Predicting and reducing cardiovascular risk

The capacity to estimate and manage risk is arguably “the revolutionary idea that defines the boundary between modern times and the past”\(^1\), underpinning decisions in financial and commodity markets, insurance, engineering, and public health. Yet the risk of an individual developing a specific condition over a fixed period of time is a relatively new concept for clinical decision making. A recent spate of publications\(^2–4\) on the presentation of cardiovascular risk estimates suitable for clinical use is joined by Jones and colleagues’ contribution published in a recent issue of Heart.\(^5\)

Their study compares the accuracy of five tables or charts of cardiovascular risk derived from the original Framingham equations. Three of the tables are from national guidelines (joint British, New Zealand, and Canadian); one is from the joint European cardiac societies and one from Ramsay’s team in Sheffield. They assess the tables using data from almost 700 patients in 12 Birmingham general practices. For each patient, risk is predicted with each table and compared to the predictions directly calculated by the Framingham equations. It is reassuring that the charts in the revised joint British guidelines compared well with results from the original equations, as these guidelines inform treatment decisions in the national service framework on coronary heart disease.\(^6\) However, questions remain about the use of risk charts or tables in routine clinical practice.

Improving effectiveness of treatment
Decisions to initiate treatment for the prevention of cardiovascular disease in individual patients requires three types of information: evidence from trials, the level of risk (based upon the biological and behavioural characteristics of the individual), and his or her view on the initiation and continuation of treatment. Trials determine whether the benefits outweigh the hazards of treatment for a group of patients at a particular level of risk, and risk may be quantified from risk factors. Combining these elements informs the decision as to whether an individual is likely to benefit from a particular treatment. The willingness of a patient to start and continue treatment is a central component of (almost) all clinical decision making; the ultimate decision about treatment is taken by the patient, not the clinician. Improvements in any of these three informational components of decision making, including the accuracy of risk prediction, will increase the impact of cardiovascular disease prevention by medical means.

Framingham risk predictions
The authors of the original Framingham papers first published their equations predicting cardiovascular risk 25 years ago, but the concept is not fully assimilated into routine clinical practice. The New Zealand guidelines popularised absolute—rather than relative—risk estimation as a key factor in the decision to treat.\(^7\)

A key finding in intervention studies is that while relative risk reduction may remain broadly constant, absolute risk reduction varies considerably because it is a function of the initial level of baseline risk. For example, if a man with a baseline risk of a cardiovascular event of 10% over 10 years and a blood pressure of 154/100 mm Hg takes effective antihypertensive treatment, his relative risk falls by about a third, while his absolute risk is reduced to 6.7%—an absolute risk reduction of 3.3%. If another man with the same blood pressure but a higher baseline risk of 30% takes effective antihypertensive treatment his relative risk also falls by about a third to 20%. However, his absolute risk reduction is 10%.

Cardiovascular risk prediction based on absolute risk is now advocated for treatment decisions for aspirin, statins, antihypertensives and, in people with atrial fibrillation, for warfarin. Risk prediction ideally should come with information detailing its sensitivity, specificity, and the predictive value. These define the extent to which all high risk individuals are identified and how many people are wrongly included in the high risk group. Information on the accuracy of the Framingham predictions is largely based on US studies; these show it to have a sensitivity of 85% and a false positive rate of 30%, better than any single risk factor alone, but with a predictive power that leaves room for improvement. There is limited information on the performance of the Framingham equations in a British population. One study found reasonable agreement at a predicted coronary event rate above 1.5% per annum but an underestimate of risk below this level.\(^8\)

The predictive power—the extent to which someone identified as being at high risk will actually go on to have a coronary event in a specified period of time—depends upon the prevalence of people at high risk among the population to which it is applied. The Framingham predictions tend to perform better in hospital outpatient departments than in general practice, where the population is more heterogeneous for coronary heart disease risk and prevalence is lower. For the same reasons the predictions perform better in elderly than young populations.

