UCLPartners Proactive Care Frameworks:

NCL Lipid Modification Primary and Secondary Prevention Pathways

UCLPartners

House keeping rules

Keep your mic muted unless you need to speak

Introduce yourself in the chat (your role, organisation, interest)

Ask your questions in the chat window

This meeting is recorded and will become available shortly after the meeting

UCLPartners Proactive Care Frameworks

UCLPartners has developed a series of frameworks for local adaptation to support proactive management of long-term conditions in post-COVID primary care.

- Led by a clinical team of GPs and pharmacists.
- Supported by patient and public insight.
- Working with local clinicians and training hubs to adapt and deliver.

Core principles:

1. Virtual where appropriate and face to face when needed.
2. Mobilising and supporting the wider workforce (e.g. pharmacists, HCAs, and others) to optimise clinical care and holistic care
3. Step change in support for self-management.
4. Digital innovation including apps for self-management and technology for remote monitoring.




Why Focus on Lipids?

- High cholesterol causes cardiovascular disease and is associated with an increased risk of cardiovascular death.[1]
- **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.
- Every 1mmol/l reduction in low-density lipoproteins (LDL) cholesterol reduces risk of a cardiovascular event by **25%**.[2]
- 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.
- 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]

References:
1. Lewington S, Whitlock G, Clarke R, et al.. Blood cholesterol and vascular mortality by age, sex, and blood pressure: a meta-analysis of individual data from 61 prospective studies with 55,000 vascular deaths. Lancet 2007;370:1829–39. 10.1016/S0140-6736
2. https://jamanetwork.com/journals/jama/fullarticle/2556125
3. https://www.nice.org.uk/guidance/cg71/chapter/Context

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 hyperlipidemia 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 dyslipidemia, 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 OD

- 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 recommended statin therapy is contraindicated or not tolerated;
- Ezetimibe monotherapy may be considered. Assess response after 3 months
  - See local statin intolerance guidance / pathway where available
  - 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 no secondary causes: suspect Familial Hypercholesterolemia (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 OD. 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 (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 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 middle-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
- 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 systemic lupus erythematosus, 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 LDL-C: low density lipoprotein cholesterol
AST: aspartate aminotransferase non-HDL-C: non-high density lipoprotein cholesterol
CHD: coronary heart disease PCSK9i: proprotein convertase subtilisin kexin 9
CKD: chronic kidney disease monoclonal antibody inhibitor
CVD: cardiovascular disease SLE: systemic lupus erythematosus
FH: familial hypercholesterolaemia SPC: summary of product characteristics
LDL-C: low density lipoprotein cholesterol
non-HDL-C: non-high density lipoprotein cholesterol
PCSK9i: proprotein convertase subtilisin kexin 9
SLE: systemic lupus erythematosus
SPC: summary of product characteristics
TC: total cholesterol

Authors: Dr Rani Khatib & Dr Dermot Neely on behalf of the AAC Clinical Subgroup. Nov 2021.
Review date: Nov 2022. NICE endorsed Dec 2021.

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/moderate 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 for primary or secondary prevention if compatible with other drug therapy. Lower starting dose maybe needed in some. See BNF.
• **Other statins** should only be used in intolerance or drug interactions.
• **Ezetimibe** when combined with any statin is likely to give greater reduction in non-HDL-C/LDL-C than doubling the dose of the statin.
• **PCSK9i** (NICE TA393,394) 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	✓	✓	✓	✓
6-9 months	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	✓ (where needed)		✓ (where needed)	

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 Secondary Prevention	Intensify lipid lowering therapy if: non-HDL-C reduction from baselineis less than 40%	non-HDL-C <2.5mmol/L (LDL-C <1.8mmol/L)
FH	Optimise lipid lowering therapy to achieve at least 50% reduction in LDL-C (or Non-HDL-cholesterol.)	

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.

	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 (Click here)

References:
JBS3. 2014. www.jbs3risk.com/pages/6.htm
Kirsten et al. 2005. Hospital Pharmacy 40(8):687-692
Navarese et al. 2015. Annals of internal medicine 163(1):40-51
Soon Jun Hong et al. 2018. Clinical therapeutics 40(2): 226-241.e4
NICE. 2016. TA385 www.nice.org.uk/guidance/ta385
NICE. 2016. TA393 www.nice.org.uk/guidance/TA393
NICE. 2016. TA394 www.nice.org.uk/guidance/TA394
NICE. 2014. CG181 www.nice.org.uk/guidance/CG181
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

Approved by the National Institute for Health and Care Excellence (NICE), Dec 2021

Subita

Subita is a 71 year old Bangladeshi woman with type 2 diabetes and hypertension

Her HbA1c is being managed initially with metformin

She is picked up by the UCLP primary prevention searches as a priority one patient as she is not currently on a statin

Her cholesterol is		
Total chol 5.4mmol/L	LDL chol 3.6mmol/L	HDL chol 0.8mmol/L

VOTING

In terms of her cholesterol Subita should be offered:

A. Risk assessment using QRisk
B. A statin
C. Lifestyle advice
D. A statin and lifestyle advice
E. Not sure

Cholesterol –Primary Prevention (no pre-existing CVD)

ARRS[$] roles/ other appropriately trained staff

Gather information:	E.g. up to date bloods, BP, weight, smoking status, run QRISK score.*
Self-management:	Education (cholesterol, CVD risk), BP monitors (what to buy, how to use), signpost to shared decision making resources.
Behaviour change:	Brief interventions and signposting e.g. smoking, weight, diet, exercise, alcohol.

