Cardiovascular Risk
Advice for Health Professionals

90% of attributable risk of ischaemic heart disease (IHD) is due to smoking, blood pressure and cholesterol; therefore, risk reduction should centre around these 3 factors. Smoking cessation advice for primary care is available here. Advice on assessing cardiovascular risk, and the assessment & management of hypertension and hyperlipidaemia is below.

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Assessing Cardiovascular Risk

This is normally done using a risk scoring system (see here), such as QRISK3 or ASSIGN. These incorporate a person's blood pressure, lipid profile and smoking status as well as age, sex, and other risk factors for developing cardiovascular disease to predict their risk of suffering from a myocardial infarction or stroke in the next 10 years.

Suggested interpretation:

10-year cardiovascular risk	Recommended action
<10%	Lifestyle modification (if appropriate) Drug therapy usually not recommended
10-20%	Lifestyle modification Consider/discuss drug therapy
>20%	Lifestyle modification Offer drug therapy (if appropriate)

Do not use these risk calculators in people with:

- Familial hypercholesterolaemia or other inherited dyslipidaemia
- Patients with established cardiovascular disease

All these groups should be on lipid-lowering therapy +/- antihypertensive therapy as appropriate.

Non-Drug Management of Cardiovascular Risk

At all levels of cardiovascular risk, lifestyle modification should be the primary intervention used to reduce cardiovascular risk. Smoking cessation is particularly important.

Lifestyle Factor	Recommendation	Further Links
Diet	• Saturated fat: aim for <30g/d if male, <20g if female • Adopting a Mediterranean diet pattern supplemented with 30g extra virgin olive oil or unsalted nuts per day • Increased consumption of fruit & vegetables	NHS Live Well NHS Scotland Eat Well Guide
Exercise	• Aim for 150min moderate-intensity exercise (or 75min high-intensity exercise) weekly • Twice weekly: physical activity to improve muscle strength.	NHS Live Well NHS Scotland: Keeping Active
Weight loss	In overweight/obese patients aim for a sustained weight loss of at least 3kg. This also reduces the likelihood of developing type 2 diabetes, hypertension, osteoarthritis etc. which are themselves cardiovascular risk factors.	NHS Live Well BMI Calculator NHS Inform 12-week Weight Management Programme Lothian Weight Management Service
Smoking	Complete sustained cessation	NHS Live Well NHS Scotland: Stopping Smoking Quit Your Way advice service
Alcohol	Aim for <14 units weekly, spread over 3 or more days.	NHS Live Well
Salt intake	• Salt intake should be reduced as much as possible • Aim for <6g/d	Action on Salt: Salt & Your Health

For more detailed clinical recommendations, see SIGN guideline 149.

Hypertension

Diagnosis

The following is based on NICE guidance 136, Hypertension in Adults: Diagnosis & Management. The threshold for diagnosis of hypertension is 140/90 (Office blood pressure) or 135/85 mmHg (Ambulatory BP Monitoring or Home BP Monitoring). Pros and cons of the various BP measurement modalities are discussed below;

Office Blood Pressure Measurement (OBPM)	
Equipment required	Electronic or calibrated analogue sphygmomanometer. Direct manual measurement is not recommended unless the patient has an arrhythmia (e.g. atrial fibrillation). More information can be found here.
Technique	• Ideally have the patient in a relaxed, temperate setting, with the person quiet and seated, and their arm outstretched and supported. • Check the patient does not have an irregular heartbeat; if they do, perform manual BP measurement and consider obtaining an ECG • Attach the cuff to the patient's arm in advance. Ensure the patient's brachial artery and heart are at the same level. • Take a measurement. If the BP is over 140/90, repeat the measurement at 5 minutes. If the two measures are substantially different, take a 3rd measure and use the mean of the last 2 measurements. • Measure BP in both arms; if the difference is >15mmHg, repeat the measurements. If the BP is consistently higher in one arm, use that for all future measurements.
Pros	Easily accessed at short notice Cheap/free Gives an instant result in front of the patient
Cons	Susceptible to white-coat effect Crude measure of patient's true blood pressure Rarely is performed in a "relaxed temperate setting", with 5 minutes rest beforehand
Notes	OBPM can generally be relied upon if normal (masked hypertension is rare), should not be relied upon for the diagnosis of hypertension NICE guidance recommends confirming hypertension with either Home or 24h Ambulatory BP measurement.

