Northern England Evaluation and Lipid Intensification guideline

Section Description	Primary Secondary prevention	Statin Intolerance	Severe Hypercholesterolaemia	Severe Hypertriglyceridaemia	Pregnancy	FH in Children and Young People	Supplementary information
Section Guideline			Simon Broome criteria for diagnosis of Familial Hypercholesterolaemia		Lipid management and medication issues in pregnancy		Lipid Clinic referral criteria Common drug interactions Regional Lipid clinics Lipoprotein (a)
Flow charts	Combined approach Management of patients with established vascular disease	Statin intolerance flow chart	Assessment pathway	Assessment pathway		Assessment pathway	

Summary of National Guidance for Lipid Management for Primary and Secondary Prevention of CVD

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INITIAL CONSIDERATIONS:

- Measure non-fasting ***full lipid profile*** (total cholesterol, HDL-C, non-HDL-C, triglycerides) and HbA1c as part of an initial baseline assessment.
- Consider secondary causes of hyperlipidaemia and manage as needed.
- Ensure appropriate baseline and follow up tests as detailed on page 2. Measure BMI.
- Identify and exclude people with contraindications/drug interactions
- If non-fasting triglyceride above 4.5mmol/L see page 2.

PRIMARY PREVENTION

Consider statin therapy for adults who do not have established CVD but fall into the categories below. Use QRISK risk assessment tool where appropriate (see page 2, *'Primary Prevention Risk Assessment'*)

- Age ≤84 & QRISK ≥10% over next 10 years
- Type 2 diabetes & QRISK ≥10% over next 10 years
- Type 1 diabetes, if they have one or more of the following:
  - Over 40 years
  - Had diabetes for >10 years
  - Have established nephropathy
  - Have other CVD risk factors
- CKD eGFR < 60 mL/min/1.73m² and/or albuminuria
- Age ≥85 years if appropriate consider comorbidities, frailty & life expectancy

Identify and address all modifiable risk factors - smoking, diet, obesity, alcohol intake, physical activity, blood pressure and HbA1c.

Consider additional risk factors, if present, together with QRISK score (treated for HIV, severe mental illness, taking medicines that cause dyslipidaemia, systemic inflammatory disorder (e.g. SLE), impaired fasting glycaemia, recent change in risk factors)

PRIMARY PREVENTION

If lifestyle modification is ineffective or inappropriate offer statin treatment.

Atorvastatin 20mg daily

- Measure full lipid profile again after 3 months (non-fasting).
- High intensity statin treatment should achieve reduction of non-HDL-C > 40% from baseline. If not achieved after 3 months;
  - discuss treatment adherence, timing of dose, diet and lifestyle
  - If at higher risk (based on comorbidities, risk score or clinical judgement – see page 2 *'Additional Risk Factors'*) consider increasing the dose every 2-3 months up to a maximum dose of atorvastatin 80mg daily.
  - For how to increase in people with CKD see *'Special Patient Populations'* (page 2).
- If patients on a high-intensity statin have side effects, offer a lower dose or an alternative statin (see page 2 *'Extent of lipid lowering with available therapies'*)
- If maximum tolerated dose of statin does not achieve non-HDL-C reduction > 40% of baseline value after 3 months consider adding Ezetimibe 10mg daily (NICE TA385)
- If statin treatment is contraindicated or not tolerated;
  - See AAC Statin Intolerance Algorithm for advice regarding adverse effects LINK
  - Ezetimibe 10mg monotherapy may be considered. Assess response after 3 months.
  - Ezetimibe 10mg/bempedoic acid 180 mg combination may be considered when ezetimibe alone does not control non-HDL-C/LDL-C well enough (NICE TA694).

If non-HDL-C reduction remains < 40% of baseline despite maximal tolerated lipid lowering therapy (including people with intolerances and contraindications) consider referral to specialist lipid management clinic according to local arrangements

SEVERE HYPERLIPIDAEMIA

If TC>7.5mmol/L and/or LDL-C >4.9mmol/L and/or non-HDL-C >5.9mmol/L, a personal and/or family history of confirmed CHD (<60 years) and with no secondary causes: suspect familial hypercholesterolaemia (possible heterozygous FH)

Do not use QRISK risk assessment tool

DIAGNOSIS AND REFERRAL

Take fasting blood for repeat lipid profile to measure LDL-C.

Use the **Simon Broome** or **Dutch Lipid Clinic Network** (DLCN) criteria to make a **clinical diagnosis of FH**.

Refer to Lipid Clinic for further assessment if **clinical diagnosis of FH** or if TC>9.0mmol/L and/or LDL-C >6.5mmol/L and/or non-HDL-C >7.5mmol/L or Fasting triglycerides > 10mmol/L (regardless of family history) (page 2)

TREATMENT TARGETS IN FH

If clinical diagnosis of FH and/or other risk factors present follow the recommended treatment management pathway for primary or secondary prevention as for non-FH, ***BUT***

Aim to achieve at least a 50% reduction of LDL-C (or non-fasting non-HDL-C) from baseline.

Consider specialist referral for further treatment and/or consideration of PCSK9i therapy IF

- they are assessed to be at very high risk of a coronary event**
- OR therapy is not tolerated
- OR LDL-C remains >5mmol/L (primary prevention)
- OR LDL-C remains >3.5mmol/L (secondary prevention)

despite maximal tolerated statin and ezetimibe therapy.

**defined as any of the following:

- Established coronary heart disease
- Two or more other CVD risk factors

SECONDARY PREVENTION

Offer statin therapy to adults with CVD, this includes angina, previous MI, revascularisation,stroke or TIA or symptomatic peripheral arterial disease. Do not delay statin treatment if a person has acute coronary syndrome. Take a lipid sample on admission (within 24 hours)

Identify and address all modifiable risk factors - smoking, diet, obesity, alcohol intake, physical activity, blood pressure and HbA1c.

SECONDARY PREVENTION

Do not delay statin treatment in secondary prevention while managing modifiable risk factors.

Prescibe a high intensity statin:

Atorvastatin 80mg daily

Use a lower dose of atorvastatin if there is a potential drug interaction, high risk of or experiencing adverse effects, or patient preference.

Offer atorvastatin 20mg if CKD (people with GFR< 60 mL/min/1.73m²).

- Measure full lipid profile again after 3 months (non-fasting).
- High intensity statin treatment should achieve reduction of non-HDL-C > 40% from baseline. If not achieved after 3 months
  - discuss treatment adherence, timing of dose, diet and lifestyle measures
  - If started on less than atorvastatin 80mg and the person is judged to be at higher risk (based on comorbidities, risk score or clinical judgement - see page 2 *'Additional Risk Factors'*), consider increasing to 80mg atorvastatin. For how to increase in people with CKD see *'Special Patient Populations'* (page 2).
- If non-HDL-C baseline value is not available*, consider target non-HDL-C < 2.5mmol/L (approximately equivalent to LDL-C < 1.8mmol/L) as recommended by Joint British Societies (JBS3).
  **this scenario is not covered by NICE CG181*
- If patients on a high-intensity statin have side effects, offer a lower dose or an alternative statin (see page 2 *'Extent of lipid lowering with available therapies'*)

If maximum tolerated dose of statin does not control non-HDL-C/LDL-C well enough after 3 months confirm statin adherence, then consider the following options based on shared decision making* with the patient

If recommended statin treatment is contraindicated or not tolerated - follow AAC Statin Intolerance Algorithm for advice regarding adverse effects LINK

If statin intolerance is confirmed, consider:

- **Ezetimibe 10mg** monotherapy. Assess response after 3 months (TA385)
- **Ezetimibe 10mg/bempedoic acid 180 mg** combination when ezetimibe alone does not control non-HDL-C sufficiently. (NICE TA694)

If non HDL-C remains > 2.5mmol/L despite other lipid lowering therapies consider Injectable therapies - arrange a fasting blood test and assess eligibility criteria (TA393/394, TA733)

Ezetimibe 10mg daily (NICE TA385). Reassess after three months. If non-HDL-C remains > 2.5mmol/L; consider **injectable therapies** arrange a fasting blood test and assess eligibility

Injectable therapies**

If non-HDL-C > 2.5mmol/L; Arrange fasting blood test to measure LDL-C to assess eligibility:

- **Inclisiran** - if fasting LDL-C ≥ 2.6mmol/L despite maximum tolerated lipid lowering therapy (TA733)

OR

- **PCSK9i** - see overleaf for LDL-C thresholds. (TA393/4)

If eligibility criteria are not met, consider **ezetimibe 10mg daily** (if not previously considered)

* See overleaf for information to support shared decision making

** Inclisiran and PCSK9i should not be prescribed concurrently

MANAGEMENT

This guidance applies to new patients and may also be taken into consideration for those already on statins at their annual review. If 40% reduction of non-HDL-C not achieved, offer high intensity statins. Discuss with people who are stable on a low- or medium-intensity statin the likely benefits and potential risk of side effects if changed to a high-intensity statin when they have a medication review and agree with the person whether a change is needed.