Stratification

Priority 1

One of:
- QRISK ≥20%
- CKD
- Type 1 Diabetes

AND
- Not on statin

Priority 2
- QRISK 15-19%

AND
- Not on statin

Priority 3
- QRISK 10-14%

AND
- Not on statin

Priority 4

On statin for primary prevention but not high intensity

Prescribing clinician

Optimise lipid modification therapy and CVD risk reduction

1. Review QRISK score*, lipid results and LFTs.
2. Initiate or optimise statin to high intensity – eg atorvastatin 20mg.
3. Titrate therapy against reduction in LDLc/non-HDLc (statin>ezetimibe).
4. Optimise BP and other comorbidities.
5. Use intolerance pathway and shared decision-making tools to support adherence.
6. Arrange follow-up bloods and review if needed.

*QRISK 3 score is recommended to assess CV risk for patients with Severe Mental Illness, Rheumatoid Arthritis , Systemic Lupus Erythematosus, those taking antipsychotics or oral steroids; [$]ARRS = Additional Role Reimbursement Scheme

[$]ARRS = Additional Roles Reimbursement Scheme

About you

Age (25-84): 71

Sex: ○ Male ◉ Female

Ethnicity: Bangladeshi

UK postcode: leave blank if unknown

Postcode:

Clinical information

Smoking status: non-smoker

Diabetes status: type 2

Angina or heart attack in a 1st degree relative < 60? ☐

Chronic kidney disease (stage 3, 4 or 5)? ☐

Atrial fibrillation? ☐

On blood pressure treatment? ☑

Do you have migraines? ☐

Rheumatoid arthritis? ☐

Systemic lupus erythematosus (SLE)? ☐

Severe mental illness?
(this includes schizophrenia, bipolar disorder and moderate/severe depression) ☐

On atypical antipsychotic medication? ☐

Are you on regular steroid tablets? ☐

A diagnosis of or treatment for erectile disfunction? ☐

Leave blank if unknown

Cholesterol/HDL ratio: 6.75

Systolic blood pressure (mmHg): 160

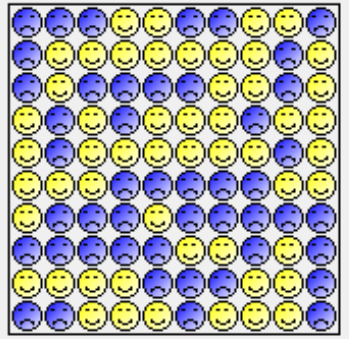
Standard deviation of at least two most recent systolic blood pressure readings (mmHg):

Your results

Your risk of having a heart attack or stroke within the next 10 years is:

47.4%

In other words, in a crowd of 100 people with the same risk factors as you, 47 are likely to have a heart attack or stroke



Risk of a heart attack or stroke

Your score has been calculated using estimated data, as some information was left blank.

Your body mass index was estimated as 29 kg/m^2.

How does your 10-year score compare?

Your score

Your 10-year QRISK®3 score	47.4%
The score of a healthy person with the same age, sex, and ethnicity*	16.7%
Relative risk**	2.8
Your QRISK®3 Healthy Heart Age***	> 84

* This is the score of a healthy person of your age, sex and ethnic group, i.e. with no adverse clinical indicators and a cholesterol ratio of 4.0, a stable systolic blood pressure of 125, and BMI of 25.

** Your relative risk is your risk divided by the healthy person's risk.

*** Your QRISK®3 Healthy Heart Age is the age at which a healthy person of your sex and ethnicity has your 10-year QRISK®3 score.

