

Abstracts

Getting away from Framingham

Gary Collins and Douglas Altman, medical statisticians from Oxford, have proposed a new model of 10-year risk of cardiovascular disease that appears to perform better than the older Anderson Framingham equation.

They independently evaluated the performance of the QRISK score for predicting 10-year risk of cardiovascular disease in an independent UK cohort of patients from general practice and compared the performance with Framingham equations.

Their study was carried out using 274 practices from England and Wales contributing to the THIN database.

The participants were 1.07 million patients, registered between 1 January 1995 and 1 April 2006, aged 35 - 74 years (5.4 million person years) with 43 990 cardiovascular events.

The main outcome measures were first diagnosis of cardiovascular disease (myocardial infarction, coronary heart disease, stroke, and transient ischaemic attack) recorded in general practice records.

This independent validation indicated that QRISK offers an improved performance in predicting the 10-year risk of cardiovascular disease in a large cohort of UK patients over the Anderson Framingham equation. Discrimination and calibration statistics were better with QRISK. QRISK explained 32% of the variation in men and 37% in women, compared with 27% and 31% respectively for Anderson Framingham. QRISK underpredicted risk by 13% for men and 10% for women, whereas Anderson Framingham overpredicted risk by 32% for men and 10% for women. In total, 85 010 (8%) of patients would be reclassified from high risk (20%) with Anderson Framingham to low risk with QRISK, with an observed 10-year cardiovascular disease risk of 17.5% (95% confidence interval (CI) 16.9 - 18.1) for men and 16.8% (15.7 - 18.0) for women. The incidence rate of cardiovascular disease events among men was 30.5 per 1 000 person years (95% CI 29.9 - 31.2) in high-risk patients identified with QRISK and 23.7 per 1 000 person years (23.2 - 24.1) in high-risk patients identified with Anderson Framingham. Similarly, the incidence rate of cardiovascular disease

events among women was 26.7 per 1 000 person years (25.8 - 27.7) in high-risk patients identified with QRISK compared with 22.2 per 1 000 person years (21.4 - 23.0) in high-risk patients identified with Anderson Framingham.

The QRISK cardiovascular disease risk equation offers an improvement over the long-established Anderson Framingham equation in terms of identifying a high-risk population for cardiovascular disease in the UK. QRISK underestimates 10-year cardiovascular disease risk, but the magnitude of underprediction is smaller than the overprediction with Anderson Framingham.

Collins GS, Altman DG. *BMJ* 2009; 339: b2584.

Statins for all – with established cardiovascular risk factors

A team of investigators from multiple centres have used published papers to show that statins are beneficial for people without cardiovascular disease, but who have established cardiovascular risk factors.

The team investigated whether statins reduce all-cause mortality and major coronary and cerebrovascular events in people without established cardiovascular disease but with cardiovascular risk factors, and whether these effects are similar in men and women, in young and older (>65 years) people, and in people with diabetes mellitus. They used a meta-analysis of randomised trials. Their sources were the Cochrane controlled trials register, Embase, and Medline.

Two independent investigators identified studies on the clinical effects of statins compared with a placebo or control group and with follow-up of at least 1 year, at least 80% or more participants without established cardiovascular disease, and outcome data on mortality and major cardiovascular disease events.

They found 10 trials that enrolled a total of 70 388 people, of whom 23 681 (34%) were women and 16 078 (23%) had diabetes mellitus. Mean follow-up was 4.1 years. Treatment with statins significantly reduced the risk of all-cause mortality (odds ratio 0.88; 95% confidence interval 0.81 - 0.96); major coronary events (0.70; 0.61 - 0.81), and major cerebrovascular

events (0.81; 0.71 - 0.93). No evidence of an increased risk of cancer was observed.

They concluded that in patients without established cardiovascular disease but with cardiovascular risk factors, statin use was associated with significantly improved survival and large reductions in the risk of major cardiovascular events.

Brugts JJ, et al. *BMJ* 2009; 338: b2376.

Male circumcision and HIV transmission to women

Previous studies have suggested that circumcision of HIV-infected men reduces the rate of transmission of HIV to their uninfected partners. Maria Wawer and colleagues, writing in the *Lancet*, found that this was not the case in their Ugandan study.

Their study population was 922 uncircumcised, HIV-infected, asymptomatic men aged 15 - 49 years with CD4 cell counts 350 cells/ μ l or more who were enrolled in this unblinded, randomised controlled trial in Rakai District, Uganda. Men were randomly assigned by computer-generated randomisation sequence to receive immediate circumcision (intervention, $N=474$) or circumcision delayed for 24 months (control, $N=448$). HIV-uninfected female partners of the randomised men were concurrently enrolled (intervention, $N=93$; control, $N=70$) and followed up at 6, 12, and 24 months, to assess HIV acquisition by male treatment assignment (primary outcome). A modified intention-to-treat (ITT) analysis, which included all concurrently enrolled couples in which the female partner had at least one follow-up visit over 24 months, assessed female HIV acquisition by use of survival analysis and Cox proportional hazards modelling.

