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module 240

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Welcome to the two hundred and fortieth module in the *Pharmacy Magazine* Continuing Professional Development Programme, which looks at pharmacist interventions in cardiovascular disease (e.g. MURs).

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GOAL

To provide an overview of cardiovascular diseases, treatments and their primary prevention.

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OBJECTIVES

After studying this module you should be able to:

- Describe cardiovascular disease, its risk factors and risk assessment
- Discuss treatments during targeted cardiovascular MURs
- Raise awareness of the primary prevention of cardiovascular disease, including the use of NHS Health Checks.

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CPD

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Cardiovascular disease

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Introduction

Cardiovascular disease (CVD) encompasses all conditions of the heart and circulation. These include coronary heart disease (CHD), angina, heart attack, congenital heart disease and stroke. Cardiovascular disease causes more than a quarter (around 160,000) of all deaths in the UK each year and there are an estimated 7 million people living with the condition.

The total cost of premature death, lost productivity, hospital treatment and prescriptions relating to cardiovascular disease is estimated at £19bn each year.[1]

Risk assessment is carried out using the QRISK2 assessment tool. Information about the patient's age, sex, ethnicity, postcode, smoking status, family history, total cholesterol/high density lipoprotein (HDL) cholesterol ratio along with

recent blood pressure and body mass index (BMI) are used in the assessment tool to calculate a 10-year risk ratio.[2,3]

Factors that increase cardiovascular risk include smoking, hypertension, high cholesterol, diabetes, being physically inactive, being overweight or obese, a family history of heart disease, ethnic background, being male and increasing age.[1] The risk of CVD increases the more risk factors a patient has.

Coronary heart disease

Coronary heart disease (CHD) is caused by the narrowing of the coronary arteries due to atherosclerosis, which leads to angina. The majority of deaths from CVD in the UK are attributed to CHD, which is responsible for around 73,000 mortalities each year – an average of 200 people each day, or one every seven minutes.

There are 2.3 million people living with CHD in the UK – over 1.4 million men and 850,000 women. Death rates from CHD are highest in Scotland and the north of England and lowest in the south of England.[1]

Treatment for CHD includes antiplatelets, statins, beta-blockers, nitrates, ACE inhibitors, angiotensin II receptor antagonists, calcium channel blockers and diuretics.[4]

Antiplatelets

Antiplatelet treatments include low-dose aspirin, clopidogrel, ticagrelor and prasugrel. A medicines use review is an opportunity to check a patient's understanding and adherence to prescribed treatments. It is worthwhile checking if patients are taking aspirin after food and whether they may be experiencing any gastric adverse effects. Clopidogrel may commonly cause bruising or nose bleeds.[5] This should be explored during a MUR as some patients may not associate these adverse effects with clopidogrel.

Statins

Statin treatment can be prescribed as primary prevention to patients with a greater than 10 per cent risk of cardiovascular disease based on the QRISK2 assessment tool. Atorvastatin 20mg is the statin offered unless the patient is committed to altering his/her lifestyle to reduce their risk to less than 10 per cent.[2] Other statins used include simvastatin, pravastatin and rosuvastatin.

Statin treatment is used as primary prevention in patients with high CVD risk

Reflection exercise 1

Think about the QRISK2 online calculator and how it could be applied to your patient population. Which of your team members would be suitable to take on the role of recruiting patients and calculating their QRISK2 scores?

Side-effects commonly caused by statins include muscular aches – something that can be explored in a MUR. It is advisable to refer any patient with adverse effects back to their doctor to be prescribed a suitable alternative.

Statins (except atorvastatin) are taken at night as cholesterol synthesis is greatest at this time. During a MUR, check that the patient is adherent to this and address any issues nightshift workers may have about not being able to take their statin before bedtime. In this scenario a nightshift worker would have to take his or her medication before going to work and advice on establishing this routine may be needed.

Grapefruit juice can increase plasma levels of simvastatin, so patients should be advised to avoid it.[6] This can be explored when discussing healthy lifestyle measures with CHD patients.

Beta-blockers

Beta-blockers such as atenolol or bisoprolol are used for preventing angina or treating hypertension.[4] They commonly cause fatigue, hypotension and coldness or numbness in the extremities.[7] These undesirable effects can be enough for a patient to feel negative about their medication, leading to non-adherence. Patients can be advised to wear gloves and socks to help reduce the feeling of coldness.

