

Effectiveness and efficiency of different guidelines on statin treatment for preventing deaths from coronary heart disease: modelling study

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Abstract

Objective To examine the potential effectiveness and efficiency of different guidelines for statin treatment to reduce deaths from coronary heart disease in the Canadian population.

Design Modelled outcomes of screening and treatment recommendations of six national or international guidelines—from Canada, Australia, New Zealand, the United States, joint British societies, and European societies.

Setting Canada.

Data sources Details for 6760 men and women aged 20-74 years from the Canadian Heart Health Survey (weighted sample of 12 300 000 people) that included physical measurements including a lipid profile.

Main outcome measures The number of people recommended for treatment with statins, the potential number of deaths from coronary heart disease avoided, and the number needed to treat to avoid one coronary heart disease death with five years of statin treatment if the recommendations from each guideline were fully implemented.

Results When applied to the Canadian population, the Australian and British guidelines were the most effective, potentially avoiding the most deaths over five years (> 15 000 deaths). The New Zealand guideline was the most efficient, potentially avoiding almost as many deaths (14 700) while recommending treatment to the fewest number of people (12.9% of people *v* 17.3% with the Australian and British guidelines). If their “optional” recommendations are included, the US guidelines recommended treating about twice as many people as the New Zealand guidelines (24.5% of the population, an additional 1.4 million people) with almost no increase in the number of deaths avoided.

Conclusions By focusing recommendations on people with the highest risk of coronary heart disease, the Canadian, US, and European societies guidelines could improve either their effectiveness (in terms of hundreds of avoided deaths) or efficiency (in terms of thousands of fewer people recommended treatment) in the Canadian population.

Introduction

Because coronary heart disease is common and lipid lowering drugs—most notably statins—are widely dispensed, statins are among the most frequently prescribed drugs in many drug plans. Lipid treatment guidelines therefore have important implications both for population health and for healthcare resources.

In this study we assessed six recent national or international lipid guidelines from a population perspective.¹⁻⁶ We considered three characteristics of

each guideline: (a) the number of people that the guidelines recommended for statin treatment, (b) the potential community effectiveness (the potential number of deaths that could be prevented if all community members were screened, treated, and compliant according to the guideline), and (c) the guideline efficiency (the overall number needed to treat). We examined these three characteristics for each guideline in the Canadian population.

Participants and methods

We used data from the Canadian Heart Health Survey, a population based survey that collected physical measures including blood pressure, weight, height, and blood lipid concentrations in 6760 people aged 20-74 years,⁷ to estimate the risk of coronary heart disease and cardiovascular disease (coronary heart disease plus stroke) of individual respondents.^{8,9}

From electronic searches (see bmj.com for details), we identified eight guidelines that were used nationally and selected the most current guideline from those countries whose population risk of heart disease and whose healthcare resources were similar to those of Canada (from Canada, Australia, New Zealand, the United States, joint British societies, and European societies).¹⁻⁶

We screened each respondent to the Canadian Heart Health Survey for coronary risk and assigned treatment according to each guideline's recommendations (see bmj.com for details). The US guideline had optional treatment recommendations, which we considered separately. We used each guideline's risk charts to assign respondents into their appropriate risk category. All guideline risk charts used the Framingham heart study data or algorithms, except the European societies, which used the SCORE (systematic coronary risk evaluation) study data in their most recent guideline.¹⁰

To compare the guidelines, we estimated five year mortality from coronary heart disease (using the Framingham algorithm¹¹) and 10 year mortality from cardiovascular disease (using the SCORE algorithm¹⁰). For respondents with cardiovascular disease, we used the observed mortality risk of Ontario residents (a third of the national population) because Framingham or similar equations are not available for people with cardiovascular disease. For those people recommended

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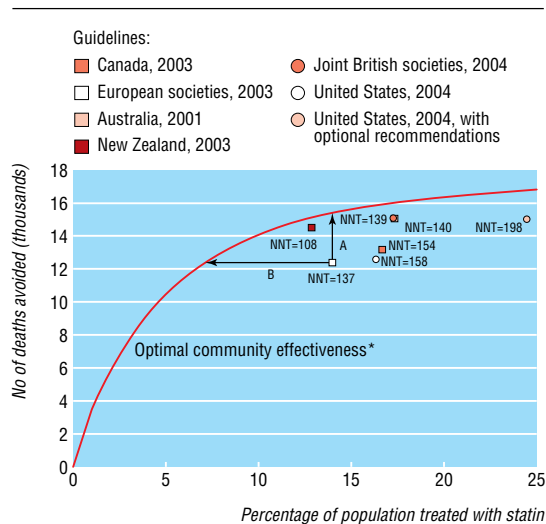
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Further details of data used and analysis methods are on bmj.com



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*The optimal community effectiveness curve shows the number of CHD deaths avoided if the highest risk people were treated first
 A=The effectiveness gap or the difference between the potential deaths avoided by the guideline recommendations compared with the optimal number of deaths avoided if the highest risk people were recommended treatment.
 B=The efficiency gap or the difference between percentage of the population recommended statin treatment compared with the minimum population that could be treated to avoid the same number of deaths.
 NNT=Number needed to treat to prevent 1 CHD death over 5 years

Number of deaths from coronary heart disease (CHD) prevented over five years by percentage of Canadian population aged 20-74 years treated with statins for different guidelines for the management of dyslipidaemia

statin treatment, we calculated the number of deaths from heart disease potentially avoided, using the product of five year baseline risk and an estimate of 27% relative reduction in mortality from cardiovascular disease.¹² We calculated population based estimates for the Canadian population aged 20-74 years in 1990-2 (12 300 000 people).