Risk prediction based on UK populations is only applicable for men.\(^9,10\) Although the current Framingham predictions were generated from data collected in the 1970s in the white US suburb of Framingham, they have proved to be reasonably robust when applied to current northern European populations. Framingham equations have acquired more support, most notably as part of the English national recommendations on coronary heart disease and hypertension, and have proved popular because of their wide age range and inclusion of both sexes.

But there are limitations to the use of the Framingham predictions in Britain. There is insufficient longitudinal data from the ethnically diverse British population or specific patient groups such as people with raised blood pressure or diabetes. In addition, a number of major risk factors are not included in the equations including family history of premature myocardial infarction and South Asian ethnicity, both of which are independent risk factors for coronary heart disease. Microalbuminuria, an important independent cardiovascular risk factor in people with diabetes, is also missing from Framingham data. The equations may underestimate risk at extremes of blood
pressure, raised serum cholesterol or obesity. These omissions mean that the risk estimation for individuals remains relatively crude, although still superior to clinical assessments alone.11

Choice of risk prediction methods
The competing cardiovascular risk charts based on the Framingham equations have been generated by different methods of graphical display. Paper versions inevitably mean that continuous variables such as age or blood pressure have to be grouped to produce a simple graph. There is an inevitable loss of accuracy when compared with computer based methods based on continuous data. There has also been disagreement as to whether coronary heart disease events or stroke events, or both, should be the outcome determining treatment. With the notable exception of people of African origin, coronary heart disease events are good predictors of stroke and can be applied more easily to current data.

The extent to which the various charts are routinely used in hospitals and general practice is not known, but as computer based methods become generally available the utility of paper based methods is likely to diminish. Computer based methods that use the full Framingham equations are more accurate not only because they avoid converting risk factors into dichotomous variables, but also because they allow more variables to be used. The omission of left ventricular hypertrophy from the joint British tables may decrease their accuracy particularly in people with raised blood pressure, a factor not investigated by Jones and colleagues.3

Screening for raised cholesterol in general practice?
The assessment of risk, based on either Framingham charts or computer programs, requires knowledge of the serum cholesterol and high density lipoprotein (HDL) cholesterol. While most people referred to outpatients for cardiovascular problems will have their serum lipids measured, there is no case for routine screening for hyperlipidaemia in general practice. It is not cost effective and the workload is prohibitive. To avoid routine measurement of lipids, “default” values for serum cholesterol and HDL, based on mean values found in population samples, may be used to calculate risk. If risk is found to be 15% or more lipids will need to be measured. This will apply to about 40% of adults over 50 years of age and very few below this age.12 13

Does risk assessment improve management?
As yet there is no evidence that risk based cardiovascular treatment decisions produce better patient outcomes than those based on individual measures, such as blood pressure or lipid profile, nor that computer based methods are superior in practice to paper based methods. In a randomised controlled trial, Montgomery and colleagues failed to show any difference in blood pressure control between patients whose general practitioners managed them with computer based decision support (incorporating numerical estimate of cardiovascular risk) and those managed by guidelines and risk charts.14 French physicians have come to similar conclusions.15 However, there is considerable doubt about the size of the difference that these studies were likely to find or their power to detect them. Studies of multiple risk factor intervention have a poor record in this respect. The detection of small differences over short periods of time is a difficult task and these studies have been based on overly optimistic assumptions about the between group differences in risk factor control that result from modest changes in professional organisation or knowledge.16 17

Despite its limitations, quantitative estimation of cardiovascular risk factors is an approach to clinical decision making that is here to stay. It identifies risk more accurately than clinical acumen alone and allows the targeting of treatment to people who will benefit most. Both paper and computer based methods are now generally available. The question is whether it will take another 25 years before it becomes as much a part of risk assessment as documenting blood pressure or smoking.

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Thanks to Brian Hurwitz for his comments on an earlier draft of this paper.