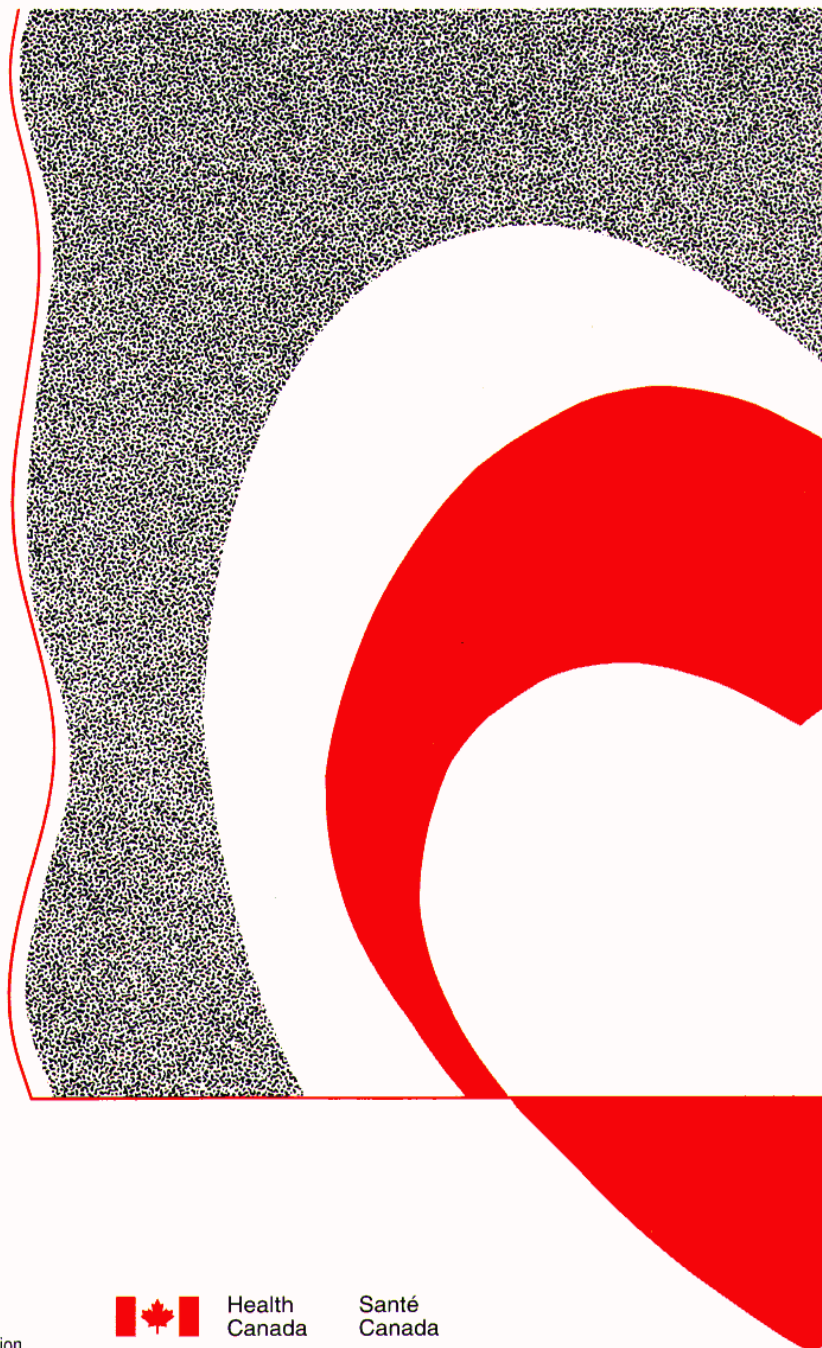




HEART DISEASE AND STROKE IN CANADA

1997



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HEART DISEASE AND STROKE IN CANADA

1997

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1. INTRODUCTION

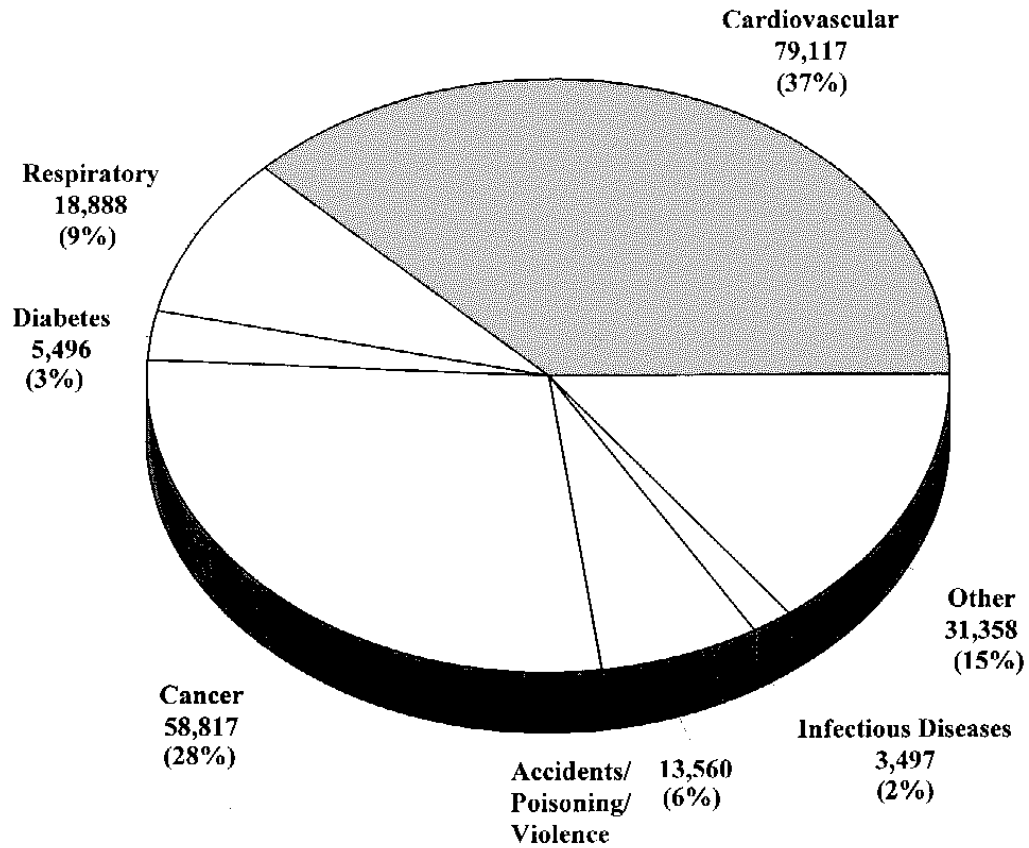
In recent years, considerable progress has been made in identifying the multiple factors that place individuals at risk of developing heart disease and stroke. Successful programs of prevention have demonstrated that through the modification of these risk factors, death and illness from these diseases can be reduced. However, despite these numerous interventions, cardiovascular disease remains the major cause of death, disability and illness in Canada. To address this burden, a number of partners are collaborating on a range of national and international efforts.

The Heart and Stroke Foundation of Canada and its affiliated provincial foundations play a major role in combating heart disease and stroke. The Foundation's mission is to "further the study, prevention, and reduction of disability and death from heart disease and stroke through research, education and the promotion of healthy lifestyle." In this respect, the Foundation provides the majority of funds for research into heart disease and stroke in Canada. Furthermore, the Foundation maintains significant health promotion activities in risk factor areas such as nutrition, blood pressure, and physical activity. Emphasis has been placed on the prevention of sudden pre-hospital death through its cardiopulmonary resuscitation (CPR) programs and on healthy, public policy in areas such as tobacco control. A current focus of many of the Foundations' activities is on cardiovascular disease in women and children.

Health Canada and the National Health Research and Development Program have also provided significant support and leadership in heart health promotion across Canada. The Canadian Heart Health Initiative, a multilevel strategy for cardiovascular disease prevention, is the result of collaboration between Health Canada, the provincial Ministries of Health and the Heart and Stroke Foundation. The Initiative promotes cardiovascular disease prevention at the community level in each province. The 1992 Victoria Declaration on Heart Health established international partnerships in policy development and program implementation aimed at heart health promotion and cardiovascular disease prevention worldwide. The 1995 Catalonia Declaration builds on these international partnerships by providing worldwide examples of heart health programs and demonstrating how those successes in turn provide economic benefits to the countries involved.

This publication is the fourth of a regular series that provides the public, health professionals and policy makers with an overview of the current trends in heart disease and stroke in Canada, as well as international comparisons. The information has been obtained from published data, including that from the Canadian Heart Health Surveys, as well as current data provided generously by the Health Statistics Division, Statistics Canada, and the Laboratory Centre for Disease Control, a division of Health Canada. This publication outlines the patterns of risk factors, mortality and disability attributable to cardiovascular disease, as well as its impact on the health care system. An analysis of the distribution of risk factor prevalence across Canada illustrates the scope for cardiovascular disease prevention programs. This issue also contains a focus section, "Stroke in Canada: Current Management and Prevention Strategies" prepared by Drs. N. Mayo, S. Phillips, and A. Shuaib.

FIGURE 1
Leading Causes of Death,
Number and Percentage of Deaths, Canada, 1995



Total Number of Deaths in 1995: 210,733

SOURCE: Laboratory Centre for Disease Control; Statistics Canada, 1997

Cardiovascular (ICD-9 390-495); Respiratory (ICD-9 460-519); Diabetes (ICD-9 250); Cancer (ICD-9 140-239); Infectious Diseases (ICD-9 001-139); Accidents/Poisonings/Violence (ICD-9 E800-E999)

This document was prepared by the Heart and Stroke Foundation of Saskatchewan Epidemiology Unit at the University of Saskatchewan, in collaboration with the Heart and Stroke Foundation of Canada, Statistics Canada, and the Laboratory Centre for Disease Control, Health Canada.

The term 'cardiovascular disease' used in this document refers to ischemic heart disease and stroke, as well as other heart and vascular diseases. For the purposes of this publication, we will use the term 'stroke' to mean 'cerebrovascular disease', even though 'stroke' is a subgroup of cerebrovascular disease, not the complete entity. 'Stroke' will be used in the clinical sense and includes all the International Classification of Diseases (ICD-9) codes 430-438. Where appropriate, the patterns of the specific disease entities are highlighted. As well, a glossary of all relevant terminology is included at the end of this document.

Age-standardization for international comparisons in this edition has been made to the European Standard Population, which is a change from previous editions of this document; therefore, comparison of international mortality rates with previous editions are not possible. Age-standardization for Canadian comparisons is based on the 1991 population of Canada, rather than the 1986 population as in previous editions and therefore, direct comparisons for these data with previous editions also are not possible.

2. DEATHS FROM CARDIOVASCULAR DISEASE

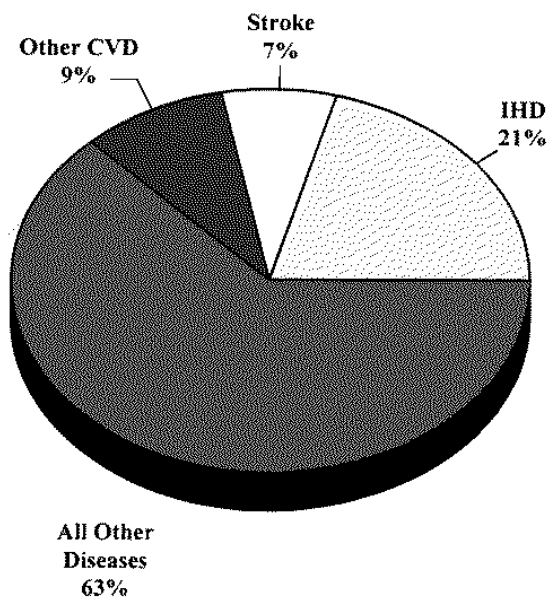
2.1 The Leading Causes of Death

In 1995, there has been an increase in the number of deaths due to cardiovascular disease, although cardiovascular disease now accounts for 37% of all deaths, down from 38% in 1992 (figure 1). In 1995, there were 79,117 deaths attributed to cardiovascular disease, compared to 75,221 in 1992. Ischemic heart disease (IHD) accounts for the greatest percentage of deaths at 21%, of which half are attributable to acute myocardial infarction (AMI) (figure 2). Stroke and other cardiovascular diseases account for 7% and 9% of deaths respectively (figure 2). Tables 1 and 2 list the actual number of deaths in each age group, for both males and females, for all cardiovascular disease, as well as ischemic heart disease, acute myocardial infarctions, and stroke. Although the percentage of all age-adjusted deaths due to ischemic heart disease has decreased from 25% in 1988 to 21% in 1995, the total number of deaths attributed to ischemic heart disease has slightly increased.

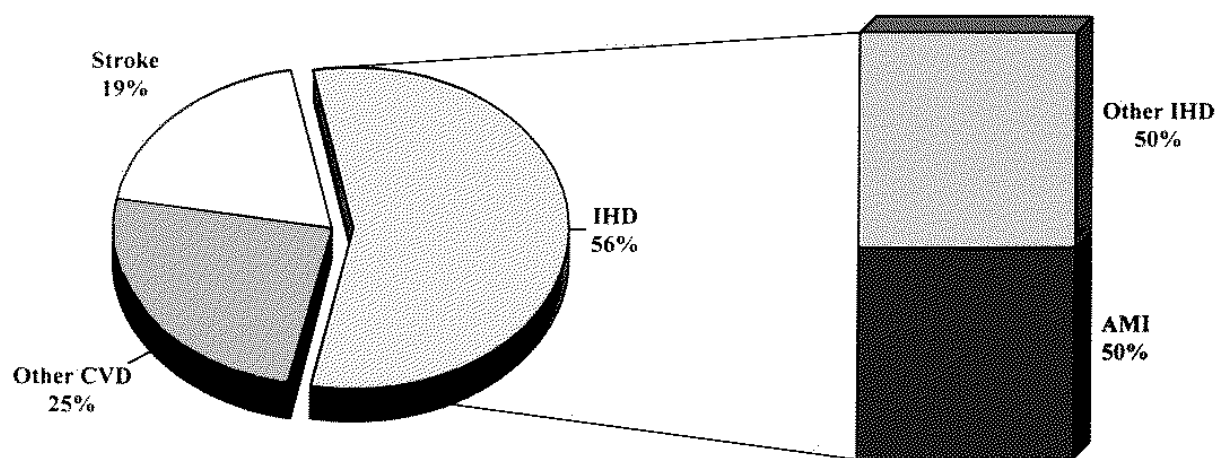
For men of all ages, 36% of deaths are attributable to cardiovascular disease, while in women, the percentage is higher, at 39%. While a greater percentage of men suffer death from ischemic heart disease and heart attacks, more women than men die of stroke (Tables 1 and 2).¹

Death from ischemic heart disease may occur suddenly in the absence of or within one hour of the onset of symptoms. Such 'sudden death' may be the only manifestation in approximately 15% of individuals suffering a first heart attack.^{2,3} In individuals with known ischemic heart disease experiencing a second heart attack, the risk of sudden death may be increased four to five-fold.^{2,3}

FIGURE 2
Major Components of Cardiovascular Disease and All other Diseases Mortality, Canada, 1995



Major Components of Cardiovascular Disease Mortality, Canada, 1995



SOURCE: Laboratory Centre for Disease Control; Statistics Canada, 1997

TABLE 1**Number and Percent of Deaths due to Cardiovascular Diseases, Males,
Canada, 1995**

AGE	All Deaths	ALL CVD ¹		IHD ²		AMI ³		STROKE ⁴	
		Number	Percent of All Deaths	Number	Percent of All Deaths	Number	Percent of All Deaths	Number	Percent of All Deaths
34	6896	255	3.7	68	1.0	38	0.6	45	0.7
35-44	4797	772	16.1	469	9.8	273	5.7	108	2.3
45-54	7426	2007	27.0	1447	19.5	828	11.2	208	2.8
55-64	13 792	4664	33.8	3317	24.1	1993	14.5	465	3.4
65-74	27 964	10 412	37.2	6696	23.9	3673	13.1	1515	5.4
75-84	32 487	13 835	42.6	8127	25.0	4113	12.7	2530	7.8
85+	18 034	8140	45.1	4209	23.3	1739	9.6	1715	9.5
All ages	111 396	40 085	36.0	24 333	21.8	12 657	11.4	6586	5.9

1 All CVD = All Cardiovascular diseases (ICD code 9th revision 390-459)

2 IHD = Ischemic heart disease (ICD-9 410-414)

3 AMI = Acute myocardial infarction (heart attack);(ICD-9 410), AMI is a sub-category of IHD

4 Stroke = (ICD-9 430-438)

SOURCE: Laboratory Centre for Disease Control; Statistics Canada, 1997.

TABLE 2
Number and Percent of Deaths due to Cardiovascular Diseases, Females
Canada, 1995

AGE	All Deaths	ALL CVD ¹		IHD ²		AMI ³		STROKE ⁴	
		Number	Percent of All Deaths	Number	Percent of All Deaths	Number	Percent of All Deaths	Number	Percent of All Deaths
34	3311	188	5.7	29	0.9	15	0.5	49	1.5
35-44	2350	268	11.4	98	4.2	56	2.4	77	3.3
45-54	4539	715	15.8	340	7.5	195	4.3	191	4.2
55-64	8117	1888	23.3	1073	13.2	644	7.9	353	4.3
65-74	18,398	5988	32.5	3357	18.2	1960	10.7	1172	6.4
75-84	30,134	13,332	44.2	7014	23.3	3692	12.3	3066	10.2
85+	32,488	16,644	51.2	7821	24.1	2995	9.2	4043	12.4
All Ages	99,337	39,023	39.3	19,732	19.9	9557	9.6	8951	9.0

1 All CVD = All Cardiovascular diseases (ICD code 9th revision 390-459)

2 IHD = Ischemic heart disease (ICD-9 410-414)

3 AMI = Acute myocardial infarction (heart attack);(ICD-9 410), AMI is a sub-category of IHD

4 Stroke = (ICD-9 430-438)

SOURCE: Laboratory Centre for Disease Control; Statistics Canada, 1997.

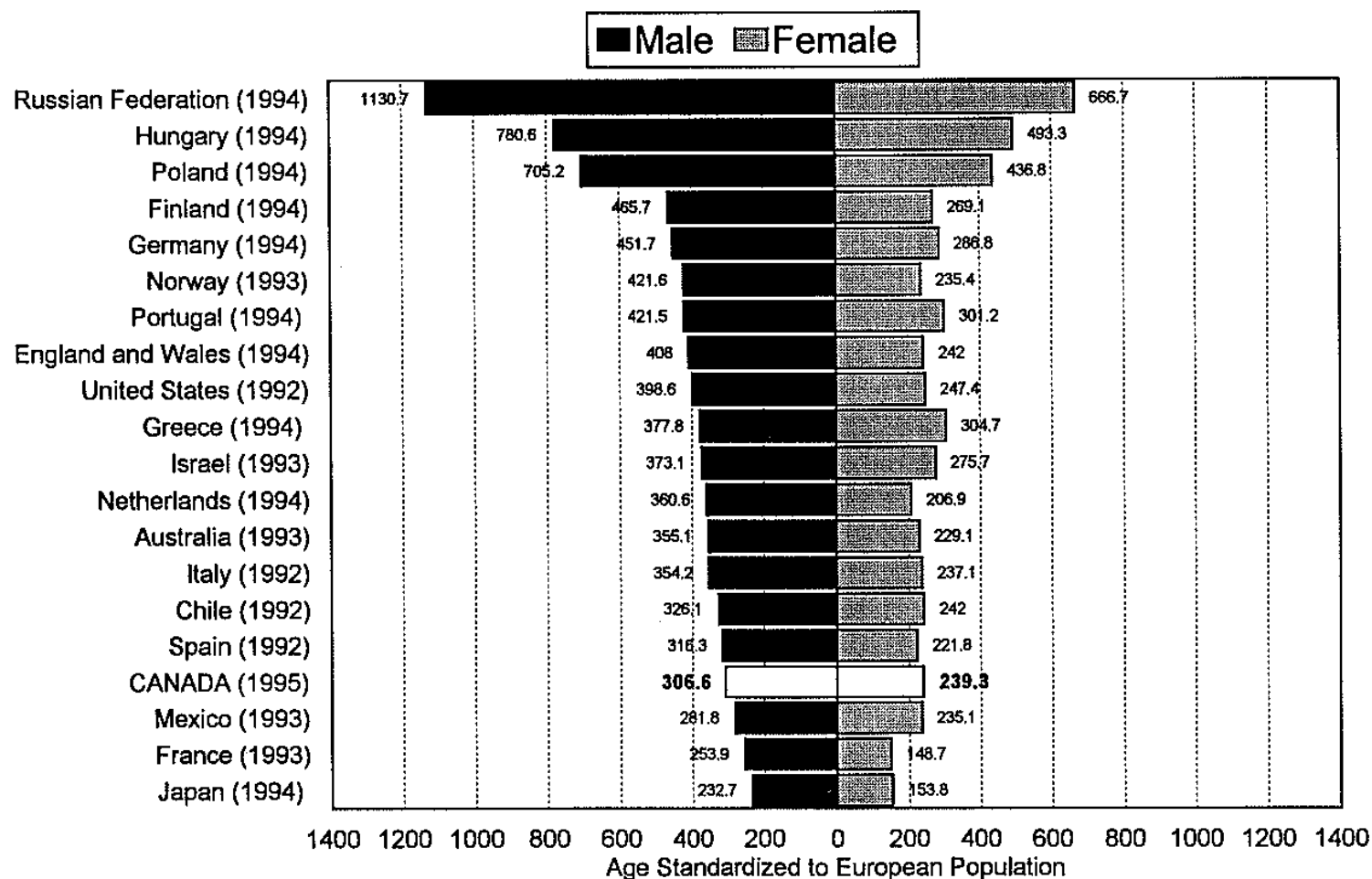
Results from the Quebec Cardiovascular Study found that 60% of the mortality from ischemic heart disease occurred outside the hospital as a first event⁴ and that 42% of all ischemic heart disease deaths were observed in men dying within one hour of the onset of their symptoms or found dead in bed. These results highlight the need for disease prevention and effective pre-hospital care.

