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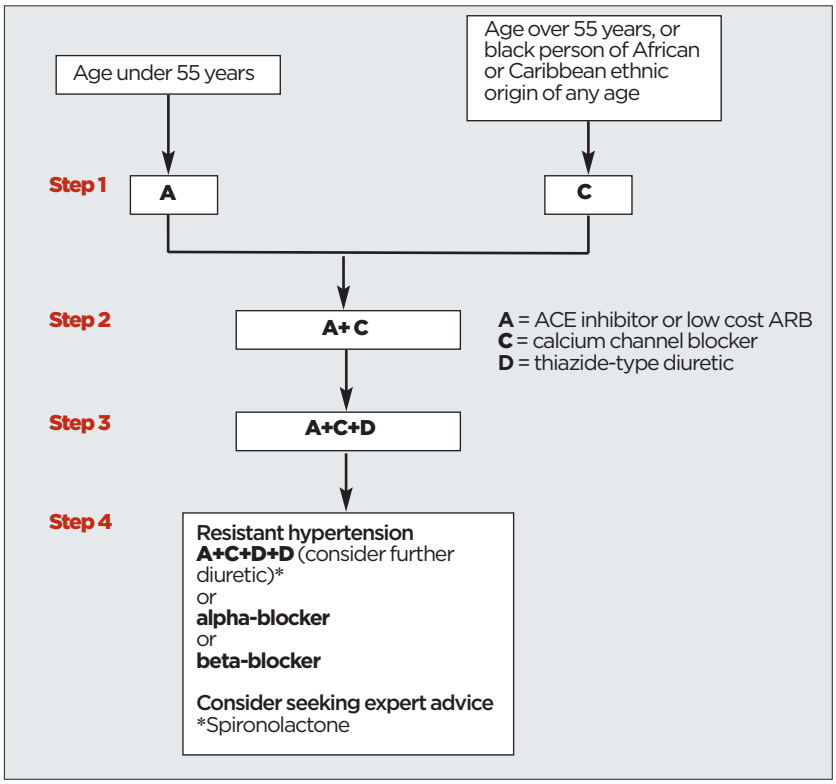


FIGURE 1
Algorithm for blood pressure lowering, adapted from NICE CG127[34]

How should CVD risk be assessed?

What are the evidence-based management approaches?

Which patients should be referred?

CARDIOVASCULAR DISEASE (CVD) AFFECTS SEVEN MILLION PEOPLE IN THE UK ALONE.[1]

CVD is a term that encompasses coronary heart disease, atrial fibrillation, aortic disease, peripheral artery disease and stroke. Given the rising prevalence of these conditions with the ageing population assessing and managing CVD effectively should be a top priority.

RISK FACTORS

The INTERHEART study which included more than 15,000 patients admitted for a first myocardial infarction (MI) at 262 centres across 52 countries, identified key modifiable risk factors for CVD. These included: smoking, abnormal lipid profile, hypertension, diabetes, abdominal obesity, psychosocial factors, diet, alcohol consumption, and lack of physical activity. The study concluded that these factors account for over 90% of the risk of MI worldwide.[2]

QRISK2, The Framingham Risk Score and ASSIGN are all widely used to help assess CVD risk. These tools are based on cohorts from England and Wales, the USA and Scotland respectively.

In 2007, the ASSIGN score was the first to address the risk from social deprivation and social inequality as a leading contributor to CVD.[3,4] Current NICE guidance however, recommends the use of the newer QRISK2 (2010) to assess CVD risk to aid primary prevention.[5] Well validated studies have suggested that QRISK2 is a better predictor of a patient's ten-year risk of CVD compared with the traditionally used Framingham equation.[6]

An important feature of QRISK2 is the inclusion of ethnicity, that has led to a greater number of Asian and Afro-Caribbean individuals subsequently identified as being at higher risk for developing CVD compared with the white population.[7] It should also be noted however, that NICE recommends that QRISK2 should not be used in patients with established CVD, chronic kidney disease, type 1 diabetes mellitus and those > 84 years.[5]

The newer QRISK3 score was recently published[8] and includes additional factors such as migraine, systemic lupus erythematosus, use of systemic corticosteroids, and atypical antipsychotics. It is thought that QRISK3 is likely to supersede QRISK2 in 2018.

