A review of the cost of cardiovascular disease

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In Canada, 74,255 deaths (33% of all deaths) in 2003 were due to cardiovascular disease (CVD). As one of the most costly diseases, CVD represents a major economic burden on health care systems. The purpose of the present study was to review the literature on the economic costs of CVD in Canada and other developed countries (United States, Europe and Australia) published from 1998 to 2006, with a focus on Canada. Of 1656 screened titles and abstracts, 34 articles were reviewed including six Canadian studies and 17 American studies. While considerable variation was observed among studies, all studies indicated that the costs of treating CVD-related conditions are significant, outlining a convincing case for CVD prevention programs.

Key Words: Cardiovascular disease; Cost of illness; Health economics; Health policy; Outcomes research; Review

Cardiovascular disease (CVD) is one of the leading causes of global mortality and morbidity, and is responsible for an estimated 16.7 million deaths worldwide (30% of all deaths) (1). In North America, 74,255 deaths (33% of all deaths) in Canada in 2003 were due to CVD and one American dies from CVD every 36 s (2,3). CVD also represents a major economic burden on health care systems in terms of direct (eg, hospitalizations, rehabilitation services, physician visits, drugs) and indirect costs associated with mortality and morbidity (eg, losses of productivity due to premature mortality and short- or long-term disability).

Because the cost of CVD is likely to continue to grow due to increased obesity rates and our aging society, it is important to gain an understanding of the cost of CVD and its main drivers. The objective of the present research was to review studies published since 1998 related to the economic cost of CVD or related conditions in Canada, the United States (USA), Europe and Australia, with a focus on Canadian studies.

METHODS

Literature review

A search strategy was developed to identify the literature related to the economic cost of CVD and associated conditions (ie, cost of illness studies). The search was limited to the English language literature published between January 1998 and August 2006, and included studies conducted in or related to Canada, the USA, European countries and Australia. The initial scope of the review included cost of illness studies presenting only costs from a national or provincial/state perspective. However, due to the small number of identified studies, the scope of the research was expanded to include all cost of illness studies, even if based on specific populations (eg, employer database) or derived from a trial. Studies presenting costs as part of a cost-effectiveness analysis were not included in the review.

The primary computerized search was performed in three databases: Ovid MEDLINE, EMBASE and the Cumulative Index to

Une analyse du coût des maladies cardiovasculaires

En 2003 au Canada, 74 255 décès (33 % de tous les décès) étaient imputables à une maladie cardiovasculaire (MCV). Puisque c'est l'une des maladies les plus coûteuses, la MCV représente un fardeau économique important sur les systèmes de santé. La présente étude visait à procéder à une analyse bibliographique des coûts des MCV sur l'économie canadienne et d'autres pays industrialisés (États-Unis, Europe et Australie) publiés entre 1998 et 2006, en s'attardant sur le Canada. Des 1 656 titres et résumés retenus, 34 ont été analysés, y compris six études canadiennes et 17 études américaines. On observait une variation considérable entre les études, mais toutes indiquaient des coûts importants pour le traitement des pathologies liées aux MCV, ce qui étaye de manière convaincante l'intérêt d'adopter des programmes de prévention des MCV.

Nursing and Allied Health Literature. In addition to the three primary databases, searches were conducted in the Office of Health Economics – Health Economic Evaluations Database, the Canadian Research Index and the Centre for Review and Dissemination, which includes the Database of Abstracts of Reviews of Effects, the National Health Services Economic Evaluations Database and the Health Technology Assessment database.

A separate search strategy was developed for each electronic database to incorporate the distinct subject headings used in each database. In addition to relevant subject headings (eg, 'cost of illness'), the search included the following key words: 'myocardial infarction', 'stroke', 'angina', 'hypertension', 'hyperlipidemia', 'acute coronary syndrome', 'coronary artery disease', 'coronary heart disease', 'cost', 'burden', 'illness' and 'economic burden'.

Titles and abstracts of identified studies were screened by one reviewer for possible inclusion or exclusion before retrieving full-text versions of the publications. When it was not clear whether a study should be included, consensus was reached by discussion with a second reviewer. References of included studies, reviews and meta-analyses were also searched to ensure that all relevant studies were identified.

Data abstraction

Using a standardized data abstraction form, the following data were abstracted: country of study, condition or disease evaluated, study design, number of patients, mean age of the population, time horizon, study perspective, total costs, direct costs, indirect costs and methods used to calculate indirect costs. In addition, any other information facilitating the interpretation of the results (eg, breakdown of costs into main cost categories, first-year costs versus lifetime costs and comparisons with other chronic conditions) was recorded when available.