Ezetimibe, alirocumab, evolocumab or inclisiran can be added when patients' LDL-C levels are not lowered enough with the maximally tolerated dose of statins. Bempedoic acid with ezetimibe is an option when statins are contraindicated or not tolerated, and when ezetimibe alone does not control LDL-C well enough. Do not offer a fibrate, nicotinic acid, bile acid binder or omega-3 fatty acids alone or in combination with statin, for the prevention of CVD (Check NICE CG181 for exceptions).

PRIMARY PREVENTION RISK ASSESSMENT

QRISK3 is the current version of the QRISK calculator. www.qrisk.org/three LINK

- Do not use this risk assessment tool for people with established CVD or those who are at high risk of developing CVD because of FH or other inherited disorders of lipid metabolism.
- Do not use a risk assessment tool to assess CVD risk in people with type 1 diabetes, or eGFR less than 60 mL/min/1.73 m² and/or albuminuria.
- Consider people aged ≥ 85 at increased risk of CVD because of age alone particularly people who smoke or have raised BP.

Additional Risk Factors

Note, standard CVD risk scores including QRISK may underestimate risk in people who have additional risk because of underlying medical conditions or treatments. These groups include the following groups of people;

- severe obesity (BMI>40kg/m²) increases CVD risk
- treated for HIV
- serious mental health problems
- taking medicines that can cause dyslipidaemia such as antipsychotic medication, corticosteroids or immunosuppressant drugs
- autoimmune disorders such as SLE, and other systemic inflammatory disorders
- non-diabetic hyperglycaemia
- significant hypertriglyceridaemia (fasting triglycerides 4.5-9.9mmol/L)
- recent risk factor changes e.g. quit smoking, BP or lipid treatment

Consider socio-economic status as an additional factor contributing to CVD risk.

If QRISK < 10% over the next 10 years - Give lifestyle advice and ensure regular review of CVD risk in line with guidance.

SPECIAL PATIENT POPULATIONS

Type 1 Diabetes

While NICE recommends offering statins to patients with Type 1 diabetes as detailed in the algorithm, it also states to consider statins in all adults with type 1 diabetes.

Chronic Kidney Disease

Offer atorvastatin 20mg for the primary or secondary prevention of CVD to people with CKD (eGFR less than 60 mL/min/1.73m² and/or albuminuria)

Increase the dose if a greater than 40% reduction in non-HDL-C is not achieved and eGFR is 30 mL/min/1.73m² or more.

Agree the use of higher doses with a renal specialist if eGFR is less than 30 mL/min/1.73m²

ABBREVIATIONS

ALT: alanine aminotransferase
AST: aspartate aminotransferase
CHD: coronary heart disease
CKD: chronic kidney disease
CVD: cardiovascular disease
FH: familial hypercholesterolaemia
LDL-C: low density lipoprotein cholesterol
non-HDL-C: non-high density lipoprotein cholesterol
PCSK9i: proprotein convertase subtilisin kexin 9 monoclonal antibody inhibitor
SLE: systemic lupus erythematosus
SPC: summary of product characteristics
TC: total cholesterol

EXTENT OF LIPID LOWERING WITH AVAILABLE THERAPIES

Approximate reduction in LDL-C					
Statin dose mg/day	5	10	20	40	80
Fluvastatin			21%	27%	33%
Pravastatin		20%	24%	29%	
Simvastatin		27%	32%	37%	42%
Atorvastatin		37%	43%	49%	55%
Rosuvastatin	38%	43%	48%	53%	
Atorvastatin + Ezetimibe 10mg		52%	54%	57%	61%

Low intensity statins will produce an LDL-C reduction of 20-30%
Medium intensity statins will produce an LDL-C reduction of 31-40%
High intensity statins will produce an LDL-C reduction above 40%
Simvastatin 80mg is not recommended due to risk of muscle toxicity

- **Rosuvastatin** may be used as an alternative to atorvastatin if compatible with other drug therapy. Some people may need a lower starting dose (see BNF).
- Low/medium intensity statins should only be used if intolerance or drug interactions.
- **Ezetimibe** when combined with any statin is likely to give greater reduction in non-HDL-C or LDL-C than doubling the dose of the statin.
- **PCSK9i** (NICE TA393, TA394) alone or in combination with statins or ezetimibe produce an additional LDL-C reduction of approximately 50% (range 25-70%).
- **Bempedoic acid** when combined with ezetimibe (TA694) produces an additional LDL-C reduction of approximately 28% (range 22-33%) but no clinical outcome evidence is currently available.
- **Inclisiran** (TA733) alone or in combination with statins or ezetimibe produces an additional LDL-C reduction of approximately 50% (range 48-52%) but no clinical outcome evidence is currently available.

MONITORING

Baseline Measurements

In addition to full lipid profile, measure renal, thyroid and liver profiles (including albumin) and HbA1c to exclude secondary causes and co-morbidities.
Measure baseline liver transaminase (ALT or AST) before starting a statin.
Measure CK if unexplained muscle pain before starting a statin.
CK should not be measured routinely especially if a patient is asymptomatic.

	Primary Prevention		Secondary prevention	
	Lipid Profile	ALT or AST	Lipid Profile	ALT or AST
Baseline	✔	✔	✔	✔
3 months	✔	✔	✔	✔
6-9months	If <40% non-HDL-C reduction, up titration required. Repeat full lipid profile and ALT or AST within 3 months of each up-titration of statin dose or addition of ezetimibe as required			
12 months	✔	✔	✔	✔
Yearly	✔*		✔*	

Provide annual medication reviews for people taking statins to discuss effectiveness of therapy, medicines adherence, lifestyle modification and address CVD risk factors.
Consider an annual non-fasting **full lipid profile to inform the discussion around effectiveness of lipid lowering therapy and any medicines non-adherence.*

Monitoring

Repeat full lipid profile is non-fasting.
Measure liver transaminase within 3 months of starting treatment and then within 3 months of every additional up titration and then again at 12 months, but not again unless clinically indicated.

If ALT or AST are greater than 3 times the upper limit of normal then do not initiate a statin or discontinue statin therapy already prescribed and repeat the LFTs in a month.

If ALT or AST are elevated but are less than 3 times the upper limit of normal then:

- Continue the statin and repeat in a month.
- If they remain elevated but are less than 3 times the upper limit of normal then continue statin and repeat again in 6 months.

TITRATION THRESHOLD / TARGETS

	NICE titration threshold	JBS3
Primary prevention	Intensify lipid lowering therapy if non-HDL-C reduction from baseline is less than 40%	non-HDL-C <2.5mmol/L (LDL-C <1.8mmol/L)
Secondary Prevention		
FH	Optimise lipid lowering therapy to achieve at least 50% reduction in LDL-C (or non-HDL-C.)	

If baseline cholesterol is unknown in the setting of secondary prevention use the use Joint British Societies' JBS3 consensus recommendation.
Non-HDL-C = TC minus HDL-C
LDL-C = non-HDL-C minus (Fasting triglycerides[a]/2.2)
[a] valid only when fasting triglycerides are less than 4.5 mmol/L

SPECIALIST SERVICES

Scope of specialist service available locally may include; lipid clinic, PCSK9i clinic (offering initiation and subsequent follow up), FH genetic diagnosis and cascade testing, lipoprotein apheresis service. NICE eligibility criteria for PCSK9i and fasting LDL-C thresholds are summarised below.