Nitrates

Nitrate treatments used for angina are isosorbide mononitrate and glyceryl trinitrate.[4] Nitrates are potent coronary vasodilators. Tolerance to nitrates can develop but twice daily dosing at set intervals can help minimise this. Standard-release nitrate preparations use an asymmetric dosing interval (e.g. 8am and 4pm or 2pm and 10pm) that can help minimise tolerance.[8] Adherence to this dosing regimen can be checked during a MUR. Modified-release preparations are given once daily to avoid tolerance.

Glyceryl trinitrate is used as a spray or sublingual tablets when rapid relief of symptoms is required. Check that the patient always carries the treatment with them and that the preparation is in date. The MUR is also an opportunity to check the dispensing interval at which these glyceryl trinitrate preparations are issued. If frequently dispensed, this could be an indicator that the angina is worsening.

Some patients may ask why they need this combination of treatments for their condition. A NICE guideline development group made a consensus recommendation that long-acting nitrates can be considered for monotherapy if beta-blockers and calcium channel blockers are not tolerated or are contraindicated.[8]

The guideline development group also agreed that the addition of a long-acting nitrate can be considered in people whose symptoms are not controlled by monotherapy with either a beta-blocker or a calcium channel blocker or if the combination of both treatments is not appropriate.[8]

Reflection exercise 2

Think about the adverse effects of some of the cardiovascular medicines, such as beta-blockers and calcium channel blockers, which may result in poor adherence. Which adverse effects could you discuss at a new medicines service (NMS) consultation in order to improve adherence?

Other treatments used for angina include nicorandil and ivabradine. Nicorandil can cause gastrointestinal ulceration (including aphthous ulcers and anal ulceration).[8] Regular purchasing of over-the-counter (OTC) antacids or mouth ulcer preparations may raise concerns that the patient is experiencing adverse effects from nicorandil, in which case an intervention MUR may be required. In this instance the patient should be referred back to his/her GP.

Nicorandil is currently not recommended as monotherapy for angina – monotherapy with a beta-blocker or a calcium channel blocker instead is the preferred first-line treatment. Nicorandil can be considered as monotherapy for the treatment of stable angina if a beta-blocker and a calcium channel blocker are not tolerated or are contraindicated.

The routine use of nicorandil as add-on therapy to standard anti-anginal treatment is not recommended as it is associated with an increased risk of adverse effects such as headaches and gastrointestinal disturbance.[8]

Treatment with ivabradine may have common adverse effects of luminous phenomena (phosphenes – brief spots or flashes of light) and blurred vision. It is vital to check this during a MUR and explore any issues patients may have with driving, particularly at night when there are changes in light intensity. Grapefruit can increase the plasma levels of ivabradine, so patients are advised to avoid it.

The NICE guideline development group concluded that monotherapy with ivabradine for angina should not be used as an alternative to monotherapy with a beta-blocker or a calcium channel blocker, but that it can be considered when beta-blockers and calcium channel blockers are contraindicated or not tolerated.[8]

ACE inhibitors

ACE inhibitors are prescribed first-line in patients with hypertension who are younger than 55 years of age and not of black African or Caribbean ethnic origin. Hypertension is a risk factor for cardiovascular disease. Enalapril, lisinopril or ramipril are the preferred ACE inhibitors. Starting and maintenance doses of ACE inhibitors are shown in Table 1.[9]

ACE inhibitors can result in hyperkalaemia and regular monitoring of renal function and urea and electrolyte tests needs to be carried out during treatment. This can be checked during a MUR and the patient advised to contact his/her GP practice if it has been more than 12 months since tests were performed. ACE inhibitors may cause a persistent dry cough that is worse at night in 15 per cent of patients.[9]

Monitoring purchases of dry cough mixtures OTC may highlight this potential issue and is an opportunity to conduct an intervention MUR. Patients who find the dry cough troublesome should be advised to return to their GP, who could consider an angiotensin II receptor antagonist as an alternative to the ACE inhibitor.

NICE reports that the combination of ACE inhibitors and calcium channel blockers in patients with hypertension was significantly better at preventing myocardial infarction than a combination of ACE inhibitors and diuretics.

