Preventing cardiovascular disease among Canadians: Is the treatment of hypertension or dyslipidemia cost-effective?

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BACKGROUND AND OBJECTIVES: The direct health care costs associated with treating hypertension and dyslipidemia continue to grow in most western countries, including Canada. Despite the proven effectiveness of hypertension and lipid therapies to prevent cardiovascular disease, the cost-effectiveness of long-term primary prevention, as currently advocated by Canadian treatment guidelines, remains to be determined.
METHODS: Therapeutic efficiency, defined as person-years of treatment per year of life saved (YOLS) and the cost-effectiveness of treatment were estimated for groups of Canadian adults, 40 to 74 years of age. The clinical indications for treatment were based on the Canadian national guidelines in 2005. Analyses focused on those without cardiovascular disease or diabetes using risk factor data from the Canadian heart health surveys and drug data from a national study, the MyHealthCheckUp survey. The expected impact of therapy was based on published results: statins would result in a 40% drop in low-density lipoprotein cholesterol and a 6% increase in high-density lipoprotein cholesterol, while hypertension therapy would result in a 6.4% drop in systolic and a 5.6% drop in diastolic blood pressure.
RESULTS: The estimated daily cost of statins was $1.98 versus $1.72 for antihypertensives. Overall, 2.33 million patients would be treated with lipid therapy and 2.34 million with antihypertensives. The average cost-effectiveness of lipid therapy would be approximately $16,700 per YOLS while hypertension therapy would be approximately $37,100 per YOLS. Lifelong lipid and hypertension therapy would be associated with 1.1 million and 472,000 life years saved at a national cost of $18.3 billion and $17.5 billion, respectively. However, hypertension treatment for some groups of Canadians appeared relatively expensive (more than $50,000 per YOLS) including men or women younger than 50 years of age. Despite attractive cost-effectiveness ratios, treatment appeared relatively inefficient (person-years of treatment per YOLS more than 100 years) for statin therapy among women younger than 50 years of age, and hypertension treatment for women younger than 60 years of age and men younger than 50 years of age.
CONCLUSIONS: Given Canadian guidelines, the treatment of dyslipidemia or hypertension in primary prevention appears economically attractive overall. However, for some groups of individuals, the forecasted future benefits appear to be relatively small given the many years of treatment that are required.

Key Words: *Cost-benefit analysis; Health economics; Hypercholesterolemia; Hypertension; Prevention*

Prévention de la maladie cardiovasculaire chez les Canadiens : Le traitement de l'hypertension ou de la dyslipidémie est-il rentable?

HISTORIQUE ET OBJECTIFS : Les coûts de santé directs associés au traitement de l'hypertension et de la dyslipidémie continuent de croître dans la plupart des pays occidentaux, y compris au Canada. Malgré l'efficacité éprouvée des traitements antihypertensifs et hypolipidémiants pour la prévention de la maladie cardiovasculaire, il reste à déterminer si la prévention primaire à long terme telle qu'elle est actuellement préconisée par les directives thérapeutiques canadiennes est rentable.
MÉTHODES : Les auteurs ont évalué l'efficience thérapeutique définie par le nombre d'années-personnes de traitement par année de vie sauvée (AVS) et le rapport coût:efficacité du traitement pour des groupes d'adultes canadiens de 40 à 74 ans. Les indications cliniques des traitements se fondaient sur les directives nationales canadiennes de 2005. Les analyses ont porté sur des sujets indemnes de maladie cardiovasculaire ou de diabète, sur des données sur les facteurs de risque provenant de sondages sur la santé cardiaque des Canadiens et sur des données pharmacologiques provenant d'une étude nationale, l'enquête MonBilanSanté. L'impact escompté du traitement provenait de résultats publiés : les statines allaient entraîner une baisse de 40 % du LDL-cholestérol et une augmentation de 6 % du HDL-cholestérol, tandis que le traitement antihypertensif allait entraîner une baisse de 6,4 % de la TA systolique et de 5,6 % de la TA diastolique.
RÉSULTATS : Le coût quotidien estimé des statines a été de 1,98 $, contre 1,72 $ pour les antihypertenseurs. Dans l'ensemble, 2,33 millions de patients allaient être traités par hypolipidémiants et 2,34 millions, par antihypertenseurs. Le rapport coût:efficacité moyen du traitement hypolipidémiant allait être d'environ 16 700 $ par AVS, tandis que celui du traitement antihypertenseur allait être d'environ 37 100 $ par AVS. Le traitement à vie des dyslipidémies et de l'hypertension allait être associé à 1,1 million et 472 000 années de vies sauvées, pour un coût national de 18,3 milliards de dollars et de 17,5 milliards de dollars, respectivement. Toutefois, le traitement de l'hypertension chez certains groupes de Canadiens a semblé relativement coûteux (plus de 50 000 $ par AVS), y compris chez les hommes ou les femmes de moins de 50 ans. Malgré les rapports coût:efficacité attrayants, le traitement a semblé relativement non efficient (années-personnes de traitement par AVS > 100 ans) dans le cas du traitement par statines chez les femmes de moins de 50 ans et dans le cas du traitement antihypertensif chez les femmes de moins de 60 ans et les hommes de moins de 50 ans.
CONCLUSIONS : Compte tenu des directives canadiennes, le traitement des dyslipidémies ou de l'hypertension en prévention primaire semble globalement attrayant sur le plan économique. Toutefois, chez certains groupes d'individus, les avantages prévus semblent relativement faibles, compte tenu du grand nombre d'années de traitement requis.

