Lipid Management: Medicines Optimisation Pathways

Developed by SEL Cardiovascular Medicines Working Group on behalf of the SEL Integrated Medicines Optimisation Committee (IMOC) and following guidance from the National Institute for Health and Care Excellence (NICE), NHS England/Accelerated Access Collaborative (AAC) and UCL Partners

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Contents

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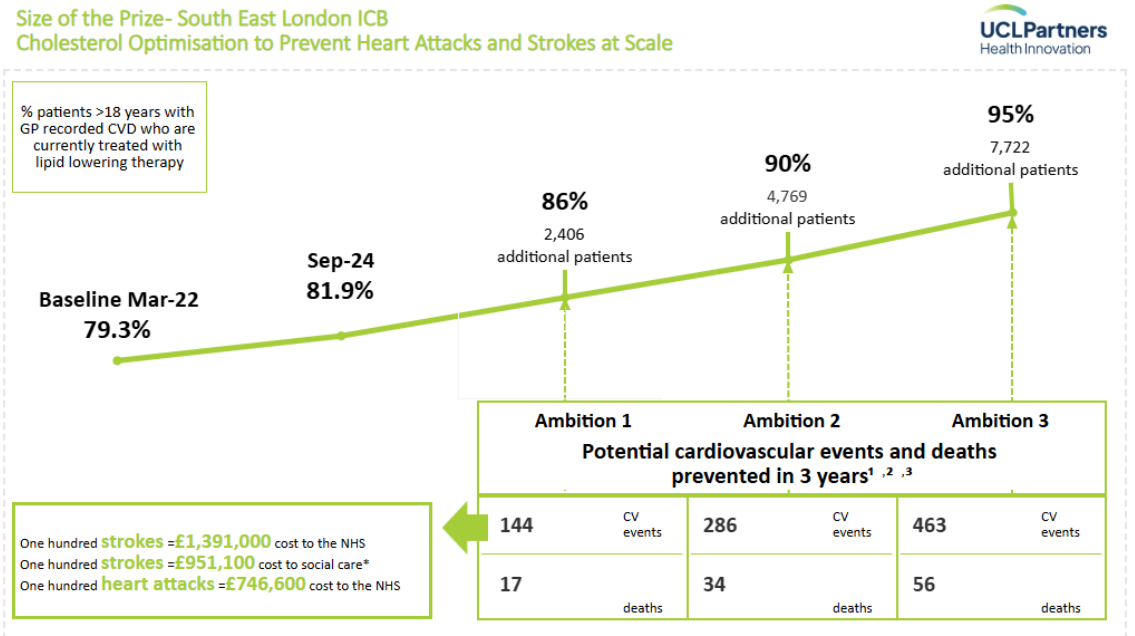
Why is Lipid Management Important?

- High cholesterol causes cardiovascular disease and is associated with an increased risk of cardiovascular death.[1]
- People with high cholesterol who also have other risk factors (e.g. high blood pressure, diabetes, smoking) are at significantly greater risk of CVD and have most to gain from a reduction in cholesterol. **Every 1mmol/l reduction in low-density lipoproteins (LDL) cholesterol reduces risk of a cardiovascular event by 25%.**[2]
- Lifestyle change is important to reduce cardiovascular risk. Where this is ineffective or in people at highest risk (e.g. pre-existing CVD or familial hypercholesterolaemia (FH), drug therapy with statins and other medications is very effective.
- Familial Hypercholesterolaemia (FH) is high-risk but very treatable. Half of men with FH will have a heart attack or stroke before age 50 and a third of women before age 60. Statins are highly effective at reducing this risk.[3]
- One in six patients with CVD are not receiving lipid lowering therapy, large numbers of people are not taking the recommended dose or intensity statins. Optimising treatment in these patients will prevent many more heart attacks and strokes.



For CVDP003CHOL: Patients with no GP recorded CVD and a GP recorded QRISK score of 20% or more, who are currently treated with lipid lowering therapy:

- NHS South East London Integrated Care Board achievement (June 2024) = 61% (national ambition 65%*).
- At least 2,547 people at high risk of a cardiovascular event would need to be treated with lipid lowering therapy to meet the national ambition

For CVDP012CHOL: Patients with GP recorded CVD (narrow definition), whose most recent blood cholesterol level is LDL-cholesterol less than or equal to 2.0 mmol/l or non-HDL cholesterol less than or equal to 2.6 mmol/l, in the preceding 12 months:

- NHS South East London Integrated Care Board achievement (June 2024) = 38%
- At least 36,215 people with known CVD have not achieved recommended lipid-lowering levels

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Based on a pathway developed by: UCLPartners

Lipid Optimisation Pathway for Patients with High Cardiovascular Risk – Primary Prevention

NHS

Review and re-enforce lifestyle and diet measures

Is patient on high intensity statin (HIS)? (atorvastatin 20mg or equivalent)

Yes

No

Initiate atorvastatin 20mg daily (or rosuvastatin 10mg daily)

After 3 months - has non-HDL-C reduced by 40% or more from baseline?[1]

Yes

No

Check adherence and lifestyle measures

Consider titrating statin up to atorvastatin 80mg or equivalent taking into account patient preferences, co-morbidities, polypharmacy, frailty and life expectancy

If non-HDL cholesterol has not fallen by 40% or more from baseline, consider adding ezetimibe 10mg daily

If statin intolerant (trialled 2 or more statins) **– offer ezetimibe (SPC).** Reassess within three months and, if not achieving target, **consider switching to bempedoic acid with ezetimibe tablets▼ (SPC)**[1]

Review annually, assessing adherence to drugs, diet and lifestyle

Lipid lowering therapy should be offered to all patients with a QRISK ≥ 10% after addressing lifestyle modification.[4]

Patients with the following conditions are high CVD risk and **require consideration** for a high intensity statin (HIS) regardless of QRISK: **familial hypercholesterolaemia** (FH), **type 1 diabetes mellitus** (T1DM), **chronic kidney disease** (CKD) and/or albuminuria.

