DEATH CERTIFICATE CODING VARIATION AND CORONARY HEART DISEASE

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ABSTRACT

The recent CHD mortality decline has been attributed to reduction of risk factors, improved management and potentially to artifact. The purpose of this thesis is to assess the impact of death certificate coding on geographic and time variations in CHD mortality rates.

Several samples of death certificates were recoded. There were samples of 400 death certificates originally coded ICD-9 410 (Acute Myocardial Infarction) and of 200 death certificates from all causes for the provinces of Nova Scotia and Saskatchewan for the years 1970 and 1984. The net effect of death certificates falsely coded ICD-9 410 and of the death certificates which should have been but were not coded ICD-9 410 did not vary significantly by province or by year. Therefore, death certificate coding errors were unlikely to explain the differential variation in CHD mortality decline by province and year. The error rates did increase significantly with age and with the number of contributing and underlying causes of death reported on the death certificates.

RESUME

Le déclin de la mortalité par maladie coronarienne observé depuis le début des années soixante est attribué à une réduction des facteurs de risques, à une amélioration des traitements, et possiblement à des artéfacts. Le but de cette thése est d'évaluer l'impact potentiel de la variation de la codification des certificats de décès sur les taux de mortalité par maladie coronarienne.

Des séries de 400 certificats de décès codifiés Infarctus Aigu du Myocarde et des séries de 200 certificats de décès par toute cause pour les provinces de Nouvelle Ecosse et de Saskatchewan pour les années 1970 et 1984 furent recodifiés. L'effet combiné des certificats qui n'auraient pas dus être codifiés ICD-9 410 et des certificats de décès qui n'etaient pas mais auraient du être codifiés ICD-9 410 ne montre pas de variation significative entre les provinces et les années.

Une variation dans la codification des certificats de décès ne peut donc expliquer meme partiellement le déclin dela mortalité par maladie coronarienne. Les taux d'erreurs dans la codification des certificats de décès augmentent de façon significative avec l'age et avec le nombre de causes contributoires et sous-jacentes au décès enumérées sur le certificat de décès.

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Finally, to my parents and to my daughter Isabelle for their love.

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TABLE OF ABBREVIATIONS

AMI	Acute Myocardial Infarction
ACLS	Advanced Cardiac Life Support
ASA	Acetyl Salycilic Acid
BCLS	Basic Cardiac Life Support
BP	Blood Pressure
CAB	Coronary Artery Bupass
CCU	Coronary Care Unit
CHD	Coronary Heart Disease
CVD	Cardio Vascular Disease
EMS	Emergency Medical System
FN	False Negative
FP	False Positive
HBP	High Blood Pressure
HDL	High Density Lipoproteins
ICD	International Classification of Diseases
ICDA	International Classification of Diseases Adapted
LDL	Low Density Lipoproteins
LRCCPPT	Lipid Research Clinics Coronary Primary Prevention Trial
MRFIT	Multiple Risk Factors Intervention Trial
RCT	Randomized Clinical Trial
SUD	Sudden Unexpected Death
VF	Ventricular Fibrillation

CHAPTER ONE

INTRODUCTION AND RATIONALE FOR THE STUDY

1. INTRODUCTION

For the last half-century, there have been important variations in mortality and morbidity rates for Coronary Heart Disease (CHD). Throughout the 1940s and the 1950s there were marked increases in CHD morbidity and mortality in industrialized countries. Some countries, including the USA and Canada, were considered to be experiencing CHD epidemics. In the 1960s, CHD mortality began to decline unexpectedly among some populations and has continued to do so. Following the initial surprise of the first report of the decline of CHD mortality in 1974 in the USA (1), several studies were conducted to explain this phenomenon.

The patterns of decline for CHD morbidity and mortality have shown national and regional inconsistencies. In the USA, Canada, and Australia, decreases were noted initially in the mid-1960s. Rates began to decline in Japan, Belgium, Finland and the Netherlands in the early 1970s. Some countries, including Spain, Greece and Switzerland, have yet to witness a CHD mortality decline (2,3).

Within countries, regional variations were observed in CHD mortality decline. The declines also varied by gender, age, ethnicity, and socioeconomic status. For example, the CHD mortality decline was particularly pronounced for young, white males of higher socioeconomic status.

In Canada, the decline in CHD mortality rates began in 1965. The onset of the decline occurred unevenly in the different provinces, generally following a west to east trend. The decline began in the Prairies (1965) and gradually moved towards the Maritimes where it was not observed until the 1970s (4). Despite declines in CHD mortality in all of the provinces, differences in CHD rates persist among the provinces. In 1978 the highest rate for fatal first AMI was in Nova Scotia, 273.0 per 100,000 person-years, 1.9 times the reported rate of 143.3 per 100,000 person-years in Saskatchewan, the province with the lowest rate.

Despite the impressive decline in mortality, CHD remains the leading cause of death in Canada today, and is the area of the most rapidly escalating health care costs (5). CHD mortality rates are a crucial source of information for health care policy making.

At one of the first major conferences organized by the National Heart Lung and Blood Institute, (NHLBI), in Bethesda in 1978 (2), the following questions were raised:

- is the CHD mortality decline due to reduction in the incidence of disease?

- is the CHD mortality decline due to reduction of case fatality?

- is the CHD mortality decline a statistical artifact?

Although there was general consensus that the total CHD mortality decline is not a statistical artifact (4), little has actually been done to examine the question of how much of the

decline could be attributable to such artifacts. In particular, no studies have assessed the degree to which changes in the nosologic coding from the death certificate could account for the reported variations in the CHD mortality decline.

2. RATIONALE FOR THE STUDY

Inaccuracies have been reported in death certification (6), particularly for the cardiovascular system (7). Moreover, quality assessment studies have reported important variations in death certificate coding. Therefore, it is pertinent to determine if death certificate coding practice varies over time and region in Canada, and the extent to which differential variations may account for the observed changes in the CHD mortality rates in Canada between the years 1970 and 1984, and between provinces.

Then the research questions are:

1- did the accuracy of death certificate coding vary between Saskatchewan and Nova Scotia between the years 1970 and 1984 ~~with regard to~~ the ICDA code 410 (AMI)?

2- what was the net effect of death certificate coding error rates variation upon the observed differences between Saskatchewan and Nova Scotia and between the years 1970 and 1984 for AMI mortality rates?

The following chapter will review the CHD epidemiology: the CHD mortality rate variations in Canada, USA, and in other countries; major CHD observational and intervention studies, their contribution and limitations; the CHD risk factors and

management; and, finally the death certification and death certificate coding for CHD. The methods used to ascertain death certificate coding variation are developed in chapter three. The data analysis and the results of this study are presented in chapter four. In the last chapter, possible explanations for the CHD mortality rates decline are discussed. Included as possibilities are the reduction of incidence, the reduction of case fatality, and in particular the potential of the effects of differential death certificate coding errors.

CHAPTER TWO

REVIEW OF LITERATURE

A. CHD MORTALITY

1 INTRODUCTION

The first report on CHD mortality decline in 1974 (1) was a great surprise. As can be seen in figure 1, the proportion of all death due to CHD had increased through the 1940s and 1950s to the point that observers thought it had reached an epidemic.

The increase in the proportion of deaths due to CHD was largely an artifact of the decline in competing causes of death such as infectious, parasitic and diarrheal diseases (8). The trends in proportion of death due to CHD were also distorted by other factors such as changes in the proportion of CVD deaths due to CHD (i.e. in the 1950s, concurrent reduction of deaths due to stroke and increase in CHD mortality), evolving medical terminology, and coding fluctuations within the CVD category and between acute and chronic CHD.

The observed CHD mortality decline since the late 50s remains largely unexplained. In the USA, the proportion of deaths due to cardiovascular diseases declined by 5.3 percentage points, and CHD declined by 7.1 percentage points between 1968 and 1982 (figure 2). The decline has reached all groups of the Canadian society and the rate of decline is increasing.

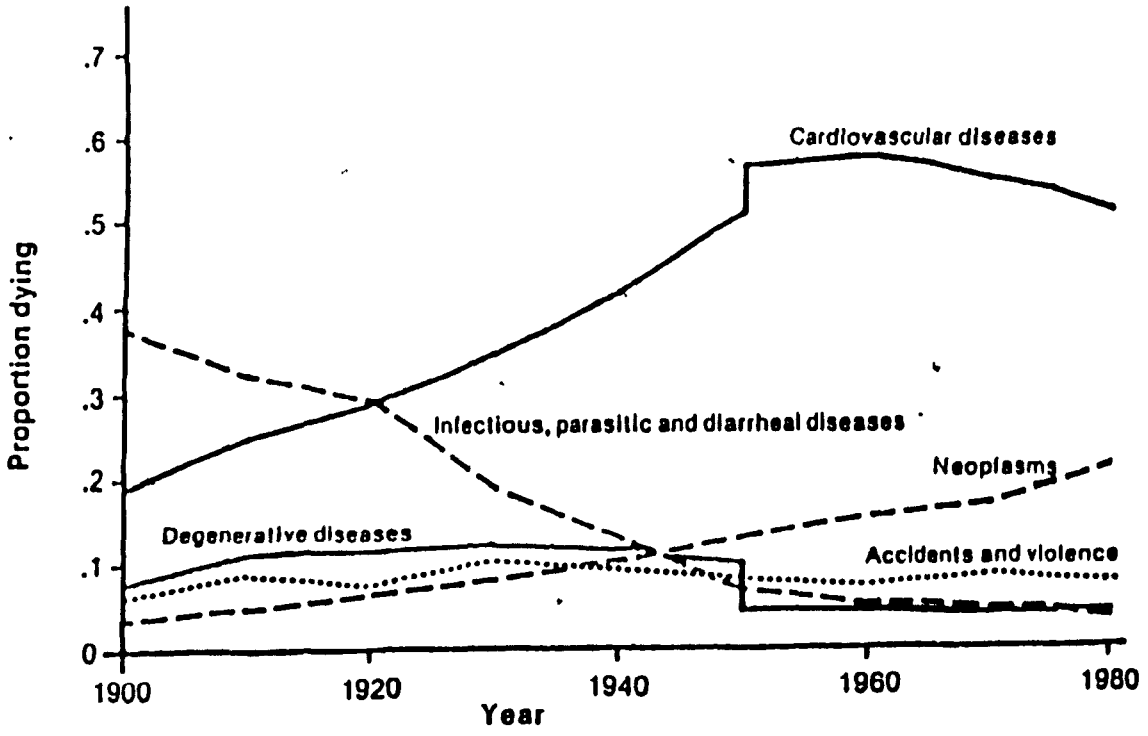


Figure 1. Proportion of life table deaths due to selected causes, US Males, 1900-1980

From the National Center for Health Statistics, Vital Statistics Report.

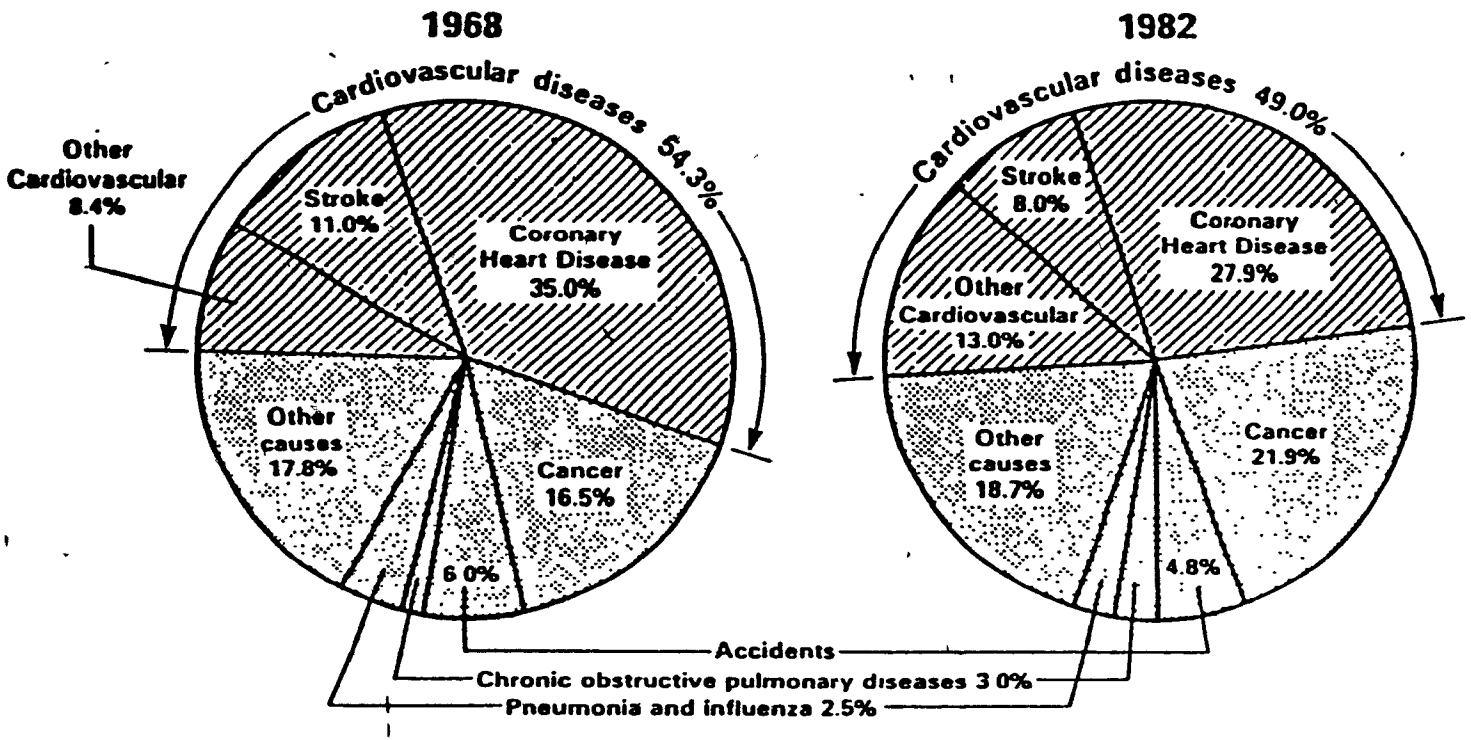


Figure 2. Deaths by cause as percentage of total deaths in the United States, 1968 and 1982. Causes of death for 1968 classified by the Eighth Revision, and for 1982 by the Ninth Revision of the International Classification of Diseases adapted for use in the United States. Data for 1982 are provisional; for 1968, final. From the National Center for Health Statistics, Division of Vital Statistics.

2. CANADIAN PICTURE

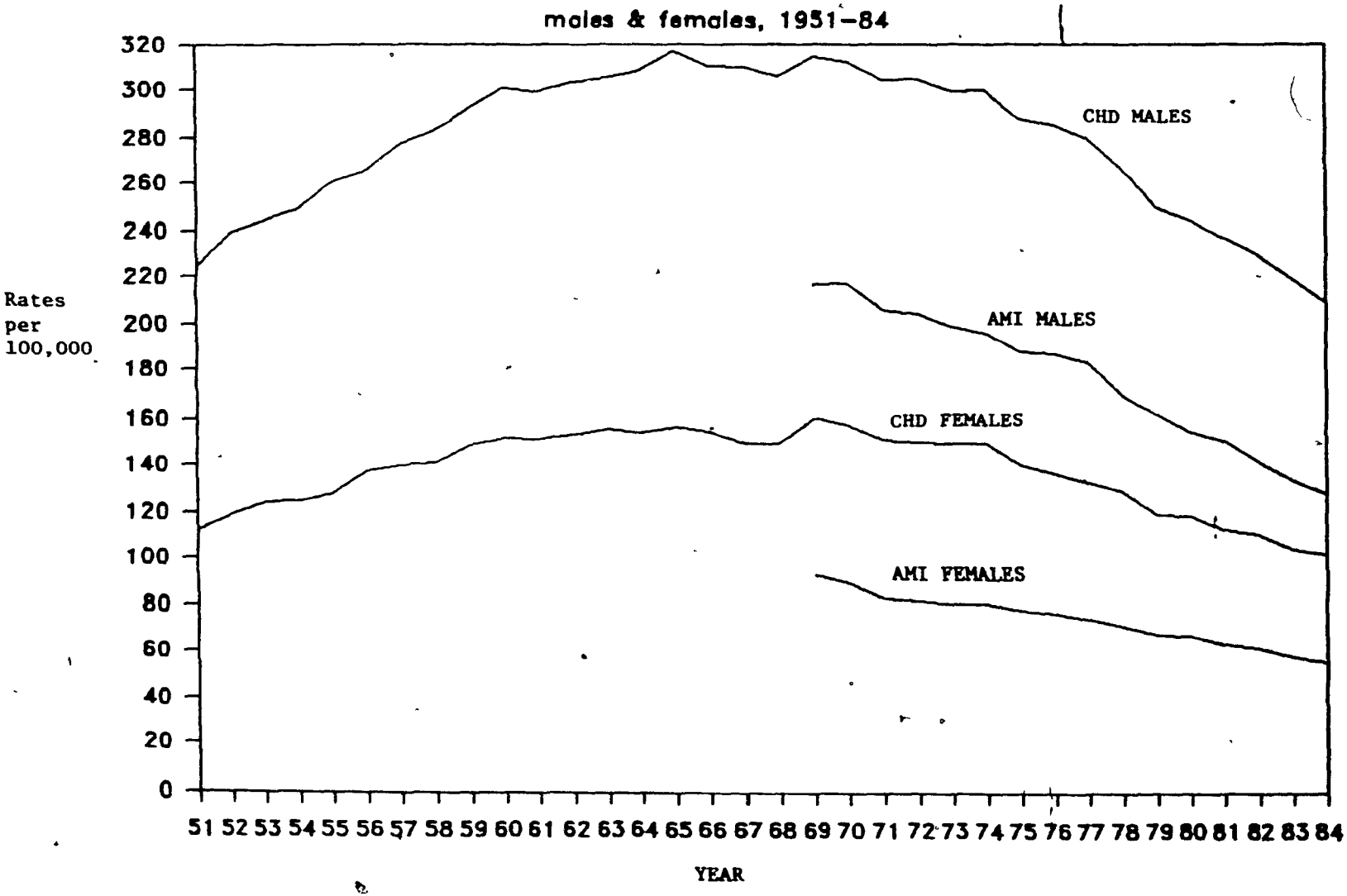
2.1. Canada

CHD age-adjusted mortality rates for males increased 0.5% annually from 1950 until 1965, then decreased 1.7% annually for the next ten years (4). For females, the CHD age-adjusted mortality rates remained stable from 1950 to 1960 at which point they began to decline 0.4% annually, and the annual rate of decline reached 2.4% in the 1970s (figure 3). In Canada, CVD mortality rates have declined 53% for women and 34% for men since 1951 (Statistics Canada).

Even though the decline in CHD was seen in both sexes and across all age groups, the young (under 45 years of age) and those of higher socioeconomic status appeared to have initially benefited the most (9). The only group showing an increase in CHD mortality were women under the age of 30.

Trends for acute and chronic CHD behaved differently from each other. Mortality data on acute CHD (available since 1969 only) shows a persistent decline across all ages and both sexes, which is, however, more pronounced among the young male group. Chronic CHD age-adjusted death rates trends over the same period are less uniform than for acute CHD. The male/female CHD mortality rate ratio of 2 remained relatively constant (4). Also, the rate of decline is increasing (4).

