Coronary Heart disease and Stroke, Primary and Secondary Prevention Guideline (Cholesterol)

DOCUMENT CONTROL			
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CONTENTS

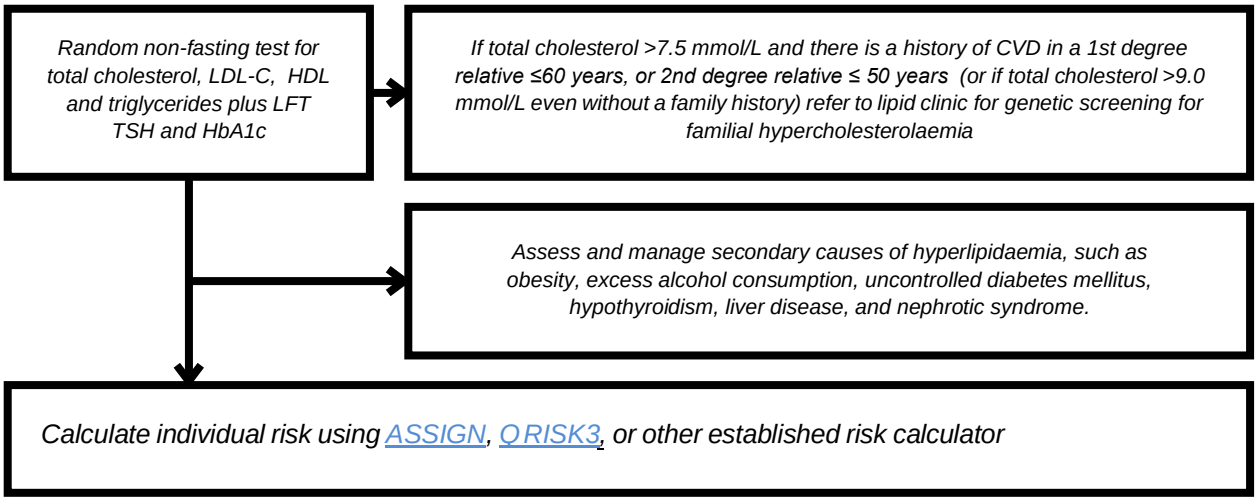
1. Purpose and Scope

This document aims to support practitioners in Dumfries and Galloway in the management of hyperlipidaemia as well as the primary and secondary prevention of Coronary Heart Disease and Stroke.

2.1 Primary Prevention of Coronary Heart Disease and Stroke

Treat all patient's ≥40 years of age who have diabetes, and patient's ≤40 years who have had diabetes ≥20 years or have target organ damage, without additional risk assessment. Treat patients with chronic kidney disease (CKD 3-5) without additional risk assessment.

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



- It should be noted that both these models may under estimate lifetime risk in younger patients and adjustment may be appropriate in those aged <50years if 10 year risk >10%
- Cardiovascular risk assessments are not validated in ≥ 75years for ASSIGN and ≥85years for QRISK3 and the risk should therefore be reviewed in the context of other co-morbidities

For patients with a 10-year cardiovascular event ASSIGN risk of ≥ 20% offer atorvastatin 20mg daily as primary prevention

See BNF for cautions, contra-indications, and clinically important drug interactions

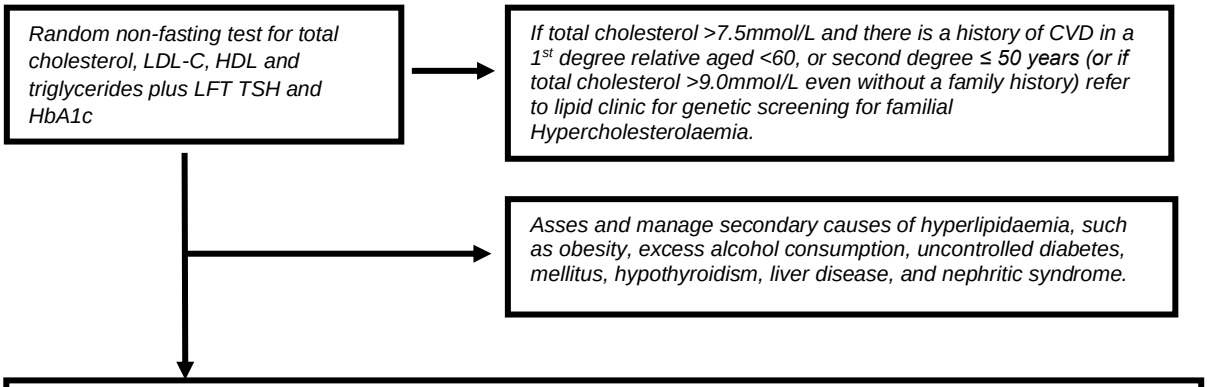
All patients should be advised of the key benefits of lifestyle modification including smoking cessation, diet, weight loss, increased exercise, and reduced alcohol consumption.