For individuals suffering a heart attack and admitted to hospital, it is estimated from the experience in Ontario that the age- and gender-adjusted case fatality rate during the first 30 days has decreased from 22% in 1981 to 16% in 1991.⁵ This decrease began before the utilization of beta-blocking agents, aspirin, and thrombolytic therapy, with a modest decrease from 22.3% in 1981 to 21.4% in 1985.⁶ However, a significant decline from 21.4% in 1985 to 16.3% in 1991 coincides with the increased use of thrombolytic therapy.⁶ An analysis of the National Hospital Morbidity File for acute myocardial infarction for 1992/93⁷ found an overall in-hospital mortality rate of 16%, 13.1% for men and 21.4% for women, which is similar to the results obtained in the Ontario experience. Recently published results from the Canadian Assessment of Myocardial Infarction (CAMI) study demonstrated lower mortality rates. The in-hospital mortality rate of all patients presenting to selected hospitals with an acute myocardial infarction from November 1991 to December 31, 1992 was 9.9%; the one-year post discharge mortality rate was 7.1%.⁸

Studies worldwide continue to assess the efficacy of one regimen of thrombolysis versus another. Regardless of the specific preparation used, a thrombolytic agent, when given within 12 hours of the onset of symptoms, reduces mortality from myocardial infarction. The reduction in mortality may be as high as 30-50% for those receiving the thrombolytic agent within 6 hours of the onset of their chest pain, to 7.5% for the patients consulting between 6 to 12 hours after the onset of symptoms.^{9, 11} Unfortunately, thrombolytic therapy is used in only 30-50% of eligible patients.¹² There are still delays in patients seeking treatment after the onset of symptoms, and delays in receiving treatment once in hospital, even for those meeting inclusion criteria for thrombolytic trials.¹³ Therefore strategies are needed to improve diagnosis, reduce "door-to-needle" time, and increase the availability of thrombolytic agents.¹⁴⁻¹⁷

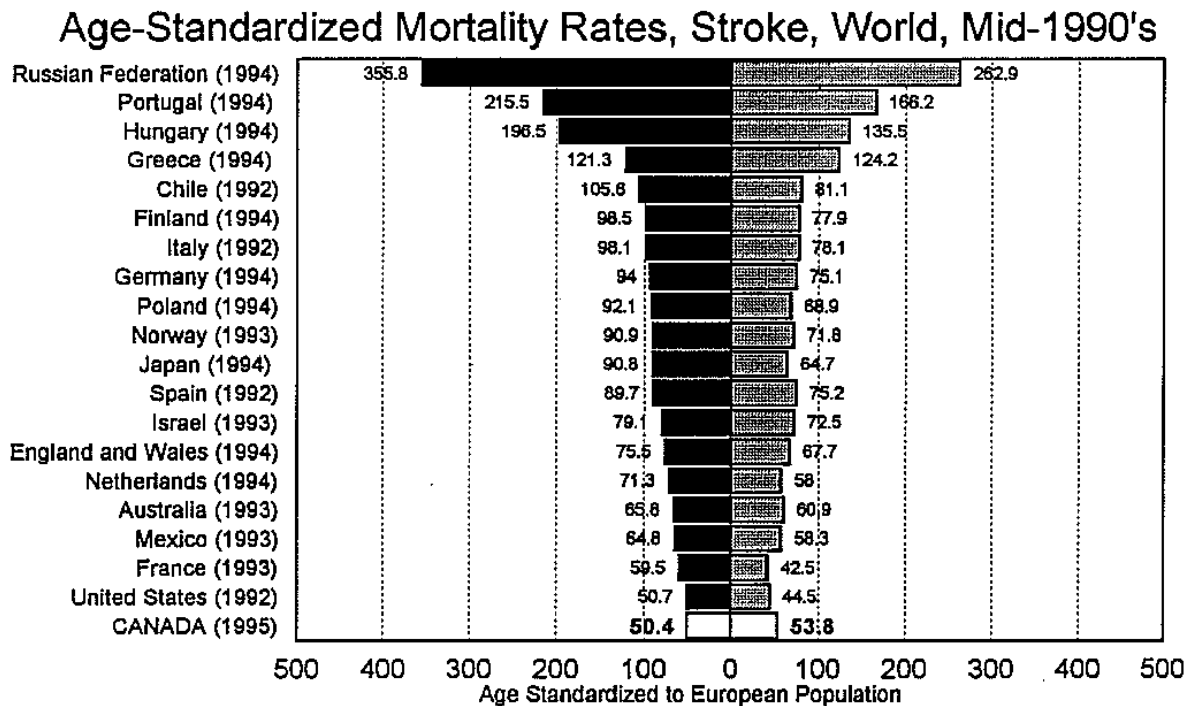
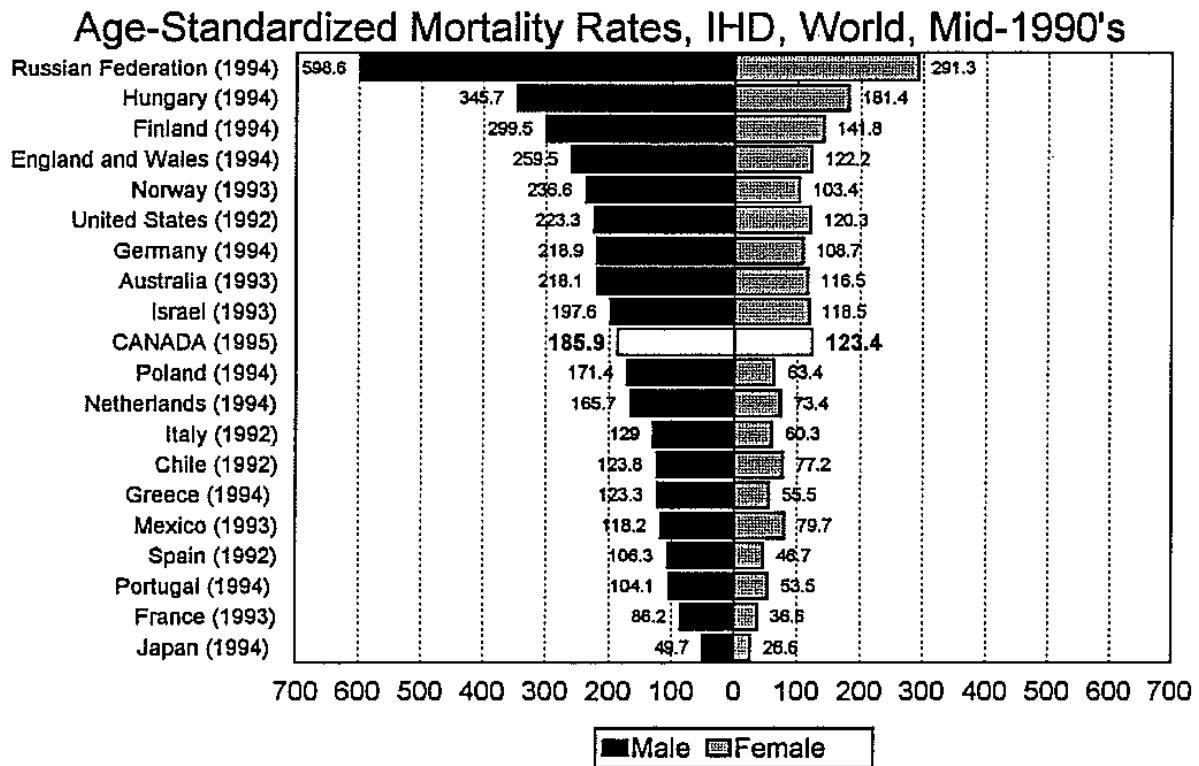
Figure 3

Age-Standardized Mortality Rates Cardiovascular Disease, World, Mid-1990's



Source: 1995 World Health Statistics Annual, WHO

Figure 4



SOURCE: 1995 World Health Statistics Annual, WHO

2.2 *International Comparisons*

Cardiovascular disease is the leading cause of death worldwide, but rates vary considerably among countries. In the mid-1990's, age standardized mortality rates for all cardiovascular disease in men ranged from 1130.7 deaths per 100,000 population in the Russian Federation, to a low of 232.7 deaths per 100,000 in Japan (figure 3). In women, the mortality rates ranged from 666.7 deaths per 100,000 in the Russian Federation, to a low of 148.7 deaths per 100,000 in France (figure 3). Canada's rates (1995) for men were 306.6 deaths per 100,000; for women, the rates were 239.3 deaths per 100,000. These international rates, while providing an overview of the worldwide situation, are derived from the different countries in different years, depending on when statistics were collated; therefore caution must be used in comparisons between countries.

Among the 20 selected countries, Canada ranks 10th in mortality rates from ischemic heart disease, at a rate of 185.9 deaths per 100,000 for men; the mortality rate for women is 123.4 deaths per 100,000 population (figure 4). In comparison, France (a comparable society to Canada) has much lower rates; 86.2 deaths per 100,000 for men and 36.6 deaths per 100,000 for women. Canada's relative position has remained essentially unchanged since the mid-1980's.

Canada maintains its enviable position among the selected countries in mortality rates from stroke. For males the rate is 50.4 deaths per 100,000 population, which is the lowest among the selected countries (figure 4). For women, the rate is 53.8 deaths per 100,000 population, the third lowest, behind the United States and France (figure 4). World rates for men range from 50.4 deaths per 100,000 in Canada, to 355.8 deaths per 100,000 in the Russian Federation. World rates for women range from 42.5 deaths per 100,000 population in France to 262.9 per 100,000 in the Russian Federation (figure 4).

Many factors may account for international differences in mortality rates: diet, smoking habits, lack of physical activity, and the control of high blood pressure in the population. Much of the difference, however, remains unexplained.

2.3 *Age- and Sex-Specific Death Rates*

Sex differences in cardiovascular disease are well documented. Up to the age of 74 years, men experience two- to five-fold greater death rates for AMI and IHD compared to women (Table 3, figure 5). The exception is stroke, for which the death rates for both men and women are approximately equal for all ages. In women, the proportion of all deaths due to cardiovascular disease increases dramatically after menopause, so that in the decades following menopause, ischemic heart disease mortality rates in women approach those of men. In men, the percentage of all deaths due to cardiovascular disease increases steadily from age 35 to 84 (figure 6). Research suggests that normal estrogen levels in pre-menopausal women confer a protective benefit against the development of ischemic heart disease.¹⁸

TABLE 3
Age-Specific Mortality Tate, per 100,000
All Cardiovascular Diseases, Males and Females,
Canada, 1995

	Sex	35-44	45-54	55-64	65-74	75-84	85+
IHD¹	M	19	78	267	702	1825	4020
	F	4	19	85	296	1029	3163
AMI²	M	11	45	161	385	924	1662
	F	2	11	51	173	542	1251
Stroke³	M	4	11	37	159	568	1639
	F	3	10	28	103	450	1688
Other CVD	M	8	19	71	231	714	2122
	F	4	10	36	129	477	2099
ALL CVD⁴	M	31	109	376	1092	3107	7781
	F	11	39	149	528	1956	6950

1 IHD = Ischemic heart disease (ICD-9 410-414)

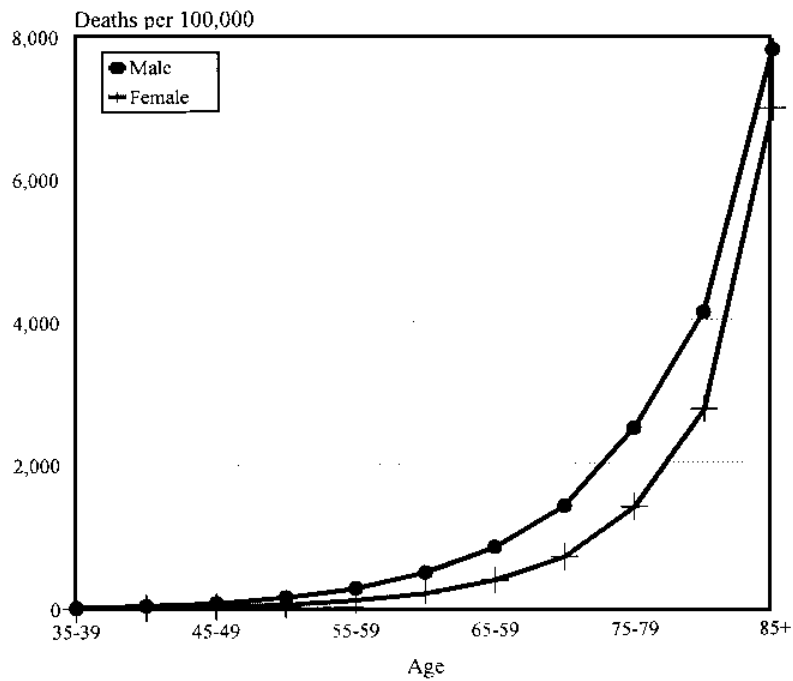
2 AMI = Acute myocardial infarction (heart attack); (ICD code 9th version 410), AMI is a sub-category of IHD

3 Stroke = (ICD-9 430-438)

4 All CVD = All Cardiovascular diseases (ICD code 9th revision 390-459)

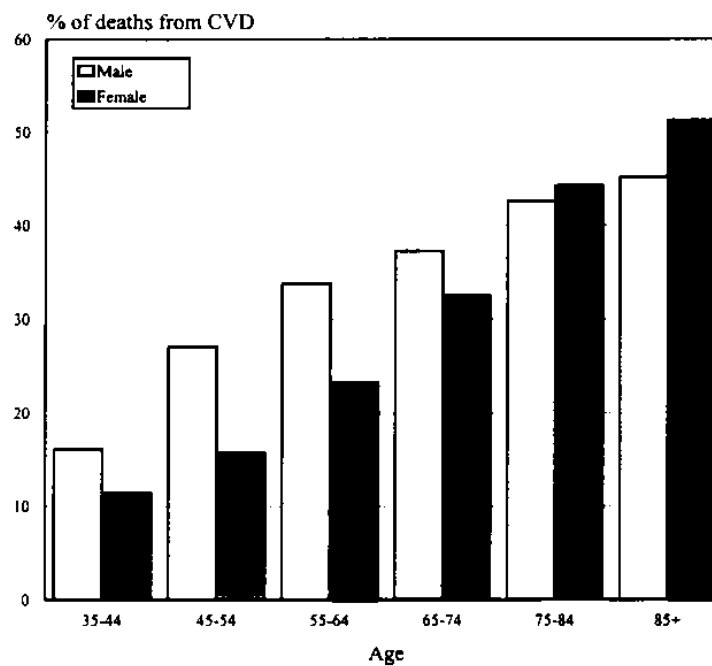
SOURCE: Laboratory Centre for Disease Control; Statistics Canada, 1997.

FIGURE 5
Age-Specific Cardiovascular Disease Mortality Rates,
Canada, 1995



SOURCE: Laboratory Centre for Disease Control; Statistics Canada, 1997

FIGURE 6
Percentage of Total Deaths due to Cardiovascular Diseases by Age Group and Sex,
Canada, 1995



SOURCE: Laboratory Centre for Disease Control; Statistics Canada, 1997

Although the age-specific cardiovascular disease mortality rates in men are more than double those in women for the age groups less than 85 years (Table 3), the actual number of deaths show that almost as many women die from cardiovascular disease as men. In 1995, 40,091 men and 39,026 women died from cardiovascular disease (Tables 1 and 2). This apparent paradox can be explained by the older average age of death of women and the high cardiovascular disease mortality rates in the older age groups.¹⁹

In both sexes, rates increase dramatically in the older age groups (figures 5 and 6). During the coming decades as the proportion of elderly (those over 65 years) within the population increases, the prevalence of, and the absolute number of deaths due to cardiovascular diseases may increase. The lower death rate in the 35-64 age group does not diminish the importance of cardiovascular disease as a health problem; it is still the leading cause of death in this age group.

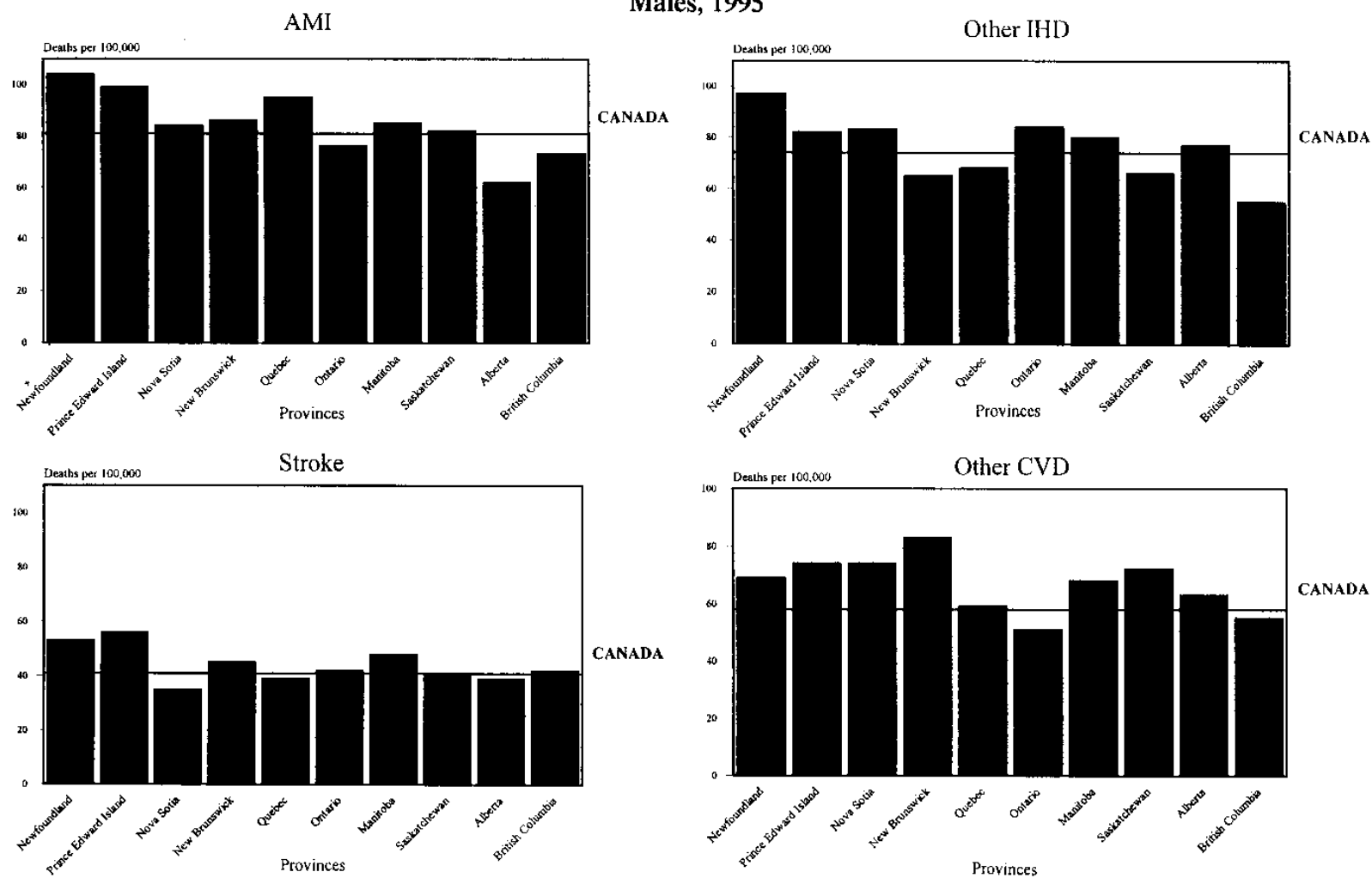
2.4 *Regional Comparisons*

Within Canada, there is an east-west gradient in cardiovascular disease mortality rates (figures 7 and 8; Tables 4 and 5). Atlantic Canada has consistently higher rates than Western Canada. Cardiovascular disease mortality rates in 1995 were highest for men and women in Newfoundland, 317 and 294 per 100,000 population, respectively. The rates were lowest for men and women in British Columbia, 226 and 219 per 100,000 population, respectively. Regional differences are more notable with respect to death rates from acute myocardial infarction and ischemic heart disease than to those from stroke. Mortality atlases (figures 9,10,11,12) show overall disease patterns in Canada for ischemic heart disease and stroke; however, the death rates given for specific census divisions should be interpreted cautiously due to the relatively small number of deaths from which they are derived.

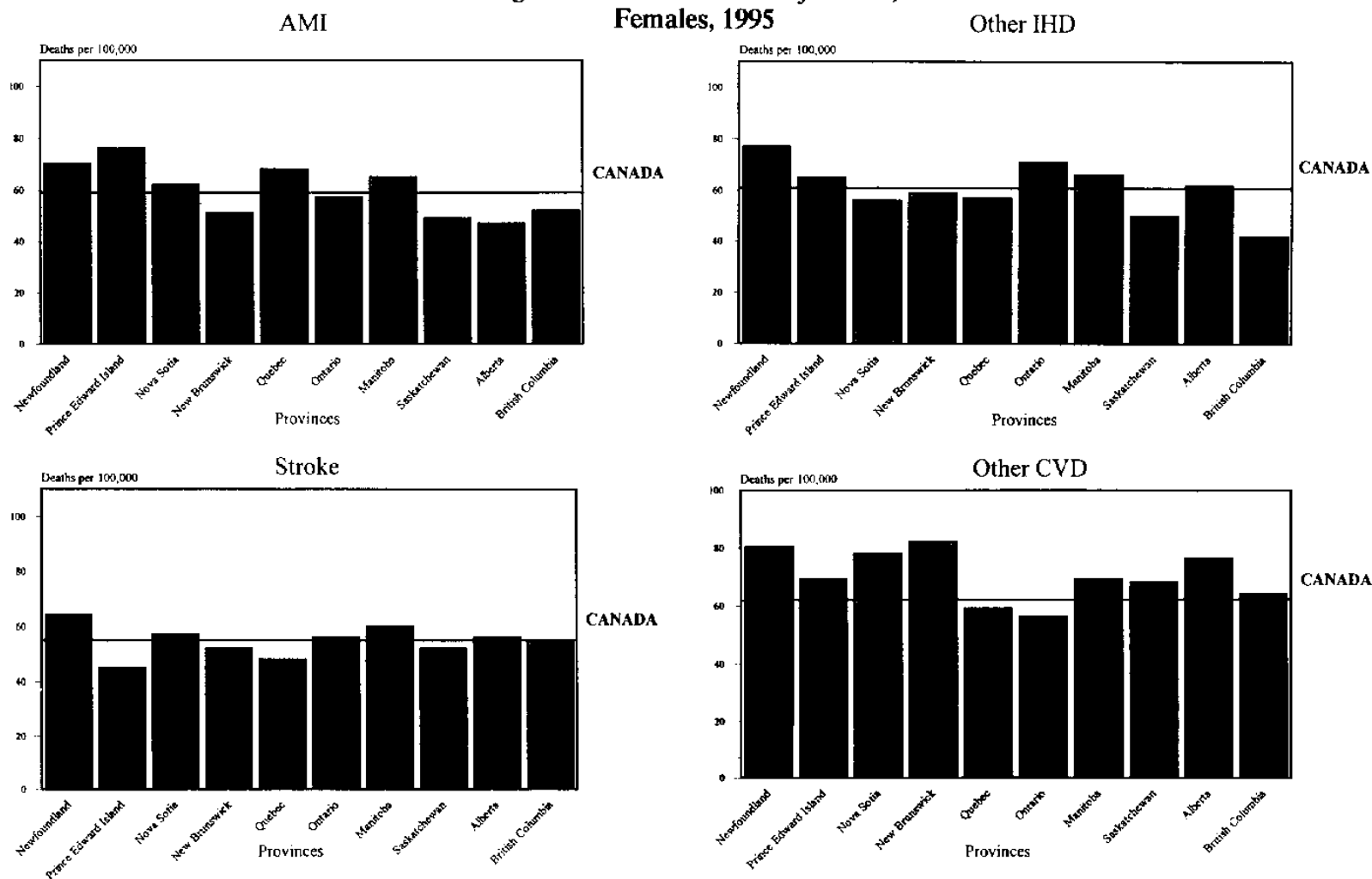
Provincial prevalence rates of smoking, high blood pressure and obesity parallel the cardiovascular disease gradient (see section 6, Risk Factors for Cardiovascular Disease). This would suggest that the variation in cardiovascular disease mortality rates in Canada is partly explained by differences in the prevalence of risk factors.

FIGURE 7

**Age Standardized Mortality Rates¹,
Males, 1995**



1. Standardized to 1991 Canadian Male Population
SOURCE: Laboratory Centre for Disease Control; Statistics Canada, 1997

FIGURE 8**Age Standardized Mortality Rates¹,
Females, 1995**¹ Standardized to 1991 Canadian Female Population

SOURCE: Laboratory Centre for Disease Control; Statistics Canada, 1997

TABLE 4

**Age-Standardized, Sex Specific Mortality Rates¹, per 100,000
All Cardiovascular Diseases, Males
Provincial Comparisons, Canada, 1995**

	IHD ³			Stroke ⁴	Other CVD	ALL CVD ⁵
	AMI ²	Other IHD	Total IHD			
Newfoundland	103	97	201	52	69	317
Prince Edward Island	99	82	181	57	74	312
Nova Scotia	84	83	167	35	74	278
New Brunswick	86	65	151	45	83	280
Quebec	95	68	163	39	59	260
Ontario	76	84	160	42	51	252
Manitoba	85	80	165	49	68	283
Saskatchewan	82	66	148	39	72	258
Alberta	61	77	139	38	63	240
British Columbia	74	55	128	42	55	226
CANADA	81	74	155	41	58	254

1 Standardized to 1991 Canadian Male Population

2 AMI = Acute myocardial infarction (heart attack);(ICD code 9th version 410), AMI is a sub-category of IHD

3 IHD = Ischemic heart disease (ICD-9 410-414)

4 Stroke = (ICD-9 430-438)

5 All CVD = All Cardiovascular diseases (ICD code 9th revision 390-459)

SOURCE: Laboratory Centre for Disease Control; Statistics Canada, 1997.

