



Cholesterol Management
A National Priority to prevent heart
attacks and strokes at scale

Overview

- National ambitions for cholesterol
- Drivers and incentives for delivery
- The national AAC / NHSE pathway and current gaps in delivery
- The UCLPartners Frameworks for cholesterol

Scale of the problem

Cardiovascular disease (CVD)
is the leading cause of death worldwide

In England, CVD causes

1 in **4** deaths

which equates to

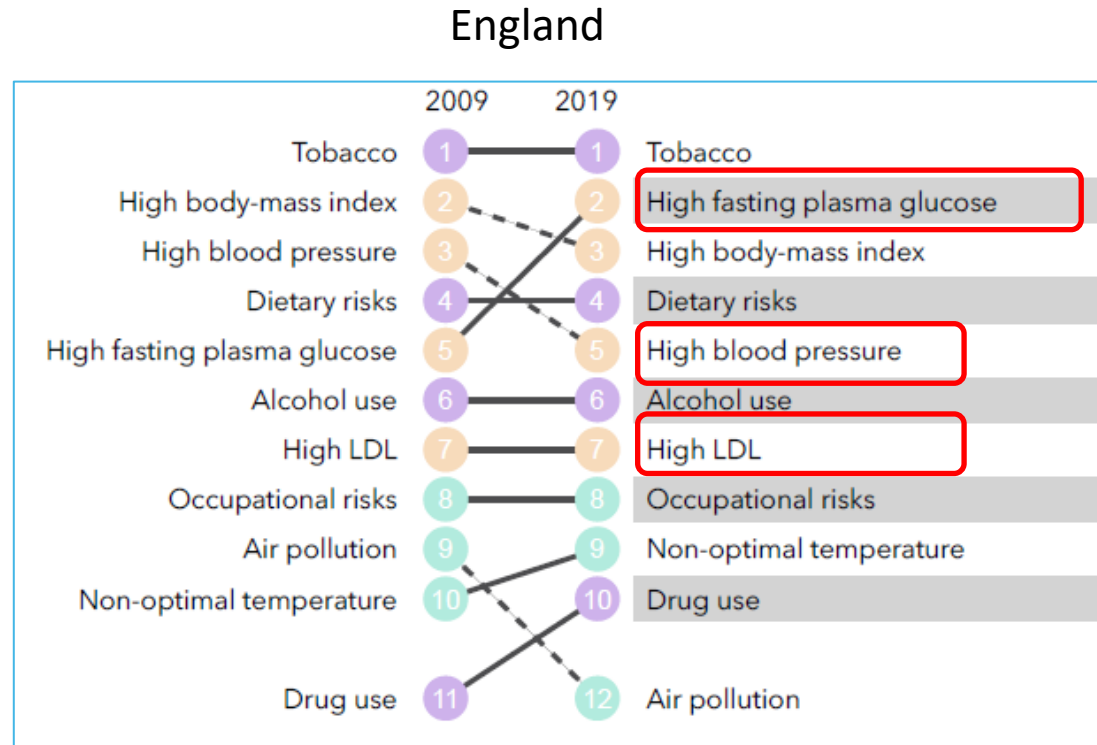
1 death every 4 minutes

Cardiovascular disease is a major cause of health inequalities

People living in the **most deprived areas** of England are almost

4 times as likely **to die prematurely from CVD** than those in the least deprived areas

What risk factors cause most death and disability?*



Treatment of high impact metabolic risk factors is very effective at preventing mortality and morbidity.
But under detection and under treatment is common.

*Global Burden of Disease Study 2019

Why cholesterol?

- Almost half of UK adults have raised cholesterol, which can lead to heart disease.
- High cholesterol is one of the most significant risk factors for CVD.
- Globally, a third of ischaemic heart disease is attributable to high cholesterol.
- It is estimated to account for 7.1% of deaths and 3.7% of disability-adjusted life years (DALYS) in England.
- Statins have been shown to reduce mortality and morbidity in patients with or at risk of CVD.

Unmet Needs In Lipid Management

7.6 million people in England with CVD¹. Of these:

- 1.9 million people may not be on a statin²
- 2.3 million people are on low or medium intensity statin³

1. <https://www.bhf.org.uk/what-we-do/news-from-the-bhf/contact-the-press-office/facts-and-figures>
2. UCLP data on file
3. Openprescribing: <https://openprescribing.net/measure/statinintensity/national/england/>

There are limited lipid incentives in QOF relating to use of statins in people with diabetes:

- DM022. The percentage of patients with diabetes aged 40 years and over, with no history of cardiovascular disease and without moderate or severe frailty, who are currently treated with a statin (excluding patients with type 2 diabetes and a CVD risk score of <10% recorded in the preceding 3 years).
- DM023. The percentage of patients with diabetes and a history of cardiovascular disease (excluding haemorrhagic stroke) who are currently treated with a statin.