Offer HIS to patients with T1DM and age> 40 years or patients with T1DM >10 years or nephropathy or with other CVD risk factors NICENG238

Offer HIS to patients with Type 2 DM with CV risk ≥ 10% and to **all patients with CKD**

Consider additional CVD risk factors, if present, together with QRISK score

People living with HIV (PLWH)

All people living with HIV aged 40 years or older should be offered a statin for primary prevention of CVD irrespective of lipid profile or estimated CVD risk[5].

Flowchart & dosage guidance of lipid - lowering management and HIV specialist contact details can be found here

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Lipid Optimisation Pathway for Patients with Established Cardiovascular Disease - Secondary Prevention

NHS

Is the patient on high dose, high intensity statin (HIS)?
(atorvastatin 80mg or equivalent)

Yes → **Review within 4 to 12 weeks**
Is LDL-C ≤ 2mmol/L or non-HDL ≤ 2.6mmol/L?[1]

Yes → **Consider adding ezetimibe (SPC) 10mg daily to maximum tolerated statin to reduce CV risk, even where the lipid target has been achieved.[1]**

No → **Initiate / increase to high dose HIS if possible**
and re-enforce lifestyle and diet measures

No → **Address any adherence issues and reinforce lifestyle measures[1]**
Consider intensifying therapy

Consider ezetimibe (SPC) 10mg daily. Reassess within three months.

Assess eligibility for injectable therapies and seek Advice & Guidance (A&G)*:

- Inclisiran▼ (SPC) - if LDL-C ≥ 2.6mmol/L
  Inclisiran initiation checklist
  OR
- **Refer to lipid clinic for PCSK9i (mAB)[6,7]** if LDL-C > 4mmol/L (or > 3.5mmol/L if recurrent events)

If statin intolerant – offer ezetimibe (SPC). Reassess within 2 to 3 months and, if not achieving target, **consider bempedoic acid with ezetimibe tablets ▼(SPC) or injectable therapies** in line with eligibility criteria.[1]

Check fasting triglyceride levels & manage

At any point consider icosapent ethyl▼(SPC) in addition to statins +/- other lipid lowering therapies **if fasting triglycerides ≥1.7 mmol/litre AND LDL > 1.04 mmol/litre and ≤2.6 mmol/litre.**

Review annually, assessing treatment to target, adherence to drugs and offering support for diet and lifestyle measures

Lipid lowering therapy should be offered to all patients with established CVD[1]

High Intensity Statin (HIS) for secondary prevention	
Atorvastatin	80mg
Rosuvastatin	20mg – 40mg (please note for rosuvastatin 40mg specialist supervision is recommended when this dose is initiated)

Dose may be limited, for example if:

- CKD: eGFR<60ml/min –recommended starting dose - atorvastatin 20mg
- Drug interactions
- Drug intolerance
- Older age / frailty

Use shared-decision making and incorporate patient preference in treatment and care decisions.

Women of childbearing age - as a precaution, most women are advised to stop taking statins for three months before trying to conceive, and during pregnancy. Refer to maternal medicine or lipid consultants for advice & guidance where appropriate

***Where an individual qualifies for injectable therapies, as per NICE technology appraisals, consider these in preference to ezetimibe to prevent lipid levels being lowered but remaining above the LDL-C target and below thresholds for initiating injectable therapies**

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Statin Intolerance Pathway

Statin intolerance is defined as the presence of clinically significant adverse effects that represent an unacceptable risk to the patient or that may reduce adherence to therapy (see AAC pathway)

Discuss with the patient if signs and symptoms are statin intolerance or due to a statin reluctance/non-adherence. *Consider that a statin at any dose reduces CV risk* - if a patient cannot tolerate a high intensity statin (HIS), aim to treat with a maximum tolerated dose of a statin, but if symptoms persist consider alternative options/lipid clinic referral.

↓

For Statin Related Muscle (SRM) symptoms: symmetrical pain/weakness in large proximal muscle groups, worsened by exercise. Measure creatine kinase (CK). See here for muscle symptoms pathway.

↓

If CK normalises and symptoms have resolved for at least 2 weeks, then rechallenge: Offer a low/moderate dose of HIS e.g. atorvastatin 10 - 20mg daily or rosuvastatin 5 - 10mg daily. Please note: Non-standard dosing may be recommended by specialist clinics e.g. rosuvastatin 5mg weekly or three times a week (off label use but accepted practice).

↓

If tolerating ezetimibe (SPC) but not achieving lipid lowering targets: consider inclisiran▼ (SPC) following specialist advice if for secondary prevention or consider initiating bempedoic acid▼ 180mg daily (SPC).