NICE TA393 Alirocumab NICE TA394 Evolocumab	Without CVD	With CVD	
		High risk [1]	Very high risk [2]
Primary non-FH or mixed dyslipidaemia	Not recommended	LDL C > 4.0 mmoL/L	LDL C > 3.5 mmoL/L
Primary heterozygous-FH	LDL C > 5.0 mmoL/L	LDL C > 3.5 mmoL/L	

[1] History of any of the following: ACS; coronary or other arterial revascularisation procedures; CHD, ischaemic stroke; PAD. [2] Recurrent CV events or CV events in more than 1 vascular bed (that is, polyvascular disease).

Bempedoic acid/ezetimibe and inclisiran are available in primary care and do not require initiation by specialist services.' PCSK9i may be available for prescribing in primary care: see local initiation pathways.

TRIGLYCERIDES

Triglyceride concentration	Action
Greater than 20mmol/L	**Refer to lipid clinic for urgent specialist review** if not a result of excess alcohol or poor glycaemic control. At risk of acute pancreatitis.
10 - 20mmol/L	Repeat the TG measurement with a fasting test (after an interval of 5 days, but within 2 weeks) and review for potential secondary causes of hyperlipidaemia. Seek specialist advice if the TG concentration remains > 10mmol/litre. At risk of acute pancreatitis
4.5 - 9.9mmol/L	If non-fasting triglycerides are greater than 4.5mmol/L, repeat with a fasting TG measurement Be aware that the CVD risk may be underestimated by risk assessment tools, optimise the management of other CVD risk factors present and seek specialist advice if non-HDL-C concentration is > 7.5 mmol/litre.

STATIN INTOLERANCE

Statin intolerance is defined as the presence of clinically significant adverse effects from statin therapy that are considered to represent an unacceptable risk to the patient or that may result in adherence to therapy being compromised.

For people who are intolerant of the recommended statin treatment see the NHSE AAC statin intolerance algorithm, available on the NHSE AAC page LINK

References:
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NICE 2008. CG71 www.nice.org.uk/guidance/cg71
NICE 2021. TA694 www.nice.org.uk/guidance/TA694
NICE 2021. TA733 www.nice.org.uk/guidance/TA733

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Flow chart for the management of patients with established vascular disease

Patient with coronary artery disease, cerebrovascular disease and or peripheral arterial disease, treated with maximum tolerated statin

Has the patient achieved a 40% reduction in non-HDL-C from baseline and is non-HDL-C ≤ 4mmol/L?

YES

Continue with standard management pathway to maintain > 40% reduction in non-HDL-C

NO

Ensure secondary causes excluded.
Blood and urine samples (request U+E, LFT, TFT, HbA1c, Urine ACR if not recent)

Assess

Current drug treatment and concordance
Lifestyle including diet (including any "fad diets") and physical activity
alcohol history
glycaemic control of diabetes

Correct any secondary causes

Intensify statin potency/ dose and add Ezetimibe as required (see box), titrating every 6 to 8 weeks until maximum tolerated or Non HDL -C ≤4mmol/l

Is non-HDL-C still > 4mmol/L?

Notes (Please also refer to the additional notes below):
If non-HDL-C > 4mmol/L and any secondary causes, including poor concordance have been corrected, consider escalation in statin intensity/dose as tolerated, titrating at 6 to 8 weekly intervals e.g. Ensure Atorvastatin 80mg OD or maximum tolerated dose.

If fail to achieve non-HDL-C ≤ 4mmol/L, consider;

- Switching to Rosuvastin 20mg or 40mg OD (or lower dose to start and titrate up if concerns about tolerability)
- If treated with optimal statin as tolerated, the addition of Ezetimibe 10mg OD.

The response should be assessed at 6 to 8 weekly intervals and treatment intensified as required
If non-HDL-C does not fall with change in treatment review concordance, ensure secondary causes excluded, consider a different agent.

* High risk of CVD i.e. history of any of the following: acute coronary syndrome (such as MI or unable angina needing hospitalisation); coronary or other arterial revascularisation procedures, coronary heart disease; ischaemic stroke, peripheral arterial disease.

** Very high risk of CVD i.e. recurrent cardiovascular events or cardiovascular events in more than 1 arterial vascular bed (that is, polyvascular disease)

NO

YES

Measure fasting lipid profile which will include a calculated LDL-C

* High risk of CVD and calculated LDL-C > 4mmol/L?
** Very High risk of CVD and calculated LDL-C > 3.5mmol/L?
ARE Triglycerides < 4.5mmol/L?

NO

Repeat fasting (12 hours) blood test for lipid profile PLUS a **measured** LDL-C (eg. Beta Quant or direct LDL-C assay)

LDL-C > 4mmmol/L (*High Risk)

or LDL-C > 3.5mmol/L (**very high risk)

YES

Refer to clinics providing PCSK9i therapy e.g. lipid or cardiology clinics. Provide comprehensive details of patient history and all management steps tried including drugs used with referral

NO

Continue current lipid lowering regime

YES

Statin Intolerance Pathway

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This resource relates to NICE guidance:
CG181, CG71, TA385, TA393/394, QS100

Person at high CVD risk reports potential intolerance to recommended high intensity statin treatment

New onset or worsening of muscle symptoms since starting statins? (pain, tenderness or weakness)

No → Consider other potential side effects for statins
- Be aware of **Statin Reluctance** and **Nocebo Effect**
- See '***Person Centred Care***'

YES

Symptoms typical for Statin Related Muscle toxicity (SRM)*?

No → Muscular symptoms not related to statins → Non SRM: Consider other causes e.g. PMR, Vit D deficiency. Check bone profile, Vit D, CRP.

*Symmetrical pain and/or weakness in large proximal muscle groups, worsened by exercise

YES

Measure Creatinine Kinase (CK)
Assess severity of symptoms
+/- repeat baseline assessment**

**Consider other causes if new onset of muscle symptoms of >2 weeks duration in a person previously tolerant of statin therapy for > 3months

Tolerable symptoms
No clinical concern
CK < 4x ULN

Improvement within 2 weeks
Resolved within 6 weeks
Patient happy to continue

No → **Stop statin for 4-6 weeks**
Document time to symptom onset and time to resolution

Intolerable symptoms
and/or clinical concern ***and/or*** CK > 4x and < 10x ULN

CK > 10x and < 50x ULN → **Renal function** stable/normal eGFR

Yes → **Stop statin for 4-6 weeks**
Document time to symptom onset and time to resolution

No → Stop statin and consider **Rhabdomyolysis**

CK > 50x ULN → **Urgently** seek specialist advice and inpatient **assessment**

Has CK normalised?

No → Consider **Statin induced necrotizing autoimmune myopathy** (SINAM) → **Seek specialist advice and consider** PCSK9i (NICE TA 393, 394)

YES

Have symptoms resolved?

No → Non-SRM. **Consider other causes**

YES

Has the patient been **symptom free for at least 2 weeks?**

No → Wait for 2 weeks before **rechallenge**

YES

Reassess and **restart** with lower dose / alternative statin (see - '***Statin-based Approaches***')
Offer low or moderate dose of a higher intensity statin (Atorvastatin 10 or 20 mg OD, or Rosuvastatin 5 or 10mg OD)

No recurrence of muscle symptoms
Titrate at 8 weeks intervals to achieve appropriate targets

Recurrence of muscle symptoms
Short time to onset
Symptoms intolerable

Symptoms tolerable
Treatment effective, goals achieved
Patient happy to continue

No → **Consider further options**
(For example add ezetimibe, or give as monotherapy and if needed add bempedoic acid)
see '***Statin-based Approaches***'

If not effective → **Seek specialist advice and consider** PCSK9i (NICE TA 393, 394)

Abbreviations

CK = Creatinine Kinase
CRP = C-Reactive protein
eGFR = Estimated glomerular filtration rate
PMR = Polymyalgia rheumatica
SINAM = Statin induced necrotizing autoimmune myopathy
SRM = Statin related muscle toxicity
ULN = Upper Limit of Normal Range
Vit D = Vitamin D

Introduction

- Statins are the cornerstone for prevention and treatment of cardiovascular (CV) disease with a substantial evidence of reduction of morbidity and mortality. Refer to Lipid Management Pathway and related NICE guidelines (CG181, CG71) for guidance on initiation, titration and monitoring of statin therapy.
- In clinical trials, statins were found to be largely well tolerated (often with a similar adverse effect (AE) profile to placebo), however this is not reflected in clinical practice where up to 75% of people started on a statin will discontinue treatment within 2 years.
- Stopping statin therapy is associated with an increased risk of major CV events and there is growing concern that clinicians are labelling patients as '**statin intolerant**' too quickly. Indeed statin discontinuation is significantly associated with negative media coverage.