Currency conversion and estimates of costs per capita

To present the cost data, all reported costs were converted from local currency to 2004 Canadian dollars, unless stated otherwise. Yearly

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Figure 1 Quorum diagram of study selection related to the cost of illness studies. CVD Cardiovascular disease

average exchange rates were used to convert to Canadian currency and Consumer Price Index rates from the Organisation for Economic Co-operation and Development (OECD) economic statistics database were used to inflate to 2004 dollars (4,5). For transparency, total costs in local currencies are also reported, along with converted costs in all tables.

In addition, a direct cost per capita was calculated for each study to obtain a common denominator for all studies. Because indirect costs largely depend on the methods used for their calculations, a direct cost per capita measure was considered to be more appropriate for comparison purposes than a total cost per capita. When country estimates were presented, the direct costs were simply divided by the total population of the country in the year of the costing study. For studies presenting a cost per patient, prevalence and population data were used to estimate the total number of cases in the studied countries. For a particular study, the cost per patient was first multiplied by the country's prevalent population and then divided by the total country population to derive the cost per capita. Several sources were used for population and prevalence data including the OECD factbook (6) for population data and the World Health Organization (7) for prevalence data. Condition and age-specific prevalence rates were used as much as possible in these estimations of the cost per capita. However, prevalence of ischemic heart disease was used as an estimate for coronary artery disease (CAD) and prevalence of cerebrovascular disease was used as an estimate for the prevalence of stroke.

RESULTS

Literature search

The initial literature search identified 1656 unique publications, as outlined in the quorum diagram in Figure 1. On review of the title and abstracts of these citations, 1538 publications were excluded because they did not focus on the economic cost of CVD. Because two studies published in 2004 and 2005 had reviewed the cost of stroke in Europe, European studies published after 2003 were selected for review only if they were not included in these two reviews. While this approach did not follow the systematic approach used for the identification of all other CVD-related conditions, it was not deemed necessary to redo previous work in light of the two

comprehensive reviews of the cost of stroke in Europe. Instead, these two reviews are briefly discussed, along with more recent articles on the cost of stroke in Europe.

A full-text review of the remaining 118 citations identified 34 unique articles that were included in the final review. Reasons for exclusion following the full-text review are identified in the quorum diagram. Of the 34 studies identified in the review, six reported cost-of-illness estimates for Canada. Of the remaining studies, 17 were conducted in the USA, one in Australia, two in Italy, two in the United Kingdom (UK), one in Germany, one in Finland and four for all of Europe (of which two studies were reviews). Because some studies were evaluating more than one CVD-related condition, these 34 studies resulted in 37 estimates of the cost of CVD.

The major findings of each study are briefly presented in the text, and the study details are reported in the tables (eg, sample size, study population age and cost figures). It is well known that directly comparing cost figures among studies is difficult due to several factors (eg, country, study design and time horizon). However, the majority of the reviewed studies reported a breakdown of the cost, allowing us to identify similarities and differences in the drivers of the cost of CVD. To facilitate the interpretation of the data, studies were first stratified according to CVD-related conditions and then by country. Due to the Canadian focus of the present article, cost figures and detailed information are only provided in the text for Canadian studies or for comparison purposes for non-Canadian studies. However, for each study, the cost figures are presented in the tables in local and converted currencies, along with an estimate of the cost per capita in 2004 Canadian dollars and other key information (eg, sample size and age). The figures presented in the text are expressed in 2004 Canadian dollars to help comparability.

COST OF ILLNESS STUDIES

CVD

Seven studies were identified that estimated the costs associated with CVD in Canada, the USA and Europe, of which two presented national estimates (8-14). Details of these studies are reported in Table 1. No Australian studies on the overall cost of CVD were found.

Canada: As reported by Health Canada (11), CVD represented 11.6% of the total Canadian cost of illness classifiable by diagnostic category. CVD was also the most costly disease in Canada (\$21.2 billion in direct and indirect costs), followed by musculoskeletal diseases (\$18.8 billion) and cancer (\$16.3 billion). Of the \$7.8 billion of direct CVD costs, hospitalizations accounted for 61%, drugs for 26% and physician care for 12%. Indirect costs associated with short-term disability (\$290.4 million), long-term disability (\$3.6 billion) and premature mortality (\$9.5 billion) totalled \$13.4 billion or 63% of the total costs of CVD in Canada in 1998 (11).

USA: In its 2006 publication, the American Heart Association (8) estimated from various sources that the one-year cost of CVD in the USA in 2006 was \$457.4 billion, of which 64% (\$292.3 billion) were direct costs. Hospital costs were the main cost category (45% of CVD direct costs), followed by drugs (19.5%) and physician visits (14.8%). While the contribution of indirect costs in the determination of the total cost of CVD was different between Canada (11) and the USA (63% and 36%, respectively), indirect costs associated with productivity losses due to premature mortality represented 75% of the total indirect costs in both studies.