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Shared Decision-Making Resources

NHS

Benefits per 10,000 people taking statin for 5 years	Events avoided
Secondary Prevention: Major CV events* avoided in patients with pre-existing CVD & a 2mmol/L reduction in LDL	1,000
Primary Prevention: Major CV events* avoided in patients with no pre-existing CVD & a 2mmol/L reduction in LDL	500

*Major CV events = CV death, non-fatal myocardial infarction and non-fatal stroke

Adverse events per 10,000 people taking statin for 5 years	Adverse events
Myopathy	5
Haemorrhagic Strokes (NICE CKS) The recommendation to avoid use of statins for secondary prevention in people with a history of intracerebral haemorrhage has been removed and information added to the basis to explain this change, based on a large trial which demonstrated no difference in adverse impact. The topic was also aligned with the recommendations contained in the updated NICE guideline [NG236])	5-10
Diabetes Cases	50-100

Shared decision-making resources:

- **BHF information on statins**
- **Heart UK: Information on statins**
- **NICE shared decision-making guide**
- **Statins - side effects**

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Muscle Symptoms Pathway

NHS

Muscle Symptoms - pain, tenderness, weakness

Measure CK

Exclude other possible causes e.g. ethnicity, rigorous exercise, physiological, infection, recent trauma, new or worsening peripheral arterial disease, drug or alcohol addiction. Stop statin if intolerable symptoms, or clinical concern

CK > 50 x ULN

Consider rhabdomyolysis. Stop statin and seek specialist advice urgently

Seek specialist advice if CK not normalised

CK >10-50 ULN

Check renal function

Renal function deteriorating?

Yes

No

CK 5-10 ULN

Discuss with patient. Continue statin and review at 2 weeks. Consider lower dose or alternative statin

CK < 5 x ULN

Reassure patients that symptoms are unlikely to be due to statin and explore other possible causes

Intolerable symptoms

Stop statin for 4-6 weeks.
2 weeks after symptoms resolved and CK normalised,
restart statin at lower dose
(Consider low dose rosuvastatin if previously on atorvastatin)

Titrate to higher dose if tolerated.

If recurrence of symptoms - Consider ezetimibe (SPC) +/- bempedoic acid ▼ (SPC), inclisiran▼ (SPC) or PCSK9i (mAB) in line with eligibility criteria

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Abnormal Liver Function Test (LFT) Pathway

NHS

Abnormal LFTs

If transaminase is raised ≥3 x ULN

Stop statin, repeat LFTs after one month and restart once LFTs normalise.
Consider rosuvastatin if previously on atorvastatin.
Seek Advice & Guidance (A&G) from specialist if patient is already on rosuvastatin

If transaminase is raised <3 x ULN

Continue and repeat after one month – if result remains <3 x ULN – continue and repeat at 6 months.

Consider other causes of abnormal LFT – alcohol, fatty liver, cirrhosis, cancer, viral hepatitis etc and investigate/treat appropriately.

Seek specialist advice if concern of causal relationship between statin and liver damage.

Check liver function (ALT/AST) at baseline, within 3 months and at 12 months after initiation of statin therapy.

Do not routinely exclude from statin therapy people who have liver transaminase levels that are raised but <3 x ULN

Most adults with fatty livers are likely to benefit from statins and this is not a contraindication.

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Lipid Management Options and LDL-C Reduction:

Approximate reduction in LDL-C						High intensity statins (HIS) reduce LDL-C >40% (highlighted green) and are more effective at preventing cardiovascular events than low / medium intensity statins. NICE/AAC recommends atorvastatin and rosuvastatin as HIS. *Simvastatin 80mg is not recommended due to muscle toxicity risk.
Drug / daily dose	**5mg**	**10mg**	**20mg**	**40mg**	**80mg**	
Pravastatin (SPC) (3rd line statin if atorvastatin and rosuvastatin are inappropriate)		20%	24%	29%		
Simvastatin (SPC) (3rd line statin if atorvastatin and rosuvastatin are inappropriate)		27%	32%	37%	42%*	
Atorvastatin (SPC)		37%	**43%**	**49%**	**55%**	
Rosuvastatin (SPC)	38%	**43%**	**48%**	**53% specialist initiation**		
Atorvastatin with Ezetimibe (SPC) 10mg		**52%**	**54%**	**57%**	**61%**	
Ezetimibe 10mg with Bempedoic acid 180mg (SPC)	Approx. 38%*					*17-18% LDL-C lowering for bempedoic acid, ezetimibe 21% approximations vary in current study data.

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Recommended Criteria For Referral to Lipid Clinic (SEL Hospital and Community Settings)

Hospital lipid clinic	Referral Criteria	Community lipid service	Referral criteria (Lambeth, Southwark and Bexley boroughs)
Severe hypercholesterolaemia	Cholesterol >9.0 mmol/L (or non-HDL-C > 7.5 mmol/L) regardless of existing heart disease / family history	**Statin intolerance**	Intolerance of 3 or more statins OR Severe adverse reaction to one statin AND not meeting target reductions in LDL-C/ non-HDL-C on ezetimibe 10mg daily
Suspected familial hypercholesterolaemia (FH)	Cholesterol >7.5 mmol/L and LDL-C >5.0 mmol/L **AND** • Premature CVD (age <60yrs) in the patient OR • Family history: 1st degree relative MI < 60 years old , 2nd degree relative MI <50 years old OR • Presence of tendon xanthomata	**Secondary prevention of CVD**	Unable to meet target reductions in LDL-C or non-HDL-C despite maximal doses of statins + ezetimibe
Family screening	Cascade screening from identified patient with familial hypercholesterolaemia with a genetic diagnosis of FH	**Medicines adherence support**	Persistent non-adherence to drug therapies despite best efforts of the GP practice
Severe Hypertriglyceridemia	• Triglyceride > 20 mmol/L OR • Triglyceride 10 - 20 mmol/L which persists on a fasting lipid profile (2 samples 1 week apart) OR • Triglyceride 4.5 - 9.9 mmol/L WITH non-HDL cholesterol > 7.5 mmol/L	Please note the community clinic will also undertake follow up of specific patients reviewed in secondary care specialist lipids services and discharged with a management plan suitable for primary care. Currently community clinics run by GSTT are available in Lambeth, Southwark and Bexley boroughs. See here for lipid clinic contact details	
Statin intolerance	Intolerance of 3 or more statins OR Severe adverse reaction to one statin AND not meeting target LDL-C/ non-HDL-C on ezetimibe 10mg daily. For primary prevention statin intolerance please refer to community lipid clinic (where available) in the first instance.		
Secondary prevention of CVD	Unable to meet target reductions in LDL-C or non-HDL-C despite maximal doses of statins + ezetimibe		