FIGURE 3


AMI & CHD mortality rates, CANADA
males & females, 1951–84
Rates per 100,000
320
300
280
260
240
220
200
180
160
140
120
100
80
60
40
20
0
CHD MALES
AMI MALES
CHD FEMALES
AMI FEMALES
51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80 81 82 83 84
YEAR

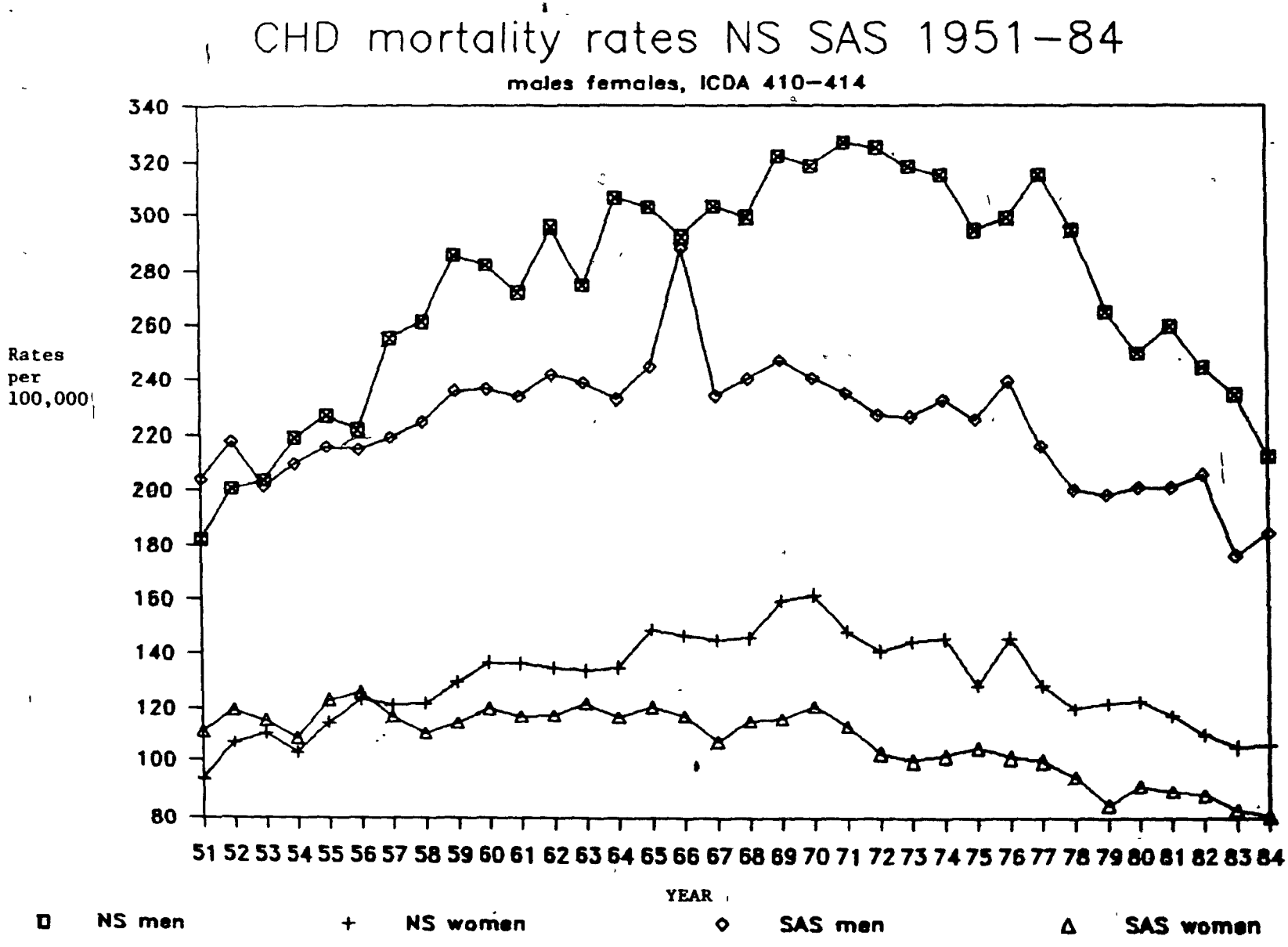
2.2. Canadian Regions

In Canada, the decline in CHD mortality rates has varied by regions. It occurred first in the Prairies in 1965, gradually moved to other provinces, and finally reached the Maritimes in the 1970s. Marked differences remain between the provinces (Appendix 1): some of the highest rates of CHD mortality have been observed in Nova Scotia, some of the lowest in Saskatchewan (figure 4). The difference between the two provinces has gradually decreased both for total CHD mortality rates (figure 4) and for AMI mortality rates (appendix 2).

The difference in rates between the two provinces remains unexplained. Greater reductions of CHD incidence rate may have occurred in Saskatchewan than in Nova Scotia, due to greater favorable changes in lifestyle or environmental factors in Saskatchewan. Also, Saskatchewan may have experienced a greater reduction in case fatality rate due to better medical care, better access to hospitals or decreased severity of the disease. The differences between the provinces may also be due to variations in diagnostic and coding practices. Finally, it could be a combination of the above.

The Nova Scotia/ Saskatchewan CVD Project was struck to examine this difference, and data were collected on the incidence of fatal and non-fatal AMI, rate of recurrent episodes, average intervals between episodes, episode fatality ratio, and the proportion of persons dying before, during or subsequent to hospitalization for the years 1977 and 1978. The study uses objective criteria developed to validate the

FIGURE 4


CHD mortality rates NS SAS 1951–84
males females, ICDA 410–414
Rates per 100,000
340
320
300
280
260
240
220
200
180
160
140
120
100
80
51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80 81 82 83 84
YEAR
NS men
NS women
SAS men
SAS women

diagnosis of AMI collected from hospital and death records. These data are available in Canada at the provincial and federal levels, and a computer data linkage system has been developed to facilitate utilization of the data.

The results show that age-adjusted incidence rates of AMI were 1.31 and 1.28 times higher in Nova Scotia than in Saskatchewan for males and females, respectively. The differences in incidence rates are most pronounced for males over 45 and for females 50 to 64 years of age with a Nova Scotia/Saskatchewan incidence rate ratio of 1.5. There were striking differences in the incidence rates of fatal first AMI; they were 1.9 and 1.53 times greater in Nova Scotia than in Saskatchewan for males and females, respectively. The recurrence rate of fatal AMI among females is 1.82 times greater in Nova Scotia than in Saskatchewan.

Most of the differences in CHD mortality rates between the two provinces are accounted for by males in Nova Scotia over 45 who have a higher incidence of fatal first AMI, and, who also more frequently die before admission to hospital.

Studies of geographically or temporally different populations are useful in identifying factors influencing cumulative incidence rates in comparison to individual studies which are better suited to assess relative risks associated with these factors (10). Wing et al. argue that the geographic pattern of onset of CHD mortality decline is similar to other patterns of social changes such as aspects of popular consumer

culture (diet, smoking and recreation) and shifts in productive economic activities, but not to diffusion of medical care (11).

3. USA

In the USA the proportion of deaths due to CVD increased from 19% in 1900 to 55% in 1950 (8).

Smith and Slater, through ordinary and cause-deleted life table analysis, examined the impact of competing causes of death; and through regression analysis examined the impact of International Classification of Diseases Adapted (ICDA) changes on trends in CVD (8). They conclude that, once changes in competing causes of death for males in the USA are taken into account, there were marked increases in CVD and CHD through the first half of the twentieth century (CVD death in the 1920s and 1930s, acute CHD death in the 1940s and 1950s). Conversely, CVD mortality for females did not increase during the same period. There was evidence of a major epidemic for the male population, but in the early 1960s there was a reversal in the epidemic patterns (8).

In the 20 year span between 1963 and 1983 in the USA, decline of CVD in general was 36% and the decline for CHD in particular was 37%. In 1982 alone, approximately 500,000 fewer deaths occurred in USA than deaths expected from the projected CVD death rates of 1963. The decline in CVD mortality accounted for a 26% decline in the overall mortality rate (i.e. deaths

due to any disease or condition), and a 2.6 year increase in life expectancy at age 35 between 1972 and 1982 (12,13).

By the mid 1970s in the USA, all groups by age, race and sex had experienced remarkably similar declines in CHD (14). However, some differences still persist such as the male excess of mortality, with a two to one CHD male/female ratio, and a three to one male/female AMI ratio. CHD mortality rates remain associated with SES levels (15). Most of the male CHD mortality declines are attributable to acute CHD while, for females, substantial declines were found for both the acute and chronic aspects of CHD. This important difference may be due to diagnostic custom, different manifestations of CHD in males and females, or to a differential impact of the factors related to the CHD mortality decline (14).

Regional variations were observed also in the USA. In the 1950s, CHD mortality rates were higher in New England, and the Southeastern and Western states. In 1968, CHD mortality rates were the highest in Southeastern states for white males and in the Northeastern states for white females (16). For the period 1950-1976, declines in CHD mortality rates were greater for all non-whites in the Southeastern states than in some other states (New York, California, Utah) where the overall CHD mortality decline was greater (17).

In the USA, the geographical variations in rates, the rates of change over time, and the rate differences in CHD mortality by sex have been studied independently and conjointly (11,14). There is inconsistency between the geographic

distribution of CHD mortality rates, and their rate of decline, (Appendices 3 and 4). This opens the possibility that the factors which account for differences in CHD mortality rates by regions may not be the same as those factors which account for the declines in mortality rates.

4 INTERNATIONAL PICTURE

CHD mortality rates vary as much as 8-fold among the countries in the world as can be seen in the rates for 27 countries. For males, Finland, Northern Ireland, and Scotland have the highest CHD mortality rates and Japan the lowest. For females, Scotland, Israel and Northern Ireland have the highest CHD mortality rates, whereas Japan and France have the lowest (18) (Appendix 5).

Since the 1960s, the most pronounced CHD mortality decline has been reported in the USA (19) (Appendix 6). Among the most industrialized countries there have been four distinct trends of CHD mortality rates over the years 1968-1977, for the 40-69 age-groups (18) (Appendix 7):

1. all countries outside of Europe experienced a CHD mortality decline among males and females (with the exception of Canadian females); the European experience is not uniform;
2. some countries experienced a decline (Finland, Belgium, Switzerland);
3. some other countries remained stable such as UK, Germany, Italy and the Netherlands;

4. some European countries experienced an increase, the most important being the increase observed in Bulgaria, Poland and Yugoslavia.

For the period 1968-1977, the greatest decreases for males were of 27% in USA, and for females 38% in Japan. The highest increases were in Poland both for males at 86%, and females at 66%.

The rate of change in CHD mortality rates does not seem to depend upon the initial CHD mortality rates. Some countries with high CHD mortality rates in 1969 experienced marked declines (USA, Finland), while others remained stable or even increased (Czechoslovakia, Ireland, Scotland, England and Wales).

Some countries with low rates of CHD mortality in 1969 experienced marked decreases (Japan, Belgium), while others experienced increases (Yugoslavia, Bulgaria, Poland). Therefore it is difficult to conclude that countries with low mortality rates are still recording an increase, and countries with high mortality rates have already reached the turning point and now are recording a decrease (18).

With regard to the proportion of CHD mortality to CVD mortality, some countries, where CHD accounts for a low proportion of CVD deaths, recorded a CHD mortality rate increase (Romania) and some a decrease (Japan). Conversely, countries with the highest proportion of CVD deaths attributable to CHD experienced a CHD mortality rate decline (USA, Canada), while others an increase (Sweden). Therefore it is difficult to

conclude that the CHD mortality decline reflects a changing pattern of proportional mortality within the greater CVD category.

The apparent CHD epidemic stimulated much research, both fundamental research trying to explore CHD mechanisms and potential therapeutic avenues, as well as epidemiologic studies trying to assess CHD risk factors and disease prone populations.

B. CHD MAJOR STUDIES

The marked increase in morbidity and mortality from CHD in the 1940s and 1950s spurred studies of related risk factors and interventions. With the unexpected and unexplained declines in CHD mortality beginning in the 1960s, major investigations were undertaken to explain the trends.

In this section the major studies, the key findings, and their significance for understanding the major CHD epidemiologic trends are presented in summary form.

1. OBSERVATIONAL STUDIES

Observational studies of CHD, at individual and population levels, have been reported since the late 1940s. Such studies were designed to explore the natural history of CHD, and to identify and assess the relative importance of various risk markers and factors to the onset of disease and mortality.

The following studies are summarized in Table 1:

- Framingham Study (20,21,22,23,24,25,26,27,28)
- Seven Countries Study (29,30)
- Minnesota Businessmen Study (31)
- San Francisco Longshoremen Study (32)
- Chicago Western Electric Co. Employees Study (33,34)
- Chicago Peoples Gas Co. Employees Study (35)
- Goteborg Sweden Study (36,37,38)
- Japanese in Honolulu Study (39,22,40,41)

TABLE 1

OBSERVATIONAL STUDIES

STUDY INVESTIGATORS	OBJECTIVES	DESIGN FOLLOW-UP CONTROLS	EXPOSURES/ INTERVENTIONS	SAMPLES EXCLUSION INCLUSION REFUSALS	ENDPOINTS	FINDINGS
FRAMINGHAM DAWBER, TR	To assess RR and IR associated with age, male gender, HBP, smoking, high serum CHOL, alcohol, diabetes, body weight, gout, sedentarism, hyperthyroidism hematocrit	Observational cohort study, zero-time 1949, follow-up for 4 to 28 years and continues.	Monitor exposure to risk factors over time: age, sex, HBP, smoking, CHOL, obesity, diabetes, physical activity	Random sample of 5209 men and women living in Framingham, Mass. aged 30-62 at entry. Refusals: 31.4% Volunteers: 14.2% Overall loss to follow-up: 2%.	5 endpoints: -angina pectoris -coronary insufficiency -AMI -sudden death -non-sudden CHD death	24-year IR CHD, men (all ages): 368. Women (all ages) 185. Identical findings for respondents and volunteers. CHD IR two most important risk factors: increasing age, and male gender particularly for AMI and SUD. If SBP>160 or DBP>95, RR=3. If SBP 140-159 or DBP 90-94, RR=1.5. If smokers, RR by age: AMI SUD age 30-39 3 4 age>50 1 2 If CHOL>260/<200, RR of AMI and CHD death=4 at age 30-39 and decreases to 2 at age 50-59. Mult (SBP, CHOL, SMK) logistic regression coefficient for AMI or CHD death: SBP CHOL SMK 0.0170 0.0068 0.1639 62% AMI attributable to HBP, CHOL, SMK. If overweight, AMI and SUD RR=2. If sedentary, weak CHD risk.
SAN FRANCISCO LONGSHOREMEN BORHANI, NO ET AL.	To assess RR and IR associated with HBP, abnormal ECG or chest x-ray, overweight, smoking, age.	Prospective cohort study, zero-time 1951, follow-up at 10 years.	Monitor exposure to risk factors over time: HBP, ECG & chest x-ray abnormalities, body weight, smoking, age.	3994 men aged 35-64 at entry; longshoremen. Exclusions: abnormality related to cardiopulmonary disease. Loss to follow-up: <1%.	-CHD death -All-cause death	IR CHD death=5.3 for 10 years; IR all-cause death=17.6 for 10 years. For CHD death: RR Age groups: 45-54 55-64 -smoking/non-smoking 3.2 4.5 -SBP>170 smokers/ SBP<130 nonsmokers 4.0 2.5 -SBP>170 nonsmokers/ SBP<130 nonsmokers 5.6 20.0 -DBP>100 smokers/ DBP<80 smokers 3.4 1.6 -DBP>100 nonsmokers/ DBP<80 nonsmokers 3.3 7.0 -DBP>100 smokers/ DBP<80 nonsmokers 14.0 7.0 -BP>160/95 smokers/ BP<160/95 smokers 4.3 1.6 -BP>160/95 nonsmokers/ BP<160/95 nonsmokers 2.5 5.9 -BP>160/95 smokers/ BP<160/95 nonsmokers 9.6 9.4 -ECG abnormal smokers/ ECG normal smokers 2.7 2.6 -ECG abnormal nonsmokers/ ECG normal nonsmokers 2.6 3.1 -ECG abnormal smokers/ ECG normal nonsmokers 6.0 7.2 Body weight: no relationship to CHD.

TABLE 1
(cont'd)

OBSERVATIONAL STUDIES

STUDY INVESTIGATORS	OBJECTIVES	DESIGN FOLLOW-UP CONTROLS	EXPOSURES/ INTERVENTIONS	SAMPLES EXCLUSION INCLUSION REFUSALS	ENDPOINTS	FINDINGS
CHICAGO WESTERN ELECTRIC CO EMPLOYEES PAUL,O.	To assess RH and IR associated with: age, HBP, diet, smoking, body fat, serum CHOL, ECG findings, Hb., lipoprotein lipase, blood sugar, fundi changes, family history, activity level, occupation.	Prospective cohort study, zero-time 1957, follow-up for 4 years.	Monitor exposure to risk factors over time. SBP, history of chest pain, cough, SOB, diet CHOL, fundi changes, ECG findings, Hb., lipoprotein lipase, blood sugar, smoking, activity, occupation, family CHD.	Random sample of 1989 men, aged 40-55 at entry, employed >1 year clerical, light/ heavy labor. Exclusions:CHD evidence from records or at first exam. Refusals. 33% Loss to follow-up: 6%	-CHD death -Angina pectoris -AMI	Refusal and study groups comparable. For CHD: if chronic cough, RR=2.0; if av nicking fundi, RR=3.2, if CHOL>256 mg/dl, RR's for angina=1.4, AMI=1.5, death=2.1. If heavy smoking, RR=1.6; if abnormal ECG, RR=4.1; if chest pain, RR=1.9; if SOB, RR=1.6; if peptic ulcer, RR=1.8. 12-year IR AMI and/or CHD death=91. No CHD relation to body weight, blood sugar, lipoprotein, diet, job type, physical activity, pulse, tension, hemoglobin.
CHICAGO PEOPLE'S GAS CO EMPLOYEES STAMLER, ET AL.	To assess risks associated with HBP, high CHOL, smoking, diabetes, diet, obesity, physical inactivity, tension.	Prospective cohort study, zero-time 1958, follow-up for 9.7 years.	Monitor exposure to risk factors over time: serum CHOL, HBP, smoking, diabetes, diet, obesity, physical inactivity, tense personality.	1329 men, aged 40-59 at entry, employees of People's Gas. Exclusions: 136 for evidence of CHD at entry. No refusals, no loss to follow-up.	-Incident CHD	IR AMI or CHD death=115/1000 for 12 years. SBP>150/SBP<130, RR=2.8. CHOL>275/<225, RR=4.6. Smoking 1 pack/day/never smoke RR=46. DBP>90 & ST-T pos/DBP<90 & ST-T neg, RR=4.5. Smoking + HBP + overweight + high CHOL/ none of these, RR=13. Smoking + HBP + overweight + high CHOL/ any 2, RR=5.7. Smoking + HBP + overweight + high CHOL/any 3, RR=1.8.
MEN BORN IN 1913 STUDY, GOTEBORG, SWEDEN TIBBLIN,G ET AL.	To assess risks of BP, CHOL and triglycerides, smoking, age of parental death, blood group, coffee, alcohol, physical activity at work, dyspnea, overweight, pulse, heart volume, geographic mobility.	Observational cohort study, zero-time 1963, follow-up for 10 years.	Monitor exposure to risk factors over time: BP, CHOL, smoking, age parental death, blood group, coffee, alcohol, activity at work, dyspnea, overweight, pulse, heart volume, high geographic mobility.	973 men, aged 50 at entry, residents of Goteborg, Sweden. Probability sample. Exclusions: AMI or angina. Refusals: 12%. Loss to follow-up: 7%.	-non-fatal AMI -CHD death -all-cause death	Non-participants: lower income, more unmarried, more alcohol problems, Sick Allowance. 10-year IR for non-fatal AMI & CHD death=59/1000 Significant risk factors for CHD: smoking (chi sq.=11.4); dyspnea (chi sq=14.2), high SBP (F=4.65); high DBP (F=3.05); CHOL (F=6.00); high triglycerides (F=2.67). No difference for blood sugar, obesity, physical activity, heart rate or volume, vital capacity, coffee.