Two other USA studies (10,14) using claims databases or population health surveys indicated that hospitalization and physician costs accounted for approximately 40% and 13% to 15% of the total direct medical costs of CVD in the USA, respectively. In another study of employed women (13), drug costs represented 16% of the direct medical costs, an estimate similar to the American Heart Association figure. A higher proportion for drug costs (32.8%) was observed in a Medicaid dataset (10).

In several USA studies using claims databases, the costs associated with CVD were compared with the costs associated with other

TABLE 1
Cost of illness studies on cardiovascular disease

Author	Country	Study design	# of patients (Mean age)	Perspective (Time Horizon)	Currency (Year of costing)	Unit of costing	Total costs, \$	Total costs 2004 CAN\$	% Direct costs	Direct cost per capita 2004 CAN\$
Health Canada 2002 (11)	Canada	cost of illness	-	societal (1 Year)	Can\$ (1998)	Canada	18.5 billion	21.2 billion	37%	234
American Heart Association 2006 (8)	USA	cost of illness	-	societal (1 Year)	US\$ (2006)	United States	403.1 billion	403.1 billion*	64%	1,071
Garis et al. 2002 (10)	USA	analysis of Medicaid database	209 (58.1)	payer (1 Year)	US\$ (1995)	per patient	2,320	3,805	100%	866
Wang et al. 2004 (14)	USA	analysis of population surveys	2472 (not reported)	payer (1 Year)	US\$ (1996)	per capita; per country	5,693 per case; 41.3 billion for country	9,139 per case; 66.3 billion for country	100%	245
Sasser et al. 2005 (13)	USA	analysis of employer database	1710 women (55.3)	payer (1 Year)	US\$ (2000)	per patient	17,045	27,772	71%	3,986
Birnbaum et al. 2003 (9)	USA	analysis of claims database	6528 women (53)	payer (Lifetime)	US\$ (2002)	incremental lifetime costs per woman with CVD vs no CVD	423,000	695,254	100%	133,665
Leal et al. 2006 (12)	Europe	cost of illness	-	societal (1 Year)	Euros (2003)	Total for EU; per country; per capita	169 billion for EU; 230 per capita	-	62% for EU	221

*2006 Canadian dollars. CAN Canada; CVD Cardiovascular disease; EU Europe; USA United States of America; vs Versus

chronic diseases or with the absence of CVD. The analysis of a state Medicaid database (10) indicated that treating CVD was more expensive than treating diabetes, hypertension or anxiety, but less expensive than treating patients with psychological diseases or depression. According to an analysis of USA population health surveys (14), people with CVD incurred more than twice the medical expenditure of people without CVD. However, among women, a three- to fourfold difference in costs was estimated in two studies assessing the one-year and lifetime costs of CVD compared with no CVD (9,13). Compared with other prevalent chronic conditions among women, the costs associated with CVD were higher than the costs of treating osteoporosis, but lower than the cost of treating breast cancer (13). The incremental lifetime costs for treating a woman with CVD was also found to be higher than the incremental lifetime medical cost of treating women with or without diabetes, or with or without stress urinary incontinence (9).

Europe: Using data derived from national sources and OECD databases, Leal et al (12) estimated that CVD accounted for 12% of the total European health care expenditures in 2006. While differences were observed among the 25 countries included in this study (eg, hospitalization costs accounted for 34% and 76% of health care costs in Malta and the UK, respectively), hospitalizations and drugs represented 57% and 27% of the overall direct costs of CVD in Europe, respectively. Indirect costs associated with productivity losses (21%) and informal care (17%) corresponded to 38% of the total cost of CVD in Europe.

Stroke

Ten studies estimating the cost of stroke (12,15-23), of which three were Canadian studies and two were European reviews, were identified and are summarized in Table 2.

Canada: Based on various public and private sources, the direct cost of stroke in Ontario was calculated to be at 2.7% of the total direct health care expenditures of Ontario (15). The costs associated with

treatment in acute care hospitals were the major cost category (49.7% of the direct medical costs), followed by costs associated with rehabilitation hospitals (12.5%), residential care facilities (11.3%), medical services (10.1%) and home care (9.0%). Drug costs and professional fees represented only 1.6% of the direct medical costs of stroke. In this study, indirect costs associated with disability (\$121.2 million) and premature death (\$279.6 million) corresponded to 38.3% of the total cost of stroke in Ontario.