- There is no formal LDL-C target for primary prevention.
- Repeat lipid profile not required as no formal primary prevention target. Repeat LFTs 3 months after initiation. Annual lipid profile not required.
- Ensure optimal management of other modifiable cardiovascular risk factors including blood pressure and glycaemic control if appropriate.
- Check CK if patient complains of myalgia.
- When undertaking medication reviews, consider switching patients established on lower intensity statins such as Simvastatin to Atorvastatin 20mg unless there is a history of intolerance, or patient preference.
- Most reported statin intolerance is due to an expectation of side-effects, but consider a reduced dose of Atorvastatin if necessary, and switch to Rosuvastatin if an alternative statin is required. There is more evidence for prognostic benefit with statin treatment than for other drug classes

  Statin Intolerance Pathway
- Statins for primary prevention in the frail elderly are not evidence based and should not be initiated in this group of patients.

2.2 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 or PCI, angina, proven Coronary Artery Disease (invasive or CT angiography) Ischaemic Stroke or TIA or Peripheral Arterial disease. Also includes patients with significant coronary calcification or atherosclerosis reported on non-cardiac imaging.



For patients with atherosclerotic disease offer atorvastatin 80mg daily as secondary prevention

See BNF for cautions, contra-indications, and clinically important drug interactions

All patients should be advised of the key benefits of lifestyle modification including smoking cessation, diet, weight loss, increased exercise, and reduced alcohol consumption.