PCN DES

- Offer statin treatment to patients with a QRISK2&3 score $\geq 10\%$, where clinically appropriate, and in line with NICE guideline CG181.
- Identify patients at high risk of Familial Hypercholesterolaemia and make referrals for further assessment where clinically indicated. This should include systematic searches of primary care records to identify those aged 30+ with Chol $> 9\text{mmol/L}$ or with Chol $> 7.5\text{mmol/L}$ aged less than 30.

<https://www.england.nhs.uk/wp-content/uploads/2021/08/B0828-ii-annex-a-pcn-plans-for-21-22-and-22-23.pdf>

IIF

- CVD-03: Percentage of patients aged between 25 and 84 years of age inclusive and with a CVD risk score (QRISK2 or 3) greater than 20 percent, who are currently treated with statins. (Value: £7m / 31points; Thresholds 48% (LT), 58% (UT))
- CVD-04: Percentage of patients aged 29 and under with a total cholesterol greater than 7.5 OR aged 30 and over with a total cholesterol greater than 9.0 who have been referred for assessment for familial hypercholesterolaemia (Value: £4.1m / 18 points; Thresholds 20% (LT), 48% (UT))

<https://www.england.nhs.uk/wp-content/uploads/2021/08/B0828-iii-annex-b-investment-and-impact-fund-21-22-22-23.pdf>

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Are negative statins stories leading to more deaths?

We look at media coverage of a story suggesting that media coverage about statins could lead to more deaths from heart disease.

Could news reports increase the risk of people dying from [cardiovascular disease](#) (CVD) and [heart attack](#) by causing them to stop taking [statins](#)? A new study by Danish scientists suggests this is the case.

Almost 700,000 people were monitored over a five-year period to see if the number who stopped taking statins within the first three months correlated with attitudes expressed in the media. They found that negative news correlated with an increase of almost 10 per cent halting their medication.

[Statins](#) are the most widely prescribed medication in the UK, and are used to reduce risk of cardiovascular disease, as well as reduce risk of a heart attack or [stroke](#).

[In people who already have cardiovascular disease](#)

Dr Børge Grønne Nordestgaard, who co-authored the study, said: "People who stop statins early have a 26% increased risk of a heart attack and an 18% increased risk of dying from cardiovascular disease."



BEHIND THE HEADLINES

[Is it really safe to drink 25 cups of coffee a day?](#)

[Does alcohol lower your heart risk?](#)

[Does anxiety put you at greater risk of heart disease and diabetes?](#)

[Are vegetables as good for your heart as we thought?](#)

[Binge-watching TV and "deadly blood clots"](#)

[Does cold weather increase the risk of a cardiac arrest?](#)

[Are people taking statins less likely to die from Covid-19?](#)

[Do eggs raise your risk of heart disease and death?](#)

[Is red meat OK after all?](#)

[Is avocado good for the heart?](#)

[Can light levels affect your blood sugar levels and how many calories you burn?](#)

[Do warmer nights raise the risk of death from heart and circulatory disease?](#)