An ACE inhibitor plus thiazide-like diuretic is recommended by NICE for people who cannot tolerate a calcium channel blocker, or those who

Table 1: Low starting, usual starting, maintenance and maximum doses of ACE inhibitors for hypertension

ACE inhibitor	Low starting doses*	Usual starting doses	Usual maintenance dose	Maximum dose
Enalapril	2.5mg once a day	5mg once a day	20mg once a day	40mg once a day
Lisinopril	2.5mg once a day	10mg once a day	20mg once a day	80mg once a day
Perindopril	2mg once a day	4mg once a day	4mg once a day	8mg once a day
Ramipril	1.25mg once a day	1.25mg once a day	2.5mg once a day or 5mg once a day	10mg once a day
Trandolapril	500 micrograms once a day	500 micrograms once a day	1-2mg once a day	4mg once a day

* Lower starting doses are required for people who are more prone to the adverse effects of ACE inhibitors (e.g. elderly, frail or renally impaired people or those on low-dose diuretics)

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have or are at risk of heart failure. Patients of African or Caribbean origin have a small increased risk of developing life-threatening angio-oedema when taking ACE inhibitors compared with other antihypertensive drugs. This group of patients are advised to use angiotensin II receptor antagonists instead of ACE inhibitors.[9]

Angiotensin II receptor antagonists

Angiotensin II receptor antagonists such as losartan, irbesartan, candesartan or valsartan may be used. These do not cause the dry cough adverse effect that is associated with ACE inhibitors but can result in hyperkalaemia – so regular monitoring of renal function and urea and electrolyte tests are required during treatment.

Losartan is recommended for the treatment of hypertension alone, while candesartan, losartan and valsartan are recommended for patients with heart failure and hypertension.[9]

Calcium channel blockers

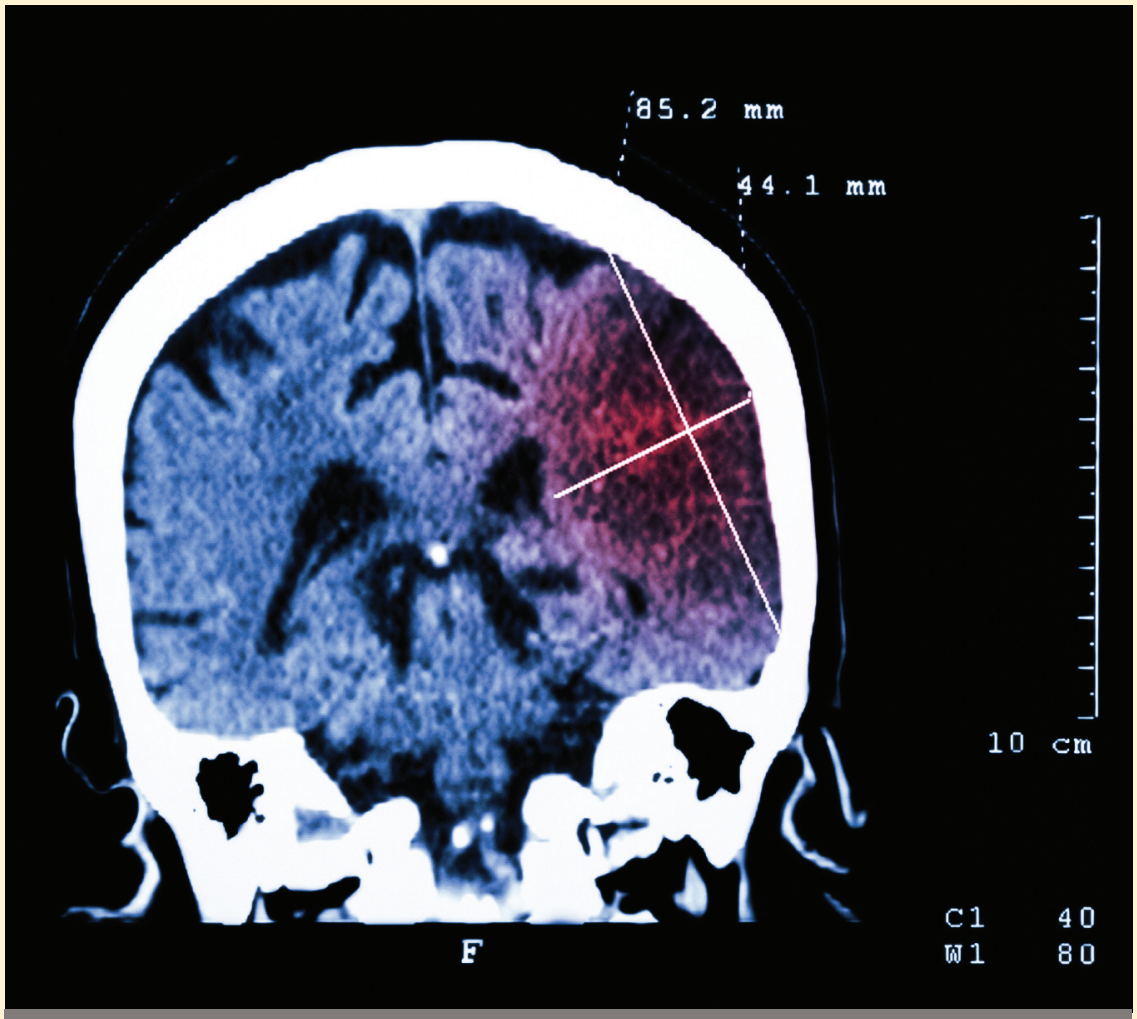
Calcium channel blockers are prescribed for people who are 55 years of age or older and those who are of black African or Caribbean ethnic origin. Examples used for hypertension and angina include amlodipine, felodipine and modified-release nifedipine.