Ambulatory Blood Pressure Measurement (ABPM)	
Equipment required	24h Ambulatory monitor + recording device
Technique	Performed in secondary care usually. Referral details available here.
Pros	• Gold-standard for measurement of blood pressure • Identifies cases of white-coat hypertension, masked hypertension, and nocturnal 'non-dippers' • Gives a clear answer
Cons	• Expensive • Time-consuming • Relies on patient attending secondary care to pick up/return device • Some patients may not be able to tolerate the cuff inflating/deflating repeatedly, including through the night • Impractical for long-term monitoring
Notes	Some GP practices may also have ABPM monitors that they can loan out to patients, mitigating some of the cons listed above. Some patient groups should have ABPM in order to assess their nocturnal dipping status: diabetes, CKD, sleep apnoea, endocrine hypertension and autonomic dysfunction.

Home Blood Pressure Measurement (HBPM)	
Equipment required	Automated BP Monitor; the BIHS keeps a list of approved validated monitors, which can be purchased from as little as £15. The Omron M2 is a cheap and basic option.
Technique	We have developed a HBPM information sheet and monitoring form for patients to use, which includes details on optimal technique: see here.
Pros	Cheap Gives accurate results (if done correctly, on a par with ABPM) Not susceptible to the white coat effect & identifies masked hypertension Suitable for long term monitoring
Cons	Patient has to fund initial cost of purchase Relies on patient motivation and use of optimal technique for accurate monitoring Patients can fail to record enough readings to allow accurate interpretation Does not assess for nocturnal 'dipping'
Notes	This is the recommended modality for monitoring of hypertension, but does require patient engagement

Monitoring blood pressure

HBPM is the recommended method, due to its low cost and accuracy. In patients who cannot perform HBPM accurately, or who cannot afford a monitor,

OBPM can be used, but is not advised if HBPM is possible.

ABPM can be used when the patient has persistently high OBPM readings despite increases to their antihypertensive medication regimen, as the white coat effect may be masking adequate BP control.

Telemonitoring (e.g. Scale-up BP) is also an option in most NHS Lothian GP practices. See here for details.

Staging of Hypertension

Management of hypertension should always incorporate non-drug management, as this is likely to have a much greater reduction on the patient's overall cardiovascular risk. Recommend lifestyle modification for all patients.

Recommended introduction of drug and non-drug management according to severity:

Stage	Systolic BP (mmHg)	Diastolic BP (mmHg)	Recommendation
I	140–159	90–99	Lifestyle advice only (reassess at appropriate interval) Consider drug treatment if: - Target organ damage (retinopathy, nephropathy, cardiac) - Cardiovascular disease - Renal disease - Diabetes mellitus - QRISK3/ASSIGN score >10% Also consider drug treatment for patients aged >80 with SBP >150.
II	160–179	100–119	Lifestyle advice Drug treatment
III	180+	120+	Lifestyle advice Drug treatment In addition, look for end-organ damage/secondary hypertension and consider referral to specialist care