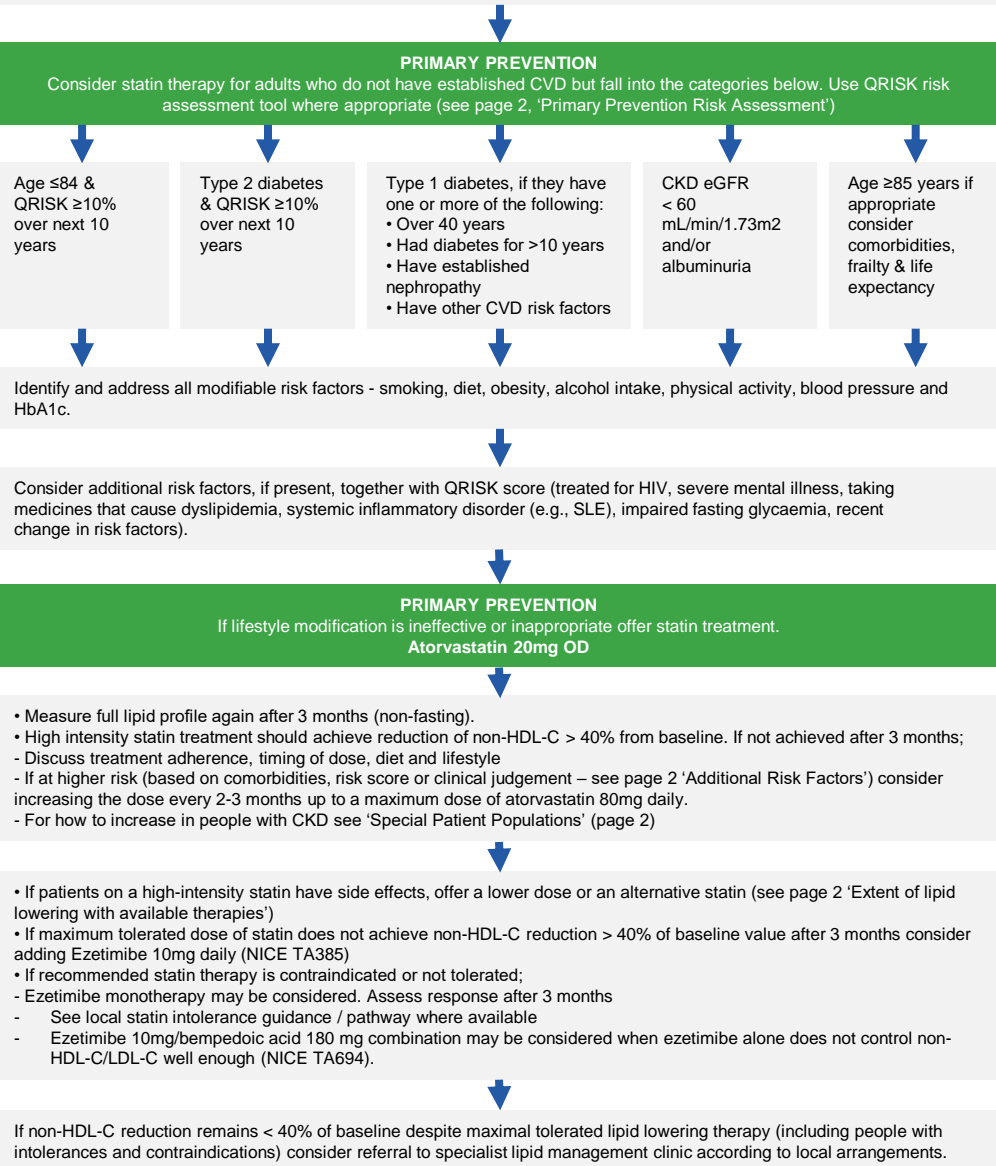
[Does eating olive oil mean you'll live longer?](#)

[Are vegetarians missing out on proteins that can prevent high blood pressure?](#)

[Salt substitute](#)

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

- 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.



INITIAL CONSIDERATIONS:

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. Prescribe 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

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

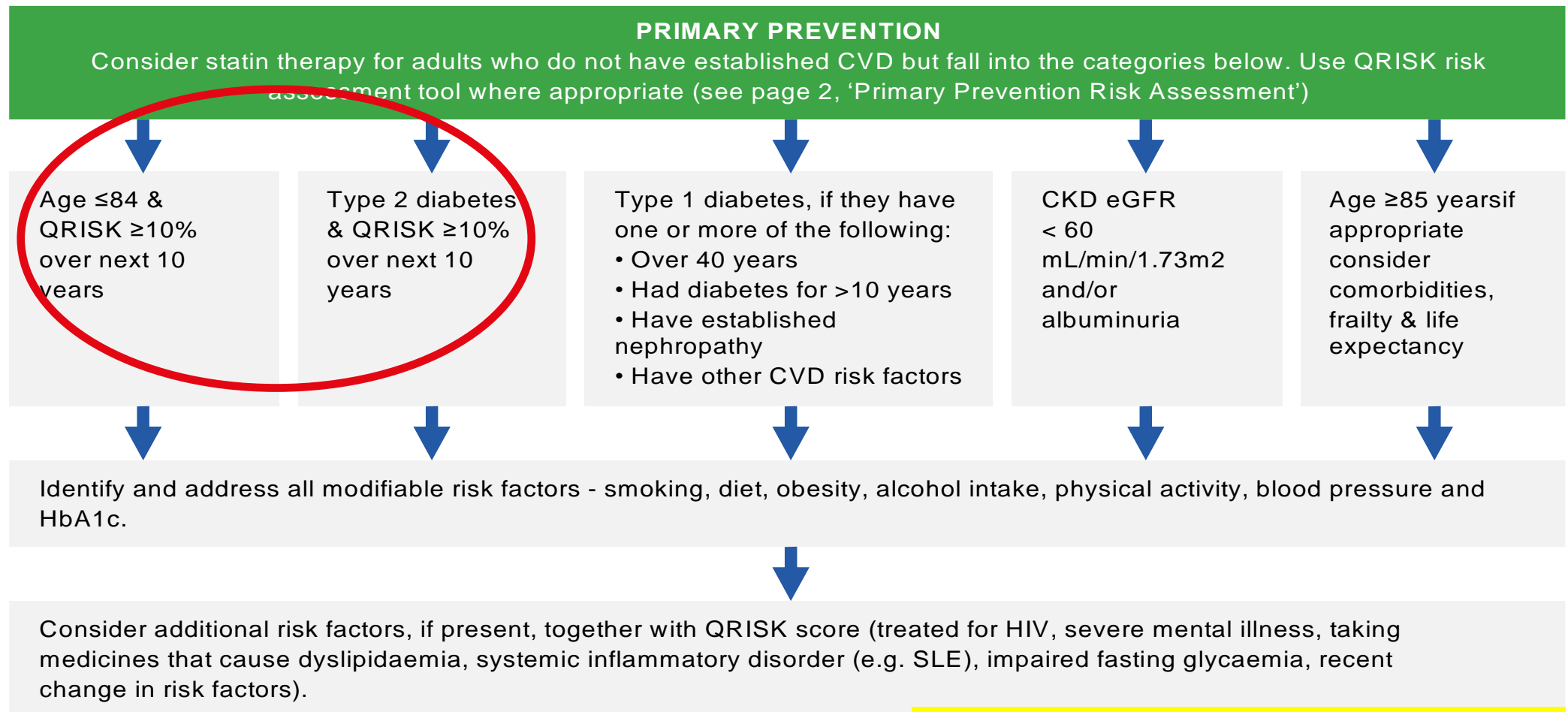
INITIAL CONSIDERATIONS:

- 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.

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.

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



What proportion of your patients have a QRisk score documented?

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

PRIMARY PREVENTION

If lifestyle modification is ineffective or inappropriate offer statin treatment.

Atorvastatin 20mg OD



Offer high intensity statin

- 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)

PCN DES / IIF alignment

STATIN INTENSITY TABLE

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

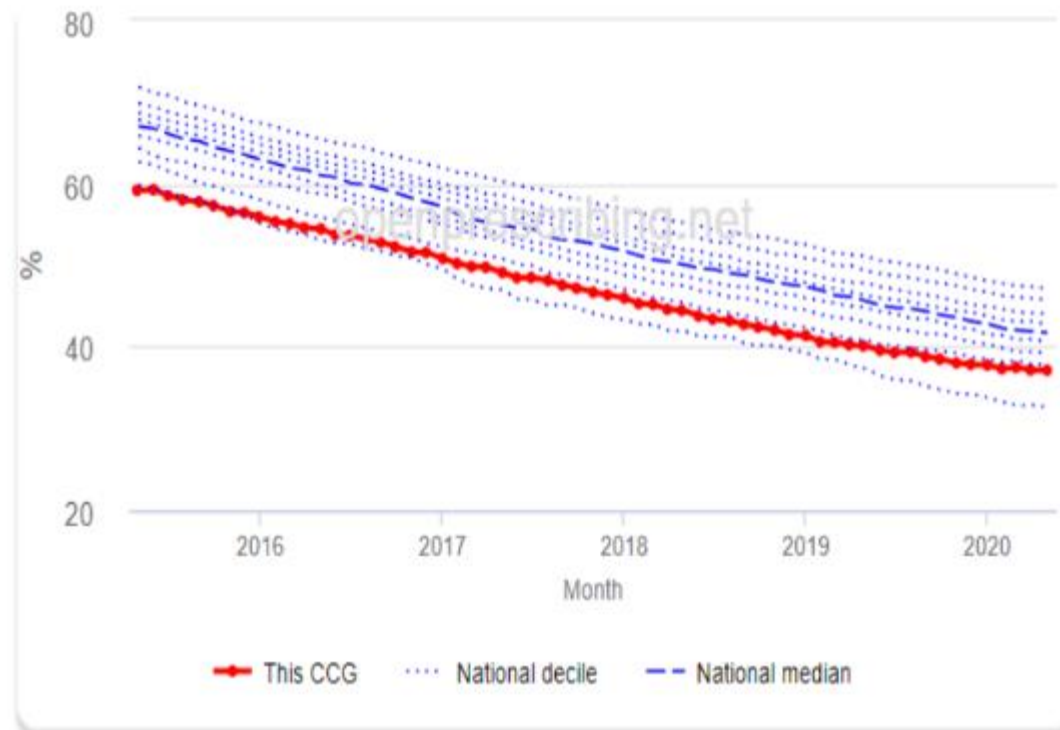
40% patients are still on low or moderate intensity statin

Prescribing of low and medium intensity statins

Low and medium intensity statins

[Link to chart](#)

Items of low and medium intensity statins as a percentage of items of all statins.



