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 current 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 died 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 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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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 are 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 conditions and found to be considerably higher. The total costs of CVD were estimated to be $18.8 billion, with hospitalization costs accounting for 45% of total CVD costs, physician visits for 14%, and drugs for 26%. Of the total direct costs, hospitalization costs accounted for 45%, physician visits for 14%, and drugs for 26%.
The cost of CVD

TABLE 1
Cost of illness studies on cardiovascular disease

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

*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 (9.2%). 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 with usual care following discharge of stroke patients requiring rehabilitation. 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).

**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...
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 a stroke. Other important categories were rehabilitation costs (24), which focused on the first-year costs following a first-time stroke, and hospitalization costs represented one-half of the costs in the first year (28), which was 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 professionals**

Drugs, hospitalization costs and costs associated with health care professionals 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 2**

<table>
<thead>
<tr>
<th>Author</th>
<th>Country</th>
<th>Study design</th>
<th># of patients</th>
<th>Perspective (Time Horizon)</th>
<th>Currency (Year of Costing)</th>
<th>Unit of costing</th>
<th>Total costs, $</th>
<th>Total costs 2004 CANS</th>
<th>% Direct costs</th>
<th>Direct cost per capita 2004 CANS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chan et al. 1998</td>
<td>Canada (Ontario)</td>
<td>modeling</td>
<td>-</td>
<td>societal (3 Year)</td>
<td>Can $ (1994/95)*</td>
<td>province</td>
<td>857 million</td>
<td>1.0 billion</td>
<td>62%</td>
<td>393</td>
</tr>
<tr>
<td>Teng et al. 2003</td>
<td>Canada</td>
<td>multi center trial</td>
<td>114 (70)</td>
<td>payer (3 Months)</td>
<td>Can $ (1997/98)*</td>
<td>per patient</td>
<td>Home: 7,784</td>
<td>Usual care: 11,065</td>
<td>100%</td>
<td>Home intensive: 123.4 Usual: 175.4</td>
</tr>
<tr>
<td>Samsa, G. 1999</td>
<td>USA</td>
<td>analysis of Medicare database</td>
<td>49,333 (1st stroke: 78.8; Recurrent: 79.0)</td>
<td>payer (2 Years)</td>
<td>US $ (1991)</td>
<td>per patient</td>
<td>First: 12,988</td>
<td>Recurrent: 13,534</td>
<td>100%</td>
<td>First: 403.67 Recurrent: 420.64</td>
</tr>
<tr>
<td>Sloan et al. 1999</td>
<td>USA</td>
<td>analysis of Medicare database</td>
<td>878 (not reported)</td>
<td>payer (6 Months)</td>
<td>US $ (1994)</td>
<td>per patient</td>
<td>16,600</td>
<td>27,707</td>
<td>100%</td>
<td>474</td>
</tr>
<tr>
<td>Ekman, M. 2004</td>
<td>6 European countries</td>
<td>review of European studies</td>
<td>-</td>
<td>-</td>
<td>Euros (2003)</td>
<td>per patient</td>
<td>21,413 (Germany) to 26,403 (Sweden)</td>
<td>Range: 34,518 (Germany) to 42,561 (Sweden)</td>
<td>100%</td>
<td>Range: 441.80-570.86</td>
</tr>
<tr>
<td>Trueben et al. 2005</td>
<td>7 European countries</td>
<td>review of European studies</td>
<td>-</td>
<td>-</td>
<td>Euros (2004)</td>
<td>per patient</td>
<td>20,239 (Germany) to 26,403 (Sweden)</td>
<td>Range: 32,726 (Germany) to 42,693 (Sweden)</td>
<td>100%</td>
<td>Range: 437.59-570.86</td>
</tr>
<tr>
<td>Leal et al. 2006</td>
<td>Europe</td>
<td>cost of illness</td>
<td>-</td>
<td>societal (3 Year)</td>
<td>Euros (2003)</td>
<td>Total for EU; per country; per capita</td>
<td>34 billion for EU; 46 per capita</td>
<td>74 billion for EU; 55 per capita</td>
<td>61% for EU</td>
<td>43</td>
</tr>
<tr>
<td>Koblimsky-Rabas et al.</td>
<td>Germany</td>
<td>analysis of population surveys linked to administrative databases</td>
<td>1,637 from stroke registry; 821 resource utilization (76.3 women; 70.6 men)</td>
<td>payer (1, 5, 10 years; lifetime)</td>
<td>Euros (2004)</td>
<td>per case</td>
<td>1 year: 15,140; 5 year: 28,837; 10 year: 36,873; lifetime: 43,129</td>
<td>1 year: 24,481; 5 year: 48,246; 10 year: 36,873; lifetime: 69,739</td>
<td>100%</td>
<td>1 yr: 327.34 5 yr: 645.11 10 yr: 797.23 Life: 932.50</td>
</tr>
<tr>
<td>Dewey et al. 2001</td>
<td>Australia</td>
<td>trial results extrapolated to Australia</td>
<td>275 (72)</td>
<td>societal (3 year; lifetime)</td>
<td>Aus $ (1997)</td>
<td>country</td>
<td>1 year: 555 million (US$420 m); Lifetime: 1.3 billion (US$985 m)</td>
<td>1 year: 661.9 million; Lifetime: 1.55 billion</td>
<td>93.9%</td>
<td>1 yr: 32.6 Lifetime: 76.4</td>
</tr>
</tbody>
</table>

