HYPERLIPIDAEMIA: INVESTIGATION, TREATMENT AND MONITORING

This guidance includes information on investigation, monitoring and management of patients with hypercholesterolaemia/dyslipidaemia (including Lipoprotein (a)) and advice on which patients to refer to secondary care specialist lipid services.

This guidance is intended for use by primary care clinicians and the Duty Biochemists at Southmead Hospital.

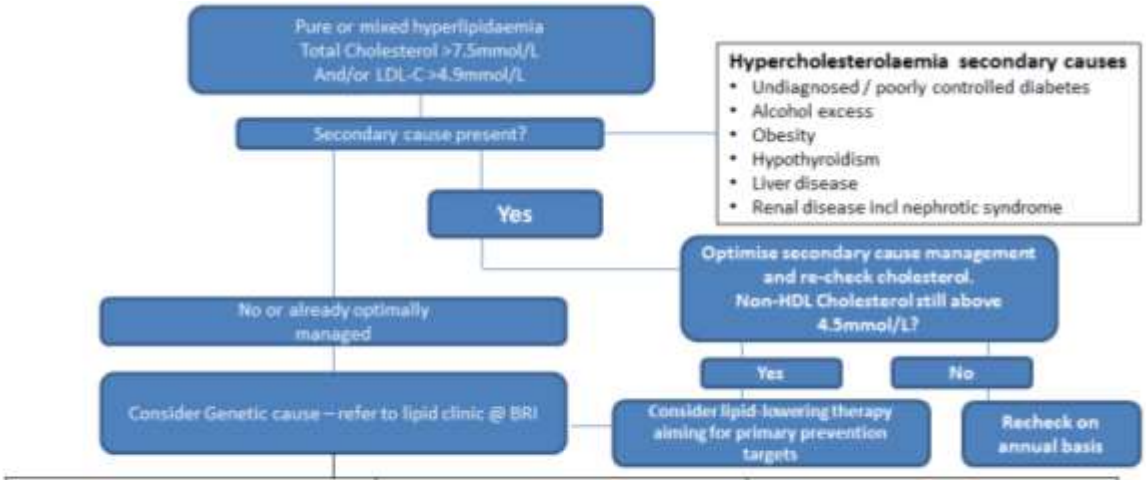
The key NICE guidelines referenced in this document are

- NICE CG 71; Familial Hypercholesterolaemia
- NICE CG 181; Lipid modification: Cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease
- NICE CG 172; Myocardial infarction: cardiac rehabilitation and prevention of further cardiovascular disease

