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COMMENTARY

Prevention of cardiovascular disease in clinical practice: The Joint British Societies' (JBS 2) guidelines

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Cardiovascular disease (CVD) represents a significant clinical and economic burden to healthcare, accounting for at least 22% of all global deaths.[1] The financial burden is equally immense; the annual cost to the European Union is estimated at €169 billion, 62% of which is directly spent on healthcare provision.[2]

Given this significant health-care burden, there exists an enormous potential for risk factor modification and preventative medicine. Ten years ago, the EUROASPIRE I (European Action on Secondary Prevention by Intervention to Reduce Events) survey of patients with established coronary heart disease (CHD) in nine European countries confirmed the substantial potential for cardiac risk factor modification.[3] A great deal of investment has taken place in many countries to improve health-care provision and in particular to target patients at high risk of CVD.

Common cardiovascular risk factors, such as hypertension feature in any cardiovascular prevention strategy.[4] However, recent surveys have even noted a significant decrease in the awareness of one's own blood pressure among the adult population-especially in small towns and villages, among less educated people, and in males.[5–7] Equally, the results of EUROASPIRE II survey[3] – conducted approximately 5 years after EUROASPIRE I – were quite disappointing, with a lack of any improvement in blood pressure management, and most CHD patients were still not achieving the cholesterol goal of less than 5 mmol/l. Smoking and obesity remained prevalent and worryingly of those patients who continued to smoke, few reported receiving appropriate advice. Of greater concern, the Health Survey for England showed that the prevalence of CVD had risen between 1994 (7.1%), and 1998 (8.5%) or 2003 (9.1%),[8] and cardiovascular risk factors remained highly prevalent.

The need for cardiovascular risk factor modification provided the impetus for a comprehensive disease prevention strategy in UK, which has materialized as the Joint British Societies' Guidelines (JBS).[8,9] This document was published first in 1998 (JBS-1),[9] with a substantial rewrite (JBS-2) published in December 2005.[8]

JBS-1 advocated a staged approach to risk factor modulation, focusing on those with greatest CHD risk first, before offering treatment to those in lower-risk categories. For example, JBS-1 suggested that for primary prevention statins should be prescribed for those with a 10-year CHD risk of greater than 30%, and if resources allowed, those at the next level of risk ($\geqslant$15%) should be treated.[9] The sceptic would argue that this recommendation was not in keeping with the scientific evidence at the time, when trials such as the Air Force/Texas Coronary Atherosclerosis Prevention Study (AFCAPS/TexCAPS) had shown a clear benefit of statins in primary prevention with CHD risk of around 10% over 10 years.[10] Since JBS-1 was published in 1998, substantial evidence has now been published on the management of hypertension, lipids and diabetes mellitus (DM), providing further impetus to revise the recommendations for CVD prevention.

In contrast to JBS-1, the JBS-2 guidelines recognise that cerebrovascular disease and peripheral vascular disease have a common set of risk factors and aetiology with CHD, and frequently patients have disease overlapping all of these diagnoses. Indeed, JBS-2 encompasses the whole spectrum of CVD, rather than just CHD *per se*, which was the main highlight of JBS-1. The tone of JBS-2 advocates focus on both those patients with established disease ('secondary prevention') and those at high risk ('primary prevention'), especially those with a CVD risk of $\geqslant$20% over 10 years. In particular, the guideline aims towards reducing the risk of atherosclerotic cardiovascular events and improving both

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the quality and length of life. The importance of both lifestyle and risk factor interventions is stressed, coupled with appropriate drug therapies to lower blood pressure, modify lipids and reduce glycaemia.

Thus, the concept strongly emphasised by the new JBS-2 guidelines is the estimation of total cardiovascular risk, an approach that is internationally promoted.[11] As CVD is multi-factorial in origin, the risk factors tend to have a multiplicative effect, and thus it is important to take into account all the risk factors when assessing the overall CVD risk of an individual as opposed to focusing on one single, individual risk factor.[12] The total CVD risk for an asymptomatic individual is estimated from several risk factors (age, sex, smoking habit, systolic blood pressure and the ratio of total to HDL cholesterol) and is expressed as a probability (percentage chance) of developing CVD over 10 years. In JBS-2, a CVD risk $\geqslant$20% over 10 years is defined as 'high risk' and justifies professional lifestyle intervention and appropriate use of antithrombotic, antihypertensive and lipid lowering therapy. Indeed, the physician should be asking the question, 'What is the person's 10 year CVD risk?' rather than 'Does the person have hypertension or hypercholesterolaemia?' when seeing a patient in the clinic. In other words, the physician should consider the person's blood pressure and lipid values (as well as other risk factors, for example, smoking) in the context of overall CVD risk, in a holistic approach.[5]

