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

The Leeds Teaching Hospitals NHS Trust

Primary Care should follow the lipid treatment guidance issued by WY & Harrogate Healthy Hearts and refer to this guidance as an additional resource.

PRIMARY PREVENTION

Consider statin therapy for adults who do not have established CVD but fall into the categories below. Use QRISK3 risk assessment tool, where available to assess CVD risk for primary prevention of CVD in people ≤ 84 years.

- Age ≤84 & QRISK3 ≥ 10% over next 10 years
- Type 2 diabetes & QRISK3 ≥ 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/1.73 m^2 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.

PRIMARY PREVENTION

If lifestyle modification is ineffective or inappropriate offer statin treatment.
Atorvastatin 20mg once daily

Target is to lower non HDL-C by 40% of baseline after 3 months. If target not achieved (and the person is judged to be at higher risk because of comorbidities, risk score or using clinical judgement) discuss adherence, timing, diet and lifestyle and consider up titrating the dose every 2-3 months up to a maximum dose of atorvastatin 80mg daily

NICE does not state an LDL-C target for primary prevention but ESC guidelines recommend LDL-C < 3 in moderate risk patients and < 2.5 in high risk patients

If LDL-C remains above threshold despite maximal tolerated lipid lowering therapy refer to **lipid clinic**

Suspect Familial Hypercholesterolaemia (FH) if TC>7.5mmol/L or LDL-C>4.9mmol/L

Refer to **lipid clinic** for further assessment

Diagnosis of FH

- 1st single agent therapy: High intensity statin e.g. Atorvastatin or Rosuvastatin.
- Ezetimibe monotherapy is recommended when statins are contraindicated or not tolerated.
- Aim for at least a 50% reduction in LDL-C from baseline.
- Ezetimibe may be co-administered with statin therapy if LDL-C is not appropriately controlled.
- The decision to offer treatment with a bile acid sequestrant or a fibrate in addition to initial statin therapy should be taken by a FH specialist.

If LDL-C remains > 5 mmol/L despite maximal tolerated lipid lowering therapy or if therapy is not tolerated refer to specialist PCSK9i clinic.

SECONDARY PREVENTION

Offer statin therapy to adults with established CVD, this includes angina, previous MI, stroke or TIA or symptomatic peripheral arterial disease.

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 to manage modifiable risk factors.
Prescibe a high intensity statin:
Atorvastatin 80mg once daily

Consider a dose reduction to Atorvastatin 40mg once daily or lower in patients who are over 75 years, due to potential drug interaction, high risk of adverse effects, or patient preference.

Offer Atorvastatin 20mg if CKD (< 60 mL/min/1.73 m^2)

- Increase the dose if non-HDL-C reduction is < 40%
- Agree the use of higher doses with a renal specialist if eGFR is less than 30 mL/min/1.73m^2

NICE recommends aiming to lower non HDL-C by 40% of baseline. If target not achieved discuss adherence, timing, diet and lifestyle.
JBS3 consensus recommends a 'lower is better approach' and targets should be non HDL-C < 2.5mmol/L (LDL-C < 1.8mmol/L).

- If maximum tolerated dose of statin does not achieve LDL-C < 1.8 consider adding Ezetimibe.
- If statin therapy is contraindicated or not tolerated:
  - Refer to **lipid clinic**.
  - Ezetimibe monotherapy can be considered, but it has no prognostic benefit

If LDL-C remains >3.5 despite maximal tolerated lipid lowering therapy refer to specialist PCSK9i clinic if criteria met.

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MANAGEMENT

- This guidance applies to new patients and may also be taken into consideration for those already on statins at their annual review. Discuss with people who are stable on a low- or middle-intensity statin the likely benefits (if not meeting LDL-C targets) 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.
- If statin therapy is contraindicated, not tolerated or not effective, do not routinely offer a fibrate, nicotinic acid, bile acid binder or omega-3 fatty acids to lower CV disease risk.

RISK CALCULATORS

Where available, please use **QRISK3**.

