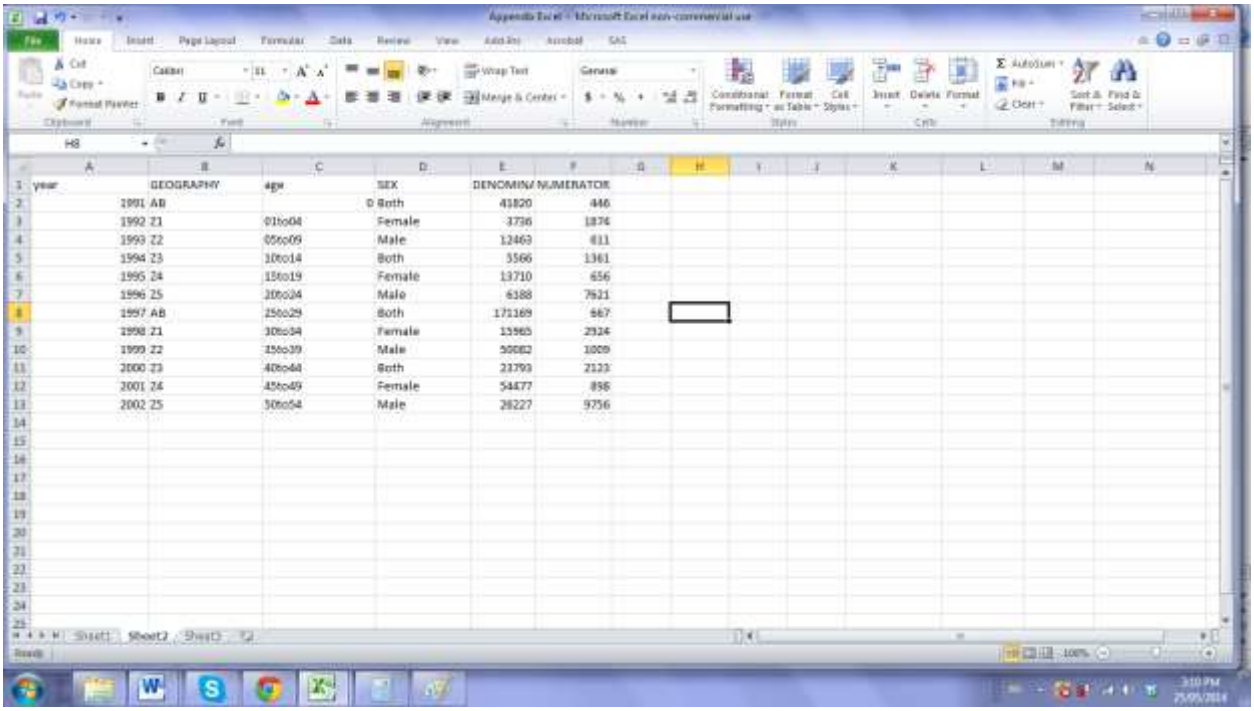
Figure 26 Screen shot of example data



	A	B	C	D	E	F	G	H	I	J	K	L	M	N
1	STANDARD_ERROR	STANDARD_SCORE	PREV_RATE	GEO_TYPE	AGE_TYPE	GEOGRAPHY	age	SEX	year	FNFLAG	DENOMINATOR	NUMERATOR	AB_VALUE	INDICATOR_TYPE
2	0.004781943	0		0 AB	GRP_5YR	AB		0 Both	1991	BOTH	41820	0	0	PERCENT
3	0.053475936	0		0 ZONE	GRP_5YR	Z1	01to04	Female	1992	BOTH	3736	0	0	PERCENT
4	0.016042352	0		0 ZONE	GRP_5YR	Z2	05to09	Male	1993	BOTH	12463	0	0	PERCENT
5	0.035906643	0		0 ZONE	GRP_5YR	Z3	10to14	Both	1994	BOTH	5566	0	0	PERCENT
6	0.014583637	0		0 ZONE	GRP_5YR	Z4	15to19	Female	1995	BOTH	13710	0	0	PERCENT
7	0.032299742	0		0 ZONE	GRP_5YR	Z5	20to24	Male	1996	BOTH	6188	0	0	PERCENT
8	0.001168409	0		0 AB	GRP_5YR	AB	25to29	Both	1997	BOTH	171169	0	0	PERCENT
9	0.012524266	0		0 ZONE	GRP_5YR	Z1	30to34	Female	1998	BOTH	15965	0	0	PERCENT
10	0.003993132	0		0 ZONE	GRP_5YR	Z2	35to39	Male	1999	BOTH	50082	0	0	PERCENT
11	0.008404421	0		0 ZONE	GRP_5YR	Z3	40to44	Both	2000	BOTH	23793	0	0	PERCENT
12	0.003671005	0		0 ZONE	GRP_5YR	Z4	45to49	Female	2001	BOTH	54477	0	0	PERCENT
13	0.007624566	0		0 ZONE	GRP_5YR	Z5	50to54	Male	2002	BOTH	26227	0	0	PERCENT

2) Data preparation, second step

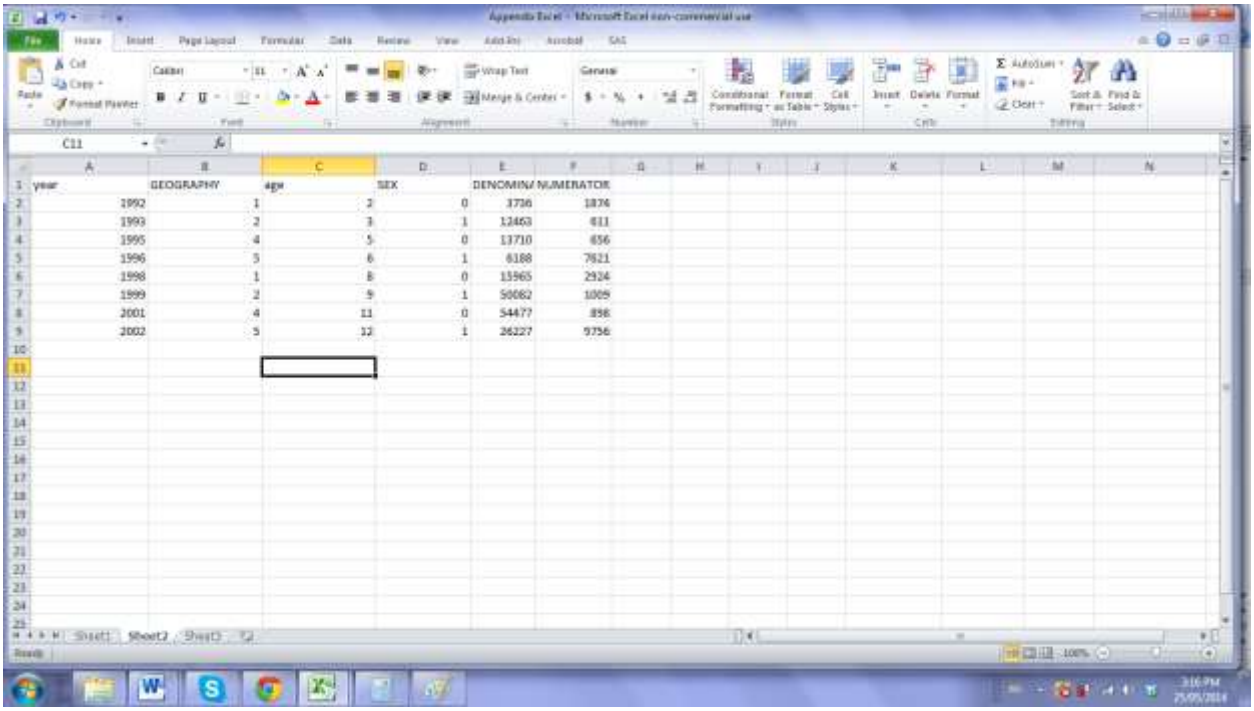
Figure 27 Screen shot of the retained data



year	GEOGRAPHY	age	SEX	DENOMIN/	NUMERATOR
1991	AB	0	Both	41820	446
1992	Z1	01to04	Female	3736	1874
1993	Z2	05to09	Male	12469	611
1994	Z3	10to14	Both	5566	1361
1995	Z4	15to19	Female	13710	656
1996	Z5	20to24	Male	6188	7621
1997	AB	25to29	Both	171169	667
1998	Z1	30to34	Female	15965	2924
1999	Z2	35to39	Male	50082	1009
2000	Z3	40to44	Both	23793	2123
2001	Z4	45to49	Female	54477	898
2002	Z5	50to54	Male	28227	9756

3) Data preparation, third step

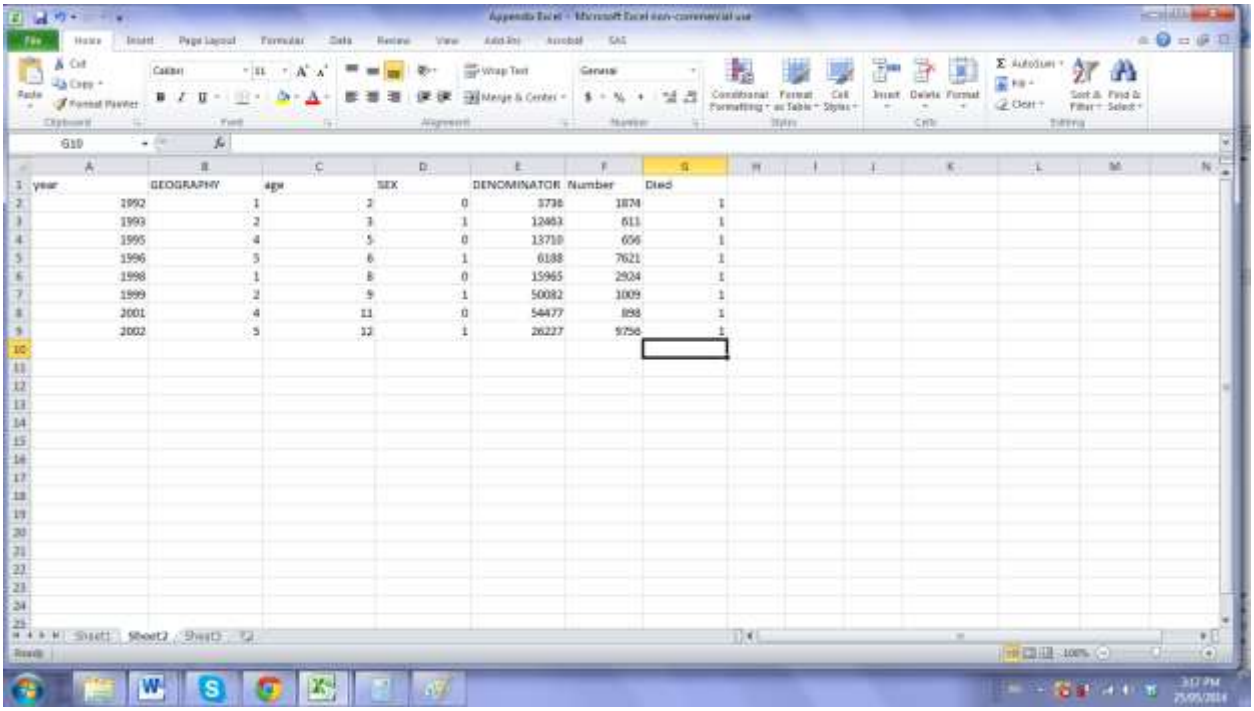
Figure 28 Screen shot of the coded data



year	GEOGRAPHY	age	SEX	DENOMIN/	NUMERATOR
1992	1	2	0	3736	1874
1993	2	3	1	12463	611
1995	4	5	0	13710	656
1996	5	6	1	6188	7821
1998	1	8	0	15965	2924
1999	2	9	1	50082	1009
2001	4	11	0	54477	898
2002	5	12	1	26227	9756

4) Data preparation, fourth step

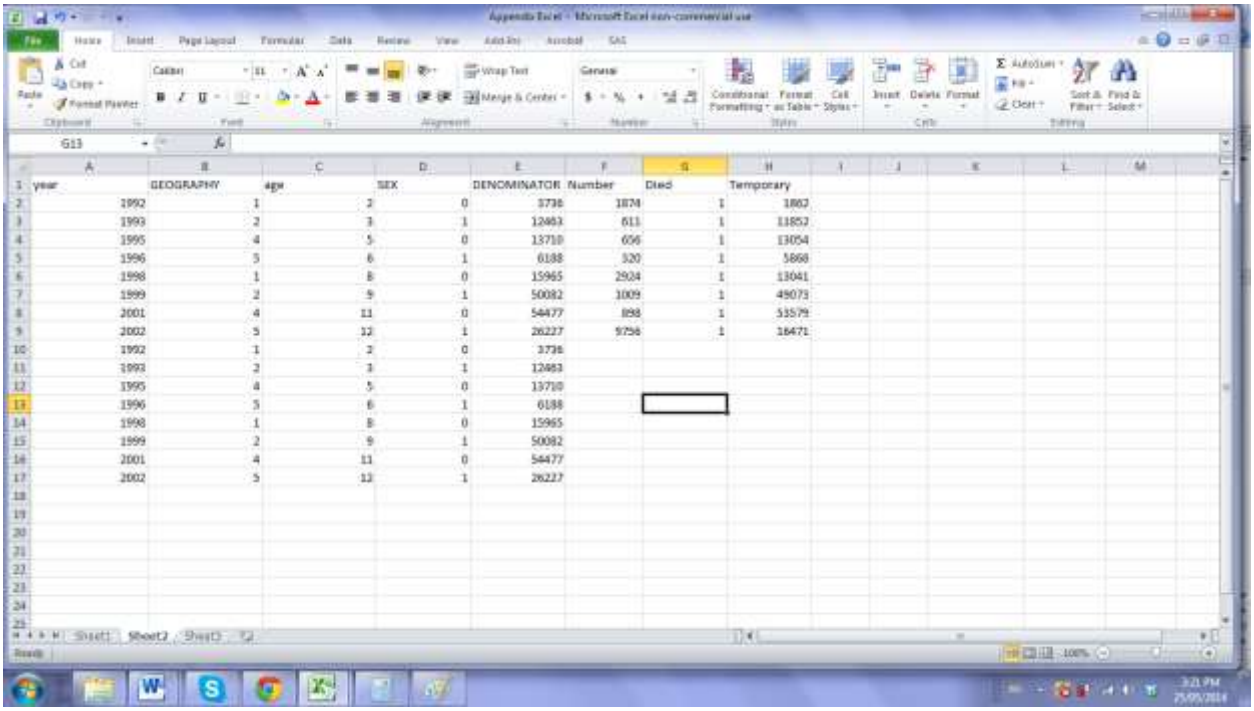
Figure 29 Screen shot of the data after the “died” variable was created



year	GEOGRAPHY	age	SEX	DENOMINATOR	Number	Died
1992	1	2	0	3736	1874	1
1993	2	3	1	12463	611	1
1995	4	5	0	13710	656	1
1996	5	6	1	6188	7621	1
1998	1	8	0	15965	2924	1
1999	2	9	1	50082	1009	1
2001	4	11	0	54477	898	1
2002	5	12	1	26227	9756	1