TABLE 5
Age-Standardized, Sex Specific Mortality Rates¹, per 100,000
All Cardiovascular Diseases, Females
Provincial Comparisons, Canada, 1995

	IHD ³			Stroke ⁴	Other CVD	ALL CVD ⁵
	AMI ²	Other IHD	Total IHD			
Newfoundland	70	77	147	65	80	294
Prince Edward Island	76	65	141	45	69	255
Nova Scotia	62	56	118	57	78	253
New Brunswick	51	59	110	53	82	245
Quebec	69	57	125	49	59	235
Ontario	57	71	128	57	56	243
Manitoba	65	66	131	60	69	259
Saskatchewan	50	50	99	52	68	222
Alberta	48	62	109	56	76	243
British Columbia	53	42	94	57	64	219
CANADA	59	61	120	55	62	239

1 Standardized to 1991 Canadian Male Population

2 AMI = Acute myocardial infarction (heart attack);(ICD code 9th version 410), AMI is a sub-category of IHD

3 IHD = Ischemic heart disease (ICD-9 410-414)

4 Stroke = (ICD-9 430-438)

5 All CVD = All Cardiovascular diseases (ICD code 9th revision 390-459)

SOURCE: Laboratory Centre for Disease Control; Statistics Canada, 1997.

TABLE 6

**Age-Standardized Mortality Rates and
Standardized Mortality Ratios for Ischemic Heart Disease (IHD) and Stroke on Indian Reserves (IR)
and in Canada, per 100,000
Ages 0-64, 1979-1991**

	Age Standardized Mortality Rates						Standardized Mortality Ratios		
	1979-82		1983-86		1987-91		1997-82	1983-86	1987-91
	IR	Canada	IR	Canada	IR	Canada			
<u>Males</u>									
IHD	85.5	88.0	74.1	72.4	51.4	55.3	0.97	1.03	0.94
Stroke	17.2	11.4	13.9	9.1	9.8	7.7	1.47	1.6	1.24
<u>Females</u>									
IHD	26.3	22.3	30.7	18.4	16.8	14.5	1.2	1.7	1.16
Stroke	25.6	9.2	14.9	7.2	11.5	5.9	2.84	1.97	1.86

SOURCE: Laboratory Centre for Disease Control, Health Canada; unpublished data.

2.5 *Aboriginal Populations*

Historical evidence suggests that aboriginal populations (both Inuit and Indian) in Canada formerly experienced a much lower cardiovascular disease mortality rate than the non-native population. Yet, during recent decades, aboriginal men have experienced death rates for ischemic heart disease similar to that of Canadian men; they have also experienced a comparable decline over time^{20,21} (Table 6). The age-standardized mortality rate from stroke in aboriginal men is decreasing as is the relative difference between their mortality rates and those of the general Canadian population (expressed as the standardized mortality ratio). Aboriginal women experience higher mortality rates than the general Canadian female population for both ischemic heart disease and stroke. The higher prevalence of risk factors for cardiovascular disease such as high blood pressure, diabetes, obesity and smoking may account, in part, for this trend.²²⁻²⁴ However, during the past decade, the differences between aboriginal and non-aboriginal women has noticeably decreased. Whether these slighter differences reflect the general trend among Canadians overall, or are the result of programs aimed specifically at aboriginal groups remains unclear.

2.6 *Time Trends*

Cardiovascular disease death rates have been declining steadily in Canada since the mid-1960's. The 1995 death rates are almost half those of 1969; this applies to all major categories of cardiovascular disease, and to rates among both men and women (figure 13).

Ischemic heart disease rates peaked in Canada in the mid 1960's (figure 13). Ontario's rates were the highest, reaching 447 deaths per 100,000 population (males) in 1970; those in Saskatchewan were the lowest at 318 deaths per 100,000 population (males) in 1969.²⁵ Since then, the decline has been steady at approximately 2% per year. The rate of decline has been greatest in Atlantic Canada and least in the Prairies, so that by 1995, considerably less regional variation is seen than two decades earlier. The decline may, like that in the United States, be explained partly by a reduction in the prevalence of smoking and consumption of dietary fat, improved identification and control of high blood pressure, improved medical and surgical care of individuals who have developed cardiovascular disease,²⁶ as well as improvements in diagnostic precision.

The decline in the death rate from acute myocardial infarction is similar to that seen for ischemic heart disease (figure 13). Statistics specific to acute myocardial infarction were not collected until 1969 and therefore death rates are not available prior to this time.

Although stroke in Canada is responsible for 7% of all deaths, the death rate from stroke is among the lowest in the world (see Section 2.2 International Comparisons). Death rates from stroke declined at approximately 2% per year since the 1950's; the percentage of deaths due to stroke has remained stable at 7% since 1988. The death rate from stroke is closely related to the prevalence of high blood pressure and smoking in the population. The decline in death rate from stroke may be related to an improved public awareness of high blood pressure and its earlier detection and treatment.

FIGURE 9

Ischemic Heart Disease, Males, Ages 35-74, 1986-1995

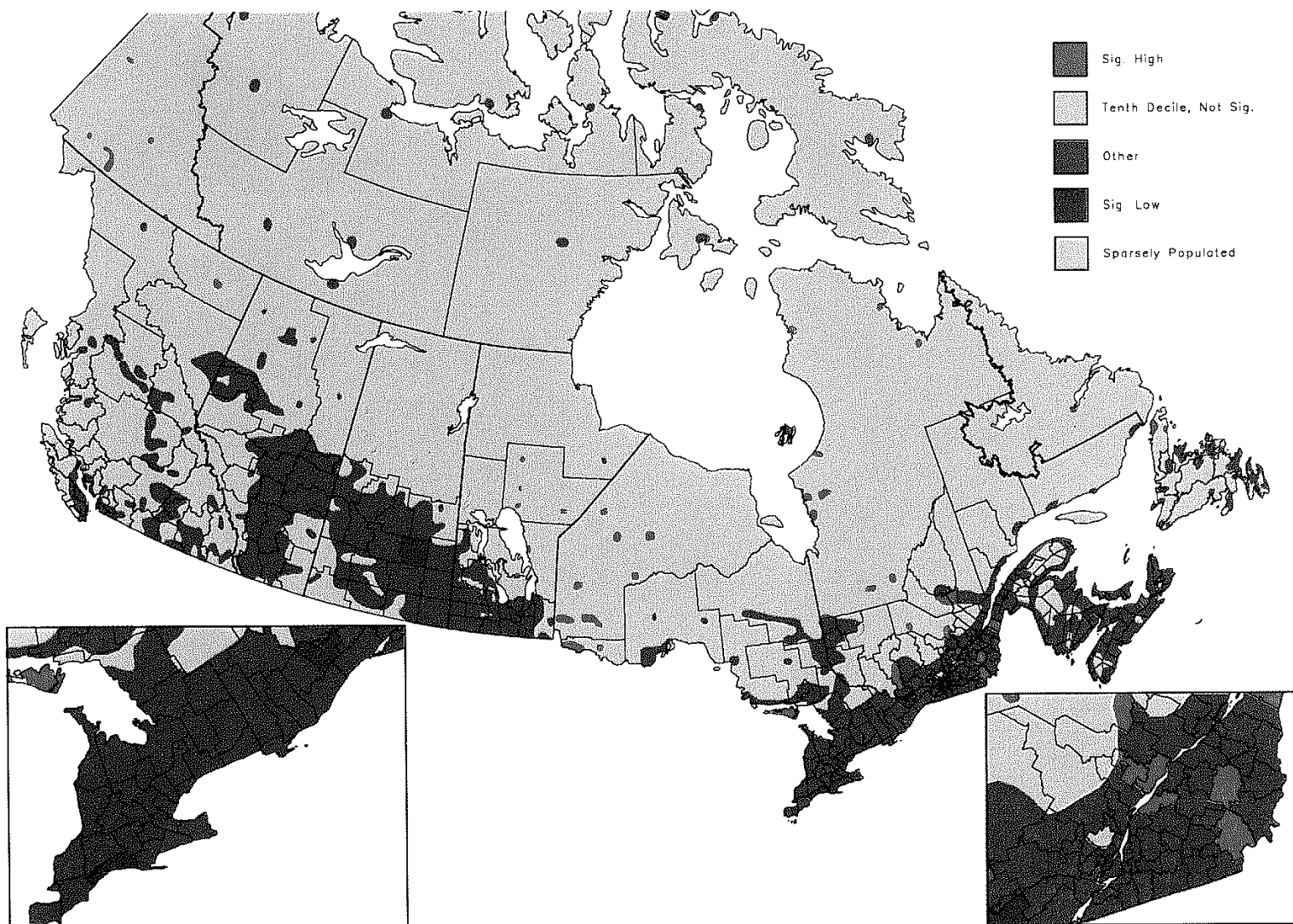


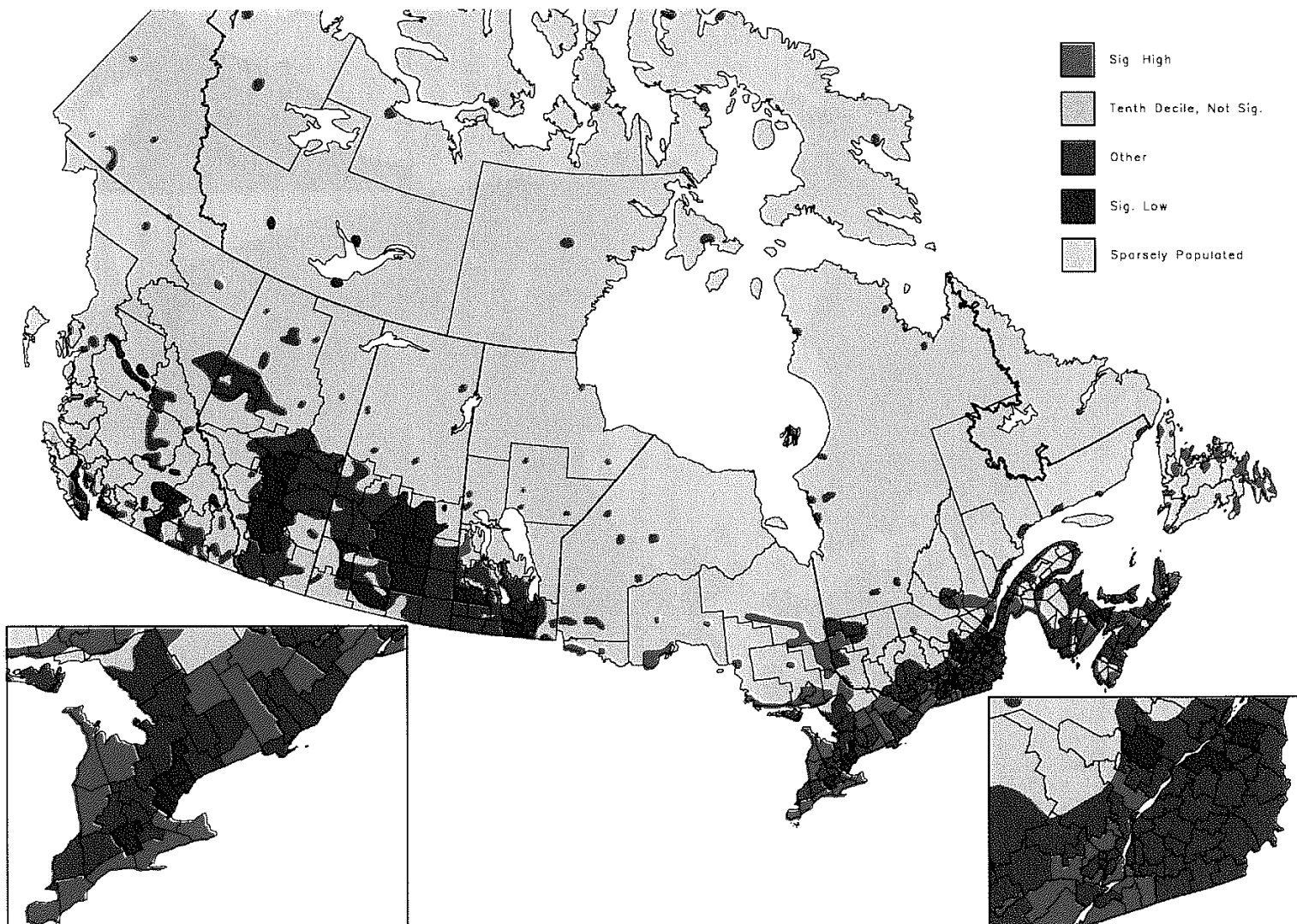
FIGURE 10**Ischemic Heart Disease, Females, Ages 35-74, 1986-1995**

FIGURE 11
Stroke, Males, Ages 35-74, 1986-1995

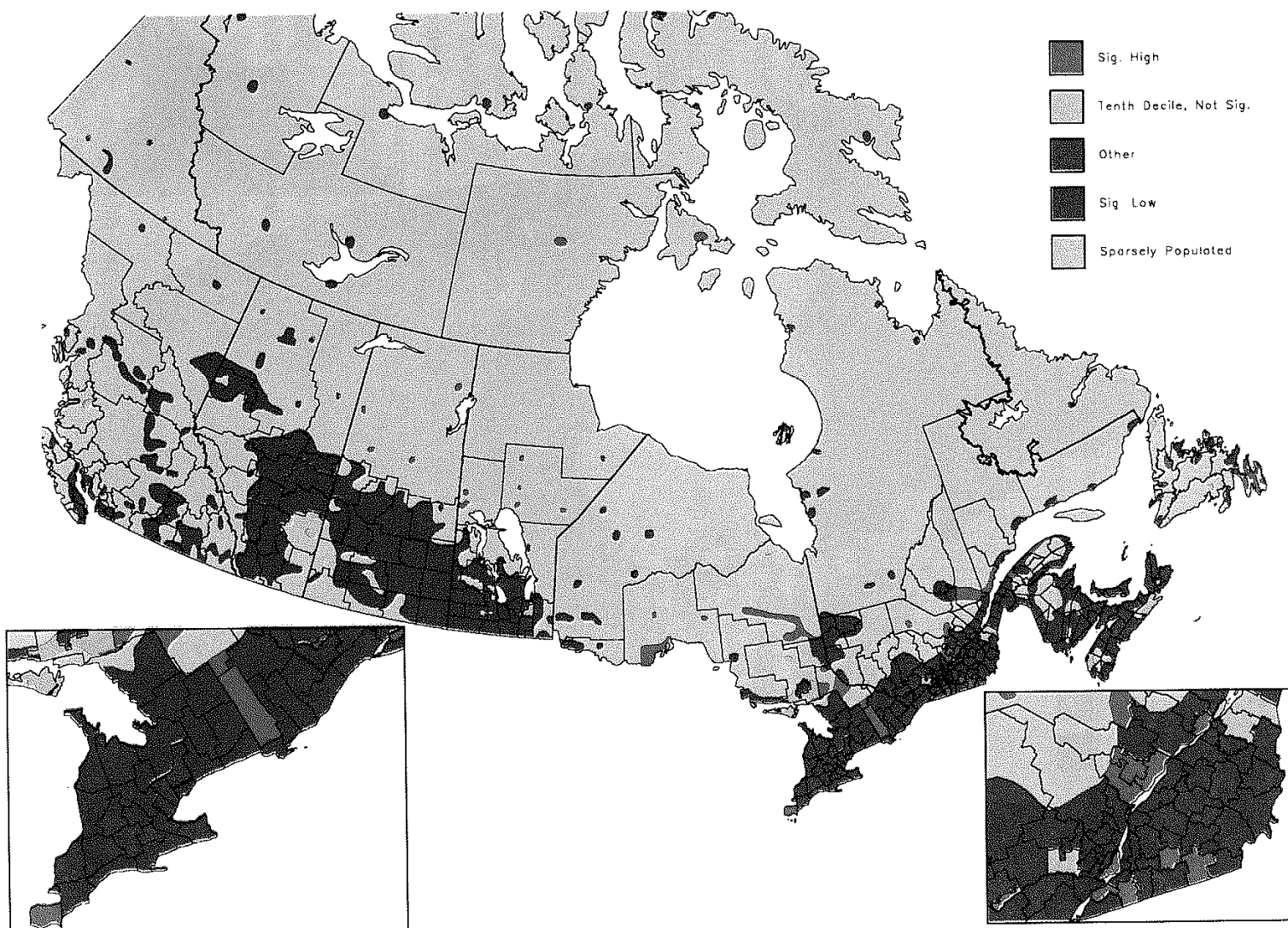
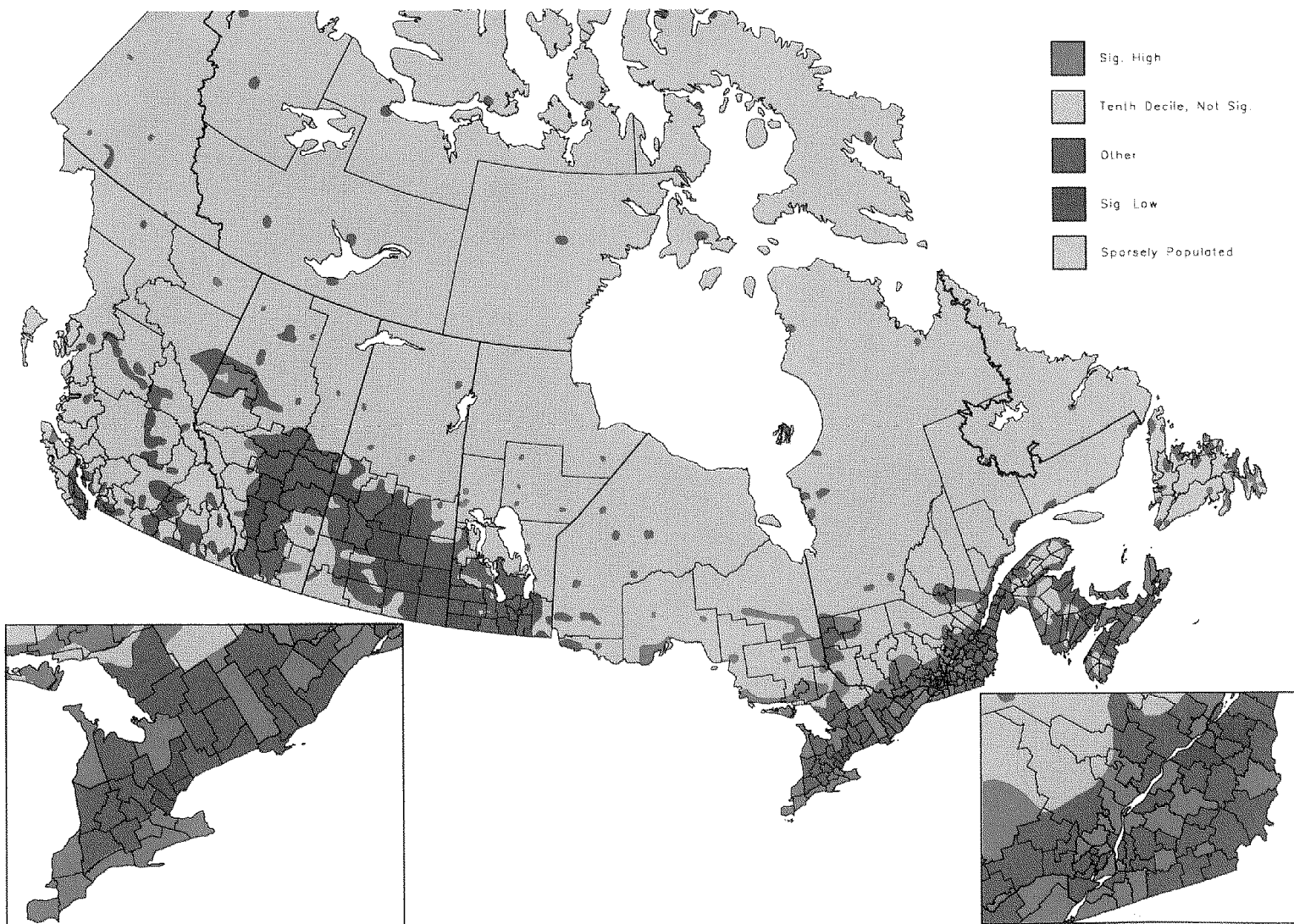


FIGURE 12
Stroke, Females, Ages 35-74, 1986-1995



While the mortality rates from ischemic heart disease have been declining in Canada and other Western countries during the past decade, it has been increasing in Eastern Europe, the Russian Federation, and in a number of countries in the developing world.

2.7 Potential Years of Life Lost

An indication of the impact of premature death on society can be obtained from the calculation of potential years of life lost. This is the sum of the number of years of life that individual Canadians "lost", that is, did not live, due to premature death (considered arbitrarily as that prior to age 75). Premature death from cardiovascular disease is responsible for an estimated 294,000 years of life lost, and is third after that from injuries and cancer (figure 14). This figure remains essentially unchanged from previous calculations. This represents a significant social and economic loss to the nation and stresses the importance of preventive health programs to decrease the number of premature deaths from cardiovascular disease.

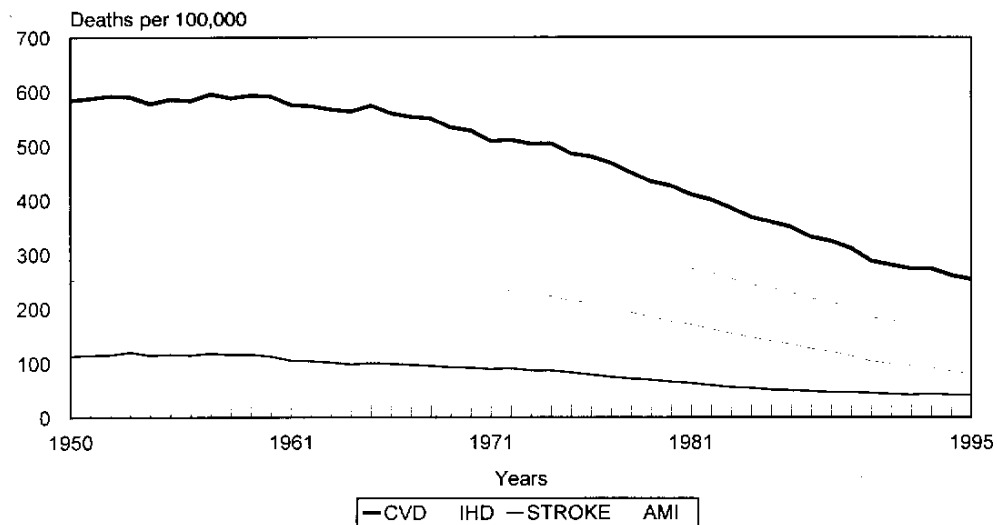
3. INCIDENCE OF CARDIOVASCULAR DISEASE

Declines in mortality from cardiovascular disease may be attributable to a decreased incidence, an improved survival, or a combination of the two factors.^{27,28} Through the determination of incidence rates, the impact of lifestyle changes and improvements in treatment may be identified. Furthermore, estimation of the incidence of cardiovascular disease is of central importance to effective health care planning.²⁸

A combined effort between Saskatchewan and Nova Scotia in the early 1980's to determine the incidence of acute myocardial infarction linked hospital discharge records with the Canadian Mortality Database.²⁹ The data were collected between 1977 and 1985. However, since this project, no provincial or national registry has been established to document and track the incidence of cardiovascular disease.