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Summary of Lipid Lowering Therapy

(*CV events defined as death, non-fatal MI and non-fatal stroke)

NHS

Lipid lowering therapy	NICE approved indication	Administration	LDL – lowering effect	CV outcome data	LT safety data
High intensity statin Atorvastatin (or Rosuvastatin) (Green)	Primary prevention, Secondary prevention, Familial hypercholesterolaemia (FH)	Oral tablet given once daily	High intensity statins can lower LDL-C by 40% -55% (depending on agent and dose)[8]	Multiple outcome studies confirming CV outcomes benefit across a wide range of patient cohorts. For every 10,000 people treated for 5 years: • In secondary prevention (established CVD): 1,000 heart attacks, strokes or deaths avoided. NNT over 5 years = 10 • In primary prevention: 500 heart attacks, strokes or deaths avoided[7]. NNT over 5 years = 20	Long term safety data has been well established over 30 years. For every 10,000 people treated for 5 years: 5 cases of myopathy 5-10 haemorrhagic strokes 50-100 new cases of diabetes [9]
Ezetimibe (Green)	With statin to reduce CV risk: primary and secondary prevention, or if statin intolerance, FH	Oral tablet given once daily	An additional LDL-C reduction of 24% in combination with statins[10]	Two CV outcomes studies in secondary prevention on top of statins[11,12] For every 10,000 people with CVD treated for 7 years: Approximately 200 major CV events* avoided. NNT 50 for preventing major cardiovascular event over 7 years. [13]	Long term safety data has been well-established over 20 years. Side effects are usually mild and transient[14].
Bempedoic acid ▼ (Amber1) Bempedoic acid with ezetimibe ▼ (Green)	With ezetimibe in statin intolerance if ezetimibe alone does not control LDL-C well enough	Oral tablet given once daily	An additional LDL-C reduction of approximately 28% (range 22-33%) when combined with ezetimibe[15]	One CV outcome study . For every 10.000 patients treated for 3 years. Approximately 130 major CV events* avoided.[16] NNT = 77	Safety data from trials of up to 3 years. Increased risk of hyperuricemia (NNH = 19) , gout (NNH = 100) and cholelithiasis (NNH = 100) reported.[16]
Inclisiran (PCSK9i) ▼ (Amber1)	Secondary prevention in patients who meet eligibility criteria	S/C injection administered every six months, once stabilised	An additional LDL-C reduction of approximately 50% (range 48-52%) alone or in combination with statins or ezetimibe[17]	No CV outcomes data. On-going studies due to report in 2026.	Short term safety data from trials of up to 2 years. Injection site reactions reported (NNH = 12).
Icosapent ethyl ▼ (Amber 2)	Secondary prevention in patients on statins who meet eligibility criteria	Two capsules taken orally twice daily with food	An 18% reduction in triglyceride levels when added to statin therapy	One CV outcomes study in secondary prevention. Given in addition to statin therapy. For every 10,000 people treated for 4.9 years approximately 370 major CV events would be avoided. NNT over 4.9 years =28 [18]	Safety data established in a trial over 5 years. Small increase in hospitalisation with atrial fibrillation / flutter (NNH =-100) and increased bleeding (NNH = 167)[18]
PCSK9i (Alirocumab/ Evolocumab) (Red)	Secondary prevention and FH in patients who meet eligibility criteria	SC injection every 2 weeks (can be self-administered)	An additional LDL-C reduction of approximately 50% (range 25-70%) alone or in combination with statins or ezetimibe. [6,7]	Two CV outcomes studies in secondary prevention on top of statins [19,20] For every 10,000 people treated for 2.5 years: Approximately 150 major CV events* avoided. NNT over 2.5 years = 65[21]	Safety data has been established over 7 years . Injection site reaction reported (NNH - 167[19] and 58[20]).

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Familial Hypercholesterolaemia (FH) Pathway

In primary care case find age <30 years:
TC >7.5mmol/L or LDL-C >4.9mmol/L or non-HDL-C >6mmol/L

In primary care case find age ≥30 years:
TC >9.0mmol/L or LDL-C >6.4mmol/L or non-HDL-C >7.5mmol/L

In primary care check bloods: repeat fasting lipid profile (TC, TG, HDL-C, LDL-C, non-HDL-C) plus LFTs (ALT/AST), TFTs, renal function, HbA1c. Check urine ACR to exclude proteinurea

If TG > 2.3mmol/L

Unlikely FH: Investigate raised triglycerides-TG (refer if indicated) and aim to reduce non-HDL-C by 40% (see primary and secondary prevention pathways).

Ensure appropriate SNOMED coding in primary care record:
hypertriglyceridemia and/or hypercholesterolaemia, not FH.