Definition of Statin Intolerance

- Intolerance to initial statin therapy is defined by NICE as the presence of clinically significant adverse effects that represent an unacceptable risk to the patient or that may reduce compliance with therapy.
- Other definition: any adverse event (AEs) considered unacceptable by the patient, and/or some laboratory abnormalities, both attributed to statin treatment and leading to its discontinuation.

Statin-associated muscle symptoms (SAMS)

- SAMS are one of the principal reasons for statin non-adherence and/or discontinuation. However, not all such symptoms should lead to a label of 'statin intolerance' as they may not be truly statin related muscle toxicity (SRM) as demonstrated by resolution on de-challenge and recurrence with re-challenge.

Non-Statin related musculoskeletal symptoms (Non SRM)

- If patients report symptoms that are not typical of SRM (e.g. asymmetric distribution, failure to resolve with de-challenge despite normal CK) consider other musculoskeletal disorders, metabolic, degenerative or inflammatory e.g. Vitamin D deficiency, polymyalgia rheumatica. Check Bone profile, Vit D, CRP.

Considerations when starting a statin to reduce risk of SRM

- Check baseline thyroid, liver and renal function, any potential drug interactions, and avoid the highest doses in at risk groups (See "Risk Factors" below).
- Ask the person if they have had persistent generalised unexplained muscle pain, whether associated or not with previous lipid-lowering therapy. If they have, measure CK. If CK levels are > 4x ULN do not start statin - investigation required.
  Do not measure CK if person is asymptomatic.
- Warn patients about AEs, specifically muscle symptoms. 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 CK

Risk factors for SRM and statin intolerance

Endogenous factors

- Female gender
- Advanced age (> 75 yrs)
- Frailty (reduced lean body mass)
- History of muscle disorder or high CK
- Impaired renal or hepatic function
- Personal or family history of intolerance to lipid-lowering therapies.
- Hypothyroidism

Exogenous Factors

- Excessive alcohol intake
- High intensity exercise
- Dehydration
- Drug interactions with statins (including herbal medicines)
- Vitamin D deficiency

Classification of statin related muscle toxicity (SRM)

Alfirevic A. et. al. Clin Pharm Ther. 2014; 96:470-476

SRM	Phenotype	Incidence	Definition
SRM 0	CK elevation <4x ULN	1.5-26%	No muscle symptoms
SRM 1	Myalgia, tolerable	190/100,000 Patient-years; 0.3-33%	Muscle symptoms without CK elevation
SRM 2	Myalgia, intolerable	0.2-2/1,000	Muscle symptoms, CK <4x ULN, complete resolution on dechallenge
SRM 3	Myopathy	5/100,000 Patient-years	CK elevation >4x ULN <10x ULN ± muscle symptoms, complete resolution on dechallenge
SRM 4	Severe myopathy	0.11%	CK elevation >10x ULN <50x ULN, muscle symptoms, complete resolution on dechallenge
SRM 5	Rhabdomyolysis	0.1-8.4/100,000	CK elevation >10x ULN with evidence of renal impairment + muscle symptoms or CK >50x ULN
SRM 6	Autoimmune-mediated necrotizing myositis (SINAM)	~2/million per year	Detection of HMGCR antibodies, HMGCR expression in muscle biopsy showing autoimmune myositis, incomplete resolution on dechallenge

HMGCR = 3-hydroxy-3-methylglutaryl coenzyme A reductase ULN = upper limit of normal

- SRM is a spectrum from myalgia to severe myopathy
- SRM 0 - does not preclude statin therapy, consider reducing starting dose
- SRM 1-3 manage according to pathway
- When SRM4 is suspected, without evidence of impaired renal function, discontinue statin therapy immediately and refer for outpatient assessment. Assess and treat possible contributory factors and re-assess the need for a statin. Intensify lifestyle modifications and consider alternative lipid lowering regimens.
- If rhabdomyolysis (SRM5) is suspected, immediately stop statins, urgently refer to inpatient assessment and management including intravenous rehydration as required to preserve renal function. Do not wait for measurement of urinary myoglobin. Post recovery, manage as for SRM4.
- Statin induced necrotizing autoimmune myositis (SINAM) (SRM6) should be suspected in patients with progressive muscle weakness and ongoing CK elevation despite statin withdrawal. Requires immunosuppressive treatment and avoidance of re-exposure to statins. Re-assess the need for lipid lowering therapy - may be eligible for treatment with PCSK9 inhibitor (NICE TA 393, 394).

Person-centred approach to address statin intolerance

Initial Consultation

- Be aware of "nocebo effect"[1] and "statin reluctance"[2]
- Reinforce healthy lifestyle habits (e.g. exercise, reducing weight)
- Listen to the concerns of each patient.
- Explain LDL-C targets and strategies to lower LDL-C/non-HDL-C
- Discuss options to reduce LDL-C/ non-HDL-C with pros and cons
- Explain the benefits of statins
- Evaluate and identify any risk factors and address (e.g. drug interactions)
- Work with patients to identify and agree best options and next steps

Follow up

- Follow up on agreed plan and address any issues/concern.
- Advise patients to contact you if they experience muscle symptoms
- Ongoing patient education and regular review helps addressing concerns around medicine safety and underline the importance of adherence.

(1) **Nocebo effect** is negative expectations of the patient regarding a treatment leading to reporting more negative effects even if they are prescribed a placebo.

(2) **Statin reluctance** is an attitudinal state of aversion to taking statins (often without prior exposure).

Statin-based approaches to manage muscle symptoms

- Adopt person-centred approach as described above.
- Therapy with a lower dose statin is preferred to no statin
- Apply a repetitive "De-Challenge" - "Re-Challenge" approach to establish if symptoms are caused by a statin(s) and the best statin regimen for each patient.
- Switch to a different statin or re-challenge with the same statin using a lower dose or frequency (intermittent dosages)
- Patients who do not tolerate statins on a daily basis, alternate day or twice-weekly dosing is a good option.
- Rosuvastatin and atorvastatin have longer half-lives, permitting their use on a non-daily regime.
- Adding ezetimibe to a lower dose statin may be better tolerated with robust reduction of LDL-C / non-HDL-C .
- Once a new regime is tolerated, dose / frequency can be up-titrated slowly to achieve LDL-C / non-HDL-C goals with minimal or no muscle complaints.

It is important to note that cardiovascular benefits have not been proven for all the above approaches but any reduction of LDL-C / non-HDL-C is beneficial.

LDL-C lowering options for patients with genuine statin intolerance

- Refer to the AAC Lipid Management Algorithm Click here
- Consider ezetimibe, (NICE TA 385) therapy as per algorithm
- Consider ezetimibe combined with bempedoic acid (NICE TA 694) as per algorithm
- Consider PCSK9i if eligible for treatment according to NICE TA 393, 394

Non-muscle related statin side effects

May vary between different statins. In clinical trials some side effects often associated with statins are not statistically different from placebo.

Most commonly reported: gastrointestinal disturbance and asymptomatic increases in hepatic transaminases (ALT or AST). May affect up to 1 in 10 statin users.

Rarer side effects include: Hepatotoxicity, new onset Type 2 Diabetes (benefits outweigh risk, do not stop statin), Renal insufficiency, proteinuria, Neurocognitive and neurological impairments (no apparent link from RCTs), Intracranial haemorrhage (conflicting evidence, benefit outweigh possible harm), Interstitial lung disease, Pancreatitis, Skin disorders including alopecia, Lupus-like reaction, Sleep disturbance, headache, dizziness, fatigue, depression, sexual dysfunction.