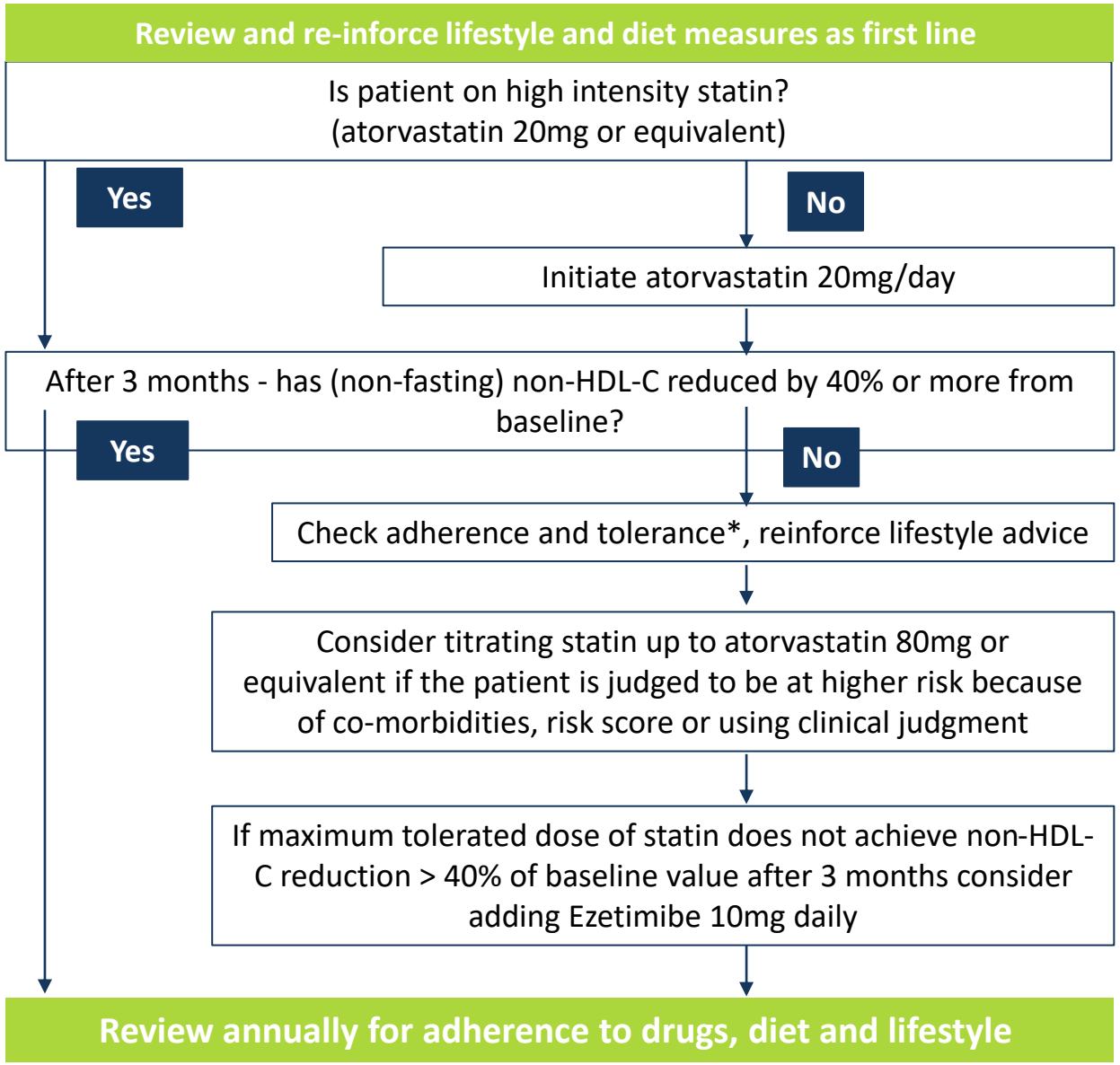
Primary Prevention

- Estimate the level of CV risk using the QRISK3 assessment tool for people without CVD aged between 24-84yrs
- Consider people aged 85yrs or older to be at increased CV risk because of age alone, especially those who smoke or have high BP
- Offer all people lifestyle advice and the opportunity to have their CVD risk reassessed after trying to change their lifestyle
- Offer people with or without diabetes atorvastatin 20 mg for the primary prevention of CVD and a QRisk score of 10% or more
  - Do not rule out statin therapy in pts with a Qrisk score < 10%
  - In older people consider factors that may make treatment inappropriate

Optimisation Pathway for Primary Prevention

North Central London
Joint Formulary Committee

UCLPartners



Optimal High Intensity statin for Primary Prevention (High intensity statins are substantially more effective at preventing cardiovascular events than low/medium intensity statins)	
Atorvastatin	20mg
Rosuvastatin	10mg

* If statin not tolerated, follow statin intolerance pathway and consider ezetimibe 10mg daily +/- bempedoic acid 180mg daily (**or** bempedoic acid monotherapy if patient is intoleratant to both statins and ezetimibe.)

Further information on management for patients with chronic kidney disease (CKD) is available in the NHS AAC lipid management guidance

Subita

- Lifestyle issues addressed first
- Offer statin, if QRisk remains > 10%
  - *unlikely to be achieved by lifestyle alone so don't delay!*
- Rigorous control of BP
- Retain control of blood sugar
- *Would your management change if she had CKD?*

VOTING *What would you recommend for Subita if she also had CKD?*

A. Risk assessment using QRisk
B. A statin
C. Lifestyle advice
D. A statin and lifestyle advice
E. Not sure

CV Risk Assessment Recommendations

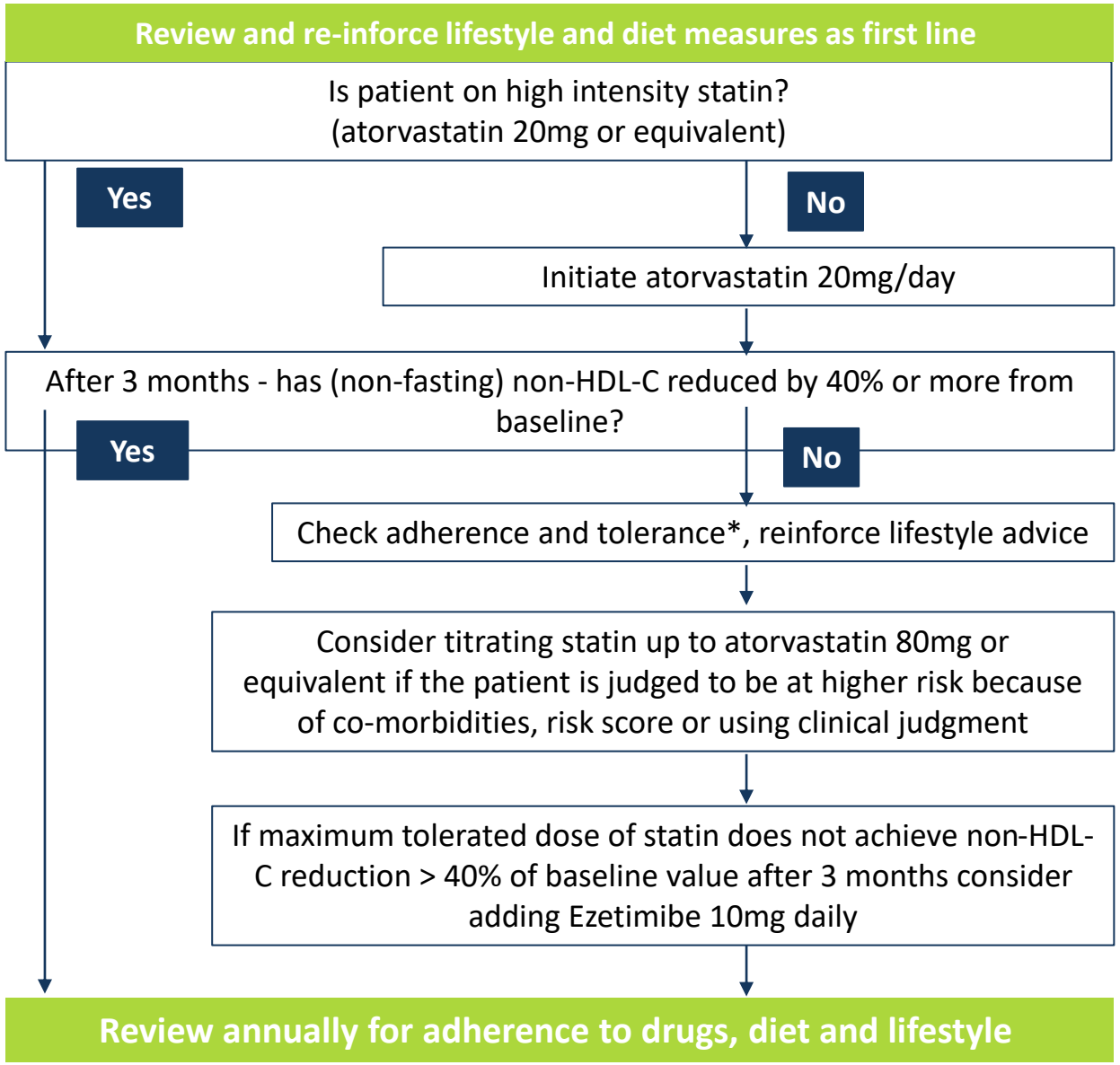
- Use the QRISK2 risk assessment tool to assess CVD risk for the primary prevention of CVD in people up to and including age 84 years
  - *except type I diabetes, CKD stage 3 or more, FH or pre-existing CVD*