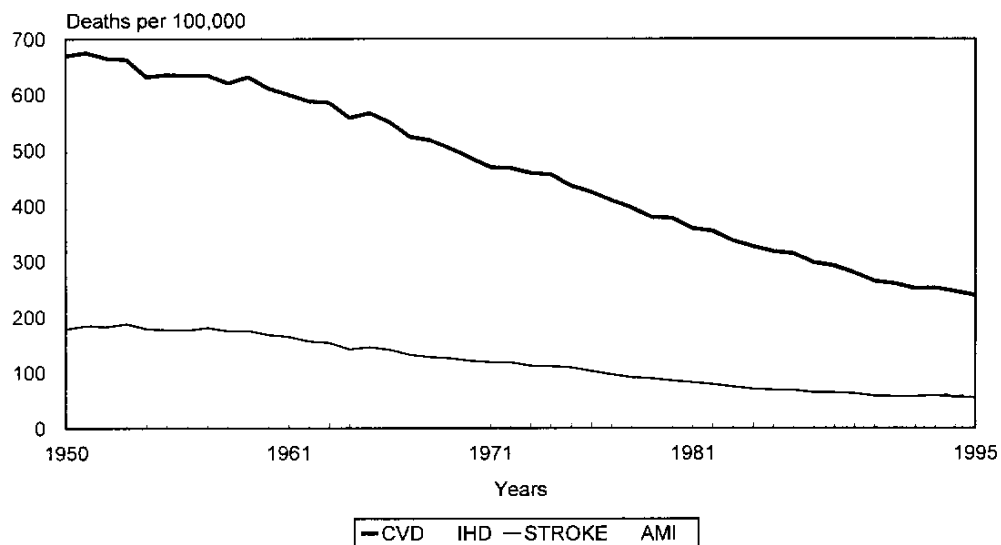
Statistics Canada and Health Canada have used the national Hospital Morbidity Data File to determine the rate of hospital discharge for myocardial infarction.⁷ This measure provides a proxy for incidence rates of myocardial infarction, however, it does not include those individuals who died prior to reaching hospital. According to this method, 32,256 men and 17,599 women experienced a myocardial infarction in the Canadian fiscal year 1992/93.⁷

FIGURE 13
Age-Standardized, Sex Specific Mortality Rate, per 100,000
Males, 1951-1995



Standardized to 1991 Canadian Male population

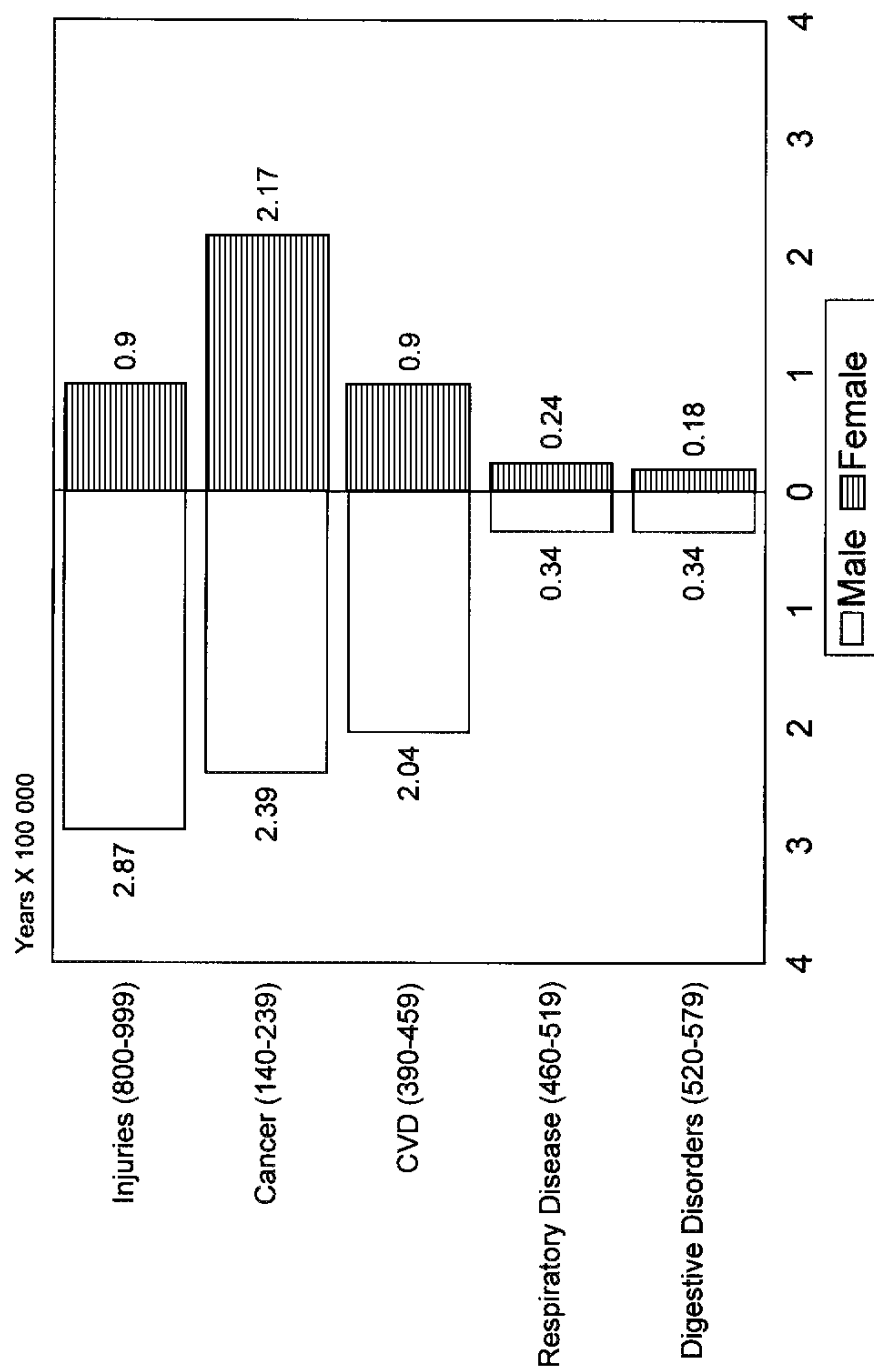
Females, 1951-1995



Standardized to 1991 Canadian Female population

SOURCE: Laboratory Centre for Disease Control; Statistics Canada, 1997

FIGURE 14
Potential Years of Life Lost (PYLL) Prior to Age 75 by Disease Category, 1995



Source: Hospital Mortality Data, Health Statistics Division, Statistics Canada

A current World Health Organization project may soon provide actual incidence rates for at least one region of Canada. The ***Monitoring of Trends and Determinants of Cardiovascular Disease*** (MONICA) project is an international cardiovascular disease surveillance study covering a total population of more than 15 million people in 41 centres.³⁰ To explain international cardiovascular disease trends, data regarding death and incidence rates, risk factor profiles and medical care are being collected in each centre using a standardized methodology. The population of Halifax County, Nova Scotia, is one of the population groups being studied.³¹ Every fatal and non-fatal case of acute myocardial infarction is validated and documented in a registry. Canadian results from this surveillance study are expected in the future.

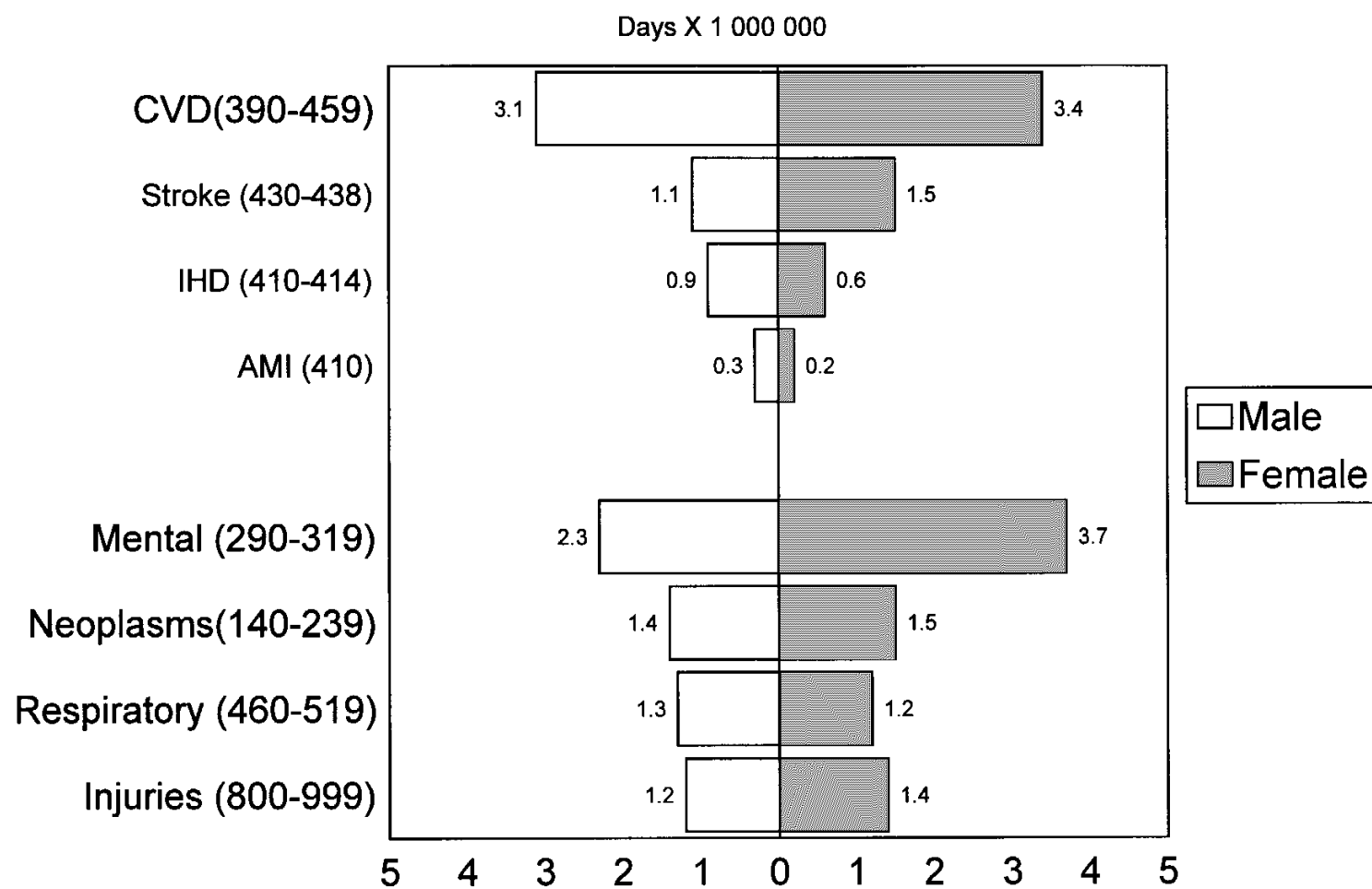
Initial results from other MONICA sites have recently been published. Age-standardized annual event rates (both fatal and nonfatal coronary events) for males ranged from 915/100,000 in North Karelia, to 76/100,000 in Beijing. For females the rates ranged from 256/100,000 in Glasgow to 30/100,000 in Catalonia. For men ages 35-64, there is 1.5-1 episode of hospitalized, nonfatal definite acute myocardial infarction registered for every death due to ischemic heart disease.³²

4. UTILIZATION OF HEALTH SERVICES

4.1 Hospitalization

Cardiovascular disease has a significant impact on Canada's health care system. In fiscal year 1994/95, the total days patients stayed in hospital for cardiovascular disease events was 6,522,117. This includes 3,076,207 days in hospital for males, and 3,445,910 days in hospital for females (figure 15). These days in hospital include all cardiovascular disease (ICD-9 390-459) as well as hospital stays for procedures or operations related to cardiovascular disease. As well, figure 15 illustrates the significant difference between the number of hospital days for stroke and ischemic heart disease (which includes myocardial infarction). A total of 2.6 million hospital days were related to stroke, while ischemic heart disease accounted for 1.5 million hospital days.

The National Hospital Morbidity File data from 1992/93 demonstrates that patients with cardiovascular disease have a longer length of stay (12 days) than the average for all causes (10.8 days).⁷ This total has decreased substantially, from a 17.5 day stay for cardiovascular disease, versus an 11.4 day stay for all causes. The average length of stay for women was higher than that for men, 13.1 days versus 11.4.⁷ The total length of stay per patient increases by age for both sexes.³³

FIGURE 15**Hospital Days for Major Causes by Sex, 1994-95**

Source: Hospital Morbidity Data, Health Statistics Division, Statistics Canada

FIGURE 16
Coronary Bypass Surgery and Angioplasty,
Total Operations, 1982-1995

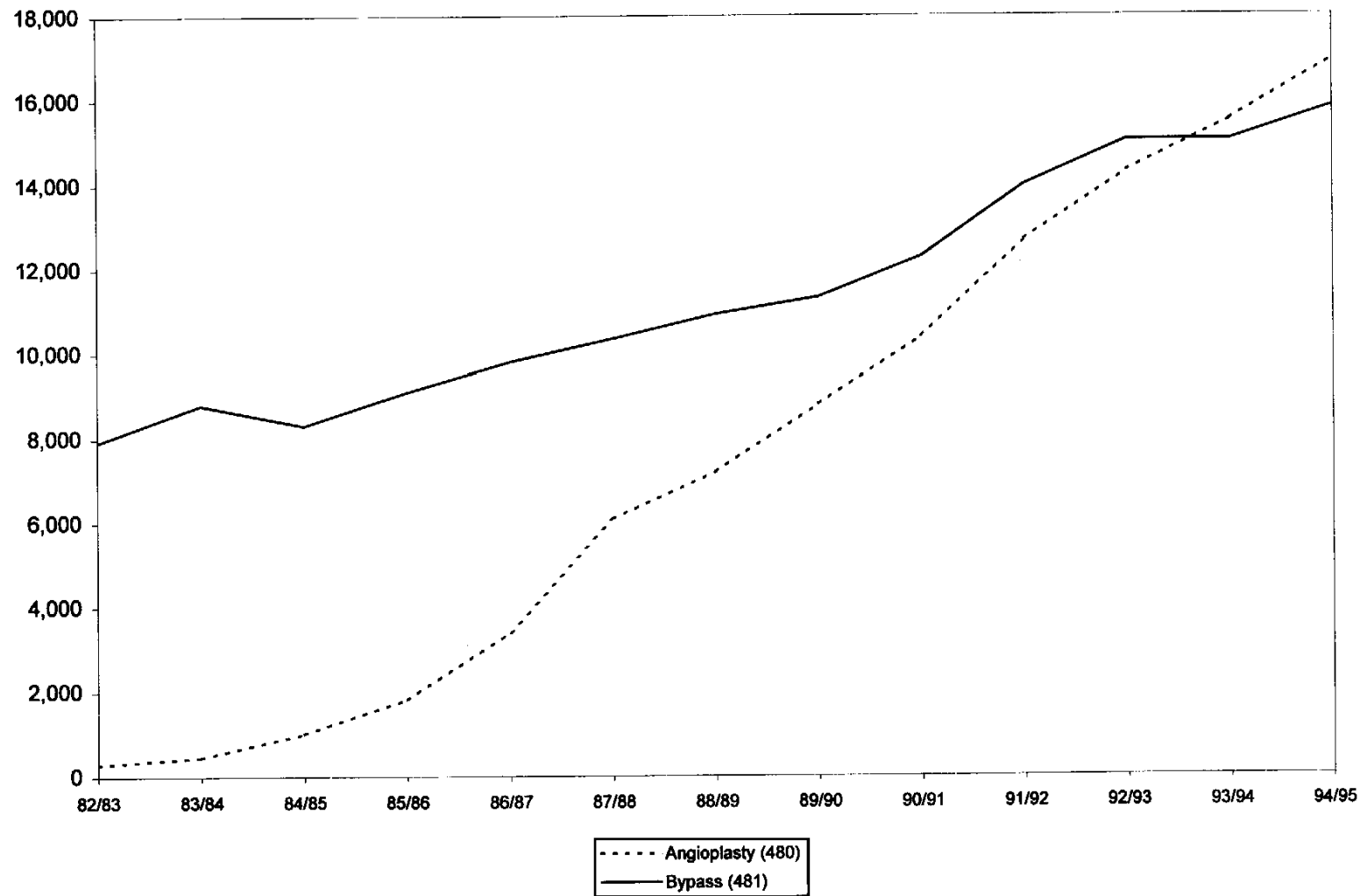


TABLE 7

**Estimated Number of Prescriptions
Dispensed in Canadian Retail Pharmacies in 1996**

	# of Prescriptions (000s)	% Share of All Prescriptions
Cardiovascular	29,994	12.8
Anti-infectives	26,322	11.2
Psychotherapeutics	24,388	10.4
Analgesics	19,704	8.4
Hormones	19,465	8.3
Contraceptives	9,641	4.1
Diuretics*	8,717	3.7
Diabetes Therapy	7,192	3.1
Others	34,855	14.9
TOTAL CANADA	234,598	100.0

* Diuretics are most often used in the treatment of cardiovascular disease.

1. Compuscript provides estimates of the number of prescriptions dispensed in Canadian retail pharmacies on a monthly basis. Information about prescriptions dispensed is collected electronically from a sample panel of almost 2,000 pharmacies. The sample of pharmacies is designed to be representative of pharmacies in Canada and is stratified by province, store type (chain or independent) and store size (large or small). After electronic processing of the raw data to check for completeness, projection factors are applied to estimate the values for all of Canada.

SOURCE: Intercontinental Medical Statistics (IMS) Canada, Compuscript, 1996

4.2 Ischemic Heart Disease-Related Procedures

The rates of both coronary artery bypass grafting (CABG) and angioplasty have increased dramatically during the past 15 years (figure 16). A total of 15,816 CABG procedures and 16,933 angioplasties were performed in Canada during the 1994/95 fiscal year. The number of angioplasties performed has been increasing more rapidly than the number of CABG procedures. Approximately one-third of the patients who have undergone an angioplasty will present with a restenosis, a narrowing similar to the one present prior to the dilatation of the narrowed vessel. To prevent such a restenosis, a stent is often inserted at the area of the dilatation. Immediate benefits and long-term re-stenosis rates from the use of stents as compared to angioplasty are still being evaluated in trials worldwide.

Of those individuals presenting to hospital with an acute myocardial infarction in 1992/93, national data indicate that 16.8% of males and 10.3% of females underwent a revascularization procedure⁷. The data also showed that women were less likely than men to undergo cardiac catheterization (a procedure used to visualize coronary artery blood flow), but once women had undergone cardiac catheterization, they were just as likely as men to undergo revascularization procedures⁷.

4.3 Utilization of Pharmaceuticals

Prescription drugs for the treatment of cardiovascular disease are estimated to account for 12.8% of the total 234.6 million prescriptions dispensed in Canada in 1996 (Table 7). An estimated 29.9 million prescriptions was dispensed for the treatment of cardiovascular disease. A breakdown of the specific drugs prescribed within this category is not available. Diuretics are analyzed separately from cardiovascular prescriptions but most are utilized in the treatment of cardiovascular disease (specifically hypertension and congestive heart failure); they account for 3.7% (8.7 million) of prescription drugs dispensed in Canada.

4.4 Physician Consultation

It is estimated that in 1994, Canadians made 264 million visits to physicians.³⁴ Nearly ten percent (9.9%) of these visits were for cardiovascular disease (Table 8). Of these cardiovascular disease-related visits, half (50%) are for the management of high blood pressure, 25% for ischemic heart disease, and 25% for other cardiovascular disease.³⁴ Of those for ischemic heart disease, 59% of visits are for myocardial infarction and 41% for angina.

TABLE 8

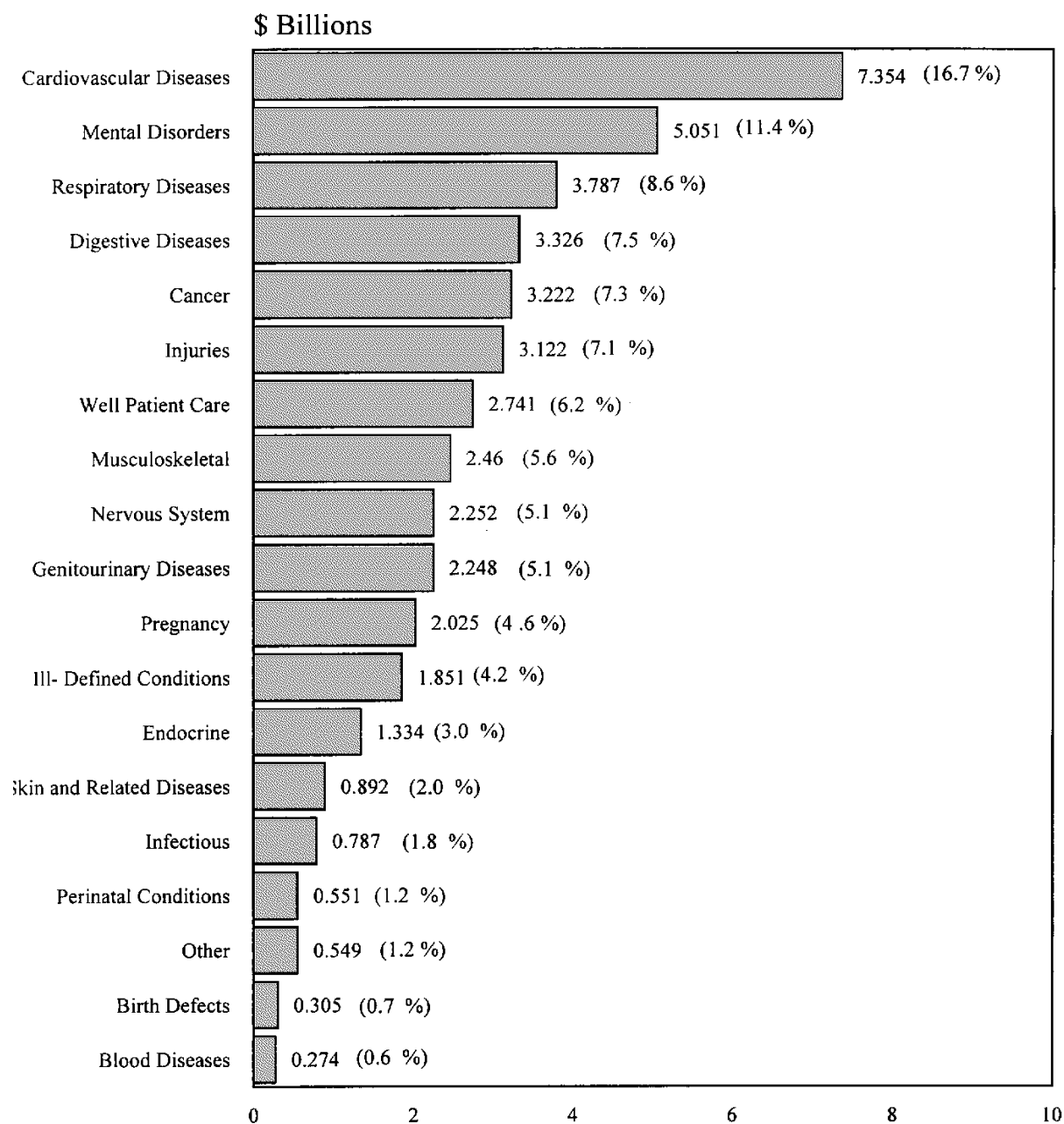
Numbers and Percentage Physicians Visits per Diagnostic Category¹
Canada, 1994

Diagnostic Category (ICD-9)	Estimated Number (Millions)	Percentage
Respiratory Diseases (460-519)	36.5	13.8
Cardiovascular Diseases (390-459)	26.0	9.9
Central Nervous System Disorders (320-389)	21.2	8.0
Mental Disorders (290-319)	22.1	8.4
Musculoskeletal Disorders (710-39)	20.3	7.7
Injury and Poisoning (800-999)	15.5	5.9
Genito-Urinary Diseases (580-629)	15.5	5.9
Skin Diseases (680-709)	13.3	5.0
Digestive Diseases (520-79)	12.3	4.7
Endocrine/Immune Disorders (240-79)	14.1	5.3
Infective/Parasitic Diseases (001-139)	10.7	4.1
Neoplasms (140-239)	8.3	3.2
Other Categories	48.2	18.3
TOTAL	263.9	100

1. Percentage drawn from the Canadian Disease and Therapeutic Index of IMS Canada. The database is comprised of self-reported practice patterns of a representative sample of 652 office-based family physicians and specialists throughout Canada surveyed four times per year.