Results

The figure shows how the six guidelines differ in the proportion of Canadians aged 20-74 years recommended statin treatment and the number of deaths from heart disease potentially avoided if all the people recommended statins took them correctly for five years. The Australian, British, and the optional US guidelines were the most effective, potentially avoiding the most deaths from heart disease over five years (> 15 000 deaths). The New Zealand guideline was the most efficient (number needed to treat= 108), potentially avoiding almost as many deaths (14 700 deaths) while recommending statin treatment to the smallest proportion of the Canadian population (12.9%). The optional US guidelines, which was the most liberal, recommended treatment to almost twice as many people (24.5%, number needed to treat= 198).

We created a curve of “optimal community effectiveness” representing the maximum number of deaths from heart disease avoided over five years of statin treatment if treatment were distributed according to individuals’ baseline risk of developing heart disease (figure). This assumes that people with the highest risk are treated first and that all people receive the same relative benefit from statin treatment. The effectiveness gap for a guideline (such as line A in the

figure) represents the extra number of deaths that could be avoided while treating the same number of people as that guideline recommends. The efficiency gap (line B) represents the minimum number of people that could be treated to achieve the same number of avoided deaths.

The New Zealand, British, and Australian guidelines had an average number needed to treat that was 95% of the optimal value, whereas the European societies, Canadian, and US guidelines had an average of 81%. In absolute terms, the European, Canadian, and US guidelines could potentially avoid 2000-3000 extra deaths over five years while recommending treatment to the same number of people. Alternatively, they could potentially avoid the same number of deaths but reduce the number of people recommended treatment by a third to a half. The guidelines with the largest effectiveness and efficiency gaps failed to recommend treatment to people at high risk of cardiovascular or heart disease, usually by introducing target lipid concentrations that excluded many high risk people (see bmj.com).

The efficiency and effectiveness gaps were similar when we estimated them for different outcomes (coronary heart disease event or death from cardiovascular disease) or used different risk algorithms (SCORE for either high or low risk populations) (data not shown).

Discussion

Different national guidelines on statin treatment varied considerably in their potential to prevent death from heart disease, and the guidelines that were potentially most effective in preventing deaths often recommended treatment to fewer people than less effective guidelines. Because the target populations for lipid treatment guidelines are large and death from heart disease is a relatively common outcome, small changes in guidelines have large consequences, potentially resulting in hundreds to thousands of avoided deaths, many thousands of people treated with statins, and millions of dollars spent each year in the Canadian population.

Possible explanations for differences

Three factors that could account for the differences in performance of the guidelines were how the guideline developers interpreted findings from clinical trials of statins, how the guidelines incorporated such findings into recommendations, and differences in the risk profile between the Canadian and other target populations.

Interpretation of clinical trials—This is similar for all current guidelines: all reviewed the same clinical trials, and all concluded that statins are effective in reducing coronary heart disease events for people who have a high risk for these events, even when they have low serum concentrations of low density lipoprotein cholesterol.¹³

Incorporation of clinical findings into recommendations—This probably accounts for the largest variation between guidelines. Unfortunately, guidelines seldom include an explicit description of how their recommendations were developed. In our study, the most effective guidelines recommended statins to almost all high risk people. The other guidelines

recommended treatment if lipid concentrations were above specific thresholds. Guidelines that recommended screening and treatment of many low risk people were less efficient. The most efficient guidelines had an explicit baseline risk below which statin treatment was not recommended unless there was familial hyperlipidaemia with high concentrations of low density lipoprotein cholesterol.

Differences in population risk—These are unlikely to have had a large influence on the differences between guidelines. The most efficient and effective guidelines focused recommendations on high risk people, who bear the vast majority of cardiovascular risk in Canada, and we would expect that to be true in most, if not all, developed countries.

Our results highlight the importance of describing statin benefit in absolute terms. Most guidelines describe statin benefit only in relative terms (that is, 20% to 40% reduction in heart disease outcomes). However, many people who were recommended statins in the Canadian and US guidelines had a low risk of heart disease and therefore had only a small absolute benefit.