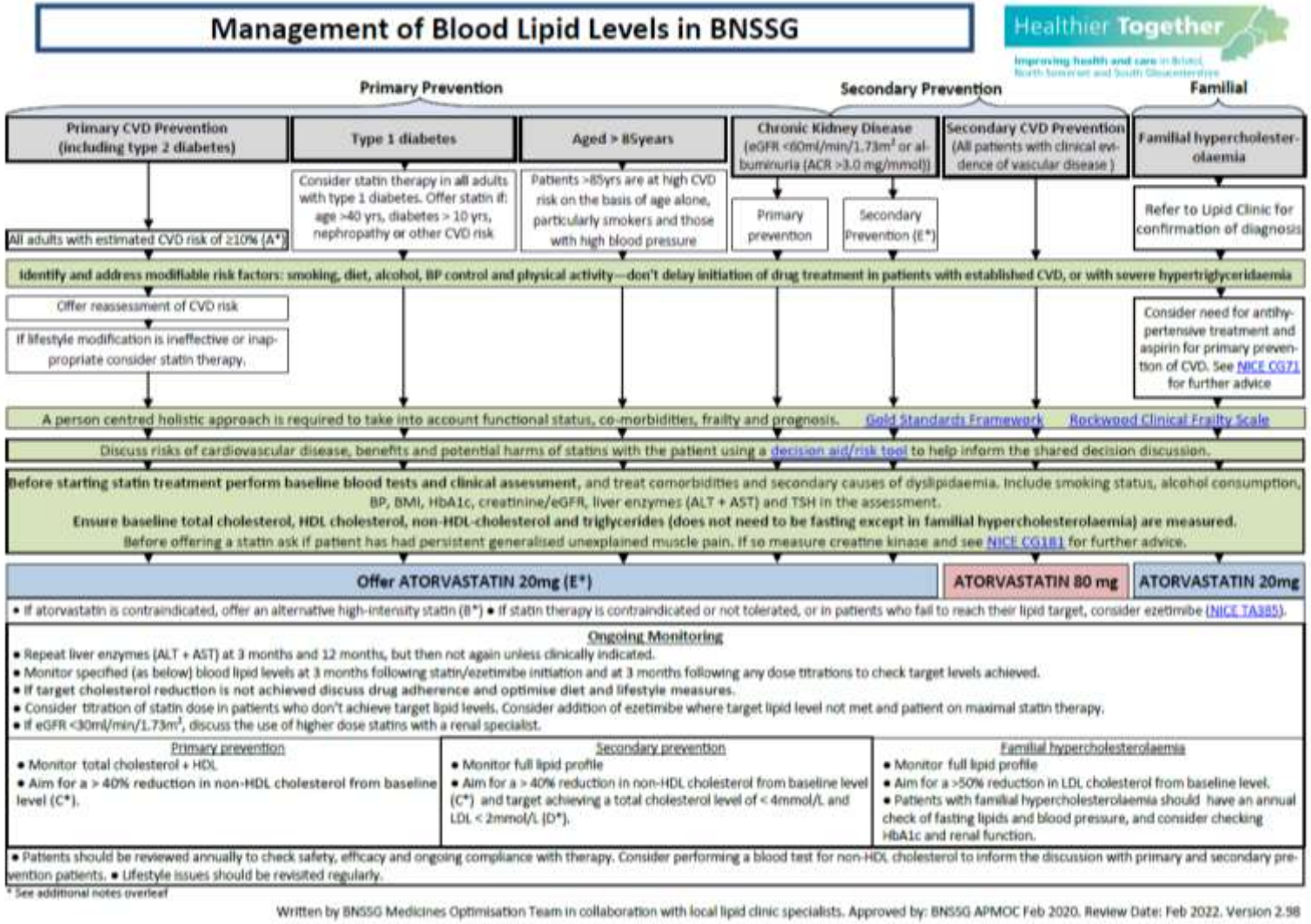
CONTENTS

SUMMARY ALGORITHMS

Investigation of hypercholesterolaemia



Familial Hypercholesterolaemia (FH)	Familial Combined Hyperlipidaemia (FCH)	Polygenic Hypercholesterolaemia
Prevalence: 1 in 250-500 (varies depending on up to date statistics) Inheritance: Autosomal Dominant Genes known to cause: - APOB - LDLR - PCSK9 Tested for on Bristol lipid genetics panel : Yes Typical Biochemistry: - TC >7.5mmol/L - LDL >4.9mmol/L - TG = normal The disease has greater severity in homozygous form and requires more aggressive management. Cascade testing of first degree relatives is indicated based on positive results.	Prevalence: 1 in 100 Inheritance: Autosomal Dominant Genes known to cause: - Not specifically testable Tested for on Bristol lipid genetics panel : No Typical biochemistry: - TC 6-9mmol/l - TG 2-6mmol/L This form is associated with other aspects of metabolic syndrome and is very responsive to lifestyle factor adjustment. Be suspicious in those with severe family history of CVD.	Prevalence: variable Inheritance: Not directly inherited Genes known to cause: - Panel of 12 genes with SNP mutations known to cause hypercholesterolemia tested in one panel. Tested for on Bristol lipid genetics panel : Yes. Typical biochemistry: - Variable - Can be anything depending on severity. In some cases TC and LDL only slightly elevated but in others may mimic FH. Those with decile score >6 given diagnosis. Not tested for specifically but included in genetic differential.


