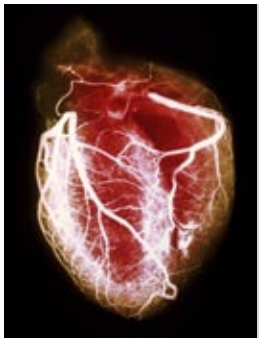
QRISK VALIDATION AND EVALUATION

QRISK may be less useful

Collins and Altman inappropriately criticise the National Institute for Health and Clinical Excellence (NICE) for not choosing QRISK to predict cardiovascular risk.[1] In doing so, they do not distinguish between assessing individual cardiovascular risk (as used by clinicians) and predicting risk of cardiovascular events in an actively managed population (as used in public health planning). As most tools predicting cardiovascular risk were developed in actively managed populations, they will underestimate the risk that clinicians and patients are initially interested in: the risk if no further treatment is initiated. This distinction seems to be overlooked in most discussion of cardiovascular risk.



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Most doctors would expect to explain the risk to patients were they left untreated. As with several other tools, however, QRISK was derived from a population cohort that may start additional treatments once found to have high rates of risk factors. Hence it is not surprising that it underpredicts cardiovascular risk. The Framingham study was conducted before the widespread use of effective treatment for cardiovascular risk factors and therefore its equations seem to overpredict cardiovascular risk when assessed in a population with active management of risk factors.

QRISK tried to adjust for baseline antihypertensive treatment, but its investigators admitted that this was a crude measure of blood pressure treatment.[2] Furthermore, it did not adjust for patients who started treatment between baseline and the end of the study.

Although QRISK seems to be more accurate in predicting cardiovascular events in a contemporary UK population, it may be less accurate in communicating risk to patients. For risk communication and individual decisions, cardiovascular risk should be based on study populations that do not receive additional treatment for cardiovascular disease.

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1 Collins GS, Altman DG. An independent external validation and evaluation of QRISK cardiovascular risk prediction: a prospective open cohort study. *BMJ* 2009;339:b2584. (7 July.)
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Bespoke cohort studies needed

Despite Collins and Altman's re-analysis of data from the THIN database to validate the QRISK equation for predicting cardiovascular disease,[1] adoption of QRISK in primary care is premature because key issues about the handling of missing data and the use of social deprivation indices remain unresolved.

Collins and Altman again highlight that complete data were available for just over a quarter of subjects. We appreciate that imputation methods were applied, but we question use of age-sex means of QRESEARCH data for lipid concentrations and blood pressures. This implies that QRESEARCH data were missing completely at random within age-sex strata—an assumption acknowledged as incorrect when the developers of QRISK revised their equation[2]. It also implies that observed QRESEARCH data reflect age-sex norms in the population—an assumption questioned by the developers' comparison of their data with the health survey for England.[3] We call for additional validation using data from bespoke cohort studies in which much greater attention has been paid to completeness of data.

Deprivation indices by their nature quickly become outdated, the Townsend index in particular being based on data from the 2001 census. It should be replaced with variables whose meaning is less context dependent, and which reflect underlying causes of inequalities in cardiovascular disease. For example, subcategorising non-smokers as either "ex-smokers" or "never smokers" would perhaps diminish some of the apparent predictive power of the Townsend index (since former smoking is likely to be more common among more deprived communities) and would allow QRISK to be more portable in its future use.

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1 Collins GS, Altman DG. An independent external validation and evaluation of QRISK cardiovascular risk prediction: a prospective open cohort study. *BMJ* 2009;339:b2584. (7 July.)
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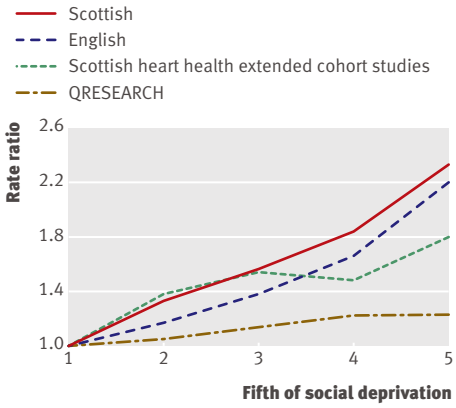
ASSIGN, QRISK, and validation

We challenge the recent QRISK validation and editorial concluding that QRISK is the cardiovascular risk score for the United Kingdom.[1 2]

ASSIGN, QRISK's precursor, was launched in Scotland before QRISK appeared.[3] Predicting that scores omitting social deprivation (socioeconomic status) as a risk factor could exacerbate social gradients in disease, we developed ASSIGN to include it. ASSIGN was adopted without external validation because it correlated highly with the gold standard Framingham score. Discriminating rather better, even after adjustment for self-testing bias, it removed Framingham's social inequity.