NB: for ABPM/HBPM the targets are 5mmHg lower, i.e. 135 instead of 140

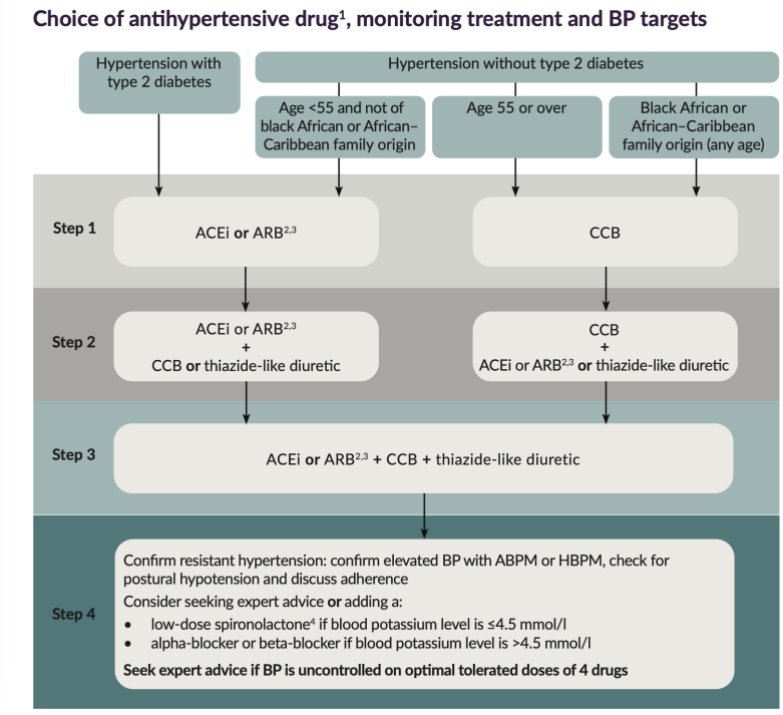
Targets for BP Control

The following are taken from NICE guidance 2019-2020:

Patient group	**Target BP (mmHg)** NB: for ABPM/HBPM the targets are 5mmHg lower, i.e. 135 instead of 140
Adults <80 years	140/90
Adults ≥80 years	150/90
Type 1 diabetic patients	135/85 If 2+ features of metabolic syndrome or albuminuria, target is 130/80
Chronic kidney disease patients	140/90 If proteinuria present, target is 130/80
Stroke patients	Systolic BP <130

Drug management of hypertension

The recommended order in which medications are started is in the flowchart below (reproduced from NICE guidance 136).



NB:

- Patients with type 1 diabetes should also be started on ACEi/ARB for first line therapy.
- Amiloride can be used in place of spironolactone if better tolerated

Link to Lothian Hypertension guidance is available. Short notes on the drugs recommended in the Lothian Joint Formulary are below.

Lisinopril	
Type/class	ACE inhibitor
Dosage	Start: 10mg daily Increase: 10mg increments Max: 80mg daily
Pharmacokinetic issues	Bioavailability: 25% Half-life: 12h Eliminated unchanged in urine
Common Adverse Drug Reactions	Postural hypotension, dizziness, cough, hyperkalaemia; less commonly angioedema (more so in black patients)
Significant Interactions	Spironolactone/amiloride – hyperkalaemia Lithium – increased lithium levels NSAIDs – renal impairment
Notes	First-dose hypotension uncommon Due to the above increased risk of angioedema, some guidelines advise using ARBs preferentially in black patients Recheck creatinine after initiation/dosage increase (a rise in creatinine of up to 25% is acceptable)
Alternatives	Ramipril (2.5mg/day, titrate to max. 10mg/day) Candesartan

Candesartan	
Type/class	Angiotensin Receptor Blocker
Dosage	Start: 8mg daily (4mg if risk of renal injury) Increase: Double dosage Max: 32mg daily
Pharmacokinetic issues	Bioavailability: 15% Half-life: 9h Elimination: 33% renal / 66% stool
Common Adverse Drug Reactions	Abdominal/back pain, dizziness
Significant Interactions	Spironolactone/amiloride – hyperkalaemia Lithium – increased lithium levels NSAIDs – renal impairment
Notes	First-dose hypotension uncommon Recheck creatinine after initiation/dosage increase (a rise in creatinine of up to 25% is acceptable)
Alternatives	ACE inhibitors Losartan (25mg/day, titrate to max. 100mg/day)

Amlodipine	
Type/class	Calcium channel blocker (dihydropyridine)
Dosage	Start: 5mg daily Max: 10mg daily
Pharmacokinetic issues	Bioavailability: 65-80% Half-life: 35-50h Elimination: 60% renal
Common Adverse Drug Reactions	Leg swelling (common reason for discontinuation) GI disturbance Flushing Rash Dizziness
Significant Interactions	P450 Inducing medication – lower drug levels of amlodipine P450 Inhibiting medication – higher drug levels of amlodipine Simvastatin – increased level of simvastatin
Notes	If stopped because of leg swelling, consider Lercanidipine
Alternatives	Lercanidipine (start 10mg/day; titrate to max. 20mg/day) Diltiazem/verapamil

Indapamide	
Type/class	Thiazide-like diuretic
Dosage	Dose is 2.5mg once daily, or 1.5mg of the modified-release preparation
Pharmacokinetic issues	Bioavailability: 100% Half-life: 14-18h Elimination: 70% renal; 23% GI tract
Common Adverse Drug Reactions	Dry mouth GI disturbance Hypokalaemia Erectile dysfunction Rash
Significant Interactions	Amiodarone – arrhythmia Lithium – Lithium toxicity
Notes	NICE guidance recommends thiazide-like diuretics (Indapamide) over thiazides (Bendroflumethiazide) Choose lowest-cost formulation
Alternatives	Bendroflumethiazide