Management: If symptoms appear statin related, consider de-challenge and re-challenge or change to a different statin (e.g. hydrophilic instead of lipophilic).

Liver enzyme abnormalities - minor increases in liver enzymes (<2x ULN) may be seen within the first three months of statin therapy; temporary discontinuation and further assessment is warranted if levels exceed 3x ULN. Several studies have confirmed that the cardiovascular benefits of statin treatment in high-risk populations outweigh the rare adverse effects, such as rhabdomyolysis.

Authors: Dr Rani Khatib & Dr Dermot Neely on behalf of the AAC Clinical Subgroup. June 2021. Review date: June 2022.
Pathway approved by NICE July 2021.

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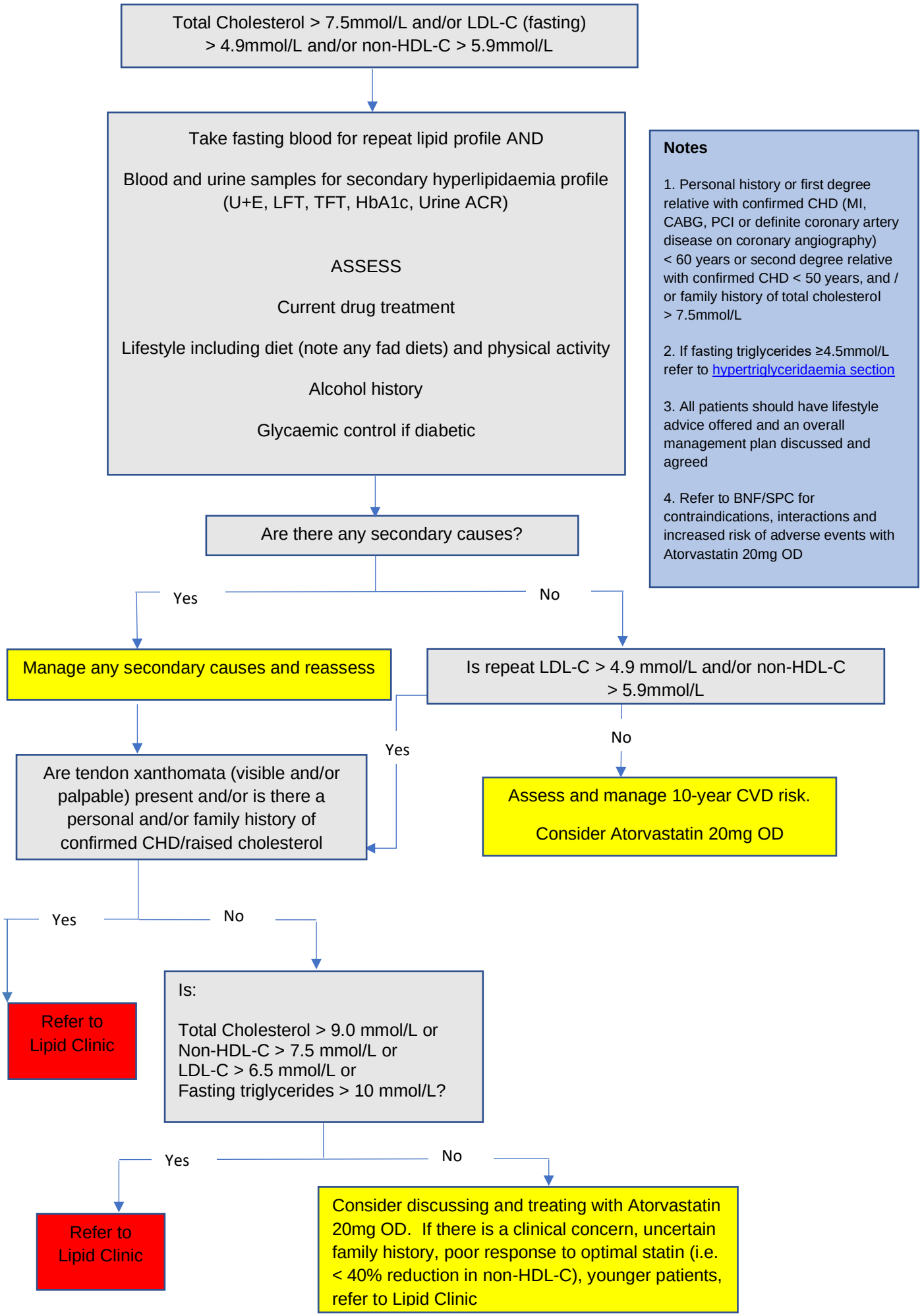
Flow chart for the assessment of severe hypercholesterolaemia



Simon Broome criteria for Familial Hypercholesterolaemia (FH)

Definite Familial Hypercholesterolaemia is defined as:

Total cholesterol > 7.5 mmol/L or LDL-C > 4.9 mmol/L in an adult
Total cholesterol > 6.7 mmol/Lor LDL-C > 4.0 mmol/L in a child (< 16 years)
(Levels either pre-treatment or highest on treatment)

Plus

Tendon Xanthomas in
- patient
- 1st degree relative (parent, sibling or child) or
- 2nd degree relative (grandparent, uncle or aunt)

Or

DNA-based evidence of a variant causing FH

Possible Familial Hypercholesterolaemia is defined as:

Total cholesterol > 7.5 mmol/L or LDL-C > 4.9 mmol/L in an adult
Total cholesterol > 6.7 mmol/L or LDL-C > 4.0 mmol/L in a child (< 16 years)
(levels either pre-treatment or highest on treatment)

Plus

Family history of premature myocardial infarction (one or the other):
- < 60 years of age in 1st degree relative
- < 50 years of age in 2nd degree relative

Or

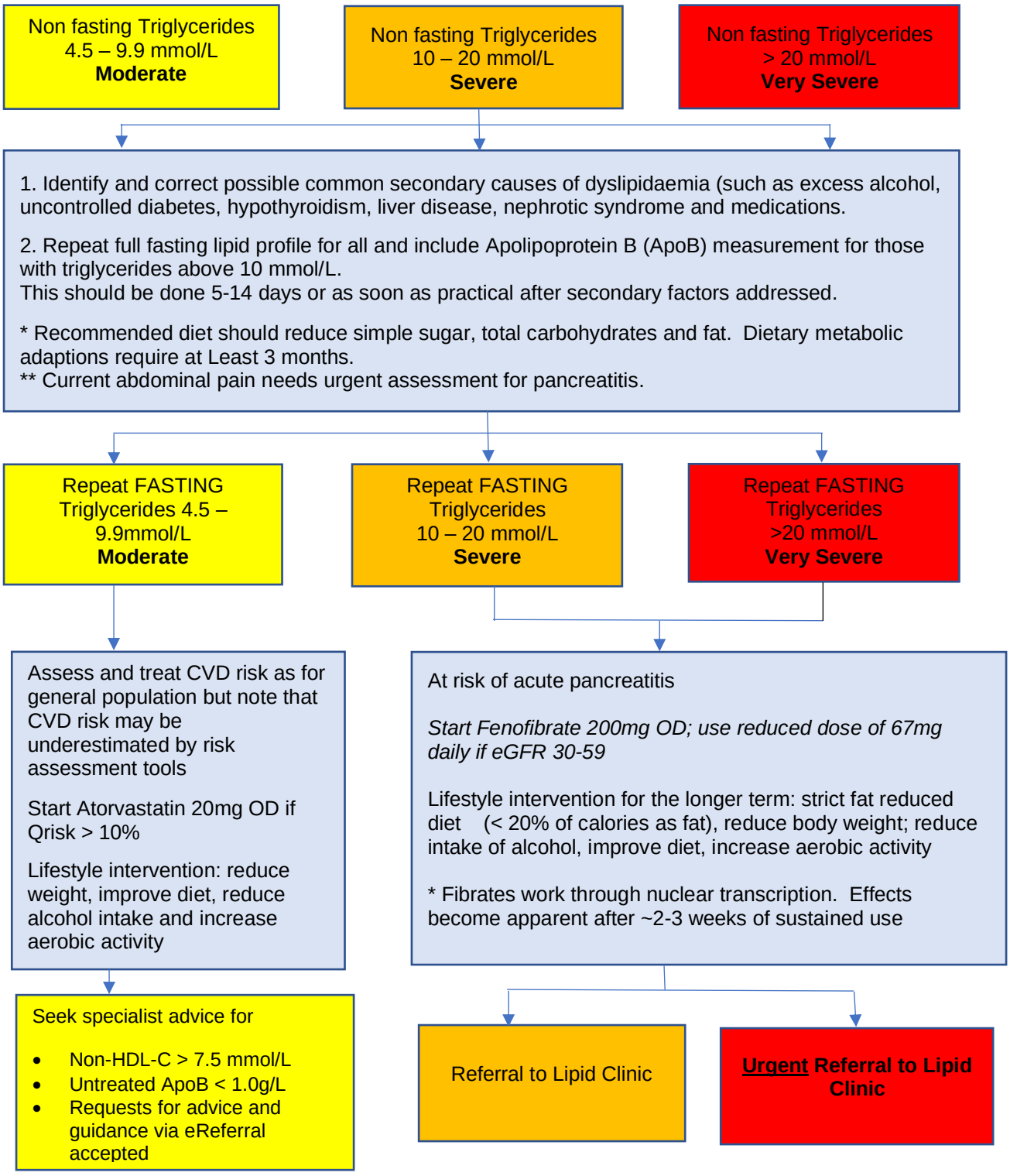
Family history of raised total cholesterol:
- > 7.5 mmol/L in adult 1st or 2nd degree relative or
- > 6.7 mmol/L in child or sibling < 16 years.