Management of Blood Lipid Levels in BNSSG
Healthier Together
Primary Prevention
Secondary Prevention
Familial
Primary CVD Prevention (including type 2 diabetes)
Type 1 diabetes
Aged > 85years
Chronic Kidney Disease (eGFR <60ml/min/1.73m² or albuminuria (ACR >3.0 mg/mmol))
Secondary CVD Prevention (All patients with clinical evidence of vascular disease)
Familial hypercholesterolaemia
Consider statin therapy in all adults with type 1 diabetes. Offer statin if: age >40 yrs, diabetes > 10 yrs, nephropathy or other CVD risk
Patients >85yrs are at high CVD risk on the basis of age alone, particularly smokers and those with high blood pressure
Primary prevention
Secondary Prevention (E*)
Refer to Lipid Clinic for confirmation of diagnosis
All adults with estimated CVD risk of ≥10% (A*)
Identify and address modifiable risk factors: smoking, diet, alcohol, BP control and physical activity—don't delay initiation of drug treatment in patients with established CVD, or with severe hypertriglyceridaemia
Offer reassessment of CVD risk
If lifestyle modification is ineffective or inappropriate consider statin therapy.
Consider need for antihypertensive treatment and aspirin for primary prevention of CVD. See NICE CG71 for further advice
A person centred holistic approach is required to take into account functional status, co-morbidities, frailty and prognosis. Gold Standards Framework Rockwood Clinical Frailty Scale
Discuss risks of cardiovascular disease, benefits and potential harms of statins with the patient using a decision aid/risk tool to help inform the shared decision discussion.
Before starting statin treatment perform baseline blood tests and clinical assessment, and treat comorbidities and secondary causes of dyslipidaemia. Include smoking status, alcohol consumption, BP, BMI, HbA1c, creatinine/eGFR, liver enzymes (ALT + AST) and TSH in the assessment.
Ensure baseline total cholesterol, HDL cholesterol, non-HDL-cholesterol and triglycerides (does not need to be fasting except in familial hypercholesterolaemia) are measured.
Before offering a statin ask if patient has had persistent generalised unexplained muscle pain. If so measure creatine kinase and see NICE CG181 for further advice.
Offer ATORVASTATIN 20mg (E*)
ATORVASTATIN 80 mg
ATORVASTATIN 20mg
• If atorvastatin is contraindicated, offer an alternative high-intensity statin (B*) • If statin therapy is contraindicated or not tolerated, or in patients who fail to reach their lipid target, consider ezetimibe (NICE TA385).
Ongoing Monitoring
• Repeat liver enzymes (ALT + AST) at 3 months and 12 months, but then not again unless clinically indicated.
• Monitor specified (as below) blood lipid levels at 3 months following statin/ezetimibe initiation and at 3 months following any dose titrations to check target levels achieved.
• If target cholesterol reduction is not achieved discuss drug adherence and optimise diet and lifestyle measures.
• Consider titration of statin dose in patients who don't achieve target lipid levels. Consider addition of ezetimibe where target lipid level not met and patient on maximal statin therapy.
• If eGFR <30ml/min/1.73m², discuss the use of higher dose statins with a renal specialist.
Primary prevention
• Monitor total cholesterol + HDL
• Aim for a > 40% reduction in non-HDL cholesterol from baseline level (C*).
Secondary prevention
• Monitor full lipid profile
• Aim for a > 40% reduction in non-HDL cholesterol from baseline level (C*) and target achieving a total cholesterol level of < 4mmol/L and LDL < 2mmol/L (D*).
Familial hypercholesterolaemia
• Monitor full lipid profile
• Aim for a >50% reduction in LDL cholesterol from baseline level.
• Patients with familial hypercholesterolaemia should have an annual check of fasting lipids and blood pressure, and consider checking HbA1c and renal function.
• Patients should be reviewed annually to check safety, efficacy and ongoing compliance with therapy. Consider performing a blood test for non-HDL cholesterol to inform the discussion with primary and secondary prevention patients. • Lifestyle issues should be revisited regularly.
* See additional notes overleaf
Written by BNSSG Medicines Optimisation Team in collaboration with local lipid clinic specialists. Approved by: BNSSG APMOC Feb 2020. Review Date: Feb 2022. Version 2.98

LIPID CLINIC REFERRALS

There is currently **no** provision for the specialist management of lipids at North Bristol NHS Trust. Enquiries and referrals should be directed to the BRI Lipidologists at University Hospitals Bristol NHS Foundation Trust; Dr Bayly, Dr Day or Dr Downie via BRI switchboard or the E-RS system E-RS system link