The results of a 12-month prospective study (18) conducted in one hospital in Hamilton (Ontario) showed that the costs of stroke also differed among the types of stroke. For example, initial hospitalization costs and follow-up costs were significantly different among hemorrhagic strokes (23% and 77%, respectively), ischemic strokes (36% and 64%, respectively) and transient ischemic attacks (9% and 91%, respectively). Included in these follow-up costs were caregiver costs, which represented 27% of total one-year follow-up transient ischemic attack costs (\$17,769), 12% of total ischemic stroke costs (\$53,576) and 11% of total hemorrhagic stroke costs (\$56,573). The results also indicated that the majority of patients included in this study were discharged home.

In a randomized controlled trial (22), a tailored home intervention was shown to significantly reduce caregiver time and save money compared with usual care following discharge of stroke patients requiring rehabilitation service and who had a caregiver at home. In this study, the three-month direct medical cost following discharge was calculated to be \$9,017 per patient in the intervention group and \$12,818 in the usual care group.

USA: Hospitalization accounted for nearly one-half of the direct cost of stroke in two studies evaluating the six-month and two-year cost of stroke based on Medicare databases (20,21). In the two-year study (20), the initial hospitalization costs and costs in the first three months accounted for more than 50% of the two-year costs for both initial and recurrent strokes.

Europe: Two recently published reviews (17,23) of the cost of stroke

TABLE 2
Cost of illness studies on stroke

Author	Country	Study design	# of patients (Mean Age)	Perspective (Time Horizon)	Currency (Year of Costing)	Unit of costing	Total costs, \$	Total costs 2004 CAN\$	% Direct costs	Direct cost per capita 2004 CAN\$
Chan et al. 1998 (15)	Canada (Ontario)	modeling	-	societal (1 Year)	Can\$ (1994/95)*	province	857 million	1.0 billion	62%	393
Goeree et al. 2005 (18)	Canada	single center trial	365 (73)	societal (1 Year)	Can\$ (2004)	per patient	TIA: 17,769 Isch: 53,576 Haem: 56,573	TIA: 17,769 Isch: 53,576 Haem: 56,573	TIA: 71% Isch: 87% Haem: 88%	TIA: 176 Isch: 652 Haem: 699
Teng et al. 2003 (22)	Canada	multi center trial	114 (70)	payer (3 Months)	Can\$ (1997/98)*	per patient	Home intervention: 7,784; Usual care: 11,065	Home intervention: 9,017; Usual care: 12,818	100%	Home interv: 123.4 Usual: 175.4
Samsa, G. 1999 (20)	USA	analysis of Medicare database	49,333 (1st stroke: 78.8 Recurrent: 79.0)	payer (2 Years)	US\$ (1991)	per patient	First: 12,988 per 2 yrs Recurrent: 13,534 per 2 yrs	First: 18,815 per 2 yrs Recurrent: 19,606 per 2 yrs	100%	First: 403.67 Recurrent: 420.64
Sloan et al. 1999 (21)	USA	analysis of Medicare database	878 (not reported)	payer (6 Months)	US\$ (1994)	per patient	16,600	27,707	100%	474
Ekman, M. 2004 (17)	6 European countries	review of European studies	-	-	Euros (2003)	per patient	Range: 21,413 (Germany) to 26,403 (Sweden)	Range: 34,518 (Germany) to 42,561 (Sweden)	100%	Range: 441.80-570.86
Truelsen et al. 2005 (23)	7 European countries	review of European studies	-	-	Euros (2004)	per patient	Range: 20,239 (Germany) to 26,403 (Sweden)	Range: 32,726 (Germany) to 42,693 (Sweden)	100%	Range: 437.59-570.86
Leal et al. 2006 (12)	Europe	cost of illness	-	societal (1 Year)	Euros (2003)	Total for EU; per country; per capita	34 billion for EU; 46 per capita	74 billion for EU; 55 per capita	61% for EU	43
Kolominsky-Rabas et al. 2006 (19)	Germany	analysis of population surveys linked to administrative databases	1,637 from stroke registry; 821 resource utilization (76.3 women; 70.6 men)	payer (1, 5, 10 years; lifetime)	Euros (2004)	per case	1 year: 15,140; 5 year: 29,837; 10 year: 36,873; lifetime: 43,129	1 year: 24,481; 5 year: 48,246; 10 year: 36,873; lifetime: 69,739	100%	1 yr: 327.34 5 yr: 645.11 10 yr: 797.23 Life: 932.50
Dewey et al. 2001 (16)	Australia	trial results extrapolated to Australia	275 (72)	societal (1 year; lifetime)	Aus\$ (1997)	country	1 year: 555 million (US\$420 m); Lifetime: 1.3 billion (US\$985 m)	1 year: 661.9 million; Lifetime: 1.55 billion	93.9%	1 year: 32.6 Lifetime: 76.4