QRISK3 provides an estimated ten-year risk of CVD based on the risk factors, taking into account demographic and clinical factors including: age (25-84 years old), gender, ethnicity, UK postcode, smoking status, the presence of diabetes, angina or heart attack in a first-degree relative < 60 years, chronic kidney disease (stage 3, 4 or 5), atrial fibrillation, blood pressure (BP) treatment, migraine, rheumatoid arthritis, systemic lupus erythematosus, severe mental illness, treatment with atypical antipsychotics, regular steroid use, a diagnosis of, or treatment for, erectile dysfunction, cholesterol/HDL ratio, BP and BMI.

A risk score is calculated using a Cox regression model depending on how many risk factors the patient presents with. Patients at low risk (< 10% according to the NICE definition) should be advised on lifestyle changes. »

Table 1

Healthy diet characteristics, adapted from the ESC guideline 2016[13]

- Saturated fatty acids to account for < 10% of total energy intake through replacement with polyunsaturated fatty acids
- Trans-unsaturated fatty acids: as little as possible, preferably no intake from processed food and < 1% of total energy intake from a natural origin
- < 5 g of salt per day
- 30-45 g of fibre per day, preferably from wholegrain products
- ≥ 200 g of fruit per day (2-3 servings)
- ≥ 200 g of vegetables per day (2-3 servings)
- Fish 1-2 times per week, one of which is oily fish
- 30 g unsalted nuts per day
- Alcoholic beverages should be limited to 2 glasses per day (defined as 20 g/d of alcohol) for men and 1 glass per day (defined as 10 g/d of alcohol) for women
- Sugar-sweetened soft drinks should be discouraged

Any relevant comorbidities should be treated and a further risk assessment should be considered in five years. These management options should also be offered to high-risk patients (risk score ≥ 10%) but the benefits and risks of lipid modification therapy should also be discussed.

However, the new SIGN guideline, published in July 2017, advises that a patient must have a risk score ≥ 20% to be deemed at high risk of a cardiovascular event.[4] SIGN has acknowledged concerns about lowering the threshold to 10% and has suggested that additional work is necessary and should be backed up with economic analysis to prove its efficacy. Until then the ASSIGN risk scoring system alongside the 20% risk figure (treatment threshold) remains in place.

The SIGN guideline attempts to devise effective strategies for the reduction of CVD that take a combined approach using both 'high-risk' and population approaches. These focus on estimating CVD risk, diet, physical activity, smoking and lipid-lowering therapies.

LIFESTYLE

Diet

SIGN states that diets low in saturated fats should be recommended to reduce the risk of cardiovascular events.[4] This recommendation is based on a Cochrane review that reports a 14% reduction in cardiovascular events in studies which replaced saturated fat with unsaturated fat.[9] SIGN also recommends adopting a Mediterranean diet supplemented with 30 ml extra virgin olive oil or 30 g unsalted nuts per day. The additional benefit is based on the PREDIMED study, a multicentre randomised controlled trial with 7,447 participants, that demonstrated that consumption of a Mediterranean diet with additional olive oil or unsalted nuts was associated with a 30% relative reduction in risk of cardiovascular mortality compared with controls who were advised to lower their dietary saturated fat only.[10]

However, only recently, data from the PURE study has challenged the guidance relating to fat consumption. The study reported that higher intakes of fats (including saturated fatty acids, monounsaturated and polyunsaturated fatty acids) and animal protein were each associated with lower mortality, whereas carbohydrate intake exceeding 60% of total energy consumption was associated with increased mortality.[11]