Referral should be considered in the following patients:

- **Any patient who may have Familial Hypercholesterolaemia (FH).** This autosomal dominant condition is one of the most common inherited disorders in the general population. The suspicion of this diagnosis and need to refer for specialist input may be raised based on:
    - An individual with biochemistry suggestive of FH. This should be considered in any patient with a total cholesterol >7.5mmol/L and/or LDL-C >4.9mmol/L with no obvious secondary cause (see below).
    - Or a family member has been identified as having FH through a lipid clinic service and genetic testing meaning cascade testing of family members is indicated.
- **Significant hypertriglycerideaemia or hypertriglycerideaemia resistant to treatment.** Triglycerides of >20mmol/L will be phoned to the GP practice/requesting clinician by the biochemistry department (unless this is a previous finding or the patient is under the care of the lipid clinic). This is in part due to the risk of acute pancreatitis secondary to hypertriglycerideaemia and secondly to prompt urgent action to identify the underlying cause and treat it. If a patient has triglycerides of >20mmol/L advise urgently contacting the UHB lipid clinic team for advice. These patients may require an insulin infusion or commencement on a fibrate (as long as there are no contraindications to do so) to help bring the triglycerides down.
  Triglycerides 10-20mmol/L should have a repeat advised between 5-14 days. if triglycerides remain >10mmol/L consider referral to the UHB Lipid Clinic. Meanwhile the patient should be counselled regarding reducing/avoiding alcohol, eating a low fat diet and diabetes control reviewed.
- **Treatment intolerance or resistance**. If there are concerns of statin intolerance in patients at high risk of CVD, established CVD or those who are intolerant to multiple statins then specialist advice should be sought through the lipid clinic in case newer agents such as PCSK9 inhibitors such as Evolocumab or Alirocumab can be prescribed
- **Inability to achieve treatment targets on available therapies**. If patients are unable to reach their optimum treatment targets on available therapies in primary care, then referral to lipid clinic would be indicated to consider other treatment options (though depending on the indication for lipid-lowering therapy the options may be limited).

If phoning abnormal results and/or adding interpretive comments to results then do mention referral to the lipid service where appropriate.

INVESTIGATING HYPERLIPIDAEMIA

When identifying a dyslipidaemia (whether mixed or a pure hypercholesterolaemia or hypertriglyceridaemia), there are 2 key paths that require investigating:

1. Identifying if a primary familial/genetic cause is present (such as Familial Hypercholesterolaemia or Familial Combined Hyperlipidaemia)
2. Or is any hyperlipidaemia secondary to another condition or co-morbidity.

FASTING SAMPLE OR NOT?

The need to perform full lipid profile on a fasting sample has gone largely out of preference. NICE guidance states that fasting samples are not required. Cholesterol testing utilises the friedwald equation for LDL calculation (LDL= TC – (HDL + TG/2.2)). This is based on the triglycerides being normal/near normal. Therefore if the TG is at the upper limit of normal/ slightly elevated then it wills falsely under-estimate the LDL level. Hence the equation is invalid if TG is significantly elevated and used with caution where TG near upper limit/slightly elevated. Advice to GP's should give the above so they can consider if samples should be taken fasted or not. Where LDL is elevated but near the limit where FH should be considered and TG is only slightly elevated – a fasted repeat can be helpful.

PRIMARY GENETIC CAUSES

There are 3 main genetic conditions which are known to commonly cause hyperlipidaemia and which are considered by the secondary care lipid service.

Familial Hypercholesterolaemia	**Familial Combined Hyperlipidaemia**	**Polygenic Hypercholesterolaemia**
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One further condition which is considered as part of the genetic causes is type 3 dysbetalipoproteinaemia. This is caused by homozygous ApoE2 genetic defects and inherited in a autosomal recessive fashion. These individuals can have equimolar concentrations of cholesterol and triglycerides in a range of 5-15mmol/L which is what signposts this condition as a possible cause. Palmar xanthomata are very indicative. Other tests include lipoprotein electrophoresis demonstrating a prominent beta band (representing elevated IDL) and a high Non-HDL-C/ApoB ratio (>5). Definitive diagnosis is made through genetic ApoE2 testing.