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Given the clinical and economic burden of cardiovascular disease (CVD) among Canadians, the treatment of modifiable risk factors such as hypertension and dyslipidemia is essential to prevent the development of this disease. CVD continues to be the leading cause of death among Canadians, with 20% and 7% of deaths attributable to coronary disease and cerebrovascular disease, respectively (1). CVD disease also remains the most expensive clinical condition, accounting for 11.6% of the total costs of illnesses and 13.9% of all drug prescriptions.

Primary prevention can potentially save lives, and reduce the morbidity and associated costs of treating coronary heart disease and stroke (2,3). Expanding clinical indications, an aging population and multiple drug therapies have resulted in rapidly increasing health care expenditures for the treatment of hypertension and dyslipidemia. Accordingly, while the benefits of primary prevention have been proven in clinical trials, the value of these interventions to society remains a matter for debate (4-7).

Evolving thresholds for initiating therapy and more aggressive treatment targets will require that greater numbers of asymptomatic adults be treated. Accordingly, these two conditions will demand a substantial portion of the national health care budget for the foreseeable future. We therefore have estimated and compared the efficiency and cost-effectiveness of treatment following compliance with Canadian national treatment guidelines.

METHODS

The cost-effectiveness of treating dyslipidemia and/or hypertension among Canadians free of CVD and diabetes was estimated from published clinical trials, drug use from the MyHealthCheckUp (MHC) national survey, population risk factor data collected by the Canadian heart health surveys, current Canadian treatment guidelines and a previously published Markov model (the Cardiovascular Disease Life Expectancy Model) to calculate the increased life expectancy and decreased morbidity associated with treating risk factors to target (2,3,8,9).

The perspective of the present health economic analysis was that of the Canadian health care system. Accordingly, all direct health care costs associated with the prevention and treatment of CVD were included in the analyses. All costs are reported in 2002 Canadian dollars, and future costs and benefits were discounted 3% annually.

The MHC national survey

The MHC national survey is a cross-Canada study designed to evaluate adults with cardiometabolic risk factors including CVD, diabetes, hypertension, dyslipidemia and obesity. Not only does it evaluate individuals receiving treatment, it can also be used to identify the characteristics of those who remain untreated, despite national treatment guidelines.

The study design was simple. Participants were screened at pharmacies and in the workplace, ensuring a representative sample of adults 40 years of age and older, both treated and untreated. After signing informed consent, each participant completed a brief questionnaire and then had the following measured: height, weight, abdominal circumference and blood pressure. Blood was then drawn by fingerprick to measure nonfasting glucose, total cholesterol and high-density lipoprotein (HDL) cholesterol levels. The MHC survey includes comprehensive drug data usually provided by the community pharmacist from the following treatment classes: hypertension, dyslipidemia, CVD, diabetes, obesity, depression and smoking cessation.

The results of these measures were then entered into a computer program onsite, based on the Cardiovascular Life Expectancy Model (9), to estimate the individual's current risk of CVD and the potential benefits of treating these risk factors. Each participant's risk profile was explained to them and an individualized action plan was discussed based on current national treatment guidelines (10). The data presented herein are based on 2121 participants including 908 taking antihypertensives and 595 on statins.

TABLE 1
Estimated costs of hypertension or statin therapy based on medication used in the MyHealthCheckup survey

Drug group	Use, %	Mean cost, $*	Cost, $†
Alpha-adrenergic blocking agents	0.4	0.76	0.01
Angiotensin II receptor antagonists	15.7	1.35	0.28
Angiotensin-converting enzyme inhibitors	24.5	1.04	0.44
Beta-adrenergic blocking agents	10.7	0.53	0.19
Central alpha-agonists	0.3	0.33	0.01
Dihydropyridines	24.4	1.42	0.44
Direct vasodilators	0.0	0.17	0.00
Loop diuretics	1.0	0.23	0.02
Mineralocorticoid (aldosterone) receptor antagonists	0.2	0.30	0.00
Miscellaneous calcium-channel blocking agents	7.6	1.26	0.14
Potassium-sparing diuretics	0.1	0.36	0.00
Thiazide diuretics	13.9	1.10	0.25
Thiazide-like diuretics	1.0	0.66	0.02
Total	100.0	–	1.80
HMG-coenzyme A reductase inhibitors			
Atorvastatin	66.3	2.26	1.37
Fluvastatin	0.4	1.30	0.01
Lovastatin	0.3	1.35	0.01
Pravastatin	8.6	1.70	0.18
Rosuvastatin	10.2	1.78	0.21
Simvastatin	14.2	1.86	0.29
Total	100.0	–	2.07