It may be that a diet lower in fat with higher carbohydrates creates smaller and denser LDL (small dense LDL is a recognised risk factor for CVD),[12] and therefore raises the risk of heart disease.[11]

The European Society of Cardiology (ESC) guideline recommends reducing saturated fat intake by substituting saturated fats with polyunsaturated fatty acids while advocating five portions of fruit and vegetables a day, see table 1, above. It also recommends a high fibre diet and two portions of fish per week in addition to adopting a Mediterranean type diet.[13]

Exercise

Regular exercise has a favourable effect on many of the established risk factors for CVD. Individuals who take part in regular moderate intensity exercise reduce their risk of a cardiac event by 50% in their fifth and sixth decades and live three to seven years longer than sedentary individuals. NICE and SIGN guidelines both support national guidance from the Department of Health:[14]

- Aim to be active daily
- Over a week, activity should add up to at least 150 minutes (2.5 hours) of moderate intensity activity in bouts of 10 minutes or more, or 75 minutes of vigorous intensity activity
- Undertake physical activity to improve muscle strength on at least 2 days a week
- All adults should minimise the amount of time spent being sedentary (sitting) for extended periods
- Those older adults (≥ 65 years) at risk of falls should incorporate physical activity to improve balance and co-ordination on at least 2 days a week.

Smoking

Smoking is a major risk factor for developing CVD.[15] The smoking ban in work places across the UK is considered one of the most effective public health interventions to promote cardiovascular health in recent times.

A large meta-analysis of more than 500,000 subjects reported the association between smoking status and cardiovascular mortality, with a hazard ratio (HR) 2.07 for current smokers and HR 1.37 for former smokers compared with lifelong non-smokers.[16]

All guidelines suggest that people who smoke should be advised to stop and be offered support to help minimise cardiovascular and general health risks. The risk of developing CVD increases by 30% on exposure to tobacco smoke even in non-smokers.[17] The new SIGN guideline suggests that exposure to passive smoking should be minimised.

In the 2015 Scottish Health Survey, 64% of smokers who had ever attempted to quit had used nicotine replacement therapy (NRT) or e-cigarettes.[18] SIGN recommends that varenicline (a nicotine partial agonist) or combination NRT should be offered.

This is supported by a Cochrane meta-analysis that indicated a large treatment effect from varenicline compared with placebo, bupropion, and single NRT, based on quit rates six months post-treatment.[19] Similarly, the ESC guideline quotes level 1A evidence to advocate using pharmacological methods such as NRT, varenicline, and bupropion individually or in combination.[13]

Alcohol

High alcohol intake is a well recognised risk factor for CVD, and worldwide 3.3 million deaths per year result from harmful use of alcohol.[20] However, there is no consensus on safe levels of alcohol consumption. NICE and SIGN have both welcomed the 2016 recommendations from the Department of Health:[21]

- Men and women are advised not to drink more than 14 units of alcohol a week
- Consumption of alcohol, is best

spread evenly over three days or more to reduce risks of death from long-term illnesses and from accidental injuries.

The ESC guideline suggests that drinking three or more alcoholic beverages per day is associated with elevated CVD risk.[13] There are studies that suggest there is a lower risk of CVD with moderate alcohol consumption.[22,23] However, a Mendelian randomisation analysis which showed that, compared with non-carriers, carriers of a gene variant associated with reduced alcohol consumption had a reduced risk of developing CHD regardless of whether they were light, moderate or heavy drinkers.[24] This therefore suggests that a lower risk of CVD with moderate alcohol consumption results from confounding rather than a cardioprotective effect and that a reduction in alcohol intake, even for moderate drinkers, is beneficial for cardiovascular health. As a result the ESC recommends no safe drinking level.

PHARMACOTHERAPY

Lipid-lowering drugs

Multiple studies have shown that lower levels of low density lipoprotein (LDL) cholesterol early in life are associated with a substantial reduction in the risk of CVD.[25] For every 1 mmol/L reduction in LDL cholesterol the CVD risk is reduced by 20%. Therefore, lowering cholesterol has been the target of primary prevention for many years.