If TG ≤ 2.3mmol/L

Primary care check:
1. Family history: 1st degree relative MI <60 years old, 2nd degree relative MI <50 years old and/or family history of raised cholesterol >7.5mmol/L
2. Tendon xanthomata, xanthelasma or corneal arcus **If either are positive refer to lipid clinic for DNA testing** for monogenic FH (Simon Broome criteria)- exclude any secondary causes before referral

If not confirmed FH

If confirmed FH*: aim to reduce LDL by >50%, **lipid clinic will initiate/recommend options:**
1. High intensity statin (atorvastatin or rosuvastatin- maximum tolerated doses-see HIS table
2. Add in ezetimibe **(SPC)**10mg daily
3. Add in bempedoic ▼ **(SPC)** acid 180mg daily (to ezetimibe) if statin intolerance or inclisiran▼ (**SPC**) if secondary prevention or alirocumab (red) or evolocumab (red) if not achieving targets

Specialist service for monogenic FH: genetic counselling and DNA test for FH mutation (this is available at all secondary care lipid clinics in SEL) and cascade testing for family members if indicated (available at GSTT)

*Ensure correct coding in primary care record for confirmed FH. SNOMED: familial hypercholesterolaemia: 398036000, homozygous FH 238078005, heterozygous FH 23807900, hypertriglyceridemia 302870006

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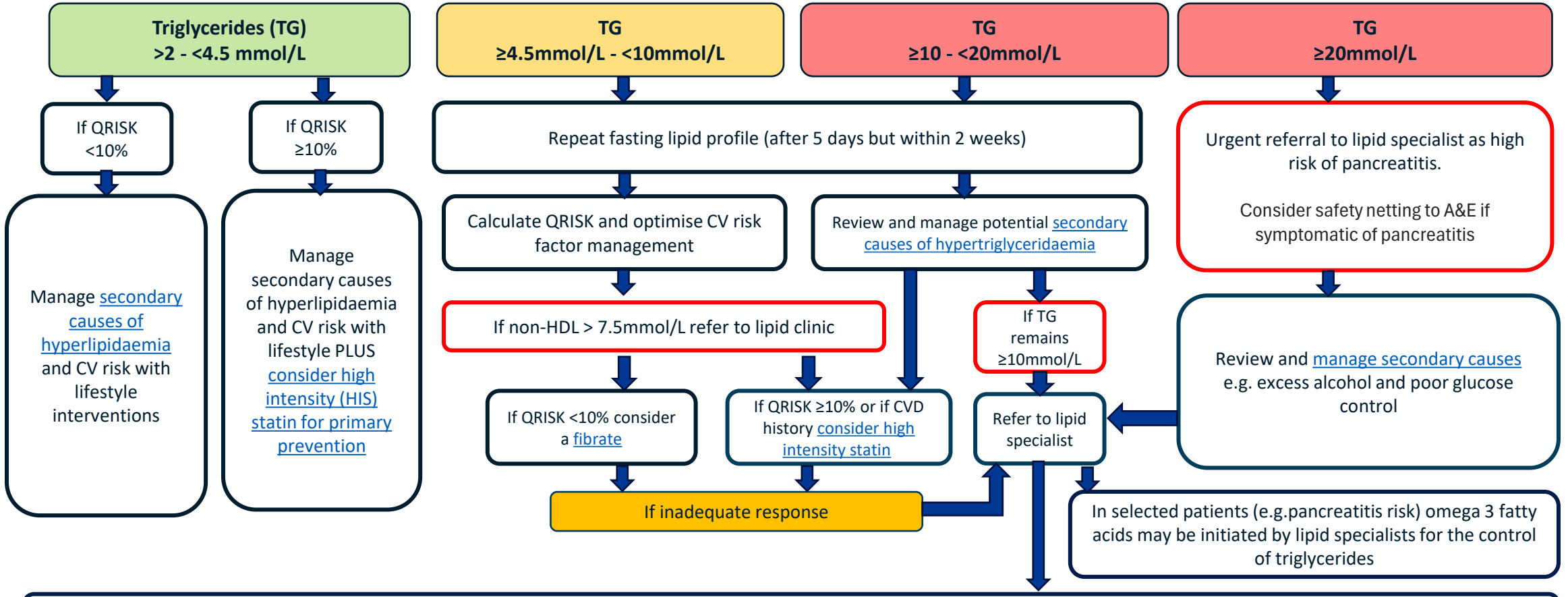
Guidance for the Management of Hypertriglyceridaemia

In all cases address any secondary causes and give appropriate lifestyle advice



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Management of Triglycerides

Address possible secondary causes and appropriate lifestyle interventions before referral to lipid clinic**:**
Excessive alcohol intake (e.g. >40 units/week) , poorly controlled/new diabetes (e.g. HbA1c >53mM/M), TG – raising medication (e.g. steroids), hypothyroidism (e.g. TSH >15), Metabolic Dysfunction-Associated Steatotic Liver Disease (see guidance) - assess risk of advanced liver fibrosis: Fibrosis (FIB) 4 score (refer to hepatology), acute/chronic liver disease (e.g. ALT >55), renal disease (e.g. CKD 3), obesity, smoking

Fibrate therapy:
Such as fenofibrate 160mg daily SPC (if contra-indicated or not tolerated seek specialist advice)

- Discontinue: if Cr increase >50% (adjust dose as per SPC) and if ALT/AST >3xULN
- Check CK if muscular symptoms: The combination of fibrate with statin increases risk of myopathy

Icosapent ethyl therapy (SPC):
Recommended by NICE for patients with CVD (secondary prevention) in combination with statin therapy where fasting TG >1.7mmol/L and LDL-C > 1.0mmol/L and ≤ 2.6mmol/L. In SEL this is amber 2 - initiation by and first prescription from a cardiovascular, diabetes or lipid specialist followed by primary care prescribing.