Limitations of study

Firstly, most guidelines suggest an individually tailored approach to lipid evaluation and treatment, which we could not achieve. However, such an approach would not appreciably change the number of patients treated or the potential benefit of statins at the population level. Secondly, we assumed that everyone for whom statins were recommended would receive and take them. Thus, we estimated a population effectiveness that is greater than would be achieved in the real world. Of further concern, there is a tendency to fail to prescribe statins to people with the greatest potential benefit.^{14 15} Thirdly, we assumed that statins have the same relative benefit for all risk groups. Some authors suggest that statin benefit is lower for low risk people,¹⁶ but, if that were the case, guidelines that recommended treatment of low risk people would be even less effective and efficient than we estimated.

Another limitation is our use of risk algorithms to estimate Canadian risk of death from heart and cardiovascular disease. However, our use of the Framingham algorithm is reasonable for at least four reasons. Firstly, it has been validated in populations similar to Canada's.¹⁷ Secondly, the results did not change when we used different algorithms and outcomes in our calculations. Thirdly, measurement error should bias results in favour of guidelines based on the Framingham algorithm compared with guidelines based on the SCORE algorithm, whereas this was not observed. Lastly, if, as has been suggested,¹⁸ the Framingham algorithm overestimated low risk of heart disease, then the least effective and efficient guidelines in our study would perform even more poorly in reality because only they recommended treatment for low risk people.

Conclusions

To improve the effectiveness of guideline recommendations, we encourage guideline developers to examine their recommendations against their population's "optimal community effectiveness" curve. Treatment recommendations should have the potential to reduce deaths from heart disease in numbers as close as possible to the optimal effectiveness. The New

What is already known on this topic

National guidelines on the use of statins to prevent coronary heart disease have important implications for population health and use of healthcare resources

What this study adds

Six national and international guidelines varied considerably in their potential to prevent death from heart disease

The three most efficient and effective guidelines recommended treatment to fewer people while at the same time potentially reducing more deaths compared with the other guidelines

The less effective and efficient guidelines failed to recommend treatment to people at high risk of cardiovascular or heart disease, usually by introducing target lipid concentrations that excluded many such people, but recommended treatment of lower risk people

Zealand, Australian, and British recommendations achieved this; the European, Canadian, and US guidelines did not.

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Commentary: Cardiovascular risk estimation: important but may be inaccurate

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Manuel and colleagues applied the recommendations from six national guidelines on statin treatment to the same Canadian population and measured each guideline's impact in terms of number of people recommended for treatment, potential number of deaths from coronary heart disease avoided, and the number needed to treat to avoid one death.¹ They show that markedly different numbers of people are recommended for treatment when different guidelines are followed.

Deciding whether to prescribe statins for a patient for the primary prevention of coronary heart disease would seem to be a relatively straightforward issue in the broader context of decision making in primary care. Over the past 10 years, 14 randomised controlled trials have established the efficacy of statins across a broad range of patient groups.² However, as Manuel and colleagues show, integration of evidence into clinical guidelines is inconsistent, particularly with regard to explicit use of Framingham and other multivariable risk functions when estimating the probability of heart disease developing in individual patients.¹

Some would argue that the results of Manuel and colleagues' study are not surprising, as the outcome for their study—death from coronary heart disease—was calculated by applying the Framingham or SCORE risk score, an example of internal validity assessment. The guidelines that go furthest in recommending calculation of absolute risk—New Zealand, British, and Australian—would be expected to perform better than those that are less explicit—US, Canadian, and European. As the relative benefits from statins are constant irrespective of initial absolute risk and the risks of treatment are small, the approach of explicit absolute risk assessment is justified: higher risk individuals are likely to gain the most in absolute terms.^{1,2}

Equally, uncritical application of absolute risk assessment for primary prevention of coronary heart disease should be discouraged. A systematic review of 27 external validity studies, of the extent to which predicted risk assessments are an accurate reflection of observed risk of heart disease, shows that the performance of the Framingham risk score varies considerably between different countries and populations.³ Predicted to observed ratios ranged from an underprediction of 0.43 in higher risk populations to overprediction of 2.87 in lower risk populations.³ Within the United Kingdom, regional differences of risk of heart disease mean that the accuracy of Framingham varies,

with overprediction in areas of low incidence of CHD⁴ and underestimation in socially deprived areas, where the incidence of heart disease is high.⁵ Even if Framingham was consistently accurate, evidence about the benefits of applying absolute risk assessment in the primary prevention of heart disease is scarce; only four randomised controlled trials implementing this approach have been published, with inconclusive results.³

In conclusion, the study by Manuel and colleagues contains an important message. Explicit absolute risk assessment is an essential starting point when considering primary preventive treatment for CHD. However, uncritical application of Framingham may mislead patients and health professionals and ongoing studies are needed to ensure CHD risk assessment is as accurate as possible for the group of patients to which it is applied.

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Endpiece

Distress

If you are distressed by anything external, the pain is not due to the thing itself, but to your estimate of it; and this you have the power to revoke at any moment.

Marcus Aurelius Antoninus (AD 121-180)

Submitted by Luke Cascarini, senior house officer, Queen Victoria Hospital, East Grinstead