TABLE 1
(cont'd)

OBSERVATIONAL STUDIES

STUDY INVESTIGATORS	OBJECTIVES	DESIGN FOLLOW-UP CONTROLS	EXPOSURES/ INTERVENTIONS	SAMPLES EXCLUSION INCLUSION REFUSALS	ENDPOINTS	FINDINGS
MINNESOTA BUSINESS & PROFESSIONAL MEN KEYS, A	To assess risks associated with HBP, CHOL, body weight	Prospective cohort study, zero-time 1948, follow-up for 15 years.	Monitor exposure to risk factors over time: relative weight, body fat, SBP, DBP, CHOL (NOT SMOKING!)	281 white men, 45-55 at entry. Volunteers: (50 overweight, 50 underweight, 50 active). Exclusions: CVD, other comorbid states.	-incident CHD -incident angina pectoris -CHD death -all-cause death	Significant risks for CHD: high SBP, high serum CHOL. Combined variables: high SBP+body weight (above 80th centile). (No data for RRs or IRs)
HONOLULU HEART PROGRAM YANO, K ET AL.	To assess risks of age, SBP, CHOL, cigarette smoking, physical activity, body weight.	Prospective cohort study, zero-time 1965-68, follow-up for 10 years.	Monitor exposure to risk factors over time: age, SBP, serum CHOL, smoking, physical activity, body weight.	7705 men of Japanese ancestry born between 1900-19, resident of Oahu since 1965. Refusals: 28%. Exclusions: CHD at entry. Loss to follow-up: 4%.	-fatal CHD, -nonfatal AMI, -angina pectoris	CHD IR=66 for 10 years (less than lowest rate for white males in other large studies). CHD risks significant in multivariate log analysis: high SBP (B=0.401), alcohol consumption (B=-0.430) smoking (B=0.264), CHOL (B=0.222), serum glucose (b0.158), age (b=0.186), serum uric acid (B=0.143), vital capacity/height (B=-0.133), physical activity index (b=-0.117).
SEVEN COUNTRIES KEYS, A.	To assess RR and IR associated with diet, age, blood pressure, CHOL, smoking, obesity, physical activity, resting pulse rate in 7 countries	16 cohorts in 7 countries: USA 1, Japan 2, Yugoslavia 5, Finland 2, Italy 3, Greece 2, Netherlands 1, zero-time from 1958 to 1964, follow-up for 10 years	Monitor exposure to risk factors age, HBP, smoking, CHOL, diet, obesity, resting pulse rate, physical activity. Varied lifestyles: urban, rural, fishing, lumbering, railroad, farming, clerical.	12763 men aged 40-59 at entry. Response rate: mean 90.4%. USA 75% to Japan 100%.	CHD prevalence at entry, 5-year CFR, 10-year IR hard=CHD death or non-fatal MI any=all diagnoses of CHD	CHD PREVALENCE AT ENTRY (%) Fin. 3.4 U.S. 4.6 Meth. 0.6 Italy 1.1 Yugo. 1.3 Greece 0.6 Japan 0.3 CHD DEATHS 10-YEAR IR 45.5 42.4 31.7 20.3 14.3 6.6 6.0 10-YEAR CHD DEATHS Multiple-logistic coefficient/standard error: U.S.A. North.Europe South.Europe Age 7.65/2.13 7.27/2.17 9.00/2.63 Smk 34.00/7.24 27.65/7.36 13.93/7.61 SBP 1.76/0.53 1.89/0.52 1.60/0.56 CHOL 0.85/0.22 0.90/0.20 0.59/0.20 -At 5 years: 23% all-cause CF and 26% disappearance of CHD. -For BP: SBP, DBP equal predictors. RR=2 for upper quintile (age, BP) in log model, coefficients vary between countries. -CHOL and CHD IR highly correlated: r=.82. -RR heavy/non-smoker range from 3 in USA Finland to 1 in Mediterranean and Japan. -Diet: great cohort variation. High correlation between % calories from saturated fats and IR (r=.73) and MR (r=.84). -Obesity, physical activity, resting pulse rate have weak to no relationship with IR.

ABBREVIATIONS USED:

CHOL	Cholesterol	Hb.	Hemoglobin
HBP	High blood pressure	SOB	Shortness of breath
AMI	Acute myocardial infarction	CV	Cardiovascular
CHD	Coronary heart disease	SC	Stepped care
SUD	Sudden unexpected death	RC	Regular care
SBP	Systolic blood pressure	SI	Special intervention
DBP	Diastolic blood pressure	UC	Usual care
SMK	Smoking	MR	Mortality rate
CVD	Cardiovascular disease	IR	Cumulative incidence rate/1000
ECG	Electrocardiogram	RR	Relative risk
CF	Cardiac failure	CFR	Case fatality rate

The focus of the discussion will be on the Framingham Study and on the Seven Countries study. The other observational studies have confirmed the findings, but they added little to the overall understanding of CHD risk factors.

The Framingham Study was the first major long-term cohort study of the natural history of CHD in a single community. The study's purpose was to define the principal risk factors of CHD, and to assess the relative risks of CHD associated with these factors. In this study, attention focused on hypertension, cigarette smoking, serum cholesterol levels, and obesity which had been postulated as major risk factors which could be modified to reduce the incidence of CHD morbidity and mortality. The Framingham Study also initiated estimations of the relative importance of risk factors through the use of multivariate analysis . The Framingham Study multiple logistic risk function coefficients accurately predicted the incidence rates for AMI, mortality from CHD, and death from all causes in four other US-based CHD observational community studies in the Pooling Project (25).

Several other major community CHD epidemiologic studies have since been conducted, most in the USA. The parent-populations for the US-based CHD studies were relatively similar. These studies confirmed the Framingham Study findings to be generalizable to white middle-aged American men.

The homogeneity of samples probably impeded better assessment of the relative strength of CHD risk factors, whether alone or combined, and also possibly prevented

identification of some components of risk factors. Variations on risk factor distribution among different populations is likely to enhance the assessment of true risk association. The Seven Countries study was designed to assess risk factors in populations in contrasting cultures and societies. The relative risks associated with the major risk factors (HBP, cigarette smoking, diet-related serum cholesterol level) varied from country to country.

For instance, the Japanese cohort, which had high proportions of smokers and hypertensives but low levels of serum cholesterol, reported a low CHD cumulative incidence rate. Conversely, the Finnish cohorts, with lower proportions of smokers and hypertensives but with higher overall levels of serum cholesterol, exhibited a high CHD cumulative incidence rate. Also, in the study of dietary differences between Greece and Finland, it was not so much the percentage of calories consumed from total fats but the percentage of calories consumed from saturated fats in the diet which best explained differences between these countries in death from CHD cumulative incidence rate.

The major CHD risk factors are age, male gender, cholesterol, smoking, elevated blood pressure and low SES. Cohort median values for systolic blood pressure and serum cholesterol as independent variables in multiple regression analysis explain two-thirds of the coronary death rate variance among the cohorts. These risk factors will be reviewed in a later section of this chapter.

2. INTERVENTION STUDIES

Once risk factors were identified, the interest shifted to assessing whether reduction of risk factors would result in reducing the disease incidence or severity. Randomized control trials (RCT) have examined that particular issue for CHD.

The following studies are summarized in Table 2:

- MRFIT (42,19,43)
- Oslo Study (44,45,19)
- Clofibrate Study (46, 19)
- Lipid Research Clinics Coronary Primary Prevention Trial (LRCCPPT) (47,19,48,49)
- Hypertension Detection and Follow up Program (HDFP) (19,50,51)
- Veterans Administration Cooperative Study (VA) (19)

The focus of the discussion will be on two RCTs, the LRCCPPT and MRFIT which illustrate the main issues associated with assessing the impact of risk factors reduction.

The LRCCPPT showed that reducing elevated plasma cholesterol levels significantly reduced CHD risk in men. The reduction of CHD risk followed a dose-response relationship with cholesterol reduction. However, the study was limited to men with very high levels of cholesterol who had not responded to dietary control alone. This and the lack of difference in all-causes mortality rates between the two study groups limits the applicability of the study results to the general population with milder risk levels. The clofibrate study showed a reduction of non fatal AMI significantly greater in

TABLE 2

INTERVENTION STUDIES

STUDY INVESTIGATORS	OBJECTIVES	DESIGN FOLLOW-UP CONTROLS	EXPOSURES/ INTERVENTIONS	SAMPLES INCLUSION EXCLUSION REFUSALS	ENDPOINTS	FINDINGS
CLOFIBRATE GELZEVOVA, H ET AL	To test the hypothesis that incidence of ischemic heart disease can be reduced by lowering serum CHOL using clofibrate.	Multi-centre (3) randomized controlled trial, double-blind. Zero-time 1965, follow-up for 5 years.	Treatment with drug clofibrate	15,745 male volunteers 30-59. 5000 high CHOL level randomized to treatment, 5000 to control. 5000 low CHOL randomized to 2nd control. Exclusions: CHD or comorbidity. Loss to follow-up: 32%	-Incident CHD: fatal AMI, non-fatal AMI	Mean reduction 9% CHOL levels in treatment group. Incident CHD reduced 20% in treatment group (nonfatal AMI reduced, fatal AMI same). IHD in treatment group=5.9/1000 per year, in high CHOL control group=7.4/1000 per year ($p<.05$). MR same in all 3 groups. Incidence gallstones higher in treatment group; non-CHD mortaltiy significantly higher in treatment group.
VA COOPERATIVE STUDY	To test efficacy of drug treatment in protecting hypertensive persons against CV consequences of uncontrolled HBP	Double-blind, randomized, placebo-controlled. Zero-time 1963, follow-up for 3 years	Stepped care (SC): Hydrochlorothiazide, reserpine, hydralazine. Regular care (RC).	523 white and black middle-aged men. Inclusions: DBP 90-129, compliance with drug regimen. Exclusions: secondary HBP, comorbidity.	-Fatal, non-fatal cardiovascular events	SC group: for DBP 90-114, events reduced 78%; for DBP=115-129, events reduced 93% (both significant). RR treated/controls=0.3. 5-year IR stroke: RC-29; SC-19.
HDFP	To test efficacy of intensive stepped care drug treatment to control BP in HBP groups of DBP 90-104, 105-114, 115+	Randomized controlled trial, zero-time 1973, follow-up for 5 years	-Control (RC): Referred to usual care -Treatment (SC): Stepped care (5 medication steps): 1. chlorthalidone, 2. reserpine/alpha methyldopa, 3. hydralazine, 4. guanethidine sulfate 5.Add or substitute additional agents.	Population-based 10940 hypertensive men & women. Black & white aged 30-69, 14 US communities. Loss to follow-up: Referred care 8.9%; Stepped care 5.2%.	5-year death from all causes	5-year all-cause death rates per 100: SC 6.4 RC 7.7 $p<.01$ For mild HBP group: SC 5.9 RC 7.4 $p<.01$ 5-year IR: Death from AMI: SC 9.3 RC 12.6 $p<.01$

TABLE 2
(cont'd)

INTERVENTION STUDIES

STUDY INVESTIGATORS	OBJECTIVES	DESIGN FOLLOW-UP CONTROLS	EXPOSURES/ INTERVENTIONS	SAMPLES EXCLUSION INCLUSION REFUSALS	ENDPOINTS	FINDINGS
LIPID RESEARCH CLINICS CORONARY PRIMARY PREVENTION TRIAL	To test efficacy of CHOL lowering to reduce CHD incidence	Multicentre (12) randomized controlled trial, double blind. Zero-time 1973, follow-up for 7.4 years.	Treatment: Cholestyramine 24g/day (6 packets). Control: placebo. Both groups had CHOL-lowering diet.	8006 men aged 35-59 at entry. Inclusions: CHOL>265 mg/dl; LDL-C>190 mg/dl. Exclusions: CHD, HBP, comorbidity. Pre-trial response to CHOL lowering diet to LDL-C<175 mg/dl. No loss to follow-up.	-CHD death -AMI -all-cause mortality -other CHD manifestations and CVD	Mean compliance: placebo-4.8 packets/day; treatment 4.2 packets/day. % reduction at 7 years: Plasma tot. CHOL LDL-C placebo: 4.9% 7.7% treatment: 13.4% 20.3% p<.001 for both 7-year IRs for primary endpoints: placebo treatment CHD death +/or AMI 98 81 p<.05 All-cause mortality 37 36 p>.05 (More violent and accidental deaths in the cholestyramine group)
OSLO HJERMANN,I ET AL.	Part I: To evaluate the effect of diet and anti-smoking counselling on incidence of CVD. Part II. To evaluate effect of: treatment of mild HBP on cardiovascular complication including CHD.	Randomized controlled trial, zero-time 1972-73, follow-up for 5 years	Part I: Intervention: dietary, anti-smoking advice to subjects and wives, examination every 6 months. Control: examination only, every year. Part II: HBP medication: Hydrochlorothiazide, Alphamethyldope Propranolol. Controls same follow-up but no treatment; no placebo.	Part I: 1232 Oslo men 40-49 at entry. Inclusions: CHOL 290-388 mg/dl, coronary risk scores in upper quartile (based on CHOL levels, smoking, BP), SBP<150. Exclusions: CHD or comorbidity. Refusals: 3% Loss to follow-up: <1% Part II: 785 men 40-49 at entry. Inclusion: 150<SBP<179, DBP<110. Exclusion: CHD, comorbidity. Loss to follow-up: 1.7%.	-fatal, non-fatal AMI -Sudden death -Stroke	Part I. Intervention, control groups comparable at baseline. Smoking decreased 45% more, CHOL 13% more in intervention group than in controls. Incident CHD & sudden death 47% lower in intervention group; significantly correlated only with change in CHOL level, not with decrease in tobacco. 7.5-year IR CHD=31 for intervention group; 57 for control group. Part II. CHD higher in treated group, not statistically significant. Treatment group mean BP decreased 17 and 10 mmHg (SBP & DBP) lower than controls. Small sample size and short follow-up time. Borderline to mild essential HBP—difficult to expect great difference.

TABLE 2
(cont'd)

INTERVENTION STUDIES

STUDY INVESTIGATORS	OBJECTIVES	DESIGN FOLLOW-UP CONTROLS	EXPOSURES/ INTERVENTIONS	SAMPLES EXCLUSION INCLUSION REFUSALS	ENDPOINTS	FINDINGS
MRFIT	To determine if modification of elevated CHOL, HBP, and cigarette smoking in persons at high risk of CHD would result in reductions of coronary death rates.	Multi-centre randomized controlled trial. Zero-time 1973-76. Follow-up (ave) 7 years.	Intervention (SI): Counselling for smoking cessation, CHOL lowering. Stepped care for hypertension. Control (UC): advised of high risk status, referred to usual care.	12,866 men aged 35-57 at entry, at high risk for CHD (by Framingham equation). Randomized to SI or UC group. Exclusion: CHD. Loss to follow-up: <1% in SI & UC.	-CHD mortality -CVD mortality -total mortality -Fatal CHD & nonfatal AMI	UC SI 7-year IR CHD mortality: 19.3 17.9 (not significantly different) Adjusted RRs: Cox Regression Coefficients for Significant Variables UC SI Difference associated with RR Age 2.30 1.85 Increase by 10 years DBP 1.21 1.38 Increase by 5 mm Hg SMK 1.39 1.46 Increase by 20 cigarettes LDL 1.25 1.28 Increase by 20 mg/dl (Coefficients were not significantly different between the SI and UC groups)

ABBREVIATIONS USED:

CHOL	Cholesterol	Hb.	Hemoglobin
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SUD	Sudden unexpected death	RC	Regular care
SBP	Systolic blood pressure	SI	Special intervention
DBP	Diastolic blood pressure	UC	Usual care
SMK	Smoking	MR	Mortality rate
CVD	Cardiovascular disease	IR	Cumulative incidence rate/1000
ECG	Electrocardiogram	RR	Relative risk
CF	Cardiac failure	CFR	Case fatality rate

the treated group (cholestyramine) than in the control group. However the rates of fatal CHD were similar in the two groups. Moreover, the all causes of death rates were significantly higher in the treated group than in the control group (46). Therefore, even if an intervention may be beneficial for a specific disease the net effect may result in more harm than good.

MRFIT failed to show beneficial effects from a multiple intervention on the three major CHD risk factors. The problems encountered in the MRFIT study demonstrate the difficulties of such studies. The 7 years follow up was short compared to the 30 years follow up in the Framingham study. MRFIT was based on risk factor rates and on disease occurrence rates from previous observation studies. Secular changes in these rates occurred between the observation studies period and that in which MRFIT was planned and then executed. The real power to detect the expected difference between the Special Intervention (SI) and Usual Care (UC) groups was reduced from a planned .8 to less than .6 (42). Several other elements of the study (volunteers, multiple examinations, different physician attitude) contributed to a greater than expected reduction in risk factors and in mortality for the UC group.

Moreover, the use of diuretics and propanolol for hypertensive subjects increased their plasma lipids even if associated with a fat-lowering diet counselling which significantly reduced plasma lipids among subjects not receiving hypertensive medication (52).

Several factors lead to difficulties with observational studies and to inconclusive or controversial results from studies of interventions on CHD.

3. DISCUSSION

The epidemiologic investigation of CHD is a challenge. One cannot directly perform decisive experimental tests of disease causation, for feasibility and ethical reasons. It is difficult to imagine CHD etiologic trials on human subjects starting in infancy, with large sample sizes, tight control of covariates, and extended follow-up until outcome events occur. Rather, we must rely on observational and intervention studies, and accept their inherent limitations.

Epidemiologic observational studies must take into account the biology of risk factors for the identification of the causal constituents of the disease, and also the relative prevalence of the risk factors in the population under study. Even if two factors are of equal biologic importance in the causation of a particular disease, such as two necessary but non sufficient risk factors, these factors can be of quite different epidemiologic importance. For instance, a rare, strongly associated risk factor will have a higher relative risk but a lower attributable risk than a weaker risk factor with greater prevalence. Relative risks, attributable risks and interactions between risk factors depend on the relative prevalence of all the disease causal components (53).

Observational and intervention studies, for reasons of feasibility, usually focus on relatively homogeneous disease

prone subpopulations, and thereby reduce the various possible combinations of risk factors under study. This in turn limits proper assessment of the various causal components of CHD, their relative causal strength, and possible interactions. Among them, measures of attributable risk and etiologic fraction, so important in public health, become difficult to assess from particularly homogeneous subpopulations under study at a particular time.

Some studies were designed to focus on several populations simultaneously so that the distribution of risk factors of interest varies across a broader range, within the study population as a whole. Such heterogeneity enhances the interpretation of the impact of risk factors. For instance, combining biologic knowledge related to fats as a risk factor in CHD with epidemiologic studies of Mediterranean and Finnish populations allowed better assessment of the impact of diet on CHD.

Even long prospective cohort studies, such as the one conducted in Framingham, remain prone to deficiencies. In these studies, the following factors were unknown: pre-study risk factors experience of the cohort members, the induction period, various chronologies of component causes leading to disease onset, the variable length of latency periods between disease occurrence and disease detection. Nonetheless, all the observational studies repeated similar findings from the 1950s and the 1960s consistently pointed towards the same risk

factors and comparable strengths of association across populations.

Most intervention studies displayed inconclusive results. The interventions were based on strongly associated risk factors with a biologic gradient, findings from several population-based cohort, studies; and they tested maneuvers coherent with the disease history and biology. But, the interventions were often unifactorial, and did not account for "effect-latency" period between time of intervention and observable beneficial effect on the disease (53).

Moreover, the interventions may not have been sufficient, or timely in the disease chronology, to affect disease outcome. The intervention studies were based on relative risks determined 10 to 20 years previously, sometimes on different populations, or on the same populations but with different risk factor levels and incidence rates.

Finally, and perhaps most importantly, risk factors may not be prognostic factors once the disease is present. Presence and severity of the disease remain the most important predictors of death from a disease. Risk factors reduction may be of minimal importance to the evolution of the disease. Therefore, the negative findings of the CHD risk factor intervention studies were perhaps only inconclusive.

C. CHD RISK FACTORS

1. INTRODUCTION

Epidemiologic studies strongly suggest that the main risk factors causally related to CHD are age, gender, HBP, smoking, and serum lipid abnormalities. There is some evidence for other less strongly associated risk factors including obesity, lack of physical exercise, personality type and socioeconomic status. These factors individually increase the risk of CHD, and a combination of several risk factors may greatly increase the overall risk of CHD or other CVD. Multivariate analysis has shown also that HBP, smoking, and cholesterol act synergistically as risk factors for CHD (54).

In this section, each of the major risk factors will be reviewed.

2. AGE

For apparently healthy men, age is the most important risk factor both, for the incidence of CHD and for death from all causes. Ideally, age should be treated as a continuous variable and age standardization should be by single years of age. Several studies (Framingham, Seven Countries, Pooling Project Research Group), give similar results: for instance, the CHD risk of a 50 year old man is 1.3 times higher than the risk of a 45 year old man; at age 59 the risk of CHD death is 10 times the risk at age 40 (Appendix 8).

3. SMOKING

Smoking is one of the major risk factors for CHD. In Canada, the population attributable risk fraction of CVD for cigarette smoking (ever) is high: 30.1% for males and 31.4% for females aged 45 to 64, 16.9% for males and 18.9% for females aged 65 to 79 (55).

Overall mortality as well as mortality from CVD, sudden death or CHD increase with the number of cigarettes smoked per day. Sudden death has the strongest relation with smoking dose (Appendix 9). Also an acute myocardial infarction (AMI) is more frequently fatal for smokers than for non smokers (56). The harmful effect of cigarette smoking on CHD decreases with age, and is greater for men. Smoking is a very strong risk factor when associated with oral contraceptive use in women age 35 or older (Appendix 10). Most of the epidemiologic studies clearly show a dose response relationship, even if the relation varies from study to study (25). To date, there is some harmful effects evidence of passive smoking among which is increased risk of CHD. A 16 year follow-up population based cohort study in Japan shows a significant increased risk of 1.30 for CHD for non-smoking wives of husbands who smoke more than 20 cigarettes per day (57).

The risk of CHD is reduced markedly after cessation of smoking. The Framingham study data (25) and other studies suggest a 50% reduction of CHD risk due to smoking, after 2 years of cessation. The exact time required for the ex-smoker

CHD mortality rate to return to the non smoker rate is still unresolved, but may be as short as 5 to 10 years (58).