*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.
The cost of CVD

Cost of illness studies on hypertension

<table>
<thead>
<tr>
<th>Author</th>
<th>Country</th>
<th>Study design</th>
<th># of patients (Mean Age)</th>
<th>Perspective (Time Horizon)</th>
<th>Currency (Year of costing)</th>
<th>Unit of costing</th>
<th>Total costs, $</th>
<th>Total costs 2004 CAN$</th>
<th>% (Direct costs)</th>
<th>Direct cost per capita 2004 CAN$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maertel et al. 2004 (33)</td>
<td>Canada (Ontario)</td>
<td>multi-center trial</td>
<td>142 (68.2)</td>
<td>societal (6 Months)</td>
<td>US$ (2000)</td>
<td>per patient</td>
<td>1,963</td>
<td>3,198</td>
<td>78.2%</td>
<td>495</td>
</tr>
<tr>
<td>Hodgson et al. 2001 (31)</td>
<td>USA</td>
<td>modeling</td>
<td>-</td>
<td>payer (1 Year)</td>
<td>US$ (1998)</td>
<td>per patient</td>
<td>1,980</td>
<td>3,283</td>
<td>100%</td>
<td>685</td>
</tr>
<tr>
<td>Druss et al. 2001 (28)</td>
<td>USA</td>
<td>analysis of population survey</td>
<td>2,161 (53.8% 18-64 yrs; 44.1% &gt;65 yrs)</td>
<td>societal (1 Year)</td>
<td>US$ (1996)</td>
<td>per patient for country</td>
<td>121.8 billion</td>
<td>195.5 billion</td>
<td>91%</td>
<td>656</td>
</tr>
<tr>
<td>Amin et al. 1999 (25)</td>
<td>USA</td>
<td>analysis of HMO database</td>
<td>3,769 (54)</td>
<td>payer (2 Years)</td>
<td>US$ (1996)*</td>
<td>per patient per year</td>
<td>1,803</td>
<td>2,957</td>
<td>100%</td>
<td>530</td>
</tr>
<tr>
<td>Garis, R. 2001 (29)</td>
<td>USA</td>
<td>analysis of Medicaid database</td>
<td>1,467 (46.5)</td>
<td>payer (1 Year)</td>
<td>US$ (1995)</td>
<td>per patient</td>
<td>1,351</td>
<td>2,216</td>
<td>100%</td>
<td>408</td>
</tr>
<tr>
<td>Goetzl et al. 2004 (30)</td>
<td>USA</td>
<td>modeling</td>
<td>-</td>
<td>societal (1 Year)</td>
<td>US$ (2002)*</td>
<td>per patient</td>
<td>392</td>
<td>-</td>
<td>23.3%</td>
<td>23</td>
</tr>
<tr>
<td>Berto et al. 2002 (26)</td>
<td>Italy</td>
<td>retrospective cohort study</td>
<td>1,651 (Range of means in cohorts: 60-66.2)</td>
<td>payer (1 Year)</td>
<td>Euros (1999)*</td>
<td>per patient</td>
<td>779.59</td>
<td>-</td>
<td>Range 6.3%-10.5%</td>
<td>Range 19.9-33.2</td>
</tr>
<tr>
<td>Degli Esposti et al. 2001 (27)</td>
<td>Italy</td>
<td>retrospective cohort study</td>
<td>1,047 (62.9)</td>
<td>payer (1 Year)</td>
<td>Euros (1998)</td>
<td>per patient</td>
<td>514</td>
<td>-</td>
<td>100%</td>
<td>208</td>
</tr>
<tr>
<td>Kiskinen et al. 1998 (32)</td>
<td>Finland</td>
<td>analysis of population survey linked to national registers</td>
<td>10,284 (not stated)</td>
<td>payer (19 Years)</td>
<td>US$ (1992)</td>
<td>per patient</td>
<td>1,987</td>
<td>3,383</td>
<td>100%</td>
<td>58</td>
</tr>
</tbody>
</table>