*Assumption for year of costing since not stated in paper. EU Europe; Haem Haemorrhagic stroke; Interv Intervention; Isch Ischemic stroke; TIA Transient ischemic attack; USA United States of America

in Europe indicated considerable variation in cost figures and cost breakdown among countries and studies. Even multicountry European studies that were reviewed showed important differences among European countries when using a similar methodology and methods to adjust for price differences among countries. These differences in country cost estimates were also observed in one recent multicountry European study (12) that evaluated the cost of CVD in Europe.

In a subsequent study (19) of a German population-based stroke registry combined with national estimates, the lifetime costs of a first-time stroke were determined to be more than twice the costs associated with the first year of treatment. In an earlier publication of this registry (24), which focused on the first-year costs following a first-time stroke, hospitalization costs represented one-half of the costs in the first year after a stroke. Other important categories were rehabilitation costs (16%), readmission costs (11%) and medication costs (9%).

Australia: The direct lifetime costs following a first-ever stroke were also found to be twice those of the first-year costs of stroke in Australia, based on an incidence-based cost-of-illness model (16). In this study, the major drivers of the costs of stroke during the first year were acute hospitalization (28%), followed by inpatient rehabilitation (27%) and nursing home care (11%). Medications accounted for 2% of the costs. Indirect costs associated with loss of production were calculated to be 6% of the total first-year costs (16).

Hypertension

Nine studies evaluating the cost of hypertension are discussed and are summarized in Table 3 (25-33).

Canada: Based on 142 hypertensive patients participating in a prospective observational study (33) conducted in Ontario, the six-month direct costs of hypertension were determined to be \$2,503 per patient.

Drug costs, hospitalization costs and costs associated with health care professional visits represented 51.2%, 23.5% and 20.4% of direct medical costs of hypertension, respectively. The six-month indirect costs associated with productivity losses due to hypertension were \$696 per patient, of which nearly two-thirds were due to lost time doing chores, including paid help. Other results indicated that the total six-month costs associated with rheumatoid arthritis (\$7,615) were higher than the costs associated with osteoarthritis (\$4,653) or hypertension (\$3,198).

USA: In 1998, the direct costs of hypertension in the USA were calculated to be 12.6% of health care expenditures (\$185 billion) when national health care expenditures were disaggregated to identify the burden of hypertension (31). A similar figure was found based on an analysis of the 1996 Medical Expenditure Panel Survey (ie, \$177 billion) (28).

In the study by Hodgson et al (31), hospital care (42%) was the most important cost category, followed by physician visits (26%), prescription drugs (17%), nursing home care (12%) and home health care (4%). Similar proportions for physician and drug costs were observed by Amin et al (25) when analyzing a Health Maintenance Organization database (hospitalization, 33%; physician visits, 28%; and drugs, 19%). In several studies, the cost of hypertension alone (ie, without comorbidities) represented only a small portion of the costs of hypertension: 13% in the study by Druss et al (28), 21% in the studies by Hodgson et al (31) and Amin et al (25), and 29% in the study by Garis and Farmer (29).

From a USA employer perspective (30), the annual cost of hypertension was estimated to be \$150 per employee, of which \$99 was attributed to drug treatments. In comparison, the annual cost of absenteeism due to hypertension was calculated to be \$77 per employee while the hypertension-related expenditures due to presenteeism

