Lipid Optimisation

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Primary & Secondary Prevention - what changed (1)

- NICE CG181
  - QRISK3 – May 23
  - Advise - Total fat intake ≤30% and saturated fat ≤7% of total energy intake.
  - Informed discussion re commencing statin therapy - 10-year QRISK3 score of ≥10%, & "should not be ruled out" if the person's QRISK3 is <10% (QRISK 2 use or ? Underestimated , ? ≥85 years or older, smoker , HT – to balance frailty risk
  - Statin primary prevention - all adults with type 1 diabetes, and offered to those with type 1 diabetes and additional CVD risk factors, *e.g.* aged >40 years, diabetes duration >10 years or established nephropathy.
  - Offer 80mg atorvastatin for secondary prevention, - lower dose if drug interactions or adverse effects, or patient preference. Lifestyle but don't delay statin , CKD 20mg atorvastatin for primary and secondary prevention of CVD.

Primary & Secondary Prevention - what changed ? (2)

- >40% reduction in non-HDL cholesterol is not achieved after 3 months , drug and lifestyle adherence optimisation to higher dose & annual reviews
- Measuring Creatine kinase : unexplained muscle symptoms before offering statin therapy. 5 x upper limit not commence, raised <5 times ULN, lower dose & unexplained muscle symptoms - measure
- Liver transaminase levels should also be measured at baseline, and within three and 12 months of starting statin treatment.
- An earlier update in February 2023 – aspirin not routinely be offered for primary prevention of CVD. Response to the findings of the ASCEND, ARRIVE and ASPREE trials, use of aspirin for primary prevention of CVD does reduce the risk of cardiovascular events, however benefit is largely offset by the increased risk of bleeding.

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

ACCELERATED ACCESS COLLABORATIVE

NHS

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 (click here)
  - 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 CHD, angina, Acute Coronary Syndrome (MI or unstable angina), 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.

Prescribe 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 currently covered by NICE CG181. NICE will consider this as part of the guideline update with publication currently expected September 2023*
- 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 (click here).

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 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

Additional CV risk reduction considerations - check fasting triglycerides levels and consider icosapent ethyl. See triglycerides section overleaf.

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 and TA805 for exceptions).

PRIMARY PREVENTION RISK ASSESSMENT

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

- 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 m^2 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/m^2) 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/1.73m^2 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/1.73m^2 or more.

Agree the use of higher doses with a renal specialist if eGFR is less than 30 mL/min/1.73m^2

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.

Icosapent ethyl (TA805)

- Check fasting triglycerides levels.
- Manage secondary causes of hypertriglyceridaemia.
- Consider icosapent ethyl (TA805) if patient has established cardiovascular disease (secondary prevention) **and**
  - on statins and fasting TG ≥ 1.7mmol/L and LDL-C* between 1.04‡ and ≤2.6mmol/L
- See table above and refer as appropriate.

* LDL-C cannot be calculated using Friedewald's formula if TG >4.5. Discuss with your lab. Consider using an alternative equation (eg Sampson, doi: 10.1001/jamacardio.2020.0013) or beta-quantification.
‡ labs don't report calculated LDL-C beyond one decimal point

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 (Click here)

References:
JBS3. 2014. www.jbs3risk.com/pages/6.htm
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Navarese *et al*. 2015. Annals of internal medicine 163(1):40-51
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NICE 2008. CG71 www.nice.org.uk/guidance/cg71
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NICE 2021. TA733 www.nice.org.uk/guidance/TA733
NICE 2022. TA805 www.nice.org.uk/guidance/ta805

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Nov 2022. Review date: Nov 2023.

NICE confirmed that its guidance is accurately represented, Nov 2022.

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NHS South West Yorkshire Partnership NHS Foundation Trust

NHS Barnsley Hospital NHS Foundation Trust

NHS South Yorkshire Integrated Care Board

Barnsley Lipid Management for Primary Prevention of Cardiovascular Disease in Adults

(A separate Barnsley Lipid Management Pathway for Secondary Prevention of Cardiovascular Disease in Adults is in development).