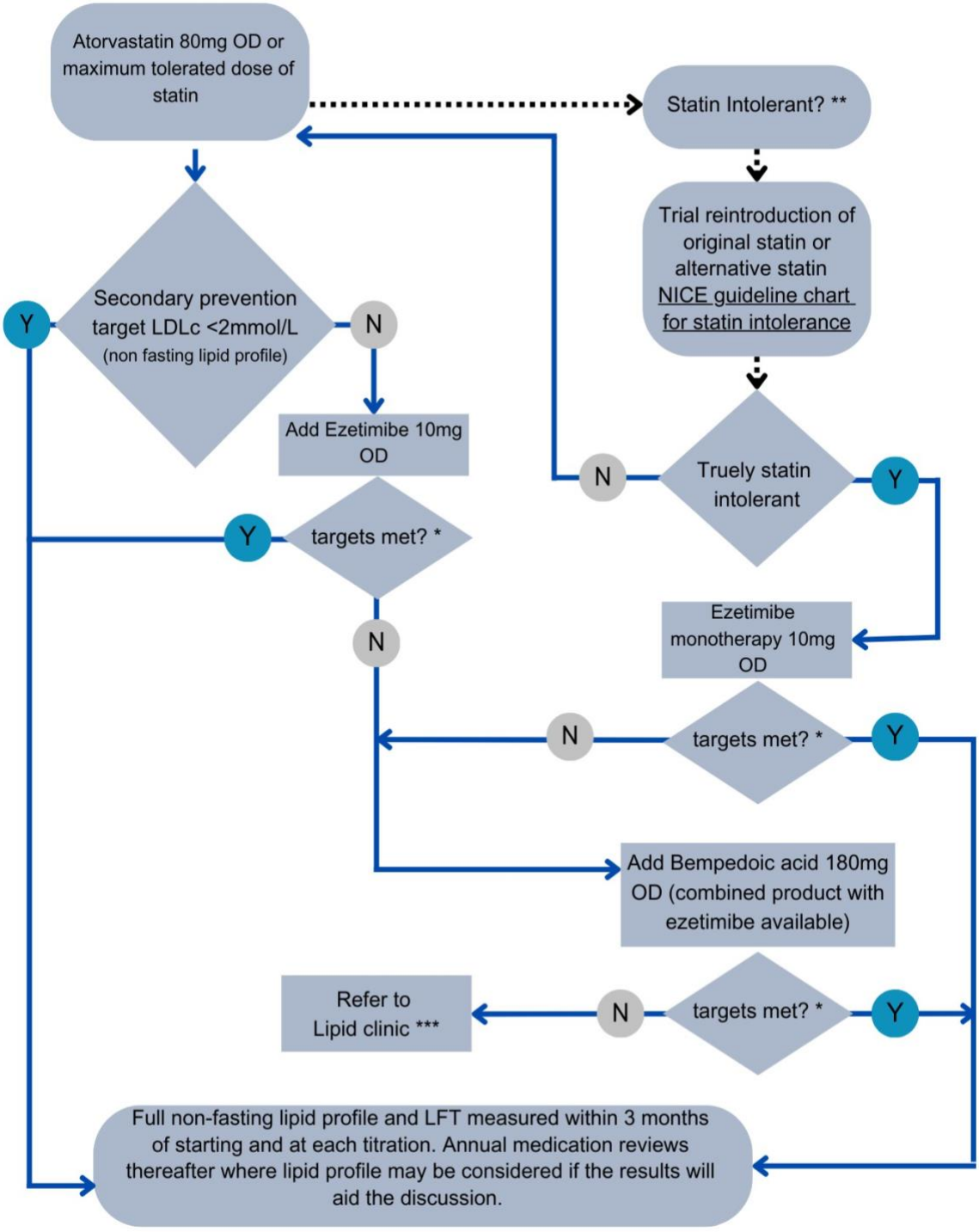
- Introduction of Lipid modification should not be delayed
- Prescribe a high intensity statin : Atorvastatin 80mg daily Target: LDLc of <2mmol/L
- Failure to reduce cholesterol concentrations significantly may be a marker of poor concordance. If cholesterol targets are not met see secondary prevention treatment flow chart.
- Ensure optimal management of other modifiable cardiovascular risk factors including left ventricular systolic dysfunction, blood pressure and glycaemic control if appropriate.
- Non fasting lipid profile and LFT measured within 3 months of starting and at each titration until optimised. Annual medication reviews should be offered to patients on lipid lowering treatments and an annual lipid profile may be considered only if it will aid this discussion.
- Check CK if patient complains of myalgia.
- Consider switching patients established on lower intensity statins such as Simvastatin to Atorvastatin 80mg unless there is a history of intolerance, or LDLc targets are met.
- Most reported statin intolerance is due to an expectation of side-effects, but consider a reduced dose of Atorvastatin if necessary, and switch to Rosuvastatin if an alternative statin is required.
- There is better evidence for prognostic benefit with statin treatment than for other drug classes

Statin Intolerance Pathway

Treatment of frail or elderly people with statins should be guided by individual circumstances and co-morbidities and need not follow guideline recommendation - clinical judgement, patient's preference and life expectancy should all be taken in to account. STOPP criteria should be used to consider deprescribing

2.3 Secondary Prevention Treatment Flow Chart

Includes patients with previous MI, previous CABG or PCI, angina, proven coronary artery disease (invasive or CT angiography) ischaemic stroke or TIA, or peripheral arterial disease. Also includes patients with significant coronary calcification or atherosclerosis reported on non-cardiac imaging.



*ensure each time a target is not met that lifestyle and concordance is reviewed
** see full guideline for advice on raised liver transaminases
*** see full guideline for treatment options offered by the specialist lipid clinic

2.4Targets

Primary Prevention

There are no targets for cholesterol in primary prevention. It is good practice to re-check full lipid profile within 3 months of initiation and optimise treatment where appropriate. There is no need for annual bloods. The aim of statin therapy is to induce a substantial reduction in LDLc concentrations, and failure to do so may be a marker of poor concordance. It would therefore be reasonable to offer an increased dose of Atorvastatin (40 or 80mg) to higher risk primary prevention patients who do not achieve a substantial reduction in LDLc following initiation of Atorvastatin 20mg daily, despite good concordance.

Secondary Prevention

The target for secondary prevention treatment is an LDLc goal of <2mmol/L Failure to reduce cholesterol concentrations significantly may be a marker of poor concordance. See Flowchart for treatment pathway.