SOURCE: Intercontinental Medical Statistics (IMS) Canada
Canadian Disease and Therapeutic Index, Year Ending 1994

FIGURE 17
Direct Costs of Illness by Disease Category,
Canada, 1993



Total Direct Costs of Illness, 1993: \$44,129,865,000
 SOURCE: Laboratory Centre for Disease Control, 1997

5 *ECONOMIC IMPACT OF CARDIOVASCULAR DISEASE*

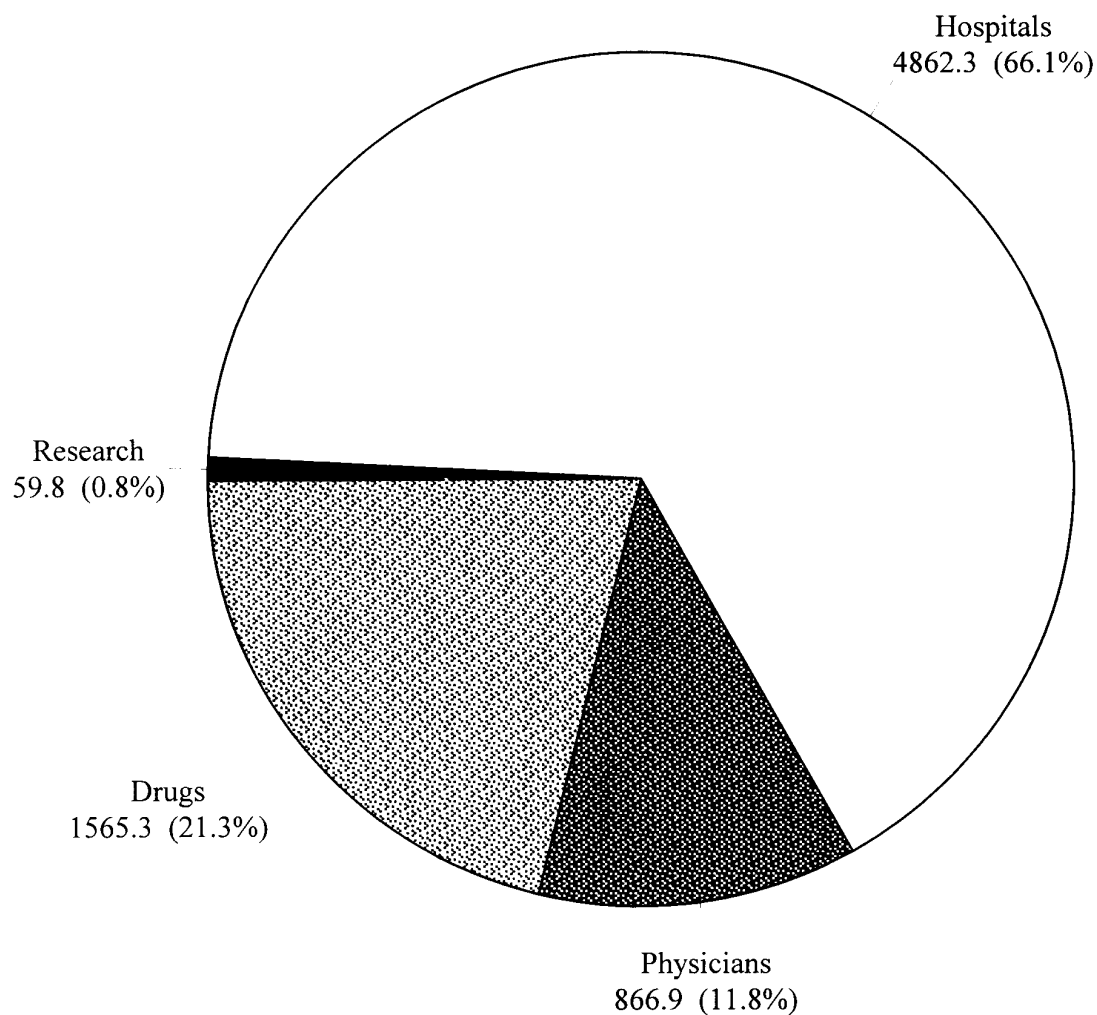
Cardiovascular diseases have a significant economic impact in Canada as measured by direct costs.³⁵ Direct costs refer to the value of resources actually expended that could have been allocated elsewhere in the absence of disease.

Cardiovascular diseases were the most expensive disease category in 1995 accounting for \$7.3 billion or 17% of the total direct costs of illness. Figure 17 illustrates the total direct costs for each diagnostic category. The sources of the direct costs of cardiovascular disease are illustrated in Figure 18. Direct costs are comprised of hospital expenditures, medical care, drugs, and research. Hospital care was the most expensive direct cost component (\$4.8 billion or 66% of the total direct costs) for cardiovascular diseases. The costs of medical services provided by physicians for the treatment of cardiovascular disease amounted to \$867 million. Prescription drugs distributed to the Canadian consumer through drug stores and hospitals for the treatment of cardiovascular diseases cost an estimated \$1.6 billion. Approximately \$59 million (0.8%) has been allocated to research.

Other costs play a significant role in the economic burden of illness in Canada. Indirect costs include the value of lost productivity due to illness or disability, and the loss of future earnings due to premature death (see Section 2.7 , Potential Years of Life Lost). Indirect mortality costs are calculated utilizing the human capital approach which estimates the current dollar value of lost future productivity due to premature death³⁶. Indirect cost estimates have been calculated for all disease categories (figures 19 and 20). Musculoskeletal disorders account for the greatest indirect costs at an estimated \$15.3 billion annually (figure 19). Cardiovascular disease is second at approximately \$12.3 billion annually or 14.5% of total indirect costs of all disease categories. This is greater than injuries, cancer and respiratory diseases. By far the greatest proportion of indirect costs for cardiovascular disease is mortality, which is 60% of the total at \$7.4 billion annually (figure 20). Long-term disability has a significant proportion at 36.4% or \$4.5 billion annually. Short-term disability is a minor component at 3.4% or \$425 million annually.³⁷

When combined, the direct costs plus the indirect costs of cardiovascular disease consume a significant portion of the health care dollar. These economic statistics do not include the personal and emotional components of the burden of cardiovascular disease. Both the economic and personal burdens of cardiovascular disease demonstrate the great need to reduce its incidence, improve the treatment of its manifestations, and reduce its long-term disability and mortality. As well, the economic analysis dramatically demonstrates the need to determine accurate incidence and prevalence rates of cardiovascular disease in Canada in order to plan the appropriate allocation of scarce health care funds.

FIGURE 18
Direct Costs of Cardiovascular Diseases, \$Millions (%),
Canada 1993



Total Direct Costs of CVD, 1993: \$7,354,253,000
SOURCE: Laboratory Centre for Disease Control, 1997

FIGURE 19
Indirect Costs of Illness by Disease Category,
Canada, 1993

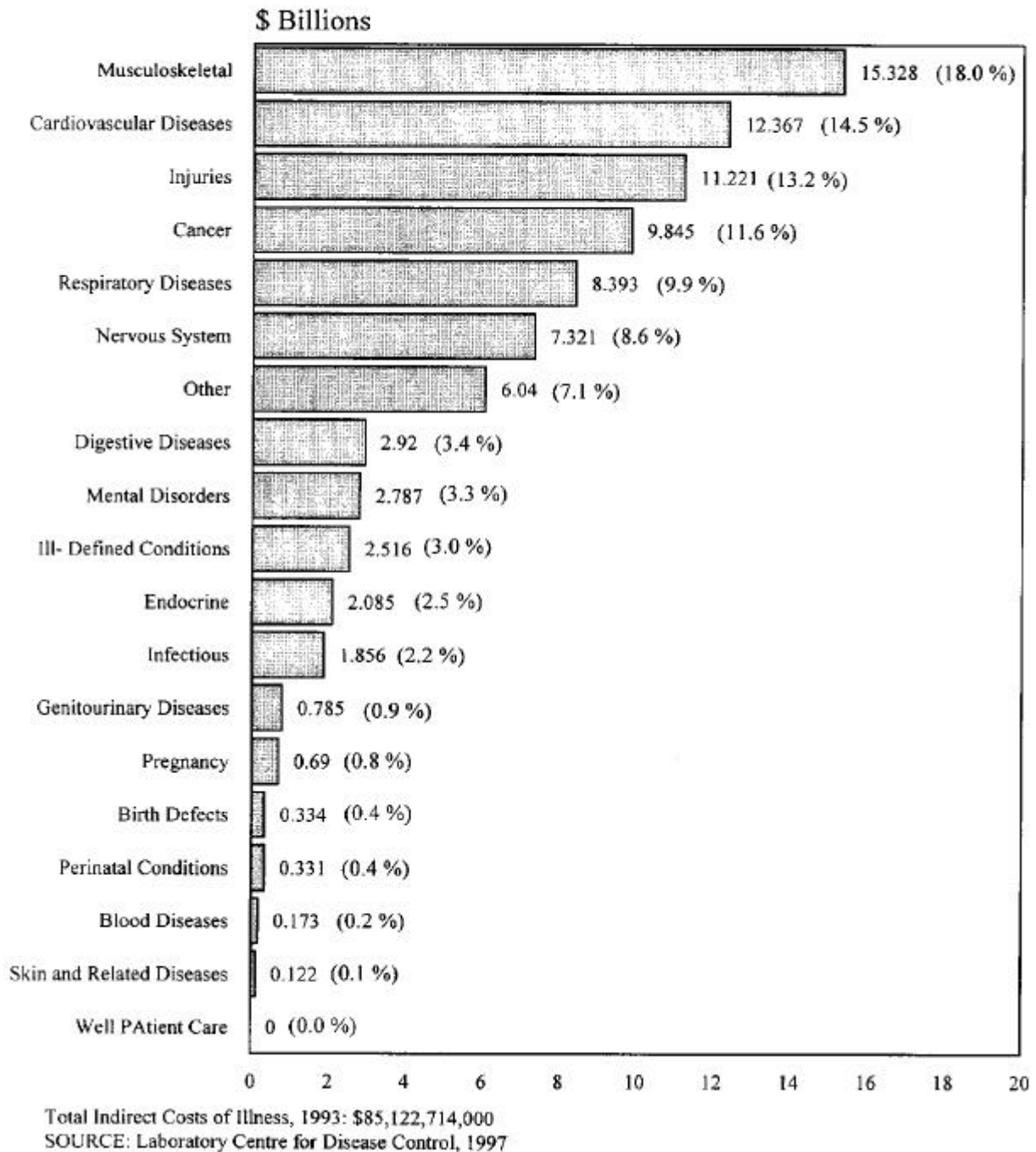
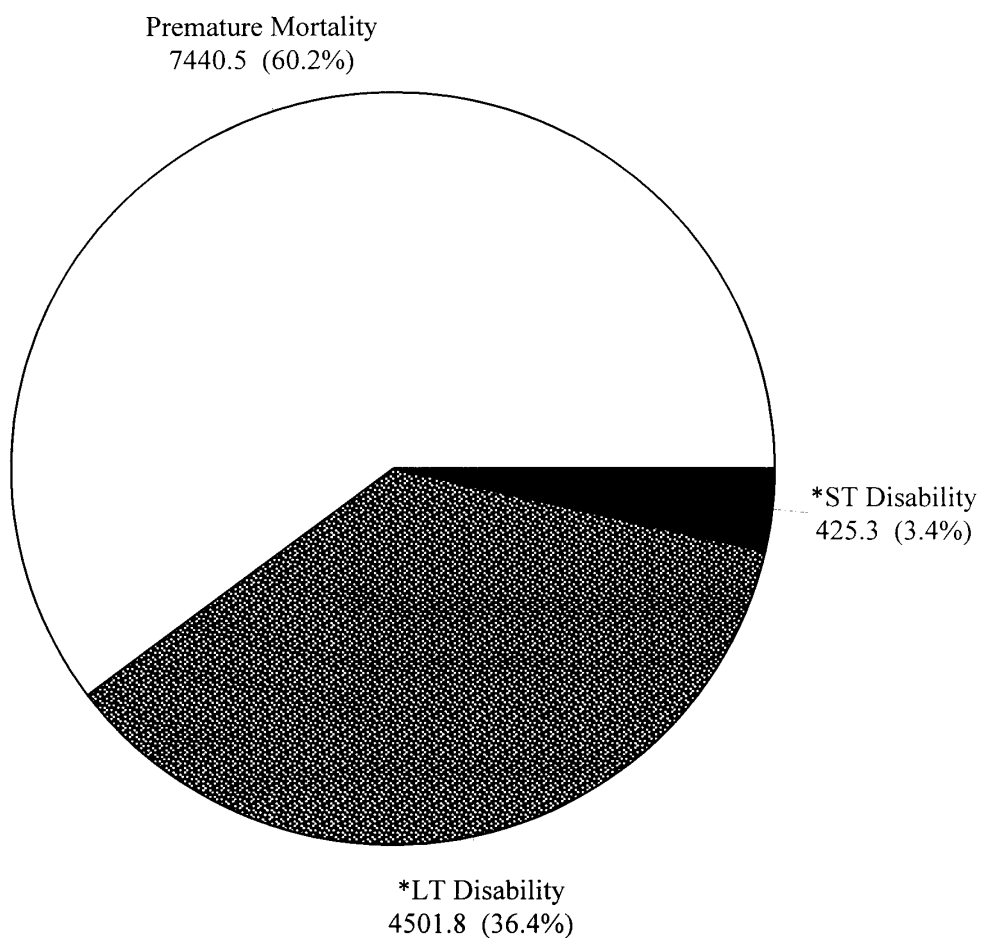


FIGURE 20
Indirect Costs of Cardiovascular Diseases, \$Millions (%),
Canada 1993



*LT = Long-Term; ST = Short-Term

Total Indirect Costs of CVD, 1993: \$12,367,592,000
 SOURCE: Laboratory Centre for Disease Control, 1997

6. RISK FACTORS FOR CARDIOVASCULAR DISEASE

6.1 Risk Factors for Ischemic Heart Disease

Considerable research has identified the major risk factors for ischemic heart disease.³⁸ Some factors such as family history of premature ischemic heart disease, age, and male sex are "non-modifiable." Smoking, elevated blood cholesterol, high blood pressure, and physical inactivity are considered "modifiable" through individual behaviour change or treatment. Both diabetes and obesity are considered to be risk factors for cardiovascular disease. There are other risk factors, not yet well defined, which may contribute to ischemic heart disease³⁹ (section 6.1.7).

As part of the Canadian Heart Health Initiative⁴⁰, the prevalence of risk factors in Canadian adults has been determined using a standardized methodology.⁴¹ Survey data were obtained from 23,251 Canadians between the ages of 18 and 74 and the results from ten provinces have been reported.^{42,43}

For the major risk factors of smoking and high blood pressure, there is a definite east to west gradient, with eastern provinces demonstrating a higher prevalence than western provinces (Table 9). The exceptions are high blood pressure in Quebec and smoking in Ontario, which have the lowest respective rates for these risk factors. There is a similar but less striking trend for sedentary lifestyle and obesity, but relative uniformity of risk from elevated blood cholesterol.

6.1.1 Smoking

In the 1986-92 Canadian Heart Health Surveys⁴³, the prevalence of smoking was highest in Atlantic Canada and Quebec, while Ontario and Saskatchewan had the lowest rates (Table 9). Percentages ranged from a high of 36% (of the 18-74 population) in Newfoundland to 23% in Ontario. Smoking rates also varied by age, with males ages 18-24 having the highest rates at 34%, while 31% of females ages 25-34 smoke regularly (Table 10); the national average of all age groups is 27%. There is little difference in the overall smoking rates of men and women (28% and 25% respectively). Approximately one-third of the population between the ages of 18-44 smoke regularly; the percentages in each age group then decline as the population ages (Table 10). As reported in the Survey on Smoking in Canada 1994, there have been no real changes in the overall prevalence of smoking since 1986.⁴⁴

The 1994 Youth Smoking Survey, Health Canada, confirms that younger people smoke more than older people, and more young people are starting to smoke. It is estimated that 29% of 15-19 year-olds are current smokers, and smoke an average of 13 cigarettes per day. As well, 14% of 10-14 year-olds are current smokers, smoking an average 10 cigarettes per day.⁴⁵ Smoking among teens 15-19 years of age has increased by 25% since 1991.⁴⁵ This increase has dire implications for the future health of Canadians, as it is estimated that 85% of smokers started smoking prior to the age 16; therefore, if this trend of more teens starting younger continues, we can then anticipate a greater number of adult smokers in the future. With the

TABLE 9
Percentage (%) of Population Aged 18-74 with Selected Risk Factors, by Province,
Canada, 1986-1992

	PROVINCES¹										
Risk Factors	BC (%)	AB (%)	SK (%)	MB (%)	ON (%)	PQ (%)	NB (%)	NS (%)	PE (%)	NF (%)	Canada² (%)
At least one major risk factor ³	59	58	61	62	61	67	67	69	65	69	63
<u>Major risk factors</u>											
Regular smoking ⁴	25	27	24	25	23	32	31	33	29	35	27
High blood pressure ⁵	13	15	16	16	17	13	19	19	20	22	15
Elevated blood cholesterol ⁶	43	37	43	44	40	48	46	44	45	43	43
Sedentary lifestyle ⁷	29	37	31	45	39	37	45	42	44	48	37
<u>Other risk factors</u>											
Obesity ⁸	27	33	35	36	31	28	36	36	37	42	31
Diabetes ⁹	4	5	5	5	4	5	5	-	4	6	4

1 British Columbia (BC), Alberta (AB), Saskatchewan (SK), Manitoba (MB), Ontario (ON), Quebec (PQ), New Brunswick (NB), Nova Scotia (NS),, Prince Edward Island (PE), Newfoundland (NF)

2 Excluding Yukon Territory and Northwest Territories

3 More than one of regular smoking, high blood pressure and elevated blood cholesterol

4 One or more cigarettes per day

5 Diastolic pressure ≥ 90 mmHg or being treated with medication, a salt-restricted diet or weight-reduction program.

6 Total plasma cholesterol level ≥ 5.2 mmol/L

7 Respondents not physically active during leisure time at least once a week during the month preceding the survey

8 Body Mass Index ≥ 27 or over (Body Mass Index = Weight in kg/(Height in m)²)

9 Self-reported; Diabetes information not collected for Nova Scotia

SOURCE: Canadians and Heart Health: Reducing the Risk; Health Canada, 1995; Canadian Heart Health Surveys

TABLE 10

Percentage (%) of Population aged 18-74 with Selected CVD Risk Factors, by Age and Sex, Canada 1986-1992

	AGE GROUPS						
Risk Factor	18-24	25-34	35-44	45-54	55-64	65-74	TOTAL
MALES							
Smoking ¹	34	32	29	27	22	17	28
High Blood Pressure ²	6	12	21	26	51	55	25
Elevated cholesterol ³	13	29	54	62	59	61	45
Sedentary lifestyle ⁴	31	35	45	44	44	38	40
Obesity ⁵	16	26	36	47	51	40	35
One or more major risk factors ⁶	39	52	65	74	85	82	64
Two or more major risk factors ⁶	6	14	28	31	36	38	24
FEMALES							
Smoking ¹	27	31	28	25	18	15	25
High Blood Pressure ²	1	3	6	22	43	58	18
Elevated cholesterol ³	17	24	31	58	78	78	43
Sedentary lifestyle ⁴	27	33	35	42	41	39	36
Obesity ⁵	15	17	25	33	46	40	28
One or more major risk factors ⁶	34	47	51	66	81	88	58
Two or more major risk factors ⁶	4	7	11	26	40	48	20

1 Prevalence in all Canadian provinces.

2 Regular cigarette smoker: one or more cigarettes per day, every day.

3 Diastolic blood pressure ≥ 90 or systolic BP ≥ 140 mm Hg and/or pharmacologic or non-pharmacologic treatment.

4 Total plasma cholesterol ≥ 5.2 mmol/L.

5 Body Mass Index ≥ 27 ; Body Mass Index = Weight in kg/(Height in Metres).

6 Major risk factors: regular smoker, high blood pressure, elevated blood cholesterol.

SOURCE: Canadian Heart Health Surveys: A Profile of Cardiovascular Risk. Canadian Medical Association Journal. 1992;146:1969-2029. Unpublished data, Canadian Heart Health Surveys.

increase in cigarette smoking among young girls and women, and the fact that smoking is one of the four major risk factors for heart disease, it can be anticipated that the mortality due to ischemic heart disease will increase and the difference between men's and women's mortality rates in the younger age-group will be reduced.

It is estimated that 41,408 deaths in Canada in 1991 were attributable to smoking,⁴⁵ which is 21% of all deaths in Canada. Of these smoking-related deaths, acute myocardial infarction accounted for 25% of male deaths and 20% of female deaths. Smoking exacts both a personal and an economic toll. In 1991, the estimated economic costs of smoking to Canadian society totalled approximately \$15 billion. This estimate included 4 million days in hospital, 3.3 million doctor visits, 1.4 million prescriptions, and 28 million days of absenteeism from work. As well, the 41,408 deaths translates into approximately \$10.6 billion in lost future income.⁴⁵

6.1.2 Elevated Blood Cholesterol

The association between elevated blood cholesterol and ischemic heart disease has long been known. Results from long-term population studies such as the Framingham study³⁸ have validated the association. Studies in other countries continue to illustrate this point. A study of 49,000 men and women in Sweden demonstrated both an increased mortality rate from coronary artery disease and cardiovascular disease, but also showed an increase in all-cause mortality at elevated cholesterol levels, even after adjustment for age, smoking, systolic blood pressure and body mass index.⁴⁶ A 2% decrease in ischemic heart disease has been associated with a 1% lowering of low density lipoprotein cholesterol (LDL-C) in middle-aged men.⁴⁷ Forty-five and forty-three percent (45% and 43%) of men and women respectively have elevated total plasma cholesterol (>5.2 mmol/L)^{43,48} (Table 10). In men, there is a rapid increase in the prevalence of elevated total cholesterol after age 34 (Table 10), whereas in women, the dramatic increase comes a decade later after age 44, then exceeds that of men after the age of 55.

Elevated low density lipoprotein cholesterol (LDL-C) and decreased high density lipoprotein cholesterol (HDL-C), particularly in the presence of elevated triglycerides, are more precise indicators of ischemic heart disease risk than total blood cholesterol.⁴⁹ Measurement of these lipid fractions may identify additional people at risk and at the same time prevent the entry into treatment of individuals who have elevated total cholesterol but low LDL-C and high HDL-C. Forty percent (40%) of men and 32% of women respectively have elevated LDL-C (>3.4mmol/L) and 13% of men and 4% of women have depressed HDL-C levels (<0.9mmol/L).⁴⁸ While elevated LDL-C and low HDL-C are risk factors for ischemic heart disease in both men and women, a consistent association between high triglyceride levels and ischemic heart disease has been found only in women. In general, when HDL-C is taken into account, triglyceride levels do not improve the prediction of cardiovascular disease. However, in women with low level of HDL-C, high triglyceride levels have been associated with increased risk of ischemic heart disease.⁵⁰⁻⁵² Recent findings from the Quebec Cardiovascular Study showed that other lipid fractions or associations may identify high risk subjects. This study, done in men, demonstrated that Apoprotein-B was the most important determinant of risk, small dense LDL-C increased the risk independently of Apoprotein-B, and the higher concentration of both of these lipid fractions increased the risk by 6-fold from baseline.^{53,54}

6.1.3 High Blood Pressure

High blood pressure is an independent risk factor for cardiovascular disease^{36,55} and can increase the risk by 2-3 fold.⁵⁶ Twenty-five percent (25%) of Canadian men and 18% of Canadian women have high blood pressure (Table 10), defined as a systolic blood pressure ≥ 140 mmHg or a diastolic blood pressure of ≥ 90 mmHg and/or are undergoing treatment.^{43,57}

At ages 18-24, 6% of men and 1% of women have high blood pressure (Table 10). From that age on in both men and women, there is a steady increase in the prevalence of high blood pressure. After the age of 64, the prevalence is approximately equal between men and women.

