Association of Temporal Trends in Risk Factors and Treatment Uptake With Coronary Heart Disease Mortality, 1994-2005

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Context Coronary heart disease (CHD) mortality has declined substantially in Canada since 1994.

Objective To determine what proportion of this decline was associated with temporal trends in CHD risk factors and advancements in medical treatments.

Design, Setting, and Patients Prospective analytic study of the Ontario, Canada, population aged 25 to 84 years between 1994 and 2005, using an updated version of the validated IMPACT model, which integrates data on population size, CHD mortality, risk factors, and treatment uptake changes. Relative risks and regression coefficients from the published literature quantified the relationship between CHD mortality and (1) evidence-based therapies in 8 distinct CHD subpopulations (acute myocardial infarction [AMI], acute coronary syndromes, secondary prevention post-AMI, chronic coronary artery disease, heart failure in the hospital vs in the community, and primary prevention for hyperlipidemia or hypertension) and (2) population trends in 6 risk factors (smoking, diabetes mellitus, systolic blood pressure, plasma cholesterol level, exercise, and obesity).

Main Outcome Measures The number of deaths prevented or delayed in 2005; secondary outcome measures were improvements in medical treatments and trends in risk factors.

Results Between 1994 and 2005, the age-adjusted CHD mortality rate in Ontario decreased by 35% from 191 to 125 deaths per 100 000 inhabitants, translating to an estimated 7585 fewer CHD deaths in 2005. Improvements in medical and surgical treatments were associated with 43% (range, 11% to 124%) of the total mortality decrease, most notably in AMI (8%; range, –5% to 40%), chronic stable coronary artery disease (17%; range, 7% to 35%), and heart failure occurring while in the community (10%; range, 6% to 31%). Trends in risk factors accounted for 3660 fewer CHD deaths prevented or delayed (48% of total; range, 28% to 64%), specifically, reductions in total cholesterol (23%; range, 10% to 33%) and systolic blood pressure (20%; range, 13% to 26%). Increasing diabetes prevalence and body mass index had an inverse relationship associated with higher CHD mortality of 6% (range, 4% to 8%) and 2% (range, 1% to 4%), respectively.

Conclusion Between 1994 and 2005, there was a decrease in CHD mortality rates in Ontario that was associated primarily with trends in risk factors and improvements in medical treatments, each explaining about half of the decrease.

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CORONARY HEART DISEASE (CHD) remains the most common cause of death worldwide and generates a large economic burden.[1,2] Rates of CHD mortality have decreased substantially over the last 3 decades.[3] Identifying the underlying factors associated with this decline is critical for planning future health policy, and prioritizing strategies for primary and secondary prevention.[4]

Previous studies have shown that the largest portion of this reduction in CHD burden can be attributed to improvements in modifiable lifestyle and dietary risk factors.[4-10] For example, from a population perspective, a reduction of 1 mmol/L in mean plasma cholesterol levels is associated with a 40% reduction in CHD mortality.[11,12] Treatment strategies also have played a pivotal role, with 25% to 55% of the decreases in CHD mortality worldwide being attributed to the improved uptake of evidence-based pharmacologi-

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cal and interventional therapies.[10] However, the relative importance of risk factor modification vs treatment uptake may vary substantially depending on the country and the period studied.[4,6-8,10,13,14]

The most recent study evaluated trends in the United States up to 2000[4]; since then, many new treatments have been introduced into contemporary practice, questioning the applicability of these previous observations. Moreover, the underlying factors associated with trends in CHD mortality in Canada have not been evaluated. Accordingly, our objective was to model CHD deaths between 1994 and 2005 in the province of Ontario to determine the contribution of prevention and treatment strategies to the Canadian decline in CHD mortality.