- **Do not** use Simon Broome LDL-C criteria for relatives of index individuals with clinical diagnosis of Familial Hypercholesterolaemia because this will result in under diagnosis.
- **Do not** use CVD risk estimation tools as people with Familial Hypercholesterolaemia are already at a high risk of premature coronary heart disease.

Homozygous Familial Hypercholesterolaemia

Consider a clinical diagnosis of homozygous familial hypercholesterolaemia in:
- adults with an LDL-C > 13 mmol/L
- children/young people with an LDL-C > 11 mmol/L

Flow chart for the assessment of Hypertriglyceridaemia



Secondary causes of Hypertriglyceridaemia

- Obesity
- Metabolic syndrome
- Diet with high fat or calories
- Excess alcohol consumption
- Diabetes Mellitus (mainly Type 2)
- Hypothyroidism
- Renal disease (proteinuria, uraemia or glomerulonephritis)
- Pregnancy (particularly in the third trimester
- Paraproteinaemia
- Systemic lupus erythematosus
- Medications (including corticosteroids, oral estrogen, Tamoxifen, thiazides, non-cardioselective beta-blockers and bile acid sequestrants, Cyclophosphamide, L-asparaginase, protease inhibitors and second-generation antipsychotic agents such as Clozapine and Olanzapine)

Lipid Management in Pregnancy

General Advice for Familial Hypercholesterolaemia (FH) / Lipid Patient Planning Pregnancy

1. Risks for future pregnancy should be discussed for women and girls when lipid lowering therapy is first considered, and should be discussed as part of annual review.

2. Discontinue lipid lowering therapy for 3 months before attempting to conceive.

3. Patient who conceive on lipid lowering therapy should stop therapy immediately and be offered urgent referral for foetal assessment.

4. Dietary advice should be offered as part of pre-conception planning. Pregnant women should limit intake of oily fish to no more than 2 portions a week and avoid shark, marlin and swordfish.

5. Commence Folic Acid 400 mcg OD prior to conception and continue until week 12 of pregnancy (give 5 mg once daily if high risk high of conceiving child with neural tube defect).

6. Do not routinely use aspirin. Aspirin should be commenced after first dating scan if risk of pre-eclampsia (NICE NG 133; see below).

7. Discuss smoking cessation.

8. Shared care arrangements for pregnancy, including expertise in cardiology and obstetrics should be made. Care should include an assessment of coronary heart disease risk; assessment for aortic stenosis is essential in women Homozygous FH.

9. Do not monitor lipid profile during pregnancy.

10. Discuss breast feeding plans – Statins and Ezetimibe can be re-started once breast feeding completed. Check Lipid profile after 6-8 weeks.

11. Infants should ideally have a buccal swab to screen for FH at 2 years. Earlier genetic testing should be considered if risk of Homozygous FH.

Women are considered to be at high risk of pre-eclampsia if they have:	
1 or more High Risk factors:	2 or more moderate risk factors :
Hypertension during previous pregnancy	First Pregnancy
CKD	Age 40 or older
Chronic Hypertension	Pregnancy interval > 10 yrs.
Type 1 or Type 2 Diabetes	BMI 35 kg/m^2 at first visit
Autoimmune disease (SLE, Antiphospholipid syndrome)	Family history of pre-eclampsia
	Multiple Pregnancy

Statins

Statins are contraindicated in pregnancy.

Advise women of childbearing potential of potential teratogenic risks and to stop taking statins if pregnancy a possibility.

Women planning pregnancy should stop statins 3 months before they attempt to conceive and not restart them until breast feeding is finished.

Ezetimibe

Ezetimibe monotherapy should not routinely be given to pregnant women and used only if clearly necessary. There is no clinical data available on the use of Ezetimibe during pregnancy.

Ezetimibe should not be given during breast feeding.

PCSK9 Inhibitors

Alirocumab should be avoided in pregnancy unless clinical conditional requires treatment. Maternal toxicity demonstrated in animal studies.

Evolocumab should be avoided in pregnancy unless treatments essential; limited information available.

Fibrates

Fibrates should not be used routinely for the prevention of cardiovascular disease.

Fibrates should be avoided in pregnancy. Embryo toxicity demonstrated in animal studies with Fenofibrate / Gemfibrozil.

Assessment of potential Familial Hypercholesterolaemia case in a child

Child identified as possible FH due to known FH gene variant in family or unknown if this family carries FH variant. Contact FH genetics nurses for help either via Advice and Guidance under FH service referrals or 0191 241 8828. They will help direct appropriate evaluation.

Child identified as potential proband
No opportunity to test adult relative OR
Adult relative's test inconclusive OR
Child tested for some other reason

Take family history, physical examination
Non -fasted lipid profile, Lipoprotein (a), if not already done

Bloods normal → Discharge

Bloods abnormal

Lifestyle advice
After 2 months
Repeat lipid profile (fasted if TGs not normal on initial sample)
TSH, free T4, HbA1c, LFT, CK, Lipoprotein (a) if not already done

TGs ≥ 2.5 mmol/L → Measure Apolipoprotein B
Consider discussion in regional MDT

TGs < 2.5 mmol/L

LDL-C over 4.0mmol/L → Activate initial genetic testing

LDL-C over 3.5 mmol/L and positive family history → Activate initial genetic testing

Pathogenic variant found → Variant Positive
Age appropriate treatment If LDL-C > 3.5mmol/L
Cascade test family

Pathogenic variant negative → Repeat lipid profile if not already done
If remains abnormal follow up and consider screening family members with lipid profiles,
Consider discussion at regional MDT

LDL-C 3.0-3.5 or Lp(a) > 200nmol/L → Follow up, repeat lipids periodically. If LDL-C (or non-HDL-C equivalent remains > 3.1 and family history suggestive of FH, consider genetic testing or discussion at regional MDT

LDL-C < 3.0 & Lp(a) <90nmol/L → Discharge

LDL-C < 3.0 & Lp(a) 90-200nmol/L → Discharge with advice to seek reassessment of other cardiovascular risk factors as an adult

Give standard letter

Child identified as having pathogenic FH variant genetic cascade testing → Refer to one of 3 Paediatric Lipid Clinics

Dr Mark Anderson, Great North Children's Hospital for Newcastle, Northumberland, Gateshead, Cumbria

Dr Neil Hopper, Sunderland Royal Hospital for Sunderland, South Tyneside and County Durham

Dr Mark Burns, James Cook University hospital for Teesside

TG – Triglycerides
Lp(a) - Lipoprotein (a)