Other genetic conditions are known to cause dyslipidaemia but for the purposes of general advice the above is worthwhile to bear in mind.

Also note that as part of the genetic testing at the Bristol genetics lab, SNP's associated with altered SLC01B1 function (which is involved in statin metabolism/excretion) are tested for. If present, the patient may have an increased risk of myalgic side-effects from statin therapy.

SECONDARY CAUSES

The secondary causes of hypercholesterolaemia / hypertriglycerideaemia largely overlap though hypertriglycerideaemia are more predominantly influenced by lifestyle factors. The following is an incomplete list but are the main differentials to consider:

- Lifestyle factors such as obesity and alcohol excess
- Undiagnosed or poorly controlled diabetes mellitus
- Profound hypothyroidism
- Renal dysfunction including nephrotic syndrome
- Liver dysfunction
- Medications (including HIV medications, some chemotherapy or immunotherapy agents)

These secondary causes should be investigated alongside any newly identified dyslipidaemia and can be mentioned in any interpretive comment to sufficiently abnormal results.

Baseline biochemical investigations for hypercholesterolaemia are primarily:

- U&E & LFT
- Hba1c
- Full lipid profile (if only total and non-HDL cholesterol has been performed)
- TFTs

Inflammatory response- After any acute illness, e.g. MI, cholesterol levels drop by up to 30% as part of the acute stress response and may not return to pre-illness levels for several weeks. Triglyceride levels also labile. This is because certain lipoproteins are acute phase response proteins.

TREATING HYPERLIPIDAEMIA

PRIMARY PREVENTION OF CARDIOVASCULAR DISEASE

An important context of managing hyperlipidaemia is its role in reducing cardiovascular disease risk. QRISK3 is now the mainstay calculator in assessing cardiovascular risk in primary prevention that takes into account demographic information, observational data (BMI etc) and biochemical information (cholesterol). If the QRISK3 score is <10% risk of cardiovascular disease over 10 years **and** the dyslipidaemia is relatively mild (total cholesterol 4-6mmol/L and/or triglycerides <10mmol/L), then secondary factors (especially lifestyle factors) can be corrected/managed in the first instance prior to commencing lipid-lowering therapy. If the QRISK3 score is >10% over 10 years then more aggressively manage lifestyle factors and more strongly consider lipid-lowering therapy.

Two other patient groups should be considered for lipid-lowering therapy as part of CVD primary prevention in their management plans:

- Those with Type 1 Diabetes - anyone who is >40 years old **or** has had the disease for >10 years **or** has established nephropathy
- Those with chronic kidney disease

Note that if patients are found to have a primary familial/genetic cause to hyperlipidaemia then the risk of CVD is higher than that which QRISK3 would predict and therefore is not appropriate to be calculated in these individuals as it may detract from the greater risk of CVD which is the genetic cause.

Also remember that quitting smoking and examining other modifiable CVD risk factors is an important mainstay of primary care management.

SECONDARY PREVENTION OF CARDIOVASCULAR DISEASE

This is an important intervention that should be instigated by cardiology specialists as part of follow-up for cardiovascular disease. Atorvastatin 80mg is typical starting dose following a cardiovascular or cerebrovascular event but this can be titrated/differed given patient preference, biochemical response and any experienced side effects.

CORRECTING SECONDARY FACTORS (INCLUDING LIFESTYLE FACTORS)

Lifestyle factors- these are very common causes for hyperlipidaemia but can be the slowest and most difficult for some patients to correct and maintain. Each of the following are management points which can be instigated in primary care prior to or alongside commencing lipid lowering therapy depending on the severity of the dyslipidaemia:

- Poor glycaemic control -
    - For those individuals who are in the pre-diabetic range (HbA1c = 42-48mmol/mol), being able to improve your diet and lose enough weight (typically 5-10% of current weight) to shift from the overweight to normal BMI range has been shown to revert individuals to normoglycaemia.
    - For those individuals with established Type 2 DM diabetes, improving overall glycaemic control (especially those HbA1c is >100mmol/mol) will concurrently improve cholesterol control. No established data states how much a reduction in HbA1c will reduce an individual's cholesterol (given how complex the contributory factors are to cholesterol) but overall improvement should pay dividends elsewhere too
- Alcohol consumption - alcohol consumption and excess should be identified through screening questionnaires and where possible steps made to ensure alcohol consumption is reduced as much as possible but to at least within recommended weekly limits if abstinence is not possible/difficult to achieve
- Obesity – improving one's diet and reducing weight/improving BMI towards normal range can confer benefits in improving both overall cardiovascular risk and reducing cholesterol levels.