4. HYPERTENSION

Over the past 30 years the concept and treatment of HBP have evolved greatly. The criterion for HBP treatment has evolved from a diastolic BP greater than 130 mmHg in 1960 to 115 mmHg in 1967 to 105 mmHg in 1970 to 95 mmHg today. If prevention of cerebrovascular disease, renal failure and heart failure has been successfully achieved by HBP treatment, it is still debated whether HBP reduction prevents CHD or not (59).

All CHD observational studies concur: elevation of both systolic and diastolic BP increases the risk of CHD for both men and women following a curvilinear dose-response relationship (Appendix 11). The Framingham Study data indicate that the relative risk of developing CHD is 1.5 with a systolic BP ≤140 mmHg and a diastolic BP ≤90 mmHg compared with a systolic BP ≥140 mmHg and a diastolic BP ≥90 mmHg. The risk becomes 2 to 3 with a systolic BP ≤160 mmHg and a diastolic BP ≤90mmHg. HBP is correlated with overweight (60) which in itself is also a risk factor for CHD (59).

CHD is considered to be the most frequent complication of HBP (59), but, except for malignant HBP, reduction of CHD incidence or mortality by antihypertensive therapy has continued to elude us (19, 61). For the few studies showing a beneficial effect of antihypertensive therapy on CHD, most of the beneficial effects were restricted to some sub-groups such

as the elderly or the markedly hypertensive. Understanding of why antihypertensive treatment has failed to show significant CHD reduction to date is of utmost importance.

One explanation could be that the relationship between HBP and CHD is one of correlation of a bidirectional causal association (61). An alternative hypothesis has received increasing attention. For moderate and mild HBP, the beneficial effects of medicated antihypertensive therapy could be offset by detrimental side-effects (59). Such effects are already known: the potassium-depleting action of diuretics (59), increased ventricular ectopic activity in long term thiazide therapy (62), increase in triglycerides and in total plasma cholesterol as well as decrease in high density lipoproteins (HDL) and HDL/LDL ratio occurring both with diuretic and beta-blocker treatments (52,63), and increase in the serum level of glucose with both diuretic and beta-blocker treatments. As antihypertensive therapy can be life-long, long term exposure to otherwise unnoticed short-term effects may have a significant impact on CHD.

5. CHOLESTEROL AND DIET

5.1. Association Cholesterol And CHD

Longitudinal studies such as the Framingham Heart Study have clearly established the contribution of blood lipids to the risk of CHD (Appendix 12). A total cholesterol level ≥270mg/100ml carries a 4 fold risk of CHD compared to a total cholesterol level ≤ 200mg/100ml (64). LDL cholesterol is the

most pertinent element with high levels of LDL increasing the risks of CHD. Increased LDL contributes to the slow process of atherosclerosis formation (65). On the other hand HDL has a protective effect against CHD mortality (Appendix 13). Coefficients for LDL and HDL appear of equal, although opposite, importance in prediction of CHD disease. It is not clear which combination or which ratio of components of blood lipids is the best predictor of CHD. The Framingham study seems to favor the ratio LDL/HDL (66).

5.2. Factors associated with cholesterol

The LRC study (66) in 4 countries (Canada, USA, USSR, Israel) confirms that both genetic and cultural factors contribute to levels of cholesterol. Cultural factors include dietary habits, particularly total calorie intake, intake of calories from fats and cholesterol, and most importantly, percentage of total calorie intake from saturated fats. Cultural factors include anthropometric factors such as weight-height index. Demographic factors include age, sex and race. Behavioral and medical factors such as smoking, exercise and alcohol habits are important as well (66).

a) Race: LDL and total cholesterol are lower and HDL higher for adult males of the black race. This is consistent with the reported lower incidence and mortality from CHD for middle-aged black males (67).

b) Hormones: hormonal supplement use by post-menopausal women appears to be protective against CHD. Hormone users showed lower LDL and total cholesterol and higher HDL values

and lower mortality rates from all causes after follow up (66). Oral contraceptive (OC) as a risk for CHD varies greatly among studies and remains very controversial (68). However there is little doubt of the increased risk of CHD with concurrent smoking and OC use (69).

c) Smoking: levels of HDL are sharply reduced by cigarette smoking in a dose response relationship (70). However it seems to be mostly related to HDL 3 which is non-related to CHD (70).

d) Diet: dietary habits correlate with serum cholesterol (total, LDL, HDL) and with CHD mortality. High intake of saturated fatty acid cholesterol and low intake of polyunsaturated and in particular monounsaturated fatty acid cholesterol (high"Keys Score") are associated with increased risk of CHD (71, 34).

Mono and polyunsaturated fatty acids cholesterol increase the HDL/total cholesterol ratio (72); removing saturated fats reduces LDL cholesterol level twice as fast as adding polyunsaturated fatty acids (73). Changing fatty acids intake can modify the average plasma cholesterol level by predictable amounts (74). Metabolic studies suggest that alcohol intake increases HDL fraction 3 rather than fraction 2; HDL fraction 2 being a stronger protective factor for CHD.

5.3. Association of Diet and CHD

Several studies suggest that dietary cholesterol per 1000 kilocalories is related to CHD mortality (34,39,71,75). Vegetable protein, polysaccharides and dietary fibers are inversely correlated with CHD. However these relationships and

the caloric intake are no longer significant once subcapsular skinfold is taken into account (39, 75). There is little doubt that dietary change can have an impact on cholesterol level (73, 76, 77, 78, 79, 80).

A WHO report states that the LDL cholesterol level for middle-aged western adults should be reduced by 20mg/100ml to approximate that of some Mediterranean populations at lower risk of CHD.

5.4. Does Reduction Of Cholesterol Decrease CHD Mortality?

a) Upper Quintile Plasma Cholesterol Level

LRCCPPT showed significant decreases in non-fatal and fatal AMIs among men in the upper quintile of plasma cholesterol level. However, the overall death rate was not reduced by the intervention.

The Oslo trial, designed to test the effect of diet and smoking intervention, after the 5 year observation period showed significant reductions in the incidence of fatal and non-fatal CHD events. The incidence of sudden death was 47% lower in the intervention group. However, it is difficult to dissociate the effect of diet change from the effect of smoking reduction (81). Therefore, a case finding strategy of high risk patients might be justified.

b) Population

Would a reduction in plasma LDL cholesterol level for the majority of the population reduce CHD mortality rates? Should we establish population-based strategies to reduce LDL

cholesterol levels? Dietary habits and exercise might be the solution.

Natives from Japan who moved to Hawaii or San Francisco and natives of India who moved to South Africa experienced an increase in cholesterol levels and in the risk of CHD after having changed their dietary habits (73).

Animal studies show that a diet-induced reduction in cholesterol produces marked regression of coronary atherosclerotic lesions. To date there is no study on humans with a diet-alone intervention to confirm these findings. There is evidence of important changes in the diet of Americans in the past 20 years with a decrease in average cholesterol intake from 600 to 800mg/day (Framingham study) to less than 500mg/day (LRC studies). Moreover, serum cholesterol levels decreased from 225mg/100ml for middle-aged persons in the 1950s (Framingham study) to 205mg/100ml in the early 1970s (LRC studies). Similarly, the mean serum cholesterol level for the upper quintile has changed in the same period from 265mg/100ml to 240mg/100ml. Despite an estimated 3% to 5% decrease accountable to methodologic and measurement variations, there is still a net 5% to 7% overall serum cholesterol level reduction in the US over the past 20 years (73).

It has been estimated (Coronary Primary Prevention Trial (82) that a 1% decrease in plasma cholesterol level induces a 2% decrease in MI incidence and sudden death. From these figures one could estimate that the American overall plasma

cholesterol level reduction of 5% over the past 20 years could account for 10% of the 26% reduction in CHD mortality.

Men who die of AMI have atherosclerotic lesions over an average 60% of their coronary artery surface area. Young (20 years old) Americans or Europeans have atheroslerosis over 1-2% of their coronary artery surface area. Reduction in the growth rate of coronary lesions can produce a major decrease in risk of death from CHD.

Since higher levels of education and income are associated with better information, better dietary habits and lower cholesterol levels it is reasonable to suggest population based campaigns for dietary changes as a strategy to reduce CHD incidence and mortality.

6. ALCOHOL

Ethanol abuse is an etiologic factor in heart disease such as congestive cardiomyopathy and arrhythmias which increase the risk of sudden death (83).

The finding that light alcohol drinking (≤2 drinks a day) has an apparent protective effect against CHD (84, 85, 86, 87) is controversial. The drinking pattern, rather than the amount of alcohol consumed, might be an important factor. Sporadic heavy drinking might be harmful in contrast to the apparent protective effect of a light regular pattern (88). Whatever protective effect alcohol may have on CHD for light drinkers must be weighted against all other detrimental health effects such as raising BP. Epidemiologic studies face problems in

obtaining valid information on the quantity of alcohol consumed (89); therefore, results must be interpreted with caution.

7. OBESITY

Numerous studies provide evidence that obesity is an important risk factor for CHD. The Framingham study (23), after 26 years follow-up, shows the Metropolitan Relative Weight Obesity Index, on initial examination, to be a good predictor of 26-year risk of CHD events, including death in men and women, independently of age, cholesterol, systolic BP, smoking, left ventricular hypertrophy or glucose intolerance. Furthermore, weight gain after the early adult years conveys an additional CHD risk.

8. EXERCISE

Despite the lack of certain evidence of the role of physical inactivity in CHD, epidemiologic evidence suggests that exercise protects against CHD (90,91,92,93). Habitually physically active men are at lower risk of CHD than their less active counterparts. Participation in vigorous sports or physical activity confers an additional protection. (92,93).

Epidemiologic studies also suggest a dose-response relationship between physical activity and reduction of CHD risk; 2000 kilocalories per week of exercising or 1 hour of hard physical activity reduces CHD risk as well as mortality from AMI once it has occurred. The risks of physical activity are minimal compared to the benefits and can be reduced by

education and guidance. Lack of physical activity is probably not as important a risk factor for CHD as smoking, cholesterol and HBP. However, physical activity helps to decrease cigarette smoking and emotional stress.

9. SOCIOECONOMIC STATUS

Socioeconomic disparities are associated with levels of CHD risk factors. The lower the level of education (proxy for socioeconomic level), the higher the CHD risk factor level (94). The biggest risk factor differences involve smoking, obesity, physical activity and alcohol intake for men age 20-69; and smoking, overweight, obesity, high diastolic BP and physical inactivity for women age 20-69 (94). If the decline in CHD risk factors is greater for higher socioeconomic levels, as it seems, it may be that the CHD decline is greater in higher socioeconomic groups and that the difference will increase in the future.

10. OTHER RISK FACTORS

Diabetes mellitus is a well known CHD risk factor. Although diabetes is associated with hypertension and hyperlipidemia, diabetes per se appears to be an independent risk factor for CHD. Fasting glucose level is an independent risk factor for CHD following a dose-response curve (70).

Thrombosis activity correlates with CHD. Acetylsalicylic acid (ASA), certain fish oils, exercise, and moderate alcohol

intake may stimulate fibrinolysis and therefore can be beneficial against CHD (70).

Type A behavior has been correlated with increased risk of CHD. However, this is uncertain since type A persons are more prone to report symptoms therefore leading to a detection bias.

Oral contraceptive (OC) use and smoking are independent risk factors for CHD but they potentiate each other. Female OC users who smoke have an 8- to 10-fold risk of CHD compared to non-OC using, non-smoking women (94).

Age, gender, cholesterol, HBP, smoking, SES and others are all factors which increase the risk of CHD. Once CHD has occurred, therapeutic maneuvers can be undertaken to reduce morbidity or death from the disease.

D. CHD MANAGEMENT

Over the last 30 years, CHD management has become more sophisticated and aggressive. Improved care has become generally more available to the population. Accessibility to care has increased, along with the public awareness and professional knowledge.

1. PREHOSPITAL RESUSCITATION AND CARE

Sixty percent of AMI deaths occur before hospitalization. Emergency medical services (EMS) are now better equipped and training in Basic Cardiac Life Support (BCLS) and Advanced Cardiac Life Support (ACLS) have become more common. Also a suspected coronary patient is much more likely to be hospitalized, evaluated and monitored (12), and therefore to benefit from CHD management. Prehospitalization cardiac resuscitation is successful when applied very early (within 5 minutes) and to patients with ventricular fibrillation (VF). However the results of EMS intervention are much less successful when observed in the population at large because of the large proportions of CHD which occurs as unwitnessed SUD, and because patients are often reached only after 5 minutes of cardiac arrest. Moreover, most of the time BCLS rather than ACLS is initially applied. Goldman (95) estimates that a maximum of 4% of the mortality decline can be attributed to EMS and prehospital care.

2. CORONARY CARE UNITS (CCU)

Control of arrhythmias and, in particular, ventricular fibrillation (VF) is a major role of CCU. VF usually occurs within 12 hours of AMI onset. Only 4.5% of hospitalized patients with AMI will present primary VF; of those, 88% will be successfully resuscitated and discharged alive (95). Arrhythmia prophylaxis is efficacious at high doses of medication but such dosages have not used been routinely in most hospitals (95). Other CCU management tools include pacemakers, intravenous nitrates, streptokinase, pulmonary arterial catheters, after-load reduction therapy and calcium channel blocking agents. All of these save individual lives (95), but it is uncertain to what extent they have had an impact on the population CHD mortality decline.

3. MEDICAL TREATMENT OF CHD

Even though drugs such as nitrates, anticoagulants and antiarrhythmic agents were available earlier, it was only with the wide use of beta blockers by the mid 1970's that CHD treatment improved with regard to symptoms (95). Only beta-adrenergic blockers have been submitted to RCT, and have shown significant improvement of survival after AMI. Based on survival rates of patients eligible for long term medical therapy after AMI, Goldman estimates that medical therapy could account for 10% of the mortality decline between 1968 and 1976 (95).

4. CORONARY ARTERY BYPASS SURGERY (CAB)

CAB procedures increased from 30,000 in 1970 to 239,000 in 1982 in the USA. CAB surgery has been shown effective with triple vessel disease and left main lesion (European Cooperative Coronary Surgery Study); but CAB does not seem to prolong life markedly for single or double vessel disease (96). Assuming maximum potential benefit from CAB (2.6% reduction in annual mortality rate for surgery patients), CAB surgery could account between 4% to 5.5% of the CHD mortality decline (3,95).

The knowledge of CHD has greatly evolved over the last half century, CHD management and accessibility to care have greatly improved in Canada. Similarly CHD diagnosis and certification has undergone various changes.

E. DEATH CERTIFICATION AND CODING

Mortality and morbidity rates are a major source of information on the health trends of populations. Increasingly, government departments, private agencies, and the public at large are using mortality and morbidity statistics as inputs in their planning and policy decisions related to health programs.

1. DEATH CERTIFICATION

Since it has legal implications, the completeness of registration of death has been justifiably assumed to be of high order. The death certificate provides information on the numbers of deaths, the socio-demographic characteristics of the deceased and on the conditions that led to death. In Canada, death certification is performed on provincial forms which contain basically similar information even if slightly different in their format (samples of the Nova Scotia and of the Saskatchewan death certificate forms are shown in the appendices 14 and 15).

In Canada, mortality reporting has attained virtual completeness (97). The death certificate is filled out by the attending physician or by the coroner, and compiled by the provinces and territories. Under the federal-provincial agreements dating back to 1919, Statistics Canada has been employing these records to produce national data on mortality. Accuracy on death certificates tends to be high for such characteristics as age, sex and date of death (98).

The physician's major contribution is certification of the cause of death. For each death, only one condition must be reported as the "underlying cause of death". With today's increased life-expectancy, people are likely to die with multiple conditions or with conditions affecting several organs. Assignment of one cause of death is becoming increasingly difficult and may not represent the disease processes resulting in death.

The diagnosis on the death certificates must conform to the International Statistical Classification of Diseases, Injuries and Causes of Death (ICD). The amount of information available for death certification depends on the familiarity of the certifying physician with the medical history of the deceased. Therefore, differences in medical practices and diagnostic labelling between areas or years can be important for comparative purposes.

If death is due to an accident, or suspicious of homicide or suicide, or if a physician was not in attendance, the death has to be certified by a coroner or a medical examiner. A medical examiner is a physician usually trained in forensic pathology, whereas a coroner need not be a pathologist or even a physician. As a result, the accuracy of death certificates may vary greatly.

The medical certificate of death includes the cause of death including immediate, antecedent and other significant conditions contributing to death (appendices 14 and 15). Accuracy of the statements of cause of death appears to be

related to the current state of medical knowledge, completeness of the information available at the time of death, and the variety of ways in which death certificates are completed.

The death certificate has been recognized as an inaccurate record of the cause of death (6,7,99). Death certificates are no more accurate for deaths occurring within an institution, where one would expect better knowledge of the patient's illnesses by the health professional certifying the death (6). In general, the diagnostic information available for death certificate coding is often sketchy and imprecise (99).

Autopsy findings, added to pertinent clinical information, could be used to improve death certificate accuracy. However, autopsies were performed only on 16% of the deaths in the United States in 1978, and the information is rarely used to supplement or revise death certificates (7).

A Connecticut study of 272 randomly selected autopsy reports and corresponding death certificates showed error rates of 25% of deaths which were falsely attributed to the circulatory system, and 18% which were not but should have been attributed to this system, leaving a net gain of 7%.

Within the circulatory system category, there was a 75% disagreement as to the specific cause of death (7). Similarly, Engel in 1980 (100) showed that vascular diseases were overreported on death certificates by about 10% when compared with autopsy report. Cameron (101) showed also that diagnostic discrepancies increased markedly with age: among those over 75

years of age, fewer than half of the death certificate causes of death were confirmed by autopsy reports.

Comparing death certificates and clinical information obtained from hospital records shows similar discrepancy. Gittelsohn (102) showed that concordance declined with patient age and length of stay, and also that error rates were associated with cause of death and with the hospital where death occurred. Concordance varied little between the years 1969 and 1975. For the Circulatory system, ICDA 3 digit agreement rate was 73% and for AMI the agreement rate was 87%.

Hospital discharge codes, if sufficiently accurate, could be used as a convenient proxy for incidence trends of AMI. However, a study in Texas found a false positive rate of 39% (of discharge diagnoses 410 (AMI) which were found to be in error by a Cardiology Surveillance study) (34). In Finland, a study found a true positive rate of 84% for AMI in hospital discharge data (104).

Accuracy of the statements of cause of death and completeness of the information are reflected in the nosological coding of the death certificate. The clearer and more precise the information of the death certificate, the better will the coding be (99).

2. DEATH CERTIFICATE CODING

The International Classification of Diseases (ICD) is the basic classification system in use for national and international morbidity and mortality statistics.

The ICD has been revised about every 10 years to reflect progress in the classification of disease. The sixth revision represented a milestone as the underlying cause of death was defined, and the international form of death certificates was devised. Recognizing the ICD-8 limitations the United States Public Health Service published the "Eighth Revision International Classification of Diseases Adapted for Use in the United States" (ICDA-8). Canada, in 1968, adopted the ICDA-8. In 1975, the Ninth Revision (ICD-9) provided for morbidity coding including primary care, multiple cause coding, and underlying cause of death coding. ICD-9, now in use worldwide, was adopted in Canada in 1979.

The ICD-9 codes appear in the "Tabular List of Inclusions and Fourth Digit Subcategories" in the ICD first volume. This is a numerical list of all the ICD-9 three digit categories and each of their subcategories. The three digit categories (001-999) are divided into seventeen broad groupings of diseases and injuries (chapters). Each chapter is divided into main "blocks" of the content of the chapter. Each "block" is formed by several three digit codes. Some are allocated to important individual conditions, others to groupings of less important conditions assignable to the "block". Three digit categories may be divided in four digit categories to further differentiate the component parts. Chapter VII, Diseases of the Circulatory System, contains the Coronary Heart Disease "block" with the ICD codes 410-414 (Appendix 16).

Such revisions as well as other factors can result in variations in the death certificate coding comparability ratios and in the accuracy of reported mortality rates.

3. DEATH CERTIFICATE CODING VARIATION

Once the death certificate has been completed, there is the possibility of error in recording the cause of death for mortality statistics data during the nosological coding phase.

Mortality rates can vary as a function of true variations in diseases overtime as well as secular changes in death certificate coding. In the latter case, variation can be due to the quality of the death certificate supplied by the recording physician (illegible data, missing documents, erroneous registration numbers), the nosologist (competency, preferences) and key entry errors (105).

Misclassifications vary with respect to their composition in terms of their ICD digits. Depending on the usage of the vital statistics, the severity of error will vary according to the digit erroneously coded.