Can be done in primary care/general paediatrics or paediatric lipid clinic

Paediatric lipid clinic

Common Drug Interactions

For full information refer to British National Formulary www.bnf.org.uk

	Severe – Avoid	Caution/Adjust Dose/Monitor
Anti-Biotics		
Clarithromycin Erythromycin Daptomycin Fusidic Acid Rifampicin Tedizolid	Atorvastatin/Simvastatin Simvastatin All Statins Atorvastatin / Fluvastatin / Rosuvastatin	Pravastatin Atorvastatin/Pravastatin All Statins / Fibrates Atorvastatin/Simvastatin
Anti-Fungals		
Fluconazole Isavuconazole Itraconazole Ketoconazole Miconazole Posaconazole Voriconazole	 Atorvastatin / Simvastatin Atorvastatin / Simvastatin Simvastatin Atorvastatin / Simvastatin Atorvastatin / Simvastatin	Atorvastatin / Fluvastatin / Simvastatin Atorvastatin/Fluvastatin/Rosuvastatin/Simvastatin Atorvastatin/Fluvastatin
Drugs used in HIV		
Multiple interactions – seek specialist advice; Consult www.hiv-druginteractions.org		
Anti-Coagulants		
Coumarins / Warfarin		All Fibrates / Fluvastatin / Rosuvastatin
Anti-Arrhythmics		
Amiodarone Dronedarone		Atorvastatin / Fluvastatin / Simvastatin Atorvastatin / Rosuvastatin / Simvastatin
Calcium Channel Blockers		
Amlodipine Diltiazem Verapamil		Simvastatin Atorvastatin / Simvastatin Atorvastatin / Simvastatin
Anti-Platelet Agents		
Clopidogrel Ticagrelor		Rosuvastatin Simvastatin
Anti-Epileptics		
Carbamazepine Eslicarbazepine Phenytoin		All Statins Atorvastatin / Simvastatin Atorvastatin / Simvastatin
Disease Modifying Drugs for Rheumatoid Arthritis		
Leflunomide Teriflunomide		All Statins All Statins
IL-6 Receptor Antagonists		
Sarilumab Tocilizumab		Atorvastatin / Simvastatin Atorvastatin / Simvastatin
Lipid Lowering Agents		
Ezetimibe Fibrates Lomitapide Nicotinic Acid Bempedoic Acid		All Statins / Fibrates All Statins / Ezetimibe Atorvastatin / Simvastatin All Statins All Statins

Androgen Receptor Inhibitors		
Apalutamiide	Simvastatin	Rosuvastatin
Darolutamide	Atorvastatin / Fluvastatin / Rosuvastatin	Pravastatin / Simvastatin
Enzalutamide		Simvastatin
Anti-Neoplastics		
Mitotane		Simvastatin
Venetoclax		All Statins
Protein Kinase Inhibitors		
Crizotinib		Atorvastatin/ Simvastatin
Fostamatinib	Rosuvastatin	Simvastatin
Idelalisib	Atorvastatin/ Simvastatin	
Imatinib		Atorvastatin/ Simvastatin
Nilotinib		Atorvastatin/ Simvastatin
Pazopanib		Atorvastatin/Pravastatin/Rosuvastatin/Simvastatin
Regorafenib		Atorvastatin / Fluvastatin / Rosuvastatin
Ribociclib	Simvastatin	Pravastatin / Rosuvastatin
Tivozanib		Rosuvastatin
Neurokinin Receptor Antagonists		
Aprepitant		Atorvastatin / Simvastatin
Netupitant		Atorvastatin / Simvastatin
Rolapitant		Rosuvastatin
Others		
Antacids		Rosuvastatin
Ciclosporin	Atorvastatin / Rosuvastatin / Simvastatin	Fluvastatin/Pravastatin/Ezetime/Fibrates
Colchicine		All Statins / Fibrates
Danazol	Simvastatin	Atorvastatin
Eltrombopag		All Statins
Glibenclamibe		All Fibrates / Fluvastatin
Grapefruit Juice	Simvastatin	Atorvastatin
Ranolazine		Atorvastatin / Simvastatin
Sacubitril + Valsartan		All Statins
St John’s Wort		Atorvastatin / Simvastatin
Ursodeoxycholic acid	All Fibrates	

Lipid Clinic referral criteria

All lipid clinics within the region offer Advice & Guidance and Electronic Booking System referrals.

For more general enquiries about Familial Hypercholesterolaemia (FH) Advice & Guidance can be accessed from the Familial Hypercholesterolaemia Specialist Nurses.

Refer to lipid clinic if:

- Clinical diagnosis of Familial Hypercholesterolaemia according to Simon Broome criteria.

- Relatives of patients with FH who may require genetic screening.

- Children with FH (Paediatric Clinic).

- Total cholesterol > 9 mmol/L or non-HDL-C > 7.5 mmol/L even if absence of first degree family history of premature heart disease.

- Triglycerides > 10 mmol/L (not due to alcohol or poor glycaemia control).
  – **refer urgently if triglycerides > 20 mmol/L**

- Patients with other inherited disorders of lipid metabolism including Familial Combined Hyperlipidaemia (FCH), Familial Hypertriglyceridaemia and Remnant Dyslipidaemia.

- Patients with existing CVD and non-HDL-C > 4 mmol/L due to intolerance of Statins/Ezetimibe.

- Patients who fulfil NICE TA 393 / 394 criteria for PCSK9i therapy (See table for thresholds in green section under 'Specialist Services')

Lipoprotein (a)

Lipoprotein (a) is a modified form of LDL (bad) cholesterol. It is a major independent risk factor for cardiovascular disease (CVD) and calcific aortic valve stenosis. It promotes atherosclerosis and has a pro-thrombotic effect.

Lipoprotein (a) level (nmol/L)	Risk
< 32	No change
32 - 90	Minor CVD risk
91-200	Moderate CVD risk
201-400	High CVD risk
> 400	Very High CVD risk

Lipoprotein (a) levels are predominantly genetically determined and therefore raised levels can run in families. The genetic inheritance pattern is autosomal co-dominant and may be more apparent at higher concentrations of lipoprotein (a). However the presence of a raised level of lipoprotein (a) does not exclude the possibility of an underlying genetic lipid disorder such as Familial Hypercholesterolaemia (FH) or Familial Combined Hyperlipidaemia (FCH) as it is possible for patients with these conditions to also have a raised lipoprotein (a) which will confer an additional risk of CVD.

Secondary causes of a raised lipoprotein (a) level;

- Chronic Kidney Disease
- Proteinuria
- Hypothyroidism
- Chronic inflammatory disease (eg Rheumatoid Arthritis, SLE, Psoriasis)

Levels may be reduced in liver disease and in postmenopausal women on HRT.

Lipoprotein (a) levels are generally 2 x higher in patients of African descent compared with Caucasian, Hispanic and certain Asian populations, with South Asian patients tending to have intermediate levels.

Measurement of lipoprotein (a)

Measurement of lipoprotein (a) should be considered in the following patients:

1. Personal or Family history of premature CVD (< 60 yrs of age)
2. 1st degree relative with raised Lipoprotein (a) (> 200 nmol/L)
3. Known genetic dyslipidaemia e.g. FH, FCH or Remnant Dyslipidaemia
4. Calcific Aortic valve stenosis
5. Borderline 10 yr CVD risk (<15%)

No fasting prior to sampling or repeat measurement is required.

Management of patients with raised Lipoprotein (a)

There are no specific therapies currently available for patients with raised levels of lipoprotein (a), although these are in development.

Management therefore needs to focus on

1. Addressing modifiable cardiovascular risk factors such as :-
    i. non-HDL Cholesterol
    ii. Blood pressure

2. Lifestyle issues such as
    i. Diet
    ii. Exercise
    iii. Weight loss
    iv. Smoking
    v. Alcohol intake.

In patients with borderline QRisk scores , lipoprotein(a) > 90 nmol/L should be considered together with other factors that predispose to premature CVD but are not included in calculated risk scores.

Patients with a lipoprotein (a) of > 200 nmol/L should have a non-HDL-C target of < 2.5 mmol/L. They should also be advised that first degree relatives should have a non fasting lipid profile and lipoprotein (a) measured.

The routine use of Aspirin therapy in patients with raised lipoprotein (a) is not recommended, unless they have confirmed CVD or have been commenced on Aspirin by their Lipid Specialist.