Statins reduce serum cholesterol levels by inhibiting HMG CoA reductase, an enzyme involved in cholesterol synthesis. They also reduce LDL-cholesterol by decreasing cholesterol production in the liver and increase clearance of LDL-cholesterol from the blood. By exerting these effects, they slow down the atherosclerotic process and potentially reverse it.

However, prior to commencing statin therapy it is important to discuss the benefits of risk factor modification. Failing this, statins should be offered to people who have ≥ 10% ten year risk of developing CVD. It is important to note that absolute risk reduction with statin therapy equates to a lower number than relative risk reduction when considering its beneficial effects. The absolute risk reduction is affected by global cardiovascular risk, with individuals who are at the highest global risk attaining the greatest absolute risk reduction from statins.[26] The side effects are well documented[27,28] but statins have overwhelmingly been shown to have a positive effect on CVD profile.

A fifth of patients on statins do not achieve a target LDL of < 1.8 mmol/L. Options in such patients include the addition of ezetimibe, a cholesterol absorption inhibitor which acts by inhibiting Niemann-Pick C1-Like 1 protein (NPC1L1). This combination has been shown to reduce LDL cholesterol by 23%-24% and lower risk of cardiovascular events by a modest 2%.[29]

Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors are a newer class of drugs that act by binding to LDL receptors to facilitate degradation, leading to increased serum LDL-cholesterol. Inhibition of PCSK9 with monoclonal antibodies decreases degradation of the LDL receptors and leads to substantial reductions in cholesterol levels.

The first large trial of PCSK9 inhibition published this year showed that evolocumab given in addition to a statin reduced LDL cholesterol by 60% and reduced risk of cardiac events, non-fatal MI, non-fatal CVA and CVD by 15%.[30] SIGN has therefore endorsed the use of PCSK9 inhibitors for specialist use in patients at high risk of vascular events with cholesterol levels remaining above target levels despite other tolerated lipid-lowering therapy. However, with an average cost of £4,000 per year there is some controversy surrounding the cost effectiveness of its use.

Lowering BP reduces the risk of CVD and mortality. A large meta-analysis which included 147 randomised controlled trials showed that lowering BP by even 10 mm Hg reduced the risk of stroke by 41% and ischaemic heart disease by 22%.[31] SIGN recommends that all individuals with BP ≥ 140/90 mmHg or a family history of hypertension should receive concomitant lifestyle advice prior to medical therapy to help reduce their BP and CVD risk. This would include a reduction in weight, salt intake, alcohol consumption and saturated fat intake, and an increase in physical activity, and fruit and vegetable consumption.

The ASCOT trial demonstrated that combined treatment with amlodipine and perindopril significantly reduced all cause mortality, total cardiovascular events and procedures, and fatal and nonfatal stroke compared with an older combination regimen of atenolol and bendroflumethiazide.[32] These findings led to the development of an algorithm published in the Joint British Societies' guideline (JBS3)[33] and used by NICE[34] (see figure 1, p13) and SIGN.

Mental health

In the UK, one in four people are affected by depression. There is an 80% increased risk of developing new or worsening CVD in adults with depression.[35] Patients with mental illness, such as depression, schizophrenia and bipolar disorder have a reduced life expectancy, with the majority of deaths being attributable to CVD.[36] These individuals also have twice the prevalence of diabetes, dyslipidaemia, hypertension, and obesity compared with the general population.[37] This could be partly explained by lifestyle factors but also by the effects of psychiatric medications on metabolic risk factors for CVD.[37] These patients are also less likely to receive preventative pharmacological therapy and interventions to treat CVD.[38]

A prospective cohort study found that the increased risk of cardiovascular events in depressed CHD patients was mostly explained by poor health behaviours, especially physical inactivity.[39] The investigators suggested that exercise interventions were likely to be more beneficial than antidepressants.