Amlodipine is the preferred choice for hypertension alone. Once-daily preparations of either verapamil or diltiazem may be used in patients without heart failure.[9] Calcium channel blockers may cause ankle swelling and patients are advised to raise their legs while seated.

Diuretics

Diuretics such as bendroflumethiazide, indapamide or chlortalidone may be used. A low dose diuretic may be required if a patient does not tolerate a calcium channel blocker or if he/she has heart failure. Renal function and electrolytes need to be checked every six to 12 months. A MUR consultation is an opportunity to check the patient is aware of these monitoring requirements. Other electrolyte imbalances may also occur.

NICE concluded that, although it could not confirm that low-dose bendroflumethiazide is ineffective, there is less evidence for its effect on clinical outcomes compared with indapamide and chlortalidone. NICE therefore recommends these latter two drugs in preference to bendroflumethiazide if a patient is to be started on a thiazide-type diuretic.[9]



Over a million people in the UK have suffered a stroke

Stroke

In the UK there are 235,000 hospital episodes attributed to stroke each year and more than 40,000 deaths. The British Heart Foundation estimates that 1.3 million people living in the UK have had a stroke. with almost half of these people under the age of 75 years.[1]

Antiplatelet treatments are prescribed for the secondary prevention of cardiovascular events in people with angina, a previous myocardial infarction or a previous stroke or transient ischaemic attack. The antiplatelet treatments of choice are:

- Clopidogrel (75mg daily)
- If clopidogrel is contraindicated or not tolerated, modified-release dipyridamole (200mg twice a day) combined with low dose aspirin is given
- If both clopidogrel and modified-release dipyridamole are contraindicated or not tolerated, aspirin alone is used
- If both clopidogrel and aspirin are contraindicated or not tolerated, modified-release dipyridamole alone is used.[10]

Patients who are at high-risk of having a gastrointestinal (GI) bleed must have a proton pump inhibitor (PPI) co-prescribed e.g. those who are elderly, have a history of GI bleeding and/or other co-morbidities such as diabetes, hypertension, and renal or hepatic impairment. This aspect can be checked during a MUR.

Myocardial infarction

Most deaths from coronary heart disease are caused by a myocardial infarction. There are up to 175,000 myocardial infarctions in the UK each year – which works out at one every three minutes. Around 110,000 men and 65,000 women suffer a MI each year.[1]

Table 2: Classification of cardiovascular and metabolic disease risk by waist circumference in people who are overweight or in obesity class I[13]

BMI	Cardiovascular and metabolic disease risk relative to normal weight and waist circumference		
	Low*	High*	Very high*
Overweight (BMI 25-29.9)	No increased risk	Increased risk	High risk
Obesity I (BMI 30-34.9)	Increased risk	High risk	Very high risk

* For men, a waist circumference of <94cm (37 inches) is low, 94-102cm (37-40 inches) is high, and >102cm (approx 40 inches) is very high. For women, a waist circumference of <80cm (31.5 inches) is low, 80-88cm (31.5-34.5 inches) is high, and >88cm (approx 34.5 inches) is very high.