Full non fasting lipid profile and LFT should be measured within 3 months of starting treatment and at each titration until optimised. Annual medication reviews should be offered to patients on lipid lowering treatments discussing:

- Adherence
- Diet and lifestyle
- Modifiable CVD risk
- Factors
- Consider a non-fasting lipid profile only if it will aid this discussion

Treatment of frail or elderly people with statins should be guided by individual circumstances and co- morbidities and need not follow guideline recommendation - clinical judgement, patient's preference and life expectancy should all be taken in to account.

2.5 Biochemistry (non fasting lipid profile)

- Total cholesterol (TC) mmol/L
- HDL cholesterol (HDLc) mmol/L
- Triglycerides (TG) mmol/L (if non fasting triglycerides 4.5-10mmol/L repeat with a fasting measurement, if >20mmol/L urgent referral)
- Calculated LDL (LDLc) mmol/L

LDLc is a better target than TC alone to guide treatment (Target <2 mmol/L). LDLc is not valid in patients with Triglycerides > 4.5mmol/L and can give an underestimated value. In patients with high triglycerides please calculate non-HDL

Non-HDL
Calculated non-HDL cholesterol = TC – HDLc (Target <2.5 mmol/L)

*LDLc and non-HDLc levels should reach target as much as possible but should also be personalised based on clinical judgement and after an informed discussion with the patient

2.6 Advice on raised Triglycerides

Triglycerides can be measured on a random sample as part of a full lipid profile.

- Raised triglycerides are most commonly due to secondary causes, e.g. poor diet, obesity, diabetes, alcohol excess, medicines.
- Any secondary causes of hypertriglyceridaemia should be identified and treated, then a further fasting sample arranged.

For patients with moderately raised non-fasting triglycerides, e.g. 4.5 to 10 mmol/L

- There is a modest increase in cardiovascular risk due to the raised triglycerides alone.
- Repeat lipid profile using a fasting sample.
- Address secondary causes and then consider treatment with Atorvastatin at a lower than usual calculated CVS risk threshold (e.g. 15%). In patients with a fasting triglyceride above 4.5mmol/L calculate non-HDL rather than LDLc.

For patients with markedly raised non-fasting triglycerides, e.g. > 10 mmol/L

- Address secondary causes and consider referral to lipid clinic if repeat fasting triglycerides remain persistently >10mmol (urgent referral if > 20mmol/L (increased risk of acute pancreatitis).

2.7 Liver Transaminases

Measure Liver Transaminases within 3 months of starting treatment and then within 3 months of each additional up titration. Does not required to be measured thereafter unless clinically indicated.

- If ALT greater than 3 times the upper limit of normal do not initiate the statin or discontinue the statin if already prescribed and repeat LFT in 1 month.
- If ALT are elevated but are less than 3 times the upper limit of normal
    - then do not routinely exclude from statin treatment
    - Continue the statin and repeat in 1 month
    - If they remain elevated but are still less than three times the upper limit of normal continue statin and repeat in 6 months.

2.8 Statin Intolerance

Please use NICE stain intolerance pathway

Statin Intolerance Pathway

2.9 Lipid Lowering Drugs

Statins

NICE categorise statins into 3 intensity categories:

- Low: LDLc reduction 20-30% (e.g. Pravastatin or Fluvastatin up to 40mg)
- Medium: LDLc reduction 31-40% (e.g. Simvastatin 40mg or Atorvastatin 10mg)
- High: LDLc reduction >40% (e.g. Atorvastatin 20mg or higher, Rosuvastatin 10mg or higher)

Atorvastatin is recommended for first line use at a dose of 20mg for primary prevention, and 80mg for secondary prevention.

- Ensure generic prescribing.
- Rosuvastatin is the preferred alternative if Atorvastatin is not tolerated, and is an alternative option if lipid targets are not met with Atorvastatin.

The use of Simvastatin 80mg is not recommended due to the increased risk of rhabdomyolysis. Patients currently on Simvastatin 80mg should be switched to Atorvastatin 80mg daily or Rosuvastatin 20mg daily.