**Mean cost of medication across all drugs in drug group (Data from IMS Health, Compuscript 2005 [Costs are in 2005 Canadian dollars]); †Cost = usage × average cost. HMG 3-hydroxy-3-methyl-glutaryl*

Clinical trial evidence

The benefits of lipid treatment were based on changes observed after 52 weeks in the rosuvastatin 5 mg and 10 mg, pravastatin 20 mg and simvastatin 20 mg arms of a randomized, double-blind trial reported by Brown et al (11). Across all treatment arms, the mean of the reported relative changes in low-density lipoprotein (LDL), HDL and total cholesterol were determined to be –40%, +6% and –29%, respectively.

For hypertension therapy, 52-week data from the chlorthalidone arm of the Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) (12) were selected. In this study, antihypertensives were titrated to achieve a goal blood pressure of less than 140/90 mmHg. After one year of therapy, 57.8% of individuals had achieved this goal. Systolic blood pressure had dropped 6.4% (approximately 10 mmHg), while diastolic pressure had dropped 5.6% (approximately 5 mmHg).

Drug costs

The costs of lipid and hypertension therapies were derived from patient drug use observed in the MHC survey, and cost data from IMS Canada Inc, which include retail markup and dispensing fees (13). The mean unit cost per pill was obtained by dividing the mean prescription cost by the mean prescription size. These costs were then weighted by their relative use by MHC participants and summed across all treated subjects to obtain the mean daily cost of treatment (Table 1). All costs were adjusted to the year 2002 using the health and personal care component of the Canadian consumer price index (14). The daily cost of statin and antihypertensive drug use in Canada was estimated to be $1.98 and $1.72, respectively.

Sensitivity analysis to maximize cost-effectiveness

To maximize the potential cost-effectiveness of therapy, a sensitivity analysis of potential treatments that would maximally lower lipids or

blood pressure at a relatively low cost was completed. For the sensitivity analysis, the 10 mg rosuvastatin arm of the the study by Brown et al (11) was selected, which was shown to be particularly effective. Treatment was initiated with rosuvastatin 10 mg and titrated according to investigator discretion. After one year of therapy, 87.5% of participants had achieved treatment goals. Mean changes in blood lipid levels included LDL cholesterol –48%, total cholesterol –34%, triglycerides –18% and HDL cholesterol +8%. Given a mean daily dose of 13.8 mg of rosuvastatin, the mean daily cost of lipid therapy was estimated to be $1.80.

For hypertension, the ALLHAT benefits were used again but the costs were estimated to be $0.57 daily, based on a weighted average of the drugs used only in the chlorthalidone arm of the study in which treatment was initiated with this low-cost diuretic (12). Among participants followed until study termination, 95% were taking chlorthalidone, in addition to drugs such as atenolol (29%), amlodipine (5%) and lisinopril (4%).

The Canadian heart health surveys

The Canadian heart health surveys (8) represent the main findings of provincial, population-based surveys completed between 1986 and 1992. Although dated, this remains the most recent national survey of cardiovascular risk factors among Canadians. Moreover, it provides reasonable estimates of baseline blood pressure and lipid measures among Canadians before treatment.

The data for men and women between 40 and 74 years of age visiting the clinic were analyzed. Survey participants who reported having had a stroke, heart attack or diabetes were excluded from the present analysis. Total plasma cholesterol (TC), HDL cholesterol and LDL cholesterol were obtained from tests performed on a blood sample collected at the clinical visit. Systolic and diastolic blood pressure were taken and recorded as the mean of the two clinical assessments made and smoking status was determined from self-reported tobacco use. Subjects taking either lipid or blood pressure medication were included in the analysis if they were not controlled to prescribed target levels. Among subjects identified for blood pressure intervention alone, 24.9% were already taking medications. Among subjects identified for lipid intervention alone, 6.7% were already taking medication. Subjects identified for both interventions included 28.2% and 4.8% who were already on blood pressure and lipid medications, respectively.

Once a representative cohort had been assembled, the potential benefits of risk factor management were estimated for each individual. The population benefits were then extrapolated using weights assigned by the Canadian heart health surveys to each individual in the sample.

Cardiovascular Disease Life Expectancy model

The Cardiovascular Disease Life Expectancy model is a Markov model that estimates the annual probability of fatal and nonfatal CVD events based on multivariate logistic regression equations developed on the 15% random sample of the Lipid Research Clinic follow-up cohort (9,15). Independent risk factors include age, sex, blood pressure, LDL cholesterol, HDL cholesterol, smoking status and diabetes, and the presence or absence of CVD at baseline.