- QRisk may underestimate risk esp:
  - *People treated for HIV, patients already taking medications which affect CV risk factors, people who recently stopped smoking, people with severe mental illness, people with autoimmune disease or systemic inflammatory disorder*

Optimisation Pathway for Primary Prevention

North Central London
Joint Formulary Committee

UCLPartners



Optimal High Intensity statin for Primary Prevention (High intensity statins are substantially more effective at preventing cardiovascular events than low/medium intensity statins)	
Atorvastatin	20mg
Rosuvastatin	10mg

* If statin not tolerated, follow statin intolerance pathway and consider ezetimibe 10mg daily +/- bempedoic acid 180mg daily (**or** bempedoic acid monotherapy if patient is intoleratant to both statins and ezetimibe.)

Further information on management for patients with chronic kidney disease (CKD) is available in the NHS AAC lipid management guidance

Subita

You contact Subita by phone to offer her a statin

She is not keen because she heard they can cause side effects

How would you manage the discussion?

Shared Decision-Making Resources

North Central London
Joint Formulary Committee

Benefits per 10,000 people taking statin for 5 years	Events avoided
Avoidance of major CVD events in patients with pre-existing CVD & a 2mmol/l reduction in LDL	1,000
Avoidance of major CVD events in patients with no pre-existing CVD & a 2mmol/l reduction in LDL	500

Adverse events per 10,000 people taking statin for 5 years	Adverse events
Myopathy	5
Haemorrhagic Strokes	5-10
Diabetes Cases	50-100

Shared decision-making resources:

- BHF information on statins
- Heart UK: Information on statins
- NICE shared decision-making guide

Collins et al 2016 Lancet Systematic Review Lancet 2016; 388: 2532–61

Digital Resources to support self-management: Cholesterol

- **Heart UK resources** Healthy Eating, blood fats explained, understanding cholesterol, and Familial Hypercholesterolemia
- **British Heart Foundation resources** Understanding Cholesterol
- **Diet** Providing information and recipes for easy ways to eat better from the 'One You' website NHS advice on lowering cholesterol levels
- **Smoking cessation** NHS support, stop smoking aids, tools and practical tips
- **Exercise:** NHS 'One You'; iPrescribe app offers a tailored exercise plan by creating a 12-week exercise plan based on health information entered by the user; Getting active around the home: tips, advice and guidance on how to keep or get active in and around the home from Sport England; Dance to health: Online dance programme especially tailored to people over 55 years old
- **Alcohol**

Heart UK alcohol guidance
NHS Drink Less guidance

- **Mental Health** Tips and suggestions for looking after your mental health
- **Peer support** Communities of people living with high cholesterol

Richard

Richard has stable angina and a history of angioplasty and stenting

He is not currently treated with a statin and is therefore picked up by the UCLP secondary prevention searches as a priority one patient

You can't see any record of a statin in his notes

His last recorded lipids are:

Total cholesterol 5.4mmol/L

Triglycerides 1.4mmol/L

HDL cholesterol 0.9mmol/L

VOTING

In terms of the statin, Richard should be offered:

A. Atorvastatin 80mg daily
B. Atorvastatin 20mg daily
C. Simvastatin 40mg daily
D. Rosuvastatin 10mg daily
E. Doesn’t matter which statin, as long as you start one

Cholesterol – Secondary Prevention (pre-existing CVD)

ARRS[$] roles/ other appropriately trained staff

Gather information e.g. Up to date bloods, BP, weight, smoking status.

Self-management e.g. Education (cholesterol, CVD risk), BP monitors (what to buy, how to use), signpost to shared decision making resources.

Behaviour change e.g. Brief interventions and signposting e.g. smoking, weight, diet, exercise, alcohol.