REFERRAL

Referral of patients to appropritae services enhances the reduction in CVD risk and hence specialist services are often cited in guidelines. Recognising that people may need support to change their lifestyle, smoking cessation services and exercise referral schemes have been central to many government campaigns promoting health.

SIGN recommends that individuals with a possible diagnosis of familial hypercholesterolaemia should be referred to a specialist clinic for investigation. However, NICE recommends that clinicians use the clinical findings, lipid profile and family history to judge the likelihood of a familial lipid disorder rather than strict lipid cut off values alone. It is also important to exclude possible common secondary causes of dyslipidaemia (uncontrolled diabetes, hypothyroidism and nephrotic syndrome) before referring for specialist review.

Mental health is now recognised as an important risk factor for CVD. Both SIGN and NICE guidelines recommend that patients who suffer from severe mental health conditions should be referred to specialist care. NICE describes the stepped care model which organises services in a structured manner where the patient can access the correct level of care.[40] The ESC guideline recommends that any patient with psychosocial risk factors (stress, social isolation, and negative emotions) should be referred to individual tailored or group counselling sessions.

»

key points

SELECTED BY

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Cardiovascular disease (CVD) affects seven million people in the UK alone. CVD is a term that encompasses coronary heart disease, atrial fibrillation, aortic disease, peripheral artery disease and stroke. Modifiable risk factors for CVD include smoking, abnormal lipid profile, hypertension, diabetes, abdominal obesity, psychosocial factors, diet, alcohol consumption, and lack of physical activity. The INTERHEART study concluded that these factors account for more than 90% of the risk of MI worldwide.

Current NICE guidance recommends the use of the QRISK2 tool to assess CVD risk in patients aged 25-84 years. Well validated studies have suggested that QRISK2 is a better predictor of a patient's ten-year risk of CVD compared with the traditionally used Framingham equation. However, it should be noted that NICE does not recommend the use of QRISK2 for patients with established CVD, chronic kidney disease and type 1 diabetes mellitus.

The European Society of Cardiology guideline recommends reducing saturated fat intake, to less than 10% of total energy intake, by substituting saturated fats with polyunsaturated fatty acids. It also recommends a high fibre Mediterranean diet with five portions of fruit and vegetables a day, and two portions of fish per week.

The Department of Health recommends that over a week, physical activity should add up to at least 150 minutes (2.5 hours) of moderate intensity activity in bouts of 10 minutes or more, or 75 minutes of vigorous intensity activity. All those who smoke should be advised to stop and offered varenicline (a nicotine partial agonist) or combination NRT. Men and women are advised not to consume more than 14 units of alcohol per week.

The clinical findings, lipid profile and family history should be used to judge the likelihood of a familial lipid disorder rather than the use of strict lipid cut-off values alone. It is also important to exclude possible common secondary causes of dyslipidaemia (uncontrolled diabetes, hypothyroidism and nephrotic syndrome) before referring for specialist review.

Before commencing statin therapy it is important to discuss the benefits of risk factor modification. If lifestyle modification is ineffective or inappropriate, statins should be offered to people who are at high risk of developing CVD.

We welcome your feedback

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CONCLUSION

It is estimated that reducing cardiovascular risk by 1% in the UK will prevent 25,000 cardiovascular events.[41] How we assess a patient's risk of CVD is constantly evolving in the era of individualised medicine. The emergence of new strategies such as QRISK3 helps clinicians to stay abreast of the latest tools to provide the best care for their patients. Despite subtle differences in guidelines regarding lifestyle recommendations such as dietary modification, there is a general consensus regarding smoking cessation, physical activity, and mental health.

Evidence-based therapies for those identified as at risk for developing CVD are continually sought after, which when coupled with public health promotion, are essential to help curb and eventually reduce the burden of CVD.

Competing interests: None

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