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 3 (including LFTs).** • Measure BMI (NICE CG189) • Identify and exclude people with contraindications/drug interactions. • If non-fasting triglyceride above 4.5mmol/L see page 4. • **If severe hyperlipidaemia** (TC>7.5mmol/L and/or LDL-C>4.9mmol/L and/or non-HDL-C>5.9mmol/L) **refer to separate Barnsley pathway.**

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 (use the current version QRISK3 where available, see page 3, *'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/1.73m^2 and/or albuminuria
- Age ≥85 years if appropriate consider comorbidities, frailty & life expectancy

Identify and address all modifiable risk factors - smoking, diet, obesity (NICE CG189), alcohol intake (less than 14units/week with several alcohol free days), physical activity, blood pressure (NG136
(Barnsley Hypertension guidelines are currently being updated)) 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)
(see page 3, *'Primary Prevention Risk Assessment'*)

Barnsley Hospital NHS Foundation Trust

Optimising Lipid Management for Secondary Prevention of Cardiovascular Disease in Barnsley

(adapted from the Accelerated Access Collaborative Summary of National Guidance for Lipid Management for Primary & Secondary Prevention of CVD Nov 21)

NHS South Yorkshire Integrated Care Board

STEP 1

Atorvastatin 80mg ON

Reassess with non-fasting lipid profile after 3m

↓

STEP 2

ADD Ezetimibe 10mg OD

Reassess with non-fasting lipid profile after 3m

Or, (if statin intolerance confirmed):

Ezetimibe 10mg OD Monotherapy

Reassess with non-fasting lipid profile after 2m

↓ ↓ ↓

FASTING LIPID PROFILE and CONSIDER ADDITIONAL THERAPIES

Advice & Guidance can be sought from: Link to BEST website to be added when available

or referral to Barnsley lipid clinic Link to BEST website to be added when available

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 (See NICE CG181 for exceptions).

Assess eligibility based on clinical criteria and shared decision making with the patient/carer.

STEP 3

If statin intolerance confirmed: **Ezetimibe 10mg and Bempedoic Acid 180mg**

or

Inclisiran 284mg

Injections initially, again at 3 months, followed by every 6 months.

or

PCSK9i

- Alirocumab 75mg, 150mg
- Evolocumab 140mg

Injections every 2 weeks

Where patients still not to target, the addition of Bempedoic Acid to statin and/or ezetimibe to be considered (with specialist advice/referral):

- Where statin intolerance PLUS ezetimibe intolerance PLUS do not want injectables
- Refer to the lipid clinic if intolerant of statins and ezetimibe.

Do not delay high intensity/dose statin treatment in secondary prevention while managing modifiable risk factors:

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

Dosing in Chronic Kidney Disease (CKD)		
eGFR	**Initiation**	**Up-titration**
>30 to <60ml/min/1.73m^2	Atorvastatin 20mg ON	Increase dose and monitor for adverse effects
<30ml/min/1.73m^2	Atorvastatin 20mg ON	Agree use of higher doses with renal specialist before increasing

- If started on less than 80mg atorvastatin and the person is judged to be at higher risk (based on comorbidities, risk score and clinical judgement) consider increasing to 80mg atorvastatin
- In patients **intolerant of atorvastatin** consider rosuvastatin (see BNF for dosage in different patient groups). Up-titrate rosuvastatin dose at 4-weekly intervals.
- In patients **intolerant of atorvastatin AND rosuvastatin** consider simvastatin 40mg or pravastatin 40mg, daily.
- Recheck lipid profile after 3 months and aim for non-HDL less than 2.5 (JBS 3 2014, QOF target) and reduction from baseline of at least 40% (NICE target. If baseline nHDL available).

Eligibility criteria for Injectable therapies

Inclisiran (TA733)

- Fasting LDL-C > 2.6mmol/L despite maximum tolerated lipid lowering therapy (TA 733)

PCSK9i (TA393, TA394)

- Non-FH or mixed dyslipidaemia:
  - Fasting LDL-C > 4.0mmol/L in high-risk patients (history of ACS, coronary or other arterial revascularization procedures, CHD, ischaemic stroke, PVD); or
  - Fasting LDL-C > 3.5mmol/L in very high-risk patients (recurrent CV events or CV events in more than one vascular bed).
- Familial Hypercholesterolaemia (*i.e. DNA confirmed genetic mutation*):
  - primary prevention if fasting LDL-C > 5.0mmol/L;
  - secondary prevention if fasting LDL-C > 3.5mmol/L.