TABLE 3
Cost of illness studies on hypertension

Author	Country	Study design	# of patients (Mean Age)	Perspective (Time Horizon)	Currency (Year of costing)	Unit of costing	Total costs, \$	Total costs 2004 CAN\$	% Direct costs	Direct cost per capita 2004 CAN\$
Maetzel et al. 2004 (33)	Canada (Ontario)	multi-center trial	142 (68.2)	societal (6 Months)	US\$ (2000)	per patient	1,963	3,198	78.2%	495
Hodgson et al. 2001 (31)	USA	modeling	-	payer (1 Year)	US\$ (1998)	per country; per capita; per hypertensive condition	For country: 108.8 billion Per capita: 403 Per condition: 3,787	For country: 185 billion Per capita: 685 Per condition: 6,440	100%	685
Druss et al. 2001 (28)	USA	analysis of population survey	2161 (55.8% 18-64 yrs; 44.1% >65 yrs)	societal (1 Year)	US\$ (1996)	per capita; for country	121.8 billion	195.5 billion	91%	656
Amin et al. 1999 (25)	USA	analysis of HMO database	3769 (54)	payer (2 Years)	US\$ (1996)*	per patient per year	1,803	2,957	100%	530
Garis, R. 2001 (29)	USA	analysis of Medicaid database	1467 (46.5)	payer (1 Year)	US\$ (1995)	per patient	1,351	2,216	100%	408
Goetzel et al. 2004 (30)	USA	modeling	-	societal (1 Year)	US\$ (2002)*	per patient	392	-	23.3%	23
Berto et al. 2002 (26)	Italy	retrospective cohort study	1651 (Range of means in cohorts: 60-66.2)	payer (1 Year)	Euros (1999)*	per patient	779.59	-	Range 6.3%-10.5%	Range 19.9-33.2
Degli Esposti et al. 2001 (27)	Italy	retrospective cohort study	1047 (62.9)	payer (1 Year)	Euros (1998)	per patient	514	-	100%	208
Kiiskinen et al. 1998 (32)	Finland	analysis of population survey linked to national registries	10284 (not stated)	payer (19 Years)	US\$ (1992)	per patient	Men: Mild HBP=146,500 Severe HBP=219,300 Women: Mild HBP=107,200 Severe HBP=165,900	Men: Mild HBP=220,474 Severe HBP=330,034 Women: Mild HBP=161,330 Severe HBP=249,670	100%	Men: Mild: 67904 Severe: 101648 Women: Mild: 49688 Severe: 76896

*Assumption for year of costing since not stated in paper. HBP High blood pressure; HMO Health Maintenance Organization; USA United States of America

(ie, loss of productivity while at work) were estimated to be \$406 per employee.

Europe: In Italy, a retrospective cohort study by Berto et al (26) indicated that drugs were the major driver (46%) of the medical costs of hypertension, followed by general practitioner visits (21%), hospital admissions (15%) and laboratory tests (13%). Another analysis of the same database (27) showed that the annual direct medical costs associated with hypertension were almost 40% lower in new hypertensive incident cases than in prevalent cases.

In a Finnish study (32), severe hypertension was shown to be associated with higher direct and indirect costs than mild-to-moderate hypertension. The records of 10,284 hypertensive respondents (25 to 59 years of age) to a 1972 survey were linked to national registries covering drug use, hospitalization, absence due to sickness, disability pensions and deaths to evaluate the 19-year cost of hypertension in Finland.

Congestive heart failure

Two studies that reported costs associated with congestive heart failure (CHF) (10,34) are summarized in Table 4. Based on an analysis (34) of a large managed care claims database, the six-month health care cost of CHF was determined to be \$3,283 per patient in the USA. Hospitalizations and prescription drugs accounted for 54% and 38% of the total direct medical costs, respectively. In comparison, the one-year cost per CHF patient was established to be \$3,802, based on an analysis of a state Medicaid dataset (10). More than one-half (52.1%) of costs were related to prescriptions. Compared with other cardiovascular conditions among this Medicaid population, the annual cost per CHF patient was similar to the cost per patient

TABLE 4
Cost of illness studies on congestive heart failure

Author	Country	Study design	# of patients (Mean Age)	Perspective (Time Horizon)	Currency (Year of costing)	Unit of costing	Total costs, \$	Total costs 2004 CAN\$	% Direct costs	Direct cost per capita 2004 CAN\$
Xuan et al. 2000 (34)	USA	analysis of managed care database	2777 (56.9)	payer (6 Months)	US\$ (1994)	per patient	1,967	3,283	100%	58
Garis et al. 2002 (10)	USA	analysis of Medicaid database	242 (69.3)	payer (1 Year)	US\$ (1995)	per patient	2,318	3,802	100%	633

USA United States of America

with CVD but higher than the costs associated with diabetes or hypertension (10).

CAD

Nine studies (12,35-42) reported costs associated with CAD overall or specifically for myocardial infarction (MI), acute coronary syndrome (ACS) and angina. These studies are summarized in Table 5 and are discussed in more detail below.

CAD: Based on a Markov model (41) and assuming an annual incidence of 616,900 CAD cases in the USA (fatal MI and nonfatal MI, stable and unstable angina), the treatment costs of CAD in the USA of these incident cases were estimated to be \$9 billion for the first year while the cumulative five-year and 10-year costs were calculated to be \$15 billion and \$20.5 billion, respectively.