Twenty-six (26%) of individuals with high blood pressure are unaware of their condition. Of those aware, only 57% are treated and controlled; that is, they have a diastolic blood pressure ≤ 90 mmHg. Women are more likely than men to be aware that they have high blood pressure, and are more likely to have their pressure under control if it is treated.^{43,57}

It is well known that hypertension predisposes to all cardiovascular disease outcomes: coronary artery disease, stroke, congestive heart failure, and peripheral artery disease. Hypertension tends to cluster with other atherogenic risk factors, including dyslipidemia, glucose intolerance, insulin resistance, obesity, and increased uric acid. Treatment of high blood pressure should be based on the multivariate risk profile.⁵⁸ Data from the ongoing Framingham study has shown no change in hypertension prevalence in four decades.⁵⁶ In hypertensive males and females 35-45% of acute myocardial infarctions are silent and/or unrecognized.⁵⁹

6.1.4 Physical Inactivity

Physical inactivity is recognized as a major risk factor for ischemic heart disease.⁶⁰ The 1988 Campbell's Survey of the Well-Being of Canadians is part of a longitudinal study examining physical activity and health patterns of Canadians.⁶¹ With age, there is a general decline in activity except for Canadians over 65 who are more active than those in the 45-64 age group. During the past 20 years, however, the Canadian population has become generally more active.^{61,63}

The Canadian Heart Health Surveys show that a sedentary lifestyle is widely prevalent (Table 9); 38% of adult Canadians are inactive in their leisure time. Almost half of individuals aged 18-74 in Newfoundland have a sedentary lifestyle; over 40% of those in the other Maritime provinces also exhibit this risk factor. British Columbia has the lowest percentage (29%) of sedentary individuals.

The Heart and Stroke Foundation of Canada, in its position statement on physical activity, recommends that regular physical activity, when properly undertaken, can be effective in preventing and limiting the disabling effects of heart disease and stroke.⁶⁴ Specific recommendations suggest that individuals of all ages should be active on a daily basis, and that individuals should incorporate fitness-enhancing activity into their normal routine. It is suggested that schools ensure that quality, daily physical and health education is provided. As well, it is recognized that physical activity is a vital component in maintaining good health, and that physical activity is often a beneficial component in cardiac and stroke rehabilitation programs.

The importance of physical inactivity as a cardiovascular risk factor has been addressed formally at several levels. The first ever U.S. Surgeon General's Report on Physical Activity was released in July, 1996, to coincide with the Olympic Games in Atlanta, Georgia.⁶⁵ The report is an exhaustive review of the benefits of exercise, thorough reviews of studies assessing the risks and benefits of exercise, and numerous recommendations for both the individual and the community. A new position is that even moderate activity on a regular basis can increase health and well-being; physical activity need not be strenuous to achieve health benefits. Sedentary individuals have a 1.2-2 fold increased risk of more premature death than active individuals. Five large cohort studies demonstrated that low levels of physical activity increased the risk of ischemic heart disease mortality. They also demonstrated a dose-response relationship; benefit occurs at moderate levels, but an increased benefit occurs with increasing levels of physical activity. The report reviewed 36 studies since 1953, looking for a specific coronary heart disease benefit, which was found to be derived from the beneficial effect on serum cholesterol, body mass index, blood pressure, and diabetes.

Twenty studies on hypertension and exercise were reviewed. The most active individuals had a 30% decreased risk of developing hypertension. One randomized trial on primary prevention of hypertension, focusing on nutrition and physical activity, found that the incidence of hypertension in the study group was one-half that of the control group, even after adjustment for gender, age, and body mass index. The report examined 22 studies on the effect on exercise on known hypertensives: aerobic exercise (30-60 minutes 3-4 times/week) decreased both the systolic and diastolic blood pressure by 6-7 mmHg.

The Surgeon General's Report places a new emphasis on amount rather than intensity of physical activity, and demonstrates that health benefits from exercise are achievable for most. It recommends cardiorespiratory fitness supplemented with strength-developing exercise at least twice per week. It has also shown that the level of decreased risk of coronary heart disease attributable to regular physical activity is similar to other lifestyle factors.

6.1.5 Diabetes Mellitus

Numerous studies have shown the clustering of cardiovascular disease risk factors in diabetics, including obesity, hypertension, elevated blood cholesterol, and smoking⁶⁶. Overall, 4% of Canadian men and 5% of women report having diabetes mellitus⁴³. This prevalence ranges from 1% in the youngest (15-34 years) to 12% in the oldest (55-74 years) age groups among men and from 3% to 9% among women respectively.⁶⁷ The true prevalence of diabetes in Canada may be double that of self-reported diabetes, based on evidence from North American studies that approximately 50% of adult with diabetes have not been diagnosed with the condition.⁶⁸ The prevalence of diabetes varies among ethnic groups. The prevalence of self-reported diabetes among the aboriginal population age 15 and over is 6.5% with a prevalence rate as high as 22% among those over 65 years of age. About two-thirds of the aboriginal population with diagnosed diabetes are women.⁶⁹

6.1.6 Obesity

Obesity, especially abdominal obesity, is associated with an increased risk of ischemic heart disease.^{70,71} Thirty-one percent (31%) of Canadian adults are obese (body mass index (BMI) ≥ 27) (Table 9) with the prevalence being greater among men than women (Table 10). With age, the prevalence of obesity increases in both men and women. Yet, for men a decrease is observed following age 65 so that in the 65-74 age group the prevalence of obesity in men and women is equal.

With increasing obesity there is a rise in the prevalence of an abdominal distribution of fat as measured by waist-hip ratio. A waist-hip ratio of > 0.9 for men and > 0.8 for women is an indication of abdominal obesity. More men (50%) than women (34%) have abdominal obesity with the prevalence also increasing with age,^{43,67}

Obesity and abdominal fat distribution are both associated with an increased prevalence of diabetes, high blood pressure and elevated plasma cholesterol. The prevalence of high blood pressure, for example, is more than doubled among individuals with abdominal obesity.⁶⁷ Therefore, it is desirable to maintain a healthy BMI in the range of 20-25 for both men and women.⁷² Data from the long-term Framingham study shows that the degree of overweight is proportional to the rate of development of cardiovascular disease. Over a follow up of 26 years, data showed that each standard deviation increase in weight was associated with a 15% and 22% increase in cardiovascular disease events in men and women respectively.⁷³ Weight control is important for the control of other cardiovascular disease risk factors. The percent of hypertension that is attributable to obesity is estimated to be 78% in men and 65% in women.⁵⁹

6.1.7 Other Factors

Recent research suggests that a number of other factors may play a role in the development of cardiovascular disease. These factors include altered thrombogenic, inflammatory and immunologic responses, dietary iron, and psychosocial factors, including anger. Anger is associated with myocardial ischemia and arrhythmias, theoretically through activation of the sympathetic nervous system which leads to sinus tachycardia, hypertension, impaired myocardial perfusion and a high degree of cardiac electrical instability.⁷⁴ Biological antioxidants such as beta carotene, ascorbic acid, vitamin E, and selenium may have a protective effect; Canada is presently directing a large international trial, called HOPE, involving 9,000 high risk men and women to determine whether or not vitamin E reduces cardiovascular mortality, myocardial infarction and stroke.⁷⁵ A recent study suggests that smokeless tobacco use is related to cardiovascular disease, as well as increasing the risk of oral cancer.⁷⁶ Recently, hemostatic variables have been included in studies of cardiovascular risk. Most myocardial infarctions and cardiac deaths are precipitated by acute occluding coronary thrombi; as well, thrombosis participates in atherogenesis. In prospective studies, fibrinogen was found to be an independent predictor of myocardial infarction in both males and females and of stroke in males; it appears that the fibrinogen level provides information on risk profile over and above that supplied by established risk factors.⁷⁷ Ongoing studies are evaluating the role of elevated homocysteine and folic acid deficiency as risk factors for cardiovascular disease. Several studies have shown that total serum homocysteine is a strong and independent risk factor for stroke⁷⁸ and that elevated

homocysteine contributes to premature arteriosclerosis, arterial thrombotic events and venous thromboembolism.⁷⁸ Further work is required before recommendations can be made regarding these factors.³⁹

6.1.8 Multiple Risk Factors

The hallmark of cardiovascular disease risk is the synergistic effect of more than one risk factor on overall cardiovascular disease risk. Even moderate elevations in more than one risk factor increases cardiovascular disease risk.⁷⁹

Seventy-five percent (75%) of Canadian adults have at least one of the major cardiovascular disease risk factors (high blood pressure, elevated blood cholesterol regular smoking and sedentary lifestyle)^{43,80} (Table 9). The prevalence of at least one risk factor increases substantially with age until it reaches a plateau at age 55 in both men and women (Table 10). Over ninety percent (>90%) of Canadian adults age 65-74 have at least one major risk factor. Men, aged 55-64, and women, aged 65-74 years of age have the highest occurrence of two or more risk factors (63% and 64% respectively) (Table 10).

TABLE 11

**Percentage of Individuals Mentioning Selected Risk Factors
as Causes of Heart Disease**

RISK FACTOR	YEARS OF EDUCATION					
	MEN			WOMEN		
	≤6	7-11	≥12	≤6	7-11	≥12
Smoking ¹	35	54	55	29	52	59
High BP ²	13	25	27	20	29	31
Elevated CHOL ³	16	30	37	16	28	36
Obesity ⁴	23	37	43	31	46	52
Lack of exercise	17	33	51	8	32	49
Stress	17	34	44	25	39	51

SOURCE: Macdonald et al. Multiple Cardiovascular Disease Risk Factors in Canadian Adults. Canadian Medical Association Journal, 1992;146:2021-29.
Unpublished data, Canadian Heart Health Surveys.

TABLE 12**Percent of Individuals with One or More Major Risk Factors¹ by Years of Education**

	YEARS OF EDUCATION			
	MEN		WOMEN	
Age (years)	≤12	≥12	≤12	≥12
18-24	71	51	64	37
25-34	75	54	70	56
35-44	83	75	70	55
45-54	87	81	85	67
55-64	91	90	89	94
65-74	92	85	95	88
Total	83	68	79	60

1. Major risk factors: regular smoker, high blood pressure, elevated blood cholesterol.

SOURCE: Macdonald et al. Multiple Cardiovascular Disease Risk Factors in Canadian Adults. Canadian Medical Association Journal, 1992;146:2021-29.
Unpublished data, Canadian Heart Health Surveys.

6.1.9 Public Knowledge on Causes of Cardiovascular Disease

More than 90% of Canadians recognize that cardiovascular disease is preventable. However, the majority do not recognize the specific risk factors⁸⁰ (Table 11), although the higher the level of education, the more likely individuals are to identify specific risk factors. Smoking was one of the most commonly reported risk factors associated with cardiovascular disease and was reported more often by smokers than by non-smokers.⁸⁰ The next most commonly reported risk factors were obesity, stress, and a lack of exercise (Table 11).

6.1.10 Socioeconomic Status and Risk Factors

Prevalence and awareness of risk factors varies with socioeconomic status. Canadians with a lower level of education (a proxy measure of socioeconomic status) are more likely to have risk factors for cardiovascular disease⁸⁰ (Table 12) yet are less likely to identify these as risk factors (Table 11). Lower socioeconomic groups are less aware than upper socioeconomic groups of high blood pressure and elevated blood cholesterol as risk factors.

6.2 Risk Factors for Stroke

Risk factors for stroke can be divided broadly into two categories: non-modifiable and modifiable. The non-modifiable risk factors include the patient's age and a family history of stroke. The presence of diabetes is associated with an increased risk of stroke, however it is not clear whether optimal diabetic control can result in a decrease in stroke incidence.

High blood pressure is the most important modifiable risk factor for stroke. Other modifiable risk factors for stroke are smoking, physical inactivity, and diabetes. Pre-existing conditions such as the presence of atrial fibrillation and a previous transient ischemic attack (TIA) are also important risk factors for stroke.⁸¹

6.2.1 High Blood Pressure

High blood pressure remains the number one preventable risk factor for stroke with an estimated 56.4% (males) and 66.1% (females) of strokes attributable to this factor.⁸² The overall age-adjusted risk of stroke among hypertensives compared to normotensives is 3.1 for men and 2.9 for women. The risk of stroke increases with both increasing systolic and diastolic pressures.

Recent evidence indicates that isolated systolic hypertension is a major risk factor for stroke in the elderly⁸³ and is a stronger predictor of stroke than elevated diastolic blood pressure.⁸⁴ Isolated systolic hypertension is defined as a systolic blood pressure of 160 mmHg or over and a diastolic pressure of less than 90 mmHg. Isolated systolic hypertension may be present in approximately 30% of women and 10% of men over the age of 80. There is good clinical evidence that treating such isolated systolic hypertension in those 60 years of age and over will decrease the incidence of stroke. Therapy also slows progression of carotid artery narrowing secondary to atherosclerosis.⁸³

6.2.2 Smoking

Cigarette smoking remains a well-known risk factor for stroke.^{85,86} The Honolulu Heart Program showed that cigarette smoking, as an independent risk factor, significantly increased the risk of stroke, intracerebral and subarachnoid hemorrhage. The risk is dose related with smoking more than 25 cigarettes per day conferring the highest risk. A recent analysis of 32 separate studies showed smoking to be a significant independent contributor to stroke incidence in both sexes and at all ages.⁸⁷ The risk of stroke was approximately 50% higher in smokers than in non-smokers and rose substantially with the number of cigarettes smoked per day in both men and women.

Based on the data from the Nurses Health Study and the Framingham study, cessation of smoking is followed by a reduction in risk of stroke to baseline over a remarkably short time. The risk of stroke falls to approximately 50% within one year and reaches the levels of those who have never smoked within five years.⁸⁸ There appears to be no age related effects as there is a decrease in risk with smoking cessation in both young and older individuals.

6.2.3 Atrial Fibrillation

Atrial fibrillation is a well-known risk factor for stroke and is a common problem, occurring in up to 10% of patients over the age of 75. Recently, several studies have shown conclusively that the risk of stroke in patients with untreated atrial fibrillation is high.⁸⁹⁻⁹¹ This may reach 7% per year in patients who, in addition to atrial fibrillation, also have a previous history of embolic disease, hypertensive heart disease, a previous history of congestive heart failure or echocardiographic evidence of a left atrial abnormality. Proper assessment and careful use of anticoagulants or antiplatelet agents can significantly decrease the risk of embolic stroke. Studies have

demonstrated that the annual incidence of a stroke in those with chronic non-valvular atrial fibrillation is 4.5%; oral warfarin decreases the incidence to 1.4%.⁹² As well, after TIA or a stroke, warfarin decreases the risk of a second stroke from 12% to 4%.⁹²

6.2.4 Transient Ischemic Attack

Patients who have had a recent TIA or a completed stroke are at a very high risk of a subsequent stroke.⁹³ This is dependent on the degree of carotid stenosis and the presence of associated risk factors. In patients with bilateral carotid stenosis, the risk may be as high as 39% in the first 18 months.⁹⁴ This risk is highest immediately after the event and then slowly decreases thereafter. In most patients, the stroke is secondary to thrombus formation in the carotid artery with subsequent distal embolization. Infrequently, an episode of hypotension in the presence of critical carotid stenosis may result in an infarction in the same arterial territory. Recognition of TIA is important because treatment can significantly decrease the risk of recurrence of stroke.⁹⁴⁻⁹⁶

6.2.5 Physical Inactivity

Leisure time activity and work-related vigorous physical activity have been shown to lower the incidence of stroke. Although most initial evidence was related to heart disease, there are now some data which show that increasing activity also leads to a decrease in the incidence of stroke.⁹⁷ Underlying mechanisms, though not fully understood, are likely multifactorial. Exercise has a beneficial effect on risk factors for cardiovascular disease; thus physical activity may help reduce elevated blood pressure and improve weight loss and the LDL-C to HDL-C ratio. These changes would then improve the risk factor profile for stroke. Exercise is also associated with positive lifestyle choices that include non-smoking, improved eating habits and maintenance of a healthy body weight.⁹⁸

6.2.6 Diabetes Mellitus

Individuals with diabetes have an increased risk of stroke. Men with diabetes have a 6-fold increased risk of death from stroke, while women with diabetes have an 8.2-fold increased risk of death.⁹⁹ Of stroke deaths, 16% of male deaths and 33% of female deaths are attributable to diabetes.⁹⁹

6.2.7 Other Risk Factors

Other risk factors for stroke include an increased hematocrit, elevated fibrinogen levels, obesity, alcohol consumption and lipid abnormalities. Prospective studies have shown that fibrinogen levels are an independent predictor of acute myocardial infarctions in both men and women, but of stroke in men only.¹⁰⁰ Several ongoing investigations are looking at the relationship between a patent foramen ovale (PFO) and subsequent embolic events. Results from a recently conducted study consisting of 140 subjects with a PFO who presented with a stroke, demonstrated that the stroke was not commonly due to a coexisting cause of stroke.¹⁰¹ Several studies have shown that total serum homocysteine is a strong and independent risk factor for stroke.⁷⁸ The relationship between the risk of stroke and the above risk factors remains controversial.⁸¹

7. PREVENTION OF CARDIOVASCULAR DISEASES

7.1 Opportunities for Prevention

A recent analyses of the secular trends in risk factor levels and improvements in treatment has demonstrated the significant impact that prevention has had on the decline in coronary heart disease mortality.¹⁰² Primary and secondary risk factor reduction may explain approximately 50% of the decline in coronary mortality. Twenty-five percent (25%) of the decline is explained by primary prevention, while 29% is explained by secondary reduction in risk factors in patients with diagnosed coronary artery disease. Improvements in treatment account for approximately 43% of the observed decline.¹⁰²

Optimal prevention requires the use of primary, secondary and tertiary prevention strategies. Primary prevention, by risk factor modification, can reduce disease incidence; secondary prevention, through early identification and management of the disease states, can increase survival; tertiary prevention, through the rehabilitation from established disease, can further reduce disability and suffering and so enhance individual quality of life.

Primary prevention of cardiovascular disease involves a three-pronged strategy that includes: a general population approach; a targeting of those at high risk; and the management of psychosocial determinants of cardiovascular disease.^{40,43} Within Canada, the differences in incidence and mortality rates that are observed between provinces leads one to believe that opportunities exist for enhanced prevention.¹⁰³ Internationally, the North Karelia project has demonstrated that effective changes can result from programs that are community-based and are targeted at both the general population and individuals at high risk of cardiovascular diseases.¹⁰⁴⁻¹⁰⁷

7.2 The Role of Research

Although cardiovascular disease constitutes one of the major health problems in Canada, funding allocation for research (\$59 million), does not reflect this, and lags behind that for cancer (\$73 million) and disorders of the nervous system (\$62 million).³⁶

Death rates from cardiovascular disease are declining, while the economic costs of cardiovascular disease are increasing. The challenge is not only to improve the quality of care and quality of life of diseased individuals but also to reduce the incidence of the disease so as to minimize its social and economic costs.

7.3 The Canadian Heart Health Initiative (CHHI)

The Canadian Heart Health Initiative is a national approach to heart health that developed from the broad consultations carried out by the Federal-provincial Working Group on Cardiovascular Disease during the mid 1980's. With the collaboration of numerous interested health and non-health sectors, a consensus was developed on strategies for cardiovascular disease prevention in Canada. The report of the working group, Promoting Heart Health in Canada¹⁰⁸ recommended an integrated multi-factorial approach toward the prevention or

control of risk factors by achieving environmental changes favourable to heart healthy lifestyles.

Promoting Heart Health in Canada serves as the policy blueprint for the CHHI. The report's strategic options —public health system leadership; community programs, intersectoral co-ordination; access to health services; public education and information; and monitoring, evaluation and research — have been adopted as CHHI strategies. This Initiative is a partnership between Health Canada and the provincial Ministries of Health, in collaboration with the Heart and Stroke Foundation of Canada (34). The CHHI accommodates the fundamental principles of health promotion as described in *Achieving Health for All: A Framework for Health Promotion*.¹⁰⁹

The main agents of the CHHI are coalitions at national, provincial and community levels. Four phases of the Initiative have been planned.

The first phase (1987-92), a cardiovascular disease risk factor survey in all 10 provinces, has been completed.⁴³ The national database documented the Canadian and provincial risk factor profiles, as well as the levels of knowledge and awareness of cardiovascular disease. This database is proving to be instrumental in planning appropriate interventions that will meet the specific needs of Canadian communities.

The second phase (1989-98), involves the implementation of demonstration heart health programs in each province. Programs underway include public and professional education, worksite programs, school health and public policy development.

Evaluation of these programs and of the Initiative as a whole comprises the third phase. This will provide information on how the programs work and will demonstrate health promotion opportunities to other Canadian communities.

The dissemination phase (1994-2002) studies processes and factors which facilitate or hinder the adoption of effective interventions. Four provinces have already started in this phase.

The Heart and Stroke Foundation of Canada and its affiliated provincial foundations play a major role in supporting activities conducted under the auspices of the Canadian Heart Health Initiative. The Foundation is broadly acknowledged for significant research and professional educational activities. Ongoing public education programs as Jump Rope for Heart, Know Your Blood Pressure by Heart, and the Heart Smart^a restaurant and cooking programs continue to provide significant exposure for the Foundation while responding to consumer demand for meaningful and practical resources.

7.4 *International Heart Health*

International conferences on Heart Health have been convened twice. The first, held in Victoria, British Columbia in 1992, proposed a worldwide partnership of policy development and program implementation towards heart health promotion and cardiovascular disease prevention, using a public health approach to eliminate or reduce risk factors.¹¹⁰

The second International Heart Health conference was convened in Barcelona in May, 1995, to address the increased burden of cardiovascular disease, the global inequalities that exist in the rates, trends, and causes of cardiovascular disease, and the resources available for control efforts. The purpose of the Catalonia Declaration is to show investing in heart health can decrease heart attacks, strokes and resulting disability and loss of life. Improved health with a resulting decrease in cardiovascular disease and thus decreased medical costs will produce economic benefits.¹¹¹ The Catalonia Declaration builds on the strategy recommendations of the Victoria Declaration and described worldwide examples of how investing in heart health can decrease the occurrence of cardiovascular disease and provide economic benefits. It is important to demonstrate these successes to government, industry, community groups, the media, educators, and health care services worldwide and thus suggest effective steps to decrease the incidence of cardiovascular disease. Effective steps will vary country to country, as differences in economics, health status, education and culture will produce different risk factor profiles, and thus different strategies. Therefore, the final policy design will be determined according to regional needs and customs. This declaration describes resources and assets available, the barriers to success and effective action to overcome them, plus examples of successes in countries around the world. These examples illustrate what can be done and may inspire others to attempt similar programs and policies to prevent and control cardiovascular disease.

Canada will host the 4th International Conference on Preventive Cardiology, entitled "Extending the Benefits of Prevention to All" in Montreal, June 29 - July 3, 1997. The previous conferences have been considered major fora for international scientific communications in cardiovascular disease prevention and epidemiology and the programme in Montreal promises to continue that precedent.

8. ***STROKE: CURRENT MANAGEMENT AND PREVENTION STRATEGIES***

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In this section, the current trends of stroke mortality and disability will be examined. As well, the mechanisms and management of acute stroke will be reviewed. To conclude, a section on prevention, primary, secondary, and tertiary, will be presented.

Trends in Stroke

It is well established that stroke is a major contributor to mortality and morbidity worldwide¹¹²⁻¹¹⁷. In Canada and other developed nations, the mortality due to stroke is declining^{113, 114, 117-121}. Today, Canada enjoys one of the lowest rates of death due to stroke^{112,115} however, morbidity and associated hospitalization remains unacceptably high¹¹⁴.

In Canada, the mortality rate due to stroke has declined approximately 50% over the past 20 years to the current level of 50 deaths per 100,000 Canadians per year, which represents 7% of all-cause mortality^{112,115}. The decline in stroke-related mortality has been attributed both to improved survival following stroke^{122,123} and to decreased incidence^{124,126}. Both risk factor management and health promotion have had a role to play in the declining incidence. Population-based public health strategies targeted towards smoking cessation, diet, exercise and weight control^{127,128} have contributed substantially as has medical management of hypertension, hyperlipidemia, diabetes, and cardiovascular disease. This combined effort has increased the public's awareness of the risk factors for cardiovascular and cerebrovascular disease.

However, despite this positive portrait, there is evidence that the rate of decline in incidence of stroke has reached a plateau^{122,129-132}. Reasons for this are still unclear¹³⁰. It may be that advances in diagnostic procedures have improved the detection of strokes. It is also hypothesized that current advances in the treatment of cardiovascular disease which have resulted in improved survival have placed a greater proportion of the population at risk to develop recurrent cerebrovascular disease¹³⁰.