Subsequent to ASSIGN's launch, QRISK authors told us that they were developing their own score. Our offer of collaborative comparison was not accepted, and QRISK coefficients were kept secret after its launch. The initial partisan publication, however, did show that ASSIGN discriminated better than Framingham in the QRESEARCH database where QRISK originated.[4]

We have not seen how QRISK deals with social deprivation in analyses similar to ours—possibly because we have full 10 year follow-up of our cohort. QRESEARCH and the validation THIN database do not. Both these databases are missing 70% of data on lipids, and probably more on family history of cardiovascular



Social gradient by deprivation fifth in men for mortality under 75 from coronary heart disease in England and Scotland, and cardiovascular event rates in QRESEARCH and Scottish heart health extended cohort studies

disease. There is a surprisingly flat social gradient in cardiovascular event rates[3-5] and in men at high risk with the Framingham score in QRESEARCH (figure).[4]

ASSIGN and QRISK scores may serve different priorities with different advantages. We welcome debate and collaborative comparisons, but question whether QRISK is the preferred score for the United Kingdom when ASSIGN is already adopted in Scotland (www.assign-score.com).

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Authors' reply

The Framingham model currently recommended by the National Institute for Health and Clinical Excellence (NICE) to predict cardiovascular risk has stood the test of time. However, it was developed several decades ago from a relatively small cohort of predominantly white middle class people in the United States. Patient characteristics have since changed (falling blood pressure, increasing obesity, reduced smoking), and health outcomes have improved. Liew and Glasziou point out that some patients in the QRISK derivation and validation cohorts may have started additional treatments once they have been identified as having high risk factors. Obtaining treatment naive population cohorts, such as the Framingham cohort, to develop risk scores is now practically and ethically impossible. Also, while natural history is important, it is not clear that prognosis is best assessed from an untreated population.

Morris and colleagues call for further validation of QRISK on bespoke cohorts, where greater attention to data collection and cleaning will enhance the completeness of data. However, such high quality cohorts, if they exist, will be highly selective and not as representative of the UK population. The Department of Health vascular risk assessment programme is designed to be applied to the whole UK population with emphasis on primary prevention of vascular disease. QRISK was developed and validated in large cohorts of patients from UK general practices.[1-3]

Morris and colleagues and Tunstall-Pedoe and colleagues mention the low level of completeness of data. The high level of unrecorded values for one component of the QRISK risk score, total serum cholesterol/HDL ratio, dramatically reduced the proportion of people with complete data.

Few risk models have undergone such extensive validation and scrutiny as QRISK on such large cohorts that are truly representative of the target population. By contrast, little attention has been paid to the unexplained and unvalidated inclusion of adjustment factors currently recommended by NICE to adjust the risk for men of South Asian origin and those with a family history of coronary heart disease.

Morris and colleagues also observe that the Townsend score used in QRISK is outdated. Although our role was to provide an independent and objective evaluation of the performance of QRISK, we are aware from the QRESEARCH website (www.qresearch.org) that QRISK is designed to reflect current practice in recording of clinical information. QRISK will be updated to reflect changes and improvements in recording of information and changing patterns of population characteristics, as well as availability of more sophisticated statistical methods. For example, Morris and colleagues question the use of age-sex reference values to replace missing data; a more sophisticated multiple imputation approach was used for QRISK2, the successor of QRISK.[4]

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NEUROPATHIC PAIN

Management is more than pills

We have one important caveat in relation to Freynhagen and Bennett's review—that evidence based non-pharmacological treatment for neuropathic pain was absent.[1]

Several randomised controlled trials show that graded motor imagery reduces pain and disability in chronic complex regional pain syndrome 1 (CRPS1) and phantom limb pain after amputation or brachial plexus avulsion injury.[2] The number needed to treat for a 50% decrease in pain and a four point drop on a 10 point scale of disability is around 4,[3] which compares favourably with any other treatment for chronic CRPS1, including spinal cord stimulation.[1] Cognitive behavioural programmes reduce disability and pain in a range of neuropathic pain states,[4] and sensory discrimination training reduces pain in chronic phantom limb pain and possibly chronic CRPS1.[5]

These treatments were devised, and continue to be refined for people with chronic neuropathic pain, since the discovery of robust and profound changes within the central nervous system, including the brain. Continuing progress in this field suggests that we can train the brain and reduce pain and disability.

Freynhagen and Bennett state that traditional acupuncture in neuropathic pain is not supported by current evidence but imply support for acupuncture on the basis that it is comparatively harmless. Other comparatively harmless non-pharmacological treatments with level I or II evidence of efficacy were not mentioned. We believe that general practitioners and clinicians should be aware of all the evidence based pharmacological and non-pharmacological treatments available to patients with neuropathic pain, not just the pills.