Stratification

Priority 1	Priority 2a	Priority 2b	Priority 3
Not on statin therapy	On suboptimal intensity statin*	On suboptimal statin dose**	Sub-optimal non-HDL (>2.5mmol/l) levels despite maximal statin therapy

Prescribing clinician

Optimise lipid modification therapy and CVD risk reduction

1. Review CVD risk factors, lipid results and liver function tests.
2. Initiate or optimise statin to high intensity – e.g. atorvastatin 80mg.
3. Titrate therapy against reduction in LDLc/non-HDLc (statin>ezetimibe>PCSK9i mAB/inclisiran).
4. Optimise BP and other comorbidities.
5. Use intolerance pathway and shared decision-making tools to support adherence.
6. Arrange follow-up bloods and review if needed.

* E.g simvastatin
** E.g atorvastatin 40mg

[$]ARRS = Additional Roles Reimbursement Scheme

Secondary Prevention (including ACS)

01

Offer atorvastatin 80mg to people with CVD, regardless of cholesterol level

Only offer a lower dose if any of the following apply:

- potential drug interactions
- high risk of adverse effects
- patient preference

02

Do not delay statin treatment in secondary prevention but discuss lifestyle changes at the same time

03

If a person has acute coronary syndrome, do not delay statin treatment. Take a lipid sample on admission and 2 to 3 months after starting treatment

Optimisation Pathway for Secondary Prevention

North Central London Joint Formulary Committee

UCLPartners

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

No → **Initiate / increase to high dose high intensity statin** ** and reinforce lifestyle and diet measures

Yes

Is (non-fasting) non-HDL-C reduced by 40% or more from baseline at 3 months? ***
(if baseline non-HDL not available, consider intensification of therapy if non-HDL-C > 2.5mmol/L)

No

Yes

Check adherence to statin and lifestyle measures. Consider adding ezetimibe 10mg daily
If statin not tolerated, follow statin intolerance pathway and consider ezetimibe 10mg daily +/- bempedoic acid 180mg daily ****
(**or** Bempedoic acid monotherapy if intolerant to both statins and ezetimibe) ****.

Is non-HDL-C reduced by 40% or more from baseline after 3 further months? ***
(if baseline non-HDL not available, consider intensification of therapy if non-HDL-C > 2.5mmol/L)

No

Yes

Consider injectable therapies
Arrange fasting blood test to assess eligibility:
- **Inclisiran** - if fasting LDL-C ≥ 2.6mmol/L despite maximum tolerated lipid lowering therapy **OR**
- **Refer for PCSK9i (Evolocumab and Alirocumab)** if fasting LDL-C > 4mmol/L (or > 3.5mmol/L if recurrent events)

Review annually for adherence to drugs and support for diet and lifestyle measures

Optimal High Intensity Statin for secondary prevention (High intensity statins are substantially more effective at preventing cardiovascular events than low/medium intensity statins)	
Atorvastatin	80mg
Rosuvastatin	20mg

* Dose may be limited if:
- eGFR<30ml/min – see product license or NHS AAC lipid management guidance
- Drug interactions
- Intolerance
- Older age / frailty

See product license or NHS AAC lipid management guidance for further information

** See statin intensity table

*** Current NICE Guidance recommends a 40% reduction in non- HDL cholesterol

**** Measure uric acid and renal function

POLLING

In terms of overall ability to lower cholesterol - which is the most potent statin?

A. Fluvastatin
B. Simvastatin
C. Rosuvastatin
D. Atorvastatin
E. Pravastatin

Statin Intensity Table – NICE recommends Atorvastatin and Rosuvastatin as First Line

North Central London
Joint Formulary Committee

UCLPartners

Approximate Reduction in LDL-C					
Statin dose mg/day	5	10	20	40	80
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/moderate 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

Targets…. Do we need them?

- NICE (2014)
  - 40% reduction in non-HDL cholesterol
- JBS-3 (2013)
  - Statins are recommended as they are highly effective at reducing CVD events with evidence of benefit to LDL-c < 2mmol/L which justifies intensive non-HDL-c lowering
    - Non-HDL-c < 2.5mmol/L
- ACC / AHA / NI (2013)
  - Escalation of therapy beyond statins where LDL> 1.8 to LDL > 2.6mmol/L depending on an individuals risk of CV events
- ESC (2019)
  - Range of target levels LDL< 1.4 to LDL < 3mmol/L depending on an individuals risk of CV events

NICE guidance (2023)

- For secondary prevention aim for LDL levels less than 2mmol/L or non-HDL cholesterol <less tham 2.6mmol/L

Non-HDL cholesterol =
Total Cholesterol – HDL cholesterol

Secondary Prevention – new messages from NICE 2023

- **New Targets**
  - For secondary prevention aim for LDL levels less than 2mmol/L or non-HDL cholesterol <less tham 2.6mmol/L
- **Intensification**
  - If on maximum dose and intensity of statin but the lipid targets have not been met consider additional lipid lowering therapy – alirocumab, evolocumab, ezetimibe, inclisiran as per Tas
  - Consider ezetimibe in additional to maximum tolerated dose of statin to reduce CV risk even if the lipid target has been met

Richard

The HCA contacts Richard to:

- Gather information — Blood results, BP, weight, smoking status
- Self-management — Education on cholesterol and CVD risk
- Behaviour change — Brief interventions and signposting e.g. smoking, weight, diet, exercise, alcohol

Robert explains that he did try a statin after his Percutaneous Coronary Intervention (PCI) and did not get on with it due to muscle pains so the HCA refers the patient to you.

You arrange a remote consultation with Richard

- *How would you approach the discussion with Richard regarding taking a statin?*

VOTING

What % of patients complain of muscle pain on statins?