5) Data preparation, fifth step

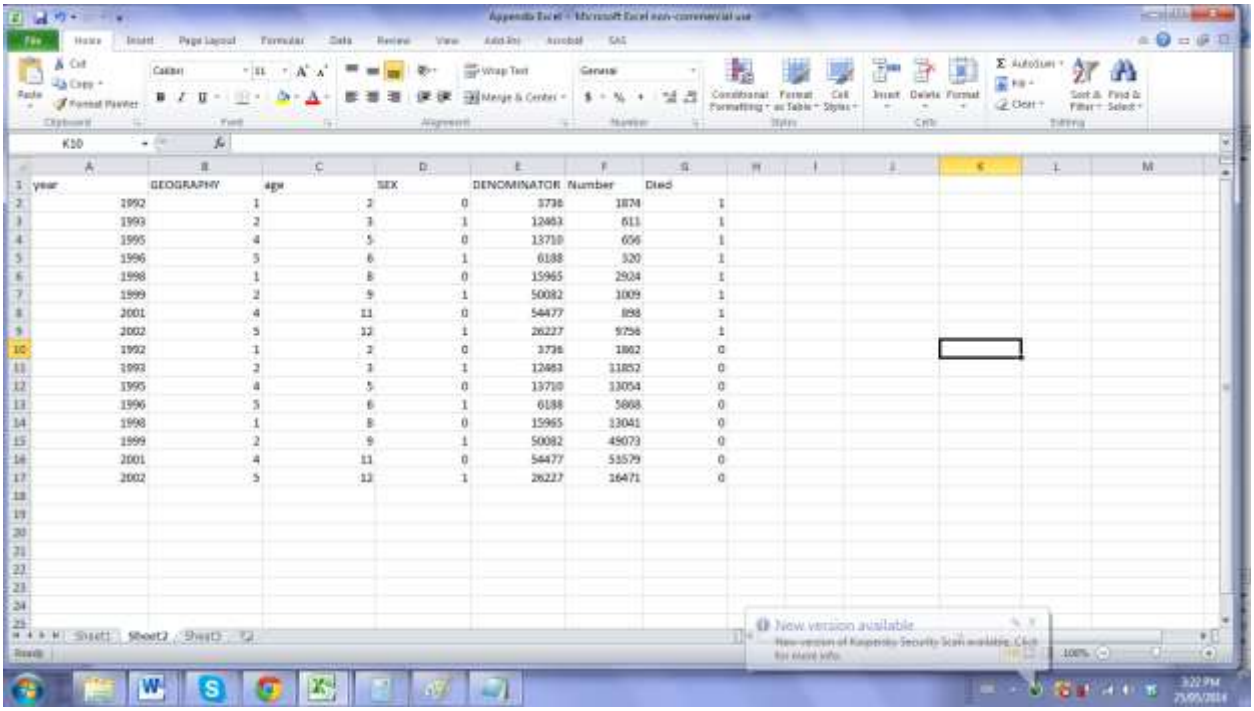
Figure 30 Screen shot of the data prepared for logistic regression



year	GEOGRAPHY	age	SEX	DENOMINATOR	Number	Died	Temporary
1992	1	2	0	3736	1874	1	1862
1993	2	3	1	12463	611	1	11852
1995	4	5	0	13710	656	1	13054
1996	5	6	1	6188	320	1	5868
1998	1	8	0	15965	2924	1	13041
1999	2	9	1	50082	1009	1	49073
2001	4	11	0	54477	898	1	53579
2002	5	12	1	26227	9756	1	16471
1992	1	2	0	3736			
1993	2	3	1	12463			
1995	4	5	0	13710			
1996	5	6	1	6188			
1998	1	8	0	15965			
1999	2	9	1	50082			
2001	4	11	0	54477			
2002	5	12	1	26227			

6) Data preparation, sixth step

Figure 31 Screen shot of the data ready for logistic regression



year	GEOGRAPHY	age	SEX	DENOMINATOR	Number	Died
1992	1	2	0	3736	1874	1
1993	2	3	1	12463	611	1
1995	4	5	0	13710	656	1
1996	5	6	1	6188	320	1
1998	1	8	0	15965	2924	1
1999	2	9	1	50082	1009	1
2001	4	11	0	54477	898	1
2002	5	12	1	26227	9756	1
1992	1	2	0	3736	1862	0
1993	2	3	1	12463	11852	0
1995	4	5	0	13710	13054	0
1996	5	6	1	6188	5868	0
1998	1	8	0	15965	13041	0
1999	2	9	1	50082	49073	0
2001	4	11	0	54477	53579	0
2002	5	12	1	26227	16471	0

Appendix 4 – An example to illustrating detailed steps in forming a logistic regression model of administrative health data

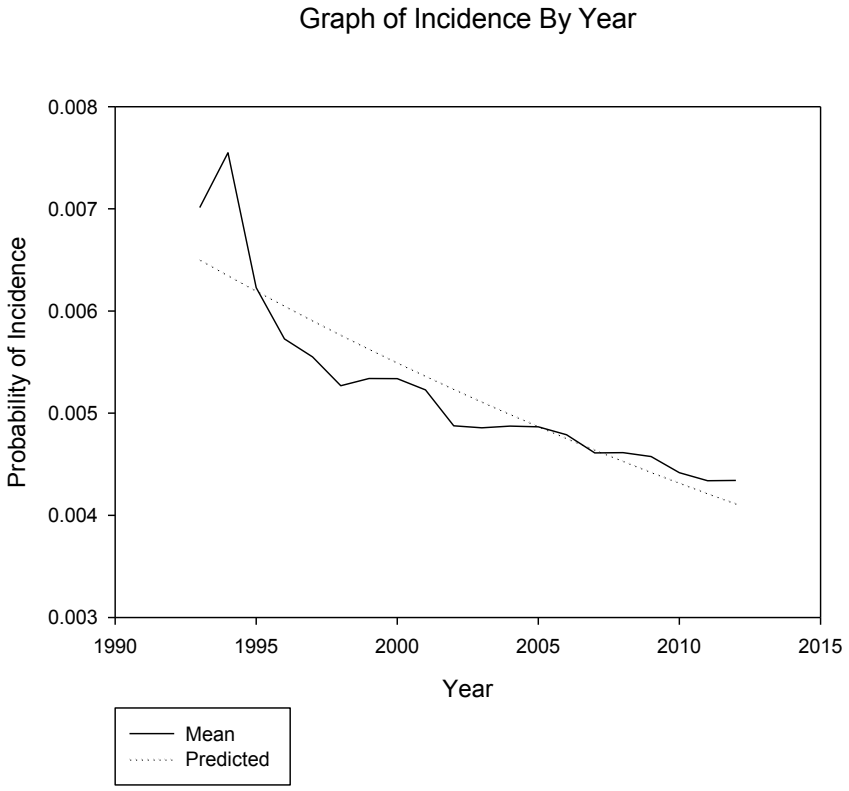
Incidence Rate Modeling Example

1) The incidence rates were regressed in a binary logistic regression with only "year" as the independent variable.

Table 16 Logistic Regression Using Year as The Independent Variable

Variable	B	Sig.	Exp(B)
Year	-0.0240	0.0000	0.9760
Constant	43.2130	0.0000	5850791346585140000.0000

Figure 32 Graph of the probability of incidence from the logistic regression model using only year as a variable



From the graph, we see that the first two incidence rates are noticeably different from the rest of the years.

2) In order to check whether we can more closely fit the original data and keep the two data points, the numerator and denominator of the rate is examined.

Table 17 Number of Cases of IHD per Year by Zone

Year	Zone 1	Zone 2	Zone 3	Zone 4	Zone 5
1983	7,462	30,813	11,241	31,188	12,136
1984	7,283	28,137	10,936	28,935	11,686
1985	7,093	27,078	10,694	27,713	11,482
1986	7,251	28,647	11,075	29,060	12,014
1987	7,221	28,519	10,985	29,001	11,761

1988	7,203	28,926	10,989	28,966	11,746
1989	7,187	29,381	11,001	29,065	11,788
1990	7,215	30,060	11,090	29,570	11,834
1991	7,240	30,527	11,204	29,805	11,870
1992	7,222	30,764	11,329	30,005	11,894
1993	7,131	30,637	11,270	30,039	11,758
1994	7,196	30,918	11,344	29,663	11,837
1995	7,259	31,322	11,436	29,295	11,939
1996	7,306	31,852	11,440	29,143	11,997
1997	7,346	32,756	11,532	29,258	12,182
1998	7,421	33,916	11,764	29,569	12,384
1999	7,521	34,940	11,934	30,107	12,494
2000	7,606	35,504	12,017	30,350	12,501
2001	7,674	36,257	12,144	30,706	12,585
2002	7,713	37,084	12,268	31,184	12,752
2003	7,724	37,604	12,304	31,466	12,791
2004	7,770	38,052	12,377	31,652	12,824
2005	7,789	38,499	12,431	31,780	12,873
2006	7,832	39,449	12,555	32,288	13,022
2007	8,016	40,598	12,869	33,313	13,370
2008	8,136	41,629	13,030	34,045	13,595
2009	8,336	43,229	13,255	35,312	13,998
2010	8,520	44,398	13,427	36,215	14,345
2011	8,654	45,571	13,610	37,042	14,715
2012	8,821	47,322	13,902	38,350	15,204

Table 18 Number of People at Risk of IHD per Year by Zone

Year	Zone 1	Zone 2	Zone 3	Zone 4	Zone 5
1983	5,770	20,556	8,753	21,508	8,403
1984	5,701	19,620	8,640	20,655	8,226
1985	5,610	19,287	8,531	20,184	8,153
1986	5,733	20,328	8,807	21,103	8,518
1987	5,750	20,531	8,813	21,287	8,435
1988	5,765	20,965	8,856	21,479	8,481
1989	5,788	21,447	8,918	21,761	8,563
1990	5,842	22,072	9,023	22,250	8,654
1991	5,885	22,532	9,133	22,607	8,725
1992	5,905	22,927	9,255	22,929	8,810
1993	5,901	23,089	9,284	23,202	8,777
1994	5,900	23,273	9,265	22,980	8,783
1995	5,920	23,572	9,275	22,760	8,834

1996	5,944	23,988	9,277	22,715	8,892
1997	5,977	24,681	9,336	22,869	9,025
1998	6,036	25,517	9,482	23,106	9,178
1999	6,120	26,318	9,620	23,562	9,290
2000	6,180	26,835	9,692	23,818	9,332
2001	6,239	27,464	9,793	24,151	9,435
2002	6,280	28,176	9,914	24,600	9,600
2003	6,312	28,731	9,984	24,926	9,692
2004	6,376	29,238	10,078	25,176	9,778
2005	6,420	29,754	10,159	25,400	9,866
2006	6,492	30,667	10,323	25,904	10,024
2007	6,676	31,699	10,614	26,804	10,336
2008	6,814	32,637	10,802	27,456	10,558
2009	6,991	33,944	11,019	28,461	10,893
2010	7,154	34,976	11,184	29,228	11,186
2011	7,277	36,024	11,368	29,940	11,498
2012	7,427	37,457	11,628	31,002	11,886

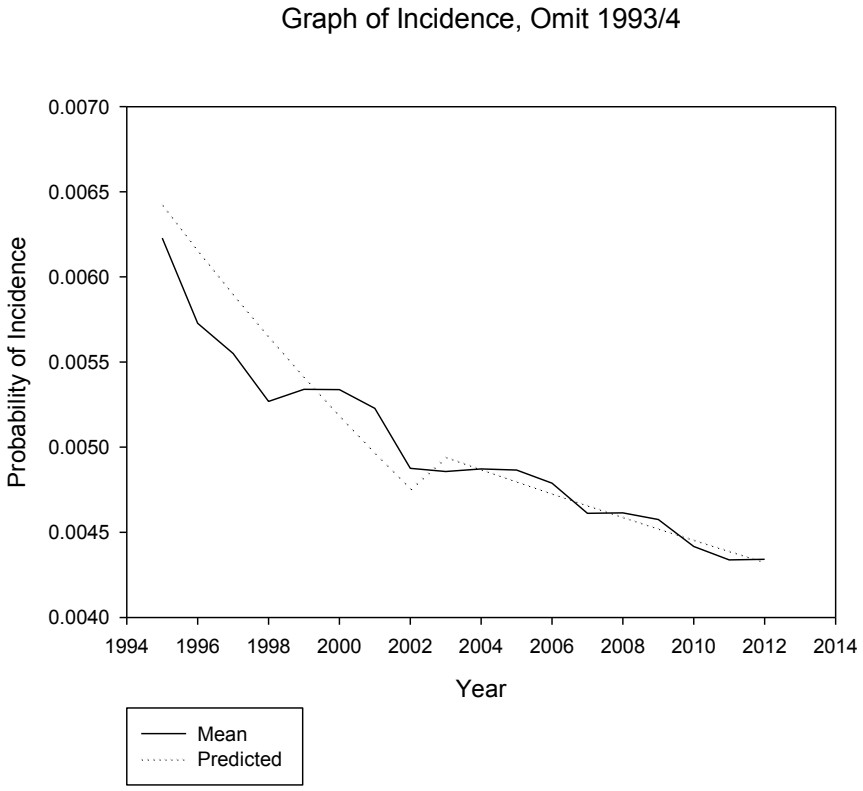
The population (denominator) shows a slight decrease between 1993 and 1994, however, the incidence cases increased by a factor greater than the decrease in population. Thus, there may be some change in the incidence recording in this time period. 1993 and 1994 data points are excluded from the analysis. Figure 1 also indicates a different slope in the probability before 2003 and after 2003

3) The first two years were omitted and new variables were added to the regression.

Table 19 Logistic Regression for Year Variables

Variable	B	Sig.	Exp(B)
Year	-0.0150	0.0000	0.9850
yearlt2003	25.0630	0.0000	76710955122.4760
Year by yearlt2003	-0.0130	0.0000	0.9880
Constant	24.5350	0.0000	45241150804.1640

Figure 33 Graph of the probability of incidence from the logistic regression model using the first three variables



The new variables improve the fit.

4) Next variable to examine is the geography (categorical). Table 20 shows the logistic regression with all the geography variables.