Bendroflumethiazide	
Type/class	Thiazide diuretic
Dosage	Start: 2.5mg daily Increase: 2.5mg increments Max: 10mg daily
Pharmacokinetic issues	Bioavailability: 100% Half-life: 3.5h Elimination: 30% urine; 70% metabolised
Common Adverse Drug Reactions	Dry mouth GI disturbance Hypokalaemia Erectile dysfunction
Significant Interactions	Amiodarone – arrhythmia Lithium – Lithium toxicity
Notes	• Normal dose is 2.5mg, but dose can be increased to 5mg daily before addition of another agent • NICE guidance recommends thiazide-like diuretics (Indapamide) over thiazides (Bendroflumethiazide)
Alternatives	Indapamide

Spironolactone	
Type/class	Potassium-sparing diuretic
Dosage	Start: 25mg daily Increase: 25mg increments Max: 100mg daily
Pharmacokinetic issues	Bioavailability: 75% Half-life: 1.4h Elimination: Hepatic → urine/bile
Common Adverse Drug Reactions	Hyperkalaemia Renal impairment Headache Weakness GI disturbance Erectile dysfunction Gynaecomastia
Significant Interactions	Ciclosporin – hyperkalaemia Lithium – Lithium toxicity Digoxin – Digoxin toxicity
Notes	Frail elderly patients can start at 12.5mg daily
Alternatives	Amiloride (starting dose 10mg daily, max. 20mg daily), Eplerenone

Bisoprolol	
Type/class	Beta-adrenoceptor antagonist
Dosage	Start: 1.25 – 2.5mg daily (lower dose in elderly) Increase: 2.5mg increments Max: 20mg daily (10mg in heart failure)
Pharmacokinetic issues	Bioavailability: 90% Half-life: 10-12h Elimination: 50% hepatic / 50% renal
Common Adverse Drug Reactions	Dizziness Headache Sleep disturbance Bradycardia Cool/numb peripheries GI disturbance Weakness
Significant Interactions	Verapamil/Diltiazem – heart block Theophylline/Aminophylline – bronchospasm Mefloquine – bradycardia
Notes	
Alternatives	Atenolol, Carvedilol, Metoprolol

Doxazosin	
Type/class	Alpha-1-adrenoceptor antagonist
Dosage	Start: 1mg daily Increase: Double every 1-2 weeks Max: 16mg daily
Pharmacokinetic issues	Bioavailability: 66% Half-life: 22h Elimination: Hepatic
Common Adverse Drug Reactions	Postural hypotension (particularly on initiating therapy) Weakness Chest pain Oedema Flu-like illness
Significant Interactions	Sildenafil – hypotension
Notes	Alpha-blockers should generally be used as a last resort.
Alternatives	Prazosin, Terazosin

Adherence Testing

In some cases it may be useful to check for adherence to the existing drug regimen, particularly when there has been no apparent response to 3 or more drugs.

This investigation should only be requested after:

- Persisting hypertension is confirmed by ABPM.
- The patient is on a 4-drug regimen, (including at least 1 diuretic).

Adherence testing is arranged through the cardiovascular risk clinic via SCI gateway referral as per guidance on Refhelp.

List of drugs that can be tested for:

ACE inhibitor	Enalapril, Lisinopril, Perindopril, Quinapril, Ramipril, Trandolapril
Angiotensin-Receptor blockers	Candesartan, Irbesartan, Losartan, Olmesartan, Valsartan
Calcium channel blockers	Amlodipine, Diltiazem, Felodipine, Lacidipine, Lercanidipine, Nifedipine, Verapamil
Diuretics	Thiazide/thiazide-like: Bendroflumethiazide, Chlortalidone, Hydrochlorothiazide, Indapamide K^+-sparing: Amiloride, Eplerenone, Spironolactone Loop: Furosemide, Bumetanide
Beta-adrenoceptor blockers	Atenolol, Bisoprolol, Labetalol, Metoprolol
Alpha-adrenoceptor blockers	Doxazosin
Centrally-acting drugs	Methyldopa, Minoxidil, Moxonidine
Other	Aliskiren, Hydralazine

Hypercholesterolaemia

Hypercholesterolaemia is a major contributor to cardiovascular disease. It is usually multifactorial, but there are some genetic conditions (discussed below) where more intensive therapy is warranted. The mainstays of therapy are identifying & treating reversible causes, lifestyle modification (particularly around smoking, diet and exercise), and prescription of statins.