The model has previously been described in detail and shown to reasonably estimate events in nine clinical trials (9) of dyslipidemia or hypertension, a published analysis of the diabetic subjects in the Scandinavian Simvastatin Survival Study (4S) (16), and the life expectancy of American and Canadian adults (17,18). It has also recently been shown to accurately estimate 10-year cardiovascular risk among Canadians, similar to the Framingham risk equations (19).

Briefly, a cohort of patients is entered into the model with specified levels of risk factors. Each year, subjects can either die of coronary heart disease, cerebrovascular disease or other causes. Surviving subjects age for one year, then re-enter the model for the following year. The mean life expectancy can be calculated by summing across the total person-years of life experienced by the cohort and dividing by the number of subjects at risk on entry into the model. To estimate the impact of modifying one or more risk factors, the cohort is re-entered into the model after the expected changes in blood lipids, blood pressure, etc, and the revised mean life expectancy is calculated. The change in the mean life expectancy before and after intervention represents the estimated impact of treatment. These 'life-years gained' are expressed as years of life saved (YOLS) for the individual. Years of life free of CVD are also calculated, as is 'therapeutic efficiency', which is defined as person-years of treatment to save one year of life. Because the present analysis focused only on primary prevention, it was assumed that all individuals would receive the same lipid or blood pressure therapy once CVD was diagnosed. Because the forecasted benefits would occur at different times, all future costs and benefits were discounted by 3% annually.

For statin therapy, a one-year delay was assumed to occur before the observed reductions in lipid levels translated into a full decrease in risk as predicted by the multivariate risk function. This is consistent with delays in benefits observed in randomized, placebo-controlled clinical trials of lipid-lowering treatments (20,21). It was also assumed that a one-year lag period would be required for the benefits of hypertension therapy to occur, and that only 50% of the predicted benefits of blood pressure reduction would actually be realized based on a meta-analysis of the results of hypertension trials by Collins et al (22).

Guidelines for lipid treatment

The 2003 Canadian Working Group guidelines for the management of dyslipidemia recommend target levels including an LDL cholesterol level less than 2.5 mmol/L and a TC:HDL ratio less than 4 for people at high risk for CVD (calculated 10-year risk of coronary heart disease at 20% or greater), an LDL cholesterol level less than 3.0 mmol/L and a TC:HDL ratio less than 5 for people at moderate risk (calculated 10-year risk between 10% to 20%), and an LDL cholesterol level less than 4.0 mmol/L and a TC:HDL ratio less than 6 for people at low risk (calculated 10-year risk of 10% or lower) (3).

The benefits of treating LDL and TC:HDL ratio to these target levels were evaluated among individuals in the Canadian heart health surveys who would qualify for treatment based on their baseline risk factors and calculated global cardiovascular risk. CVD risk was assessed using the Framingham global risk assessment equation recommended by both the American National Cholesterol Education Program, Adult Treatment Panel III (NCEP ATP III) and the Canadian Working Group (3,23).

Guidelines for hypertension management

The 2005 Canadian Hypertension Education Program recommended systolic blood pressure levels of 140 mmHg or less and a diastolic blood pressure of 90 mmHg or less (2). Among individuals with baseline blood pressure values over these targets, the benefits of treating blood pressure to these targets were evaluated.

Estimating health care costs

The economic perspective adopted in the present analysis was that of a Canadian third-party payer providing comprehensive coverage of all health care services. CVD treatment costs included the costs of hospitalizations, physician fees, outpatient care and emergency services, where applicable. Physician fees, outpatient care, emergency services and drug prescriptions, which were also included in the model, have previously been reported in detail (24).

Treatment costs were assigned to each of the following acute, nonsurgical events: sudden death, fatal myocardial infarction, nonfatal myocardial infarction (with or without cardiac catheterization), congestive heart failure (with or without complications, age younger than 70 years or 70 years and older), arrhythmia (with or without complications, age younger than 70 years or 70 years and older), stroke and transient ischemic attack. Treatment costs for each CVD medical event included the costs of hospitalization, physician fees, and outpatient and emergency services when applicable.