Table 20 Logistic Regression for Geography Variables

Variable	B	Sig.	Exp(B)
igeo		0.0000	
igeo(1)	0.2020	0.0000	1.2240
igeo(2)	-0.1090	0.0000	0.8970
igeo(3)	0.2020	0.0000	1.2240
igeo(4)	-39.1370	0.0000	0.0000
Year	-0.0220	0.0000	0.9790
yearlt2003	22.6000	0.0000	6531909983.4100

Year by yearlt2003	-0.0110	0.0000	0.9890
Year by igeo4	0.0200	0.0000	1.0200
igeo4 by yearlt2003	-0.1790	0.0000	0.8360
igeo5 by yearlt2003	-0.1800	0.0000	0.8350
Constant	37.7960	0.0000	25986095465390900.0000

Figure 34 Graph of the probability of incidence for zone 1 obtained from the logistic regression model using the significant zone 4 and 5 interaction variables

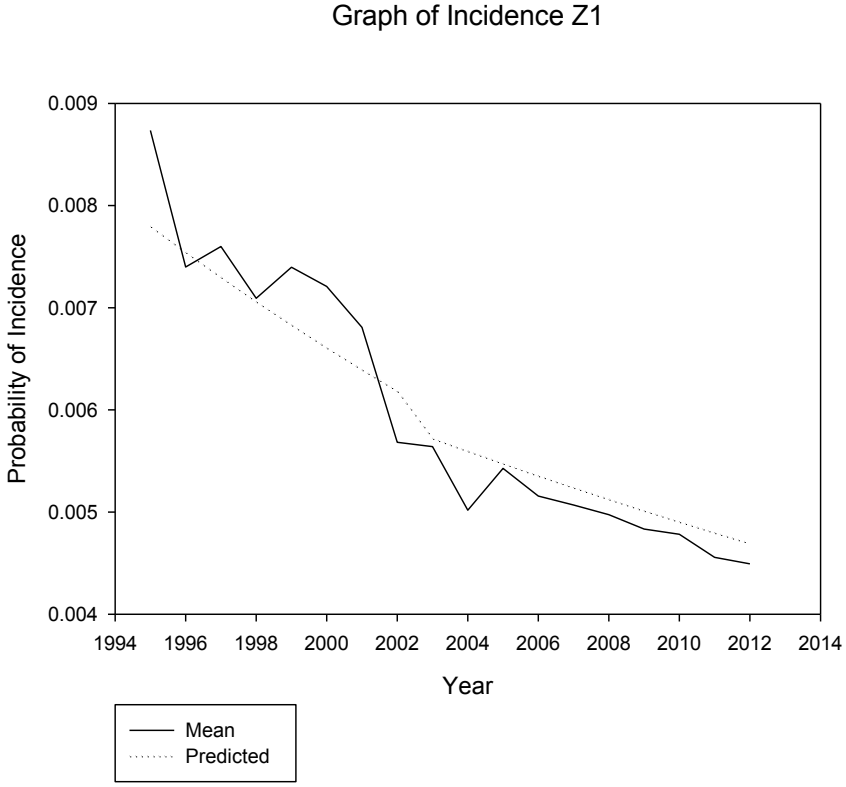


Figure 35 Graph of the probability of incidence for zone 2 obtained from the logistic regression model using the significant zone 4 and 5 interaction variables

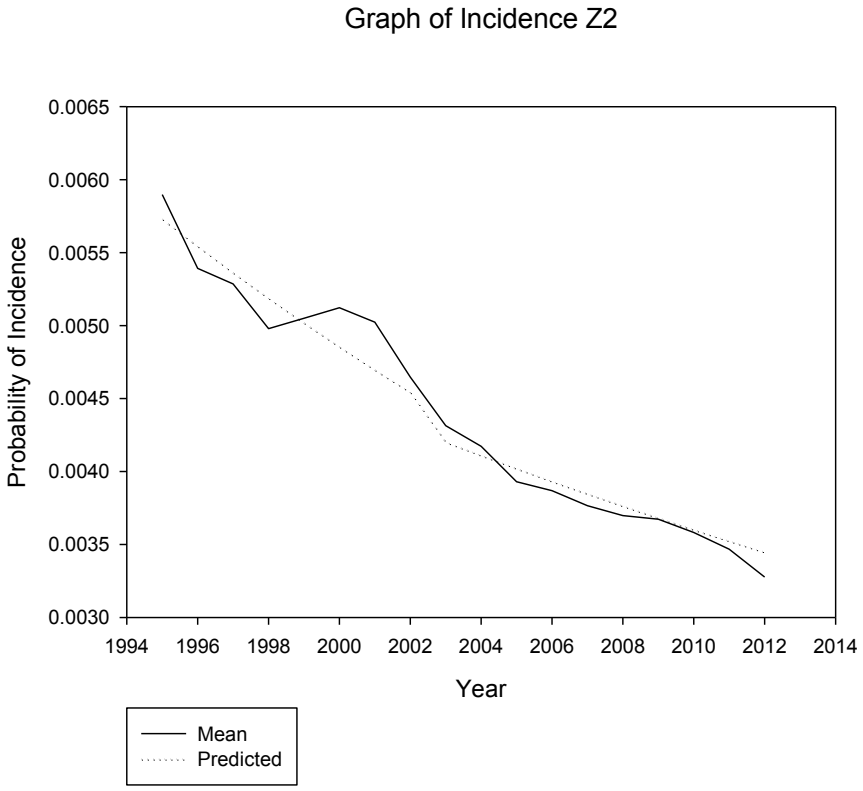


Figure 36 Graph of the probability of incidence for zone 3 obtained from the logistic regression model using the significant zone 4 and 5 interaction variables

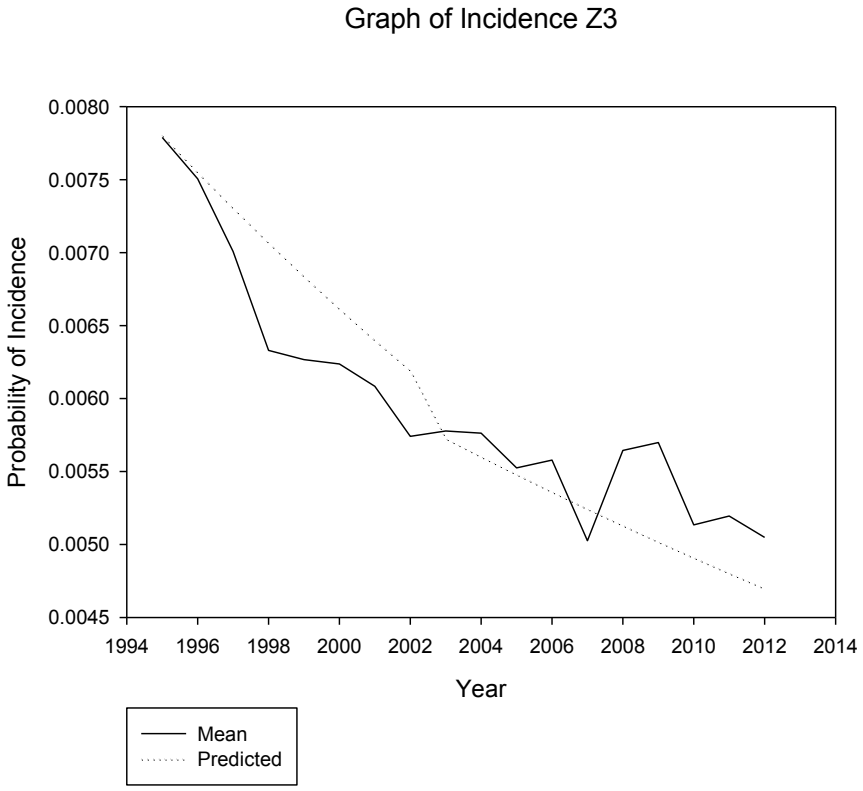


Figure 37 Graph of the probability of incidence for zone 4 obtained from the logistic regression model using the significant zone 4 and 5 interaction variables

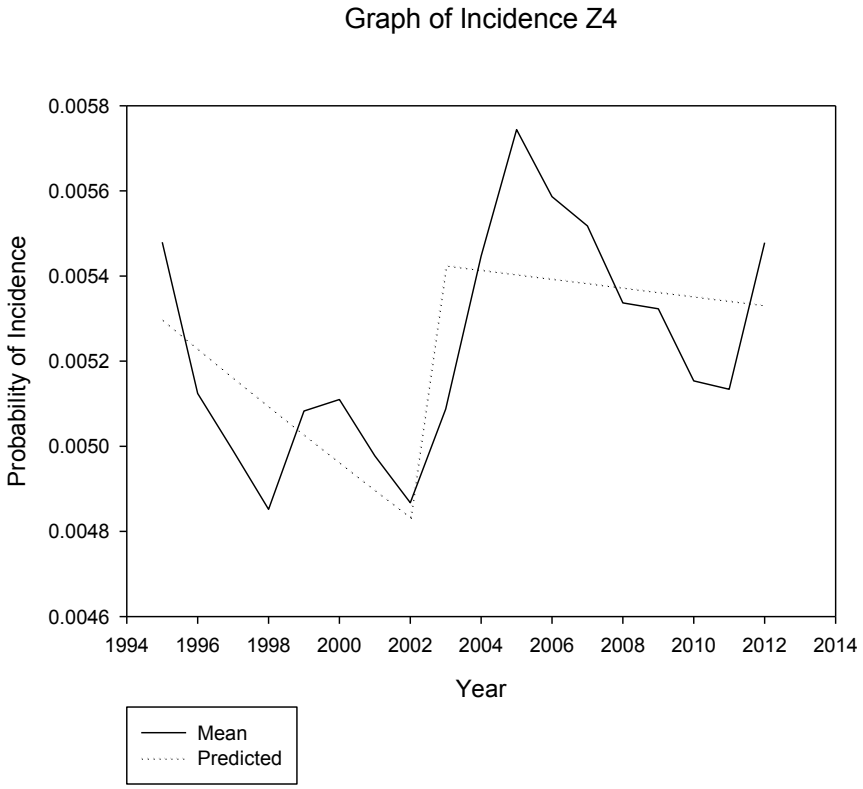
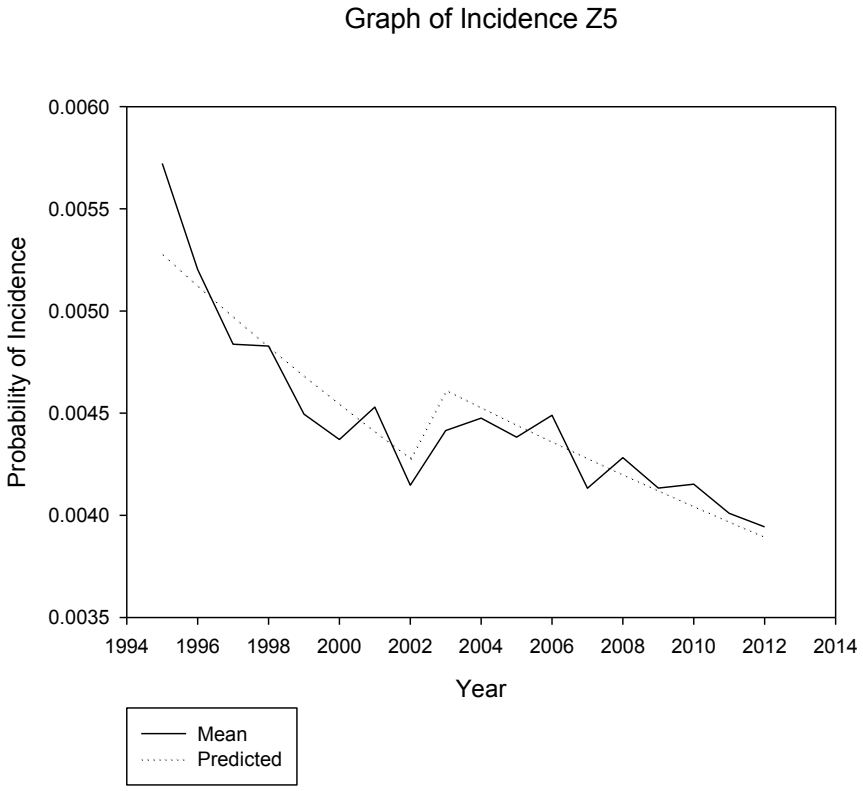


Figure 38 Graph of the probability of incidence for zone 5 obtained from the logistic regression model using the significant zone 4 and 5 interaction variables



The interaction terms with zone5 improved the model fit for zone 5 incidence probabilities.

5) The next variable to regress with year is sex. Table 21 shows the model for relationship between incidence rate, year and sex

Table 21 Logistic Regression for Year and Sex Variables

Variable	B	Sig.	Exp(B)
isex	-13.3950	0.0000	0.0000
Year	-0.0260	0.0000	0.9740
yearlt2003	24.6900	0.0000	52805594406.0870
Year by yearlt2003	-0.0120	0.0000	0.9880
Year by isex	0.0070	0.0000	1.0070
Constant	46.0100	0.0000	95941904629693300000.0000

Figure 39 Graph of the probability of incidence for females obtained from the logistic regression model using the significant sex and year variables

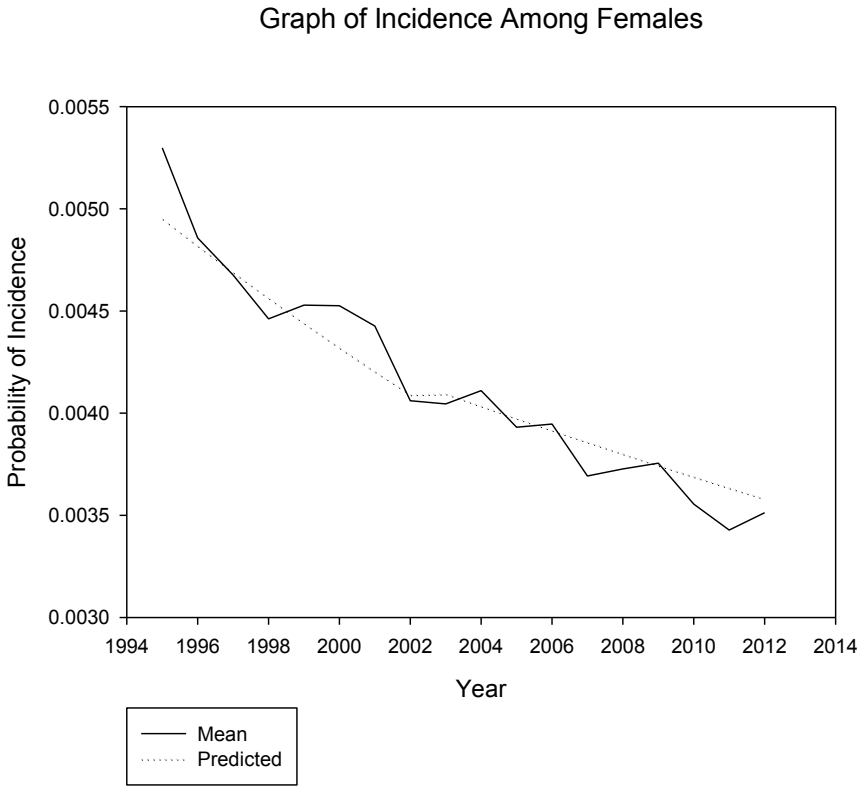
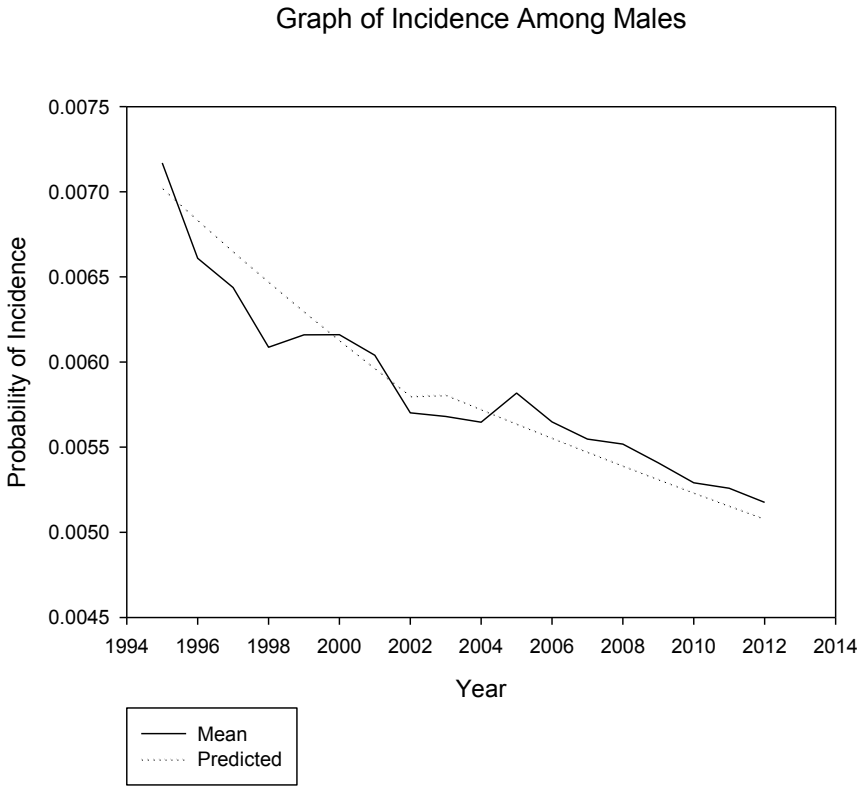


Figure 40 Graph of the probability of incidence for males obtained from the logistic regression model using the significant sex and year variables



The predicted values seem to model the actual values quite well. The fit may improve with more independent variables.