The trial was discontinued early because of futility. Ninety-two couples in the intervention group and 67 couples in the control group were included in the modified ITT analysis. Seventeen (18%) women in the intervention group and 8 (12%) women in the control group acquired HIV during follow-up ($p=0.36$). Cumulative probabilities of female HIV infection at 24 months were 21.7% (95% confidence interval (CI) 12.7 - 33.4) in the intervention group and 13.4% (6.7 - 25.8) in the control group (adjusted hazard ratio 1.49; 95% CI 0.62 - 3.57; $p=0.368$).

Circumcision of HIV-infected men did not reduce HIV transmission to female partners over 24 months; longer-term effects could not be assessed. Condom use after male circumcision is essential for HIV prevention.

Wawer M, *et al. Lancet* 2009; 374: 229-237.

Getting to the heart of the Mediterranean diet

Conventional wisdom now tells us that the Mediterranean diet is good for us, but just what is it about the diet that leads to the decreased risk of cardiovascular disease and type 2 diabetes?

Antonia Trichopoulou and colleagues from the universities of Athens and Harvard looked at the relative importance of the individual components of the Mediterranean diet to its known benefits. They used a prospective cohort study of the Greek segment of the European Prospective Investigation into Cancer and nutrition (EPIC).

Participants were 23 349 men and women, not previously diagnosed with cancer, coronary heart disease, or diabetes, with documented survival status until June 2008 and complete information on nutritional variables and important covariates at enrolment. The main outcome measure was all-cause mortality.

After a mean follow-up of 8.5 years, 652 deaths from any cause had occurred among 12 694 participants with Mediterranean diet scores of 0 - 4 and 423 among 10 655 participants with scores of ≥ 5 . Controlling for potential confounders, higher adherence to a Mediterranean diet was associated with a statistically significant reduction in total mortality (adjusted mortality ratio per two unit increase in score 0.864, 95% confidence interval 0.802 - 0.932). The contributions of the individual components of the Mediterranean diet to this association were moderate ethanol consumption 23.5%, low consumption of meat and meat products 16.6%, high vegetable consumption 16.2%, high fruit and nut consumption 11.2%, high monounsaturated to saturated lipid

ratio 10.6%, and high legume consumption 9.7%. The contributions of high cereal consumption and low dairy consumption were minimal, whereas high fish and seafood consumption was associated with a non-significant increase in mortality ratio.

The dominant components of the Mediterranean diet score as a predictor of lower mortality are moderate consumption of ethanol, low consumption of meat and meat products, and high consumption of vegetables, fruits and nuts, olive oil, and legumes. Minimal contributions were found for cereals and dairy products, possibly because they are heterogeneous categories of foods with differential health effects, and for fish and seafood, the intake of which is low in this population.

Trichopoulou A, *et al. BMJ* 2009; 338: b2337.

BRIDGET FARHAM

Single suture

Oops!

An exposé of a dodgy 'open access' publisher is laid bare at <http://scholarlykitchen.sspnet.org/2009/06/10/nonsense-for-dollars>. A scientific article created using software that generates grammatically correct but 'context-free' (nonsensical) papers was submitted to *The Open Information Science Journal*, a journal that claims to enforce peer review. The paper purported to be from authors affiliated to the Centre for Research in Applied Phrenology (CRAP). The publisher confirmed receipt of the paper the next day, and about 4 months later – lo and behold – the article was accepted. Producer-pays-to-publish models of publishing should watch out for their credibility.

Single suture

Before or after death?

Existing forensic techniques are limited in their ability to determine exactly when a stab wound was inflicted. However, Manfred Oehmichen and colleagues from the University Hospital of Schleswig-Holstein in Kiel may have found a new technique that will make this task easier.

They counted mast cells in and around the edges of the wounds of 64 stab victims. After releasing their wound-healing granules, mast cells lose the ability to make the enzyme chloroacetate esterase and no longer show up when exposed to a dye that reacts with the enzyme. The team found that fewer enzyme-positive mast cells showed up in the wounds of people stabbed to death than in neighbouring undamaged skin. However, when the team stabbed cadavers, the number of these cells was the same everywhere.

Oehmichen says that if the person were alive when stabbed there would be a reduction in mast cells.

New Scientist 2009; 11 July: 17.