- Cautions (SPC): avoid in patients prescribed dual antiplatelets or an antiplatelet with an anticoagulant- refer to CRUSADE score for post-MI bleeding risk or ORBIT bleeding risk score for AF to assess individual risk: benefits. MHRA alert
- Adherence: In order for this medication to be effective it must be taken as prescribed and so adherence and tolerability should be monitored at each review. If patients cannot take 2 capsules twice a day, then STOP therapy. Pulse checks are also recommended at each review to identify potential AF, refer for ECG if indicated and manage associated stroke risk if AF is diagnosed.

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Resources/supporting materials

- The UCLPartners search and stratification tools, part of the UCLPartners Proactive Care Frameworks, stratify patients with high impact conditions so that care may be optimised according to clinical priority and capacity, see below for some useful links:
- UCLPartners Proactive Care Search and Stratification tools- Register here
- Cholesterol search tool
- Familial hypercholesterolaemia
- Size of the Prize for cholesterol

- **PrescQIPP and SEL supporting materials:**
- Deprescribing statin algorithm (registration required)
- SEL lipid management webinars
- PrescQIPP lipid modification e-learning (registration required)
- Bempedoic FAQ
- Inclisiran FAQ

Approval date: April 2025 **Review date: April 2027 (or sooner if evidence or practice changes)**

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Optimising lipid management for patients in primary care: Supporting a review of priority cohorts in secondary and primary prevention of CVD

EMIS / UCLP search to identify

Secondary prevention: Patients with a CVD history and not currently prescribed a statin

Review clinical information and full lipid profile results - recheck lipid profile and BP measurements if not from within the last year

Discuss with the patient their reasons for not being prescribed a statin:

1. Non-adherence e.g stopped after a period of time
2. Statin intolerance- has tried 2/3 different statins with adverse outcomes- consider alternative options/rechallenges (see statin intolerance pathway)
3. Statin hesitancy- patient is reluctant to be prescribed a statin following discussions of risk: benefit - see shared decision making table
4. Statin contra-indication- interacting medications, co-morbidities, frailty- document clearly decision made with patient and coding in medical notes.
5. Statin refusal- despite best efforts and risk:benefit discussion- document clearly decision made with patient and coding in medical notes. Offer alternative. LLT.
6. Document reason using SNOMED code and/or restart HIS prescription- refer to community pharmacy for adherence support and schedule a follow up within 3 months.

Consider lifestyle / behavioural interventions

Potential Outcomes:

1. Prescribe atorvastatin 80mg daily or rosuvastatin 20mg daily. Reduce dose according to renal function/drug interactions
2. Follow statin intolerance pathway consider ezetimibe and/or bempedoic acid
3. Refer to lipid specialist for further advice if statin intolerance (>3 statins)
4. Schedule a follow up with practice pharmacist or community pharmacist to support adherence
5. Refer to social prescriber as indicated to support lifestyle interventions
6. Documentation of statin contra-indication or refusal and alternative management strategies considered

Primary prevention: Patients with high CVD risk on suboptimal intensity statin and/or not reaching lipid management targets

Review clinical information, full lipid profile and liver function test (AST/ALT) results- recheck lipid profile and BP measurements if not from within the last year:

1. Calculate up to date QRISK2 or QRISK3 score- focus review on QRISK >10% as well as those with high CV risk conditions such as FH, diabetes or CKD
2. Initiate or optimise HIS therapy (atorvastatin or rosuvastatin).
3. Add in ezetimibe and escalate therapy if non-HDL has not reduced by 40% from baseline after 3 months of maximum tolerated HIS therapy
4. Document statin intolerance / hesitancy / contra-indications (as box above)
5. Refer to lipid clinic or advice and guidance (A&G) as indicated. Lipid clinic contact details

Potential outcomes:

1. Escalation of lipid management therapy eg. maximum tolerated HIS dosing and/or ezetimibe
2. Review therapy in 3 months: Titrate medication to achieve 40% reduction on non-HDL-C or <2.6mmol/L
3. Review and support adherence to medication, diet and lifestyle interventions

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Familial Hypercholesterolaemia (FH) review in primary care: Supporting identification, diagnosis, management and coding

Priority One: Review of patients coded as FH

EMIS / UCLP search to identify

Priority Two: Identification of FH- age and lipid profile:

- <30 years: TC >7.5 or LDL-C >4.9 or nonHDL-C >6.0 (mmol/L)
- ≥30 years: TC >9.0 or LDL-C >6.4 or nonHDL-C >7.5 (mmol/L)

Review medical records for patients coded as FH (see SNOMED codes listed below).
Consider the following:

1. Has FH been confirmed by genetic? If yes go to Q2, if no go to Q3
2. If FH genetically confirmed: has the patient been reviewed by lipid specialist in last 5 years?
    - If no recent review: consider Advice & Guidance (A&G) to ensure fully optimised.
    - Has cascade testing been provided to family members? Lipid clinic may refer to genomics nurse clinic
3. If FH is not genetically confirmed: amend coding (highlight code and replace with new code e.g. hypercholesterolaemia). Add EMIS note that coding has changed, let patient know by letter / text message if a review as appropriate. Use SNOMED codes listed in box below and review all of below:
    - Review lipid profile (high TC or LDL or non-HDL levels according to age may indicate FH- see priority 2 cohort below)
    - Review triglyceride (TG) level - if >2.3mmol/L unlikely FH but need to investigate cause e.g. fatty liver and code for hypertriglyceridaemia)
        - Review Simon Broome criteria (e.g. family history of MI <60 years, tendon xanthomata) or Dutch Lipid Clinic Network (DLCN) criteria
    - Exclude secondary causes: e.g. alcohol >40 units/week, ALT >55, TG >5, HbA1c >53mM/M, TSH >15, CKD 3, liver failure, non-alcoholic fatty liver disease, and manage as appropriate (e.g fatty liver)
    - Consider CV risk : ensure QRISK score is up to date (if primary prevention): check BP, weight, lifestyle and blood tests: manage with appropriate interventions as indicated (e.g. if QRISK >10% start HIS)
- Refer to lipid clinic (if lipid profile and Simon Broome criteria indicate FH but NOT if TG levels and secondary causes exclude FH)