METHODS

The Ontario population, aged 25 to 84 years between 1994 and 2005, was evaluated using an updated version of the IMPACT model. This is a cell-based model, constructed using Microsoft Excel (Microsoft Corporation, Redmond, Washington), which integrates available country-specific epidemiological data to explain an observed decrease in CHD mortality. Specifically, the IMPACT model (1) incorporates temporal trends in major CHD risk factors including smoking, diabetes, systolic blood pressure, total cholesterol level, exercise, and obesity, in addition to the uptake of evidence-based medical and surgical treatments for CHD at 2 cross-sectional time points, and (2) estimates the relative reduction in CHD mortality associated with each. The IMPACT model has been validated in the United States, New Zealand, China, and Europe.[6-9,13,14]

Whenever possible, Ontario-specific data sources were used. The 2 time points for the Ontario model were 1994 and 2005, based on the availability of high-quality data. Data used to construct the Ontario IMPACT model are described in detail in the eAppendix (see http://www.jama.com). Briefly, data on the Ontario population and age distribution and specific CHD death counts based on the *International Classification of Diseases, Ninth Revision,* and the *International Statistical Classification of Diseases, Tenth Revision*, were obtained from Statistics Canada, while the prevalence of major cardiovascular risk factors came from Ontario-specific self-reported population health surveys, such as the National Population Health Survey, the Canadian Heart Health Database, and the Canadian Community Health Survey.[15] To determine the number of eligible patients and their 1-year mortality for specific medical and surgical treatments, linked administrative databases at the Institute for Clinical Evaluative Sciences were used. These databases included the Canadian Institute for Health Information discharge abstract database, which has records on the frequency and type of all acute and chronic care hospitalizations in the province; the Ontario Health Insurance Plan database, which includes fee-for-service claims submitted by physicians and other licensed health professionals; and the Ontario Drug Database, which has comprehensive drug use information on patients older than 65 years. All individual patients were identified by a unique, encrypted identifier, thereby allowing linkage between all administrative databases. The use of linked administrative databases represented a substantial methodological improvement in data acquisition compared with previous models because it allowed accurate accounting for potential overlaps between patient groups. This data was supplemented with use data on specific medical and surgical treatments from Ontario-specific clinical registries, including the Southwestern Ontario database for outpatient information, the Global Registry of Acute Coronary Events, and the Enhanced Feedback for Effective Cardiac Treatment (EFFECT) 2 trial for inpatient therapies, and others (see eTable 1 at http://www.jama.com).

The primary output of the IMPACT model was the number of deaths prevented or delayed in 2005 due to the reduction in CHD mortality rates. This was calculated as the difference between the observed 2005 CHD deaths and the expected CHD deaths in 2005 had 1994 mortality rates remained constant. Change in population size and age was considered using indirect standardization. The expected number of CHD deaths was calculated by multiplying age- and sex-specific mortality rates in 1994 by the population size for each 10-year age-sex stratum in 2005. Having calculated the total number of deaths prevented or delayed in 2005, the proportion associated with either trends in risk factors or treatment uptakes between 1994 and 2005 was determined.

The treatment group of the model consisted of 8 mutually exclusive CHD subgroups. These included patients hospitalized for an acute myocardial infarction (AMI), an acute coronary syndrome, or heart failure due to ischemic cardiomyopathy within the last year. In addition, the model evaluated community-dwelling patients who were AMI survivors, patients with stable coronary artery disease (with and without percutaneous or surgical revascularization), and patients with heart failure. Finally, individuals with hypertension and hypercholesterolemia eligible for primary prevention with pharmacological therapy were examined. Within each of these groups, a total of 42 medical and surgical therapies were assessed (TABLE 1). These included aspirin, thrombolytic therapy, and primary angioplasty for AMI; β-blockers, angiotensin-converting enzyme inhibitors, and spironolactone for heart failure; and statin therapy for chronic stable coronary artery disease.

The deaths prevented or delayed attributable to a specific CHD treatment within a disease subgroup were estimated by taking the product of the number of individuals in the subgroup, the proportion of those patients who received a particular treatment (see eTable 2 at http://www.jama.com), the 1-year mortality rate (eTable 3), and the relative risk reduction attributed to that specific treatment based on the published literature (eTable 4).[4,7-10,16] For

Table 1. Deaths Prevented or Delayed Due to Treatments for Coronary Heart Disease