Following a MI the medications prescribed are an ACE inhibitor, beta-blocker, statin and antiplatelet treatment. ACE inhibitors and statins are continued indefinitely following an attack. Beta-blockers are continued for at least 12 months post-MI in people without left ventricular systolic dysfunction or heart failure. Aspirin plus a second antiplatelet drug, such as clopidogrel, prasugrel or ticagrelor, are usually advised for up to 12 months after a MI (dual antiplatelet therapy).

The length of treatment and second antiplatelet drug recommended depends on factors such as the type of MI, treatments given in hospital, such as percutaneous coronary intervention and the type of stent used.[11] The length of treatment can be explored with the patient during a MUR. Some GP practices will state the end date of the second antiplatelet treatment on repeat prescriptions.

Atrial fibrillation

Over one million people in the UK have been diagnosed with atrial fibrillation (AF).[1] Warfarin or novel oral anticoagulant drugs (NOACs), such as rivaroxaban, dabigatran or apixaban, are used to treat the condition.

NOACs are prescribed to patients who are unable or unwilling to take warfarin and comply with its monitoring requirements, as these drugs do not have the same INR blood test requirements. However they do have a short half-life, so their anticoagulant effects subside rapidly.

A MUR consultation is a time to check whether patients taking NOACs are adhering to their prescribed regimen and whether any adverse effects of bleeding are experienced.

Warfarin's maintenance dose range for AF is 3-9mg (although this can vary between 1-15mg in some patients) and the dose must be taken at the same time each day. Warfarin treatment is long-term for AF with a target INR of 2.5.[12]

Regular INR blood tests are required to ensure the patient's results stay within range. Patients will carry an oral anticoagulant book with them, which has the most recent INR result and dose. It is useful to refer to the book during a MUR to check the consistency of in-range INR results, identify any out-of-range results and explore the reasons for this. The following checklist of questions may be useful as a guide to identifying reasons for out-of-range results:

- Have you missed a dose or taken too many?
- Have you purchased any OTC medicines or started any other prescribed medicines?
- Have you increased your alcohol intake recently?
- Have you changed your food or drink intake? (Green vegetables can change the INR result if eaten in different quantities that the patient is used to. Cranberry juice affects INR as well)
- Any weight loss or gain?
- Any recent illness or changes in your general health?

The MUR is also a time to check patients' awareness of the foods and medicines that may interact with warfarin. Patients are advised to carry their anticoagulant card with them **at all times** and to ensure they know when their next INR appointment is.

Prevention of cardiovascular disease

The risk of cardiovascular disease developing can be reduced by adopting lifestyle changes.

Smoking cessation

This is an opportunity to signpost patients to (for example) a NHS Stop Smoking scheme, which may be offered at the pharmacy. Behavioural and pharmacological support can also be offered. Some areas have patient group directions for Champix for those unsuccessful with NRT.

Table 3: Benefits of a 10kg weight loss in a person with obesity[13]

Aspect	Benefit
Mortality	20-25% reduction in total mortality 30-40% reduction in deaths related to diabetes 40-50% reduction in obesity-related cancer deaths
Blood pressure (in people who are hypertensive)	10mmHg reduction in both systolic and diastolic values
Diabetes (in people who are newly diagnosed)	30-50% reduction in fasting glucose 15% reduction in HbA1c
Lipids	10% reduction in total cholesterol 15% reduction in low density lipoprotein cholesterol (LDL-C) 30% reduction in triglycerides 8% increase in high density lipoprotein cholesterol (HDL-C)
Other benefits	Improved lung function, insulin sensitivity and ovarian function Reduced back pain, joint pain, breathlessness and sleep apnoea

Weight loss

Body mass index is used to measure obesity. Table 2 shows the relation between BMI and cardiovascular disease risk. Advise overweight patients to lose weight in order to reduce this risk. Weight loss can be a sensitive subject with some patients, so a careful approach is required. Pharmacy weight management services can provide patients with the encouragement and support needed to achieve their goals. Table 3 shows the benefits of 10kg weight loss.