[Download data](#)

Why it matters: 2014 NICE guidance on [primary and secondary lipid modification](#) recommends the use of a high-intensity statin (i.e. one that reduces LDL cholesterol by 40% or more) with a low acquisition cost. A table showing the percentage reduction of LDL cholesterol by statin doses can be found [here](#) and you can read our research paper on suboptimal statin treatment regimens in the [British Journal of General Practice](#). Please note, we have excluded liquid preparations from this measure.

Explore:

- [Break the overall score down into individual presentations](#)
- [Split the measure into charts for individual practices](#)
- [Compare all CCGs in England on this measure](#)
- [View this measure on the analyse page](#)
- [View technical details for this measure](#)

Tagged as: [Cardiovascular system](#), [Efficacy](#), [NICE](#)

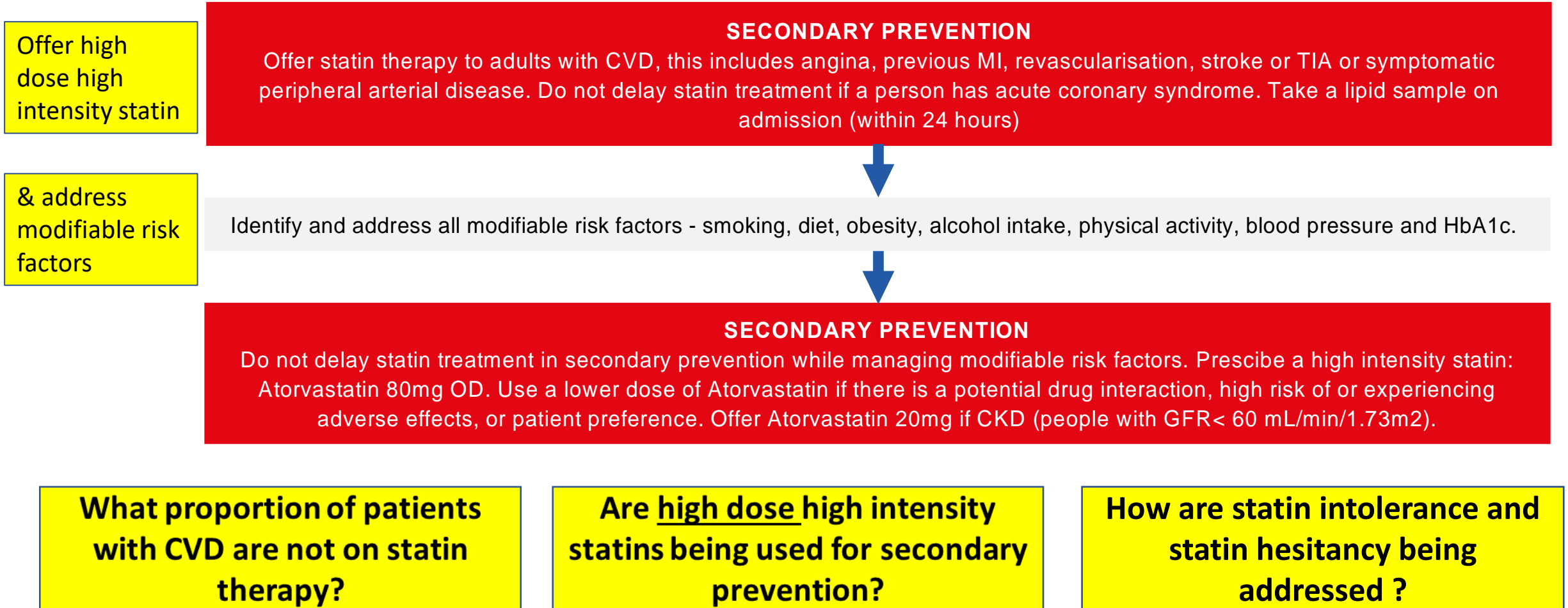
Summary of National Guidance for Lipid Management for Primary and Secondary Prevention of CVD

- 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.

Summary of National Guidance for Lipid Management for primary and secondary Prevention of CVD



- 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’)

**How are lipid levels communicated in local systems
What intensification thresholds / targets are being used?**

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

Are patients being identified for intensification of lipid lowering therapies beyond statins?