Each of the ICD revisions has produced some disruption in the comparability of cause-of-death statistics. The Ninth Revision assigned different codes for some diseases within the circulatory system category; chronic CHD, 412 in ICDA-8, became 414 in ICD-9. According to the Ninth Revision, Cardiovascular Disease unspecified (ICD-9 No. 429.2) has been separated from CHD (ICDA-8 No. 410-414). This separation accounts for a large

part of the reduction in chronic CHD mortality rates in 1979 (97).

A recent American study showed that preferences for generalized cardiovascular terms rather than terms specific to the heart resulted in artifactual changes in chronic CHD mortality rates between 1978 and 1979 (106). Whereas the AMI mortality rates (ICD-9 No. 410) remained stable, the overall CHD mortality rates (ICD-9 No. 410-414) artificially decreased by 12% (appendix 17), when ICDA-8 coded death certificates were recoded according to ICD-9 (97). However, the CHD mortality rates data from Statistics Canada do not show that difference in the yearly trend for Canada or for regions.

The change between the Eighth and Ninth Revisions of the ICD did not affect the coding of AMI (ICD-9 No. 410). The AMI comparability ratio of deaths assigned according to ICD-9 to deaths assigned according to ICDA-8 is 1.0003 with a 0.9898 to 1.0108 95% confidence limits (Appendix 17). Therefore, differences observed in AMI mortality rates would not be due to the changes in the Ninth Revision of the ICD.

Accuracy of nosological coding of cause of death was studied by Curb et al. in 1983 (107). Inter-observer variability showed different agreement rates for different causes of death (three digit ICDA code agreement among three nosologists). The three nosologists agreed on 86.5% of death certificates; two of the three nosologists agreed on 88% of the death certificates . Intra-nosologist agreement varied from 94.6% to 96.6% for CHD.

In Canada, death certificates are nosologically coded at the provincial level, then collected at the federal level in Statistics Canada. Because there are only one or two nosologists per provinces coding differences among provinces may arise. Any important systematic differences between them would lead to apparent important differences in mortality statistics between provinces.

A quality assessment study from the Health Division at Statistics Canada in 1981 (98) reported an overall 7.18% coding error rate for "Cause of Death". Two thirds of the errors involved the first two digits of the 4 digit code. The location of the erroneous digit is of importance. A first digit error results in death being attributed to causes related to the wrong body system, (e.g. diseases of the circulatory system and mental disorders). A second digit error involves two different diseases in the same system (i.e. hypertensive disease and CHD). A third digit error involves different forms of the same disease (i.e. AMI and Angina Pectoris). A similar study in 1979-1980 (105) showed important variation between provinces over time. Overall cause of death coding error rate varied from 2.2% to 18.1% between provinces.

Therefore, there is some possibility that death certificate coding variation explains some of the differences observed in CHD mortality rates between the years 1970 and 1984 and between the Provinces of Nova Scotia and Saskatchewan.

The following two chapters will cover the Methods and the Analysis and Results of this study.

CHAPTER THREE

METHODS

1. DEATH CERTIFICATE CODING VARIATION ASCERTAINMENT

The objective of the study is to determine if there have been variations in CHD death certificate coding in Canada, and if so, what the net effect of such variations has been on the time and geographic differences observed in the reported Canadian CHD mortality rates.

In order to compare coding practices between years and provinces, a standard has to be used. In Canada, death certificate coding is performed provincially, but nosology training is done nationally by a member of the Nosology Department from the Health Division in Statistics Canada. This nosologist is also responsible for the adjudication of any death certificate questionable in Canada, and is the resource person for all of the nosologists in Canada. Therefore, this nosologist was accepted as the standard for this study and recoded the samples of death certificates according to the ICD-9.

Depending upon the result of the recoding of a death certificate by the study nosologist, we can define true or false positives and negatives in the original coding as indicated below:

death certificate	original code (410/other)	study recoding (410/other)
true positives	410	410
false positives	410	other
true negatives	other	other
false negatives	other	410

2. SAMPLING STRATEGY

Since the Ninth Revision of the ICD introduced changes in chronic CHD but not in AMI death certificate coding, we decided to focus the study on AMI death certificate coding. In Canada, Nova Scotia is the province with the highest CHD mortality rates, Saskatchewan with the lowest. Also, Nova Scotia and Saskatchewan are the focus of a larger study on CHD, the Nova Scotia Saskatchewan Cardiovascular Study. For these reasons, this study focuses on the same two provinces. Since AMI was introduced in 1969 in the ICD, it was decided to examine death certificates from 1970 so that errors due to the adaptation to a new classification would no longer apply. Also, we decided to examine death certificates from 1984, the last year with complete data available.

A stratified random sampling procedure was employed with the two provinces, Nova Scotia and Saskatchewan, and the two years, 1970 and 1984, representing the four strata.

The samples were selected using the death certificate registration numbers. The sample list of death certificate registration numbers was obtained with a random sample selection computer program. Because of confidentiality of the death certificate, the sampling procedure was performed within the Health Division in Statistics Canada.

Two series of samples were obtained. The first series was obtained to examine the true and false positives rates, and included random samples of death certificates originally coded ICD-9 No. 410. In the first series the nosologist knew that 410 was the code originally assigned. The second series was obtained to examine the true and false negatives rates, and included random samples of all death certificates for each stratum. In the second series, the death certificates were submitted to the study nosologist for recoding without masking the ICD code originally assigned.

In order to examine the effect of the knowledge of the original code upon recoding by the study nosologist, the second series of death certificates were submitted again for recoding six months later, after the ICD code originally assigned was blocked out. The six month interval prevented the nosologist from remembering the code assigned the first time.

3. SAMPLE SIZE

Between 1970 and 1984, age adjusted mortality rates for ICDA codes 410 and 410-414 in Nova-Scotia, Saskatchewan and Canada declined by a minimum of 24% for 410-414 in Saskatchewan for males between 1970 and 1984 and by a maximum of 47% for 410-414 in Nova Scotia for males between 1970 and 1984.

Table 3

Age-adjusted mortality rates for 410 and 410-414
Canada, Nova Scotia and Saskatchewan

MALES	1970	1984	% DECLINE
NOVA-SCOTIA			
410	254.4	133.2	47%
410-4	318.1	211.9	34%
SASKATCHEWAN			
410	169.5	124.9	27%
410-4	240.2	183.5	24%
CANADA			
410	217.5	128.4	41%
410-4	312.3	210.1	33%
FEMALES	1970	1984	%DECLINE
NOVA-SCOTIA			
410	108.3	62.6	42%
410-4	161.7	106.2	34%
SASKATCHEWAN			
410	72.7	49.0	32%
410-4	120.9	80.5	33%
CANADA			
410	89.9	55.9	38%
410-4	157.2	101.7	36%

In order to explain the CHD mortality rate decline between 1970 and 1984, the combination of false positive (FP) and false negative (FN) error rates variation would need to produce an overall effect leading to a 24% decrease in CHD mortality

rates. Since there is no available study on AMI or CHD death certificate coding error rates variation, computations are based on the Canadian estimate error rate of 8% for overall death certificate coding in 1979 (37).

3.1. False Positive

Sample size computation are based on the following premises:

- we are interested in performing pair-wise comparisons between the four strata on the outcome variable, the false positive rate.

- we are also interested in performing several pair-wise comparisons on different combinations of strata.

- we wish to be able to detect a difference of at least five percentage points between the two strata on the outcome, if such a difference exists.

- we assume a type-I error of 0.05, and a type-II error of 0.20.

- we assume a binomial distribution of the outcome variable, with a maximum variance of $\sqrt{p(1-p)}=0.5$.

When testing hypotheses concerning differences between independent population proportions, the detectability of a given effect size, under fixed conditions of type-I error and sample size, will vary depending upon where the proportions fall along the scale between zero and one. However, when the proportions are submitted to an arcsin transformation, equal differences are equally detectable (108).

According to the arcsin transformation tables provided by Cohen (108), assuming a two-sided type-I error of 0.05, a sample size of 400 per stratum gives a power of .81 to detect a difference of 5 percentage points between false positive rates for different strata.

3.2. False Negative

Similar assumptions apply to the false negative rates as the false positive rates. However, because of considerations of time and cost, we were limited to sample of n = 200 death certificates per stratum.

According to tables using the arcsin transformation and provided by Cohen (108), assuming a two-sided type-I error of 0.05, a sample size of 200 per stratum gives a power of .80 to detect a difference of 8 percentage points between the strata false negative rates.

4. DATA COLLECTION

Random samples of death certificates from Saskatchewan and Nova Scotia for the years 1970 and 1984 were obtained from the Health Division of Statistics Canada. In order to avoid any breach of confidentiality, the data obtained were stripped of all personal identification.

The study nosologist recoded the death certificates on a coding sheet (Appendix 18) according to a coding manual. The following variables were examined:

- age and sex

- proportion of D.C. recoded as 410
- distribution of codes used for D.C. not recorded 410
- place of death

The data were entered on an IBM P.C. computer using the DBase III Plus software. The dbase data set was then transferred to a PC SAS dataset for examination and analysis.

CHAPTER FOUR

ANALYSIS AND RESULTS

1. NET EFFECT OF MISCLASSIFICATION

The status of initial coding (e.g. by the province) when compared with a standard (e.g. federal coding) can be displayed as a 2X2 table:

		Study Nosologist positive	Study Nosologist negative	
provincial coding	positive	a	b	a+b
	negative	c	d	c+d
		a+c	b+d	N

(a+b)/N is the provincial estimate of positive rate.
(a+c)/N is the study (standard) estimate of positive rate.
(b+c)/N is the proportion of misclassified positives.
However, given the study nosologist coding as the standard, the net effect of misclassification, i.e. the difference between the study and the provincial rates is:

$$(a+b)/N - (a+c)/N = b-c/N$$

Example: for a province with a population of one million, a 7/1000 death rate, a provincial estimate of 20% deaths due to AMI, and the following distribution of death certificate status after federal recoding:

		federal coding		
		AMI	Other	
provincial coding	AMI	1260	140	1400
	Other	70	5530	5600
		1330	5670	7000

Even if the death certificate misclassification rate is 30/1000, the net effect of misclassification creates a provincial overestimate of 10/1000 deaths due to AMI when compared with the study standard.

2. AMI CODING VARIATION NET EFFECT

The sample size for each of the four strata (years 1970 and 1984, and provinces of Nova Scotia and Saskatchewan) for the first series of death certificates (with AMI as the cause of death assigned by the province) were the same (n=400). Also, the samples sizes for the second series of death certificates (with the cause of death assigned by the province being different from AMI) were equal (n=200). Therefore, in order to compare the net effect of death certificates misclassification on AMI mortality rates between the provinces and the years, it is not necessary to adjust the samples to the population estimates of the proportion of deaths due to AMI. As the samples are the same for each strata the relative rates of false positives and false negatives within each strata can be directly compared amongst the samples drawn.

The goal of the analysis was to determine if systematic variations in coding errors contributed to the differences in

AMI mortality rates by year and by province. Agreements in coding do not contribute to our understanding of errors so the concordant pairs of coding were excluded in the analysis. If the errors were random, the discordant pairs should be equally distributed between the false positive and false negative cells of the table. The McNemar test can be used to determine if the errors in any one table equal numbers of discordant pairs in these two cells (109).

Where there are two or more 2 X 2 tables, the chi square test of association can be used to determine if the distribution of discordant pairs is consistent across the tables (109). This test was used to compare the distributions of discordant pairs by year and by province, as can be seen in Table 4.

Table 4
Distribution of false positives and of false negatives, Nova Scotia and Saskatchewan, 1970 and 1984.

	NOVA SCOTIA		SASKATCHEWAN	
	1970	1984	1970	1984
false positives	9	5	17	3
false negatives	1	1	0	1

$X^2=3.87$, 6df, $p \leq .10$

There were no significant differences. However, as five of the eight cells had expected values less than five, the chi square estimate of the probability of association is not very stable or reliable. Consequently the Fisher's exact test was for pairwise comparisons of discordant pairs amongst the

different combinations of strata. None of the comparisons were statistically significant (table 5), which means that the relative distributions of false positives and false negatives were equal in the 1970 and 1984 samples for Saskatchewan and Nova Scotia.

Table 5
Pairwise comparisons of discordant pairs
Nova Scotia and Saskatchewan, 1970 and 1984

comparing	Fisher's exact test p-value (two tailed)
Saskatchewan 1970 and Saskatchewan 1984	.19
Nova Scotia 1970 and Nova Scotia 1984	1.00
Nova Scotia 1970 and Saskatchewan 1970	.37
Nova Scotia 1984 and Saskatchewan 1984	1.00
Nova Scotia and Saskatchewan	.56
1970 and 1984	.17

By submitting the same samples of death certificates twice to the nosologist, we were able to estimate the nosologist intra-rater agreement: of the 800 death certificates submitted, 19 were discordant (percent agreement = 98.9%; kappa= .93) (table 6).

Table 6
Nosologist inter-rater agreement

		First Coding: AMI	First Coding: NOT AMI	
Second Coding	AMI	142	7	149
	Not AMI	12	639	651
		154	646	800

3 FALSE POSITIVES

3.1. Samples Description

3.1.1. Sex

Examination of samples with regard to the male/female ratios of death from AMI (ICD No.410) are consistent with the data for Canada as a whole.

	Statistics Canada Mortality Data % males	Sample % males (with 95% confidence intervals)
Canada 1970	66.9	66.8 (+- 3.3)
Canada 1984	61.6	59.5 (+- 3.4)
Saskatchewan 1970	69.0	67.4 (+- 4.6)
Saskatchewan 1984	65.5	64.3 (+- 4.7)
Nova Scotia 1970	66.2	66.2 (+- 4.6)
Nova Scotia 1984	59.0	54.7 (+- 4.9)

The observed decrease in the male/female AMI mortality ratio in the sample is similar to the general population trend observed over the same period.

3.1.2. Age

Data examination of samples with regard to age at death from AMI reveals some important differences.

Table 7
Mean Age of Death from AMI
by Province, Year and Sex
(with 95% confidence intervals)

	1970		1984	
	men	women	men	women
SASK	69.0 (1.4)	77.4 (1.5)	71.0 (1.4)	79.4 (1.6)
NS	67.0 (1.3)	74.5 (2.1)	70.0 (1.5)	76.3 (1.7)

As expected, the mean age at death from AMI is higher for females than for males. There is a significant ($p<.001$) difference of 7.7 years in favor of the women (76.9 +/-.9 years) over the men (69.2 +/-.7 years).

Also the mean age at death from AMI increased between 1970 and 1984 for both provinces. It increased significantly by 2.3 years in Saskatchewan (71.7 to 74.0), and by 3.3 years in Nova Scotia (69.5 to 72.8). This is consistent with the increase in life expectancy observed in the general population during the same period of time.

However, a significant ($p=.05$) difference of 1.7 years in mean age at death from AMI between Saskatchewan (72.9 years) and Nova Scotia (71.2 years) was observed. This could reflect a real difference in age distribution between the two provinces, or it could be due to the large samples.

3.1.3. Place of Death

Examination of the frequency distribution of place of death from AMI shows some significant differences.

Table 8
Frequency distribution of place of death from AMI
(with 95% confidence intervals)

	SASKATCHEWAN		NOVA SCOTIA	
Death	1970	1984	1970	1984
within an institution	66.4 (4.7)	71.9 (4.4)	54.9 (4.9)	70.4 (4.5)
outside an institution	26.3 (4.3)	27.6 (4.4)	39.3 (4.8)	23.4 (4.1)
Unknown	7.3 (2.6)	0.5 (0.7)	5.8 (2.3)	6.3 (2.4)

$X^2 = 52.97$, 6df, $p < .001$

Nova Scotia observed a significant ($p < .05$) increase (15.5%) in death from AMI within an institution between 1970 and 1984 (54.9% to 70.4%). Saskatchewan observed a significant decrease in unknown place of death between the years 1970 and 1984. The very low proportion of unknown place of death for Saskatchewan in 1984 remains unexplained since there is no apparent reason for such a dramatic difference.

The difference in proportion of death from AMI observed in an institution between Saskatchewan and Nova Scotia was significant in 1970 (66.4% and 54.9%), but the differences were not significant in 1984.

The mean age at death from AMI varies whether death occurs within an institution (72.7 +/-.7 years) or outside (70.3 +/-1.1 years).

3.2. Univariate Analysis

All of the death certificates in the sample were coded AMI (ICDA 410) as the cause of death. The death certificates recoded with AMI (ICDA 410) as the cause of death were then considered as true positives. Accordingly, the death certificates recoded with a cause of death other than AMI (ICDA 410) were considered as false positives.

The variables Age, Year and Province show some significant differences in the proportions of true and false positives. Examination of the mean age at death shows a significant difference of 4.3 years between true positives (71.9 +/-.6 years) and false positives (76.2 +/-3.3 years).

The proportion of false positives was significantly (p=.002) greater in 1970 (3.28%) than in 1984 (1.01%). The proportion of false positives was significantly (p=.003) greater in Saskatchewan in 1970 (4.3%).

Table 9
Distribution of True and False Positives
Saskatchewan and Nova Scotia, 1970 and 1984

	Saskatchewan		Nova Scotia	
	1970	1984	1970	1984
True positives	379	395	388	393
False positives (percent)	17 (4.3)	3 (.8)	9 (2.3)	5 (1.3)

X^2=13.93, 3 df, p<.003

Inspection of the contribution of each province for each year to the chi square reveals that Saskatchewan contributes 9.04 to the total chi square figure of 13.93. The variables sex and place of death do not show any significant differences in the proportions of true and false positives.

Examination of the distribution of place of death does not show any significant ($p=.09$) difference between true and false positives. Nor are there significant differences in the sex distribution of true and false positives examined either by subgroup of year, province or province by year.

Table 10
Sex Distribution of True and False Positives

	true positives	false positives
Men	977 (97.4%)	26 (2.6%)
Women	578 (98.9%)	7 (1.1%)

$X^2=2.88$, 2 df, $p=.089$

We examined whether the number of underlying and contributing causes of death influenced the rate of false positives

Table 11
Comorbidity distribution of true and false positives

Comorbidity	0	1	2	3	4	5
True positive	346	535	415	188	60	11
False positive	1	9	11	8	3	2
Proportion of false positive	.003	.017	.026	.041	.048	.154

$X^2=18.27$, $p=.00002$

A chi square for trend was used (109), and the trend was significant. Therefore, the error rate increases

significantly with the number of comorbid conditions listed on the death certificate.

3.3. Multivariate Analysis

We examined the samples with the use of a logistic regression model with false positive/true positives as the dependent variable and Year and Province as the independent variables. The results show a significant coefficient for the variable Year. The odds ratio of a false positive death certificate coding in 1984 compared to 1970 is .299 (95% CI: .134 - .665).

Table 12
Logistic regression coefficients
(with Year and Province)

	coefficient	std.error	Z
year (0=1970, 1=1984)	-1.206	.407	-2.96
province (0=SASK. 1=NS)	-.368	.353	-1.04

A model with Province, Year, Sex as categorical independent variable and Age as a continuous variable yields significant predicting values for Year, Sex and Age. None of the interaction terms between Province, Year and Sex was significant.

Table 13
Logistic regression coefficients
(with Year, Province, Sex and Age)

	PROVINCE 0=SASK. 1=NS	YEAR 0=70 1=84	SEX 0=F 1=M	AGE in years
coefficient	-.289	-1.368	1.305	.058
std.error	.357	.419	.408	.016
Z	-.81	-3.27	3.2	3.5
odds ratio	.75	.25	3.68	1.06
95%CI: lower	.37	.11	1.65	1.02
upper	1.50	.57	8.21	1.09

The odds of having a death certificate coded false positive increased with the year 1970, male gender and increasing age.

CHAPTER FIVE

DISCUSSION AND CONCLUSION

1. CHD MORTALITY RATES

CVD and CHD proportional mortality rates increased markedly through the first half of the century (8). This was largely due to important declines in competing causes of death (8). Factors such as evolving medical terminology, and death certificate coding fluctuation concurrently occurred (8). Taking into account these potential source of artifacts, there remained marked increases in CVD and CHD mortality rates through the first half of the twentieth century.

In the late 50s and early 60s, the patterns reversed. In Canada, between 1970 and 1984, CHD mortality rates declined by 33% for the males and by 36% for the females. By the mid 1970s, all age, race and sex groups and all regions had experienced declines in CHD mortality rates (14). However, the differences between provinces between gender, ages, and socioeconomic status remained; the young and those of high socioeconomic status having benefited the most.