NOTE: Inclisiran and PCSK9i should not be prescribed concurrently

Statins

- **Atorvastatin – first line, high intensity & low cost - 20mg for primary prevention**
- **Rosuvastatin** (second choice statin on the Barnsley Formulary) may be used as an alternative to atorvastatin.
- **Simvastatin or Pravastatin** ONLY if intolerance or drug interactions.
- **Avoid Fluvastatin** - high cost in relation to alternative statins & awareness of MHRA simvastatin drug interactions

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%	
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Rosuvastatin	38%	43%	48%	53%	
Atorvastatin + Ezetimibe 10mg		52%	54%	57%	61%

Low intensity statins will produce an LDL-C reduction of 20-30%

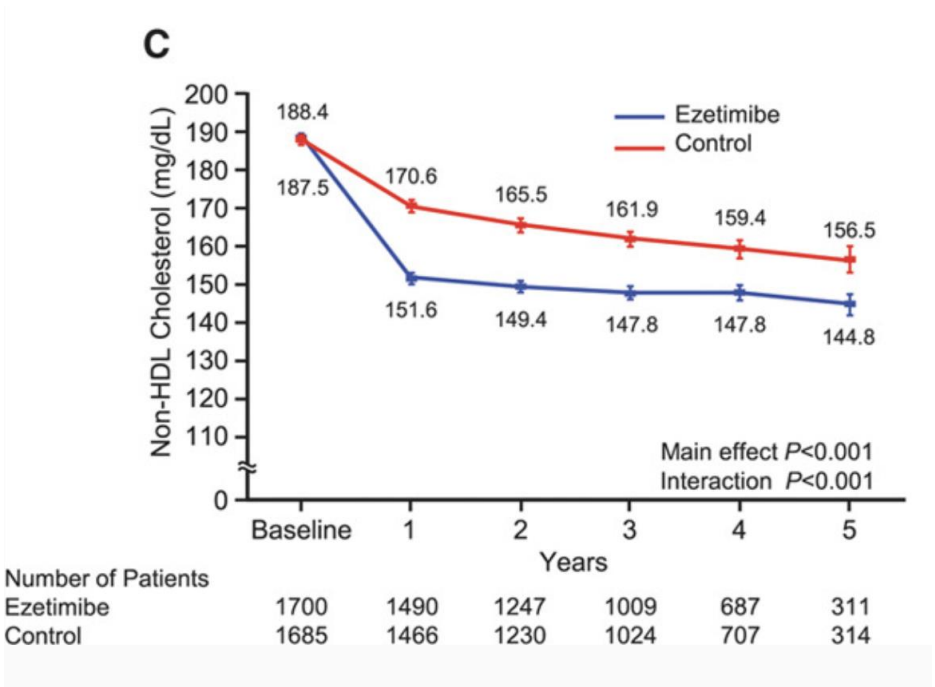
Medium intensity statins will produce an LDL-C reduction of 31-40%

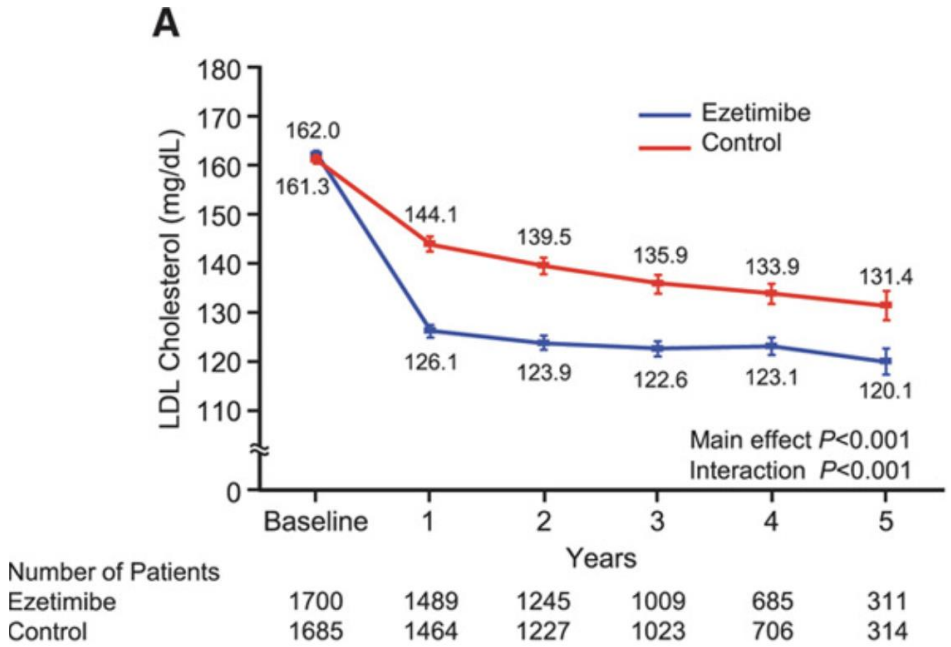
High intensity statins will produce an LDL-C reduction above 40%