Hypothyroidism- If a patient is found to be profoundly hypothyroid, replacement therapy should be commenced and TSH corrected prior to starting lipid-lowering therapy as dyslipidaemia may mostly correct after TFTs go back to normal and hypothyroidism is a risk factor for the side-effect profile of statin therapy.

Other secondary causes- CKD and liver disease may be irreversible therefore lipid-lowering therapy should be considered if there are no other secondary factors to correct.

LIPID LOWERING PHARMACOLOGICAL OPTIONS

Baseline full lipid profile, LFTs and renal function should be performed prior to commencing therapy.
.Mainstays of pharmacological management for hyperlipidaemias are:

1. Statin therapy - the most common therapy prescribed to primarily reduce LDL-C by inhibiting HMG Co-A reductase to block the cholesterol synthesis pathway. Different statins have different levels of intensity with expected reductions in LDL-C. Table 1 below is taken from the NICE guidance on statin effectiveness. If patients are unable to tolerate a particular statin then an alternative which is of lower intensity may be tolerated. If that is not tolerated then dropping down the dose frequency to once a week or less can be trialled. Only after failed trials of 3 different statins (either due to side-effects or not achieving treatment targets) should alternate therapies need to be considered.
   Standard starting dose - Atorvastatin 20mg OD for primary prevention but can vary depending on risk factors for myalgia/rhabdomyolysis and treatment targets. Rosuvastatin 5mg OD or every other day or even once a week and titrated to tolerance can be a next step if atorvastatin is not tolerated. Fluvastatin 20mg may be the last option for those with very bad tolerance.
2. Ezetemibe - Acts to reduce cholesterol absorption from the gastrointestinal tract. Has a smaller side effect profile compared to statins or fibrates but also less effective in reducing LDL-C or triglycerides. Can also be used as an adjunct alongside a statin to give an extra reduction in LDL-C if not reaching ideal treatment targets on statin alone. Can be used as a single agent if a patient is completely intolerant of statins but not very effective.
   Standard starting dose - 10mg OD
3. Fibrates – Acts on the PPAR alpha gene transcription process. PPAR receptors modulate the genes that stimulate synthesis of triglycerides and HDL whilst also affecting the action of lipoprotein lipase which metabolises VLDL. Similar side effect profile as statins so should be cautioned in those at risk of rhabdomyolsis. It can be used as a first line agent in pure hypertriglycerideaemia especially if >20mmol/L and no contraindications.
   Standard starting dose - Fenofibrate 160mg OD which can be titrated up to 200mg capsule
4. PCSK9 inhibitors - PCSK9 in its physiological purpose acts to breakdown LDL receptors (whose purpose is to take up LDL-C into the liver for breakdown amongst). PCSK9 therefore has the end effect of increasing peripheral circulation of LDL-C. Some forms of FH involve gain of function mutations in PCSK9 which cause increased LDL-R breakdown and increased LDL in the circulation. PCSK9 inhibitors are sub-cut injections given every 2 weeks but only can be started from the lipid service as requires counselling and witnessed trial of first dose.
   Standard starting dose - Evolocumab 140mg 2-weekly (only to be prescribed from secondary care)

	Reduction in low-density lipoprotein cholesterol				
Dose (mg/day)	5	10	20	40	80
Fluvastatin	-	-	21%[1]	27%[1]	33%[2]
Pravastatin	-	20%[1]	24%[1]	29%[1]	-
Simvastatin	-	27%[1]	32%[2]	37%[2]	42%[3,4]
Atorvastatin	-	37%[2]	43%[3]	49%[3]	55%[3]
Rosuvastatin	38%[2]	43%[3]	48%[3]	53%[3]	-

[1] 20%–30%: low intensity.

