The National Cholesterol Education Program III scoring system for CHD risk estimation cannot be used with European recommendations

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Abstract

To target statin therapy effectively in primary coronary heart disease (CHD) prevention, recommendations increasingly advocate the assessment of absolute CHD risk. Using methods from two recent sets of national recommendations, we estimated absolute CHD risk in 412 men and women whose general practitioners requested it on clinical grounds. Substantially fewer men and women had CHD risk exceeding 15%, 20% and 30% over 10 years with the National Cholesterol Education Program III (NCEP III) scoring system than with the Joint British charts. The latter agreed closely with the 1990 version of the Framingham risk equations.

Key words: cholesterol, coronary heart disease, hypertension, statins.

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Introduction

Randomised, clinical trials of statin therapy have been conducted in people whose annual coronary heart disease (CHD) risk has ranged from below 1% to 5%.[1-4] Recommendations for primary CHD prevention have made absolute, rather than relative, risk a major consideration in the clinical decision as to whether to introduce lipid-lowering drug therapy[5-7] to ensure that it is directed towards people at greatest risk, thus limiting cost and avoiding the needless exposure of people who are unlikely to benefit to the potential harmful effects of medication.

European and American recommendations for lipid lowering agree that the identification of high CHD risk should, whenever possible, be by clinical syndromes such as pre-existing atherosclerosis or familial hypercholesterolaemia. In other patients the recommendations advise an assessment of CHD risk based on the results of the Framingham study. In the recent National Cholesterol Education Program III (NCEP III) recommendations,[7] a new scoring system has been used.[8] This omits the prediction of stable and unstable angina included in the end point of the 1990 Framingham equation,[9] on which the Joint British Societies (JBS) charts, typical of those used outside the US, are based.[5,6] We estimated the degree of discordance of the American and British methods of CHD risk prediction in a series of patients whose general practitioners had requested CHD risk estimation in the course of their routine practice.

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Method

Between November 2000 and October 2001, the Clinical Biochemistry Laboratory at Manchester Royal Infirmary offered CHD risk calculation to general practitioners requesting serum lipids, if they provided information about patients' blood pressure and cigarette smoking. Such information was provided for 412 patients aged between 35 and 74 years whose blood pressure and lipids were in the Framingham range. Diabetes mellitus was not considered because the NCEP III scoring system does not include it (diabetes is considered a CHD risk equivalent in the US). Family history is not a factor in either of the Framingham risk equations, and was not included either.

We thus used age, gender, serum cholesterol, high density lipoprotein (HDL) cholesterol and smoking status to assess CHD risk using the NCEP III scoring system[7] and the JBS charts.[6,10] We also calculated CHD risk using the same parameters by the 1990 Framingham equation[9] programmed into a computer. The study was conducted according to the criteria for medical audit and student projects approved by the Central Manchester Research Ethics Committee. No file of identifiable patient data was created for the purpose of this investigation.

The men (n=230) were aged 57±10 years (mean ± SD) and the women (n=182) were aged 61±9 years. Of the men, 37% smoked. Their systolic blood pressure was 147±17 mmHg, serum cholesterol 5.61±1.10 mmol/L, HDL cholesterol 1.15±0.27 mmol/L and triglycerides 1.95 (1.27–3.04) (median [interquartile range]) mmol/L. In the women, systolic blood pressure was 148±19 mmHg, serum cholesterol 6.01±1.18 mmol/L, HDL cholesterol 1.33±31 mmol/L and triglycerides 1.96 (1.28–2.64) mmol/L. Some 30% of them smoked. The percentages of patients in different 10-year CHD risk categories

Table 1. The percentages (95% CI) of 230 men and 182 women who were found to be at various levels of coronary heart disease (CHD) risk critical for the US and British guidelines for lipid-lowering therapy using the National Cholesterol Education Program (NCEP) III scoring system,[7] Joint British Societies charts (JBS)[10] and the Framingham equation.[9] Results are statistically significantly different when CIs do not overlap. JBS charts do not allow calculation of CHD risk in the < 10% and 10–20% categories

	Percentage at risk		
CHD risk (% over 10 years)	**NCEP**	**JBS**	**Framingham**
Men			
< 10	26.5 (20.8–32.2)	-	18.7 (13.7–23.7)
10–20	59.1 (52.7–65.5)	-	31.3 (25.3–37.3)
> 15	51.3 (44.8–57.8)	63.9 (57.7–70.1)	65.2 (59.8–71.4)
> 20	14.3 (9.8–18.8)	47.4 (40.9–53.9)	50.0 (43.5–56.5)
> 30	4.8 (2.0–7.6)	11.3 (7.2–15.4)	12.6 (8.3–16.9)
Women			
< 10	84.6 (79.4–89.8)	-	36.8 (29.8–43.8)
10–20	13.7 (8.7–18.7)	-	40.7 (33.6–47.8)
> 15	3.3 (0.7–5.9)	37.4 (30.4–44.4)	39.6 (32.5–46.7)
> 20	1.6 (0–3.4)	22.0 (16.0–28.0)	22.5 (16.4–28.6)
> 30	0	3.8 (1.0–6.6)	4.9 (1.8–8.0)

according to the methods of risk assessment are shown in table 1. The categories were chosen because > 10% and > 20% are critical to the NCEP III recommendation,[7] > 20% to the European ones[5] and > 15% and > 30% to the British guidelines.[6,10]