It is believed, however, that strokes are becoming, if not less frequent, less devastating. Unfortunately, there is no systematic way in Canada for this important information to be documented. However, there is indirect evidence of this effect over time, as a greater proportion of patients have been able to return home after a stroke. In fact, each year over a ten-year period from 1982-1991, 1,000 more persons in Canada were affected by stroke. The numbers of people dying from stroke or being so severely disabled that they required permanent institutional care, however, did not increase at the same rate. In fact, the case-fatality rate for stroke declined over the period. The major gain appears to be in the

number of persons able to return home. Hospital discharge patterns provide a proxy measure for severity of stroke, thus, without a mechanism to collect data on stroke systematically in Canada, such conclusions are speculative.

Mechanisms and Management of Acute Stroke

Due to enhanced awareness of the problem of stroke and intensive research, the mechanisms of neuronal injury during cerebral ischemia are becoming better understood¹³³. While it has been known for over fifty years that brain cells die within minutes after the onset of ischemia, it has only recently become apparent that neuronal damage does not proceed uniformly across vascular territories. In infarction in the middle cerebral artery (MCA) distribution, for example, the most distal region in the vascular territory with reduced blood flow shows signs of damage very early after an acute arterial occlusion^{134,135}. Adjacent regions with collateral blood flow may survive for several hours before permanent damage becomes evident^{136,137}. This knowledge offers hope for therapeutic intervention to improve outcome¹³⁸.

One key to successful outcome after an acute stroke lies in rapid evaluation, localization of the lesion and definition of the mechanism of the disease process. Patients admitted to an acute stroke care unit do better than individuals with similar lesions admitted to a general medical service. In addition to a shortened hospital stay, such patients also have a better long-term prognosis^{139,140}. Appropriate evaluation requires an adequate knowledge of the anatomy of the cerebral vasculature, potential mechanisms of the arterial occlusion and possible therapies to prevent further insults. In most patients, a cranial computerized tomography scan and a carotid Doppler study are necessary to rule out an intracranial hemorrhage or define the extent of carotid stenosis¹⁴¹⁻¹⁴³. In some patients, more detailed investigations may be necessary to look for uncommon etiologies for the stroke.

Another key factor in obtaining a successful outcome is the provision of therapy to limit damage to the brain tissue. At the present time most patients who suffer an acute stroke present late to the hospital, with less than 5% of individuals appearing within six hours of the insult. This has presented a major challenge to the use of thrombolytic or neuroprotective agents in the treatment of an acute ischemic stroke¹³⁶. Every effort should be made to educate both individuals at risk and their family members to bring patients with acute stroke symptoms to an acute care facility as soon as possible after the onset of symptoms. Early arrival to a hospital with an acute stroke care unit may considerably improve prognosis.

The recognition and prompt management of complications following stroke is important. For several hours after the onset of symptoms, patients with an acute stroke are medically unstable. Several important measures, which could potentially prevent complications, can be applied to the patient with acute stroke. Most patients have an acute transient increase in their blood pressure. Unless the blood pressure is very high (more than 240/130 mm Hg) or if thrombolytic therapy is being offered to the patient, it is wise not to decrease the blood pressure acutely after the insult. Patients with a large hemispheric stroke or a brainstem stroke are at an increased risk for aspiration pneumonia; therefore, oral feeding should be withheld until a swallowing assessment has been completed. The presence of fever and hyperglycemia may also adversely affect prognosis and may require prompt attention¹⁴³⁻¹⁴⁵.

A major advance in the management of acute stroke which has generated excitement has been the introduction of therapies that may decrease the size of the ischemic infarction and improve outcome. Such therapies fall into two broad categories; thrombolytic and neuroprotective drugs. While there is considerable experimental evidence that they may have additive potential when used in combination, to date the two classes of medication have not been tested together in stroke patients.

Several different types of thrombolytic agents are used to dissolve blood clots that have led to the stroke. The three drugs used extensively in stroke research include tissue plasminogen activator (tPA), streptokinase, and urokinase¹⁴⁶. A major problem with the use of thrombolytic therapy after an acute stroke is the risk of intracerebral hemorrhage. This risk increases if therapy is delayed. Evidence for protection with tPA has led to its approval by the Food and Drug Administration in the United States provided the drug is administered within three (3) hours of the onset of symptoms by a team competent in the management of stroke and having 24-hour access to computerized tomography and neurosurgical services. The risk of intracerebral hemorrhage is the major limitation for general use. Intra-arterial urokinase may have fewer side effects and is currently undergoing clinical trials in acute stroke. A recent report suggests that low molecular weight heparin may also improve functional outcome if given within 24-48 hours of the onset of symptoms and continued for the first few days.

With better understanding of the mechanisms involved, it has become possible to develop medications that limit or attenuate the extent of neuronal damage. There are several types of neuroprotective drugs, which when given prior to the insult, may either prevent or significantly limit the size of the infarction. A number of such neuroprotective agents are currently undergoing clinical trials in acute stroke and subarachnoid hemorrhage¹³⁶⁻¹³⁸. An advantage to the use of such medications in acute stroke is that a cranial computerized tomography scan is not necessary prior to administration of the initial dose of the drug. As well, the neuroprotective agent may potentially be offered in the ambulance, thus saving valuable time. For these agents to be clinically relevant, the drug should show protection when given after the insult, have few side effects, and be easy to administer. While no neuroprotective therapy has been shown to provide significant protection, we hope to see promising results in the next few years.

Primary Prevention

The primary prevention of stroke is achieved through risk factor modification, by either lifestyle changes or by medical intervention. Secondary prevention alters a disease process after it has become clinically apparent. However, in the context of vascular disease, the distinction between primary and secondary prevention becomes somewhat blurred. Secondary prevention is targeted at *patients* whereas primary prevention is aimed at *populations*. Secondary prevention generally involves treating patients who are at high risk of serious vascular events. Primary prevention largely falls in the domain of policy makers and governmental public health departments, and is concerned with interventions such as the restriction of tobacco advertising. The two approaches are complementary. While individuals at high risk may benefit greatly from a given intervention, only a small proportion of all

serious vascular events occur in people at the highest risk. Most events occur among those at moderate risk. The paradox clearly mandates a multifaceted approach¹⁴⁷. Furthermore, because of the overlap between coronary artery disease, peripheral vascular disease, and cerebral vascular disease, stroke prevention should not be seen in isolation but as part of a bigger strategy to prevent all forms of vascular disease.

Secondary Prevention

For the purposes of this discussion, comments will be confined to the prevention of stroke after a transient ischemic attack (TIA) or after a first stroke.

Risk Factor Modification

1. Hypertension

Antihypertensive drug treatment reduces the risk of first stroke by about 40%¹⁴⁸. The efficacy of therapy for secondary prevention is less clear as only two small trials have been conducted among stroke survivors, and none have involved only TIA patients. The place of antihypertensive treatment in the setting of acute stroke remains unclear¹⁴⁹. Most physicians would probably treat hypertensive TIA patients and stroke survivors as they would patients who had not yet suffered a serious vascular event¹⁵⁰. For stroke patients, decisions about long-term antihypertensive treatment are best deferred for a few days after the stroke since blood pressure usually falls spontaneously during this time.

2. Hyperlipidemia

The role of hyperlipidemia in the pathogenesis of stroke, and the place of lipid lowering drugs in the prevention of stroke remain uncertain. The picture is clearer for coronary heart disease, and because TIA patients and survivors of ischemic stroke are at high risk of coronary events it seems reasonable to lower elevated plasma cholesterol levels in these individuals. The results of one trial (The Scandinavian Simvastatin Survival Study)¹⁵¹ suggest that any patient with a history of ischemic stroke or TIA, and a previous myocardial infarction, and a cholesterol level greater than 5.2 mmol/L is likely to benefit from cholesterol reduction with a statin drug. Further randomized trials are required to define more clearly who should be treated and how.

3 Smoking

Smoking is a risk factor for cerebral infarction and for subarachnoid hemorrhage¹⁵². It is well known that all tobacco users should be advised to quit. Several randomized trials have demonstrated the effectiveness of nicotine replacement therapy¹⁵³. Long-term abstinence, however, can be difficult to achieve, and requires a combination of behavioural and pharmacological approaches.

4. Alcohol

Observational studies have shown a J-shaped relationship between alcohol intake and stroke. Occasional to light alcohol consumption is protective, whereas heavy alcohol use (5 or more drinks per day) is an independent risk factor for ischemic stroke¹⁵⁴. How alcohol protects against stroke is unknown. Heavy alcohol intake aggravates hypertension, and may induce emboligenic cardiac problems such as atrial fibrillation and congestive cardiomyopathy. Alcohol may also have prothrombotic effects on platelet function and hemostatic mechanisms. Clinical trials of the influence of alcohol on stroke are not feasible, but prudence would seem to dictate that controlled alcohol intake is an important component of secondary stroke prevention.

5. Diet

The links between diet and stroke remain obscure. Nutrition counseling for patients who have had a stroke or TIA usually focuses on optimizing blood glucose control (in diabetic subjects), and on reducing saturated fat intake and increasing the intake of vegetables, fruit, and dietary fibre.

6. Exercise

Lack of physical exercise is associated with an increased risk of stroke¹⁵⁵. It is not known whether a program of increased physical activity after a stroke or TIA protects against recurrent vascular events, but there is evidence that exercise reduces mortality after myocardial infarction. Patients who have had a stroke or TIA are usually encouraged to return to normal activities and take regular moderate exercise to promote self-confidence and independence, and to help with weight control.

Antithrombotic Treatment

1. Antiplatelet Therapy

Antiplatelet treatment started a few weeks after an ischemic stroke or TIA and continued for several years reduces the risk of recurrent serious vascular events by about 25%¹⁵⁶. Two recent large randomized controlled trials (The International Stroke Trial¹⁵⁷, and the Chinese Aspirin Stroke Trial¹⁵⁸) have shown that additional benefit can be obtained by starting aspirin immediately after an acute ischemic stroke. Most of the data from randomized trials of antiplatelet therapy concern aspirin; yet there remains uncertainty about the most efficacious dose. Depending on their point of view, physicians may prescribe doses ranging from 80mg on alternate days to 1,300 mg daily. Other antiplatelet agents — dipyridamole, ticlopidine, and clopidogrel — although clearly effective, are not unequivocally superior to aspirin^{156,159,160}. These drugs may, however, be used in patients who cannot tolerate aspirin, or in those who experience ischemic vascular events while taking aspirin.

2. *Anticoagulant Therapy*

Although anticoagulants were first used to treat cerebrovascular disease more than 50 years ago, randomized controlled trials have only recently provided data to guide practising clinicians¹⁶¹⁻¹⁶³. Warfarin, at a dose sufficient to produce an International Normalized Ratio in the range 2.0 - 3.0, is the treatment of choice for the prevention of stroke in patients under age 75 who have atrial fibrillation and a history of hypertension, diabetes, congestive heart failure, or a thromboembolic event (including a TIA or nondisabling ischemic stroke). In such patients, a relative risk reduction of two-thirds or more is afforded by carefully controlled anticoagulant therapy. Atrial fibrillation occurring in young patients in the absence of the above mentioned risk factors is less ominous and does not require anticoagulant treatment. Among patients over age 75, the benefits of warfarin are less clear because of an increased risk of bleeding complications. In this group of patients, many physicians would opt to use aspirin instead of warfarin. In one trial involving patients with prosthetic heart valves, the combination of aspirin and warfarin was superior to warfarin alone for the prevention of stroke¹⁶⁴. Except in patients with atrial fibrillation or prosthetic heart valves, warfarin does not have a clearly established (evidence-based) role in secondary stroke prevention.

3. *Carotid Endarterectomy*

In patients who experience a carotid territory TIA or nondisabling stroke and have angiographic evidence of severe (70% or more) ipsilateral carotid stenosis, successful carotid endarterectomy performed within 6 months of the attack almost completely abolishes the risk of ischemic stroke in the territory of the operated artery over the subsequent few years¹⁶⁵⁻¹⁶⁶. Because surgery is so superior to medical treatment (i.e. antiplatelet therapy and risk factor modification), establishing — at the earliest opportunity — the presence (or absence) of severe carotid stenosis is the imperative of contemporary management of the patient who presents with a carotid territory TIA or minor ischemic stroke. The role of carotid endarterectomy in the management of asymptomatic carotid stenosis is much less clear. In the Asymptomatic Carotid Atherosclerosis Study¹⁶⁷ the absolute benefit afforded by surgery was small, such that about 170 patients had to be operated on in order to prevent one disabling stroke. It has been argued that this is not cost-effective medicine, particularly since the risk of a serious cardiac event is considerably higher than the risk of stroke. In Canada, there is consensus against endarterectomy for asymptomatic carotid stenosis¹⁶⁸.

Tertiary Prevention

Prevention does not stop once someone has had a stroke. There is much to be done to prevent the distressing sequelae of stroke. Early mobilization reduces respiratory difficulties, thrombosis in leg veins, skin break down, contractures, incontinence, urinary tract infections, and depression. Rehabilitation increases independence, the ability of the person to return home and take up pre-stroke activities, and the ability of the family to be able to provide care. Continued participation in physical, recreational, educational, and social activities will contribute to improvement in health and quality of life. There are increasing numbers of persons in the community who are living with the sequelae of stroke and who are at risk for

diminished activity level, social isolation and recurrent stroke. Services targeted at tertiary prevention are, therefore, essential if the outcome of stroke is to improve. Currently, in Canada, access to these services are minimal and threatened as provinces look for ways of cutting costs.

Increased awareness of risk factors and lifestyle changes to reduce these risk factors even after stroke will go a long way towards preventing a recurrence. The perception that "you can't teach an old dog new tricks (especially one with a stroke)" needs to be dispelled. Prevention of stroke at all levels can improve the health of Canadians.

9. GLOSSARY

ACUTE MYOCARDIAL INFARCTION: (ICD-9 410) A manifestation of ischemic heart disease, describing a severe sudden onset of myocardial necrosis due to the formation of a thrombus in the coronary arterial system obstructing arterial blood flow to that section of cardiac muscle.

AGE-STANDARDIZED RATES: The standardized rate represents what the crude rate would be if the population under study had the age distribution of the standard population. It is the weighted average of age-specific rates applied to a standard distribution of age.

ANGINA PECTORIS: (ICD-9 413) A symptomatic manifestation of ischemic heart disease, describing a severe squeezing or pressure-like thoracic pain, brought on by exertion or stress.

CARDIOVASCULAR DISEASE: All diseases of the circulatory system classified according to ICD-9 390-459. They include acute myocardial infarction, ischemic heart disease, valvular heart disease, peripheral vascular disease, arrhythmias, high blood pressure and stroke.

CASE FATALITY RATE: The proportion of persons contracting a disease, who die of that disease.

DIABETES: Diabetes mellitus is an illness associated with a disturbance of blood glucose control. In the provincial heart health surveys, individuals were considered to have diabetes if they reported ever having been so diagnosed by a physician.

ELEVATED SERUM CHOLESTEROL: Elevated serum cholesterol is here defined as a total serum cholesterol level greater than or equal to 5.2 mmol/litre.

HIGH BLOOD PRESSURE: High blood pressure is defined as diastolic blood pressure equal to or greater than 90 mmHg or systolic blood pressure equal to or greater than 140 mm Hg and/or on treatment, either pharmacologic or non-pharmacologic (weight control and/or salt restriction), for the purpose of lowering blood pressure.

ICD: International Classification of Diseases - 9th Revision, 1977.

INCIDENCE: The number of instances of illness commencing, or of persons falling ill, during a given period in a specified population.

ISCHEMIC HEART DISEASE: (ICD-9 410-414) Any condition in which heart muscle is damaged or works inefficiently because of an absence or relative deficiency of its blood supply; most often caused by atherosclerosis, it includes angina pectoris, acute myocardial infarction, chronic ischemic heart disease, and sudden death.

OBESITY: Individuals are considered obese if they have a Body Mass Index [weight in kilograms/(height in metres)²] greater than or equal to 27.

PERSON-ORIENTED DATA: Information derived by Statistics Canada by linking the diagnosis of acute myocardial infarction with hospital discharge records from the National Hospital Morbidity File and using a personal identifier.

PHYSICAL ACTIVITY: In the Canada Fitness Survey, 1981, individuals were considered physically inactive or sedentary if they reported a usual daily leisure-time energy expenditure of less than 1.5 kcal/kg/day.

POTENTIAL YEARS OF LIFE LOST: The sum of the number of years of life that individual Canadians 'lost' due to premature death. It is calculated with death prior to age 75 being considered premature. Since the average life expectancy for men is 75 years, and 81 years for women, death prior to age 75 can be considered an average for both men and women.

PREVALENCE: The number of instances of a given disease or other condition in a given population at a designated time; the term usually refers to the situation at a specified point in time.

RELATIVE RISK: The ratio of the risk of disease or death among the exposed to the risk among the unexposed.

SMOKING: Individuals are considered to be smokers if they regularly smoke at least one cigarette per day.

STANDARD MORTALITY RATIO (SMR): The ratio of the number of events observed in the population to the number that would be expected if the population had the same specific rates as the standard population, multiplied by 100.

STROKE: (ICD-9 430-438) Sudden development of a focal neurologic deficit due to disease of one or more blood vessels of the brain.

THROMBOLYSIS: The action of pharmacologic lysis of a coronary artery occlusion. Occlusions are thrombi composed of platelets, fibrin, erythrocytes, and leukocytes and are usually superimposed on or adjacent to atherosclerotic plaques. The pharmacologic agents used are streptokinase and tissue-plasminogen activator, in combination with other adjunctive therapy, such as heparin and aspirin.

TRANSIENT ISCHEMIC ATTACK: Reversible neurological or retinal deficits secondary to a decrease in blood flow. Symptoms last for less than 24 hours, usually less than half an hour. There is complete recovery of function within 24 hours.

WAIST-HIP RATIO: The ratio of waist circumference (cm) to hip circumference (cm).

10. REFERENCES

1. Health Statistics Division, Statistics Canada. Unpublished data.
2. Kannel, W.D., Gagnon, D.R., and Cupples, L.A. Epidemiology of sudden coronary death: Population at risk. Canadian Journal of Cardiology, 1990; 6:439-444.
3. Wannamethee, G., Shaper, MacFarlane, P.W., and Walker, M. Risk factors for sudden cardiac death in middle-aged British men. Circulation, 1995; 91:1749-1756.
4. Dagenais, G.R., Cantin, B., Dagenais, F., et al. Importance of outside hospital mortality as a first acute ischemic heart event: The Quebec Cardiovascular Study. Canadian Journal of Cardiology, 1996; 12:914-918.
5. Naylor, C.D. and Chen, E. Population-wide mortality trends among patients hospitalized for acute myocardial infarction: The Ontario experience, 1981-1991. Journal of American College of Cardiology, 1994; 24:1431-1438.
6. Rogers, W.J., Bowlby, L.J., Chandra, N.A., et al. Treatment of myocardial infarction in the United States (1990 to 1993): Observations from the national registry of myocardial infarction. Circulation, 1994; 90:2103-2114.
7. Johansen, H., Nair, C, Taylor, G. Person-based information for acute myocardial infarction (AMI) from 1992/93 Canadian hospital discharge data with projections to the year 2016. Unpublished manuscript.
8. Rouleau, J. L., Talajic, M., Sussex, B., et al. Myocardial infarction patients in the 1990's - their risk factors, stratification and survival in Canada: The Canadian Assessment of Myocardial Infarction(CAMI) Study. Journal of American College of Cardiology, 1996; 27:1119-27.
9. Figuerdo, V.M., Amidon, T.M., and Wolfe, C.L. Thrombolysis after acute myocardial infarction: who should be added to inclusion criteria: Postgraduate Medicine, 1994 Dec; 96(8):30-4, 37-40.
10. Fowles, R.E. Myocardial infarction in the 1990's. The importance of early thrombolysis therapy. Postgraduate Medicine 1995 May; 97(5):135-8,141-2,145-6.
11. Alpert, J.S. (ed.) Cardiology for the Primary Care Physician. St. Louis, Mosby, 1996 pg.153.
12. Alpert, J.S. (ed). Cardiology for the Primary Care Physician. St. Louis, Mosby, 1996, pg.154.
13. Cox, J.L., Lee, E., Langer, A., et al. Time to treatment with thrombolysis therapy: determinants and effect on short-term non-fatal outcomes of acute myocardial infarction. Canadian Medical Association Journal, 1997; 156:497-505.

14. Lee, K.L., Califf, R.M., Simes, J., et al. Holding GUSTO up to the light. Annals of Internal Medicine, 1994; 120:876-881.
15. Ridker, P.M., O'Donnell, C.J., Marder, V., et al. A response to "Holding GUSTO up to the light". Annals of Internal Medicine, 1994; 120:882-885.
16. Cairns, J., et al. Canadian Consensus Conference on Coronary Thrombolysis - 1994 Update. Canadian Journal of Cardiology, 1994; 10:517-521.
17. Canadian Consensus Conference on Coronary Thrombolysis - 1994 Recommendations. Canadian Journal of Cardiology, 1994; 10:522-528.
18. Hanes, D.S., Weir, M.R. and Sowers, J.R. Gender considerations in hypertension pathophysiology and treatment. American Journal of Medicine, 1996; 101(3A):10S-21S.
19. Johansen, H.L., Nargundkar, M., Nair, C., et al. Women and cardiovascular disease. Chronic Diseases in Canada, 1990; 11(3):41-46.
20. Mao, Y., Morrison, H., Semenciew, R., and Wigle, D. Mortality on Canadian Indian Reserves - 1977-82. Canadian Journal of Public Health, 1986 ;77:263-268.
21. Mao, Y., Moloughney, B.W., Semenciew, R., and Morrison, H. Indian Reserve and Registered Indian Mortality in Canada. Canadian Journal of Public Health, 1992; 83:350-353.
22. Young, T.K. Cardiovascular Disease and Risk Factors Among North American Indians. Winnipeg, MB: Northern Health Research Unit, 1990.
23. Young, T.K. Self-perceived and clinically assessed health status of Indians in northwestern Ontario: Analysis of a health survey. Canadian Journal of Public Health, 1982; 73:272-277.
24. McIntyre, L., Shah, C.P. Prevalence of hypertension, obesity and smoking in three Indian communities in northwestern Ontario. Canadian Medical Association Journal, 1986; 143:345-349.
25. Nair C., Nicholls E. Cardiovascular Disease in Canada. Ottawa, ON: Canadian Centre for Health Information, Statistics Canada, 1990.
26. Goldman L., Cook, E.F. The decline in ischemic heart disease mortality rates. Annals of Internal Medicine, 1984; 101:825-836.
27. Nova Scotia-Saskatchewan Cardiovascular Disease Epidemiology Group. Estimation of the incidence of acute myocardial infarction using record linkage. A feasibility study in Nova Scotia and Saskatchewan. Canadian Journal of Public Health, 1989; 80(6):412-416.

28. Wielgosz, A.T. Establishing surveillance of cardiovascular disease incidence in Canada. Canadian Journal of Cardiology, 1992; 8(3):249-251.
29. Nova Scotia-Saskatchewan Cardiovascular Disease Epidemiology Group. Trends in incidence and mortality from acute myocardial infarction in Nova Scotia and Saskatchewan 1974-1985. Canadian Journal of Cardiology, 1992; 8(3):253-258.
30. WHO MONICA Principal Investigators. The World Health Organization MONICA Project (Monitoring of Trends and Determinants in Cardiovascular Disease): A major international collaboration. Journal of Clinical Epidemiology, 1988; 41:105-114.
31. Gregor, R.D., Guerensey, J.R., Mackenzie, B.R., et al. Prevalence of ischemic heart disease and its treatment in Halifax County; results of the MONICA survey. Nova Scotia Medical Journal, 1990; 69:146-149.
32. Tunstall-Pedoe, H., Kuulasmaa, K., Amouyel, P. et al. Myocardial infarction and coronary deaths in the World Health Organization MONICA Project. Registration procedures, event rates and case-fatality rates. Circulation, 1994 Jul; 90(1):583-612.
33. Johansen, H., Nair, C. and Taylor, G. Unpublished report.
34. Intercontinental Medical Statistics Canada. Unpublished data.
35. Bureau of Chronic Disease Epidemiology, Laboratory Centre for Disease Control, Health Canada. Unpublished data.
36. Moore, R. et al. Economic Burden of Illness in Canada, 1993. Final draft July 22nd, 1996. Laboratory Centre for Disease Control, Health Canada.
37. Bureau of Chronic Disease Epidemiology, Laboratory Centre for Disease Control. Unpublished data.
38. Dawber, T.R. The Framingham Study: The epidemiology of Atherosclerotic Disease. Cambridge, Ma: Harvard University Press, 1980, p.257.
39. National Institutes of Health. Epidemiology and Prevention of Cardiovascular Disease. U.S. Department of Health and Human Services, National Institutes of Health. 1994.
40. Health Canada. The Canadian Heart Health Initiative: a policy in action. Health Promotion, 1992; 30(4):1-19 (insert).
41. MacLean, D.R., Petrasovits, A., Nargundkar, M., et al. Canadian heart health surveys; a profile of cardiovascular risk: survey methods and data analysis. Canadian Medical Association Journal, 1992; 146(11, suppl):1969-1974.
42. Canadian Heart Health Surveys Research Group. The Federal-Provincial Canadian Heart Health Initiative. Canadian Medical Association Journal, 1992; 146(6):1-2.