Review medical records and invite appropriate patients for a face- to- face screening appointment:

1. Repeat full lipid profile (TC, TG, HDL-C, LDL-C)
2. Shared decision with the patient to start HIS or escalate lipid management therapy as appropriate:
3. Consider clinical signs of FH and family history: Simon Broome criteria or Dutch Lipid Clinic Network (DLCN) criteria
4. Rule out and manage secondary causes: e.g. high alcohol intake, liver impairment, high triglycerides, uncontrolled diabetes, hyperthyroidism, renal impairment and liver failure; also consider in females if TC increase is due to menopause or in pregnancy or breastfeeding. Add exception note to GP record alongside hypercholesterolaemia or "possible FH" code to show a primary care review has occurred.
5. Refer to lipid clinic for genetic diagnosis as indicated- code as "possible" or "probable FH" in primary care record until clinic review
6. Signpost to patient information for FH and lifestyle interventions: Familial hypercholesterolaemia| British Heart Foundation (bhf.org.uk); familial-hypercholesterolaemia.pdf (heartuk.org.uk)

Potential Outcomes:

1. Use FH referral form to refer to specialist lipid clinic in secondary care as indicated: for diagnosis or management support
2. Ensure coding is correct for each patient adjust as required
3. Consider lifestyle and medication interventions and schedule follow up

Suggested SNOMED Coding:

- **Single gene FH**: Familial hypercholesterolemia (disorder) SCTID: 398036000 Family history of familial hypercholesterolemia (situation) SCTID: 443454007
- **Other high cholesterol coding**: Hypercholesterolemia (disorder) SCTID: 13644009 Family history: Hypercholesterolemia (situation) SCTID: 160314003

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SEL Lipid Specialist Services and Contact Details

Before referral to lipid clinic: Identify and address potential secondary causes of hyperlipidaemia, such as uncontrolled diabetes mellitus, obesity, excess alcohol consumption, untreated hypothyroidism, proteinuria and some medications, for example, thiazide diuretics, ciclosporin, steroids and antipsychotics:

SEL Lipid Clinic	Lipidologist for referrals	Contact Details
GSTT	Prof AS Wierzbicki/Prof MA Crook	Via eRS or gst-tr.diabetesandendocrine@nhs.net
KCH	Dr Nandini Rao	Via eRS or to book an appointment/query re appointment/blood test request forms Tel: 02032994181 or email: Laura.Gonzalez@nhs.net
PRUH	Dr Nandini Rao	Via eRS or kch-tr.br-referrals@nhs.net
LGT	Prof MA Crook	Via eRS or tlh-tr.LewishamReferrals@nhs.net or endocrinology at QEH: lipidology clinics at the Bromley diabetes centre, Outpatients QEH: Tel 02088364969
Community	Lambeth, Southwark and Bexley boroughs	Via eRS and/or email: gst-tr.KHPCommunityCVD@nhs.net

The aim of hospital and community clinics is to focus on patients with primary hyperlipidaemia, before referral please exclude:

- For hypercholesterolaemia exclude hypothyroidism (check TSH), chronic renal disease or nephrotic syndrome, variant diets (zero carbohydrate; protein supplements)
- For hypertriglyceridaemia exclude new/uncontrolled diabetes (check HbA1c), excess alcohol intake and fatty liver (may require referral to gastro if FIB-4 score indicates)
- For suspected familial hypercholesterolaemia exclude secondary causes and refer to the hospital based lipid clinic not the community clinic.