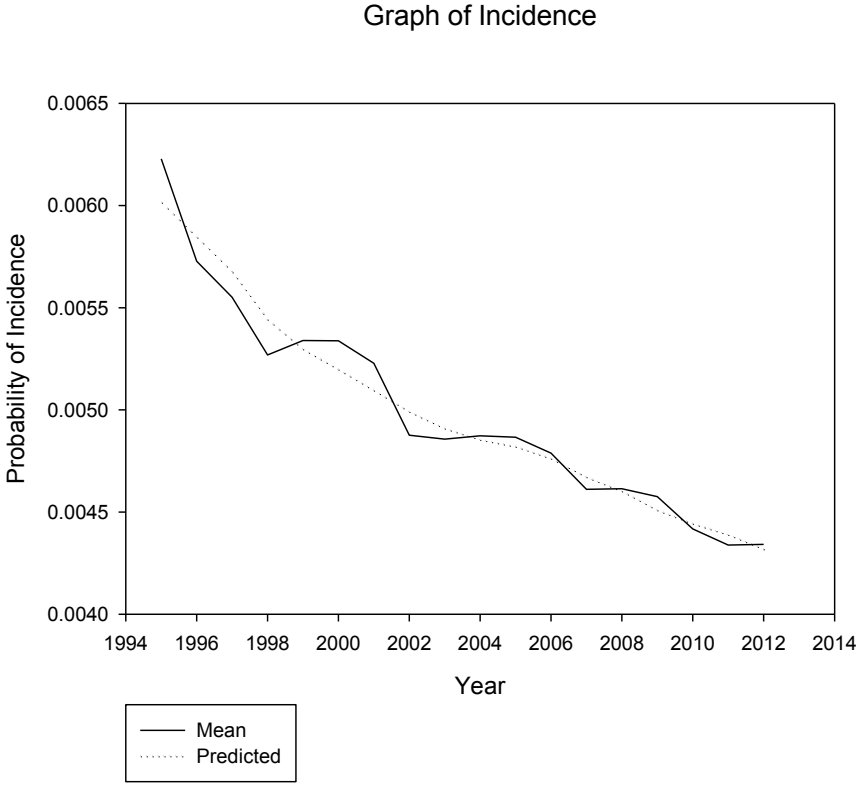
6) The next step is to examine the age and incidence probability relationship.

Table 22 Logistic Regression for Year and Age Variables

Variable	B	Sig.	Exp(B)
Year	0.0330	0.0000	1.0340
yearlt2003	12.4830	0.0000	263814.4460
Year by yearlt2003	-0.0060	0.0000	0.9940
iage	8.0280	0.0000	3065.9520
iage by yearlt2003	0.0040	0.0700	1.0040
Year by iage	-0.0040	0.0000	0.9960
Constant	-76.3610	0.0000	0.0000

Iage by yearlt2003 was not significant but the rest of the variables were significant.

Figure 41 Graph of the probability of incidence for males obtained from the logistic regression model using the age and year variables



The graph is not visually different from the previous figure but some of the new variables are significant.

7) Table 23 shows the relationship between age and other variables.

Table 23 Logistic Regression for Year, Age and Geography Variables

Variable	B	Sig.	Exp(B)
iyear	-0.0230	0.0000	0.9770
yearlt2003	0.0760	0.0000	1.0790
iyear by yearlt2003	-0.0070	0.0000	0.9930
iage	0.3800	0.0000	1.4620
isex(1)	-0.6020	0.0000	0.5480
igeo		0.0000	
igeo(1)	-0.1240	0.0030	0.8830
igeo(2)	-0.3680	0.0000	0.6920
igeo(3)	-0.0260	0.4940	0.9750
igeo(4)	0.0350	0.2650	1.0360
iage * igeo		0.0000	
iage by igeo(1)	0.0060	0.0230	1.0060
iage by igeo(2)	0.0150	0.0000	1.0150

iage by igeo(3)	0.0000	0.9050	1.0000
iage by igeo(4)	-0.0050	0.0210	0.9950
Constant	-9.1190	0.0000	0.0000

Figure 42 Graph of the probability of incidence for 5 year age groups in zone 1 obtained from the logistic regression model without the <25 age group

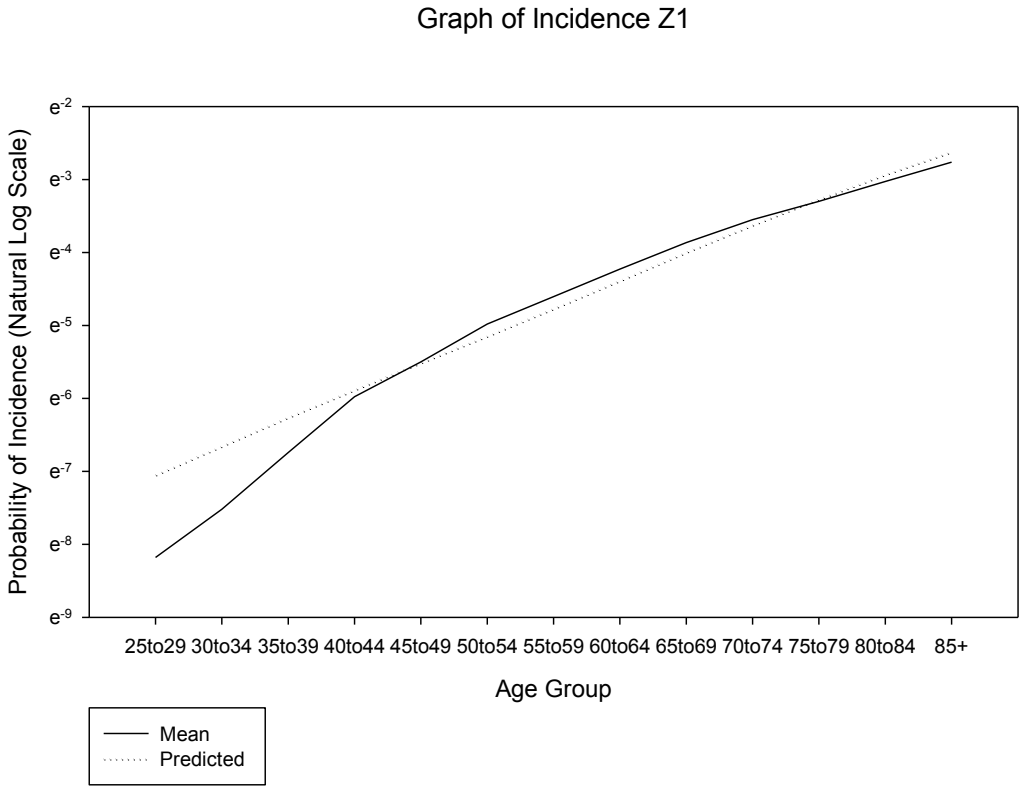


Figure 43 Graph of the probability of incidence for 5 year age groups in zone 2 obtained from the logistic regression model without the <25 age group

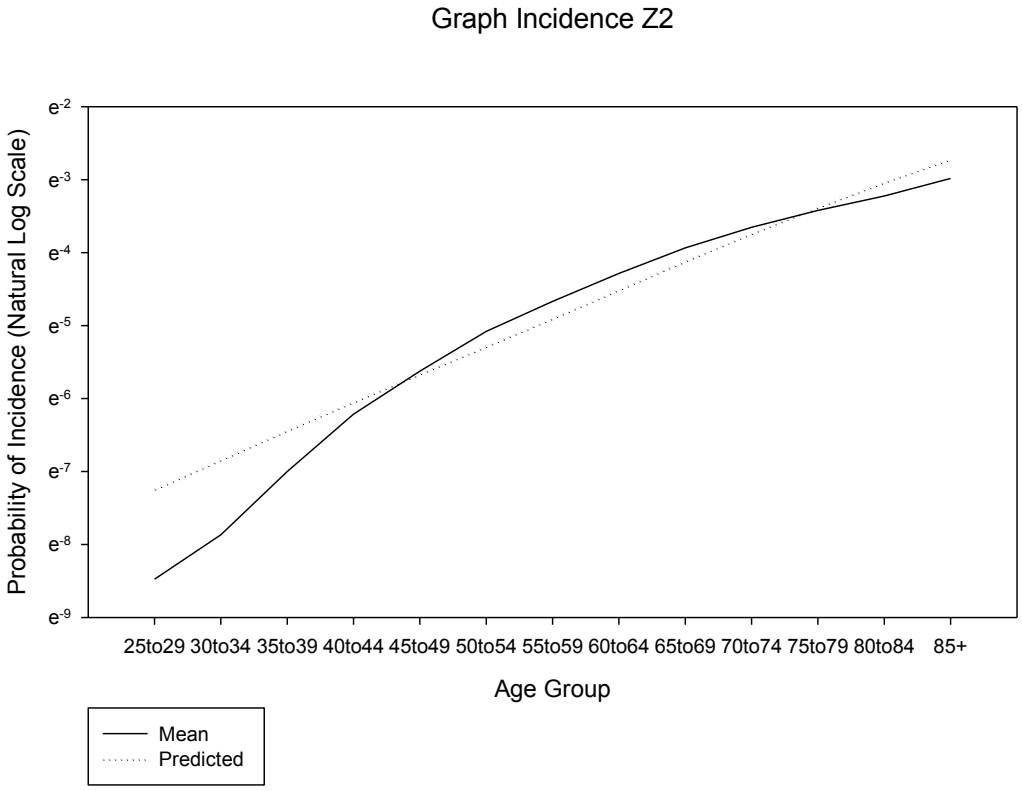


Figure 44 Graph of the probability of incidence for 5 year age groups in zone 3 obtained from the logistic regression model without the <25 age group

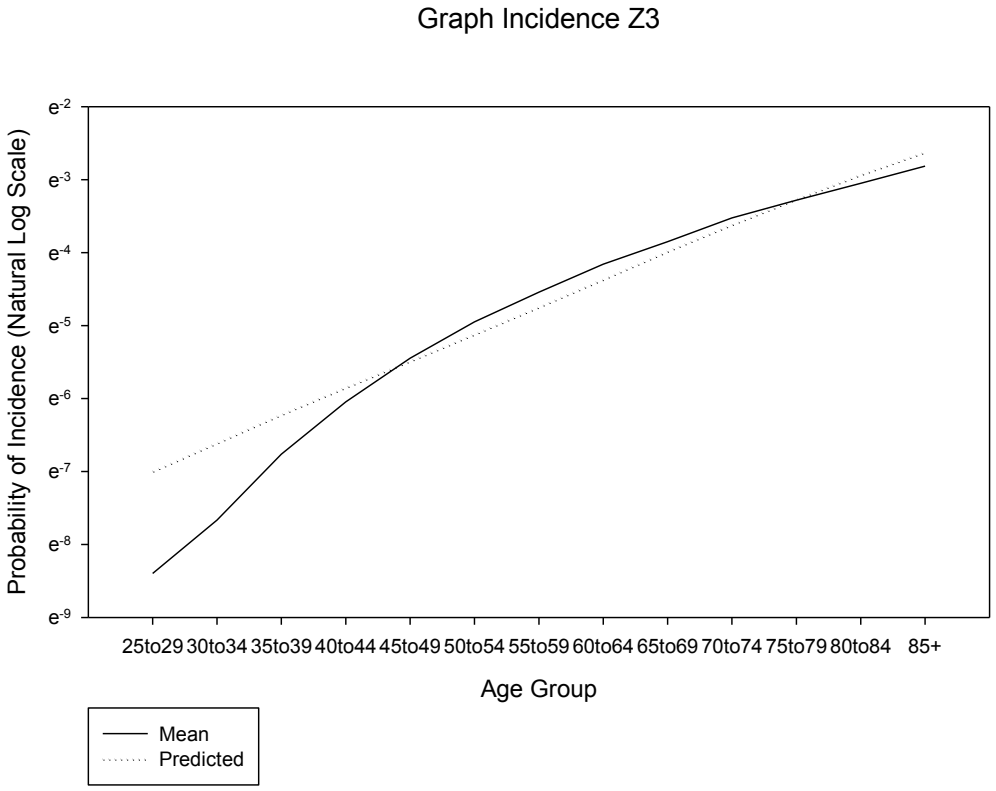


Figure 45 Graph of the probability of incidence for 5 year age groups in zone 4 obtained from the logistic regression model without the <25 age group

