This study uses the 1998 version of the Framingham algorithm, which relies on multiple sub-categories of LDL-cholesterol (LDL-C) to fine tune risk estimates. In the UK, as in many other countries and commercial computer programs, the original simpler 1991 algorithm is used. Given the high biological, analytical and mathematical variation in calculated LDL-C, we would contend that this more modern version may be less accurate than the older algorithm. The basic problem lies in the high biological variability of triglycerides and their consequent effect on the Friedewald equation — a foundation stone of modern cardiology anchored on the shifting sands of a small number of patients. Direct measurement of LDL-C, though likely more accurate, is rarely performed and is subject to methodological differences between assays.

Despite these limitations, both risk calculators did predict high-risk groups but over-estimated the likely burden of disease. However, only proportions of events predicted were assessed. When attempting to predict risk of an event in an individual using a population-based function, identical proportions from two assessment systems may identify profoundly different populations. This is the problem of concordance. Concordance between events predicted in high-risk individuals and actual individual outcomes was not assessed in this study and may represent a further source of error in risk calculation. Indeed even minor modifications to risk assessment programs can result in significant changes in concordance. Similarly evolution of risk factor distributions (e.g., increase in diabetes) is likely to cause drift in algorithm coefficients (as is clearly shown in Table 2 in the paper) leading to further reductions in concordance between predicted and actual events.

Given these limitations we would contend that the interpretation of cardiovascular risk calculation algorithms is an art. Clinicians should avoid excessive reliance on spuriously accurate computer predictions but should instead critically review the individual risk factors in each patient and base their judgements on initiation of intervention on a broad view of the likely risks.

References

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Screening for cardiovascular disease: reply

Dear Editor
Thank you for giving us the opportunity to reply to Dr AS Wierzbicki and please consider the present letter.

Dr Wierzbicki addressed two questions on the external validation study of the Framingham and PROCAM risk functions in healthy middle aged-men from low (France) and high-risk (Belfast) European countries.

First, the author raised the question of the impact of evolving definitions of categorical risk factors, wide variation in the interpretation of their definitions and lack of precision in biological risk factors measurements on the assessment of CHD risk. Most of these points have been discussed in our paper. The concern regarding the greater variability in the measurement of LDL-cholesterol (1998 algorithm) than in that of total cholesterol (1991 algorithm) is a priori well sounded. However, both

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Screening for cardiovascular disease

Sir

The paper by Empana et al.1 reviewing the utility of the Framingham and PROCAM cardiovascular risk calculation algorithms in a validation study against the PRIME cohort raises many issues. Firstly definitions of critical importance for defining categorical variables.2 The definitions of diabetes and family history have either changed dramatically or are subject to wide differences in interpretation. This has profound effects on calculated risks. Given the results of this study, it is interesting to note that methods for measurement of HDL-cholesterol (HDL-C) have advanced since these algorithms were devised and modern assays give results 10–20% higher than the methods used in Framingham resulting in an underestimation of risk due to low HDL-C in the original algorithm.

More fundamentally, all risk calculators have wide confidence intervals for predictions due to underlying biological variation in risk factors.3 We have previously shown that the 95% confidence interval at the accepted risk threshold is 20±6% for single measurement and 20±3.3% for triplicate measurements. These wide confidence intervals limit the power of any algorithm to reliably identify high-risk individuals as is clearly demonstrated in this paper.

References
1991 and 1998 Framingham algorithms had only slightly different discriminatory power in our populations (c-statistics of 0.68 and 0.69, respectively in Belfast and France for the 1991 algorithm as compared to 0.66 and 0.68 for the 1998 one). This suggests in practice that the variability in the measurement of LDL-cholesterol only partially contributed to the “quality” of the algorithms.

Second, the author pointed out the problem of the concordance between estimated individual’s probability of CHD events and the actual outcomes. Although we did not develop this point in our paper, we gave c-statistics (area under the receiving operative characteristics curve) at Table 4, which precisely represents this concordance for the different algorithms (Framingham and PROCAM) and populations (Belfast and France).

Finally, we agree with Dr Wierzbicki that individual risk calculation by algorithm may be largely spurious and should be interpreted critically in the light of clinical judgment.

References


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Cardioversion threshold, IRAF and beyond

We read with great interest the report of De Simone et al. in the August 2003 issue of the journal. The main finding of their study was that verapamil, added to flecainide or amiodarone reduced recurrences of atrial fibrillation after cardioversion. They also report that patients on flecainide required less shocks and had a lower mean cumulative energy to defibrillate than patients on amiodarone. They state that this illustrates the favourable effect of flecainide on defibrillation energy requirements. However, on the basis of their definition of successful cardioversion (i.e. at least three beats of sinus rhythm, probably indicating 3 or more atrial complexes irrespective of the site of origin in the atria) it is impossible to correctly determine and compare defibrillation thresholds in the treatment groups. In stead, absence of electrical activity in the atria immediately after a shock should have been used. The definition of De Simone et al. gauges cardioversion threshold, resumption of sinus rhythm and suppression of hyperacute immediate recurrence of atrial fibrillation (IRAF), all at the same time. In other words, the higher ‘cardioversion threshold’ may in fact have been due to a more marked depressing effect of amiodarone on atrial pacemaker activity compared to flecainide. Such an effect may impede resumption of normal sinus rhythm and facilitate IRAF. Considering the above, the authors could have taken the opportunity to report the effects of various drug combinations on threshold as well as on IRAF, i.e. recurrences occurring within 1–2 min after cardioversion. The fact that verapamil added to amiodarone was not associated with increased energy requirements is not discussed, but suggests a favorable effect due to reduction of IRAF. We feel it is important to dissect the different drug effects on threshold, resumption of normal pacemaker activity and IRAF. Considering the meticulous monitoring of the heart rhythm around the cardioversion, the study by De Simone et al. could have added valuable information in this respect. Such information may enhance a targeted use of antiarrhythmic drugs in the suppression of consecutive recurrence mechanisms in patients undergoing cardioversion of persistent atrial fibrillation.

References


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