This concept needs to be re-emphasized, because despite the guidelines (including JBS-1), many patients remain suboptimally treated. For example, a study in 2002 involving five general practices showed that 64% of subjects had a CHD risk of $>$15% but only 15% were prescribed a statin; moreover, 20% had CHD risk $\geqslant$30% over 10 years, but yet only 7% had statin.[13] Also, less than half of hypertensive patients had their serum cholesterol and HDL cholesterol measured.[13] Similar suboptimal prescribing has been noted by other investigators.[14] Of note, Green *et al.*[13] calculated that overall CVD risk was reduced from 29 to 22% on antihypertensive therapy and to 20% on statins; but would be reduced to 15% over 10 years, if a combination of statins and antihypertensive therapy were used. This would certainly translate to better clinical outcomes, with combination therapy.[15] A holistic approach is therefore needed when addressing the risk factors for CVD disease.

One potential disadvantage of this approach to CVD prevention in the asymptomatic population is that inevitably treatment will be concentrated towards older people (especially those $>$70 years), unless the lifetime risk factor exposure is taken into account. The new JBS-2 risk assessment charts[8] differ from earlier assessment tools significantly, although it still uses data extrapolated from the Framingham study in 1991.[12] The current JBS charts allow assessment for three age ranges: $<$50, 50–59 and $\geqslant$60 years. Curiously, these broad groups are based on risk assessment for patients of age 49, 59 and 69 years, respectively. However, this method naturally implies that patients in the lower end of each age range will have a greater calculated CVD risk.

Where previous methods tended to target treatments away from younger patients, this method tries to redress that balance, thereby taking into account that younger patients have a greater lifetime risk. Indeed, this will direct more antihypertensive and lipid lowering medication towards those high-risk patients in the younger age group.[8]

However, there are certain additional CVD risk factors not included in the risk prediction chart, of which a physician should be aware when assessing the cardiovascular risk. People originating from the Indian subcontinent, for example, the South Asians have a higher prevalence of CHD and cardiovascular mortality compared with white Europeans. The differences in risk between ethnic groups cannot be fully explained by conventional risk factors, suggesting alternative explanations.[16] South Asians may be genetically more susceptible to develop abdominal obesity and insulin resistance when exposed to a 'toxic' Westernized environment of reduced energy expenditure and increased caloric consumption.[17] Similarly, those with a positive family history of premature CVD (men $<$55 years and women $<$65 years) or those with raised triglycerides ($>$1.7 mmol/l) have 1.3 times more risk than that calculated from the charts.[8]

As the Framingham study assessed mainly Caucasian patients, extrapolating these data to other ethnic groups (e.g., South Asians and black African/Caribbean) is fraught with difficulties. JBS-2 tries to get round this by suggesting that South Asians have a CVD risk 1.4 times greater than that predicted by the charts.[8] The latter correction factor is not evidence based and is inappropriately derived from Standardized Mortality Rates. Of note, many studies,[18–21] which have attempted validations of different scores in different ethnic groups in the UK, have suggested different approaches. A cross-sectional survey comparing 10-year risk of CHD, stroke and combined CVD using the Framingham equation[18] suggested that by lowering the thresholds for risk of CHD to 12% in South Asians and 10% in people of African origin (compared to $\geqslant$15% that identifies risk of combined CVD $\geqslant$20%, using the Framingham equation in white people) would increase the probability to identify those at risk from 81 to 100% (South Asians) and 81 to 97% in people of African origin. On the other hand, Aarabi and Jackson[21] suggested adding 10 years to the age of South Asian people would be the simplest way of calculating CHD risk with acceptable accuracy. Hence, an ethnic risk score has been proposed.[22]