However, the annual medical costs of CAD in the USA, including both incident and prevalent cases, were documented to be \$53.7 billion when CAD was the first listed diagnosis and \$121.9 billion when CAD was listed in any position, based on various public and private USA

TABLE 5
Cost of illness studies on various aspects of coronary artery disease (CAD)

Author	Disease	Country	Study design	# of patients (Mean Age)	Perspective (Time Horizon)	Currency (Year of costing)	Unit of costing	Total costs, \$	Total costs 2004 CAN\$	% Direct costs	Direct cost per capita 2004 CAN\$
Russell et al. 1998 (41)	CAD	USA	modeling (Markov)	N/A (N/A)	payer (1 Year)	US\$ (1995)	per patient	Fatal MI: 17,532 Nonfatal MI: 15,540 Stable angina: 2,569 Unstable angina: 12,058 Sudden CAD death: 713	Fatal MI: 28,756 Nonfatal MI: 25,489 Stable angina: 4,214 Unstable angina: 19,778 Sudden CAD death: 1,169	100%	Fatal: 850.30 Nonfatal: 753.69 Stable angina: 124.60 Unstable angina: 124.60 Sudden C death: 34.58
Javitz et al. 2004 (37)	CAD; chronic angina	USA	modeling	-	payer (1 Year)	US\$ (2000)	per country	Chronic Angina: 1st listed: 1,883 million Any position: 8,893 million CAD: 1st listed: 32,975 million Any position: 74,798 million	Chronic Angina: 1st listed: 3 billion Any position: 14.5 billion CAD: 1st listed: 53.7 billion Any position: 121.9 billion	100%	Chronic Angina: 1st listed: 6.67 Any position: 31.51 CAD: 1st listed: 116.23 Any position: 265.06
Migliaccio-Walle & Caro 2005 (40)	MI	Canada (Sask.)	retrospective administrative database	15559 (66.9)	payer (5 Years)	Can\$ (2002)	per patient	48,578	50,849	100%	633
Levy et al. 2003 (38)	MI	8 European countries	modeling (decision tree)	-	payer (2 Years)	Euros (1999)*	per patient	Range: 9,512 (Belgium) to 18,293 (Austria)	-	100%	Range: 190.24-365.86
Etemad & McCollam 2005 (36)	ACS	USA	analysis of HMO database	13731 (54.2)	payer (2 Years)	US\$ (1999)*	per patient per month	2,312	3,873	100%	23
Eisenstein et al. 2001 (35)	ACS	USA	single center trial	9876 (median = 62)	payer (10 Years)	US\$ (1997)	per patient	All ACS: 52,517 Unstable angina: 54,078 MI: 51,523	All ACS: 84,250 Unstable angina: 86,754 MI: 82,655	100%	All: 525.17 Unstable: 540.78 MI: 151.23
Stewart et al. 2003 (42)	angina	UK	modeling	-	payer (-)	GBP (2000)	per country	669 million	1.7 billion	100%	11
Liu et al. 2002 (39)	CHD	UK	modeling	-	societal (-)	GBP (1999)	per country	7.06 billion	19.1 billion	24.5%	29
Leal et al. 2006 (12)	CHD	Europe	cost of illness	-	societal (-)	Euros (2003)	Total for EU; per country	44.7 billion for EU; 50 per capita	72 billion for EU; 81 per capita	51% for EU	26

*Assumption for year of costing since not stated in paper. ACS Acute coronary syndrome; CHD Coronary heart disease; EU Europe; GBP United Kingdom Pounds; HMO Health Maintenance Organization; MI Myocardial infarction; N/A Not applicable; Sask Saskatchewan; UK United Kingdom; USA United States of America

databases (37). Hospitalization costs represented more than two-thirds of the total direct medical costs associated with CAD and prescription drugs – between 2% (CAD diagnosis listed in any position) and 15% (CAD listed first) of the medical cost. Compared with the cost of chronic angina, which was also evaluated in this study, the cost of CAD was reported to be 10 to 20 times higher.

MI: In Canada, the 2002 average five-year direct medical costs per patient hospitalized as a result of an MI was determined to be \$50,849 based on an analysis (40) of an administrative database of 15,559 Saskatchewan residents (mean age 66.9 years) who experienced an MI between January 1, 1990, and December 31, 1995. Results indicated that the MI costs were higher for the first year compared with the subsequent years.

Acute costs of MI and one-year follow-up also represented the largest proportion of the costs of MI in Europe when a decision tree model was used to estimate the two-year cost of MI in eight European countries (38).

ACS: In a retrospective analysis of a managed care database (36), hospitalization and drug costs represented 72% and 7% of the two-year medical costs associated with new-onset ACS patients, respectively. Using patient-level information and modeling techniques to calculate the 10-year costs of ACS, Eisenstein et al (35) reported that approximately 50% of the medical costs associated with ACS occurred in the acute phase.