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

Cost of illness studies on congestive heart failure

<table>
<thead>
<tr>
<th>Author</th>
<th>Country</th>
<th>Study design</th>
<th># of patients (Mean Age)</th>
<th>Perspective (Time Horizon)</th>
<th>Currency (Year of costing)</th>
<th>Unit of costing</th>
<th>Total costs, $</th>
<th>Total costs 2004 CAN$</th>
<th>% (Direct costs)</th>
<th>Direct cost per capita 2004 CAN$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xuan et al. 2000 (34)</td>
<td>USA</td>
<td>analysis of managed care database</td>
<td>2,773 (56.9)</td>
<td>payer (6 Months)</td>
<td>US$ (1994)</td>
<td>per patient</td>
<td>1,967</td>
<td>3,283</td>
<td>100%</td>
<td>58</td>
</tr>
<tr>
<td>Garis et al. 2002 (10)</td>
<td>USA</td>
<td>analysis of Medicaid database</td>
<td>342 (80.3)</td>
<td>payer (1 Year)</td>
<td>US$ (1995)</td>
<td>per patient</td>
<td>2,318</td>
<td>3,862</td>
<td>100%</td>
<td>633</td>
</tr>
</tbody>
</table>

USA United States of America

(ie, loss of productivity while at work) were estimated to be $426 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 registers 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 35% 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 (12). 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 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
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 represented 25% of the cost of CVD.

**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 following an MI 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).

**ACCS:** 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 expenditure.

### TABLE 5

<table>
<thead>
<tr>
<th>Author et al.</th>
<th>Disease</th>
<th>Country</th>
<th>Study design</th>
<th># of patients (Mean Age)</th>
<th>Perspective (Time Horizon)</th>
<th>Currency (Year of costing)</th>
<th>Unit of costing</th>
<th>Total costs, $</th>
<th>% Direct costs</th>
<th>Direct cost per capita 2004 CAN$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Russell et al. 1998 (41)</td>
<td>CAD</td>
<td>USA</td>
<td>modeling (Markov)</td>
<td>N/A (N/A)</td>
<td>payer (1 Year)</td>
<td>US$ (1995)</td>
<td>per patient</td>
<td>Fatal MI: 17,732 Nonfatal MI: 15,540 Stable angina: 2,569 Unstable angina: 12,058 Sudden CAD death: 713</td>
<td>100%</td>
<td>650.30</td>
</tr>
<tr>
<td>Migliaccio-Walle &amp; Caro 2005 (40)</td>
<td>MI</td>
<td>Canada (Sask.)</td>
<td>retrospective administrative database</td>
<td>15559 (66.8)</td>
<td>payer (5 Years)</td>
<td>Can$ (2002)</td>
<td>per patient</td>
<td>48,578</td>
<td>100%</td>
<td>633.00</td>
</tr>
<tr>
<td>Levy et al. 2003 (38)</td>
<td>ACS</td>
<td>USA</td>
<td>analysis of HMO database</td>
<td>13731 (54.2)</td>
<td>payer (2 Years)</td>
<td>Euros (1999)*</td>
<td>per patient</td>
<td>Range: 9.512 (Belgium) to 18,293 (Austria)</td>
<td>-</td>
<td>100%</td>
</tr>
<tr>
<td>Eisenstein et al. 2001 (35)</td>
<td>ACS</td>
<td>USA</td>
<td>single center trial</td>
<td>9876 (median = 62)</td>
<td>payer (10 Years)</td>
<td>US$ (1997)</td>
<td>per patient</td>
<td>2,312</td>
<td>100%</td>
<td>23.00</td>
</tr>
<tr>
<td>Stewart et al. 2003 (42)</td>
<td>angina</td>
<td>UK</td>
<td>modeling</td>
<td>-</td>
<td>payer (-)</td>
<td>GBP (2000)</td>
<td>per country</td>
<td>669 million</td>
<td>1.7 billion</td>
<td>11</td>
</tr>
<tr>
<td>Liu et al. 2002 (39)</td>
<td>CHD</td>
<td>UK</td>
<td>modeling</td>
<td>-</td>
<td>societal (-)</td>
<td>GBP (1999)</td>
<td>per country</td>
<td>7.06 billion</td>
<td>19.1 billion</td>
<td>24.5%</td>
</tr>
<tr>
<td>Leal et al. 2006 (12)</td>
<td>CHD</td>
<td>Europe</td>
<td>cost of illness</td>
<td>-</td>
<td>societal (-)</td>
<td>Euros (2003)</td>
<td>Total for EU per country</td>
<td>44.7 billion for EU; 50 per capita</td>
<td>72 billion for EU; 81 per capita</td>
<td>51%</td>
</tr>
</tbody>
</table>

*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
The impact of certain variables on cost estimates. Indirect costs were only 13% of the studies to identify factors influencing cost figures. A cost-effectiveness analyses may provide valuable information on cost, results. Even in comparable studies (same country and condition), in different settings; therefore, caution should be used when comparing studies conducted since 1998 that were missed in the electronic database searches. Even after transformation to Canadian currency or a base 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 majority 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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