Many cases of hypercholesterolaemia are related to lifestyle. Secondary causes include:

- Uncontrolled diabetes mellitus
- Obesity
- Excess alcohol consumption
- Untreated hypothyroidism
- Some medications, such as thiazide diuretics and ciclosporin.

If any of these are present, interventions to target these risk factors should be initiated.

Assessment

Assessment should focus on identifying secondary causes, evidence of end-organ damage and other risk factors for cardiovascular disease.

History	Past or Family History CVD Current lifestyle – smoking, alcohol, diet, exercise Drug history: thiazides, β-blockers, retinoids, anti-retrovirals, oestrogen/progesterone, anti-psychotics, corticosteroids & immunosuppressants
Examination	BP BMI Fundoscopy Look for signs of heart failure, peripheral vascular disease, dyslipidaemia.
Investigations	ECG (if suspect arrhythmia) Urine for blood, protein, glucose Lipid profile U+E TFTs LFTs (particularly ALT & GGT) Blood glucose/HbA1c

After this, calculate cardiovascular risk as above. If the 10-year risk is >20%, offer drug therapy. If risk is 10-20%, discuss starting drug therapy with the patient.

Note: CVD risk calculators underestimate risk up to 2-fold in those with:

- Obesity
- Interited dysplipidaemias (e.g. Familial hypercholesterolaemia or Familial combined hypercholesterolaemia)

- Hypertriglyeridaemia
- HIV
- Systemic inflammatory conditions
- Serious mental health problems
- Those already on antihypertensive treatment
- Certain ethnic populations, particularly south asian men

Drug Management of Hypercholesterolaemia

Statins

Statins are the mainstay of treatment. High-intensity statins (atorvastatin & rosuvastatin) are the most cost-effective, and produce the greatest reduction in LDL. Levels of LDL reductions with various statins are given in the table:

Intensity	Drug	Daily dosage		
		20mg	40mg	80mg
High	Rosuvastatin	48%	53%	58%
	Atorvastatin	43%	49%	55%
Moderate	Simvastatin	32%	37%	42%*
	Pravastatin	24%	29%	33%

*Simvastatin 80mg/d is no longer recommended due to significantly increased incidence of myositis, and expense when compared to atorvastatin 20mg/d, which provides a similar reduction in LDL

For primary prevention of cardiovascular disease in patients with a 10-year risk of >20%, prescribe atorvastatin 20mg/d. This lowers LDL more than the maximal doses of moderate-intensity statins and is well tolerated.

For secondary prevention, we recommend atorvastatin 40-80mg/d (according to tolerability).

If a patient is already on a moderate-intensity statin discuss switching to a high-intensity statin, unless they have previously been intolerant of such therapy.

Choosing a statin

- First-line: High-intensity statins – atorvastatin, then rosuvastatin
- Second-line: Moderate-intensity statins – simvastatin, then pravastatin

Atorvastatin and simvastatin are both metabolised by CYP3A4 – patients taking drugs which inhibit 3A4 (e.g. Azole antifungals, HIV protease inhibitors, macrolide antibiotics, verapamil/diltiazem, amiodarone, grapefruit juice) are more likely to develop myositis/rhabdomyolysis – use alternatives instead. Rosuvastatin and pravastatin are not metabolised by CYP3A4.

Rosuvastatin is now off-patent, and provides the most intense LDL-lowering effect per dose.

Statin intolerance

Myalgia is commonly reported in patients starting statins, but statin myopathy (raised CK with myalgia) or rhabdomyolysis is rare. ~80% of patients reporting intolerance to statins can be successfully rechallenged. If a patient reports intolerance to statin therapy, we recommend the following:

- Check Creatinine Kinase if the symptom is myalgia; if raised, discontinue the drug.
- Consider reintroducing the same drug at the same dosage.
- If symptoms recur, reduce the dosage of the same drug (atorvastatin 10mg reduces LDL by 37%); most of the benefit can be obtained with small doses of statin.
- If symptoms persist, switch to a lower-intensity statin (e.g. simvastatin).
- As a last resort, consider rosuvastatin 5mg 3x/week.