TABLE 2
Characteristics of Canadian men between 40 and 74 years of age free of cardiovascular heart disease and diabetes

	Total population (n=8.44 million)	Subpopulation requiring lipid intervention (n=2.33 million)	Subpopulation requiring intervention for hypertension (n=2.34 million)
Male, %	48	68	53
Age, years	53.6 (40–74)	57.4 (40–74)	58.2 (40–74)
Systolic blood pressure, mmHg	129 (83–224)	134 (91–224)	149 (118–224)
Diastolic blood pressure, mmHg	80 (49–127)	82 (52–127)	89 (49–127)
Taking blood pressure medications, %	11	17	25
Total cholesterol, mmol/L	5.5 (2.3–17.1)	6.4 (2.9–17.1)	5.7 (2.3–11.9)
Low-density lipoprotein cholesterol, mmol/L	3.4 (0.4–12.0)	4.3 (1.4–12.0)	3.6 (0.9–8.6)
High-density lipoprotein cholesterol, mmol/L	1.3 (0.3–3.8)	1.1 (0.3–2.7)	1.3 (0.4–3.8)
Taking lipid medications, %	7	7	5
Smoking, %	20	28	16
Body mass index, kg/m^2	26.3 (17.0–42.9)	27.3 (17.0–42.9)	27.7 (17.0–42.9)
10-year Framingham risk, %	6 (<1–60)	12.4 (<1–60)	9.6 (1–60)

Data presented as mean (range) unless otherwise specified

Hospital costs for each medical event were estimated using the Canadian Institute for Health Information methodology (25). Over 85% of all Canadian acute care inpatient discharges (4.5 million patient records per year) are categorized into Case Mix Groups (CMGs). Each CMG is assigned a relative cost based on the intensity of resource use (the corresponding Resource Intensity Weight for that CMG). The Resource Intensity Weight cost weights were developed by the Canadian Institute for Health Information to adjust inpatient costs for the systematic differences in resource utilization across diagnoses.

Costs of surgical inpatient care for patients experiencing CVD events also included probability-weighted costs of the following procedures: coronary artery bypass grafting (with or without catheterization, complications and comorbidities), angioplasty (with or without complications and comorbidities), coronary catheterization (with or without complex diagnoses), permanent and temporary pacemaker insertion and pacemaker replacement (with or without complications and comorbidities). Costs per admission for surgical procedures were calculated as previously described for acute medical hospitalizations.

The mean costs of physician services for emergency, inpatient and outpatient care, and laboratory services were based on reimbursement fee schedules from the provinces of Quebec and Ontario (26-28). All costs were calculated in 2002 Canadian dollars (29).

RESULTS

Among 8.44 million Canadian adults 40 to 74 years of age, free of CVD or diabetes, 2.33 million would be eligible for dyslipidemia treatment while 2.34 million would be treatable for hypertension. The clinical characteristics of each of these populations are summarized in Table 2. Among Canadians requiring lipid therapy, 68% would be male and 28% would smoke. Among those requiring hypertension therapy, 53% would be male and 16% would smoke. The calculated 10-year Framingham risk of coronary heart disease would be 12.4% for those requiring lipid therapy and 9.6% for those with uncontrolled hypertension. The mean age for initiating lipid therapy would be 57 years (56 years for men and 60 years for women), while the mean age for initiating hypertensive therapy would be 58 years (56 years for men and 61 years for women).

If all individuals diagnosed with dyslipidemia received statin therapy, the lifetime costs of treatment would average $14,000 per individual (Table 3). However, these therapeutic costs would be offset in part by cost savings of $6,200 associated with delaying or preventing cardiovascular events such that the mean lifetime net cost per individual would be $7,800 or $510 annually. The incremental cost-effectiveness of lipid therapy would average $16,700 per YOLS, at a total cost to the Canadian health care system of $18.3 billion. However, these costs would be associated with substantial benefits including 1.1 million person-YOLS due to the prevention or delay of coronary events and strokes. For the individual patient, this would translate into 1.51 years free of CVD and 0.47 years of increased life expectancy or YOLS. The overall therapeutic efficiency was also estimated. On average, it would require 38 years of statin therapy to save one year of life. Stratifying by age and sex demonstrated a wide range of results. While the increased life expectancy was approximately 0.3 to 0.5 YOLS across the board, the person-years of treatment to save one year of life ranged from 27 years for men 70 to 74 years of age, up to 102 years for women 40 to 49 years of age. Similarly, while cost-effectiveness ratios tended to congregate between $10,000 and $20,000 per YOLS, treating younger women, particularly those 40 to 49 years of age, would be less cost-effective ($43,800 per YOLS).

Results focusing on the treatment of hypertension are presented in Table 4. The costs of treatment average $12,500 per individual and are offset by cost savings of $5,000 due to cardiovascular events delayed or avoided. The net cost per individual treated would be $7,500 or $480 annually. The incremental cost-effectiveness of hypertension therapy would average $37,100 per YOLS at a total cost to the Canadian health care system of $17.5 billion. Again, these costs would be associated with substantial benefits including 472,100 person-YOLS due to the prevention or delay of CVD. For the individual patient, this would translate into 0.44 years free of CVD and 0.20 YOLS. On average, it would require 95 years of hypertension therapy to save one year of life. As with lipids, these results were highly variable for different subgroups. Among younger (age 40 to 49 years) men and women, the cost-effectiveness ratios associated with treating hypertension ($63,900 and $70,500 per YOLS, respectively) were substantially higher than other age groups. Therapeutic efficiency also varied widely, ranging from 53 to 157 person-years of treatment to save one year of life.