[2] 31%–40%: medium intensity.

[3] Above 40%: high intensity.

[4] Advice from the MHRA: there is an increased risk of myopathy associated with high-dose (80 mg) simvastatin. The 80 mg dose should be considered only in patients with severe hypercholesterolaemia and high risk of cardiovascular complications who have not achieved their treatment goals on lower doses, when the benefits are expected to outweigh the potential risks.

Table 1 –showing the relative effectiveness of different statins, at different doses, on LDL-C concentrations. Taken from NICE guidance CG181 Appendix A (https://www.nice.org.uk/guidance/cg181/chapter/appendix-a-grouping-of-statins)

POTENTIAL CAUTIONS/CONTRAINDICATIONS TO LIPID LOWERING MEDICATIONS

MYALGIA/CK RISE/RHABDOMYOLYSIS:

- If a patient has myalgia or risk factors for rhabdomyolysis prior to starting statins a creatinine kinase (CK) should be measured at baseline.
- **Statins should be avoided in patients with a CK of persistently >5 times the upper limit of normal**. If the CK is lower than 5x ULN a lower dose statin can be commenced with close monitoring and seeking specialist advice if concerned.
- Advise people who are being treated with a statin to seek medical advice if they develop muscle symptoms (pain, tenderness or weakness). If this occurs, measure creatinine kinase. If this occurs with >1x statins then consider seeking lipid clinic advice.
- Some of the risk factors for rhabdomyolysis include;
    - Age >65 years
    - Renal impairment
    - Uncontrolled hypothyroidism
    - Personal or familial history of hereditary muscular disorders
    - Previous history of muscular toxicity with a statin or fibrate

- Alcohol abuse
- Concomitant use of other lipid lowering agents i.e. fibrates
- Concomitant use of cytochrome P450 3A4 inhibitors including macrolide antibiotics, cyclosporine, azole antifungals (e.g. ketoconazole and itraconazole) and protease inhibitors

LIVER FUNCTION TESTS:

- Statins should be avoided in patients with liver transaminases (ALT or AST) of >3 times the upper limit of normal. If liver transaminases (ALT or AST) > x3 ULN withhold statin and assess the trend in ALT. If the ALT normalises the statin may be tried again however a dose reduction or alternative statin could be considered.
- If the ALT remains > 3 x ULN or there is concern of active liver disease or liver fibrosis the statin should be stopped and a full liver screen should be carried out to investigate the aetiology, only re-starting the statin if liver fibrosis and active live disease is excluded.
- An ALT rise up to 3x ULN does not require the statin to be withheld. However, a review of other possible medications should take place.

RENAL IMPAIRMENT:

- Avoid high dose statins in mild renal impairment. When eGFR <30 ml/min/1.73m^2, do not start a statin but seek specialist advise.
- If considering fibrate therapy; the dose of fibrate should be reduced when eGFR < 60 ml/ min/1.73m^2 and fibrates avoided use when eGFR <40 ml/min/1.73m^2.

MONITORING HYPERLIPIDAEMIA

TREATMENT TARGETS FOR LIPID-LOWERING THERAPY

NICE guidance has become more simplified regarding the targets used for biochemical monitoring of lipid lowering therapy. Whether for primary or secondary prevention the initial treatment target advised by NICE is a 40% reduction in non-HDL cholesterol from the baseline/pre-treated level.

NICE guidance advises a LDL-C reduction of 50% for those found to have FH. For those with established cardiovascular disease or those with a primary familial cause to hypercholesterolaemia, a tighter target aiming for total cholesterol <4mmol/L and LDL cholesterol <2mmol/L may be used by the lipid clinic. This is rooted in good evidence from clinical trials which show that reducing LDL-C right down to even <1mmol/L confers reduction in risk of future cardiovascular deaths.

If targets are not being met then options for improving management include:

- Reviewing secondary factors/lifestyle adherence
- Increasing current pharmacological therapy (caution should be taken where risk of myalgia/previous intolerance to statins if that is prime therapy)
- Addition of adjunct agent (such as ezetimibe or a fibrate depending on whether triglyceride dominated lipid profile or LDL-C dominated profile)

- Referral to lipid clinic if multiple statin intolerance or unable to reach targets with options available. If established cardiovascular disease or familial cause to hypercholesterolaemia a PCSK9 inhibitor may be an option depending on the LDL-C concentration and severity of disease.