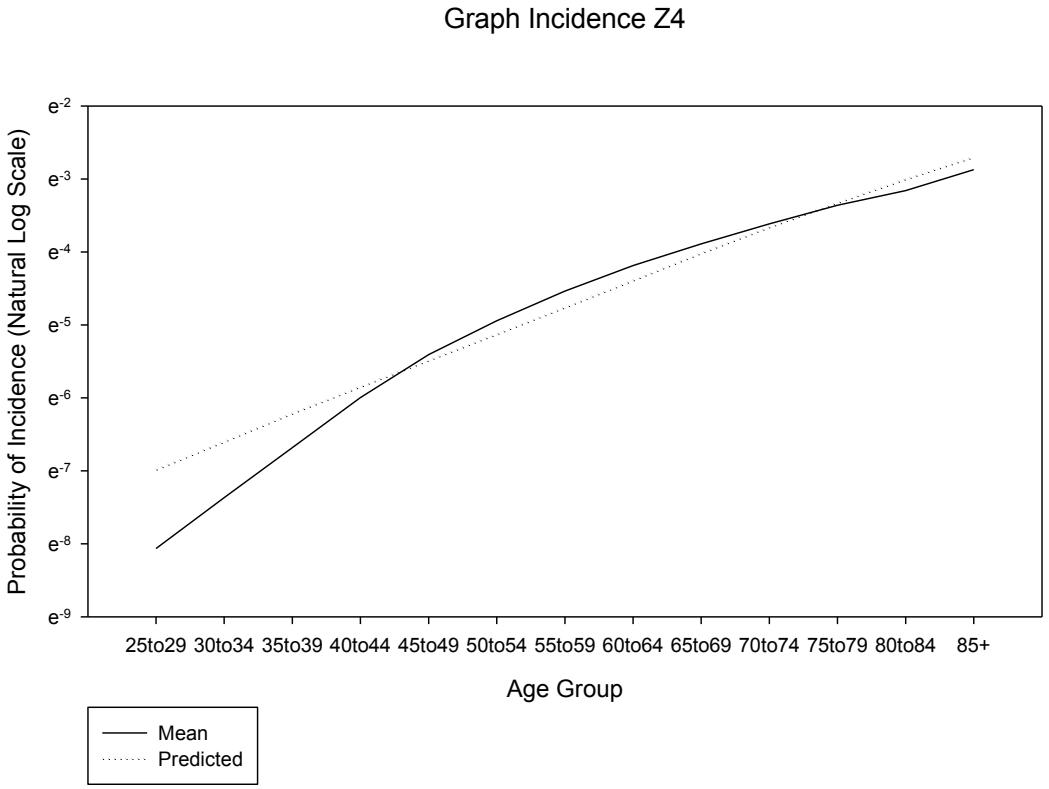
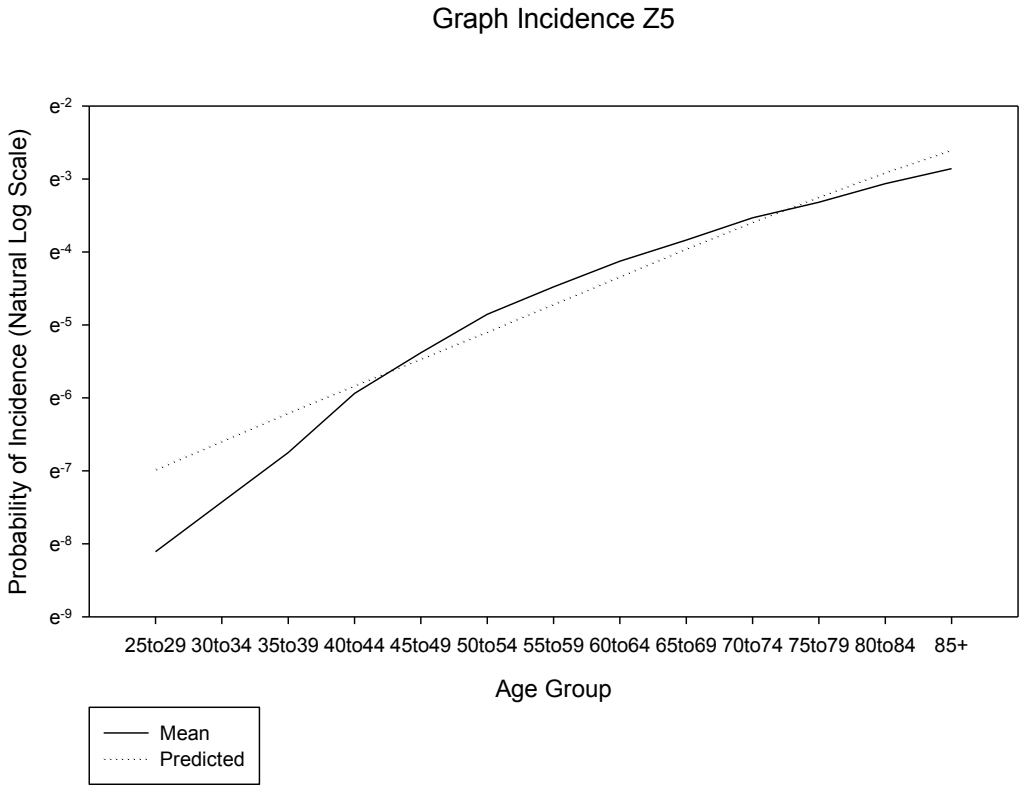


Figure 46 Graph of the probability of incidence for 5 year age groups in zone 5 obtained from the logistic regression model without the <25 age group



The graphs for all zones show an overestimation for those under the age of 45 and over 74 while underestimating those in the 45-74 age group.

8) This next step adds in variables that were previously found to be significant from the individual variable analyses as well as new variables which improved the model fit.

Table 24 Logistic Regression of the Preliminary Model

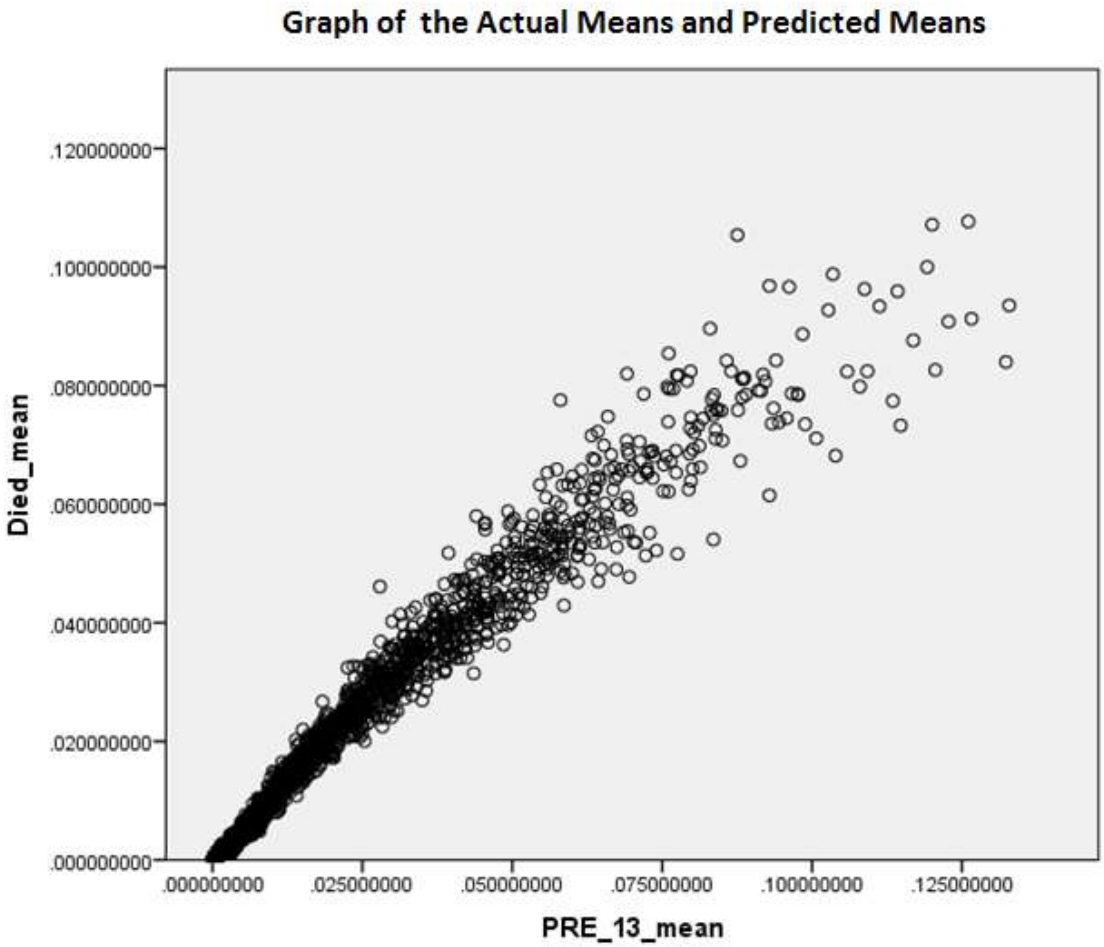
Variables	B	Sig.	Exp(B)
iyear	0.0350	0.0000	1.0360
yearlt2003	0.1350	0.0000	1.1440
iyear by yearlt2003	-0.0060	0.0000	0.9940
iage	0.3570	0.0000	1.4300
isex(1)	-1.1560	0.0000	0.3150
igeo		0.0000	
igeo(1)	-0.3240	0.0000	0.7230
igeo(2)	-0.4100	0.0000	0.6640
igeo(3)	-0.3190	0.0000	0.7270

igeo(4)	-0.2640	0.0000	0.7680
agelt45	-4.6620	0.0000	0.0090
agelt45 by iage	0.4180	0.0000	1.5190
iage by isex(1)	0.0400	0.0000	1.0410
geolt4 by iage	0.0160	0.0000	1.0160
geo2 by isex(1)	-0.0590	0.0000	0.9430
iage by iyear	-0.0040	0.0000	0.9960
geo4 by yearlt2003	-0.1640	0.0000	0.8490
geo4 by iyear	0.0200	0.0000	1.0200
geo5 by yearlt2003	-0.1440	0.0000	0.8660
Constant	-8.6150	0.0000	0.0000

This regression adds "age less than 45 by geo1" into the equation to make the three-variable interaction term (agelt45 by geo1 by iage) hierarchically well formulated. Two interaction terms become insignificant, and are taken out of the formula.

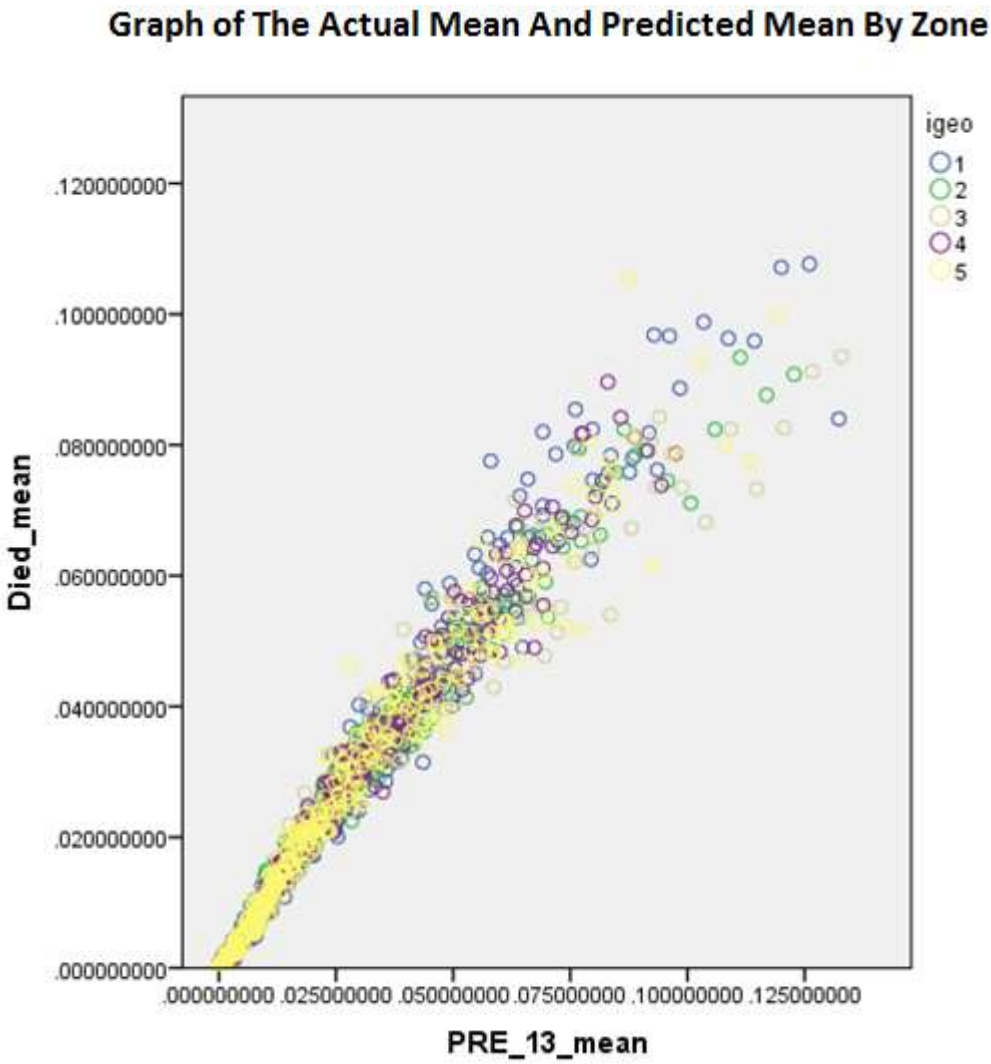
9) The next step in model building is to evaluate how well the formula fits the actual data and add variables if needed.

Figure 47 Graph of the actual means and predicted mean incidence



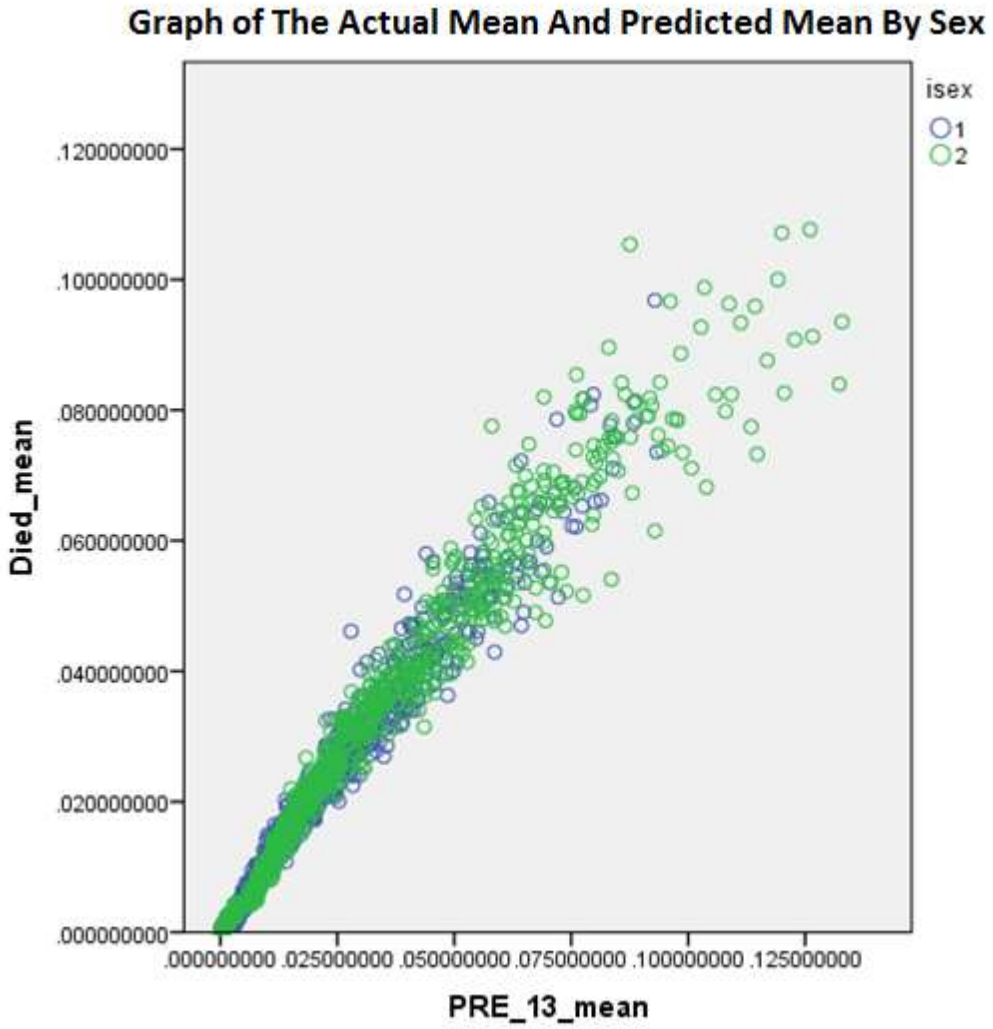
A straight 45-degree line would infer the predicted values are closer to the mean. The further the points from the 45-degree line, the larger the difference between the actual and predicted. The graph shows that larger incidence values are not as accurately captured by the model compared to smaller incidence values.