A. 3%
B. 15%
C. 34%
D. 67%
E. 87%

Muscle Pain with Statins

- 87% people on statins complain of muscle pain …… BUT

  85% of people not on statins complain of muscle pain

JAMA Intern Med. 2013;173(14):1318-1326

- A meta-analysis of over 4million patient records concluded the rate of complete statin intolerance was 9.1%

European Heart Journal, ehac015, https://doi.org/10.1093/eurheartj/ehac015

- In n=1 trials of patients reporting statin intolerance; muscle symptoms were no more common with statins than with placebo and more than half of patients were re-initiated on a statin successfully

JAMA. 2021;325(16):1602. doi:10.1001/jama.2021.4801

Muscle Symptoms Pathway

North Central London Joint Formulary Committee

UCLPartners

Muscle Symptoms

Check CK

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

CK>50x ULN

Consider rhabdomyolysis. Stop statin and seek specialist advice urgently

CK >10-50 ULN

Check renal function

Renal function deteriorating?

Yes

No

CK >4-10 ULN

CK 0-4x ULN

No improvement in CK or symptoms intolerable

Tolerable symptoms

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

Monitor CK , continue statin and review at 6 weeks

Stop statin for 4-6 weeks. **2 weeks after symptoms resolved and CK normalised,** restart statin at lower dose (or consider low dose rosuvastatin if on atorvastatin and titrate up)

Seek specialist advice if CK not normalised

Review every 3 months and titrate to higher dose if tolerated.

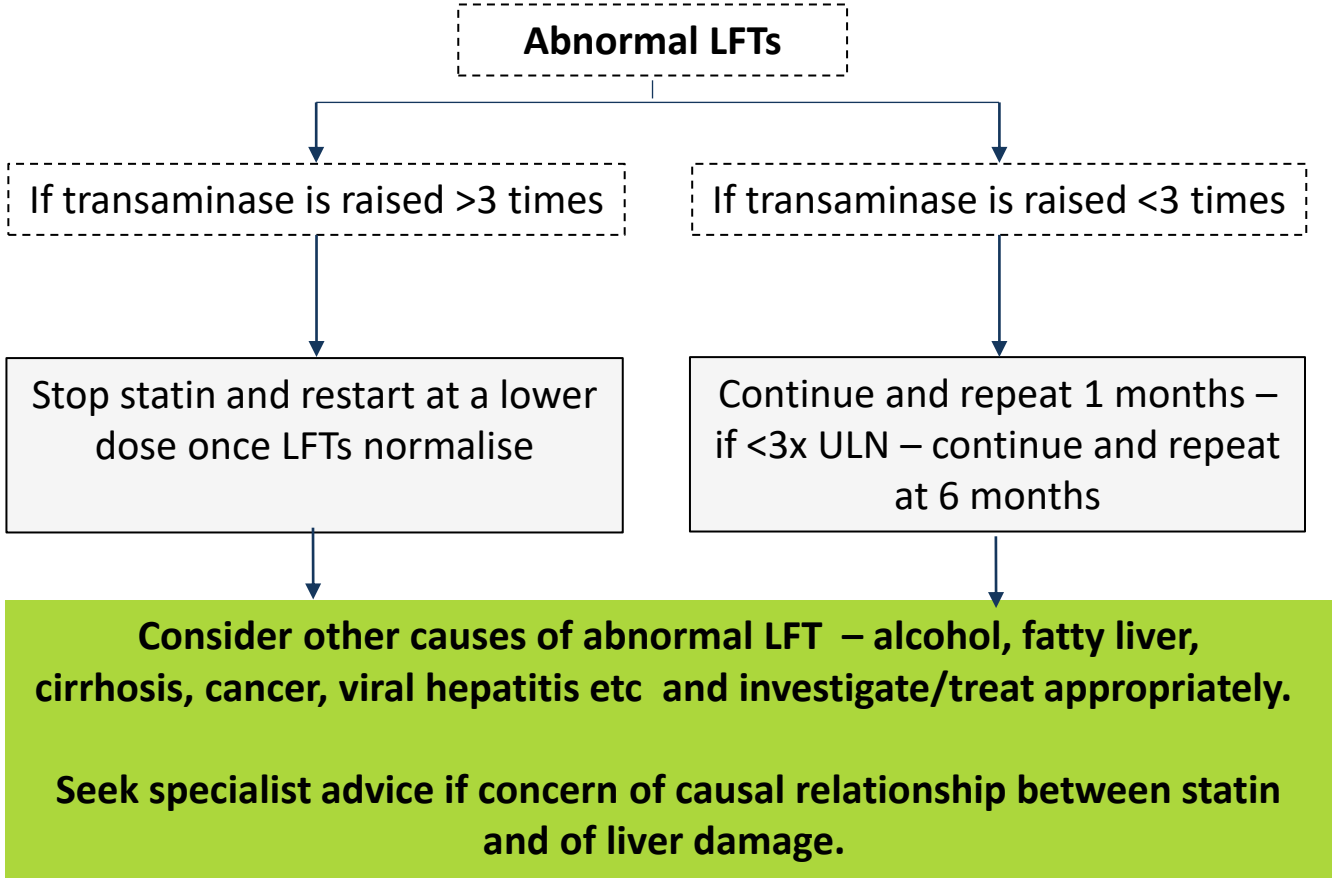
If recurrence of symptoms - Consider ezetimibe +/- bempedoic acid and/or inclisiran and/or referral for PCSK9i (mAB) in line with eligibility criteria

Detailed guidance:
https://www.england.nhs.uk/aac/wp-content/uploads/sites/50/2020/08/Statin-intolerance-pathway-January-2022.pdf

Abnormal Liver Function Test (Transaminitis) Pathway

North Central London
Joint Formulary Committee

UCLPartners



- Do not routinely exclude from statin therapy people who have liver transaminase levels that are raised but are less than 3 times the upper limit of normal.
- Most adults with fatty livers are likely to benefit from statins and this is not a contraindication.
- Check liver function at baseline, at 3 months and 12 months after initiation of statin therapy.