Use of LDL thresholds for injectable therapies – need a fasting sample

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

ACCELERATED
ACCESS
COLLABORATIVE



SEVERE HYPERLIPIDAEMIA

If TC > 7.5 mmol/L and/or LDL-C > 5.0 mmol/L and/or non-HDL-C > 5.9 mmol/L and/or family history of CVD (50 years) and no secondary prevention (Familial Hypercholesterolaemia or Heterozygous FH)

Do not use QRISK risk assessment

PCN DES / IIF alignment

DIAGNOSIS AND REFERRAL

Take fasting blood for repeat measure LDL-C.

Use the Simon Broome or Diagnostics Network (DLCN) criteria to make diagnosis of FH.

Refer to Lipid Clinic for further clinical diagnosis of FH

or if TC > 9.0 mmol/L and/or LDL-C > 6.5 mmol/L and/or non-HDL-C > 7.5 mmol/L or

fasting triglycerides > 10 mmol/L (regardless of family history)

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 > 5 mmol/L (primary prevention)
- OR LDL-C remains > 3.5 mmol/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

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	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-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 ÷ 2.2)
 ÷ 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
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 NICE 2021. TA694 www.nice.org.uk/guidance/TA694
 NICE 2021. TA733 www.nice.org.uk/guidance/TA733

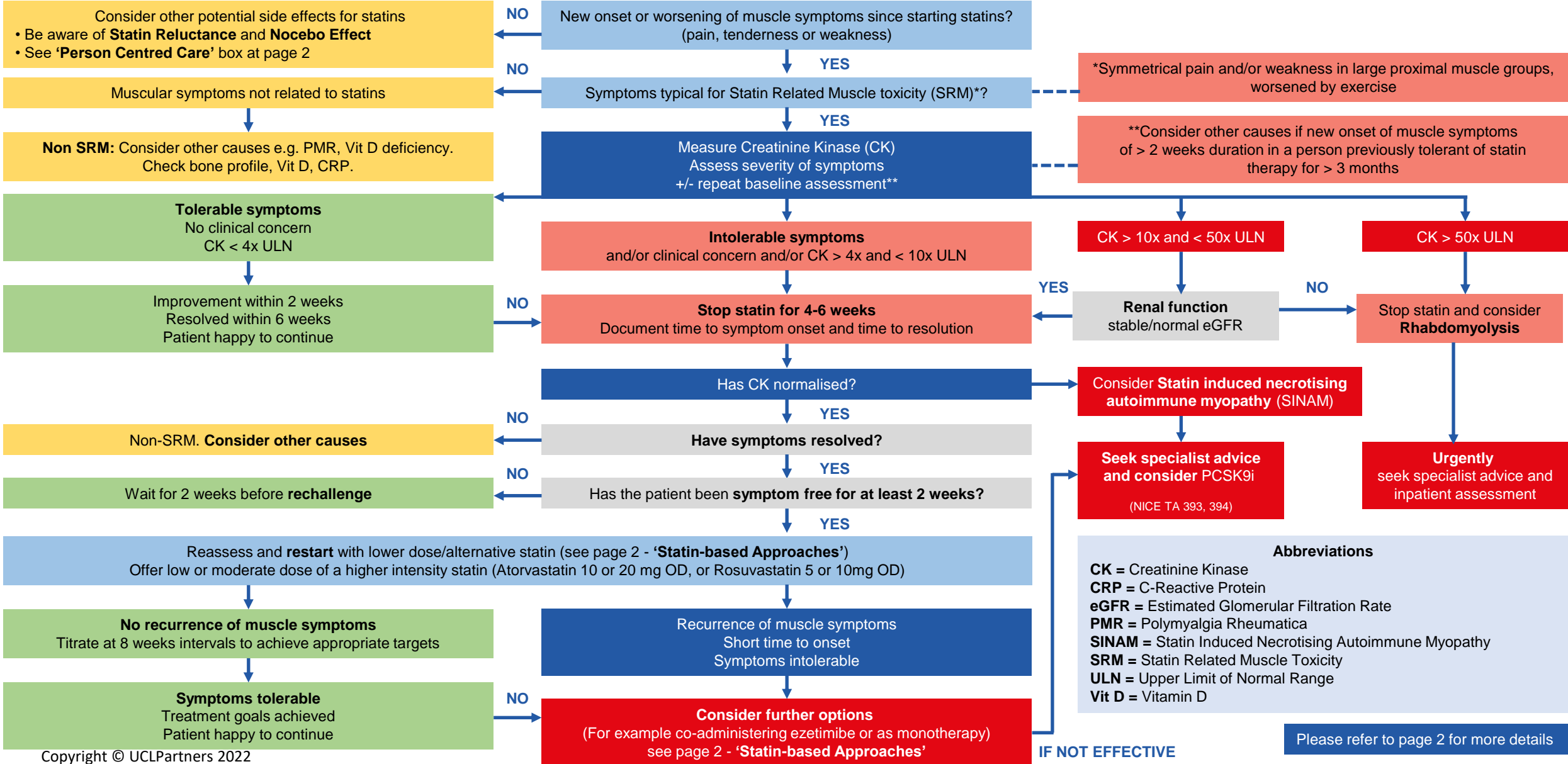
Approved by the National Institute for Health and Care Excellence (NICE), Dec 2021

