# Cardiovascular Risk and Risk Scores: ASSIGN, Framingham, QRISK and others: how to choose

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Coronary heart disease and stroke contribute significantly to premature mortality and morbidity. Largely preventable, they demand prevention. Emphases range from responsibilities of governments to individuals, and the clinic nurses or doctors advising and treating them. The risk of cardiovascular disease varies. To be efficient and effective, medical interventions must focus on those at highest risk.

The strongest marker of risk is existing cardiovascular disease (diabetes often included) demanding secondary prevention, now routine medical therapy. Next comes age, the criterion the polypill's promoters proposed for medicating the population.[1] Age, sex and existing disease are major determinants of cardiovascular risk, but work begun 60 years ago in Framingham, USA,[2] gave us risk factors—individual characteristics identifying increased risk. Combined as multifactorial risk they predict more than individual factors (see table 1). Since the Framingham classics (age, sex, smoking, blood pressure and lipids) other risk factors and scores have been proposed. The accompanying paper published in this issue of *Heart* examines some scores used currently in the UK (***see page 491***).[3] How to choose?

The first criterion is utility. If a score is user-friendly, motivates the clinic nurse or doctor and the patient to start and persist with preventive action, it is a good score. A sheathed sword cannot cut. Any score that gives positive weighting to age, smoking, blood pressure and lipids will largely agree with another. Debate should not encourage nihilism. Easy implementation matters: factors included should be available, or justify their addition.

Chauvinism is a questionable criterion, but motivates new scores. From the USA came Framingham and preventive (not …tative) cardiology.[4] Framingham is often depreciated as based on outdated, middle-aged Americans. In 1991 specifications for developing the Dundee coronary risk disk[5] stipulated a British population base, anticipating criticism that risk factors might not behave in the same way. Likewise for European development of SCORE.[6] Biological risk factors are now known to behave similarly across diverse populations—we are the same species. Although Framingham competes strongly with scores from elsewhere, there is still a prejudice that recent, local scores are more credible.

Complexity arises from 'risk prediction' and 'validation'. We cannot accurately predict a future myocardial infarction as if it were an eclipse of the sun despite claims to 'predict absolute risk'. Single measurements of fluctuating risk factors and the unpredictable distribution and behaviour of individual atherosclerotic plaques guarantee imprecision.

In deriving a score we record the experience of a cohort followed for some years in terms of their initial risk factor levels and subsequent cardiovascular morbidity and mortality; then project it onto new disease-free populations to anticipate the future. If cardiovascular risk were determined exclusively by classic risk factors incidence rates of disease would be predictable. Long ago American risk scores were shown to overpredict event rates in Parisians.[7] Similar recent observations, and the need for SCORE itself to be recalibrated for different European populations, are not surprising. It would be coincidence were a score from one population at one time to be exactly calibrated to another. There are other and unknown determinants. Calibration, a part only of validation, has been overemphasised. It is secondary.

Risk scores are not crystal balls for prophesying. They are for prioritising preventive treatment. Individuals have risk factor values entered into a multifactorial score and are ranked according to this estimated risk to assess whether they justify treatment. More important than calibration is the score's discrimination between future cases and non-cases, by concentrating future cases at the top end of the distribution, the crucial component of validation. Table 1 shows how different factors and two scores discriminate in terms of the percentage of subsequent 10-year cardiovascular events occurring in the top 20% of risk, calculated from baseline risk factors in the Scottish heart health extended cohort (SHHEC). The best result approaches 50%. Two scores concentrating 50% of future cases in the top 20% have similar discrimination even if they are calibrated differently—the cutpoint to pick out this top 20% may be different, as it was for individual risk factors. Which individuals are high risk also differs. Good scores discriminate better than poor ones. Sophisticated statistical tests explore this in different ways.

Picking up half (for simplicity) of future cases when designating one fifth of the population as high risk for treatment is the paradox of risk scoring. Is the glass half full or half empty? Treatment is 20% of that treating everybody. Numbers needed to treat, to anticipate one case, are 40%, saving resources and side effects. The top 20% has four times the risk of the remainder, but it contains many false positives. Half the future cases are false negatives, not categorised high risk, therefore untreated, unless assessment of borderline cases is repeated at intervals. We are far from 'predicting' future cases with certainty.