QRISK3 replaces **QRISK2** and includes more parameters.

https://www.qrisk.org/three/

Do not use this risk assessment tool for people 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 severe obesity (BMI>40kg/m^2) .
Consider people aged ≥ 85 at increased risk of CVD because of age alone particularly people who smoke or have raised BP.

If QRISK3 < 10% over the next 10 years - Give lifestyle advice and ensure regular review of CVD risk in line with guidance.

QINTERVENTION is a tool that produces a graphical representation to demonstrate the risk of diabetes, heart disease or stroke over the next 10 years for an individual. It shows how that risk could change with interventions e.g. taking statins and also the risk of side effects from statins. The Qintervention tool can be a useful decision making aid especially for patients aged >70 years.

http://www.qintervention.org/index.php

STATIN INTENSITY TABLE

	Reduction in LDL-Cholesterol				
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%	

Low intensity statins will produce an LDL-C reduction of 20-30%
Medium intensity statin will produce an LDL-C reduction of 31-40%
High intensity statins will produce an LDL-C reduction above 40%

Rosuvastatin may be used as an alternative to Atorvastatin. Other statins should only be used in intolerance or drug interactions.

MONITORING

	Primary Prevention		Secondary Prevention	
	Lipid Profile	ALT or AST	Lipid Profile	ALT or AST
Baseline	✓	✓	✓	✓
3 months	✓	✓	✓	✓
6 months	✓ (if target not achieved)			
9 months	✓ (if target not achieved)			
12 months	✓	✓	✓	✓
Yearly	✓(where needed)		✓(where needed)*	

Consider an annual non-fasting full lipid profile to inform the discussion during annual review around effectiveness of lipid lowering therapy and any medicines non-adherence.

- Primary prevention - check baseline lipid profile and repeat lipid profile at 3 monthly intervals with lifestyle modification or statin titration if target not achieved.
- Measure baseline liver transaminase enzymes (alanine aminotransferase or aspartate aminotransferase) before starting a statin.
- Measure liver transaminase within 3 months of starting treatment and 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.

TARGETS

	NICE Target	JBS3 Target	ESC Target
Primary Prevention	40% non-HDL-C reduction from baseline		LDL-C < 3 in moderate risk patients and <2.5 in high risk patients
Secondary Prevention	40% non-HDL-C reduction from baseline	non-HDL-C <2.5mmol/L (LDL-C <1.8mmol/L)	LDL-C < 1.8
FH	at least a 50% reduction in LDL-C from baseline (or LDL-C<5).		LDL-C < 1.8

- If baseline cholesterol is unknown see ESC recommendations.
- Joint British Societies' consensus recommends a 'lower is better approach'.
- **Non-HDL-C** = TC minus HDL-C

REFERENCES

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STATIN INTOLERANCE

What to do if a patient has a statin intolerance and interpretation of CK levels.
Please see the following guidance:

http://www.leedsformulary.nhs.uk/docs/2.12GuidanceonStatinIntolerance.pdf?UNLID=288744321201791415392 4

CK levels should not be measured routinely especially if a patient is asymptomatic.

SPECIALIST SERVICES

Specialist services available at LTHT:

- Lipid Clinic
- PCSK9 inhibitors clinic
- FH Genetic testing

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 20 mg for the primary or secondary prevention of CVD to people with CKD.
Increase the dose if a greater than 40% reduction in non−HDL-C is not achieved and eGFR is 30 mL/min/1.73 m^2 or more.
Agree the use of higher doses with a renal specialist if eGFR is less than 30 mL/min/1.73 m^2

TRIGLYCERIDES (TG)

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
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 > 10 mmol/litre.
4.5 - 9.9mmol/L	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.

ABBREVIATIONS

CVD - *cardiovascular disease*
CKD - chronic kidney disease
FH - *Familial Hypercholesterolaemia*
HDL-C - *high density lipoprotein cholesterol*
LDL-C - *low density lipoprotein cholesterol*
PCSK9i - *proprotein convertase subtilisin 9 inhibitor,*
TC - *total cholesterol*