	No. of Patients	% Treatment Uptake 2005	% Treatment Uptake 1994	RR Reduction	1-Year Case Fatality	Deaths Prevented or Delayed, Mean (%) (Range)
AMI	16 640				0.164	630 (8.3) (–5.1 to 39.9)
Fibrinolysis		35	31	24		20 (0.2) (0.1 to 0.4)
Aspirin		94	78	15		70 (0.9) (0.5 to 7.4)
β-Blocker		82	40	31		25 (1.4) (–0.4 to 1.7)
ACE inhibitor or ARB		63	23	4		50 (0.3) (0.1 to 1.5)
Clopidogrel		60	0	4		35 (0.5) (–0.6 to 2.3)
Primary PCI		16	0	7		105 (0.7) (0.3 to 1.0)
Primary CABG		0	0	39		5 (0)
Statin		88	9	22		320 (4.2) (–5.6 to 23.8)
CPR						
In the community		2.5	1	5		10 (0.1)
In the hospital		2	2	33		0
Acute coronary syndrome	10 180				0.054	150 (2.0) (0.7 to 2.4)
Aspirin and heparin		80	72	33		15 (0.1) (0 to 0.1)
Aspirin alone		11	9	15		5 (0)
Glycoprotein IIB/IIIA receptor blocker		7	0	9		0
ACE inhibitor or ARB		55	23	7		10 (0.1) (0 to 0.1)
β-Blocker		79	50	0		10 (0)
Clopidogrel		51	0	7		15 (0.1) (0 to 0.1)
CABG surgery		3	0	43		10 (0)
PCI		18	0	32		30 (0.1) (0 to 0.2)
Statin		78	8	22		60 (0.8) (0.6 to 1.9)
2 Previous AMIs	37 500				0.026	170 (2.3) (2.0 to 10.0)
Aspirin		91	74	15		10 (0.2) (0.1 to 0.7)
β-blocker		85	51	23		35 (0.4) (0.4 to 2.0)
ACE inhibitor		67	25	20		40 (0.5) (0.5 to 2.6)
Statin		88	9	22		55 (0.8) (0.6 to 3.3)
Warfarin		14	0	22		15 (0.2) (0.2 to 1.0)
Rehabilitation		15	0	26		15 (0.2) (0 to 0.1)
Chronic stable CAD	292 210					1305 (17.2) (7.0 to 35.4)
Aspirin in community		78	64	15	0.030	130 (1.7) (0.7 to 3.6)
Statins in community		78	8	23	0.030	725 (9.5) (3.9 to 19.8)
ACE inhibitor		53	20	17	0.030	375 (5.0) (2.0 to 10.3)
CABG surgery		5880[a]	3470[a]	21	0.048	60 (0.8) (0.3 to 1.4)
Angioplasty		5260[a]	1440[a]	13	0.023	15 (0.2) (0 to 0.3)
Heart failure						
In the hospital	3365				0.356	80 (1.0) (0.4 to 2.2)
ACE inhibitor		62	89	20		–45 (–0.6) (–0.2 to –1.2)
β-Blocker		55	29	35		70 (0.9) (0.4 to 1.9)
Spironolactone		21	3	30		40 (0.5) (0.2 to 1.1)
Aspirin		52	42	15		10 (0.1) (0.1 to 0.3)
In the community	50 440				0.112	750 (9.9) (6.1 to 31.1)
ACE inhibitor/ARB		70	89	20		–125 (–1.7) (–1.1 to –5.5)
β-Blocker		67	29	35		760 (10.0) (6.5 to 32.8)
Spironolactone		5	3	30		35 (0.4) (0.3 to 1.5)
Aspirin		52	42	15		85 (1.1) (0.4 to 2.3)
Hypertension treatment	459 900	46	28	13	0.005	50 (0.7) (–0.2 to 0.9)
Hyperlipidemia treatment	565 295				0.004	90 (1.2) (0.4 to 2.6)
Statins		45	20	35		85 (1.1) (0.5 to 2.3)
Gemfibrozil		6	0	7		5 (0.1) (0 to 0.3)
Niacin		2	0	5		0
Total treatment						3280 (42.6) (11.2 to 123.6)

Abbreviations: ACE, angiotensin-converting enzyme; AMI, acute myocardial infarction; ARB, angiotensin II receptor blocker; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CPR, cardiopulmonary resuscitation; PCI, percutaneous coronary intervention (with or without stenting); RR, relative risk.
[a] Instead of percentages, the actual numbers of patients receiving treatment (determined from an administrative database) are presented.