Figure 48 Graph of the actual and predicted mean incidence by zones



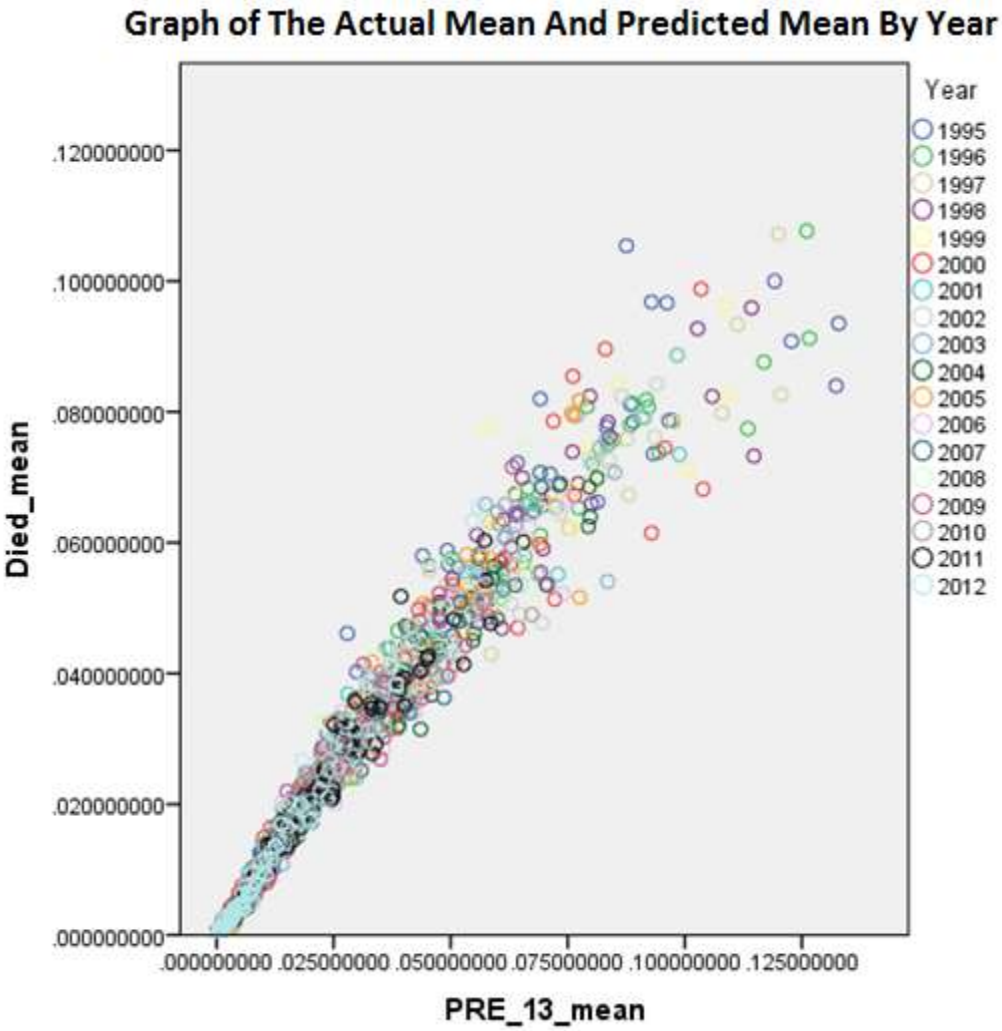
Zone 4 does not seem to contribute to the higher means or departure from the 45-degree line as much as the other zones

Figure 49 Graph of the actual and predicted mean incidence by sex



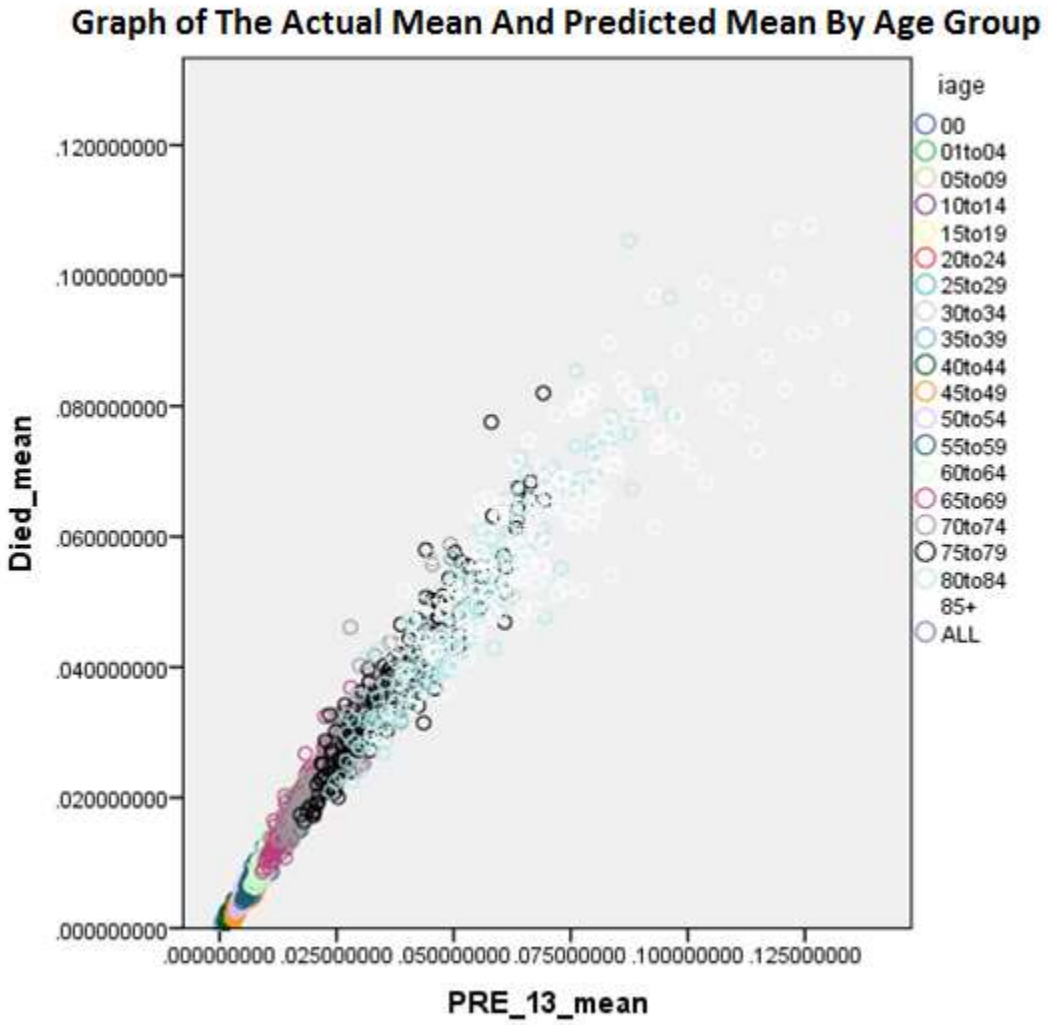
Men contribute to the higher rates and departure from the 45-degree line than women.

Figure 50 Graph of the actual and predicted mean incidence by year



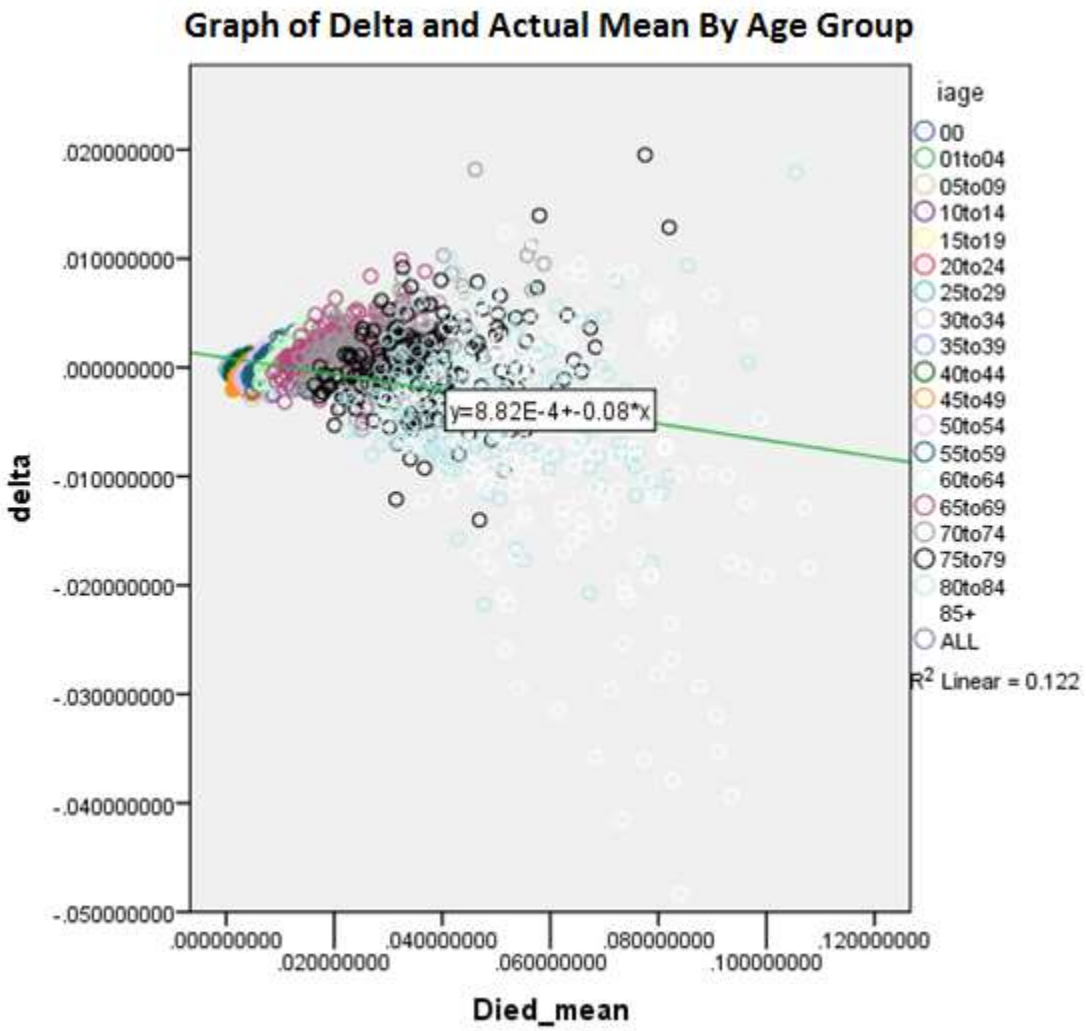
The earlier years tend to have higher rates and departure from the 45-degree line than later years.

Figure 51 Graph of the actual and predicted mean incidence by age group



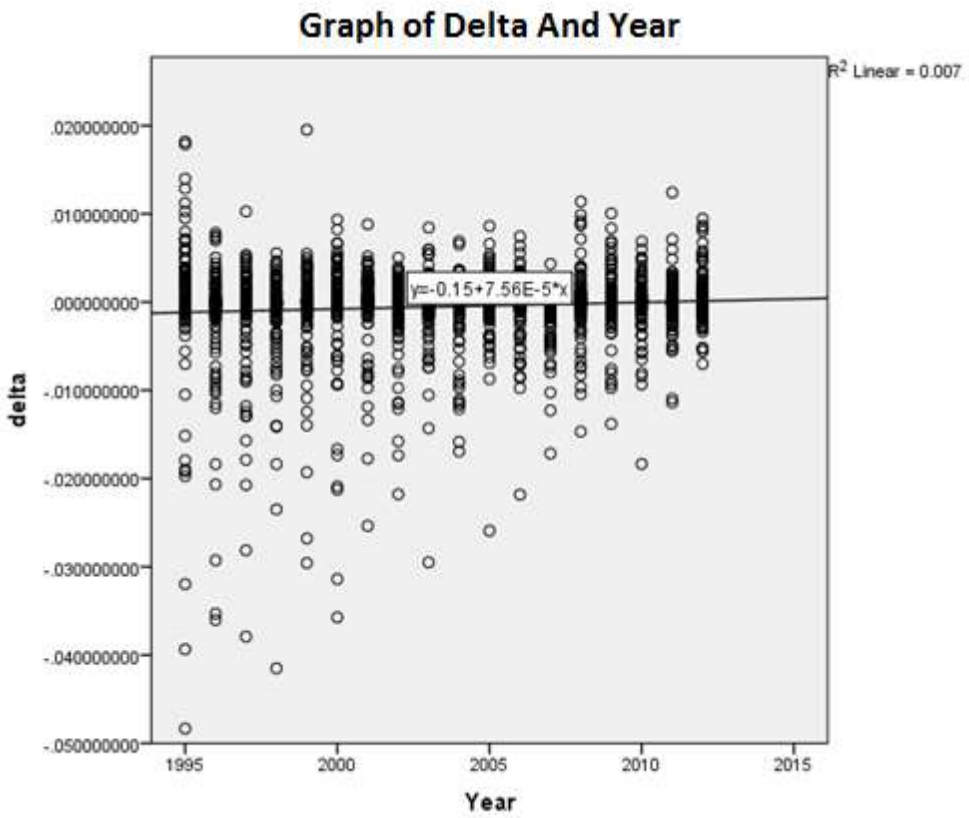
The older the age group, the larger the incidence. The departure from the 45-degree line is mostly due to the 85+ category

Figure 52 Graph of the delta and mean incidence by age group



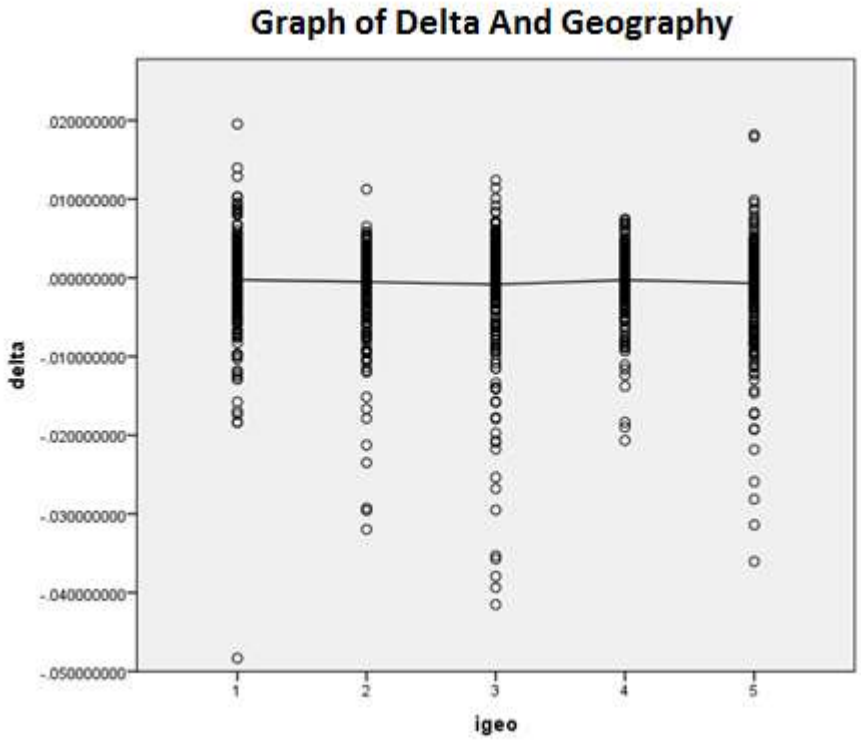
Delta is the difference between the actual and predicted incidence rate. Mostly older age groups contribute to a decreasing delta value. This means the predicted overestimates the incidence in this 85+ age group.