Sensitivity analyses, minimizing costs and/or maximizing benefits lower the cost-effectiveness of treatment. For statin therapy, lifetime costs of treatment average $12,700 per individual, and cost savings of $7,300 are associated with delaying or preventing cardiovascular events, resulting in a mean lifetime net cost per individual of $5,400 or $350 annually (Table 5). The incremental cost-effectiveness of statin therapy averages $9,900 per YOLS at a total cost to the Canadian health care system of $12.6 billion. However, these costs are associated with substantial benefits, including 1.3 million person-YOLS due to the prevention or delay of coronary events and strokes. For the individual patient, this translates into 1.84 years free of CVD and 0.54 years of increased life expectancy or YOLS. On average, it would require 34 years of lipid therapy to save one year of life.

The reduced costs of treating hypertension are presented in Table 6. The costs of treatment would average $5,800 per individual, offset by

TABLE 3
Estimated costs and benefits of statin therapy

Age, years	Population treated, n	Lifetime cost of treatment, $	Lifetime net health costs, $	Annual net health costs, $	Cost per year of life saved, $	National costs associated with treatment, $ (millions)	Total person-years of life saved	Years of life saved	Years free of cardiovascular disease	Person-years of treatment to save one year of life
Women										
40–49	134,300	19,400	13,800	650	43,800	1,848	42,200	0.31	1.46	102
50–59	198,800	16,200	9,200	520	25,000	1,837	73,300	0.37	1.69	55
60–69	281,700	12,600	4,700	340	11,600	1,314	112,900	0.4	1.67	38
70–74	142,700	9,900	2,500	230	7,100	357	50,500	0.35	1.37	33
Total	757,700	14,200	7,100	450	19,200	5,357	279,000	0.37	1.58	53
Men										
40–49	487,900	17,600	11,400	590	20,100	5,539	276,200	0.57	1.81	37
50–59	424,600	14,500	8,500	530	14,900	3,594	241,600	0.57	1.57	30
60–69	496,700	11,400	6,200	500	13,300	3,076	230,900	0.46	1.22	29
70–74	167,400	9,100	4,300	430	10,900	713	65,500	0.39	1.01	27
Total	1,576,600	13,900	8,200	540	15,900	12,922	814,200	0.52	1.47	31
Overall	2,334,300	14,000	7,800	510	16,700	18,279	1,093,200	0.47	1.51	38

TABLE 4
Estimated costs and benefits of hypertension therapy

Age, years	Population treated, n	Lifetime cost of treatment, $	Lifetime net health costs, $	Annual net health costs, $	Cost per year of life saved, $	National costs associated with treatment, $ (millions)	Total person-years of life saved	Years of life saved	Years free of cardiovascular disease	Person-years of treatment to save one year of life
Women										
40–49	131,700	17,000	11,700	550	70,500	1,539	21,800	0.17	0.53	157
50–59	354,600	14,300	8,600	480	45,900	3,041	66,200	0.19	0.57	120
60–69	397,400	11,300	5,300	380	24,800	2,110	85,100	0.21	0.55	81
70–74	218,900	9,000	3,700	330	19,300	813	42,100	0.19	0.48	73
Total	1,102,800	12,500	6,800	440	34,900	7,503	215,200	0.20	0.54	101
Men										
40–49	400,500	16,300	11,800	580	63,900	4,729	74,100	0.18	0.34	128
50–59	324,800	12,700	7,900	510	33,800	2,579	76,300	0.23	0.38	78
60–69	371,500	10,100	5,900	470	28,100	2,189	77,800	0.21	0.37	71
70–74	138,900	7,700	3,700	390	18,000	517	28,700	0.21	0.33	53
Total	1,235,700	12,500	8,100	520	39,000	10,014	256,900	0.21	0.36	89
Overall	2,338,400	12,500	7,500	480	37,100	17,517	472,100	0.20	0.44	95

cost savings of $3,700 due to cardiovascular events delayed or avoided, resulting in mean net costs per individual of $2,100 or $130 annually. The incremental cost-effectiveness of hypertension therapy would average $10,200 per YOLS at a total cost to the Canadian health care system of $4.8 billion. For some specific patient groups, cost-effectiveness ratios would be extremely low (less than $5,000 per YOLS) and cost savings are forecasted for women 70 to 74 years of age.

DISCUSSION

Given the evidence that primary prevention works over the duration of a clinical trial (usually three to five years), the following question remains: how well does it work over a lifetime? Disease simulation models are necessary to address this question. Using current Canadian treatment guidelines, we have estimated that primary prevention lipid therapy for specific subgroups of adult men and women will require between 27 and 102 person-years of treatment to save one year of life, while hypertension therapy will require 53 to 157 years of treatment. These lipid treatment estimates can be compared with a similar analysis of Americans by Goldman et al (7). Using the Coronary Heart Disease Policy model, they estimated that primary prevention lipid therapy prescribed for high-risk American adults would result in five to 39 quality-adjusted life-years per 1000 person-years of treatment or approximately 26 to 200 person-years of treatment to save one year of life. It should be noted that the treatment time horizon for their analysis was 21 years rather than a lifetime, and benefits were restricted to the prevention of coronary events rather than coronary events and stroke, as presented in the present article.