Back to Richard…

Following a discussions about the benefits and risk of statins, Richard agrees to try rosuvastatin

You decide to start him on a low dose (5mg daily) and increase if tolerated – aiming for high dose high intensity statin (20mg daily).

You make a plan to contact him again by phone in 2 weeks to see how he is getting on

You recommend that he also talks to the community pharmacist, as they can provide adherence support through the new medicines service

If he tolerates the statin, you plan to recheck his lipid levels in 3 months to review response to therapy

Optimisation Pathway for Secondary Prevention

North Central London Joint Formulary Committee

UCLPartners

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

No → **Initiate / increase to high dose high intensity statin** ** and reinforce lifestyle and diet measures

Yes

Is (non-fasting) non-HDL-C reduced by 40% or more from baseline at 3 months? ***
(if baseline non-HDL not available, consider intensification of therapy if non-HDL-C > 2.5mmol/L)

No

Yes

Check adherence to statin and lifestyle measures. Consider adding ezetimibe 10mg daily
If statin not tolerated, follow statin intolerance pathway and consider ezetimibe 10mg daily +/- bempedoic acid 180mg daily ****
(**or** Bempedoic acid monotherapy if intolerant to both statins and ezetimibe) ****.

Is non-HDL-C reduced by 40% or more from baseline after 3 further months? ***
(if baseline non-HDL not available, consider intensification of therapy if non-HDL-C > 2.5mmol/L)

No

Yes

Consider injectable therapies
Arrange fasting blood test to assess eligibility:
- **Inclisiran** - if fasting LDL-C ≥ 2.6mmol/L despite maximum tolerated lipid lowering therapy **OR**
- **Refer for PCSK9i (Evolocumab and Alirocumab)** if fasting LDL-C > 4mmol/L (or > 3.5mmol/L if recurrent events)

Review annually for adherence to drugs and support for diet and lifestyle measures

Optimal High Intensity Statin for secondary prevention (High intensity statins are substantially more effective at preventing cardiovascular events than low/medium intensity statins)	
Atorvastatin	80mg
Rosuvastatin	20mg

* Dose may be limited if:
- eGFR<30ml/min – see product license or NHS AAC lipid management guidance
- Drug interactions
- Intolerance
- Older age / frailty

See product license or NHS AAC lipid management guidance for further information

** See statin intensity table

*** Current NICE Guidance recommends a 40% reduction in non- HDL cholesterol

**** Measure uric acid and renal function

Adherence to new medication

Table 2 Adherence to new medication

	Still taking medication at 10 days (n = 226/239)	Still taking medication at 4 weeks (n = 171/197)
Adherent	159 (70%)	128 (75%)
Non-adherent	67 (30%)	43 (25%)
Partial non-adherence	49	26
Complete non-adherence	18	17

Table 3 Examples of problems caused by medicines

Nature of problem	Examples
Side effects	Numbness, oral thrush, nausea, vomiting, giddiness
	Stopped taking new medicine because of side effects
Concerns	Not keen – don't believe in taking pills
	Worried about taking new medicine, for example because of previous side effects, allergy, potential interactions
Practical aspects	Tablets difficult to swallow
	Hard to remember complicated regime
	Have to take half a tablet and hard to break accurately

Barber N *et al*. *Qual Saf Health Care* 2004;13:172–175

Effective treatments

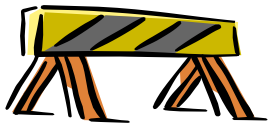
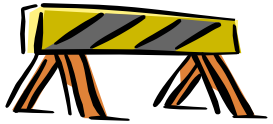
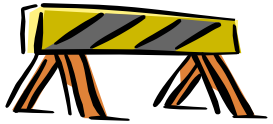
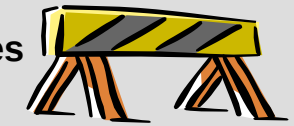
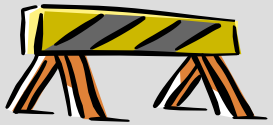
BEHAVIOUR

Practitioner – prescribing

Patient – adherence

Optimum outcomes

There are many reasons why people don't get the most out of medicines

Barriers to optimal use of medicine		Examples
Professional		Inappropriate prescribing Mistakes in dispensing or administration
Practical		Forgetfulness Inability to open containers
Information		Instructions not understood Poor understanding of condition/treatment
Lifestyle choices		Unpleasant side effects Inconvenience No perceived benefit
Beliefs about medicine		Unnatural Addictive Poisonous Diminishing efficacy

Non-Intentional

Intentional

Bempedoic acid for use in statin intolerance

- Bempedoic acid with ezetimibe is recommended as an option for treating primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia as an adjunct to diet in adults. It is recommended only if:
  - statins are contraindicated or not tolerated
  - ezetimibe alone does not control low-density lipoprotein cholesterol well enough
- Bempedoic acid with ezetimibe can be used as separate tablets or a fixed-dose combination
- The recommended dose is one film-coated tablet of 180 mg taken once daily
- Bempedoic acid lowers LDL-C by an additional 28% (range 22-33%) when combined with ezetimibe
- Bempedoic acid was associated with a slightly increased risk of tendon rupture, involving the biceps tendon, rotator cuff, or Achilles tendon. Other more commonly reported adverse events in clinical trials were upper respiratory tract infection, back pain, abdominal pain or discomfort, bronchitis, pain in extremity, anaemia, and elevated liver enzymes
- More information on bempedoic acid can be found at: https://www.medicines.org.uk/emc/product/11743/smpc#gref