Angina: Using a prevalence-based model assuming that 1.1% of the UK population suffered from angina pectoris, the direct cost of angina pectoris in the UK (\$1.7 billion) was estimated to be 1.3% of the UK national health expenditures (42). In-hospital

procedures (35%) were the highest cost category, followed by hospital bed use (31%), drug treatment (12%), postdischarge outpatient department visits (8%) and physician outpatient department referrals (5%).

Using another prevalence approach, Liu et al (39) determined the direct cost of CAD in the UK to be \$4.7 billion, an estimate four times higher than the UK cost of CAD given in the previous study (42). Direct costs of CAD were mainly driven by hospitalization costs (53%) and drug treatment (32%). Indirect costs associated with productivity losses due to morbidity and mortality accounted for more than 75% of the total cost of CAD in the UK (\$19.1 billion) (39).

In a multicountry European study (12) evaluating the cost of CAD in Europe, inpatient care and prescription expenditures contributed to 62% and 23% of the medical costs, respectively. While differences were observed among the 25 European countries involved in this study, the cost of CAD represented 25% of the cost of CVD.

DISCUSSION

Thirty-four studies assessing the cost of CVD or related conditions in North America, Europe and Australia were reviewed in the present report. While it is difficult to directly compare all of the studies due to different methods of analysis, time horizon and countries or settings, all of the studies concluded that the costs of treating CVD-related conditions are significant from both a payer and societal perspective.

CVD contributed to 11.6% of the total Canadian cost of illness and 12% of the UK health care expenditures (11,12). The direct cost of stroke was estimated to be nearly 3% of the health care expenditures in Ontario, the cost of hypertension was 12.6% of the USA health care

expenditures, and the cost of angina was 1% of the UK national health care expenditures (15,31,42). In addition, caregiver costs and losses of productivity due to CVD premature mortality or morbidity were shown to be considerable. With the exception of hypertension, for which drug cost was the main cost category, hospitalization costs were the main drivers of the direct cost of CVD-related conditions. However, follow-up costs have been shown to be significant in all studies, suggesting that follow-up care and associated costs should be considered in economic evaluations of CVD or strategies aimed at decreasing the burden of CVD. Several USA studies using administrative databases have also shown that the cost associated with CVD conditions was higher than other chronic conditions.

Several limitations were associated with the present review due to the broad research question and the challenges associated with developing a literature search strategy that includes all relevant studies. This increases the risk that some studies were missed in the initial screening process or were not identified. To minimize this risk, all the references listed in the included studies were manually searched to identify any studies conducted since 1998 that were missed in the electronic database searches. Even after transformation to Canadian currency or a direct cost per capita, it is difficult to directly compare studies conducted in different settings; therefore, caution should be used when comparing results. Even in comparable studies (same country and condition), important differences were observed among cost estimates and, consequently, it is difficult to compare costs across these studies. Although cost-effectiveness analyses may provide valuable information on cost, they were excluded from our review. As a result, other important information on the cost of CVD may have been missed.

While cost-of-illness studies have the potential to identify the main cost drivers of a disease, the majority (82%) of the studies reviewed did not provide any information on the predictors of the costs. In fact, multivariable regression analyses were conducted in only 13% of the studies to identify factors influencing cost figures. A minority of studies (28%) conducted sensitivity analyses to examine the impact of certain variables on cost estimates. Indirect costs were evaluated in only 33% of the studies, and productivity losses associated with premature mortality were the main drivers of the indirect costs. However, the majority of these studies used the human capital

approach (ie, valuation of lost earnings from time of premature death to age of retirement) to estimate these indirect costs, which may have resulted in an overestimation of the indirect costs compared with a valuation using the friction cost method (ie, valuation of lost earnings from death to time until worker is replaced).

The present review identified the need to conduct additional research in Canada to gain a better understanding of the cost of CVD or other chronic conditions. Of the seven Canadian studies reviewed in the present paper, two were cost-of-illness studies using a top-down approach, one used modeling techniques, three were based on short-term trials, and only one was based on an analysis of a provincial administrative dataset. Considering the number of national and provincial databases available in Canada, it is surprising that so few studies used databases to estimate the burden of CVD in Canada. While some limitations are associated with administrative databases (eg, validity of diagnosis), they provide a wealth of information to better understand the economic burden of CVD. Such analyses also allow for comparisons among different conditions or diseases in a particular population, and may be less expensive to conduct than trials.

The present review of the cost of CVD, which includes six studies conducted in Canada, outlines the importance of prevention of the disease and its consequences, providing a convincing case for CVD prevention programs in Canada. While some CVD risk factors such as age, sex and familial history cannot be changed, preventive action can be taken against other CVD risk factors such as physical inactivity, high blood pressure, high cholesterol, diabetes and stress.

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