An attribute of scores newly questioned by us and others is equity or fairness, the antithesis of discrimination. If a score is to be nationally adopted for preventive action it should not neglect sections of the population at excess risk for reasons incompletely identified by classic risk factors. Application of a Framingham score[8] across populations with large social gradients in disease like the UK will result in relative under-treatment of the socially deprived, and over-treatment of the socially privileged, frustrating national policies for diminishing social gradients in disease.[9] Harmful effects of social deprivation are only partly mediated by smoking, blood pressure and lipids. We were the first to propose a solution in the ASSIGN cardiovascular risk score in Scotland based on SHHEC,[10 11] a carefully standardised study, by adding in social deprivation and also family history. This was emulated 7 months later by QRISK[12] based on QRESEARCH, a much larger, predominantly English general practice population but with much missing data. ASSIGN[3 10] is shown to compensate for the social bias

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**Table 1** Percentage of 10-year cardiovascular events occurring in high-risk category (top 20% for continuous variables) (Scottish Heart Health Extended Cohort). Sexes combined.

| Variable | % High risk | % Age of 10-year events in baseline high-risk category |
|---|---|---|
| Continuous | | |
| Age | 20.0 | 36.5 |
| Systolic blood pressure | 20.0 | 36.0 |
| Cigarettes ≥20/day* | 21.9 | 32.4 |
| HDL-cholesterol† | 20.0 | 30.9 |
| SIMD | 20.0 | 29.0 |
| Total cholesterol | 20.0 | 28.0 |
| Binary | | |
| Diabetes mellitus | 1.4 | 3.8 |
| Age ≥55 years | 26.2 | 44.8 |
| Male sex | 49.2 | 63.8 |
| Positive family history | 29.6 | 38.9 |
| Score | | |
| ASSIGN top 20%[10] | 20.0 | 46.3 |
| ASSIGN score ≥20[10] | 16.0 | 41.6 |
| Framingham top 20%[9 10] ‡ | 20.0 | 45.6 |
| Framingham score ≥20[9] ‡ | 20.8 | 49.2 |
| Denominator | 13297 | 1165 |

(QRISK algorithms not available for comparison).
*Highest 20% falls in the middle of 20 per day so all of these included.
†Lowest 20%, not highest, for high-density lipoprotein (HDL)-cholesterol.
‡Framingham cardiovascular score (several Framingham scores exist).
SIMD, Scottish Index of Multiple Deprivation.

from Framingham[9] but it is not clear how well QRISK does.[3 13] These feature in the accompanying paper.[3]

One effect of adding social deprivation and family history, powerful risk factors (see table 1), to classic factors in the ASSIGN score was a statistically significant improvement in discrimination, but disappointingly modest.[10] Diminishing returns is a common finding on adding new factors to the Framingham dataset.[14] Improvement is not inevitable; more does not mean better. The present paper[3] independently confirms our own finding in SHHEC[10] that ASSIGN discriminated better than a Framingham score[9] but not by much; also shown, but not emphasised, in the original QRISK paper on the QRESEARCH population.[12]

The problem of calibration is resolvable by moving cutpoints for high-risk treatment. It has been suggested that ASSIGN and Framingham may lead to over-treatment,[12] but the converse argument for QRISK is that it may be identifying too few, particular in younger age groups, in which the number of positives may be too small to justify its use.[13] Framingham scores come both sides of ASSIGN: the Framingham cardiovascular score scores higher on average, more results exceeding a score of 20[8 10] (see table 1), but the composite of coronary plus stroke scores, and also the Cox Framingham score, frequently score lower,[3 12] results differing by age and sex and subject. Thresholds for treatment are coming down. 'Absolute risk' rises rapidly with age. If the same cutpoint is used regardless of age, all scores will identify a useful minority of the population for treatment over only a limited range of middle age; below this hardly anyone qualifies, above almost everybody. The paradigm needs re-examining.

Current testing of ASSIGN[3] in the THIN, largely English general practice population, had problems experienced in the QRESEARCH studies that much, and for some variables most, data (notably lipids and family history) were missing. The social gradient in disease for QRISK, QRESEARCH and THIN appears implausibly shallow. Maybe the indexing of social deprivation was unsatisfactory.[3 13] Scotland has its own Scottish index of multiple deprivation based on the postcode (see http://www.scotland.gov.uk/Topics/Statistics/SIMD (accessed 6 Jan 2011)). It would be nice to think that better data, especially for variables additional to Framingham, would improve discrimination by ASSIGN further, but that would be supposition. Data held in general practice need to be improved and standardised to get the full benefit from any system of risk factor scoring.

We launched ASSIGN for use in Scotland on grounds of social equity,[9 11] an argument now being heard as prominently outside Scotland. It is here shown to discriminate as well, if not marginally better, than its rivals, Framingham and possibly QRISK, in an independent study. Marginally better or equivalent discrimination may not prove a strong argument in itself, so the major rationale for ASSIGN is that of social equity. Implementation in place of the Framingham score modifies the distribution of high-risk cases across the population—increasing the primary care workload in socially deprived neighbourhoods, a challenge for health service support. We are currently revising ASSIGN,[15] incorporating the 2009 update of the SIMD.

**Patient consent** Obtained.

**Sole contributor's statement of interest** The sole contributor, Hugh Tunstall-Pedoe, developed the ASSIGN cardiovascular risk score jointly with Mark Woodward in 2006, in relation to the revised SIGN (Scottish Intercollegiate Guidelines Group) guideline 97 'Risk estimation and the prevention of cardiovascular disease'.[10 11] It is adopted by SIGN and the Scottish Government Health Directorates as the current cardiovascular risk score of choice in Scotland.

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