Heartbeat: Challenges in primary prevention of cardiovascular disease

Catherine M Otto

In addition to encouraging a healthy lifestyle and treating modifiable risk factors, one of the mainstays for primary prevention of cardiovascular disease (CVD) is the use of statin therapy in people with increased CVD risk. However, it is confusing for clinicians and patients that guidelines from different organisations make different recommendations about who to treat and how to set treatment goals.[1] In my editorial in this issue of *Heart*, the 3 major differences between guidelines are summarised: (1) how CVD risk is calculated, (2) the risk threshold for recommending statin therapy and (3) the use of treatment with a fixed statin dose versus therapy adjusted to achieve a serum low density lipoprotein (LDL) target. The rationale for different risk scores in each guideline is because CVD risk prediction varies in different populations; ideally the risk score was derived from the population being treated. Evidence suggests that statin therapy is beneficial even for lower risk patients; thus, the threshold chosen for treatment depends on estimates of the likelihood (and acceptance) of side effects, as well as cost considerations. The decision to recommend fixed dose versus LDL level targeted therapy is primarily an economic decision given that more intensive treatment requires more monitoring and may increase risk. The UK National Institute for Health and Care Excellence (NICE) guidelines recommend offering fixed dose atorvastatin 20 mg to people whose 10-year risk of developing cardiovascular disease is ≥10% using the QRISK assessment tool, which includes all patients over age 84 years.

Another approach to primary prevention of CVD is the use of a single pill that includes a statin and antihypertensive agents given to entire populations, an approach known as the 'polypill'. In a microsimulation model, Ferket and colleagues[2] found that the optimal strategy for this approach was treatment with the polypill when 10-year CVD risk was greater than 20%. This approach was predicted to gain 123 quality adjusted life years (QALYs) per 10K individuals at an extra cost of £1.45 million.

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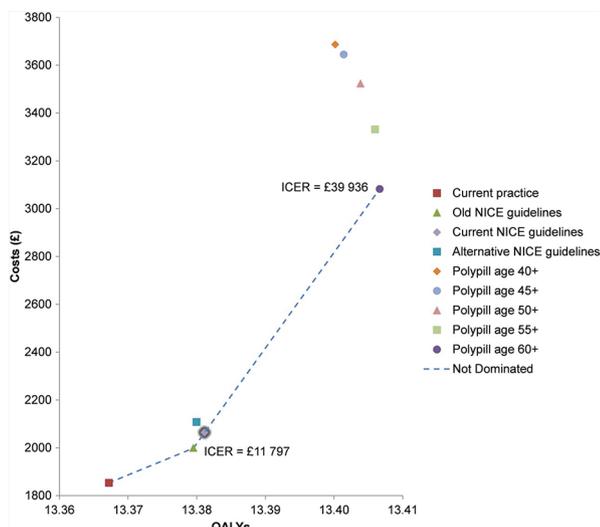
Figure 1 Cost-effectiveness graph of base-case analysis results. Costs (in UK pounds) and quality-adjusted life-years (QALYs) are means in the UK Biobank study population. The grey shaded area indicates that the scenario has been eliminated by extended dominance. Extended dominance implies that the programme is less costly than the next not absolutely dominated programme, but also has a larger incremental cost-effectiveness ratio (ICER) than this next programme. NICE, National Institute for Health and Care Excellence.
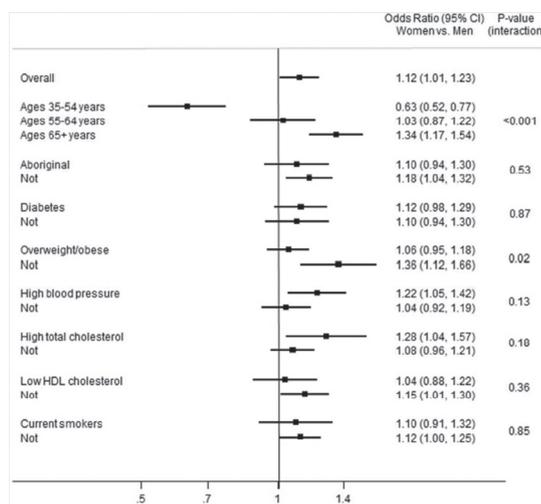

Figure 2 Multiple-adjusted female to male odds ratios and 95% confidence intervals for guideline recommended medication prescription amongst the patients in the cardiovascular disease/high cardiovascular risk subgroup CI: confidence interval; HDL: high density lipoprotein. Indigenous: Aboriginal and/or Torres Strait Islander; overweight/obese: body mass index ≥25 kg/m2; high blood pressure: systolic blood pressure ≥140 mmHg and diastolic blood pressure ≥90 mmHg; high total cholesterol: total cholesterol ≥5.5 mmol; and low HDL cholesterol: HDL cholesterol ≤1 mmol. Each variable in the figure is adjusted for all the others.