If the patient is truly intolerant of statins, consider use of the alternatives below.

Ezetimibe

Ezetimibe is a cholesterol absorption inhibitor. It has few significant side effects, and reduces LDL by 15-20%. Indications for starting Ezetimibe 10mg daily are:

- Primary prevention in statin-intolerant patients
- Secondary prevention in patients on maximum-tolerated doses of statins where LDL targets have not been attained.

PCSK9 Inhibitors

These are monoclonal antibodies which prevent LDL-receptor degradation, resulting in more LDL being removed from the systemic circulation and lower plasma LDL cholesterol. Two drugs are available, Evolocumab (£680/month) and Alirocumab (£340/month). Use of these drugs is restricted in Lothian. If you think a patient should be considered for PCSK9 inhibitor therapy, please refer them to the lipid clinic at RIE.

Targets for Lipid Control

Primary prevention: There is no specific LDL reduction target

Secondary prevention: Aim for a 1mmol / 40% reduction in non-HDL cholesterol. If this is not obtained:

- Increase statin dose
- Consider addition of other lipid-lowering therapies.
- Revisit lifestyle modification
- Consider nonadherence

Familial Hypercholesterolaemia (FH)

Suspect FH in adults with:

- Total cholesterol >7.5 mmol/l or
- Past or family history of premature coronary heart disease (<60 years in patient or their first-degree relative).

In such patients apply the Simon Broome Criteria:

Definite FH	TC >7.5 (or LDL-C >4.9) AND tendon xanthomas, or evidence of these signs in first or second degree relative OR DNA-based evidence of an LDL-receptor mutation, familial defective apo B-100, or a PCSK9 mutation
Possible FH	TC >7.5 (or LDL-C >4.9) and family history of one of the following: • Myocardial infarction in first-degree relative <60yrs, or second-degree relative <50yrs. • TC >7.5 mmol/l in adult first or second degree relative OR >6.7 mmol/l in child, brother or sister aged <16 years

Refer patients who meet definite or possible Simon Broome criteria for DNA testing via Refhelp.

Cardiovascular risk calculators (QRISK3/ASSIGN) should not be used in patients with confirmed FH, as they are already at markedly increased risk of cardiovascular disease.

Familial Combined Hypercholesterolaemia (FCH)

Definition
This condition has a high prevalence (~1%), and presents as marked elevation of LDL and triglycerides. It is commonly associated with type 2 diabetes and the metabolic syndrome. The origin is polygenic, but the condition runs in families.

Assessment
If you suspect a patient has FCH, perform a full lipid screen and obtain past medical and family history of cardiovascular disease (including age at which cardiovascular events occurred). There is no formal genetic diagnosis (though a raised serum ApoB is suggestive)

Management
Treatment should consist of lifestyle modification and medication to reduce cholesterol (statins) and triglycerides (fibrates; rarely used, and only in combination with a statin). We are able to discuss and advise on cases via email.

Hypertriglyceridaemia

Definition

A non-fasting triglyceride level above the normal range (>2 mmol/L) – repeat with patient fasted to confirm the diagnosis.

Assessment

Exclude secondary causes:

- Alcohol excess
- Obesity
- Diabetes
- Drugs causes (e.g. steroid hormones)
- Hypothyroidism
- Fatty liver disease of any cause

Management

Fasting triglyceride level (mmol/L)	Action
4.5-9.9	Lifestyle interventions to reduce cardiovascular risk. No specific drug treatment is indicated
>10	Seek specialist advice – patient is at risk of pancreatitis Consider starting a fibrate

Be aware that risk assessment tools will underestimate the CVD risk

Links & References

Hypertension

- NICE guidance NG136: Hypertension in adults: diagnosis and management
- BIHS Statement on Implementation of NG136

Hyperlipidaemia

- SIGN 149: Risk estimation and the prevention of cardiovascular disease
- NICE guidance CG71: Familial hypercholesterolaemia: identification and management
- 2016 ESC/EAS Guidelines for the Management of Dyslipidaemias

Links

- LJF – hypertension
- LJF - Hyperlipidaemia
- Our page on Refhelp
- QRISK3 calculator
- ASSIGN score calculator