Biochemical monitoring of pharmacological therapy

NICE guidance advises that the following monitoring is performed on patients in receipt of lipid-lowering therapy. This is both to monitor for side effects of therapy and ensure treatment targets are being worked towards/achieved:

- LFTs and renal function performed at 3 months following starting statin therapy to check for side-effects
- Repeat full lipid profile at 3 months after starting or altering pharmacological therapy to check if achieved targets/check response
- LFTs, renal function and full lipid profile conducted at least annually once treatment targets are met
- CK **only** if patients start to exhibit symptoms of myalgia. Do not measure routinely in asymptomatic patients

Lipoprotein (a)

Background

Lipoprotein (a) is a molecule made up of Apolipoprotein B-100, Apolipoprotein a (lower case a rather than A) as well as a core of LDL. It has been found to be pro-thrombotic as well as artherogenic as it acts not only to cause lipid plaques like normal LDL-C but also shows homology to plasminogen and can disrupt fibrinolysis giving it its pro-thrombotic action. As such it is considered to be an independent risk factor for cardiovascular disease separate to LDL-C. Those who have significantly elevated Lp(a) levels (>400nmol/L) have a CVD risk profile similar to those who have heterozygous FH and hence do require further action and consideration of familial testing.

The blood test is done on an serum sample and processed at the BRI labs using the Optilite turbidimetric method. The reference range is <75nmol/L. Some older Lp(a) results reported on ICE may be in mg/dL units where the reference range is <30mg/dL. Conversion of results is approximately (but not always precisely): [nmol/L] = [mg/dL] x 2.4. Once performed, Lp(a) does **not** require repeating unless due to a secondary cause.

Current management of Lp(a) in the Bristol Lipid Service

As with other hyperlipidaemia's there are both primary genetic and secondary causes to elevated Lp(a) which are of a similar profile to that listed in above sections:

- Nephrotic syndrome
- CKD
- Profound hypothyroidism

The Bristol Lipid service is developing guidance surrounding the actions required on elevated Lp(a) levels for general practice to follow. The mainstay of actions required are based on the Lp(a) result:

- 90-200nmol/L : Consider treating cholesterol to primary prevention targets utilising lifestyle factors or pharmacological therapy
- 200-400nmol/L : Aggressively treat cholesterol to TC <4mmol/L and LDL-C <2mmol/L using a high intensity statin (atorvastatin 20mg OD for example) as well as consider screening 1st degree relatives for elevated Lp(a). If their result is of a similar level then they should be recommended similar management by their GP. This can be managed in primary care and does not necessarily require referral to secondary care
- >400nmol/L : As above and consider CT coronary angiogram to identify any underlying undiagnosed coronary disease. A familial cause is possible and should be referred to secondary care lipid service for management.

At present there are no specific treatments for Lp(a). Statin therapy aggressively treats LDL-C to secondary prevention targets so that LDL-C is as little a contributory risk factor as possible. Anti-sense oligonucleotide therapy is currently in development but not going to be used in practice for at least a few years. Anti-platelet therapy like low dose aspirin may help mitigate against the pro-thrombotic effects where Lp(a) levels are significantly elevated but due to the side effect profile of regular aspirin, it should **not** be started routinely without a case by case consideration of the risk/benefit profile.

REFERENCES AND RELEVANT DOCUMENTS

1 NICE CG 71; Familial Hypercholesterolaemia (August 2008 updated November 2017)

2 NICE CG 181; Lipid modification: Cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease (June 2014 revised September 2016)

3 NICE CG 172; Myocardial infarction: cardiac rehabilitation and prevention of further cardiovascular disease (November 2013)

4 NICE Pathways; Lipid modification therapy for preventing cardiovascular disease (August 2018)

5 NICE TA394; Evolocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia (June 2016)

6 British National Formulary, Number76, September 2018: bnf.org

7 QRisk®3: 2018 risk calculator

8 Management of Lipoprotein(a) - UHB trust guidance