Lowering the risk threshold to 10% increased cost by £40K per QALY gained. As long as the polypill cost less than £240 per year, the most cost-effective scenario was to start the polypill in all patients at age 60 years (figure 1).
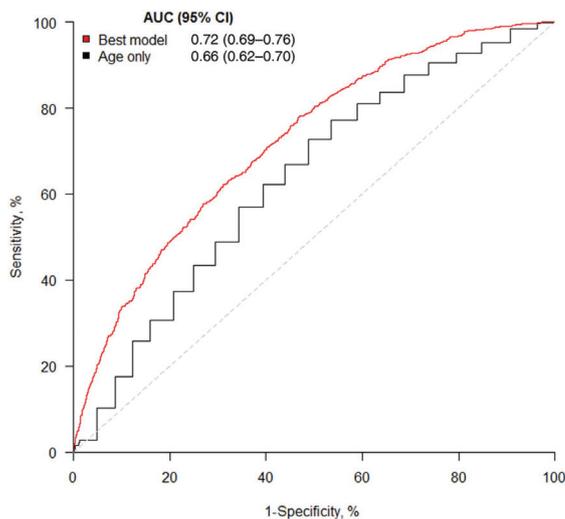
Figure 3 Receiver operating characteristic curve showing results for two selected models, applied to the testing cohort. Sensitivity versus one minus specificity plotted for every observed threshold, and expressed in percentage terms. Logistic models, applied to the data on Glaswegian women, were used to obtain the test results, which were then tested against the actual outcomes in the non-Glaswegian data. The two models illustrated in this plot are those that predict cardiovascular disease using (1) age as the single prognostic variable; (2) the model with the best (lowest) Akaike information criterion; that is, using age, systolic blood pressure, total cholesterol, high-density lipoprotein-cholesterol, smoking and diabetes. AUC, area under the receiver operating characteristic curve.

The first step in primary CVD prevention is risk factor assessment and management. In order to evaluate any differences in clinical care between men and women, Hyun and colleagues[3] reviewed data on over 53K Australian patients in the Treatment of Cardiovascular Risk using Electronic Decision Support (TORPEDO) study. They found that women were less likely to have CVD risk factor assessment (OR 0.88, 0.81–0.96) but more likely to receive guideline recommended medications than men. There was marked heterogeneity in CVD risk factor treatment by age in women compared with men. High risk younger women (age 35–54 years) less likely to be prescribed medications (OR, 0.63, 0.52–0.77) whereas older high risk women (aged ≥65 years) were more likely to be prescribed the medications (OR 1.34, 1.17–1.54). (figure 2)

In the accompanying editorial, Thompson and Daugherty[4] comment that 'A particularly important finding of this study is the lower rate of smoking status screening in women compared with men (82% vs 85.3%, p<0.001). Smoking is a significant risk factor for CVD in women. Women smokers have a 25% greater risk of CVD than male smokers,

independent of smoking intensity or other cardiovascular risk factors.' They also note that this study 'adds to the growing evidence that many of the gender differences seen in CVD care are age dependent. Similar to what has been

shown in management for hypertension and mortality after acute myocardial infarction, this study demonstrated that young women (age <54 years) with high risk of or prevalent CVD were least likely to be prescribed preventive medications.' They conclude: 'Although gender stereotypes and bias may contribute to gender disparities in care, changing attitudes among all health care providers is an ambitious task. Efforts to ensure equity in care for women and men may be better spent by supporting decisions based on evidence appropriate to a patient's objective clinical data rather than clinicians' stereotypes.'

Our series of articles on Graphics and Statistics for Cardiology[5–7] continues in this issue with a review of how to optimally present the data in paper validating a new clinical prediction tool[8] by Woodward, Tunstall-Pedoe and Peters. We hope this article will assist authors in preparing visual displays to inform and attract readers. (figure 3)

The Education in Heart article discusses bleeding associated with management of acute coronary syndromes (ACS).[9] Patients with ACS typically are treated with percutaneous coronary intervention followed by antiplatelet and/or anticoagulant therapy, often for prolonged periods of time. Management of bleeding complications in these patients can be complex because the risk of holding antithrombotic

therapy must be balanced against bleeding risk, and because these patients often have multiple comorbidities. Current guidelines recommend that: (1) minor bleeding be managed without interruption of therapy, (2) major bleeding requires interruption of antiplatelet and anticoagulant therapy unless bleeding can be adequately controlled by other means, (3) blood transfusion should be avoided in hemodynamically stable patients without overt bleeding and a haemotocrit over 25%, and (4) endoscopic procedures generally should be performed without interruption of antiplatelet therapy.

The Image Challenge[10] asks you to diagnose a finding in the left ventricular apex on echocardiography in a patient with a recent myocardial infarction; it certainly has an unusual appearance. Take a look!

Competing interests None declared.

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