example, in Ontario in 2005, about 2790 men aged 55 to 64 years were hospitalized with AMI, of whom, 94% were given aspirin. Aspirin reduces the case-fatality rate by 15%.[17] The underlying 1-year case-fatality rate in these men was 6.4%. The approximate number of deaths prevented or delayed attributable to aspirin use in AMI was therefore calculated as:

Patient numbers × treatment uptake × relative mortality reduction × 1-year case-fatality rate = 2790 × 94% × 15% × 6.4% = 25 deaths prevented or delayed.

There is a paucity of data on the efficacy of treatment combinations. Simply assuming that the efficacy of multiple treatments was additive would overestimate the treatment effect. The Mant and Hicks method[18] was used instead to estimate case-fatality reduction by polypharmacy. This approach estimates the cumulative relative benefit as follows:

Relative benefit = 1 – (1 – relative reduction in case-fatality rate for treatment A) × (1 – relative reduction in case-fatality rate for treatment B) . . . × (1 – relative reduction in case-fatality rate for treatment N).

(See the eAppendix for further details and examples at http://www.jama.com.) Because many of the therapeutic interventions studied were widely used in 1994, the net benefit of an intervention was calculated by subtracting the expected number of deaths prevented if the 1994 use rates remained constant from the observed deaths prevented as calculated in the example above.

Risk factors included diabetes mellitus, total cholesterol level, systolic blood pressure, body mass index, smoking, and physical inactivity. Two approaches were used to estimate the number of deaths prevented or delayed as a consequence of changes in CHD risk factors. The regression coefficient approach was used for the risk factors of systolic blood pressure, total cholesterol level, and body mass index (expressed in continuous data).[4,7-10,16] Three variables were used for this approach: (1) the expected number of CHD deaths in 2005, (2) multiplied by the absolute change in risk factor prevalence, (3) multiplied by a regression coefficient that quantified the change in CHD mortality expected for the change in risk factor level (see eTable 5 at http://www.jama.com).[4,7-10,16] For example, in 2005, there were 448 expected CHD deaths among 476 670 women aged 55 to 64 years. The mean systolic blood pressure in this group decreased by 6.9 mm Hg (from 139.3 mm Hg in 1994 to 132.4 mm Hg in 2005). The largest meta-analysis evaluating the effect of blood pressure treatment on mortality estimated age- and sex-specific reduction in mortality to be 50% for every 20-mm Hg reduction in systolic blood pressure, generating a logarithmic coefficient of –0.035.[11] The number of deaths prevented or delayed as a result of this change was estimated as:

(1 – [*EXP*(coefficient × change)] × expected deaths in 2005) = (1 – [*EXP* (–0.035 × 6.88)] × 448) = 96 deaths prevented or delayed.

The second approach used was the population-attributable risk fraction (PARF).[4,7-10,16] This approach was used to determine the mortality benefit due to changes in the prevalence of dichotomous risk factors of smoking, diabetes, and physical inactivity.[4,7-10,16]

$$PARF = [P \times (RR - 1)]/[1 + P \times (RR - 1)]$$

where *P* is the prevalence of the risk factor and RR is the relative risk for CHD mortality associated with the presence of that risk factor. Deaths prevented or delayed were then estimated as the expected CHD deaths in 2005 multiplied by the difference in the PARF between 1994 and 2005. For example, the prevalence of diabetes among men aged 65 to 74 years was 13.5% in 1994 and increased to 18.3% in 2005. Assuming a relative risk of 1.93,[5] the PARF was calculated as 0.112 in 1994 and 0.145 in 2005. The approximate number of deaths attributable to the increase in diabetes prevalence from 1994 to 2005 was calculated as:

Expected deaths in 2005 × (PARF in 2005 – PARF in 1994) = (3196) × (0.145 – 0.112) = 105 additional deaths.