Inclisiran for secondary prevention

- Inclisiran is indicated only for patients:
  - With established CVD
  - On optimal oral lipid lowering therapy including high intensity statins where tolerated
  - Where LDL-C remains ≥ 2.6mmol/L
- Inclisiran lowers LDL-C by approx. 50%, but there are currently no long term CVD outcome data or safety data which should be taken into account when making a shared decision with the patient about appropriate treatment choices
- Inclisiran (Leqvio®) is administered at a dose of 284mg by subcutaneous injection
- It should be given at month 0 (initiation), month 3, month 9 and then every 6 months thereafter.
  - If a planned dose is missed by more than 3 months, a new dosing schedule should be started – inclisiran should be administered initially, again at 3 months, followed by every 6 months.
  - It should be administered by a healthcare professional into the abdomen; alternative injection sites include the upper arm or thigh.
- The only adverse reactions associated with inclisiran reported to date are injection site reactions (8.2%)
- More information on inclisiran can be found at: https://www.medicines.org.uk/emc/product/12039/smpc#gref

Icosapent ethyl in secondary prevention (NICE TA* recommendation)

- Icosapent ethyl is recommended as an option for reducing the risk of cardiovascular events:
  - in adults with established CV disease who are taking statins
  - where fasting triglycerides are ≥ 1.7 mmol/litre or above AND where LDL-C levels are >1.04 mmol/litre and ≤2.60 mmol/litre.
- The recommended daily oral dose is 4 capsules taken as two 998 mg capsules twice daily. Icosapent should be taken with or after a meal. The capsules should be swallowed whole.
- In the REDUCE-IT study, icosapent ethyl lowered triglyceride levels by 18%, resulting in a 26% reduction in major cardiovascular events (Death, MI, stroke) .
- Icosapent ethyl should be used with caution in patients with known hypersensitivity to fish and/or shellfish.
- The most frequently reported adverse reactions associated with icosapent ethyl were bleeding (11.8%), peripheral oedema (7.8%), atrial fibrillation (5.8%), constipation (5.4%), musculoskeletal pain (4.3%), gout (4.3%) and rash (3.0%).
- More information on icosapent ethyl can be found at: https://www.medicines.org.uk/emc/product/12964/smpc

TA: Technology Appraisal

Summary of lipid lowering therapies

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

UCLPartners

Drug class	NICE approved indication	Administration	LDL-lowering efficacy	CV outcomes evidence	Safety data
Statins	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)[1]	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 [7]
Ezetimibe	Primary prevention, Secondary prevention and FH where statins are contraindicated, not tolerated or ineffective	Oral tablet given once daily	An additional LDL-C reduction of 24% in combination with statins[2]	Two CV outcomes studies in secondary prevention on top of statins[8,9] 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. [10]	Long term safety data has been well-established over 20 years. Side effects are usually mild and transient.
PCSK9i (Alirocumab/ Evolocumab)	Secondary prevention and FH in patients who meet eligibility criteria	Self-administered S/C injection every two weeks	An additional LDL-C reduction of approximately 50% (range 25-70%) alone or in combination with statins or ezetimibe. [3,4]	Two CV outcomes studies in secondary prevention on top of statins [11,12] For every 10,000 people treated for 2.5 years: Approximately 150 major CV events* avoided. NNT over 2.5 years = 65[13]	Safety data has been established over 7 years . Injection site reaction reported (NNH - 167[11] and 58[12]).
Bempedoic acid	For use where statins are not tolerated only in combination with ezetimibe, 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[5]	One CV outcome study . For every 10.000 patients treated for 3 years. Approximately 130 major CV events* avoided.[14] 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.[14]
Inclisiran	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[6]	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	Secondary prevention in patients on statins who meet eligibility criteria	Two capsules taken orally twice daily	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 [15]	Safety data established in a trial over 5 years. Small increase in hospitalisation with atrial fibrillation / flutter (NNH =- 100) and increased bleeding (NNH = 167) [15]

References:
1. NICE CG181 2014 https://www.nice.org.uk/guidance/cg181/chapter/1-recommendations; 2. NICE TA385 2016 https://www.nice.org.uk/guidance/ta385; 3. NICE TA393 2016. https://www.nice.org.uk/guidance/ta394 4. NICE TA394 2016. https://www.nice.org.uk/guidance/ta394 5. NICE TA694 2021. https://www.nice.org.uk/guidance/ta694 6. NICE TA733 2021. https://www.nice.org.uk/guidance/ta733. 7. Collins et al. 2016. Lancet 2016; 388: 2532–61. 8. Cannon CP et al. 2015. N Engl J Med 2015; 372:2387-2397; 9. Amerenco P et al. 2020. N Engl J Med 2020; 382:9-19; 10. Can Fam Physician. 2015 Mar; 61(3): 251. 11. Sabatine et al. 2017: N Engl J Med 2017; 376:1713-1722; 12. Schwarz GG et al. 2018. N Engl J Med 2018; 379:2097-2107; 13. Can Fam Physician. 2018 Sep; 64(9): 669. 14. N Engl J Med 2023; 388:1353-1364. https://www.nejm.org/doi/full/10.1056/nejmoa1812792 . 15. N Engl J Med 2019; 380:11-22

UCLPartners

Supporting primary care clinicians to optimise clinical care and self-management and release capacity

www.uclpartners.com/proactive-care