

IMPLICATIONS OF THE JOINT EUROPEAN CARDIOVASCULAR PREVENTION GUIDELINES

In May, the European Society of Cardiology issued new guidelines to prevent heart disease and improve management of patients. Dr John Cannon looks at the implications for primary care

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These guidelines are predicated on the fact that in the past 30 years there has been a reduction in age-adjusted coronary artery disease (CAD) mortality by more than 50% – largely due to better management of heart disease, reduced smoking, reduced lipids and improved BP – but there are persistent inequalities related to increased obesity, type 2 diabetes mellitus (T2DM) and poor concordance with lifestyle advice. The improvement of health risk behaviours would prevent 80% of cardiovascular diseases (and 40% of cancers).

It is suggested that a lifetime approach to cardiovascular risk is imperative, as both risk and prevention are dynamic and related to patient age and/or accumulated comorbidities. Therefore, the advice in these guidelines is to include younger patients with these increased risks.

In 2009, costs related to cardiovascular disease (CVD) exceeded €100 billion (84.5 billion) – approximately 10% of the total EU healthcare expenditure.

NICE has stated that reducing cardiovascular risk by 1% in the population would prevent 25,000 cardiovascular cases and save €40 million (£33 million) annually. Therefore, the guidelines suggest stronger legislation and policies affecting food, smoking and physical activity are required if such savings are to be made.

The guidelines promote a 10-year CVD risk assessment system (titled SCORE and based on large representational European cohort datasets) for screening men over 40 years of age and women over 50 years of age every five years and younger patients at higher risk (e.g., those with family history of premature CVD).

The notion of 'risk age' is used, this being relative to the number of CVD risk factors in an individual of the same gender compared to a person with an ideal level of risk factors. This uses levels of systolic BP, total cholesterol and smoking status, and is particularly useful in younger people with high relative risk (RR), but a low absolute risk (which might indeed increase their absolute risk by up to a factor of 12).

In spite of SCORE's elegant and simple tabular

depiction, the ESC does not currently recommend lifetime risk stratification for treatment decisions.

These guidelines also point out the effect of stress on cardiovascular events, e.g. after the death of a significant person in that individual's life the incidence rate of acute myocardial infarction (AMI) is increased up to 21-fold in the first 24 hours.

Chronic work stress increases coronary heart disease in men (RR 1.2-1.5), as does long-term stress in the family life (RR 2.7-4.0) and post-traumatic stress disorder (RR 1.3). All these conditions lead to

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alteration of haemostatic and inflammatory markers, endothelial function and myocardial perfusion.

The use of coronary-artery calcium assessment for CVD prediction is not recommended as it has poor predictive value and increases radiation exposure. It is particularly bad for women.

The guidelines recognise that while ankle-brachial pressure index and aortic pulse wave velocity are indicators of vascular pathology, they add little to further CVD risk prediction. Additionally, there is recognition that influenza increases the risk of AMI or stroke (RR 4 in the early phase) as do, to a lesser extent, comorbidities of rheumatoid arthritis, ankylosing spondylitis, severe psoriasis, obstructive sleep apnoea and erectile dysfunction. Female-specific exacerbating conditions include obstetric issues such as pre-eclampsia, pregnancy-related hypertension and PCOS.

The guidelines offer advice as to how best to intervene at the individual level in effecting behavioural change to reduce risk factors. For example:

- There are evidence-based benefits of psychological intervention to facilitate lifestyle changes employing CBT with class IA evidence
- Collaborative care for depression has been shown to reduce the risk of developing CAD events eight years after such treatment by almost 50% compared to usual care
- Encouragement of physical activity (PA) with class IA evidence improves hypertension, reduces LDL-C, reduces non-HDL-C, reduces BMI and T2DM
- Smoking cessation is the most effective strategy for CVD prevention. A lifetime smoker has 50% probability of dying from smoking and will lose an average 10 years of life. Passive smoking for example in the spouse increases cardiovascular risk (RR 1.3)
- The importance of diet is also underlined. Trans-fats increase total cholesterol and reduce HDL-C. Reduction in salt by 1g per day will see a reduction in systolic BP by more than 3mmHg with attendant benefits. For each serving of fruit or vegetables (up to 5/day) per day there is a 4% reduced risk of cardiovascular disease. Eating 30g of nuts daily reduces cardiovascular risk (RR 0.71) as does consuming one portion of fish a week (RR 0.85) (but not fish oil as a substitute)
- The guidelines conclude that there is no certainty about alcohol in terms of the benefit or risk. However, sugar sweetened drinks (not artificially) convey increased risk. A Mediterranean diet taken over five years will reduce CVD risk (RR 0.71)
- Bodyweight is debated with all-cause mortality lowest with a BMI 20-25kg/m². Increased weight

leads to increased BP, lipids, insulin resistance, systemic inflammation, pro-thrombotic state, albuminuria, T2DM and all CVD events (AMI, CHF, AF, CVAs). The recommendation is to reduce waist circumferences below 94cm for a male and 80cm for a female adult.

Medical interventions

The guidelines draw attention towards the issue of lipids. Both raised LDL-C and reduced HDL-C increase CV events, and although reducing LDL-C has a beneficial effect on cardiovascular well-being, increasing HDL-C by therapeutic manoeuvres has not been shown to do so. For every 1mmol/litre reduction in LDL-C there is a 20-25% reduction in cardiovascular deaths. CKD is characterised by a mixed dyslipidaemia (high triglycerides/high LDL-C/ low HDL-C) raising the prevalence of CVD in this condition.