Because of the uncertainty surrounding many of the values, multiway sensitivity analyses were performed.[4] For each model parameter, minimum and maximum plausible values were assigned using the 95% confidence intervals from the source documentation; if these were unavailable, these limits were defined as 20% above and below the best estimate.[4] The minimum and maximum plausible values were introduced into the model, generating the minimum and maximum estimates for deaths prevented or delayed. This represents a conservative estimation of uncertainty; in selected simulations, this approach has consistently yielded broader confidence bounds than those represented by 99% confidence intervals.

This study was based on secondary analyses of multiple deidentified clinical, survey, and administrative databases, and was approved by the ethics review board at Sunnybrook Health Science Centre. Where required under privacy legislation, informed patient consent or a waiver of informed consent has been obtained by the principal investigators of these various databases, prior to the data being made available for these secondary analyses.

RESULTS

Between 1994 and 2005, the age-adjusted CHD mortality rate in Ontario decreased by 35% from 191 to 125 deaths per 100 000 inhabitants. Of the 8.4 million Ontario residents between the ages of 25 and 84 years in 2005, there were 10 060 CHD deaths. In contrast, there were 13 010 CHD deaths in 1994 despite an overall population of only 7 million residents between the ages 25 to 84 years. With indirect age standardization, the IMPACT model estimated that there were 7585 deaths prevented or delayed in 2005; given the observed mortality rates compared with

the deaths expected, the 1994 CHD mortality rates remained constant.

Risk factor changes were associated with 48% (range, 28%-64%) of the total mortality decrease, whereas new medical and surgical treatments were associated with 43% (range, 11%-124%) of the decrease. Of the observed reduction in CHF mortality, 9% (range, 0%-61%) was not associated with factors studied in the IMPACT model. The decrease in observed CHD deaths was concentrated in older patients aged 75 to 84 years (FIGURE).

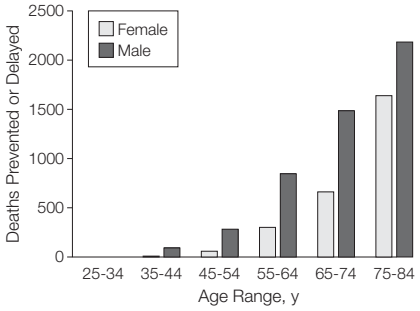
An estimated 3280 of the total deaths prevented or delayed were associated with improvements in medical and surgical treatments between 1994 and 2005 (Table 1). The most substantial contributions came from the management of patients with chronic stable coronary artery disease (1305 fewer deaths; 17% of total [range, 7%-35%). In 1994, 8% of patients with chronic stable coronary artery disease were taking statins compared with 78% in 2005. This improvement in use rates was associated with 725 deaths prevented or delayed (9% of total; range, 4%-20%). In contrast, percutaneous and surgical revascularizations were associated with only 1% (range, 0%-2%) of the overall deaths prevented or delayed.

Improvements in the treatment of patients with heart failure in the community were associated with approximately 750 fewer deaths (10% of total; range, 6%-31%). In 1994, 29% of patients were taking β-blockers compared with 67% in 2005. Interestingly, use of angiotension-converting enzyme inhibitors or angiotensin II receptor blockers decreased from 89% in 1994 to 69% in 2005. However, this was outweighed by the improved uptake of other medications including β-blockers and aldactone. An important limitation in this cohort is the inability to distinguish between heart failure from systolic and diastolic dysfunction because many of the evaluated therapies are of proven benefit only for systolic dysfunction.

Deaths prevented or delayed from treatments for the acute hospital-based subgroups were relatively modest (Table 1). Although improvements in the treatment of AMI patients represented 8% (range, –5% to 40%) of the overall deaths prevented or delayed; new acute treatment modalities, such as primary angioplasty, prevented or delayed only 105 deaths. Even in this subgroup of patients, improved secondary prevention with statin therapy represented the most important advance in treatment over the model period, contributing to 320 deaths prevented or delayed.