Figure 53 Graph of the delta and year



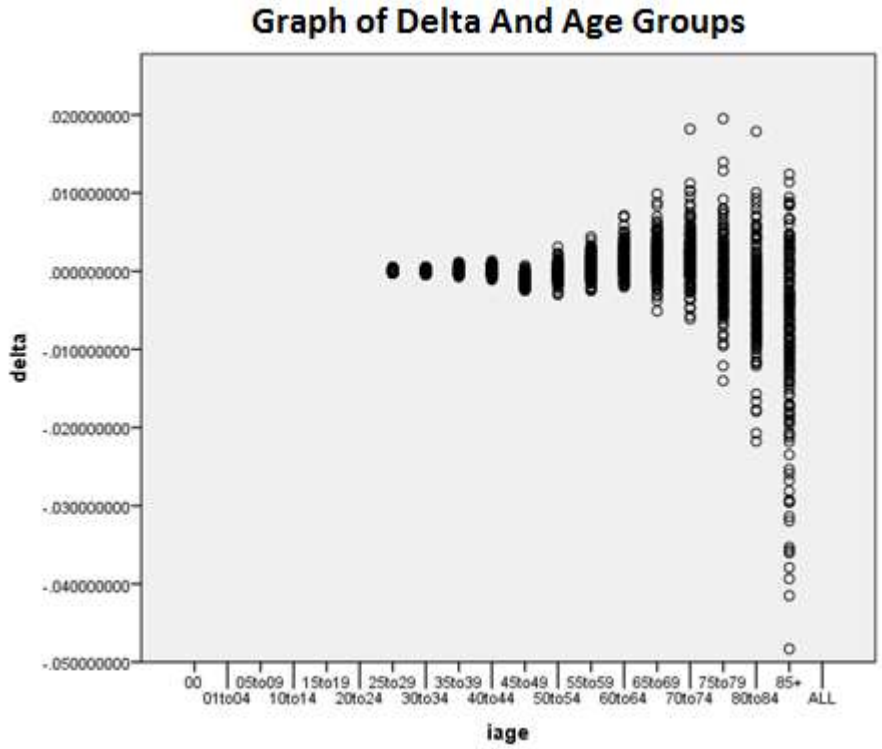
There is consistently an overestimation by the model in all the variables: earlier years, older age groups, zone 3.

Figure 54 Graph of the delta and geography



There appears to be a consistently larger number of negative delta values for each zone.

Figure 55 Graph of the delta and age group



The 85+ age group has the largest spread of delta values, with more underestimates than overestimates.

The next tables show frequencies of outliers defined as "mean incidence" greater than 0.04 and delta greater than 0. This allows the identification of variables with high frequencies of outliers; these variables in turn need to be added to the regression

Table 25 Frequency of Outliers by Year

Year	Frequency	Percent	Valid Percent	Cumulative Percent
1995	19	15.3	15.3	15.3
1996	7	5.6	5.6	21
1997	6	4.8	4.8	25.8
1998	7	5.6	5.6	31.5
1999	9	7.3	7.3	38.7
2000	7	5.6	5.6	44.4
2001	7	5.6	5.6	50
2002	7	5.6	5.6	55.6
2003	6	4.8	4.8	60.5
2004	5	4	4	64.5
2005	8	6.5	6.5	71
2006	3	2.4	2.4	73.4
2007	2	1.6	1.6	75
2008	8	6.5	6.5	81.5
2009	8	6.5	6.5	87.9
2010	4	3.2	3.2	91.1
2011	3	2.4	2.4	93.5
2012	8	6.5	6.5	100
Total	124	100	100	

Table 26 Frequency of Outliers by Sex

Sex	Frequency	Percent	Valid Percent	Cumulative Percent
1	53	42.7	42.7	42.7
2	71	57.3	57.3	100
Total	124	100	100	

Table 27 Frequency of Outliers by Geography

Zone	Frequency	Percent	Valid Percent	Cumulative Percent
1	36	29	29	29
2	13	10.5	10.5	39.5
3	24	19.4	19.4	58.9
4	24	19.4	19.4	78.2
5	27	21.8	21.8	100
Total	124	100	100	

Table 28 Frequency of Outliers by Age

Age Group	Frequency	Percent	Valid Percent	Cumulative Percent
70to74	19	15.3	15.3	15.3
75to79	30	24.2	24.2	39.5
80to84	31	25	25	64.5
85+	44	35.5	35.5	100
Total	124	100	100	

Table 29 Frequency of Outliers by Sex and Geography

isex * igeo Crosstabulation

	Zone					
Sex	1	2	3	4	5	Total
1	15	5	9	8	16	53
2	21	8	15	16	11	71
Total	36	13	24	24	27	124

Table 30 Frequency of Outliers by Year and Geography

Year * igeo Crosstabulation

	Zone					
Year	1	2	3	4	5	Total
1995	7	4	1	2	5	19
1996	0	1	2	2	2	7
1997	1	0	1	1	3	6
1998	2	1	0	3	1	7
1999	3	1	0	4	1	9
2000	5	0	0	2	0	7
2001	3	0	0	2	2	7
2002	1	2	0	3	1	7
2003	2	2	2	0	0	6
2004	0	2	1	0	2	5
2005	2	0	2	2	2	8
2006	0	0	1	0	2	3
2007	1	0	1	0	0	2
2008	1	0	3	1	3	8
2009	2	0	4	1	1	8
2010	2	0	2	0	0	4
2011	1	0	2	0	0	3
2012	3	0	2	1	2	8
Total	36	13	24	24	27	124

More males over the age of 85 in zone 1 seem to be exhibiting higher incidence rates. After these observations, appropriate variables were added to the regression to improve the model fit.

10) After repeating step 9 for a variation of models, the final incidence probability model was complete.

Table 31 The Final Incidence Model

Variable	B	Sig.	Exp(B)
iyear	0.0350	0.0000	1.0360
isex(1)	-1.2510	0.0000	0.2860
igeo		0.0000	
igeo(1)	-0.3270	0.0000	0.7210
igeo(2)	-0.4120	0.0000	0.6620
igeo(3)	-0.3220	0.0000	0.7250
igeo(4)	-0.2640	0.0000	0.7680
yearlt2003	0.1340	0.0000	1.1440
agelt45	-4.6240	0.0000	0.0100
iyear by yearlt2003	-0.0060	0.0000	0.9940
agelt45 by iage	0.4150	0.0000	1.5150
iage	0.3580	0.0000	1.4310
iage by isex(1)	0.0470	0.0000	1.0480
geolt4 by iage	0.0160	0.0000	1.0160
geo2 by isex(1)	-0.0590	0.0000	0.9430
iage by iyear	-0.0040	0.0000	0.9960
geo4 by yearlt2003	-0.1640	0.0000	0.8490
geo4 by iyear	0.0200	0.0000	1.0200
geo5 by yearlt2003	-0.1430	0.0000	0.8670
age85plus by isex(1)	-0.1080	0.0000	0.8980
Constant	-8.6270	0.0000	0.0000

Appendix 5 -- Recording Instances of Disease: ICD codes

The International Classification of Disease codes are the standard for recording diseases around the world and it used extensively in epidemiology. The code is used to record health problems on many types of medical records including death certificates and hospital records. These ICD codes have been used to monitor incidence, prevalence, and mortality of diseases (morbidity and mortality) in The World Health Organization member states. The ICD codes have also been used for resource allocation and decision-making by many countries. [10]

ICD codes were first created in 1900; the two most current versions used are the ICD-9 and ICD-10 codes. ICD-9 was created in 1979 and was used till 1998. ICD-10 was created in 1999 and is still being used today. [74] ICD-9-CM is based on the ICD-9 codes and used coding diagnoses and procedures associated with hospital utilization in the United States of America. [74,75] ICD-10-CA is the Canadian modification to the ICD-10 codes by the Canadian Institute for Health Information. [76, 77] The ICD-10-CM was a revised version of the WHO's ICD-10 by the Center for Health Policy Studies in the U.S. There is, however, no implementation date for the ICD-10-CM. [76] Alberta used the ICD-9 codes from 1994-2000, then ICD-9CM codes were used in 2001, and finally ICD-10-CA codes were used from 2002 onwards. [78]

The ICD codes differentiate between different types of ischemic heart disease, some of which are indicative of the amount of heart damage. IHD is clinically defined as ICD-9 codes 410 to 414 [79] or ICD-10 codes I20 to I25. [3] In both versions of ICD codes, the main components of IHD are: acute myocardial infarction and angina pectoris. Acute myocardial infarction is used to describe damage to the heart muscle due to complete blockage of the coronary artery. Angina pectoris is

the reduced blood flow to areas of the heart during exertion. ICD codes allow for the classification of the extent of the arterial blockage, the cause of blockage, extent of necrosis, and whether there are coronary artery problems before and after angina or MI.

ICD Code Details

For ICD-9 codes, the fifth digits denote episode of care. The fifth, digit of 0 denotes unspecified care when the document does not give sufficient information for an assignment of 1 or 2. The fifth digit of 1 designates the first episode of care for a newly diagnosed myocardial infarction. The first digit of 1 is assigned regardless of the number of times a patient is transferred during the first episode of care. The fifth digit of 2 denotes an episode of care following an initial episode; where a patient is admitted for further observation, evaluation or treatment for a myocardial infarction that was previously treated but less than 8 weeks old. [80]

Aside from the MI and angina pectoris, other diseases are classified as IHD. Post-myocardial infarction syndrome is also known as Dressler's syndrome. Dressler's syndrome occurs after a heart attack, the outer layer of membrane surrounding the heart wall (pericardium) becomes inflamed. The patient feels chest pain and develops a fever. [81] Intermediate coronary syndrome (ICS) as the name implies is an ill-defined group of heart disease that is the grey area between MI and angina pectoris. The duration and severity of the intermediate coronary artery syndrome is between that of an MI and angina. It is characterized by one or more bouts of prolonged chest pain, each bout lasting 15 minutes to several hours. ICS responds poorly to nitrites and is usually unrelated to angina but similar to MI. ICS is rarely associated with heart muscle damage. [82] Acute coronary occlusion without MI is a condition where the heart vessel is blocked but the

blockage does not results in MI. This may occur when the blockage is gradual rather than sudden as with most MIs, and when there are alternative coronary arteries supplying the muscle group. [83] "Other acute and subacute forms of ischemic heart disease" have not been specified, so the specific diseases that are classified under this code are unclear. Old myocardial infarctions are diagnosed when there are abnormalities in the heart wall. [84] Aneurysms are the widening or ballooning of a portion of an artery due to the weakening of the muscle in the artery wall. In addition to the arteries, an aneurysm can occur in the heart wall if the heart muscle becomes weak. Chronic total occlusions of coronary arteries are complete blockages of a coronary artery lasting 3 months or longer. [85]

Angina Pectoris has 3 subcategories in the ICD-9 code. The first is Prinzmetal angina which is a decrease in blood supply to the heart muscled due to spasms in the coronary arteries. Prinzmetal angina usually occurs in younger patients and the spasms are a result of cold weather, stress, medicine, smoking, and cocaine use. [86] Angina decubitus occurs when a person lies down; the angina recedes when the patient sits or stands. [87] The third type, "other unspecified angina pectoris" has no listed examples in the ICD-9 code.

The ICD codes also specify the type of artery that is hardening or grafted. Coronary atherosclerosis occurs when arteries harden from plaque buildup, as mentioned earlier. Coronary atherosclerosis can occur in the original "native vessel," in vessels which were grafted during the CABG treatment, or in vessels of a transplanted heart. Grafts can be autologous (from the patient's body) or non-autologous (from a source other than the patient).

References

1. Public Health Agency of Canada. 2009 tracking heart disease and stroke in canada. http://www.phac-aspc.gc.ca/publicat/2009/cvd-avc/summary-resume-eng.php. Updated 2009. Accessed 10/19, 2013.

2. Heart and Stroke Foundation. Heart disease. http://www.heartandstroke.com/site/c.ikIQLcMWJtE/b.3483991/k.34A8/Statistics.htm#heartdisease. Updated 2011. Accessed 10/19, 2013.

3. Alberta Health. Chronic disease and injury. http://www.health.alberta.ca/documents/Trends-2007-chronic.pdf. Updated 2007. Accessed 09/01, 2013.

4. Chan B, Young W. Burden of cardiac disease: Cahpter 1. *Cardiovascular Atlas*. 1999:1.

5. Tu JV, Nardi L, Fang J, et al. National trends in rates of death and hospital admissions related to acute myocardial infarction, heart failure and stroke, 1994-2004. *CMAJ*. 2009;180(13):E118-25.

6. Lee LM, Teutsch SM, Thacker SB, St. Louis ME, eds. *Principles and practice of public health surveillance.* 3rd ed. New York: Oxford University Press; 2010.

7. Ashley EA, Niebauer J. Chapter 5: Coronary artery disease. http://www.ncbi.nlm.nih.gov/books/NBK2216/. Updated 2004. Accessed 10/19, 2013.

8. Lilly LS, ed. *Pathophysiology of heart disease.* 5th ed. New York: Wolters Kluwer; 2011.

9. Lipoprotein-associated phospholipase A_2 (lp-PLA_2). http://www.bhlinc.com/clinicians/clinical-references/reference-manual/chapter12. Updated 2015. Accessed April 15, 2015.

10. World Health Organization. International classification of diseases (ICD). http://www.who.int/classifications/icd/en/. Updated 2013. Accessed 10/21, 2013.

11. World Health Organization. Public health surveillance. http://www.who.int/topics/public_health_surveillance/en/. Updated 2013. Accessed 10/22, 2013.

12. Koepsell TD, Weiss NS. *Epidemiologic methods*. 1st ed. New York: Oxford University Press; 2003.

13. Luepker RV. WHO MONICA project: What have we learned and where to go from here? *Public Health Reviews*. 2012;33(2):373.

14. Tu JV, Brien SE, Kennedy CC, Pilote L, Ghali W. Chapter 1: Introduction to the candian cardiovascular outcomes research team's candian cardiovascular atlas project. *Canadian Cardiovascular Atlas*. 2003:1.

15. Manuel DG, Leung M, Nguyen K, Tanuseputro P, Johansen H. Chapter 3: The burden of CardioVascular disease in canada. *Canadian Journal of Cardiology*. 2003;19(9):997-1004.

16. Alberta Health and Wellness. Chronic disease projections 2006 to 2035: Ischemic heart disease. http://www.health.alberta.ca/documents/Chronic-Disease-Projections-2008.pdf. Updated 2008. Accessed 22/10, 2013.