The most useful pharmacotherapy for dyslipidaemia are statins, since they reduce LDL-C with the consequent reduction in cardiovascular morbidity, mortality and reduced need for coronary-artery interventions. Those that reduce LDL-C by more than 50% halt progression and may indeed lead to regression of atherosclerosis. While there is no evidence that statins increase non-cardiovascular mortality there is a slightly increased risk of T2DM, but the benefits greatly outweigh the risk. The guidelines refer to a meta-analysis of statin and ezetimibe that shows the combination offers a further benefit, suggesting LDL-C is the key target. There is no support for bile acid sequestrants, fibrates or niacin in these guidelines. There is promise for a novel approach via PCSK9 inhibitor which leads to a sharp decline in LDL-C by up to 60%, either as monotherapy or added to statins at maximum dose. As yet there is no outcome data available but preliminary results are promising.

Diabetes

The guidelines highlight the need for optimal management of diabetes mellitus with a need to concentrate on weight reduction and increased physical activity, as well as aiming for target SBP below 140 and DBP below 85mmHg (T1DM less than 130/80mmHg).

With an SBP below 130mmHg there are additional benefits of reducing CVA, retinopathy and albuminuria. All patients older than 40 years of age (and those younger with increased risk) with T1/2DM require statins. Patients with established CVD should be considered for early use of SGLT2 inhibitors which reduce cardiovascular disease (RR 0.62), total mortality (RR 0.68) and heart failure hospitalisation (RR 0.65) without major adverse effects.

For those patients with raised BP, an RAAS blocker (e.g., ACEi/ARB) is most beneficial particularly in

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the presence of proteinuria or microalbuminuria (for MAU treat regardless of baseline BP). Antiplatelet therapy is not advised unless there is pre-existent CV disease. Interestingly, and possibly counterintuitively, several trials have demonstrated that intensive glycaemic control increases cardiovascular deaths and total mortality. The guidelines therefore endorse the safety and efficacy of reducing total cholesterol and optimising BP control preferentially.

At present there is no evidence of benefit of GLP-1 agonists or DPP-4 inhibitors in diabetics at high-risk of CVD. In spite of all the evidence these guidelines suggest that many patients older than 40 years of age continue to smoke, don't take statins and have poor BP and blood sugar control.

Hypertension

Hypertension has a prevalence of 30-45% in those over 18 years of age, and this issue is addressed in the new guidelines. Hypertension is well recognised as a major risk factor for CAD, CHF, cerebrovascular disease, PAD, CKD and AF. Combination therapy is needed in most patients to hit targets and the guidelines suggest initiation with dual combination in a single pill (to improve concordance) where there is markedly elevated baseline BP or patients are at high CV risk. Evidence suggests the extra BP reduction gained from the combination of two different drug classes is five times greater than doubling the dose of one drug; this also minimises potential side-effects. The combination of beta-blockers and thiazides is not recommended due to the metabolic side-effects which also potentially increase the risks of diabetes.

Unlike NICE/BHS (where the 'ACD' algorithm is predicated on renin levels related to age and ethnicity), the ESC recommend all groups for initiation and maintenance of BP. It is, however, acknowledged that ACEIs/ARBs are effective at reducing left ventricular hypertrophy, microalbuminuria, proteinuria and preserving renal function.

In approximately 20% of patients there is a need for three drugs to hit target and the guidelines suggest a 'Polypill' combination of ideally ACD at fixed dosage in a single tablet as the most rational choice. It is recognised there may be a J-shaped curve in patients with atherosclerosis hitting a SBP target of below 130mmHg.

Regarding the issue of resistant hypertension, there is a need to consider treatment concordance, white coat effect, increased salt or alcohol in the diet, use of recreational drugs or the presence of secondary hypertension. The ESC guidelines suggest anti-aldosterone drugs (with a caveat if eGFR is less than 45 or K⁺ greater than 4.5mmol/l), amiloride or alpha-blockers should be fourth or fifth line drugs. Antiplatelet drugs are not recommended if the hypertensive patient is free from CVD.

There is a great emphasis placed on a healthy lifestyle in these guidelines, based on the paradigm

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that small shifts in the risk of disease across a whole population leads to greater reductions of disease-burden, rather than a large shift in high risk individuals only. To this end, there is an aim to reduce childhood obesity, to tax foods which are rich in sugar, fats and alcohol (such legislation already exists in some EU countries), to encourage physical activity from kindergarten (physical inactivity affects more than half the world's population), to reduce smoking, with the aim of making Europe smoke-free by 2030, to reduce alcohol consumption and to reduce air and water pollution, all of which are recognised to increase cardiovascular disease.

The key professional to provide long-term all follow-up for CVD prevention is the primary care physician. In most countries GPs provide more than 90% of consultations, as well as prescribe public-health medicine. The difficult step is gaining patient engagement with lifestyle change and concordance with medication.

The successful implementation of these guidelines relies greatly on GPs providing risk factor evaluation, intervention and patient education. We know from EUROASPIRE III (primary prevention arm) that many high risk patients (e.g., hypertensives, diabetics, patients on statins) continue to smoke, are obese and failed to adhere to treatments, meaning they did not achieve the respective targets. There needs to be greater involvement of the patient and their caregivers with appropriate treatment and behavioural plus lifestyle education. As an example, it is well recognised that coronary rehabilitation programmes reduce hospital admissions, increase health-related quality of life and reduce mortality.

At both national and European level legislation should be developed regarding nutrition, smoke-free policies and environments, restrictions on marketing of unhealthy foods, promoting physical activity and reducing air and water pollution.

The emphasis needs to be decisively placed at the primary care level underpinned by powerful public-health legislation where the evidence is incontrovertible.