While a similar analysis for blood pressure treatment is not available, the Coronary Heart Disease Policy model has been used to estimate the decline in mortality from coronary heart disease in the United States between 1980 and 1990 (30). In that analysis, lipid therapy was estimated to be responsible for 16% of the observed decline in coronary heart disease mortality while the control of hypertension was responsible for 7%. In our analyses, the lifetime benefits of lipid therapy were also forecast to result in population benefits that are approximately twofold greater than those associated with blood pressure treatment. This is due to a number of issues (18). The Canadian lipid guidelines base treatment targets an individual's calculated Framingham risk, while the blood pressure guidelines focus only on blood pressure levels. Accordingly, those receiving statin therapy will

TABLE 5
Potential costs and benefits of efficient statin therapy

Age, years	Population treated, n	Lifetime cost of treatment, $	Lifetime net health costs, $	Annual net health costs, $	Cost per year of life saved, $	National costs associated with treatment, $ (millions)	Total person-years of life saved	Years of life saved	Years free of cardiovascular disease	Person-years of treatment to save one year of life
Women										
40–49	134,300	17,500	10,900	510	30,100	1,461	48,500	0.36	1.78	90
50–59	198,800	14,700	6,500	360	15,300	1,287	84,000	0.42	2.04	49
60–69	281,700	11,400	2,100	150	4,500	588	129,500	0.46	2.02	33
70–74	142,700	9,000	200	20	500	31	58,100	0.41	1.66	29
Total	757,700	12,900	4,400	280	10,500	3,367	320,100	0.42	1.92	47
Men										
40–49	487,900	16,000	8,600	440	13,100	4,196	320,200	0.66	2.21	32
50–59	424,600	13,200	6,000	370	9,000	2,549	282,400	0.67	1.93	26
60–69	496,700	10,400	4,100	320	7,500	2,040	270,800	0.55	1.50	25
70–74	167,400	8,300	2,500	250	5,300	412	77,100	0.46	1.25	24
Total	1,576,600	12,600	5,800	380	9,700	9,197	950,500	0.60	1.81	27
Overall	2,334,300	12,700	5,400	350	9,900	12,564	1,270,500	0.54	1.84	34

TABLE 6
Potential costs and benefits of efficient hypertension therapy

Age, years	Population treated, n	Lifetime cost of treatment, $	Lifetime net health costs, $	Annual net health costs, $	Cost per year of life saved, $	National costs associated with treatment, $ (millions)	Total person-years of life saved	Years of life saved	Years free of cardiovascular disease	Person-years of treatment to save one year of life
Women										
40–49	131,700	7,900	3,900	190	23,800	520	21,800	0.17	0.53	157
50–59	354,600	6,700	2,100	120	11,400	752	66,200	0.19	0.57	120
60–69	397,400	5,300	400	30	1,700	148	85,100	0.21	0.55	81
70–74	218,900	4,200	–400	–30	CS	–79	42,100	0.19	0.48	73
Total	1,102,800	5,800	1,200	80	6,200	1,341	215,200	0.20	0.54	101
Men										
40–49	400,500	7,600	4,700	230	25,600	1,895	74,100	0.18	0.34	128
50–59	324,800	5,900	2,700	170	11,700	892	76,300	0.23	0.38	78
60–69	371,500	4,700	1,600	130	7,900	612	77,800	0.21	0.37	71
70–74	138,900	3,600	600	60	2,900	83	28,700	0.21	0.33	53
Total	1,235,700	5,900	2,800	180	13,600	3,483	256,900	0.21	0.36	89
Overall	2,338,400	5,800	2,100	130	10,200	4,825	472,100	0.20	0.44	95

CS Cost savings

have a higher risk than those receiving hypertension therapy. Another issue is that statin therapy appears to be more effective at lowering lipids than blood pressure treatments are at lowering blood pressure. Accordingly, the CVD event reduction observed in lipid trials is greater than that observed in hypertension trials.

The results of the present pharmacoeconomic analysis demonstrate that the cost-effectiveness of treating dyslipidemia or hypertension among most Canadians without diagnosed CVD or diabetes is economically attractive with average cost-effectiveness ratios of $16,700/YOLS and $37,100/YOLS, respectively. In the present analysis, these results were driven by the distribution of risk factors among Canadians, current treatment guidelines, the forecasted benefits of treatment and the estimated costs associated with treatment strategies. Among most age- and sex-specific subgroups, cost-effectiveness ratios of lipid therapy were extremely attractive (below $20,000/YOLS) for men 50 years of age or older and women older than 60 years of age. The cost-effectiveness ratios of hypertension therapy were substantially higher but remained below $50,000/YOLS for men and women 50 years of age or older.