Healthy diet

Adopting a healthy diet will help to reduce CVD risk. Advise patients to:

- Reduce their intake of saturated fats to less than 7 per cent
- Eat at least five portions of fruit and vegetables per day
- Eat at least two portions of fish a week, one of which should be oily
- Eat at least four to five portions of unsalted mixed nuts and seeds (30g portion) a week
- Reduce salt intake to less than 6g a day. Minimise the salt added to foods and processed foods (which already have a high salt content)
- Use olive oil rather than butter.

Alcohol consumption

Men should not drink more than 21 units and women no more than 14 units of alcohol a week. Binge drinking should be avoided and patients should have at least two alcohol-free days per week. Table 4 shows examples of popular alcoholic drinks and their equivalent units.[14]

Exercise

Patients are advised to be physically active by undertaking at least 150 minutes of moderate intensity exercise or 75 minutes of vigorous intensity exercise a week. Moderate activities such as brisk walking, using stairs or cycling can be incorporated into daily life. In addition to moderate intensity activities, patients should be advised to undertake muscle-strengthening activities on two or more days a week that work all major muscle groups (legs, hips, back, abdomen, chest, shoulders and arms).

Pharmacists should stress the importance of regular exercise to prevent CVD

NHS Health Checks

The NHS Health Check programme helps to prevent the onset of cardiovascular disease and vascular dementia by supporting changes to and management of behavioural and physiological risk factors. The Health Check is a national risk assessment and management programme for those aged 40 to 74 years living in England, who do not have any existing vascular disease, and

Reflection exercise 3

Think of the strengths and skill mix of your team and how they can promote healthier lifestyles.

Table 4: Popular alcoholic drinks and their equivalent units

Alcoholic drink	Units
125ml glass of red/white/rose wine (12%)	1.5
1 pint of lager/beer/cider (3.6%)	3
330ml bottle of lager/beer/cider (5%)	1.7
275ml alcopop (5.5%)	1.5
25ml small shot of spirits (40%) (e.g. gin, rum, vodka, whisky)	1

Reflection exercise 4

How can your team help to increase recruitment to the NHS Health Check service? Find out where patients can be signposted if it is not provided at your pharmacy.

who are not currently being treated for certain risk factors.

NHS Health Checks are aimed at preventing heart disease, stroke, diabetes and kidney disease, and raising awareness of dementia, for those aged 65-74 years. The check, which includes an alcohol risk assessment, should be offered every five years.[15] A consultation typically lasts about 30 minutes and involves asking questions about:

- **Age**
  Cardiovascular disease risk increases with age
- **Ethnicity**
  Some ethnic groups (e.g. people from south Asian and African-Caribbean backgrounds) are at increased risk of cardiovascular disease
- **Smoking status**
  Smokers are at increased risk of developing cardiovascular disease
- **Family history**
  There is an increased risk of cardiovascular disease if there is a family history of it
- **Physical activity**
  A sedentary lifestyle leads to an increased risk of cardiovascular disease
- **Alcohol consumption**
  Drinking above the recommended limits increases cardiovascular disease risk.

The health check also includes a cholesterol test, blood pressure measurement, body mass index measurement and blood glucose test (if a patient is found to be at increased risk of developing type 2 diabetes) to give an overall risk score, which is described as low, moderate or high:

- **Low**
  Less than 10 per cent chance of a heart/circulation problem in the next 10 years
- **Moderate**
  10-20 per cent chance of a heart/circulation problem in the next 10 years
- **High**
  More than 20 per cent chance of a heart/circulation problem in the next 10 years.

Healthcare professionals can also calculate a patient's 'heart age' using the information supplied. A calculator works out the lifetime risk and heart age using information such as family history of heart disease and lifestyle choices (e.g. smoking). You can check your own heart age at: **nhs.uk/Conditions/nhs-health-check/Pages/check-your-heart-age-tool.aspx**.

In conclusion, cardiovascular disease remains a common and fatal condition for a significant proportion of the population in this country. Its prevention through the promotion of healthy living is a tangible way in which community pharmacists and their teams can influence the health of the nation by making positive interventions.

References & further reading

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