Discussion

The NCEP III scoring system gave significantly lower estimates of risk in both men and women, particularly in the higher categories of risk, compared to the Framingham equation; the JBS charts gave similar results to the Framingham equation. It could be said that, because some of the CHD end points are omitted from the NCEP III scoring system, this result was predictable. However, the extent of the difference and its effect on the various risk categories could only have been appreciated from a real clinical evaluation such as the present one.

The main justification for changing from the all-inclusive CHD end point in the NCEP III recommendations was that predicting only fatal and non-fatal myocardial infarction is closer to the end point of CHD incidence employed in the statin trials.[1-4] The counter-argument is that the object of a CHD risk estimation is to identify people from the general population who have not yet developed clinical atherosclerosis, but who are at high risk of doing so. Because stable or unstable angina is not as certain an indicator of the development of CHD as definite myocardial infarction, excluding it as an end point in a clinical trial provides a more rigorous test of the hypothesis that statin therapy decreases CHD incidence.

In fact, people destined to develop angina are an important high-risk group for CHD death or non-fatal myocardial infarction, particularly since in the Framingham study the diagnosis of angina was made by a physician. They are also a high-risk group for intervention procedures, such as coronary surgery or angioplasty, which have been end points in all the statin trials.[1-4] Future guidelines will also be expected to identify people at high risk of stroke as well as CHD, not only to guide the management of high blood pressure, but also because statin therapy is now known to prevent stroke as well as CHD.[1,3,4] Whatever the resolution of these arguments, it is certain from the present study that methods of risk estimation and the thresholds for intervention from different sets of recommendations are not interchangeable.

Estimation of CHD risk is recommended by NCEP III in the primary prevention of CHD only in those whose low density lipoprotein (LDL) cholesterol is less than 4.0 mmol/L (160 mg/dl) and when two or more risk factors are present. Statin therapy is, however, recommended regardless of risk if the LDL cholesterol exceeds 4.0 mmol/L and two or more risk factors are present; and if the LDL cholesterol is above 4.8 mmol/L (190 mg/dl) if one or no risk factors are present. Even then, physician and patient may opt to treat LDL cholesterol levels as low as 4.0 mmol/L. Examination of our results revealed that, according to these recommendations, many people with LDL levels above 4.0 mmol/L would receive statin treatment although they were at lower risk than those whose LDL cholesterol levels were less than 4.0 mmol/L. Although not the primary purpose of our study, it raises concerns that the NCEP III scoring system, even when used with the NCEP III recommendations for statin therapy, will not lead to the most effective deployment of these drugs in the US in the primary prevention of CHD, that is to those in whom the likelihood of cardiovascular events is greatest.

The British recommendations give more prominence to risk calculation once the LDL cholesterol exceeds 3 mmol/L (equivalent to serum cholesterol 5 mmol/L). Our results indicate that these recommendations, properly applied, should mean that in primary prevention statin therapy is more consistently directed at those at highest risk, in whom it can be most effective. A number of studies, including the present one, provide evidence that the JBS charts are a faithful, two-dimensional version of the Framingham risk equation, which is easy for nurses and general practitioners to use.[11-15]

The relatively high yield of participants in our study whose CHD risk exceeded 15% over 10 years (65% of men and 40% of women) would be anticipated, because general practitioners requesting lipid measurements would probably have aimed their screening at people who on other clinical criteria might be anticipated to be at higher than average risk.[16] This is the way CHD risk estimation is intended to be employed in Britain.[16,17] The present study design (rather than risk assessment in the

Key messages

- The new American method of CHD risk estimation, which predicts only fatal and non-fatal myocardial infarction, but not stable or unstable angina, should not be used with recommendations for statin therapy such as those in Britain based on the original inclusive Framingham end point
- Now that we know that statin therapy prevents not only myocardial infarction but also angina and stroke, moves towards prediction methods which include only fatal and non-fatal myocardial infarction appear retrogressive. An even more inclusive measure of cardiovascular risk, including stroke, would seem the best future direction to take
- The Joint British Societies CHD risk prediction chart published in the British National Formulary gives results very close to those computed from the Framingham risk equation

general population) is therefore, we would argue, the most clinically relevant way to compare risk assessment methods.

In conclusion, using the NCEP III scoring system with British recommendations which are based on the 1990 Framingham equation will lead to substantial undertreatment with statins. Concern is also raised by this study about whether, even in the US, it will contribute to the underefficient use of statins, with some patient groups being treated at much lower risk than those to which it is applied.

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Conflict of interest

Professor Paul Durrington is a member of the Joint British Societies Committee making recommendations on cardiovascular disease prevention.

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