Ezetimibe

Ezetimibe 10mg daily

- as an add-on to statin therapy for secondary prevention if cholesterol goals are not achieved on the maximum tolerated dose of statin
- as monotherapy for secondary prevention in the event of persistent statin intolerance

BNF - Ezetimibe

Adenosine Triphosphate Citrate Lyase (ACL) Inhibitor

Bempedoic Acid 180mg tablets (Nilemdo®)

Bempedoic acid 180mg/ezetimibe 10mg tablets (Nustendi ®)

- Not for use in primary prevention
- Indicated in primary hypercholesterolaemia or mixed dyslipidaemia in patients who have not responded adequately to other appropriate measures
- In combination with a statin, or a statin with other lipid-lowering therapies in patients unable to reach low-density lipoprotein cholesterol (LDLc) goals with the maximum tolerated dose of a statin
- alone or in combination with other lipid-lowering therapies in patients who are statin-intolerant, or for whom a statin is contra-indicated

BNF - Bempedoic acid (Nilemdo)
BNF - Bempedoic acid/ Ezetimibe (Nustendi)
SMC - Bempedoic acid (Nilemdo)
SMC - Bempedoic acid/ Ezetimibe (Nustendi)

Referral for Specialist initiation only

PCSK9-inhibitors

Alirocumab (Praluent®) – Homecare

Licensed indication:

- adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, as an adjunct to diet:
    - in combination with a statin or statin with other lipid lowering therapies in patients unable to reach LDLc goals with the maximum tolerated dose of a statin or,
    - alone or in combination with other lipid-lowering therapies in patients who are statin-intolerant, or for whom a statin is contraindicated

BNF-Alirocumab
SMC-Alirocumab

Evolocumab (Repatha®) - Homecare

Licensed Indication:
Adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, as an adjunct to diet:

- in combination with a statin or statin with other lipid lowering therapies in patients unable to reach LDL-C goals with the maximum tolerated dose of a statin or,
- alone or in combination with other lipid-lowering therapies in patients who are statin-intolerant, or for whom a statin is contraindicated
- Adults and adolescents aged 12 years and over with homozygous familial hypercholesterolaemia in combination with other lipid-lowering therapies.
- Adults and adolescents aged 12 years and over with homozygous familial hypercholesterolaemia in patients on apheresis in combination with other lipid-lowering therapies

BNF-Evolocumab
SMC-Evolocumab

Small Interfering Ribonucleic Acid (siRNA)

RNA interference mediated reduction of PCSK9 production

Inclisiran (Leqvio®) requires an IPTR

Licensed Indication:
Adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, as an adjunct to diet:

- In combination with a statin or statin with other lipid lowering therapies in patients who are unable to reach LDL-C goals with the maximum tolerated dose of a statin,
- or alone or in combination with other lipid lowering therapies in patients who are statin intolerant, or for whom a statin is contraindicated.

BNF-Inclisiran
SMC-Inclisiran

2.10 Drugs not recommended for use in D&G

The following lipid-lowering drugs are not recommended for routine use:

- Fibrates (not to be used to achieve LDLc targets only for use for the treatment of hypertriglyceridemia with triglycerides >10mmol/L)
- Anion exchange resins
- Omega-3 preparations (including icosopental ethyl)

3 References

- NICE guideline [NG238], Cardiovascular disease: risk assessment and reduction, including lipid modification Published: 14 December 2023 https://www.nice.org.uk/guidance/ng238/chapter
- SIGN 149 • Risk estimation and the prevention of cardiovascular disease Published July 2017 https://www.sign.ac.uk/assets/qrg149.pdf
- European Society of Cardiology, Guidelines on Dyslipidaemias (Management of) Published; 31 August 2019 https://www.escardio.org/Guidelines/Clinical-Practice-Guidelines/Dyslipidaemias-Management-of
- European Society of Cardiology, Lipidology update: targets and timing of well-established therapies Published 05 March 2024 https://www.escardio.org/Councils/Council-for-Cardiology-Practice-(CCP)/Cardiopractice/lipidology-update-targets-and-timing-of-well-established-therapies

4 Document Information

4.1 Monitoring:

Monitoring as per DG RefHelp Right Decision Service standard operating procedure – managing the content lifecycle

4.2 Equality and diversity:

Not impact assessed, negative impact on individuals is not anticipated.

4.3 Key Contacts

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4.4 Document control

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Name	**Responsibility**	**Version Number**
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Fergus Donachie	Upload the guideline to RefHelp	1.0
Implementation plan		
Lead Officer:	**Action:**	**Timeframe:**