Simvastatin 80mg is not recommended due to risk of muscle toxicity

Ezetimibe & Oral Bempedoic Acid

- Reduces absorption of cholesterol
- Back in 2011 evidence base challenging - ? reduction in CVD events & expensive. Widely used in Barnsley
- 2015 IMPROVE-IT trial – significant benefit reducing cholesterol and CVD events - sub analysis conferred greater benefit in diabetes & > 75 yrs. groups.
- 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 (at a lower cost)
- **Bempedoic acid (Amber-G classification)** when combined with ezetimibe (NICE TA694) produces an additional LDL-C reduction of approximately 28% (range 22-33%) – however no clinical outcome evidence & expensive !





Ezetimibe Lipid-Lowering Trial on Prevention of Atherosclerotic Cardiovascular Disease in 75 or Older :
Ouchi et al ; Aug 2019 ; Circulation; Vol 40, No 12

Traffic Light Status Inclisiran

- Inclisiran – Injection
- TL will be harmonised across SY - currently
  - Barnsley & Rotherham Amber
  - Sheffield Green
  - Doncaster - Green with Guidance

Local Incentives (1)

- **Practice Delivery Agreement**
  - Training attended & review of high risk most deprived cohort(s)
- **Inclisiran – within Specialist Drugs (Shared Care) Service**
- **BHNFT Lipid Clinic**

Regional & National Incentives (1)

- **<u>Primary Care Administration Income</u>**
- Inclisiran £45, which is payable 30 days personally administered item reimbursed via FP34D form or on an FP10 prescription, Reimbursed Amount £55 per injection : Income £10 per injection
- Initial consultation counselling, initial subcutaneous injection, 3 months and then every 6 months : 4 injections in 1st year. Two per year thereafter
- Income would cover administration costs of the injection after initial counselling undertaken.
- Larger clinics running over wider area with more patients would be more efficient.

Regional & National Incentives (2)

- **QoF – two new indicators - circa £150K (ave £5K/practice)**
  - CHOL001 – Patients on therapeutic registers prescribed a statin or LLT (70-95% & 14points)
  - CHOL002 – Treatment to target , non HDL- C < 2.5mmol/L OR LDL-C <1.8mmol/L (20-35% & 16points)
- **SY AHSN InHIP (Innovation Health Improvement) Work**
  - A&G (Doncaster FT) , Training & Incentive(s) TBC

Eclipse (PROTECT)

PDA –Population Health Management

- PHM-02b – 25 Points (Minimum threshold 10, Maximum Threshold 25)
- Practices should review patients with coronary heart disease and optimise lipid lowering treatment and onward referrals where appropriate.
- For those patients identified by Eclipse as from the 20% most deprived communities (IMD1) practices should proactively follow up to ensure they are reviewed as priority.
- Patients who have commenced lipid lowering treatment and onward referrals where appropriate.
- Outcome is looking for chnagein size of this cohort

Eclipse (PROTECT)

- Eclipse VISTA Icon – Lipid Optimisation – select view & select “Priority Patients”

Cholesterol > 7.5	256789	**1113**
Cholesterol > 7.5mmol/L and no test in last 12 months	256789	**509**
Cholesterol > 7.5mmol/L and current smoker	256789	**224**
Cholesterol > 7.5mmol/L and BP >140/90	256789	**263**
Cholesterol > 7.5mmol/L and on statin	256789	**228**
Cholesterol > 7.5mmol/L and not on statin	256789	**885**
Cholesterol > 7.5mmol/L and ischaemic heart disease	256789	**47**
Cholesterol > 7.5mmol/L and peripheral vascular disease	256789	**22**
Cholesterol > 7.5mmol/L and history of Stroke / TIA	256789	**13**
Cholesterol > 7.5mmol/L and diabetes	256789	**102**
Cholesterol > 9mmol/L aged >=30 and not referred for FH screening	256789	**44**
Cholesterol > 9mmol/L at any time and not referred for FH screening	256789	**376**
Cholesterol > 7.5mmol/L and estimated QRISK3 Score > 20% not on a statin	256789	**187**
Patient on Ezetimibe and Statin with HDL > 2.5	256789	**4**

Eclipse (PROTECT)

- Can apply Core 20 plus 5 filter to list – choose to apply Deprivation Decile 1-2. Can sort or select from the list.