17. Heart and Stroke Foundation. Heart disease prevention. http://www.heartandstroke.com/site/c.ikIQLcMWJtE/b.3483919/k.EB14/Heart_disease__Prevention_and_risk_factors.htm. Updated 2012. Accessed 10/24, 2013.

18. Oxford University Press. Concise medical dictionary. http://www.oxfordreference.com/view/10.1093/acref/9780199557141.001.0001/acref-9780199557141-e-452?rskey=9i7fNS&result=490. Updated 2012. Accessed 10/19, 2013.

19. National Heart Lung and Blood Institute. What is a heart attack? http://www.nhlbi.nih.gov/health/health-topics/topics/heartattack/. Updated 2013. Accessed 10/19, 2013.

20. Britannica. Human cardiovascular system. http://www.britannica.com/EBchecked/topic/95628/human-cardiovascular-system/33560/Wall-of-the-heart. Updated 2013. Accessed 10/19, 2013.

21. John's Hopkins Medicine. Anatomy and function of the coronary arteries. http://www.hopkinsmedicine.org/healthlibrary/conditions/cardiovascular_diseases/anatomy_and_function_of_the_coronary_arteries_85,P00196/. Updated 2013. Accessed 10/19, 2013.

22. Cox JL, Bata IR, Gregor RD, Johnstone DE, Wolf HK. Trends in event rate and case fatality of patients hospitalized with myocardial infarction between 1984 and 2001. *Can J Physiol Pharmacol*. 2006;84(1):121-127. doi: 10.1139/Y05-141.

23. Reeder B, Taylor G. The burden of cardiovascular diseases in canada. *Can J Cardiol*. 1999;15 Suppl G:20G-4G.

24. Brophy JM. The epidemiology of acute myocardial infarction and ischemic heart disease in canada: Data from 1976 to 1991. *Can J Cardiol*. 1997;13(5):474-478.

25. Nova Scotia-Saskatchewan Cardiovascular Disease Epidemiology Group. Trends in incidence and mortality from acute myocardial infarction in nova scotia and saskatchewan 1974 to 1985. *Canadian Journal of Cardiology*. 1992;8(3):253-258.

26. Bata IR, Gregor RD, Eastwood BJ, Wolf HK. Trends in the incidence of acute myocardial infarction between 1984 and 1993 - the halifax county MONICA project. *Can J Cardiol*. 2000;16(5):589-595.

27. Nicholls ES, Jung J, Davies JW. Cardiovascular disease mortality in canada. *Can Med Assoc J*. 1981;125(9):981-992.

28. Tunstall-Pedoe H, Kuulasmaa K, Mahonen M, Tolonen H, Ruokokoski E, Amouyel P. Contribution of trends in survival and coronary-event rates to changes in coronary heart disease mortality: 10-year results from 37 WHO MONICA project populations. monitoring trends and determinants in cardiovascular disease. *Lancet*. 1999;353(9164):1547-1557.

29. Naylor CD, Chen E. Population-wide mortality trends among patients hospitalized for acute myocardial infarction: The ontario experience, 1981 to 1991. *J Am Coll Cardiol*. 1994;24(6):1431-1438.

30. Davies JW, Semenciw RM, Mao Y. Cardiovascular disease mortality trends and related risk factors in canada. *Can J Cardiol*. 1988;4(Suppl A):16A-20A.

31. James PD, Manuel DG, Mao Y. Avoidable mortality across canada from 1975 to 1999. *BMC Public Health*. 2006;6:137.

32. Bata IR, Eastwood BJ, Gregor RD, et al. Decreasing mortality from acute myocardial infarctions: Effect of attack rates and case severity. *J Clin Epidemiol*. 1997;50(7):787-791.

33. Alberta Health Services. AHS zone map. http://www.albertahealthservices.ca/1532.asp. Updated 2013. Accessed 10/28, 2013.

34. Alberta Health Services. AHS in my zone. http://www.albertahealthservices.ca/zones.asp. Updated 2013. Accessed 10/28, 2013.

35. Alberta Health and Wellness. Interactive health data application. http://www.ahw.gov.ab.ca/IHDA_Retrieval/. Updated 2013. Accessed 10/22, 2013.

36. Alberta Health, Surveillance & Assessment Branch. Interactive health data application – age-sex specific mortality rates. http://www.ahw.gov.ab.ca/IHDA_Retrieval/ShowMetaDataNotesServlet?1192. Updated 2012. Accessed 10/21,2013.

37. Alberta Health Surveillance & Assessment Branch. Interactive health data application – age-sex specific prevalence of ischemic heart disease. http://www.ahw.gov.ab.ca/IHDA_Retrieval/ShowMetaDataNotesServlet?122. Updated 2012. Accessed 10/21,2013.

38. Alberta Health Surveillance and Assessment Branch. Interactive health data application – age-sex specific incidence rates of ischemic heart disease. http://www.ahw.gov.ab.ca/IHDA_Retrieval/ShowMetaDataNotesServlet?684. Updated 2012. Accessed 10/21, 2013.

39. Alberta Health and Wellness. Health and wellness: Alberta health care insurance plan statistical supplement 2007/2008. http://www.health.alberta.ca/documents/AHCIP-Stats-Supplement-08.pdf . Updated 2009. Accessed 09/29, 2014.

40. Alberta Municipal Affairs. Alberta's municipal population total: From 1960 to 2013 . http://municipalaffairs.gov.ab.ca/documents/LGS/Alberta_Municipal_Population_History.pdf. Updated 2013. Accessed 09/29, 2014.

41. Excel (Part of Microsoft Office Professional Edition) [computer program]. Microsoft; 2010.

42. Kleinbaum DG, Klein M, eds. *Logistic regression A self-learning text.* 3rd ed. New York: Springer; 2010. 10.1007/978-1-4419-1742-3.

43. SPSS Inc. SPSS [computer program]. Version 22.0. Chicago, IL: SPSS Inc; 2013.

44. Tunstall-Pedoe H, Kuulasmaa K, Amouyel P, Arveiler D, Rajakangas AM, Pajak A. Myocardial infarction and coronary deaths in the world health organization MONICA project. registration procedures, event rates, and case-fatality rates in 38 populations from 21 countries in four continents. *Circulation*. 1994;90(1):583-612.

45. Hu J, Waters C, Ugnat AM, et al. Trends in mortality from ischemic heart disease in canada, 1986-2000. *Chronic Dis Can*. 2006;27(2):85-91.

46. Filate WA, Johansen HL, Kennedy CC, Tu JV. Regional variations in cardiovascular mortality in canada. *Can J Cardiol*. 2003;19(11):1241-1248.

47. Cairns J, Theroux P, Armstrong P, et al. Unstable angina-report from a canadian expert roundtable. *Canadian Journal of Cardiology*. 1996;12(12):1279.

48. Wielgosz A. Living with heart disease: The 2001 annnual report card on the health of canadians. *Canadian Journal of Cardiology*. 2001;17(2):148.

49. Filate WA, Johansen HL, Kennedy CC, Tu JV. Regional variations in cardiovascular mortality in canada. *Canadian Journal of Cardiology*. 2003;19(11):1241.

50. Mitzgala HF. Decline in ischemic heart disease mortality. *Can J Cardiol*. 2002;18(3):246-247.

51. Currie CJ, Morgan CL, Peters JR. Patterns and costs of hospital care for coronary heart disease related and not related to diabetes. *Heart*. 1997;78(6):544-549.

52. McManus DD, Piacentine SM, Lessard D, et al. Thirty-year (1975 to 2005) trends in the incidence rates, clinical features, treatment practices, and short-term outcomes of patients <55 years of age hospitalized with an initial acute myocardial infarction. *Am J Cardiol*. 2011;108(4):477-482.

53. McGovern PG, Pankow JS, Shahar E, et al. Recent trends in acute coronary heart disease--mortality, morbidity, medical care, and risk factors. the minnesota heart survey investigators. *N Engl J Med*. 1996;334(14):884-890. doi: 10.1056/NEJM199604043341403.

54. Manuel DG, Lim JJ, Tanuseputro P, Stukel TA. How many people have had a myocardial infarction? prevalence estimated using historical hospital data. *BMC Public Health*. 2007;7:174. doi: 10.1186/1471-2458-7-174.

55. The world health organization MONICA project (monitoring trends and determinants in cardiovascular disease): A major international collaboration. WHO MONICA project principal investigators. *J Clin Epidemiol*. 1988;41(2):105-114.

56. Tunstall-Pedoe H, Kuulasmaa K, Amouyel P, Arveiler D, Rajakangas AM, Pajak A. Myocardial infarction and coronary deaths in the world health organization MONICA project. registration procedures, event rates, and case-fatality rates in 38 populations from 21 countries in four continents. *Circulation*. 1994;90(1):583-612.

57. McGovern PG, Pankow JS, Shahar E, et al. Recent trends in acute coronary heart disease--mortality, morbidity, medical care, and risk factors. the minnesota heart survey investigators. *N Engl J Med*. 1996;334(14):884-890. doi: 10.1056/NEJM199604043341403.

58. Rosamond WD, Chambless LE, Folsom AR, et al. Trends in the incidence of myocardial infarction and in mortality due to coronary heart disease, 1987 to 1994. *N Engl J Med*. 1998;339(13):861-867.

59. Levy D, Thom TJ. Death rates from coronary disease--progress and a puzzling paradox. *N Engl J Med*. 1998;339(13):915-917. doi: 10.1056/NEJM199809243391309.

60. Sytkowski PA, D'Agostino RB, Belanger A, Kannel WB. Sex and time trends in cardiovascular disease incidence and mortality: The framingham heart study, 1950-1989. *Am J Epidemiol*. 1996;143(4):338-350.

61. Immonen-Raiha P, Arstila M, Tuomilehto J, et al. 21 year trends in incidence of myocardial infarction and mortality from coronary disease in middle-age. *Eur Heart J*. 1996;17(10):1495-1502.

62. Rouleau JL, Talajic M, Sussex B, et al. Myocardial infarction patients in the 1990s--their risk factors, stratification and survival in canada: The canadian assessment of myocardial infarction (CAMI) study. *J Am Coll Cardiol*. 1996;27(5):1119-1127. doi: 10.1016/0735-1097(95)00599-4.

63. Tu JV, Austin PC, Filate WA, et al. Outcomes of acute myocardial infarction in canada. *Canadian Journal of Cardiology*. 2003;19(8):893.

64. Tu JV, Naylor CD, Austin P. Temporal changes in the outcomes of acute myocardial infarction in ontario, 1992-1996. *CMAJ*. 1999;161(10):1257-1261.

65. Wolf HK, Bata IR, Gregor RD. Ten year trends of myocardial infarction rates, measured by MONICA and by hospital discharge diagnosis. *Canadian Journal of Cardiology*. 2000;16(Suppl):192F.

66. World Health Organization. Mortality from ischaemic heart disease in industrialized countries. *Weekly epidemiological record*. 1987;62(32):233.

67. Gordon T, Thom T. The recent decrease in CHD mortality. *Preventive Medicine*. 1975;4(2):115.

68. Stern MP. The recent decline in ischemic heart disease mortality. *Ann Intern Med*. 1979;91(4):630-640.

69. Public Health Agency of Canada. ARCHIVED - cardiovascular disease morbidity surveillance information. http://www.phac-aspc.gc.ca/cd-mc/cvd-mcv/cvd_morbidity-mcv_morbidite-desc-eng.php#mrbpie. Updated 1996. Accessed 10/22, 2013.

70. Canadian Institute for Health Information. Discharge abstract database (DAD) metadata. http://www.cihi.ca/CIHI-ext-portal/internet/en/document/types+of+care/hospital+care/acute+care/dad_metadata#. Updated 2013. Accessed 10/28, 2013.

71. Statistics Canada. Hospital morbidity database. http://www23.statcan.gc.ca/imdb/p2SV.pl?Function=getSurvey&SDDS=3203&Item_Id=21966. Updated 2013. Accessed 10/27, 2013.

72. Alberta Health. Overview of administrative health datasets . http://www.health.alberta.ca/documents/Research-Health-Datasets.pdf. Updated 2012. Accessed 10/27, 2013.

73. Statistics Canada. Vital statistics - death database. http://www23.statcan.gc.ca/imdb/p2SV.pl?Function=getSurvey&SDDS=3233&Item_Id=144261&lang=en. Updated 2013. Accessed 10/25, 2013.

74. Centre for Disease Control and Prevention. International classification of diseases,Ninth revision (ICD-9). http://www.cdc.gov/nchs/icd/icd9.htm. Updated 2009. Accessed 10/21, 2013.

75. Centre for Disease Control and Prevention. International classification of diseases,Ninth revision, clinical modification (ICD-9-CM). http://www.cdc.gov/nchs/icd/icd9cm.htm. Updated 2013. Accessed 10/21, 2013.

76. Canadian Institute for Health Information. The canadian enhancement of ICD-10. http://www.cihi.ca/CIHI-ext-portal/pdf/internet/PDF_CODINGCLASS_ICD10ENHAN_EN. Updated 2001. Accessed 10/21, 2013.

77. Canadian Institute for Health Information. ICD-10-CA. http://www.cihi.ca/cihi-ext-portal/internet/en/document/standards+and+data+submission/standards/classification+and+coding/codingclass_icd10. Updated 2013. Accessed 10/21, 2013.

78. Walker RL, Hennessy DA, Johansen H, Sambell C, Lix L, Quan H. Implementation of ICD-10 in canada: How has it impacted coded hospital discharge data? *Biomed Central*. 2012;12:149.

79. Centres For Medicare and Medicaid Services. ICD-9 code lookup. http://www.cms.gov/medicare-coverage-database/staticpages/icd-9-code-lookup.aspx. Accessed 10/19, 2013.

80. Centre for Disease Control and Prevention. Index of /pub/Health_Statistics/NCHS/publications/ICD9-CM/2011/. ftp://ftp.cdc.gov/pub/Health_Statistics/NCHS/Publications/ICD9-CM/2011/. Updated 2011. Accessed 10/19, 2013.

81. Mayo Clinic. Dressler's syndrome. http://www.mayoclinic.com/health/dresslers-syndrome/DS00666. Updated 2013. Accessed 10/19, 2013.

82. Vakil RJ. Intermediate coronary syndrome. *Circulation: Journal of The American Heart Association*. 1961;24:557-571.

83. MILLER RD, BURCHELL HB, EDWARDS JE. Myocardial infarction with and without acute coronary occlusion; a pathologic study. *AMA Arch Intern Med*. 1951;88(5):597-604.

84. Bolooki HM, Askari A. Acute myocardial infarction. http://www.clevelandclinicmeded.com/medicalpubs/diseasemanagement/cardiology/acute-myocardial-infarction/. Updated 2013. Accessed 10/19, 2013.

85. Garrat K. Chronic total occlusion of the coronary artery. http://www.cdc.gov/nchs/data/icd9/att1_CTO_mar06.pdf. Updated 2006. Accessed 10/19, 2013.

86. American Heart Association. Prinzmetal's angina, variant angina and angina inversa. http://www.heart.org/HEARTORG/Conditions/HeartAttack/SymptomsDiagnosisofHeartAttack/Prinzmetals-Angina-Variant-Angina-and-Angina-Iversa_UCM_435674_Article.jsp. Updated 2013. Accessed 10/19, 2013.

87. Lockwood W. Angina. http://www.rn.org/courses/coursematerial-210.pdf. Updated 2013. Accessed 10/24, 2013.