Lipoprotein (a) only needs to be measured once as concentrations are generally stable throughout life. Lipoprotein (a) values are generally unaffected by Lipid lowering therapies.

Lipoprotein (a) is distinct from Apolipoprotein A1, which is a major component of HDL (good) cholesterol.

Lipid Clinics in the North East and North Cumbria Cardiovascular Network

Clinic address	Consultant(s)
Adult Clinics	
Lipid and Metabolic Clinic Royal Victoria Infirmary Queen Victoria Road Newcastle Upon Tyne Tyne and Wear NE1 4LP	Dr Ahai Luvai Dr Fiona Jenkinson Dr Purba Banerjee 0191 282 4301
Lipid Clinic Sunderland Royal Hospital Kayll Road Sunderland Tyne and Wear SR4 7TP	Dr Peter Carey 0191 565 6256 Secretary Ext 47449
Healthy Hearts Lipid Clinic Morpeth NHS Centre Dark Lane Morpeth Northumberland NE61 1JY	Dr Stewart Pattman 0191 293 2546
Healthy Hearts Lipid Clinic Hexham General Hospital Northumberland NE46 1QJ	Dr Stewart Pattman 0191 293 2546
Healthy Hearts Lipid Clinic Pathology Department Rake Lane North Shields Tyne and Wear NE29 8NH	Dr Stewart Pattman 0191 293 2546
Lipid Clinic Shotley Bridge Community Hospital Consett County Durham DH8 0NB	Dr Shafie Kamaruddin Dr Srikanth Mada Dr Paul Peter Dr Azmi Mohammed 0191 333 2333
Lipid Clinic University Hospital of North Durham North Road Durham County Durham DH1 5TW	Dr Shafie Kamaruddin Dr Srikanth Mada Dr Paul Peter Dr Azmi Mohammed 0191 333 2333

Lipid Clinic Queen Elizabeth Hospital Queen Elizabeth Avenue, Sheriff Hill, Gateshead Tyne and Wear NE9 6SX	Dr Jola Weaver 0191 445 2181
Trinity Square Diabetes Clinic Trinity Square Gateshead Tyne and Wear NE8 1AG	Dr Jola Weaver 0191 497 1530
Lipid Clinic Bishop Auckland Hospital Cockton Hill Road Bishop Auckland County Durham DL14 6AD	Dr Shafie Kamaruddin Dr Srikanth Mada Dr Paul Peter Dr Azmi Mohammed 01388 455 000
Specialist Lipid and Metabolic Clinic James Cook University Hospital Marton Road Middlesborough Cleveland TS4 3BW	Dr Arutchelvam Vijayaraman Dr Isaac Oluwatowoju 01642 850 850
Lipid and Metabolic Clinic James Cook University Hospital Marton Road Middlesborough Cleveland TS4 3BW	Dr Isaac Oluwatowoju 01642 855 106
Lipid Clinic at The University Hospital of Hartlepool University Hospital of North Tees Hardwick Rd, Hardwick, Stockton-on-Tees S19 8PE	Dr Harish Datta 01642 624 898
Lipid and Metabolic Clinic Cumberland Infirmary Newtown Road Carlisle Cumbria CA2 7HY	Prof Olusegun Mojiminiyi 01228 814 028
Lipid and Metabolic Clinic West Cumberland Hospital Hensingham Whitehaven Cumbria CA28 8JG	Prof Olusegun Mojiminiyi 01946 523428

Paediatric Clinics	
Paediatric Lipid Clinic Royal Victoria Infirmary Queen Victoria Road Newcastle upon Tyne NE1 4LP	Dr Mark Anderson 0191 233 6161
Paediatric Lipid Clinic City Hospitals Sunderland Kayll Road Sunderland SR4 7TP	 Dr Neil Hopper 0191 565 6256
Paediatric Lipid Clinic James Cook University Hospital Marton Road Middlesborough Cleveland TS4 3BW	Dr Mark Burns 01642 850 850
Familial Hypercholesterolaemia Specialist Nurses	
Institute of Genetic Medicine International Centre for Life Central Parkway Newcastle upon Tyne NE1 3BZ	Susan Musson Aimee Potter 0191 2418828

Membership of the NEELI Clinical Guidelines Steering group

- Dr Peter Carey, Consultant Endocrinologist, South Tyneside and Sunderland Hospitals NHS Foundation Trust and Chair of Northern England Clinical Networks Lipids Specialist Advisory Network
- Dr Ahai Luvai, Consultant Chemical Pathologist, Newcastle Hospitals NHS Foundation Trust
- Dr Neil Hopper, Consultant Paediatrician, South Tyneside and Sunderland Hospitals NHS Foundation Trust
- Susan Musson, Familial Hypercholesterolaemia Specialist Nurse, Northern Genetics Service, Newcastle upon Tyne NHS Foundation Trust
- Aimee Potter, Familial Hypercholesterolaemia Specialist Nurse, Northern Genetics Service, Newcastle upon Tyne NHS Foundation Trust
- Dr Isaac Oluwatowoju, Consultant Chemical Pathologist, South Tees NHS Foundation Trust
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- Susan Turner, Prescribing Pharmacist and Professional Secretary for Pharmacy Committee
- Dr Dermot Neely, Specialist Adviser on Lipids, Academic Health Science Network, North East and North Cumbria

With thanks to the following colleagues for their input and expertise regarding lipid management in pregnancy

- Dr Shafie Kamaruddin, Consultant Endocrinologist, County Durham and Darlington NHS Foundation Trust
- Dr Dermot Neely, Consultant in Clinical Biochemistry and Metabolic Medicine, Newcastle upon Tyne
- Dr Aarti Ullal, Consultant in Obstetrics and Gynaecology, South Tyneside and Sunderland NHS Foundation Trust
- Dr Alexandra Thompson, Consultant Cardiologist, Newcastle upon Tyne Hospitals
- Dr Shahid Junejo, Consultant Cardiologist STS

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- Dr Robin Mitchell, Clinical Director, Northern England Clinical Networks
- Elaine Stephenson, Clinical Networks Delivery Manager, Northern England Clinical Networks
- Karen Pellegrino, Business Support Assistant, Northern England Clinical Networks

Approval of the guideline

This guideline was endorsed by the Local Pharmacy Committees on the following dates

- Northumberland, Tyne & Wear, Cumbria -13th October 2020
- Sunderland South Tyneside -7th October 2020
- County Durham and Darlington -12th November 2020

Declared conflicts of interest

AL has received conference fees and travel from Amgen and Sanofi, is an investigator for clinical trials sponsored by Novartis, Evidera and Regeneron, has received speaker honoraria from Amgen, Sanofi and MSD and acts on advisory boards for Sanofi, Akcea, MSD and Novaritis. PC is the Clinical Lead for the Lipid Specialists Advisory Group and has received conference fees from Sanofi, Lilly and Novo Nordisk, is on advisory boards for Amgen and Novartis, has received speaker fees from Lilly and Sanofi and has undertaken research involving Sanofi and Novartis products. SJP has received conference fees and travel from Sanofi, is involved in study work sponsored by Diiachi Sankyo and has received funding for NHSE AAC rapid uptake product work involving Sanofi and Amgen. RDGN has speaker honoraria previously from Novartis, Amgen and Sanofi and acts as a trustee for the NHSE AAC rapid uptake product work involving Sanofi and Amgen. No DOI reported by SK, SM, IO, HD.

- **Date of review**

1 April 2023 to align with NICE review of CG 181.

Should significant further changes occur to the embedded NHS England AAC documents (in green and red sections) following their review dates, this document will be reviewed in advance of this above review date.

- **Contact Person for enquiries**

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- **Version number & list of Amendments**

Version February 2022.1:

GREEN SECTION: Amended to include updated AAC National Guidance for lipid management pathway (November 2021) to incorporate Bempedoic acid and Inclisiran

RED SECTION: Amended to include updated AAC Statin intolerance pathway (June 2021) to incorporate new therapeutic options

YELLOW SECTION: Amended to advise FASTING lipid profile as follow up investigation

PURPLE SECTION: Minor amendment with removal of arrows, no pathway change.