These forecasted benefits and cost-effectiveness of lipid therapy in primary prevention can be compared with published pharmacoeconomic analyses of the West of Scotland Coronary Prevention (WOSCOP) study (31). In this primary prevention study of men (mean age 55 years) receiving pravastatin 40 mg daily, LDL cholesterol was reduced 26% compared with placebo. This treatment was associated with a 31% reduction in definite nonfatal myocardial infarction or death from coronary heart disease. Over five years of follow-up, approximately 7% of participants in the placebo group suffered a definite cardiac event. This event rate is similar to the 12.4% 10-year Framingham risk estimated for Canadian men and women who would be targeted for lipid therapy (Table 2). Subsequently, published economic analyses have estimated the effectiveness of primary prevention with pravastatin at US$22,000 to US$34,000 per YOLS (32,33). However, at the time of these analyses, the daily cost ($3.32 to $4.44) of Pravachol (Bristol-Myers Squibb Canada) was approximately two-fold greater than the cost of statins used in our analyses, while the observed 26% reduction in LDL cholesterol was substantially less than the 40% used in the present study. Combining a doubling in statin

efficacy with a 50% reduction in treatment costs would result in cost-effectiveness ratios reduced by approximately one-quarter.

Comparisons with other pharmacoeconomic analyses of hypertension therapy are more problematic given the paucity of definitive clinical trials evaluating the benefits of primary prevention. To the best of our knowledge, the results of the ALLHAT study have not been previously evaluated in a pharmacoeconomic analysis focusing specifically on primary prevention. Nonetheless, estimates of the cost-effectiveness of antihypertensives over a lifetime range from approximately $11,000 to $71,000 per YOLS for a wide range of patients including those with diagnosed CVD or diabetes (6).

Despite acceptable cost-effectiveness ratios, a number of potential barriers to treatment remain. One of the most important is long-term adherence by the patient. The national costs of lifelong treatment are significant, including $18.3 billion for lipid therapy and $17.5 billion for antihypertensives. For the individual patient, this includes cumulative drug costs ranging from $9,100 to $19,400 for lipid therapy, and $7,700 to $17,000 for blood pressure therapy. While these drug costs are offset to some extent by the cost savings associated with preventing cardiovascular events, these financial benefits to the health care system only occur many years into the future. On the other hand, the annual drug costs of $723 or $629 for treating dyslipidemia or hypertension, respectively, start immediately. Any portion of these costs borne directly by the patient may undermine adherence to therapy.

The costs of preventive treatments may be substantial, but so are the benefits to society and the individual. Even after discounting, the increased life expectancy following the risk reduction associated with lipid or hypertension therapy ranges from 0.31 to 0.57 years and 0.17 to 0.23 years, respectively. The development of CVD would also be delayed 1.01 to 1.81 years or 0.33 to 0.57 years, respectively. Once again, these benefits will only be realized after many years of treatment. The poor patient adherence to blood pressure and lipid therapies that has been documented by others will also substantially increase the estimated cost-effectiveness ratios presented herein (34,35). The forecasted person-years of treatment required to save one year of life (Tables 3 to 6) are large for some groups of patients and raise the possibility that some individuals may prefer to avoid the costs and inconvenience of lifelong treatment given the potential future benefits. Perhaps poor adherence reflects this implicit expectation.

There are a number of strengths associated with these analyses, including recently collected drug use data from the MHC national survey and a Markov model that has been shown to reasonably estimate the results observed in clinical trials. There are also a number of important limitations that must be acknowledged. Current treatment guidelines will target Canadians who, in the absence of CVD or diabetes, will have a baseline 10-year Framingham risk of approximately 10% to 12% (Table 2). Before initiating treatment, average baseline LDL cholesterol (4.3 mmol/L) and blood pressure values (149/89 mmHg) would also be only modestly elevated compared with the values often observed in major clinical trials. Nonetheless, the results presented herein assume that the benefits observed in clinical trials will translate into fewer events after using the model to adjust for the lower baseline risk and risk factor levels. Given an additional assumption of 100% adherence with treatment, one must recognize that the resulting estimates represent a best case scenario of what the guidelines might achieve in a perfect world.

CONCLUSION

The cost-effectiveness of treating dyslipidemia or hypertension to prevent CVD appears to be economically attractive among most groups of Canadians who would be eligible for therapy. Nonetheless, the costs of nationwide implementation would be substantial, as would be out-of-pocket costs of prescription drugs for many individuals. Moreover, significant reductions in morbidity and mortality will only be observed after many years of treatment. Poor adherence to long-term treatment remains a major barrier that must be addressed if the potential benefits of preventative care are to be fully realized.

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