Also, there were important differences in CHD mortality rate patterns among the countries in the world. It is difficult to conclude that countries with low mortality rates are still recording an increase, and countries with high mortality rates have already reached the turning point and now are recording a decrease (18).

Also, within some countries (Canada, USA), the geographic distribution of CHD mortality rates differs from the geographic distribution of the rate of decline. This opens the possibility that the factors, which past cumulative experience is most important for the level of CHD mortality, may not be the same as those factors which had the greatest impact on the CHD mortality decline (11,14).

2. CHD MAJOR STUDIES

The Framingham Study assessed the relative risks associated with the main CHD risk factors: age, male gender, hypertension, cigarette smoking, high serum cholesterol levels and obesity. Other studies confirmed the Framingham Study findings to be generalizable to the white middle-aged American men.

The Seven Countries study established that the relative risks associated with CHD risk factors vary in populations with contrasting cultures.

Prospective cohort studies on homogeneous disease-prone sub-populations, and secular changes of risk factors make the assessment of attributable risks and etiologic fractions difficult for larger populations for a particular time.

Nonetheless, repeated findings from all the observational studies in the 1950s and the 1960s consistently pointed towards the same risk factors and comparable strengths of association across populations.

Several studies failed to show positive effects upon populations from interventions designed to reduce CHD risk

factors. The interventions were on strong CHD risk factors but did not account for the "beneficial effect latency" period, or for secular trends of risk factors. Moreover, the relatively short follow-up period favored the cases to come from the subjects who, at entry, were between disease occurrence and disease detection; these subjects, in whom disease may have already occurred, were probably those who would benefit the least from risk factor reduction since presence of risk factors may not be important predictors of disease outcome.

Therefore, in the light of these conflicting findings, one can question whether the CHD mortality rate decline reflects a decline in incidence rates secondary to risk factor reduction, a reduction in case fatality rates or are simply due to artifacts.

3. INCIDENCE RATE DECLINE

A reduction in risk factor levels in the population at large will lead to reduced incidence rates of disease. However, most CHD cases in the population occur among the vast proportion of low risk subjects rather than the few high risk ones. This supports large population based interventions (110). What evidence is there of CHD risk factor reduction in the population?

3.1. Age

Since mortality rates are age standardized, the aging of the population should not affect CHD mortality rates. However, cohort effects can influence age adjusted mortality rates. It

can be argued that a fifty year old male in 1970 would have a better health status than his counterpart in 1950 because of better lifestyle and higher socioeconomic status and better access to care. The cohort effect would then tend to reduce the CHD relative risk of age.

3.2. Gender

There is no indication of change in gender proportion that could influence CHD mortality rates.

3.3. Fat Consumption and Cholesterol

Undoubtedly there are problems with the validity of measurement of dietary intake over the last 20 years. However, food consumption data from the US Department of Agriculture shows that per capita consumption of whole milk has decreased by 25%, butter by 33%, and eggs by 15%. As well, per capita consumption of vegetables and fruits has increased by 75% (73).

Data based on the Framingham study show that daily cholesterol intake decreased from 600mg to 800mg in the early 50s to less than 500mg in the early 1970s for a middle aged man (26,73). During the same period, the plasma cholesterol levels decreased from 225mg/100ml to 205mg/100ml (73). Even when taking into account possible changes due to measurement differences, the overall cholesterol level decreased by 5% between the 1950s and the 1970s (73).

A longitudinal study in Minneapolis and other studies (Oslo study, Western Electric study and MRFIT) showed similar results. Moreover, the LRCCPPT shows that a 1% reduction in

cholesterol (mainly Total and LDL) results in a 2% reduction of AMI and sudden death incidence (49). Attempts at predicting CHD mortality decline from serum cholesterol reduction vary from a 4.3% CHD mortality rate decline for a 5mg/dl cholesterol reduction (111), to a 19% CHD mortality decrease for a 8% cholesterol decrease (49). However, these estimates are based on the absolute initial values of the populations under study. One can then question how these estimates apply to the general population or to populations from other countries.

3.4. Cigarette Smoking

In December 1983, 5.8 millions Canadians over 15 years old (31%) were regular cigarette smokers (34% of men and 28.3% of women). These proportions reflect sharp decreases from 1970, particularly for men: 9.5 percentage points for the adult population (14.9 percentage points for males and 4.1 percentage points for females). This decline is consistent for all ages and both sexes, although to a varying degree. There is evidence that regular cigarette smokers are smoking more cigarettes per day. Between 1970 and 1983, the percentage of persons who smoked 25 or more cigarettes per day increased by 31% for males and by 57% for females.

There is no doubt that cigarette smoking is a risk factor for CHD and that there is a dose-response relationship. However there are questions about the shape of the dose-response curve (exponential, linear or logarithmic) (112). The estimated decline in CHD mortality rate due to smoking reduction varies from 14% to 47% of the overall decline

according to the different studies (112). There is some uncertainty as to how long it takes for an ex-smoker to reach the never-smoked risk level. Also, there is some discrepancy between total sales of cigarettes and reported prevalence of smoking in surveys (113).

3.5. Weight reduction and exercise

There is some evidence which establishes the beneficial effect of exercise and weight control in reducing CHD risk (114). However, despite apparent changes in exercise habits (114), the average height corrected weight of Americans did not change between 1960 and 1974 (95). Therefore it is very difficult to extrapolate the data on physical activity from studies to population and it is thus difficult to assess the impact of physical activity on CHD mortality decline (114).

3.6. Hypertension

Even if the potential value of HBP treatment to reduce CHD mortality risk is substantial, there is conflicting evidence of its reality. Data from the U.S. National Health Survey indicate no reduction in HBP prevalence between 1960 (18.2%) and 1971 (18.1%) (95). However, data from studies such as the Framingham study and the Hypertension Detection and Follow up Program indicate a two to four fold increase in the proportion of HBP patients treated effectively between 1960 and 1970. Therefore it is difficult to estimate the impact of HBP treatment on CHD mortality decline. A comparison of life style, risk factors, and CHD management changes in 11 countries

seems to favor improvement in lifestyle and in the risk factor situation supporting primary prevention in a major role for CHD mortality rates declines (4). .

Therefore, there is evidence that risk factors reductions had a role in CHD mortality decline (115). However, if there is a threshold to the beneficial effect of risk factor modification, this would influence the population based strategies where risk factor modification would be minimal for the majority of the population (116). General CHD management has evidently improved, but the question is to what extent that improvement contributed to CHD mortality decline.

4. REDUCTION OF CASE FATALITY

It seems likely that the combination of CCUs, surgical treatment, prehospitalization care and medical treatment is partially responsible for the observed CHD mortality rate decline. Gillum et al. observed a reduction of 8% for men and 26% for women, 30 to 74 years old in hospital mortality rates for AMI between 1970 and 1980 (21).

Similarly, in Goteborg (Sweden) a declining trend was noted between 1968 and 1977 in mortality rates after AMI. The differences were not statistically significant but samples were small (117).

In a large employed population, Pell et al (118) found that beginning in 1969 the 24 hour case fatality rate declined moderately and there was a sharp drop in the 30-day case fatality rate for those who survived 24 hours after onset of attack (118).

Weinblatt et al. examined the post-AMI prognosis of men enrolled in the Health Insurance Plan in the 1960s and 1970s. They showed no difference in long term prognosis between the two decades (119).

WHO data from seventeen centers does not show any mortality rate difference for secondary prevention after AMI (120). Altogether, about 40% of the CHD mortality decline could be attributed to medical care (secondary prevention) distributed as CCU 13.5%, HBP treatment 18% (?), long term medical treatment of CHD 10%, CAB surgery 4%. However, it is difficult to evaluate if the reduction in case fatality is directly due to better management or to reduced severity of the disease as a consequence of risk factor reduction.

However, better knowledge of the disease, and better diagnostic methods have led to decision-making, diagnostic and coding changes.

5. DIAGNOSTIC AND CODING ARTIFACT

It is possible that secular trends in disease diagnosis, death certification and coding practices have affected CHD mortality rates.

Secular changes in diagnostic practices have occurred following increases in knowledge on the natural history of the disease, increased availability of evolving diagnostic procedures, increased accessibility to care and increased expectations from the populations. Several attempts have been made towards diagnostic validation (Cardiology Surveillance Study, Monica Project, Nova Scotia Saskatchewan Cardiovascular

Study). The false positive rate has been as high as 39% (103). One can imagine that better knowledge and diagnostic procedures would reduce the false positive rates, therefore artificially reduce CHD mortality rates.

Some death certification factors would favor artificial increases in CHD mortality rates: death certification tends to over-report CVD when compared to autopsy report (100); over-reporting of CVD also increases with age particularly over 75 years of age, and the population is aging. Conversely the increased proportion of death within institutions would favor better knowledge of the individual disease process leading to death; this would favor a decrease in the over-reporting tendency.

Death certificate coding practices have undergone secular changes also. The last revision, the Ninth Revision of the International Classification of Diseases, introduced in Canada in 1979, produced an artificial reduction in chronic CHD mortality rates.

If the decline was a coding artifact, there likely would have been a shift from CHD to other cardiovascular diseases. However, mortality rates for other CVD categories declined as well: rheumatic heart disease (ICDA 390-398) by 34.7%, hypertensive heart disease (ICDA 400 to 404) by 48.9% and cerebrovascular disease (ICDA 400 to 404) by 27.9%. Together with CHD, these categories represent 90% of all CVD mortality. Moreover, the mortality rate from all CVD declined by 21.4%.

Thus the CHD decline cannot be explained solely by a coding shift to other CVD.

It cannot be explained by a coding shift to another cause of death either since mortality rates for most other causes of death declined as well, the major exception being the increase of cancers. A coding shift from CHD to malignant neoplasms would be hard to imagine (121).

This study shows that for AMI death certificate coding the error rates do not vary significantly between the years 1970 and 1984. Therefore, AMI death certificate coding practice variation cannot explain, even partially, the CHD mortality rate decline observed during that period of time.

Also the death certificate coding error rates do not differ significantly between the provinces of Nova Scotia and Saskatchewan for either year, 1970 or 1984. Therefore, death certificate coding error rates cannot explain these two provinces CHD mortality rate differences.

It is interesting to notice that death certificate coding error rates increase significantly with age. This is similar to the findings observed for error rates in diagnosis and death certificate accuracy.

Also death certificate coding error rates increase significantly with the number of comorbid conditions noted on the death certificate.

6. CONCLUSION

The CHD mortality rate decline observed in Canada over the last quarter of the century is probably real. There is little doubt the reduction of CHD risk factors in the population leads to reduction in incidence rates. The geographic and chronologic pattern of onset of the decline in CHD mortality rates appear to be more similar to other patterns of social changes (diet, smoking) and shifts in productive economic activities than to diffusion of medical care (11).

Individuals have benefited from reducing their risk factors and from improved CHD management. However, the impact of CHD management on CHD mortality rates is difficult to assess at a population level.

Diagnostic and death certification inaccuracies may have lead to artificial reductions in CHD mortality rates. However, the lack noticeable shifts within the CVD category or with another category makes it difficult for the diagnostic and death certification inaccuracies to explain an important part of the CHD mortality rates decline.

This study shows that death certificate coding variation cannot explain, even partially, CHD mortality rates decline. The study also shows that death certificate coding error rates increase with age and the number of comorbidity expressed on the death certificate.

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APPENDIX I

Age Standardized Mortality Rates, of 1984, By Province, Ages 25-74

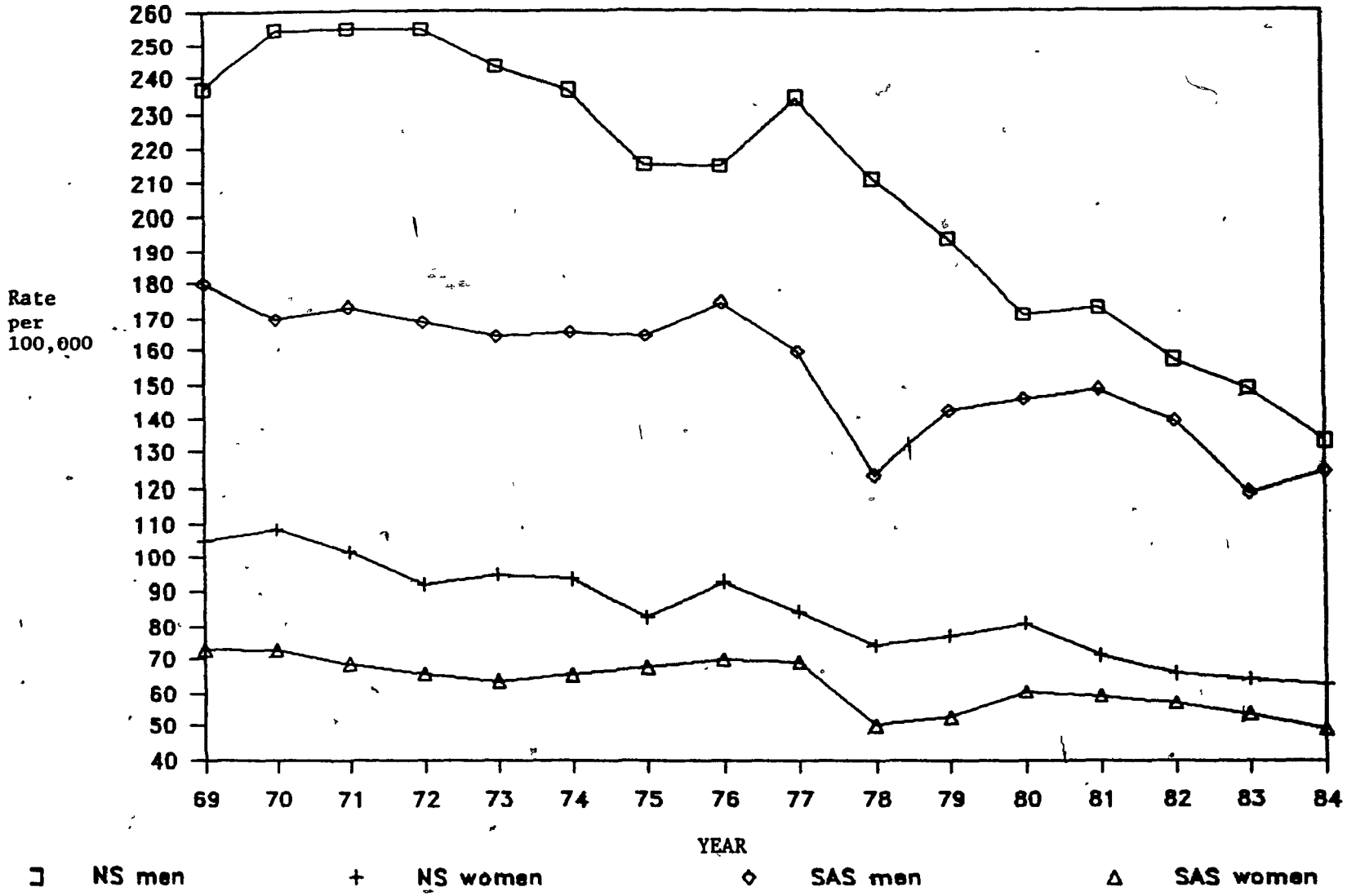
		B.C.	ALTA	SASK.	MAN.	ONT.	QUE	NB	NS	PEI	NFLD
Ischemic Heart	M	207.8	203.5	214.3	229.1	252.9	259.8	240.5	260.0	267.6 +	270.3 *
Disease	F	64.8	64.7	57.8	78.8	87.2	89.7	104.3 *	85.2	65.0	100.8 +
Cerebrovascular	M	30.0	36.2	32.2	36.5	35.8	41.8 *	34.9	34.7	31.1	39.9 +
Disease	F	23.8	24.9	23.0	25.1	24.8	25.8 +	28.6 *	23.0	22.1	23.4
Cancer of Trachea/											
Bronchus/Lung	M	60.2	70.2	66.8	76.9	90.6	117.4 +	117.9 *	96.0	107.2	85.9
and Other	F	31.2	27.4	23.1	30.9	32.4 +	28.5	22.8	37.4 *	17.5	17.7
Breast Cancer	F	36.2	34.3	32.9	39.8	43.4 +	42.4	35.4	39.7	45.2 *	36.9
Diabetes Mellitus	M	8.1	9.7	7.4	15.0	11.4	16.1	16.5 +	21.4	19.3 *	14.1
	F	6.7	5.7	7.0	10.9	9.1	11.4 +	10.3	10.4	6.6	15.1*
Chronic Bronchitis,											
Emphysema and	M	23.3	28.7	24.0	18.4	24.7	33.3 *	33.2 +	28.9	25.6	43.7
Asthma	F	11.4	9.7	8.9	9.5	9.1	9.7	11.7 +	13.9 *	8.5	8.2
Cirrhosis of Liver	M	17.1	25.5 *	17.5	17.1	20.3	20.4 +	16.2	14.1	6.7	7.4
	F	8.1	11.0 +	9.6	11.2 *	8.9	7.1	5.7	6.0	6.1	3.2
Kidney Disease	M	4.5	3.6	5.6	4.1	5.7	7.4 *	4.3	5.0	4.9	6.9 +
	F	3.8	4.1	4.5 +	3.5	3.9	3.8	3.3	5.1 *	1.9	3.6
MVT Accidents	M	20.4	27.9	35.0 *	14.4	16.2	23.4	28.5	19.3	33.1 +	13.1
	F	11.0	11.7	11.3	6.2	7.3	6.6	12.0 +	11.6	16.7 *	3.1
Suicide	M	26.4	35.4 *	28.9	20.7	23.4	32.3 +	28.2	24.9	30.0	14.0
	F	7.5	13.5 *	6.3	9.1	9.6	9.7 +	4.0	2.8	7.1	1.5

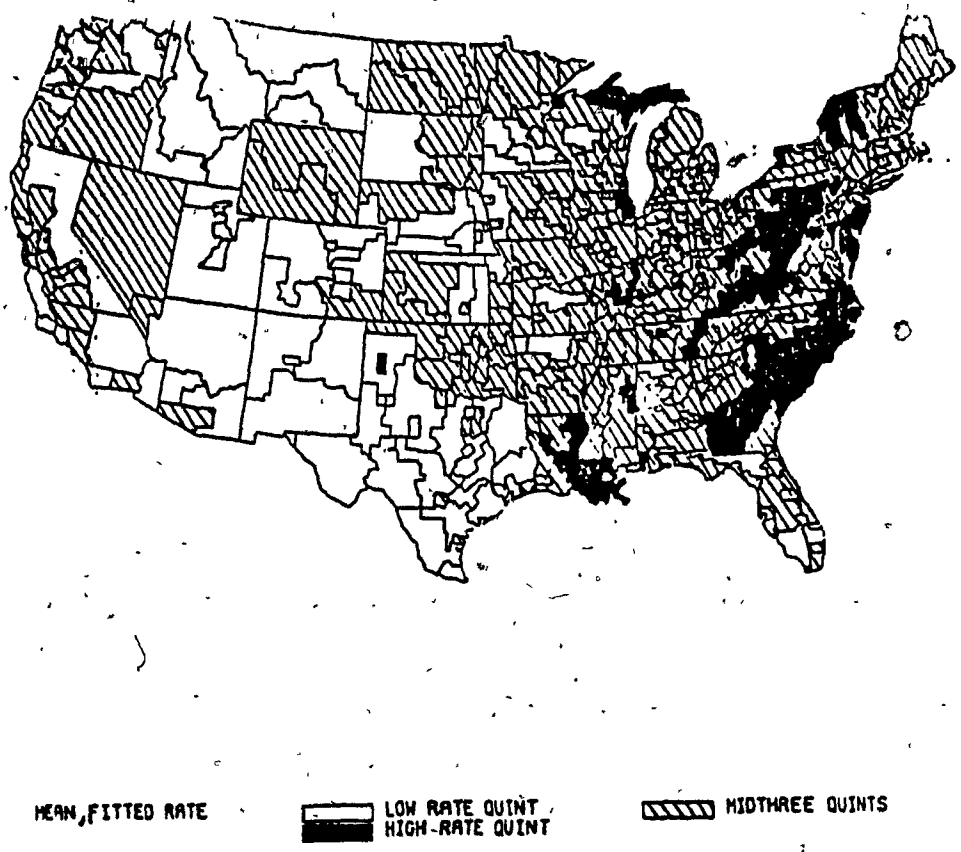
* highest rate among provinces
\+ second highest rate among provinces

