

## CLINICAL GUIDELINE

# CORONARY HEART DISEASE AND STROKE, PRIMARY AND SECONDARY PREVENTION GUIDELINES (CHOLESTEROL)

A guideline is intended to assist healthcare professionals in the choice of disease-specific treatments.

Clinical judgement should be exercised on the applicability of any guideline, influenced by individual patient characteristics. Clinicians should be mindful of the potential for harmful polypharmacy and increased susceptibility to adverse drug reactions in patients with multiple morbidities or frailty.

If, after discussion with the patient or carer, there are good reasons for not following a guideline, it is good practice to record these and communicate them to others involved in the care of the patient.

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# Primary prevention of coronary heart disease and stroke

**High risk patients (predicted cardiovascular event rate 20% or more over 10 years) should be offered treatment with a statin**

**This includes all patients  $\geq 40$  years of age who have diabetes, and all patients with chronic kidney disease (CKD 3-5), without additional risk assessment.**

Random non-fasting test for total cholesterol, HDL and triglycerides and also LFT's TSH and HbA1c

If total cholesterol  $>7.5$  mmol/L and CVD in 1<sup>st</sup> degree relative aged  $<60$ , (or total cholesterol  $>9.0$  mmol/L even without family history) refer to lipid clinic for genetic screening for familial hypercholesterolaemia

Consider and manage secondary causes of hyperlipidaemia, such as excess alcohol consumption, uncontrolled diabetes mellitus, hypothyroidism, liver disease, and nephrotic syndrome

Calculate individual risk using ASSIGN or Joint British Societies risk prediction models

**For patients with a 10 year cardiovascular event risk  $\geq 20\%$  offer atorvastatin 20mg daily as primary prevention**

- Consider using a lower dose of statin in patients who experience side-effects of treatment. Consider changing to an alternative statin if side-effects persist. NB Any dose of any statin is preferable to alternative drug classes (see supplement).
- **There is no target for cholesterol for routine primary prevention. There is no evidence to support up-titration of statin dose, or the use of alternative medications in the event of intolerance.**
- **Maintenance of existing statin therapy is an acceptable alternative for patients already established on treatment.**
- See BNF for cautions, contra-indications and clinically important drug interactions (e.g. clarithromycin). Recheck LFT's after 1 month. Check CK if the patient complains of myalgia.
- Treatment of frail or very elderly people with statins should be guided by individual circumstances and co-morbidities and need not follow guideline recommendations.

# Secondary prevention of coronary heart disease and stroke

**Patients with established atherosclerotic arterial disease are at high risk and should be offered treatment with a statin regardless of total blood cholesterol concentration**

**Includes patients with: previous MI / previous CABG / previous PCI / angina / proven coronary artery disease (invasive or CT angiography) / ischaemic stroke or TIA / peripheral arterial disease**

Random non-fasting test for total cholesterol, HDL and triglycerides and also LFT's TSH and HbA1c

If total cholesterol >7.5 mmol/L and CVD in 1<sup>st</sup> degree relative aged <60, (or total cholesterol >9.0 mmol/L even without family history) refer to lipid clinic for genetic screening for familial hypercholesterolaemia

Consider and manage secondary causes of hyperlipidaemia, such as excess alcohol consumption, uncontrolled diabetes mellitus, hypothyroidism, liver disease, and nephrotic syndrome

**For patients with atherosclerotic disease offer atorvastatin 40-80mg daily as secondary prevention (80mg for high risk ACS / stroke)**

- Restrict the dose of atorvastatin to 40mg if the EGFR is <30 mls/minute/1.73m<sup>2</sup>, or if there are significant drug interactions. Also consider a reduced dose or an alternative statin in patients who experience significant side effects (see supplement). NB Any dose of any statin is preferable to alternative drug classes.
- The target for treatment is a total cholesterol concentration <4.0mmol/L, or a reduction by ≥ 40% from baseline for secondary prevention.
- Consider switching patients who are established on lower potency statins to high dose atorvastatin particularly if their cholesterol concentration is ≥ 4.0mmol/L.
- See BNF for cautions, contra-indications and clinically important drug interactions (e.g. clarithromycin). Recheck total cholesterol, triglycerides and LFT's after 1 month. Check CK if the patient complains of myalgia.
- Treatment of frail or very elderly people with statins should be guided by individual circumstances and co-morbidities and need not follow guideline recommendations.

**Cholesterol Goals Achieved**  
Annual review to ensure continued concordance.

**Cholesterol goals not achieved** Discuss adherence to treatment. Only if goals are not met on the maximal tolerated dose of statin should the addition of ezetimibe 10mg daily be considered. Other classes of lipid-lowering agents are not recommended without specialist advice.

## SUPPLEMENT – ADDITIONAL COMMENTS AND ADVICE

### **1. MAIN CHANGES TO THE GUIDELINE**

Atorvastatin is now recommended as the statin of choice for both primary and secondary prevention. A dose of 20mg daily is recommended for primary prevention, and a dose of 40-80mg daily for secondary prevention (80mg preferred for high risk ACS and stroke, reduced dose if EGFR <30 mls/minute/1.73m<sup>2</sup>) as per NICE CG181.

All patients aged >40 years with diabetes or CKD stages 3-5 should be offered treatment with a statin.

The target cholesterol concentration (for secondary prevention only) should now be <4.0 mmol/L or a reduction of at least 40% from baseline (see S3).