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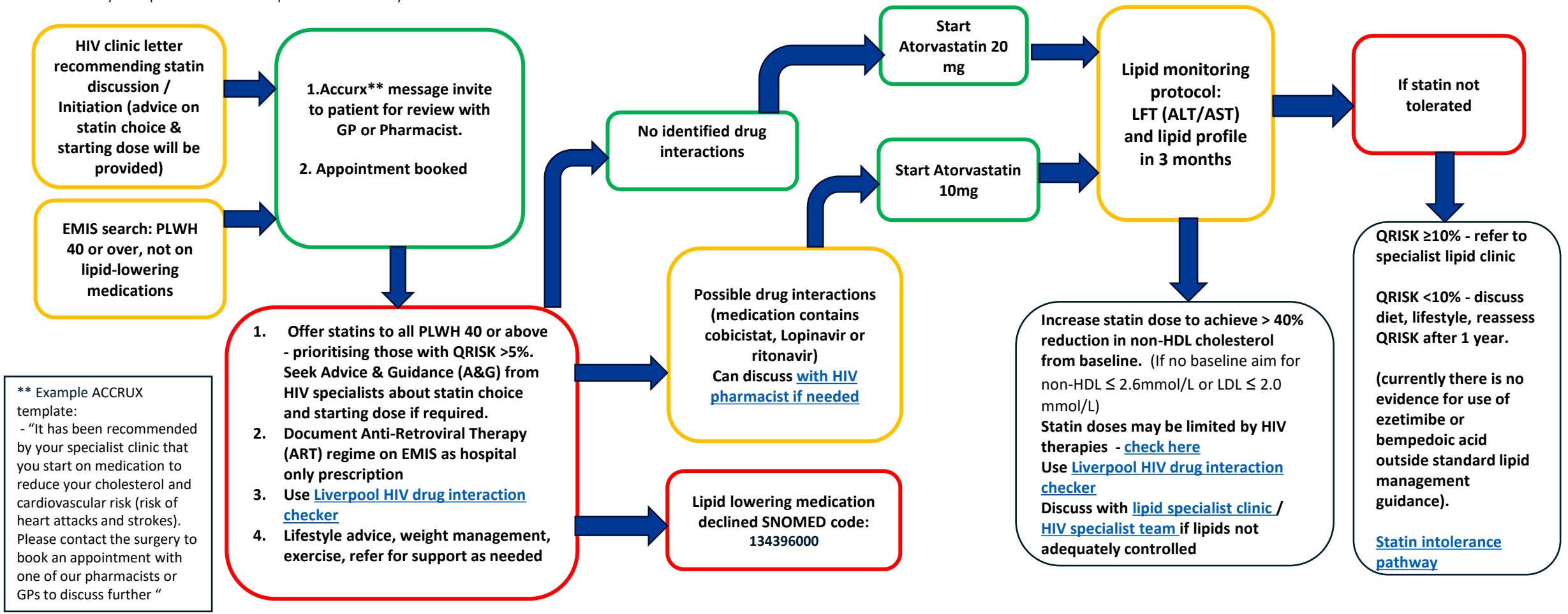
Statin Initiation for Primary Prevention for People Living with HIV (PLWH) 40 years and above*

*adapted from Statin Initiation for Primary Prevention for PLW HIV over 40 years created by multiple SEL GP HIV champions and Dr. Hamlyn



** Example ACCRUX template:
- "It has been recommended by your specialist clinic that you start on medication to reduce your cholesterol and cardiovascular risk (risk of heart attacks and strokes). Please contact the surgery to book an appointment with one of our pharmacists or GPs to discuss further "

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Common Statin/ARV Interactions and Recommended Doses for PLWH

For further information and advice about interactions please see: https://www.hiv-druginteractions.org/checker or seek Advice & Guidance from HIV Specialist team

ARV Regimen	Effect on Statins	Recommended atorvastatin starting dose	Maximum atorvastatin dose	Recommended rosuvastatin starting dose	Maximum rosuvastatin dose
Ritonavir- or cobicistat-boosted darunavir	Increased atorvastatin and rosuvastatin concentrations.	10mg	40mg	5mg	20mg
Ritonavir- or cobicistat-boosted elvitegravir	Increased atorvastatin and rosuvastatin concentrations.	10mg	40mg	5mg	20mg
Ritonavir- or cobicistat-boosted atazanavir	Significantly higher atorvastatin and rosuvastatin levels.	10mg	10mg	5mg	10mg
Lopinavir/ritonavir	Significantly higher atorvastatin and rosuvastatin levels.	10mg	20mg	5mg	10mg
Efavirenz	Variable reductions in atorvastatin. Rosuvastatin preferred first line.	20mg	80mg	10mg	40mg
Other ARV regimens	See https://www.hiv-druginteractions.org/checker or seek Advice & Guidance from HIV Specialist team				

Please note some antiretrovirals, such as boosted protease inhibitors (e.g. darunavir/ritonavir/cobicistat/atazanavir) and efavirenz can increase lipids, while others are more lipid-friendly. Consider referring patients with persistently elevated lipids to their HIV clinic for optimisation of their antiretroviral regimen.

Standard dosing of Ezetimibe is advised for all ARV regimes.

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Contact Details for HIV Pharmacy Teams

Trust	HIV Pharmacy Team
KCH PRUH	0203 299 3851 kch-tr.sexualhealth.pharmacists@nhs.net
GSTT	020 7188 2618 (option 2) gst-tr.hw.pharmacy@nhs.net
Lewisham Greenwich Bexley	02083333000, Extn 8603 02031926752 Lh.alexisclinic@nhs.net 02088366206 Lg.trafalgarpatientqeh@nhs.net

For further guidance:
Home - REPRIEVE Trial
BHIVA-rapid-guidance-on-the-use-of-statins.pdf

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Glossary

Abbreviations used for lipid profiles:

- TC: total cholesterol
- TG: triglycerides
- HDL-C: high density lipoprotein-cholesterol
- LDL-C: low density lipoprotein cholesterol
- Non-HDL-C: non-high density lipoprotein cholesterol

Calculating non-HDL-C
non-HDL-C = total cholesterol - HDL cholesterol

- mAB: monoclonal antibody
- FH: familial hypercholesterolaemia
- ICS: integrated care system
- CV: cardiovascular
- CVD: cardiovascular disease
- LFTs: liver function tests
- DM: diabetes mellitus
- CKD: chronic kidney disease
- BP: blood pressure
- HIS: high intensity statin
- AST/ALT: aspartate aminotransferase/alanine transaminase
- ULN: upper limit of normal
- TSH: thyroid stimulating hormone
- Cr: creatinine
- CK: creatine kinase
- ECG: electrocardiogram
- AF: atrial fibrillation
- PCSK9i: proprotein convertase subtilisin/kexin type 9 inhibitors
- CrCl: creatinine clearance
- NNH: number needed to harm
- NNT: number needed to treat

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