APPENDIX 2

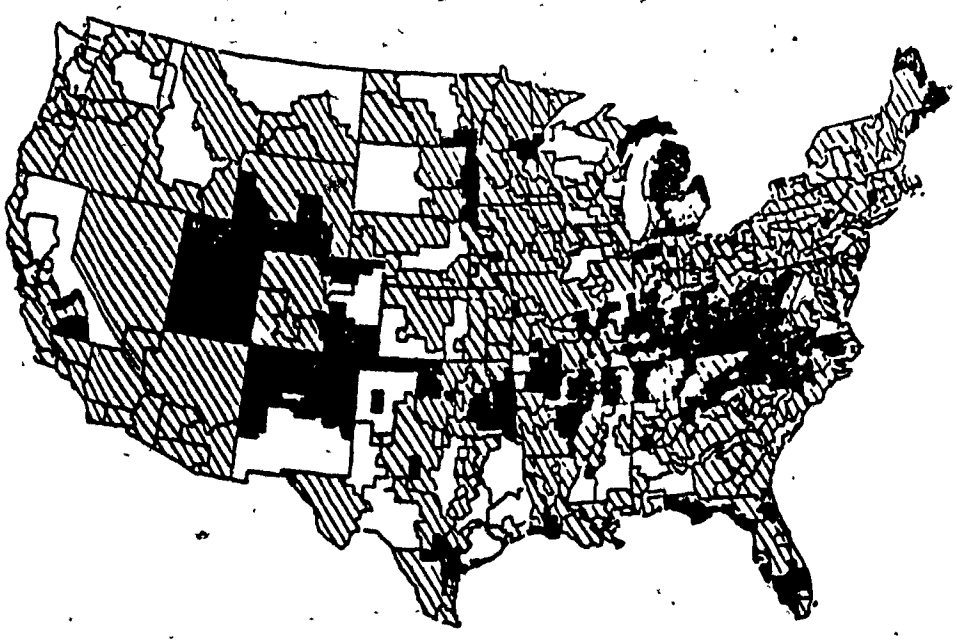
AMI mortality rates NS SAS 1969–84

males and females, ICD No.410



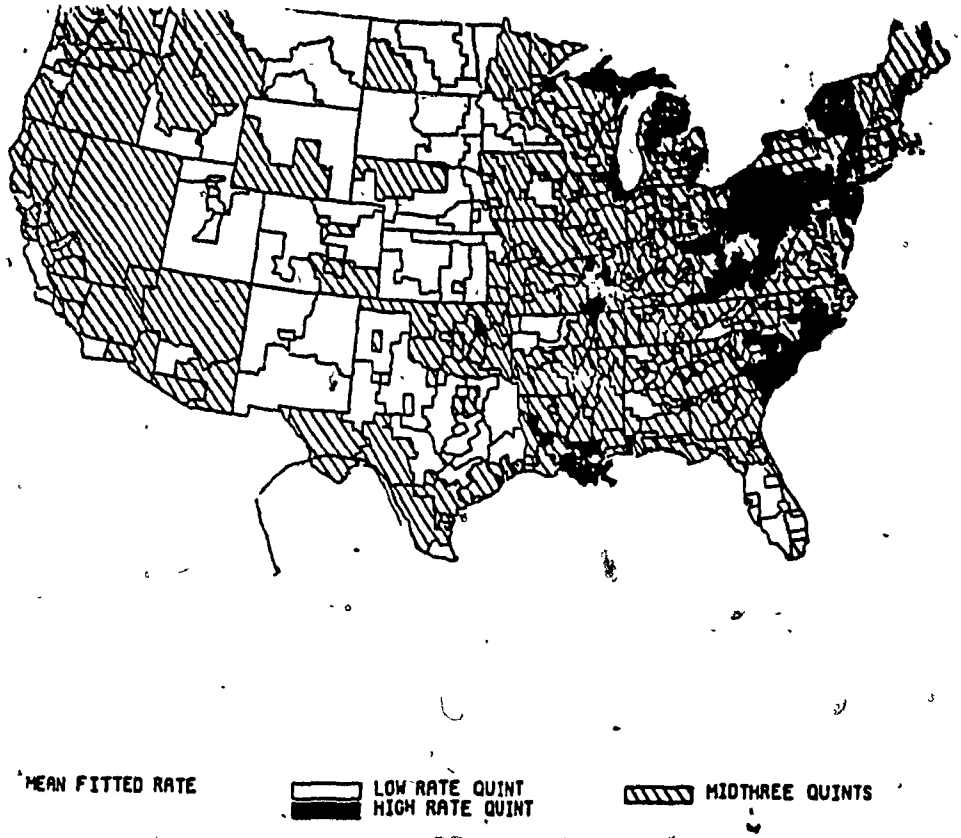


Mean fitted mortality rates, 1968–1978, ischemic heart disease, white males, aged 35–74 years, United States, by state economic area.

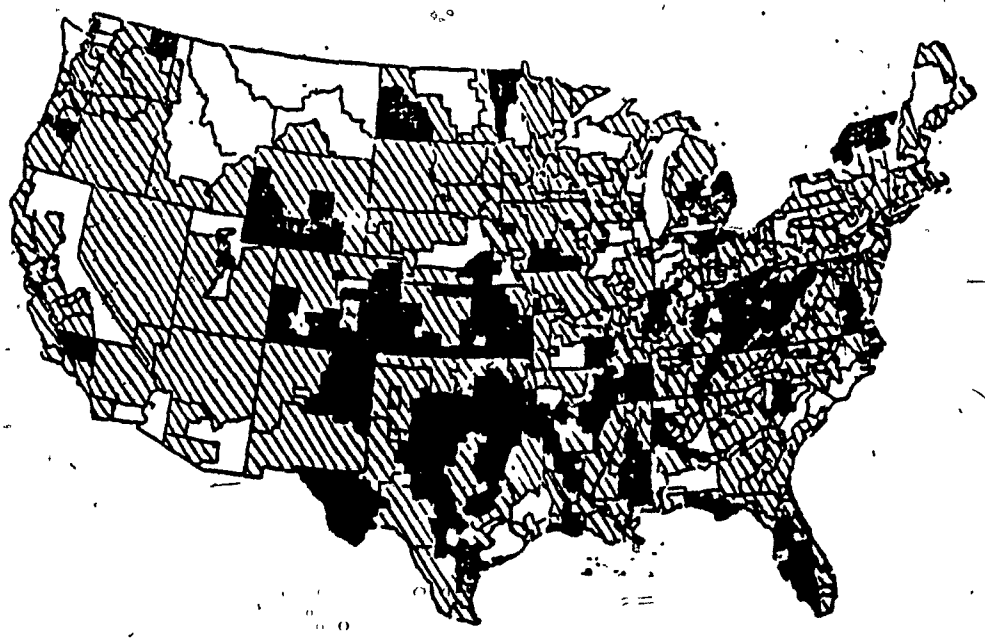


Estimated per cent change in ischemic heart disease mortality rates, 1968–1978, white males aged 35–74 years, United States, by state economic area.

APPENDIX 4

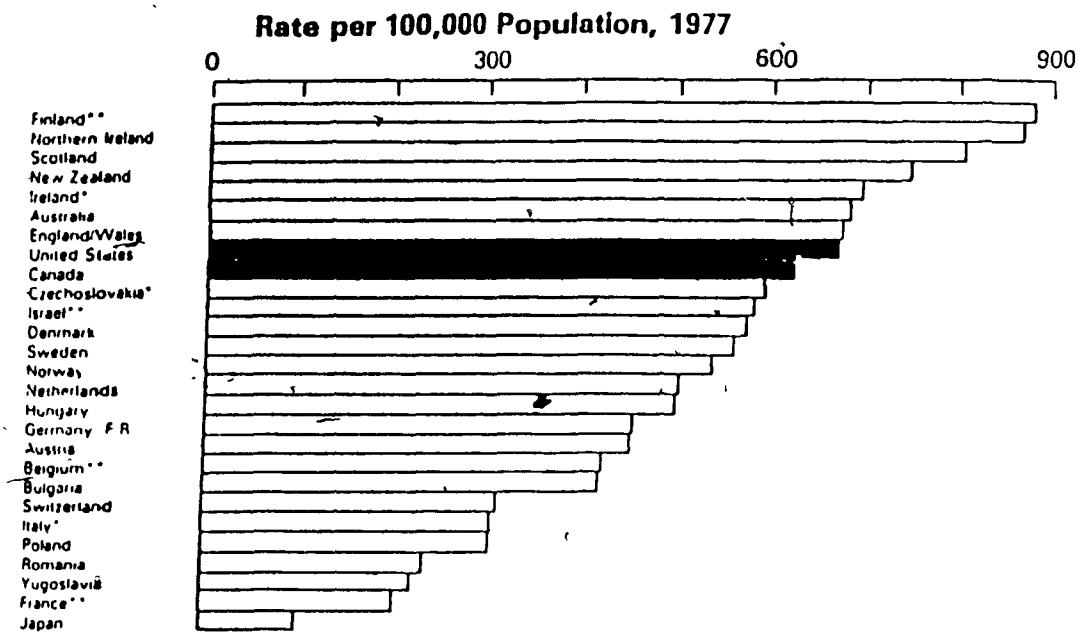


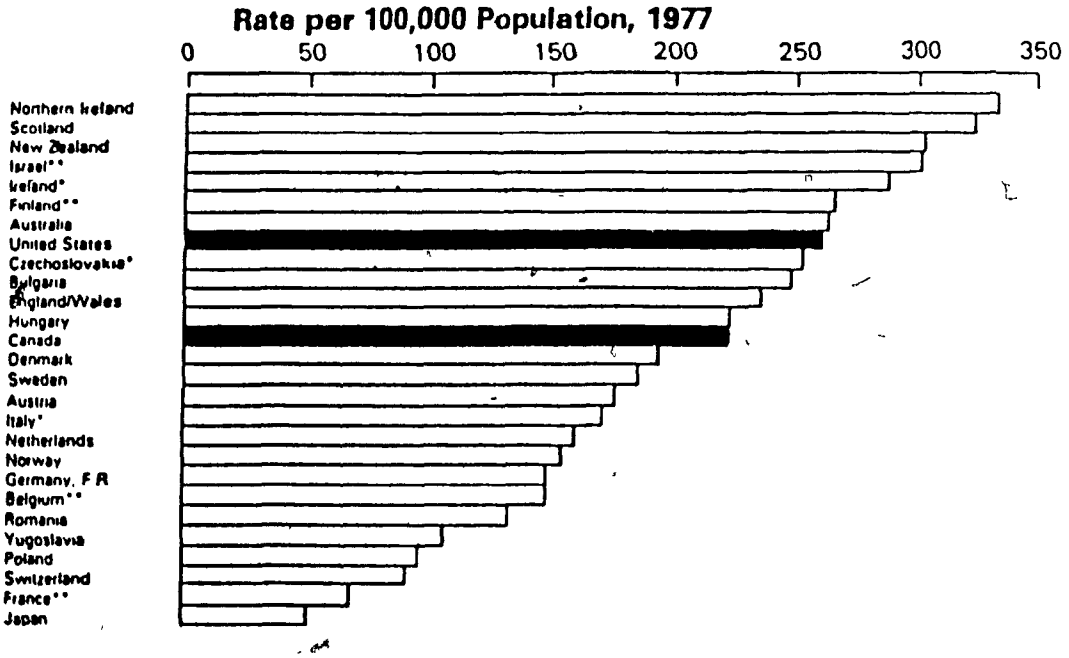
Mean fitted mortality rates, 1968–1978, ischemic heart disease, white females aged 35–74 years, United States, by state economic area.



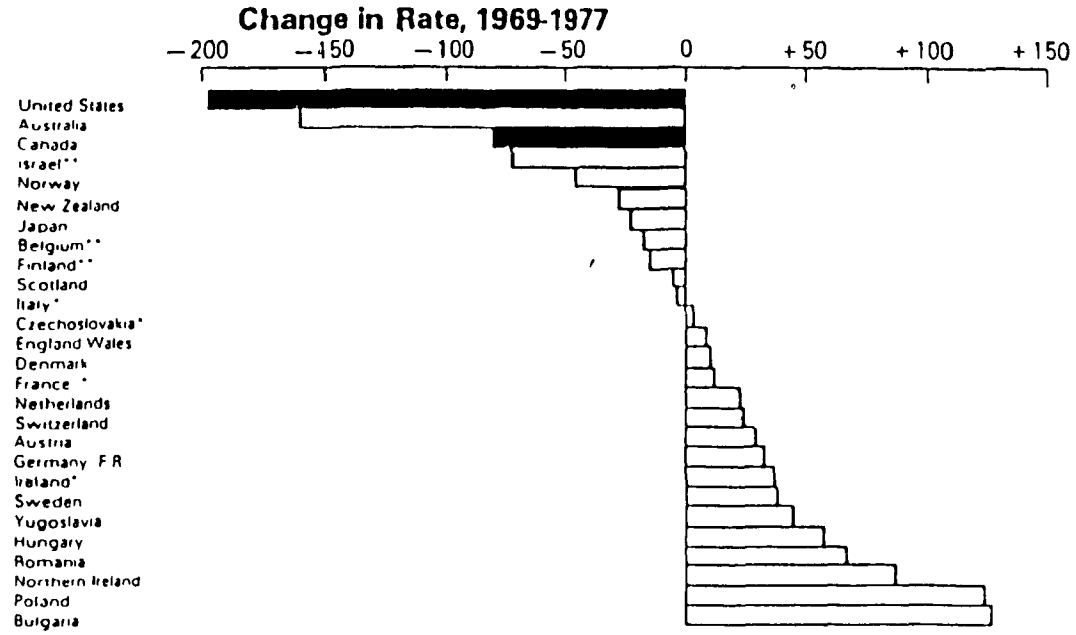
Estimated per cent change in ischemic heart disease mortality rates, 1968–1978, white females aged 35–74 years, United States, by state economic area.

APPENDIX 5

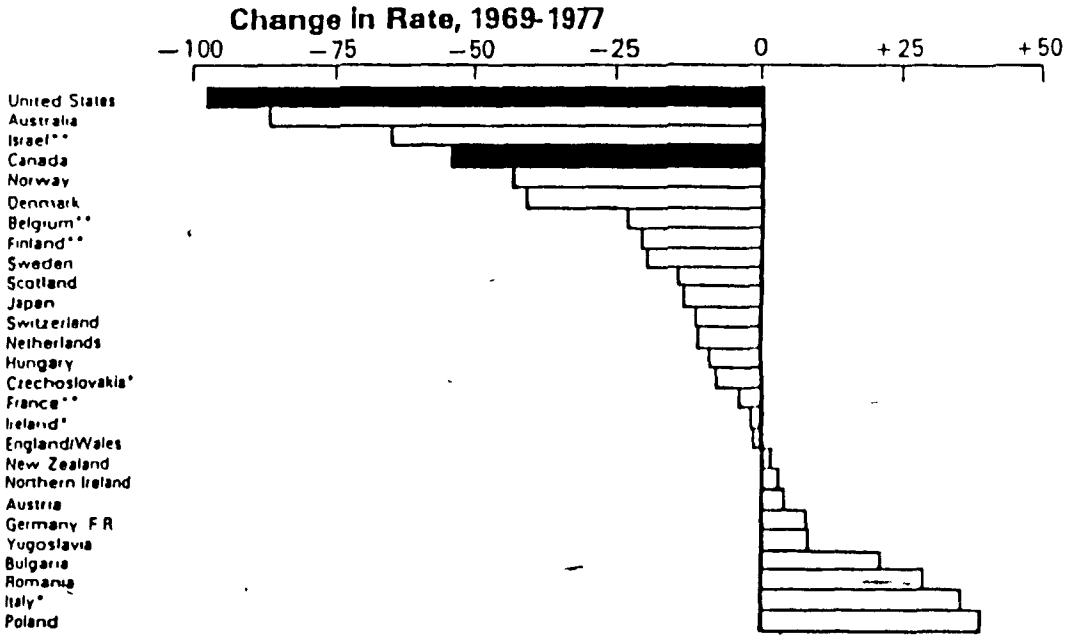




Death rate for coronary heart disease by country, 1977 for men (TOP) and women (**BOTTOM**) 35 to 74 years of age.



*1975 data
**1976 data
Source Prepared by NHLBI data from the World Health Organization



*1975 data
**1976 data
Source Prepared by NHLBI, data from the World Health Organization.

Change in death rate for coronary heart disease by country, 1969 to 1977, for men (TOP) and for women (BOTTOM) 35 to 74 years of age.

APPENDIX 7

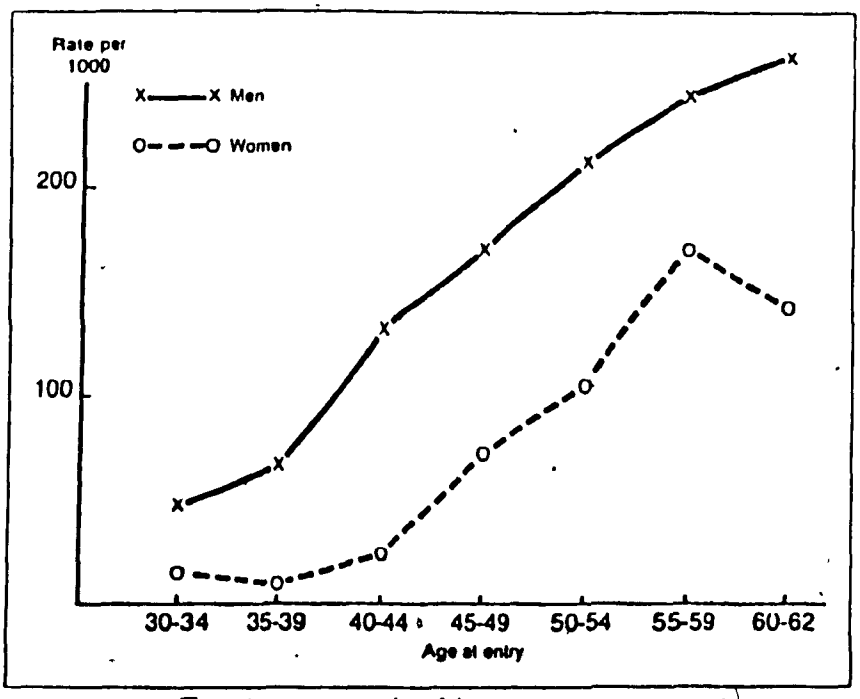
GROUPS OF COUNTRIES LISTED ACCORDING TO THE TRENDS OF THE ANNUAL CHANGE (%) OF MORTALITY FROM ISCHAEMIC HEART DISEASE FOR THE 40-69 YEAR AGE GROUPS IN 1968-1977*

Change	Males		Females	
Decrease —	Australia	—	Australia — Australie	—
	Belgium	—	Belgium — Belgique	—
	Canada	—	Finland — Finlande	—
	Finland	—	France	—
	Israel	—	Israel — Israël	— —
	Japan	—	Italy — Italie	—
	New Zealand	—	Japan — Japon	— —
	Norway	—	New Zealand — Nouvelle-Zélande	—
	United States of America	— —	Switzerland — Suisse	— —
			United States of America — Etats-Unis d'Amérique	— —
Increase —	Bulgaria	+ + +	Bulgaria — Bulgarie	+
	Denmark	+	Hungary — Hongrie	+
	France	+	Poland — Pologne	+ + +
	Ireland	+	Romania — Roumanie	+ +
	Hungary	+	Sweden — Suède	+
	Poland	+ + +	UK: England and Wales — R-U: Angleterre et Galles	+
	Romania	+ +	Yugoslavia — Yougoslavie	+ +
	Sweden	+		
	UK Northern Ireland	+		
	Yugoslavia	+ + +		
No change —	Austria		Austria	
	Czechoslovakia		Canada	
	Germany, Federal Republic of		Czechoslovakia	
			Denmark	
	Netherlands		Germany, Federal Republic of	
	Italy			
	Switzerland		Netherlands	
	UK England and Wales		Ireland	
			Norway	
	UK Scotland		UK: Northern Ireland	
			UK Scotland	

* Symbols + and — represent degrees of percentage increase or decrease per year respectively as follows —

— — 3% 4.9%	+ + + >5%
— 1%-2.9%	+ + 3%-4.9%
	+ 1%-2.9%

APPENDIX 8



Fourteen-year incidence of coronary heart disease (all clinical manifestations) according to age and sex.