### **2. STATIN INTOLERANCE**

NB The evidence for the use of statins is much stronger than for other agents for both primary and secondary prevention of cardiovascular disease. It is important to emphasise this to patients, and to ensure that there is genuine intolerance before considering an alternative. This should include trying different statin preparations and/or lower than usual doses - for example:- atorvastatin 80mg → atorvastatin 10 - 40mg → simvastatin 20mg / rosuvastatin 5mg / pravastatin 20mg

#### **Primary prevention (i.e. those with no diagnosis of atherosclerotic arterial disease)**

Ensure patients are genuinely intolerant of statins before making any changes (see above). Reinforce dietary and lifestyle measures. There is insufficient evidence to support the use of agents other than statins for primary prevention, however if familial hyperlipidaemia is suspected then the patient should be referred to a lipid clinic for specialist advice.

#### **Secondary prevention (i.e. those with a diagnosis of atherosclerotic arterial disease and also patients with diabetes or CKD)**

Ensure patients are genuinely intolerant of statin before making any changes (see above). Reinforce dietary and lifestyle measures. In exceptional circumstances consider alternative agents, but there is much less evidence for efficacy, and they are usually more expensive. It may be appropriate to seek a specialist opinion if the patient is intolerant of two classes of lipid-lowering drugs for secondary prevention. Guidance for the use of PCSK9 inhibitors is currently under review.

### **3. FAILURE TO REACH CHOLESTEROL TARGETS**

#### **Primary prevention (i.e. those with no diagnosis of atherosclerotic arterial disease or diabetes)**

There is no primary prevention cholesterol target. It is not recommended to carry out further cholesterol checks or dose titration after starting treatment.

#### **Secondary prevention (i.e. those with a diagnosis of atherosclerotic arterial disease or diabetes)**

If patients fail to reach the cholesterol target of 4.0mmol/L or at least a 40% reduction from baseline using atorvastatin 80mg it may be appropriate to add in ezetimibe 10mg daily.

### **4. LIPID-LOWERING DRUGS – FORMULARY COMMENTS**

Statins listed in the GGC formulary include atorvastatin and simvastatin, as well as pravastatin (restricted indication – drug interactions or intolerance) and rosuvastatin (3<sup>rd</sup> line use with restricted indication of intolerance to other statins, or familial hyperlipidaemia). NB Ensure generic prescribing where available.

PCSK9 Inhibitors Guidance for the use of PCSK9 inhibitors is currently under review.

Ezetimibe Ezetimibe can be used as an add-on to statin therapy if cholesterol goals are not achieved on the maximal tolerated dose of atorvastatin, after ensuring adherence, and addressing lifestyle issues as far as possible.

Anion exchange resins Cholestyramine is listed in the GGC formulary .

Fibrates listed in the GGC formulary include fenofibrate and bezafibrate, but there is conflicting evidence regarding efficacy. Fibrates reduce triglycerides more effectively than statins.

Omega-3 preparations None are not listed in the GGC formulary.

Nicotinic acid derivatives These agents are not listed in the GGC formulary, and their use is not recommended except on specialist advice.

**NB non-formulary processes apply to drugs not on formulary**

## 5. DRUG INTERACTIONS

Significant interactions are seen between statins and a wide range of other drugs. The BNF provides comprehensive guidance.

## 6. TRIGLYCERIDES

Triglycerides can be measured on a random sample as part of a full lipid profile. Elevated triglyceride levels on a random sample may be due to the presence of dietary triglycerides. A raised triglyceride level should therefore be repeated on a fasting sample to confirm. Raised triglycerides are most commonly due to secondary causes, e.g. obesity, diabetes, alcohol excess, medicines. Any secondary causes should be identified and treated. A lipid clinic referral should be arranged for any patient with a suspected familial dyslipidaemia, e.g. patients with high lipid levels and a family history of premature ischaemic heart disease or pancreatitis

***For patients with moderately raised fasting triglycerides, e.g. 5 to 10 mmol/L***

There is a slight increase in cardiovascular risk due to the raised triglycerides alone. Address secondary causes and consider statin treatment at lower risk threshold (eg 15%)

***For patients with markedly raised triglycerides, e.g. > 10 mmol/L***

Address secondary causes and consider referral to lipid clinic if triglycerides persistently > 10mmol (urgent referral if > 20mmol/L unless due to alcohol excess or poor glycaemic control)

## 7. OTHER COMMENTS

**It is important to stress that prevention of atherosclerotic arterial disease requires control of all risk factors. No single factor, including cholesterol, should be viewed in isolation. Do not delay offering lipid-modification therapy where indicated however while these measures are being addressed.**

- Addition of other medication should be considered in the secondary prevention of vascular disease where appropriate (e.g. anti-platelet therapy, ACE-inhibitors, beta-blockers etc).
- All other risk factors (e.g. smoking, hypertension, glycaemic control in diabetes) should be addressed.
- Dietary and other lifestyle advice (e.g. alcohol, exercise, weight management) should be given.

## APPENDIX

# NHS GREATER GLASGOW AND CLYDE CORONARY HEART DISEASE AND STROKE, PRIMARY AND SECONDARY PREVENTION GUIDELINES REVISION

*This 2017 update is based on guidelines originally drawn up in 1996, and revised in 1998, 2003, 2004, and 2008, 2009, 2012 and 2013.*

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### CONFLICTS OF INTEREST DECLARED:

Dr A Brady	Chief UK Investigator and member of Steering Committee, IMPROVE-IT trial
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