Other risk factors that physicians need to be aware of when assessing the overall cardiovascular risk profile are women with premature menopause,

those with impaired glucose regulation and obesity. Obesity (body mass index $\geqslant 30\,kg/m^2$), particularly those with central obesity (waist circumference for Caucasians $\geqslant 102$ or $\geqslant 88$ cm and for Asians $\geqslant 90$ or $\geqslant 80$ cm in men and women, respectively). A highly significant association between myocardial infarction risk and central obesity (waist-to-hip ratio) has been reported worldwide, across major ethnic groups from 52 countries involving more than 25 000 subjects.[23]

Indeed, optimal blood pressure control is an important component, if one has to maximize CVD risk reduction. Approximately two-thirds of the CVD burden and half the ischaemic heart disease burden are attributable to poor blood pressure.[24] Indeed, the risk of ischaemic heart disease and cerebrovascular mortality also increases steeply with increasing quintiles of systolic, diastolic and pulse blood pressure.[25–27] In adults, control of hypertension to a systolic blood pressure of 140 mm Hg is estimated to potentially prevent 21 400 deaths from stroke and 41 400 ischaemic heart disease deaths each year in the UK alone.[28]

Reassuringly, the emphasis on blood pressure control in the JBS-2 guidelines sets clear targets of optimal blood pressure control of $<140/85$ mm Hg and a recommended target of $<130/80$ mm Hg for people with established CVD, DM or chronic renal disease.[8] The JBS-2 guidelines have also adopted the British Hypertension Society 'AB/CD' treatment algorithm, which makes greater (and more appropriate) use of combination drugs, recognizing that monotherapy is often insufficient for achieving blood pressure control in most hypertensive patients.[29,30] This AB/CD algorithm may well be revised soon, given recent data that beta-blockers may be not be ideal first-line agents for hypertension, except in the presence of heart disease.[31] The release of the revised joint NICE and BHS guidelines are imminent.

In addition, modification of lipid abnormalities cannot be overemphasized, when one considers measures to maximize CVD risk reduction. The benefits were apparent even before the introduction of statins. When the results of a meta analysis from 28 randomized trials had demonstrated a 25% reduction in the incidence of CHD after 5 years, with just 10% reduction in plasma cholesterol, whether by diet, drugs or other means.[32] However, the introduction of statins has revolutionalized lipid modification therapy, as strong evidence supports their use both in primary as well as secondary prevention of CVD.[33] Whether statins *per se* have a blood pressure lowering effect *per se* has been subject of recent debate.[34,35] Whereas the frequency of lipid lowering therapy in CHD patients is relatively high, there still remains a treatment gap,[36] and the new JBS-2 guidelines provides clear guidelines that will hopefully help bridge these gaps in management and facilitate measures geared towards achieving targets. The recommended targets in JBS-2 are a serum total cholesterol <4.0 mmol/l and LDL cholesterol <2.0 mmol/l, or a 25% reduction in total cholesterol and a 30% reduction in LDL cholesterol, whichever gets the person to the lowest absolute level.[8]

Furthermore, guidelines on CVD risk reduction remain incomplete without an assessment and management of impaired glucose regulation. Present knowledge indicates that many patients with type 2 DM either have coexisting CVD or are at high risk for developing future cardiovascular events. Indeed, the risk of myocardial infarction or stroke with type 2 DM is increased two to threefold, whereas total mortality is increased twofold.[37] What is worth re-emphasizing is that type 2 DM is an independent risk factor for CVD, but when associated with other risk factors such as serum cholesterol levels, systolic blood pressure and smoking, the risk is multiplied.[38–41] Some have even advocated defining type 2 DM as a 'CHD risk equivalent'.[42] As emphasized by JBS-2, multi-factorial cardiovascular risk reduction strategies are essential.

Finally, majority of the primary and secondary prevention of cardiovascular disease now occurs in the primary care setting. The Government has recognized the need for a comprehensive approach by linking financial remuneration to achieved health targets through the Quality Outcome Framework and the new GMS contract. Whereas significant improvements have been seen in the detection, management and control of cardiovascular risk factors, the recommended targets fall short of those we would recommend based on evidence, as set in JBS-2. This represents a significant gap between what the evidence suggests it should be achieved for the benefit of the patient and what the health economy of the NHS commits to provide. One wonders whether patients should not be more involved in the final decision on which route to follow.

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