APPENDIX 9

Risk of mortality according to cigarette habit (men 45 to 74 years, Framingham Study, 20-year follow-up)

Cigarettes per day	Average annual incidence per 1000 (age-adjusted)			
	Cardiovascular mortality	Sudden death	Coronary disease mortality	Overall mortality
None	7.0	1.3	2.4	12.0
< 20	8.4	1.7	3.1	11.8
20	10.2	2.3	4.0	18.2
> 20	12.4	3.1	5.2	22.4
t value	3.80	2.66	3.11	5.47
Risk ratio (> 20/none)	1.77	2.38	2.17	1.87

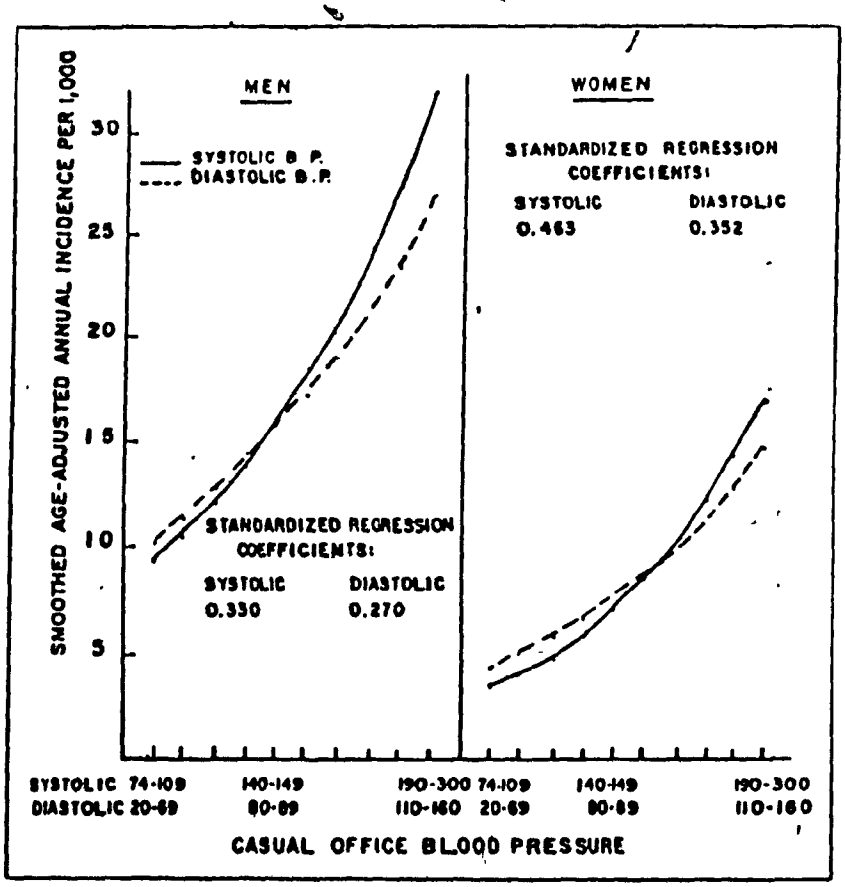
APPENDIX 10

	Oral contraceptive death rate per 100,000	
Age (yrs)	*Alone*	*Plus > 15 cig's/day*
30-34	2	16
35-39	4	23
40-44	7	83

Cig's = cigarettes.
Source: Andruth K. Jain, Population Council.

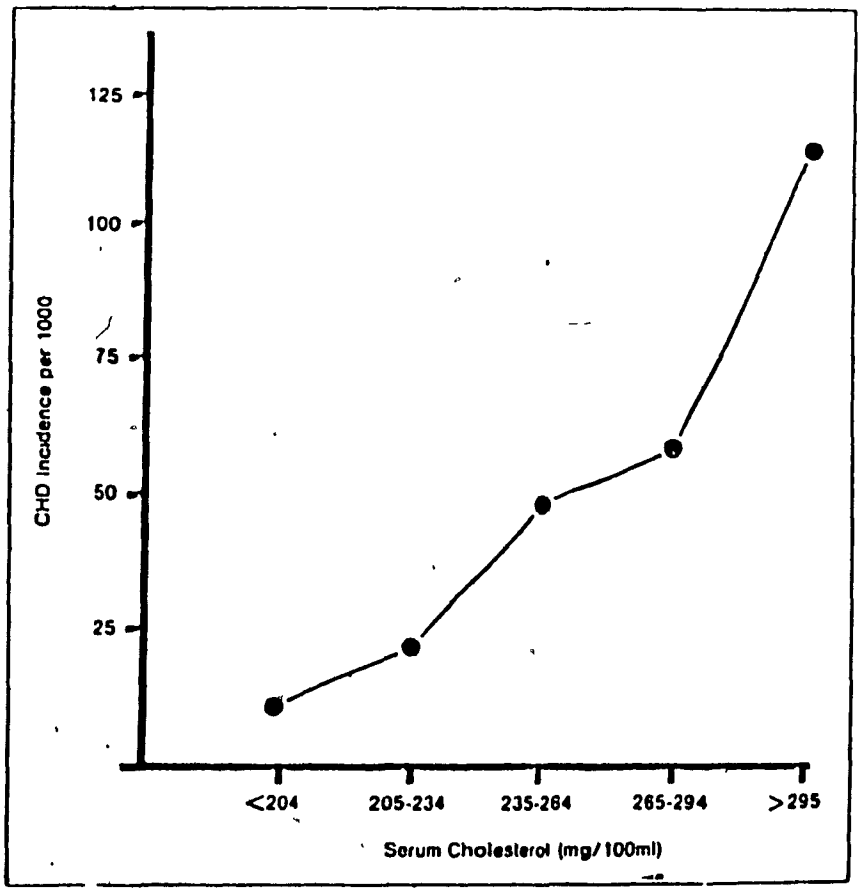
Death rates for users of oral contraceptives according to cigarette smoking status

APPENDIX 11



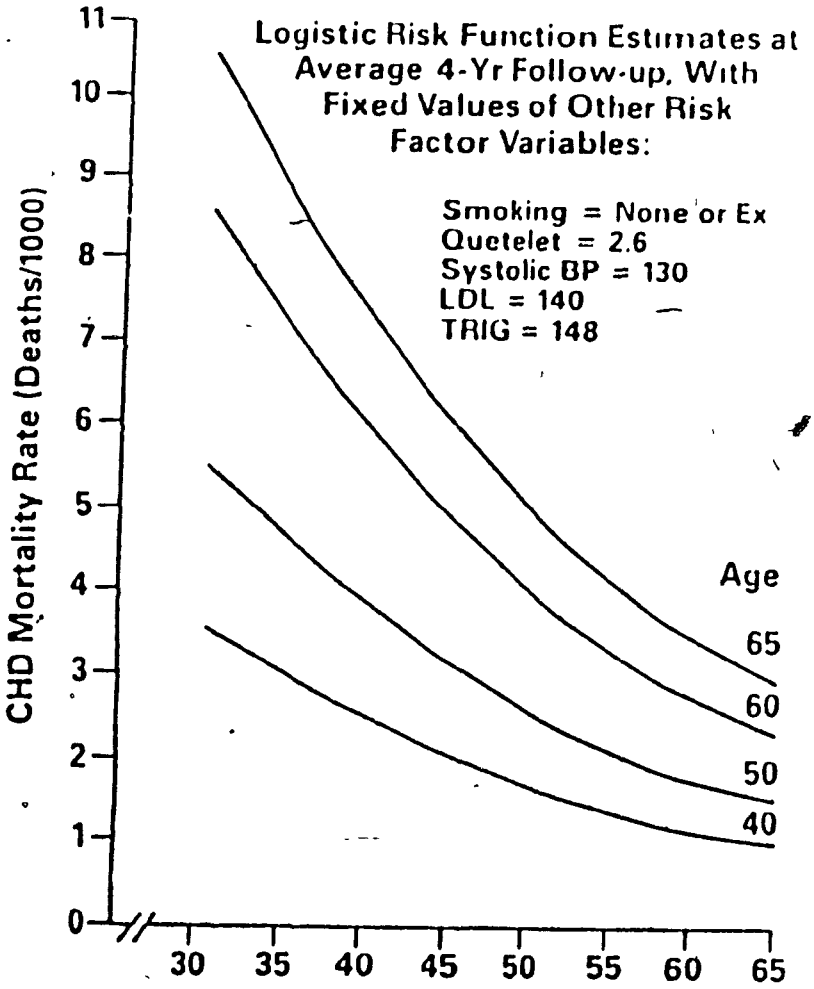
Incidence of coronary heart disease according to systolic versus diastolic blood pressure in men and women aged 45 to 74 years; Framingham study, 20-year follow-up.

APPENDIX 12



Risk of coronary heart disease over six years in men aged 30 to 49 years, according to serum cholesterol levels.

APPENDIX 13



Coronary heart disease mortality rates by level of high-density lipoprotein (HDL) cholesterol in United States white males. From the Lipid Research Clinics population. LDL = low-density lipoprotein; TRIG = triglycerides.

FORM 6

PROVINCE OF
NOVA SCOTIA
(Canada)
Office of the Registrar General

REGISTRATION OF
DEATH

Registration No (Department use only)

THIS IS A PERMANENT LEGAL RECORD
TYPE OR PRINT PLAINLY AND COMPLETE ALL ITEMS

This record must be completed and filed with the Division Registrar and burial permit obtained before burial or other disposal takes place.

NAME OF DECEASED
1. Surname of deceased (print or type) | All given names (in order) (print or type) | 2 SEX | Social Insurance Number (if available)

PLACE OF DEATH
3. Name of hospital or institution (otherwise give exact location where death occurred) | City, town, village or other place (by name) | County

USUAL RESIDENCE
4. Complete address. If rural give exact location (not Post Office or Rural Route address) | City, town, village or other place (by name) | County | Province (or country)

MARITAL STATUS
5. Single, married, widowed or divorced (specify) | 6. If married, widowed, or divorced, give full name of husband or full maiden name of wife

OCCUPATION
7. Kind of work done during most of working life
8. Kind of business or industry in which worked

BIRTHDATE
9. Month (by name), day, year of birth

AGE
10. Age (years) | (Months) If under 1 year | (Days) If under 1 day | (Hours) | (Minutes)

BIRTHPLACE
11. City or place | Province (or country) of birth

FATHER
12. Surname and given names of father (print or type)
13. BIRTHPLACE – City or place | Province (or country)

MOTHER
14. Maiden surname and given names of mother (print or type)
15. BIRTHPLACE – City or place | Province (or country)

SIGNATURE OF INFORMANT
16. Signature of informant
17. Postal address of informant
18. Relationship to deceased | 19. Date signed (month day year)

DISPOSITION
20. Burial, cremation or other disposition (specify) | 21. Date of burial or disposition Month (by name) day year
22. Name and address of cemetery, crematorium or place of disposition

FUNERAL DIRECTOR
23. Name and address of funeral director or firm

SPECIMEN

MEDICAL CERTIFICATE OF DEATH

24. DATE OF DEATH Month (by name) day year | Approx. interval between onset & death

25. CAUSE OF DEATH
Part I
Immediate cause of death (a)
due to or as a consequence of
Antecedent causes, if any, giving rise to the immediate cause (a) above, stating the underlying cause last (b)
due to or as a consequence of
(c)
Part II
Other significant conditions contributing to death but not causally related to the immediate cause (a) above

26. Autopsy? Yes [ ] No [ ]
27. Does the cause of death stated above take account of autopsy findings? Yes [ ] No [ ]
28. May further information relating to the cause of death be available later? Yes [ ] No [ ]
29. If accident, suicide, homicide or undetermined (specify)
30. Place (injury) (e.g. home, farm, highway, etc.)
31. Date of injury
32. How did injury occur? (describe circumstances)
33. I certify that the above named person died on the date and from the causes stated herein. Signature (attending physician or medical examiner)
34. Designation: Last attending physician [ ] Medical examiner [ ] Date certified Month (by name) day year
35. Name of last attending physician or medical examiner (print or type) | Address

For Office Use Only

CERTIFICATION OF DIVISION REGISTRAR
I certify this return was made to me
this day of
Signature

V.S.
orm 3

SASKATCHEWAN
DEPARTMENT OF HEALTH
Division of Vital Statistics

REGISTRATION OF
DEATH

Registration No. Department use only)

SPECIMEN

NAME OF DECEASED	1. Surname *(print or type)* Given names in full *(print or type)* / 2 SEX
PLACE OF DEATH	3 Name of hospital or institution *(otherwise give exact location where death occurred)*
	City, town, village, or other place *(by name)* If rural give sec., tp., rge., and mer
USUAL RESIDENCE	4. Full street address — or, if rural give sec., twp., range, and meridian
	City, town, village, or other place *(by name)* / Province *(or country)*
MARITAL STATUS	5 Single, married, widowed, or divorced *(Specify)* / 6 If married, widowed, or divorced, give full name of husband or full maiden name of wife
OCCUPATION	7 Kind of work done during most of working life / 8 Kind o business or industry in which worked
BIRTHDATE	9 Month *(by name)*, day, year of birth / 10 AGE (years) / *(Months)* If under 1 year / *(Days)* / *(Hours)* If under 1 day / *(Minutes)*
BIRTHPLACE	11 City or place *(if known)* / Province *(or country)* of birth
INDIAN ONLY	12 Name of Band / Treaty No
FATHER	13 Surname and given names of father *(print or type)* / 14. BIRTHPLACE — Place *(if known)* Province *(or country)*
MOTHER	15 Maiden surname and given names of mother *(print or ty* / BIRTHPLACE — Place *(if known)* Province (or country)
SIGNATURE OF INFORMANT	17 Signature of informant X / 18 Relationship to deceased
	19 Address of informant / 20 Date signed — Month, day, year
DISPOSITION	21 Burial, cremation or other disposition *(specify)* / Date of burial or disposition (month, day, year)
	23 Name and address of cemetery, crematorium or pla
FUNERAL DIRECTOR	24 Name and address of funeral director *(or person in* *a) (print or type)*

MEDICAL CERTI OF DEATH

DATE	25 Month *(by name)*, day, year of death

A PERMANENT LEGAL RECORD
E PLAINLY AND COMPLETE ALL ITEMS
ol requirements under the Vital Statistics Act)

THIS IS A PERMA

TYPE OR WRITE PLAINL

(See reverse for legal requirer

DIRECTOR — [redacted] (print or type)

MEDICAL CERTI[redacted] OF DEATH

DATE OF DEATH

25 Month (by name), day, year of death [redacted]

Approx. interval between onset & death

CAUSE OF DEATH

26

Part I

Immediate cause of death — (a) [redacted]

due to, or as a consequence of

Antecedent causes, if any, giving rise to the immediate cause (a) above, stating the underlying cause last — (b)

due to, or as a consequence of

(c)

Part II

Other significant conditions contributing to the death but not causally related to the immediate cause (a) above

AUTOPSY PARTICULARS

27 Autopsy being held? Yes ☐ No ☐

28. Does the cause of death stated above take account of autopsy findings? Yes ☐ No ☐

29. May further information relating to the cause of death be available later? Yes ☐ No ☐

ACCIDENT OR VIOLENCE *(If applicable)*

30. If accident, suicide, homicide or undetermined (specify)

31. Place of injury (e.g. home, farm, highway, etc.)

32. Date of injury (Month (by name), day, year)

33. How did injury occur? (describe circumstances)

OTHER MEDICAL PARTICULARS

34 If a woman, did death occur either during pregnancy or within 90 days following termination of pregnancy? Yes ☐ No ☐

35 Was there a surgical operation? Yes ☐ No ☐

36 If "yes" give date of operation

37 Operative findings?

CERTIFICATION *(attending physician, coroner, etc.)*

38 I certify that the above-named person died on the date and from the causes stated herein. Signature (attending physician, coroner, etc.) X

39 Attending physician ☐ Physician attending after death ☐ Coroner ☐

40. Name of physician or coroner (print or type) Address

Date Month, day, year

Notations

CERTIFICATION OF DIVISION REGISTRAR

Registration Division

I certify this return was accepted by me on this date

Date Month, day, year

Signature of Division Registrar

4—2302—3 12 25-10-7

ISCHAEMIC HEART DISEASE (410-414)

Includes: with mention of hypertension (conditions in 401-405)

Use additional code, if desired, to identify presence of hypertension

410 Acute myocardial infarction

Cardiac infarction
Coronary (artery):
- embolism
- occlusion
- rupture
- thrombosis

Infarction:
- heart
- myocardium
- ventricle

Rupture:
- heart
- myocardium

Subendocardial infarction
Any condition in 414.1-414.9 specified as acute or with a stated duration of 8 weeks or less

411 Other acute and subacute forms of ischaemic heart disease

Coronary:
- failure
- insufficiency (acute)

Intermediate coronary syndrome
Microinfarct of heart
Preinfarction syndrome
Postmyocardial infarction or Dressler's syndrome

412 Old myocardial infarction

Healed myocardial infarct
Past myocardial infarction diagnosed on ECG or other special investigation, but currently presenting no symptoms

413 Angina pectoris

Angina:
- NOS
- cardiac
- decubitus
- of effort

Anginal syndrome
Stenocardia

414 Other forms of chronic ischaemic heart disease

Excludes: cardiovascular arteriosclerosis, degeneration, disease or sclerosis (429.2)

414.0 *Coronary atherosclerosis*

Atherosclerotic heart disease
Coronary atheroma
Coronary (artery) sclerosis

414.1 *Aneurysm of heart*

Aneurysm:
- coronary
- mural

Ventricular aneurysm

414.8 *Other*

Ischaemia, myocardial (chronic)
Any condition in 410 specified as chronic or with a stated duration of over 8 weeks

414.9 *Unspecified*

Ischaemic heart disease NOS

APPENDIX 17

MONTHLY VITAL STATISTICS REPORT

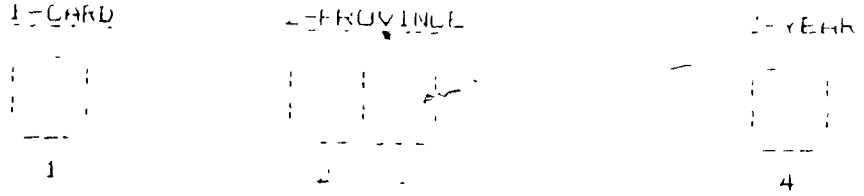
Table 1. COMPARABILITY RATIOS FOR 72 SELECTED CAUSES: BASED ON A STRATIFIED RANDOM SAMPLE OF 1976 DEATHS ASSIGNED ACCORDING TO TH NINTH REVISION AND ON ALL DEATHS ASSIGNED ACCORDING TO THE EIGHTH REVISION OF THE INTERNATIONAL CLASSIFICATION OF DISEASE UNITED STATES

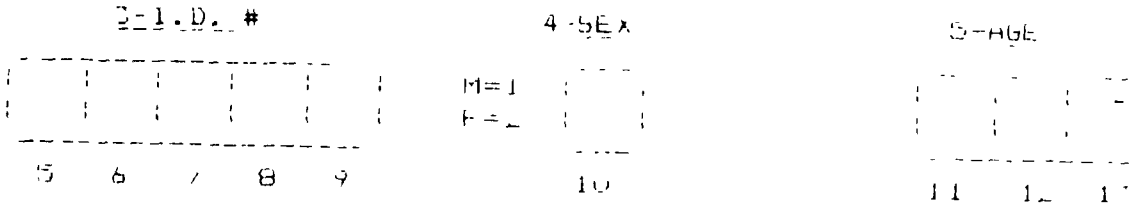
[Denominators of ratios were selected from the List of 70 Selected Causes of Death used during 1968-78 for the Annual Summary]

Cause of death (Ninth Revision of the International Classification of Diseases, 1975)	Number of deaths assigned according to—		Estimated comparability ratio[2]	Error of the estimate of the ratio in (3)		95 percent confidence limits[3]	
	Ninth Revision (estimated from sample)	Eighth Revision (total count)[1]		Standard error	Relative standard error	Upper	Lower
	(1)	(2)	(3)	(4)	(5)	(6)	(7)
Ischemic heart disease....410-414	567,520	646,073	0.8784	0.0038	0.4	0.8859	0.8709
Acute myocardial infarction....410	319,562	319,477	1.0003	0.0054	0.5	1.0108	0.9898
Other acute and subacute forms of ischemic heart disease....411	4,924	4,028	1.2224	0.0661	5.4	1.3519	1.0929
Angina pectoris....413	195	186	1.0484	0.0666	6.4	1.1789	0.9179
Old myocardial infarction and other forms of chronic ischemic heart disease....412,414	242,839	322,382	0.7533	0.0055	0.7	0.7640	0.7426
Other diseases of endocardium....424	5,154	4,195	1.2286	0.0227	1.8	1.2731	1.1841
All other forms of heart disease....415-423,425-429	124,701	49,810	2.5036	0.0257	1.0	2.5539	2.4531

APPENDIX 18

410 CODING VALIDATION FORM.





6=CAUSE OF DEATH

410 = 1
OTHER = 2

14

IF OTHER:
FULL CODE

15 16 17 18 19

7=CONTRIBUTING CAUSE OF DEATH: FULL CODES