Overall, risk factor changes accounted for an estimated 3660 fewer CHD deaths prevented or delayed (48% of total; range, 28%-64%). Over the 11-year period of the model from 1994 to 2005, there was an absolute reduction of 0.05 mmol/L in the mean total cholesterol level of the Ontario population (TABLE 2). After controlling for increased use of lipid-lowering pharmacological treatments, 1730 CHD deaths were prevented or delayed due to reductions in cholesterol level from lifestyle and dietary changes from 1994 to 2005, representing 23% (range, 10%-33%) of the overall reduction in CHD mortality. There was also an absolute decrease of 1.4 mm Hg in mean systolic blood pressure from 1994 to 2005. This was associated with 1545 fewer deaths (20% of total; range, 13%-26%) after subtracting deaths pre-

Figure. Deaths Prevented or Delayed in 2005, Stratified by Age and Sex



For the 25- to 34-year age group, the value for female is 4 and for male is 2.

Table 2. Deaths Prevented or Delayed Due to Population Risk Factor Changes

Risk Factors	Changes in Risk Factors, %[a] Absolute	Changes in Risk Factors, %[a] Relative	Relative Risk[b]	Deaths Prevented or Delayed, Mean (%) (Range)[c]
Smoking prevalence	–6	–20		725 (9.5) (7.6 to 11.4)
Male			2.52	
Female			2.14	
Diabetes prevalence	1	24		–470 (–6.2) (–4.1 to –7.8)
Male			1.93	
Female			2.59	
Physical inactivity	–11	–17		310 (4.1) (3.3 to 4.9)
Male			1.27	
Female			1.33	
Systolic blood pressure, mm Hg	–1.39	–1	β[d]	1545 (20.4) (12.7 to 26.0)
Male			–0.033	
Female			–0.041	
Total cholesterol, mmol/L	–0.05	–1		1730 (22.8) (9.8 to 32.6)
Male			–0.922	
Female			–0.901	
Body mass index[e]	0.37	1		–180 (–2.3) (–1.3 to –3.6)
Male			0.029	
Female			0.028	
Total risk factors				3660 (48.3) (28.1 to 63.5)

SI conversion factor: To convert cholesterol to mg/dL, divide by 0.0259.
[a] Changes in 2005 compared with 1994.
[b] The comparator is the gender-matched patient without the risk factor.
[c] Percentages may not sum to 100 due to rounding.
[d] The units of comparison are the weighted average of the log-transformed β coefficients. The untransformed coefficients are shown in eTable 5 with units (see http://www.jama.com).
[e] Calculated as weight in kilograms divided by height in meters squared.

vented due to advances in pharmacological therapies (Table 2).

Reductions in smoking (6%) and physical inactivity (11%) were associated with 725 and 310 fewer CHD deaths, respectively. However, there was an increase in both diabetes prevalence (1%) and body mass index (calculated as weight in kilograms divided by height in meters squared; absolute change of 0.37), both increasing mortality by 470 (6% of total; range, 4%-8%) and 180 (2% of total; range, 1%-4%) more CHD deaths, respectively.

COMMENT

Using Ontario-specific epidemiological data, we observed a reduction in the burden of CHD comparable with that reported in other Western countries. From 1994 to 2005, this 35% decrease in CHD mortality translated into 7585 fewer CHD deaths. The bulk of this mortality reduction was associated with improvements in traditional CHD risk factors, particularly total cholesterol levels and systolic blood pressure. These positive trends were offset by adverse trends in the prevalence of obesity and diabetes. The CHD mortality reduction associated with advances in surgical and medical treatments were principally observed in community-dwelling patients with chronic stable coronary artery disease and heart failure.

Understanding the underlying mechanisms for past trends in CHD mortality is critical for strategic planning and prioritization of health policy. The IMPACT model has been applied to a wide range of populations. Past studies have consistently explained 80% to 99% of the observed CHD mortality decline, with more than 50% being attributed to temporal trends in CHD risk factors and less than half to treatment.[4,6-9,13] Our analysis builds on this previous work by assessing a more recent period from 1994 to 2005, thereby incorporating relevant contemporary medical and surgical therapies and recent trends in risk factors, such as the increase in obesity rates.