43. Health Canada. Canadians and Heart Health: Reducing the Risk. Ottawa, ON: Health Canada, 1995.
44. Health Canada. Survey on Smoking in Canada. Ottawa, ON; Health Canada, 1994.
45. Health Canada. 1994 Youth Smoking Survey. Ottawa: Minister of Supply and Services Canada, 1996
46. Monique-Verschuren ,W.M. Total cholesterol concentration and mortality at a relatively young age; do men and women differ? British Medical Journal, 1995 Sept; 23:311(7008):779-813.
47. Lipid Research Clinic Program. The Lipid Research Clinics Coronary Primary Prevention Trial Results 1: Reduction in incidence of coronary heart disease. Journal of the American Medical Association, 1984; 251:351-364.
48. Connelly, P.W., MacLean, D.R., Horlick, L., et al. Plasma lipids and lipoproteins and the prevalence of risk for coronary heart disease in Canadian adults. Canadian Medical Association Journal, 1992; 146(11, suppl):1977-1987.
49. Canadian Conference on Cholesterol: Final report. Canadian Medical Association Journal, 1988; 139:1-8.
50. Gordon, T., Castelli, W.P., et al. High density lipoproteins as a protective factor against coronary heart disease. American Journal of Medicine, 1977; 62:707-714.
51. Criqui, M.H., Heiss, G., and Cohn, R. Triglycerides and coronary heart disease mortality: Lipid Research Clinics program follow-up study. American Heart Association 27th Conference on Cardiovascular Disease, 1987.
52. Austin, M.A. Plasma triglyceride as a risk factor for coronary heart disease: The epidemiologic evidence and beyond. American Journal of Epidemiology, 1989; 129:249-259.
53. Lamarche, B., Moorjani, S., Lupien, P.J., et al. Apolipoprotein A-1 and B and the risk of ischemic heart disease during a five-year follow-up of men in the Quebec Cardiovascular Study. Circulation, 1996; 94:273-278.
54. Lamarche, B., Tchernof, A., Moorjani, S., et al. Small dense low-density lipoprotein particles as a predictor of the risk of ischemic heart disease in men. Prospective results from the Quebec Cardiovascular Study. Circulation, 1997; 95:69-75.
55. MacMahon, S. et al. Blood pressure, stroke and coronary hear disease. Part 1, prolonged differences in blood pressure: prospective observational studies corrected for regression dilution bias. The Lancet, 1990; 335:765-774.
56. Kannel, W.B. Blood pressure as a cardiovascular risk factor: prevalence and treatment. Journal of the American Medical Association, 1996 May; 22-29; 275(20):1571-6.

57. Joffres, M.R., Hamet, P., Rabkin, S.W., et al. Prevalence, control and awareness of high blood pressure among Canadian adults. Canadian Medical Association Journal, 1992; 146(11, suppl):1997-2005.
58. Kannel, W.B. Cardioprotection and antihypertensive treatment: the key implications of addressing the associated coronary risk factors (the Framingham experience). American Journal of Cardiology, 1996 Feb; 22; 77(6):6B-11B.
59. Kannel, W.B. Framingham Study insights into hypertensive risk of cardiovascular disease. Hypertension Research 1995 Sept; 18(3):181-96.
60. American Heart Association. The Committee on Exercise and Cardiac Rehabilitation of the Council on Clinical Cardiology. Benefits and recommendations for physical activity programs for all Americans. Circulation, 1992; 86(1):340-344.
61. Stephens, T., Craig, C.L. The Well-Being of Canadian: Highlights of the 1988 Campbell's Survey. Ottawa, ON: Canadian Fitness and Lifestyle Research Institute, 1990.
62. Caspersen, C.J., Merritt, R.K., and Stephens, T. International physical activity patterns: a methodological perspective. In Advances in Exercise Adherence, Dishman, R.K. (ed.). Human Kinetics, Champaign, IL, 1994.
63. Haskell, W.L., Montoye, H.J., and Orenstine, D. Physical activity and exercise to achieve health-related physical fitness components. Public Health Reports, 1985; 100:202-212.
64. Heart and Stroke Foundation of Canada. Position Statement on Physical Activity. Ottawa: Heart and Stroke Foundation of Canada, May 1993.
65. United States Department of Health and Human Services. Physical Activity and Health: A Report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, 1996.
66. Connolly, V.M., Kesson, C.M. Socioeconomic status and clustering of cardiovascular disease risk factors in diabetic patients. Diabetic Care 1996 May; 19(5):419-22.
67. Reeder, B.A., Angel, A., Ledoux, M. et al. Obesity and its relation to cardiovascular disease risk factors in Canadian adults. Canadian Medical Association Journal, 1992; 146(11, suppl):2009-2019.
68. Harris, M.I., Hadden, W.C., Knowler, W.C., et al. Prevalence of diabetes and impaired glucose tolerance and plasma glucose levels in the U.S. population aged 20-74 years. Diabetes, 1987; 36:523-534.
69. Statistics Canada. 1991 Aboriginal Peoples Survey. Statistics Canada, 1991.

70. Hubert, A.B., Feinleib, M., McNamara, P.M., et al. Obesity as an independent risk factor for cardiovascular disease: a 26-year follow-up of participants in the Framingham Heart Study. Circulation, 1983; 67:968-977.
71. Larsson, B., Svardsudd, K., Welin, L., et al. Abdominal adipose tissue distribution, obesity and risk of cardiovascular disease; 13-year follow-up of participants in the study of men born in 1913. British Medical Journal, 1984; 288:1401-1404.
72. Canadian Guidelines for Healthy Weights: Promoting Healthy Weights (discussion paper), Health and Welfare Canada, Health Services and Promotion Branch, Ottawa, 1988.
73. Kannel, W.B. Effect of weight on cardiovascular disease. American Journal of Clinical Nutrition, 1996 Mar; 63(3 suppl):419S-422S.
74. Verrier, R.L. Life-threatening cardiovascular consequences of anger in patients with coronary heart disease. Cardiology Clinics, 1996 May; 14(2):289-307.
75. Dagenais, G., Universite de Montreal., personal communication.
76. Pershagen, G., Smokeless tobacco. British Medical Bulletin 1996 Jan; 52(1):50-7.
77. Ernst, E. Fibrinogen as a cardiovascular risk factor: meta-analysis and review of the literature. Annals of Internal Medicine 1993; 118:956-63.
78. Perry, I.J. Prospective study of serum total homocysteine concentration and risk of stroke in middle-aged British men. The Lancet 1995 Nov; 346(8987):1395-8.
79. Wilhelmsen, L. Synergistic effects of risk factors. Clinical and Experimental Hypertension, part A, 1990; 12:845-863.
80. MacDonald, S., Joffres, M.P., Stachenko, S.J., et al. Multiple cardiovascular risk factors in Canadian adults. Canadian Medical Association Journal, 1992; (11, suppl):2021-2029.
81. Wolf, P.A., Cobb, J.L., and D'Agostino, R.B. Epidemiology of stroke. In Stroke: Pathophysiology, diagnosis and management. Barnett, JJ (eds). New York, NY: Churchill Livingstone, 1992: 3-29.
82. Lerner, D.J., and Kannel, W.B. Patterns of coronary heart disease morbidity and mortality in the sexes: a 26-year follow-up of the Framingham population. American Heart Journal, 1986; 111:383-390.
83. SHEP Cooperative Research Group. Prevention of stroke by antihypertensive drug treatment in older persons with systolic hypertension. Journal of the American Medical Association, 1991; 265:3255-3264.

84. Lindenstrom, E. Influence of systolic and diastolic blood pressure on stroke risk: a prospective observational study. American Journal of Epidemiology,. 1995 Dec; 15:142(12):1279-90.
85. Donnan, G.A., You, R., Thrift, A., and McNeil, J.J. Smoking as a risk factor for stroke. Cerebrovascular Disease, 1993; 3:129-138.
86. Wolf, P.A., D'Agostino, R., Kannel, et al. Cigarette smoking as a risk factor for stroke. The Framingham Study. Journal of the American Medical Association, 1988; 259:1025-1029.
87. Shinton, R., and Beevers, G. Meta-analysis of the relation between cigarette smoking and stroke. British Medical Journal, 1989; 298:789-793.
88. Colditz, G.A., Bonita, R., and Stampfer, M.J. Cigarette smoking and the risk of stroke in middle aged women. New England Journal of Medicine, 1988; 318:937-941.
89. Petersen, P., Boysen, G., Godtfredsen, J., et al. Placebo-controlled randomized trial of warfarin and aspirin for prevention of thromboembolic complications in atrial fibrillation. The Lancet, 1989; 1:175-179.
90. The Boston Area Anticoagulation Trial for Atrial Fibrillation Investigators. The effect of low dose on the risk of stroke in patients with nonrheumatic atrial fibrillation. New England Journal of Medicine, 1990; 323:1505-1511.
91. Anonymous. Preliminary report of the stroke prevention in atrial fibrillation study. New England Journal of Medicine, 1990; 322:863-868.
92. Koeford, B.G. Atrial Fibrillation and apoplexy - risks and prevention. Nord Med, 1996 June; 111(6):171-5.
93. Sorenson, P.S., Marquadsen, J., Pederson, J., et al. Long-term prognosis and quality of life after reversible cerebral ischemic attacks. Acta Neurologica Scandinavica, 1989; 79:204-213.
94. North American Symptomatic Carotid Endarterectomy Trial Collaborators. Beneficial effects of carotid endarterectomy in symptomatic patients with high-grade stenosis. New England Journal of Medicine, 1991; 325:445-453.
95. Barnett, H.J.M. Drug and surgical issues in stroke prevention. Cerebrovascular Disease, 1994; 1(4 suppl):16-25.
96. Feinberg, W.M., Albers, G.W., Barnett, H.J.M., et al. Guidelines for the management of transient ischemic attacks. From the Ad Hoc Committee on Guidelines for the Management of Transient Ischemic Attacks of the Stroke Council of the American Heart Association. Stroke, 1994; 25:1320.
97. Wannamethee, G., and Shaper, A.B. Physical activity and stroke in British middle-aged men. British Medical Journal, 1992; 304:597-601.

98. Fletcher, G.F., Blair, S.N., Blumental, J., et al. Statement on Exercise. Benefits and recommendation for the physical activity programs for all Americans. Circulation, 1992; 86:340-344.
99. Tuomilehto, J., Rastenyte, D., Jousilahti, P., et al. Diabetes mellitus as a risk factor for death from stroke. Prospective study of a middle-aged Finnish population. Stroke, 1996 Feb; 27(2):202-5.
100. Heinrich, J. Fibrinogen and cardiovascular risk. Journal of Cardiovascular Risk, 1995 June; 2(3):197-205.
101. Bogousslavsky, J., Garazi, S., Jeanrenaud, X., et al. Stroke recurrence in patients with patent foramen ovale: the Lausanne Study, Lausanne Stroke with Paradoxical Embolus Study Group. U, 1996 May; 46(5):1301-5.
102. Hunink, M.G.M., Goldman, L., Tosteson, A.N.A., et al. The Recent decline in mortality from coronary heart disease, 1980-1990. The effect of secular trends in risk factors and treatment. Journal of the American Medical Association, 1997; 277:535-542.
103. Wong, T., and Wilkins, K. How many deaths from major chronic disease could be prevented: Chronic Disease in Canada, 1990; 11:573-575.
104. Farquhar, J.W. Effects of community wide education on cardiovascular disease risk factors: The Stanford Five-City Project. Journal of the American Medical Association, 1990; 264(3):359-365.
105. Puska, P., Tuomilehto, J., et al.. The North Karelia Project: Evaluation of a comprehensive community programme for control of cardiovascular disease in 1972-77 in North Karelia, Finland. Copenhagen, Denmark, World Health Organization/EURO Monograph Series, 1981.
106. Vartiainen, E., Puska, P., Pelckanen, J., et al. Changes in risk factors explain changes in mortality from ischemic heart disease in Finland. British Medical Journal, 1994; 309:23-27.
107. Shea, S., and Basch, C.E. A review of the five major community based cardiovascular disease prevention programs. Part 1: Rationale, design, and theoretical framework. American Journal of Health Promotion, 1990; 4(3):302-313.
108. Federal-Provincial Working Group on the Prevention and Control of Cardiovascular Disease. Promoting Heart Health in Canada: A Focus on Cholesterol. Ottawa, ON, 1992.
109. Health and Welfare Canada Achieving Health for All: A Framework for Health Promotion. Ottawa, ON: Health and Welfare Canada, 1986.

110. The Victoria Declaration on Heart Health. Advisory Board, International Heart Health Conference (Victoria, Canada, May 28, 1992). Health Canada, Ottawa, 1992.
111. The Catalonia Declaration: Investing in Heart Health. Advisory Board. 2nd International Heart Health Conference (Barcelona, Spain, June, 1995). Department of Health and Social Security, Autonomous Government of Catalonia, Barcelona, 1996.
112. Kalache, A., and Aboderin, I. Stroke: the global burden. Health Policy and Planning, 1995; 10(1):1-21.
113. Gordon, M. Monograph Series on Aging-related Disease: III. Stroke (Cerebrovascular Disease). Chronic Disease in Canada, 1993; 14(3):64-89.
114. Mayo, N.E. Hospitalization and case-fatality rates for stroke in Canada from 1982 through 1991. The Canadian collaborative study group of stroke hospitalizations. Stroke, 1996; 27:1215-20.
115. Petrasovits, A., and Nair, C. Epidemiology of stroke in Canada. Health Reports 1994; 6:39-44.
116. Asplund, K., Bonita, R., Kuulasmaa, K., et al. Multinational comparisons of stroke epidemiology. Evaluation of case ascertainment in the WHO MONICA Stroke Study. World Health Organization Monitoring Trends and Determinants in Cardiovascular Disease. Stroke, 1995; 26:355-60.
117. Thorvaldsen, .P. et al. Stroke incidence, case fatality, and mortality in the WHO MONICA project. World Health Organization Monitoring Trends and Determinants in Cardiovascular Disease. Stroke, 1995; 26:361-7.
118. Whisnant, J.P.. The decline of stroke. Stroke, 1984; 15:160-8.
119. Brown, R.D., Whisnant, J.P., Sicks, J.D., et al. Stroke incidence, prevalence, and survival: secular trends in Rochester, Minnesota, through 1989. Stroke, 1996; 27:373-80.
120. Modan, B., and Wagener, D.K.. Some epidemiological aspects of stroke: mortality/morbidity trends, age, sex, race, socioeconomic status. Stroke, 1992; 23:1230-6.
121. Wolf, P.A., D'Agostino, R.B., O'Neal, M.A., et al. Secular trends in stroke incidence and mortality. The Framingham Study. Stroke, 1992; 23:1551-5.
- 122 Gillum, R.F. Cerebrovascular disease morbidity in the United States, 1970-1983. Age, sex, region, and vascular surgery. Stroke, 1986; 17:656-61.

123. Bonita, R., and Beaglehole, R. Monitoring stroke. An international challenge. Stroke, 1995; 26:541-2.
124. Garraway, W.M., Whisnant, J.P. and Drury, I. The continuing decline in the incidence of stroke. Mayo Clinic Proceedings, 1983; 58:520-3.
125. Gillum, R.F., Gomez-Marin, O., Kottke, T.E., et al. Acute stroke in a metropolitan area, 1970 and 1980. The Minnesota Heart Survey. Journal of Chronic Disease, 1985; 38:891-8.
126. Kotila, M. Declining incidence and mortality of stroke? Stroke, 1984;15:255-9.
127. Folsom, A.R., et al. Improvement in hypertension detection and control from 1973-1974 to 1980-1981. The Minnesota Heart Survey experience. Journal of the American Medical Association, 1983; 250:916-21.
128. Garraway, W.M., Whisnant, J.P., Furland, A.J., et al. The declining incidence of stroke. New England Journal of Medicine, 1979; 300:449-52.
129. Broderick, K.J.P., Phillips, S.J., Whisnant, J.P., et al. Incidence rates of stroke in the eighties: the end of the decline in stroke? Stroke, 1989; 20:577-82.
130. Kuller, L.H. Incidence rates of stroke in the eighties: the end of the decline in stroke? Stroke, 1989; 20:841-3.
131. Mayo, N.E., et al. Changing rates of stroke in the province of Quebec, Canada: 1981-1988. Stroke, 1991; 22:590-5.
132. Terent, A. Increasing incidence of stroke among Swedish women. Stroke, 1988; 19:598-603.
133. Siesjo, B.K., Zhao, Q., Pahlmark, K, et al. Glutamate, calcium and free radicals as mediators of ischemic brain damage. Annals of Thoracic Surgery, 1995; 59:1316-1320.
134. Obrenovitch, T.P. The ischemic penumbra: Twenty years on. Cerebrovascular and Brain Metabolism Reviews, 1996; 7:297-323.
135. Ginsberg, M.D. Injury mechanisms in the penumbra: approaches to neuroprotection in acute ischemic stroke. Cerebrovascular Disease, 1997; 7(suppl 2):7-12.
136. Baron, J.C., von-Kummer, R. and del-Zoppo, G.J. Treatment of acute stroke. Challenging the concept of a rigid and universal time window. Stroke, 1995;26:2219-2221.
137. Giroux, C., and Scatton, B. Ischemic stroke: treatment on the horizon. Eur Neurol, 1996; 36:61-64.
138. Wilgren, N. Neuroprotection in late clinical development - a status report. Cerebrovascular Disease, 1997; 7(suppl 2):13-17.

139. Langhorne, P., Williams, B.O., Gilchrist, W., et al. Do stroke units save lives? The Lancet, 1993; 342:395-398.
140. Kalra, L. The influence of stroke unit rehabilitation on functional recovery from stroke. Stroke, 1994; 25:821-825.
141. Adams, H.P. Jr. Investigation of the patient with ischemic stroke. Cerebrovascular Disease, 1991; 1Suppl.1:54-60.
142. Donnan, G.A. Investigations of patients with stroke and transient ischemic attacks. The Lancet, 1992; 339:473-477.
143. Feinberg, W.M., et al. Guidelines for the management of transient ischemic attacks: From the Ad Hoc Committee on Guidelines for the Management of Transient Ischemic Attacks of the Stroke Council of the American Heart Association. Stroke, 1994; 25:1320.
144. Adams, H.P., Brott, T.G., Crowell, R.M., et al. Guidelines for the management of patients with acute ischemic stroke: A statement for healthcare professionals from a special writing group of the Stroke Council, American Heart Association. Stroke, 1994; 25:1901-1914.
145. Adams, H.P., Brott, T.G., Crowell, R.M., et al. Guidelines for the management of patients with acute ischemic stroke. Stroke, 1994; 25:1901-1914.
146. The National Institute of Neurological Disorders and Stroke (NINDS) rt-PA stroke study group. Tissue plasminogen activator for acute ischemic stroke. New England Journal of Medicine, 1995; 333:1581-1587.
147. Rose, G. Strategy of prevention: lessons from cardiovascular disease. British Medical Journal, 1981; 281:1847-1851.
148. MacMahon, S., and Rodgers, A. Blood pressure, antihypertensive treatment and stroke risk. Journal of Hypertension, 1994; 12(suppl.10):S5-14.
149. Phillips, S.J. Pathophysiology and management of hypertension in acute ischemic stroke. Hypertension, 1994; 23:131-136.
150. Phillips, S.J., and Whisnant, J.P. On behalf of the National High Blood Pressure Education Program. Hypertension and the brain. Archives of Internal Medicine, 1992; 152:938-945.
151. Scandinavian Simvastatin Survival Study Group. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: The Scandinavian Simvastatin Survival Study (4S) The Lancet, 1994; 344:1383-1389.
152. Donnan, G.A., et al. Smoking as a risk factor for stroke. Cerebrovascular Disease, 1993; 3:129-138.

153. Silagy, C., Mant, D., Fowler, G. and Lodge, M. Meta-analysis on efficacy of nicotine replacement therapies in smoking cessation. The Lancet, 1994; 343:139-142.
154. Sacco, R.L., Lin, I.F., Boden-Albala, D.E., et al. Alcohol and the risk of ischemic stroke: Verification of a J-shaped relationship from the Northern Manhattan Stroke Study. Stroke, 1997; 28:250.
155. Shinton, R., and Beevers, G. Lifelong exercise and stroke. British Medical Journal, 1993; 307:231-234.
156. Antiplatelet Trialists' collaboration. Collaborative overview of randomised trials of Antiplatelet therapy. I. Prevention of death, myocardial infarction, and stroke by prolonged Antiplatelet therapy in various categories of patients. British Medical Journal, 1994; 308:81-106.
157. International Stroke Trial Collaborative Group. The International Stroke Trial (IST); a randomised trial of aspirin, subcutaneous heparin, both or neither among 19,435 patients with acute ischaemic stroke. The Lancet, 1997, in press.
158. CAST (Chinese Acute Stroke Trial) Collaborative Group. CAST: a randomised placebo-controlled trial of early aspirin use in 19,975 patients with acute ischaemic stroke. The Lancet, 1997, in press.
159. Diener, H., et al. European Stroke Prevention Study 2. Dipyridamole and acetylsalicylic acid in the secondary prevention of stroke. J Neurol Sci, 1996; 143:1-13.
160. CAPRIE Steering Committee. A randomised, blinded trial of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE). The Lancet, 1996; 348:1329-1338.
161. Atrial Fibrillation Investigators. Risk factors for stroke and efficacy of antithrombotic therapy in atrial fibrillation. Analysis of pooled data from five randomized controlled trials. Archives of Internal Medicine, 1994; 154:1449-1457.
162. European Atrial Fibrillation Trial Study Group. Secondary prevention in nonrheumatic atrial fibrillation after transient ischaemic attack or minor stroke. The Lancet, 1993; 342:1255-1262.
163. European Atrial Fibrillation Trial Study Group. Optimal oral anticoagulant therapy in patients with nonrheumatic atrial fibrillation and recent cerebral ischemia. New England Journal of Medicine, 1995; 333:5-10.
164. Turpie, A.G.G., Colly, L.P., Heijboer, H., et al. A comparison of aspirin with placebo in patients treated with warfarin after heart valve replacement. New England Journal of Medicine, 1993; 329:524-529.
165. North American Symptomatic Carotid Endarterectomy Trial Collaborators. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. New England Journal of Medicine, 1991; 325:445-453.

166. European Carotid Surgery Trialists' Collaborative Group. MRC European Carotid Surgery Trial: interim results for symptomatic patients with severe (70-90%) or with mild (0-29%) carotid stenosis. The Lancet, 1991; 337:1235-1243.
167. Asymptomatic Carotid Atherosclerosis Group. Carotid endarterectomy for patients with asymptomatic internal carotid artery stenosis. Journal of the American Medical Association, 1995; 273:1421-1428.
168. Perry, J.R., Szalai, J.P., and Norris, J.W., for the Canadian Stroke Consortium. Consensus against both carotid endarterectomy and routine screening for asymptomatic carotid artery stenosis. Archives of Neurology, 1997; 54:25-28.