Despite the different study period, we observed similar mortality reductions associated with risk factor improvements compared with the United States between 1980 and 2000, particularly total cholesterol level and systolic blood pressure.[4] These trends may reflect the general improvement in socioeconomic status at the population level, which in turn may support healthier lifestyles and dietary habits. However, this may also lead to overconsumption, which may partially explain the recent epidemic of obesity and diabetes mellitus. Our results suggest that we have not reached the nadir of population cholesterol or blood pressure levels. Strategies to improve these areas will continue to be of importance. Conversely, policies to address the increasing prevalence of obesity and diabetes mellitus will be crucial if the gains realized over the last decade are not to be lost.

Despite the exponential increase in expenditures on medical technologies and drugs, the Ontario IMPACT model found that less than half of the observed CHD mortality reduction was associated with treatment improvements. Although this overall result appears similar to that seen in the United States from 1980 to 2000, there were substantial differences in the relative importance of disease subgroups.[4] While primary pharmacological prevention for hypertension and hyperlipidemia played an important role in the United States (7% and 4.9%, respectively), these accounted for only 2% of the total mortality reduction in Ontario.[4] In contrast, improvements in chronic stable coronary artery disease management in Ontario represented 17.3% of the mortality reduction, whereas this subgroup accounted for only 5.4% in the United States.[4]

We believe several factors are important in understanding these results. First, because the baseline year of our analysis was 1994, many of the treatment strategies evaluated were already in use unlike in the US model, which had a much earlier base year of 1980.[4,7-9] Any effect on CHD mortality was due to the incremental change in use between 1994 and 2005. Although use rates improved for most treatments over this period, these were modest in areas such as fibrinolysis and aspirin use. In contrast, there was a marked increase in the use of statins and angiotensin-converting enzyme inhibitors, which in turn had a dramatic reduction in overall mortality. Second, the majority of new treatments developed over the last decade, such as primary angioplasty for AMI, glycoprotein IIb/IIIa receptor inhibitors and clopidogrel for acute coronary syndrome, or automated internal cardiac defibrillators for severe cardiomyopathy, were applicable to only a small proportion of CHD patients. Patients with chronic stable coronary artery disease continued to represent the largest burden of CHD disease; thus, treatment improvements in these patients translated to the greatest overall effect. This highlights an important potential use of models such as IMPACT for strategic planning by identifying the areas in which future gains are likely to be in optimizing treatment uptake from a population perspective. This may be of particular importance in low- and middle-income countries in which health care resources are limited.

Our results must be interpreted within the context of several limitations, most importantly, the use of multiple data sources for populating the mathematical model. Despite the use of linked administrative databases to mitigate this issue, residual double counting of some patients may have occurred despite our best efforts. In addition, efficacy data derived from clinical trials may not be generalizable to real-world practice, and may therefore overestimate the clinical benefits. Our analyses were limited to 2005 because it represented the most contemporary period in which comprehensive data were available; however, we do not believe that the trends in risk factors and medical therapies seen in our study would be qualitatively different in a more updated model. As seen in our sensitivity analyses, there was sub-

stantial uncertainty in our estimates, most pronounced in the treatment group of the model. In comparison with the best estimate of 43%, the overall treatment effect ranged from a minimum of 11% to a maximum of 124%. Although, the uncertainty surrounding the risk factor estimates was less, there remained a range from 28% to 63% around the best estimate of 48%. Finally, 91% of the observed CHD mortality decline was associated with factors studied in our model; the residual portion may reflect imprecision around our estimates or failure to quantify other important factors, such as the consumption of fruits and vegetables, psychosocial stress, and abdominal obesity.[5] The INTERHEART study investigators examined the relationship of these factors with the risk of AMI and found a population-attributable risk that ranged from 10% to 25%.[5] This emphasizes the importance of collecting population-level data on these and other known risk factors, such as exposure to secondhand smoke and incorporating them into future studies.

In conclusion, our results suggest that approximately half of the CHD mortality reduction in Ontario between 1994 and 2005 was associated with improvements in major risk factors and approximately 43% to evidence-based treatments. However, obesity and diabetes mellitus both increased substantially. Although our study was not designed to establish a causal relationship between these trends and mortality, these results may inform decision making at all levels with the goal of ensuring that the gains in CHD mortality reduction during the previous decade are not lost in the next decade.

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Online-Only Material: eAppendix and eTables 1-5 are available at http://www.jama.com.

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