Statin Intolerance Pathway

ACCELERATED
ACCESS
COLLABORATIVE



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



UCLPartners Proactive Care Frameworks

Supporting primary care recovery post pandemic



← Main website

Proactive care frameworks

We have developed a series of proactive care frameworks to support primary care teams to manage patients with cardiovascular and respiratory long-term conditions.



www.uclpartners.com/proactive-care

UCLPartners Proactive Care Frameworks

High Impact Conditions

CVD prevention

1. Atrial Fibrillation
2. Blood pressure
3. Cholesterol
4. Type 2 Diabetes

Respiratory

5. Asthma
6. COPD

In development

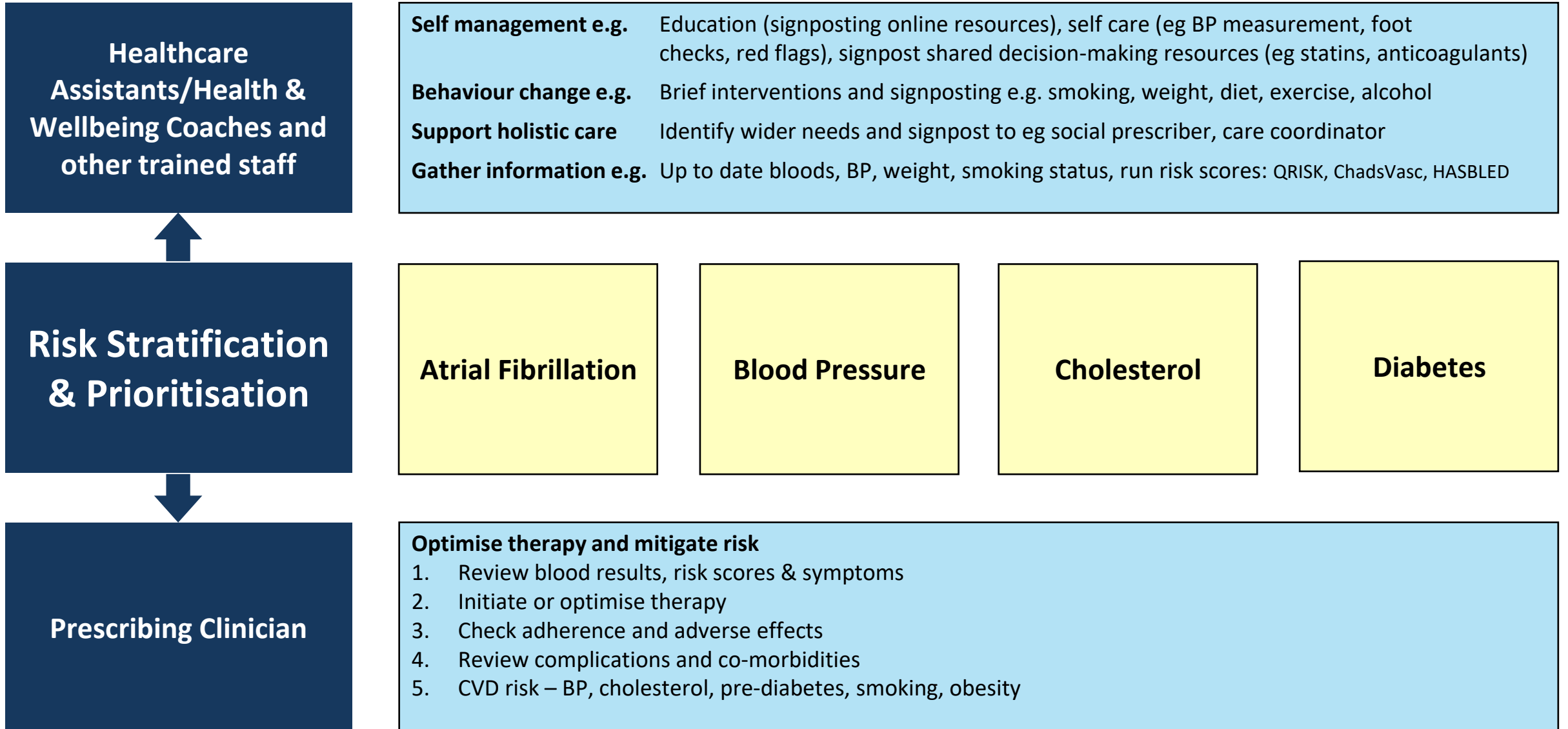
7. Heart Failure
8. SMI

Framework Principles

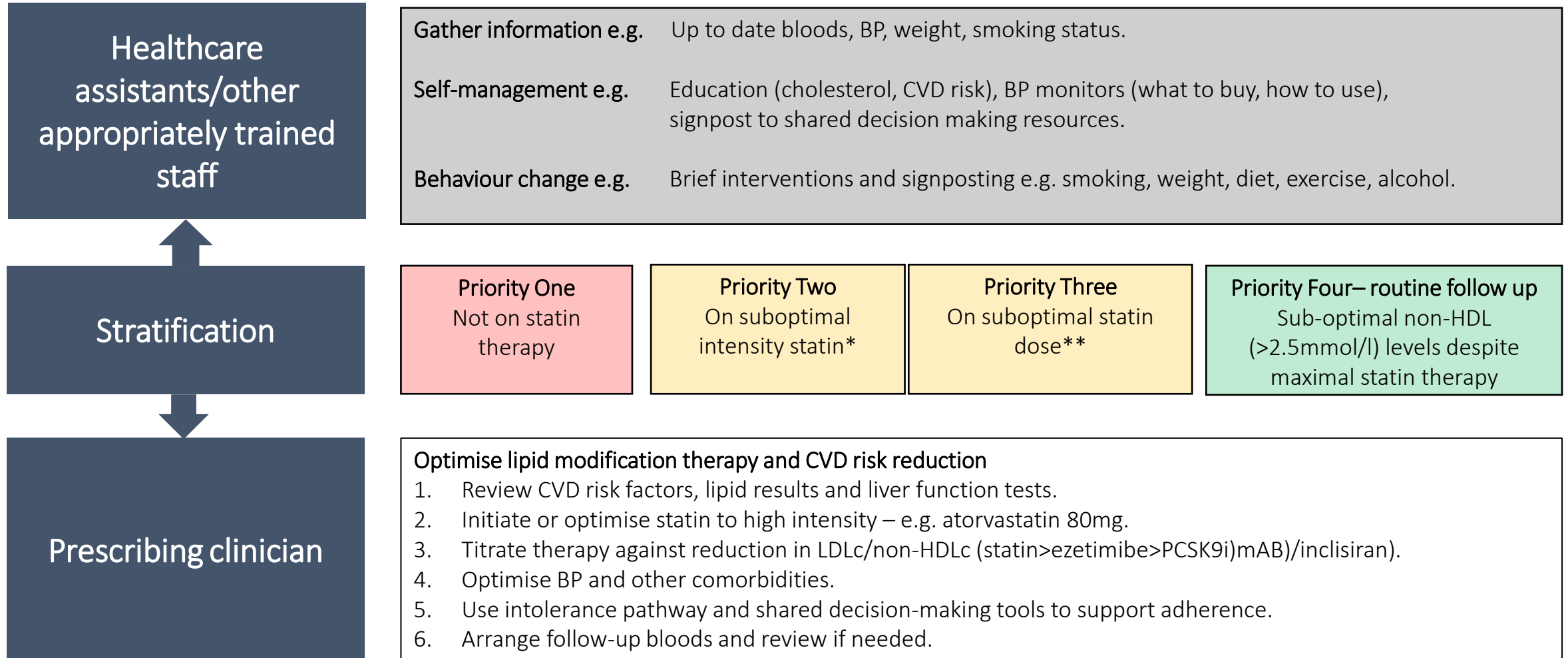
- Primary care led with PPI support
- Improve clinical care and self-care
- Free clinician capacity

Population Health Management Approach

- Risk stratification based on NICE guidance
- Prioritisation to optimise treatment early in those with greatest need
- Deploy wider workforce to support self-management and personalisation of care



Cholesterol – Secondary Prevention (pre-existing CVD)



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

Secondary prevention cholesterol search outcomes

- One London borough - population ~ 440,000
- Secondary prevention population = 9,232

Priority Cohort	Definition	No. of pts	% population
Priority Group 1	CVD not on a statin	2,383	26%
Priority Group 2	CVD on sub-optimal intensity statin	1,103	12%
Priority Group 3	CVD on sub-optimal dose of statin	4,108	44%
Priority Group 4	CVD on maximal statin with non-HDL chol > 2.5mmol/L	528	6%

Cholesterol –Primary Prevention (no pre-existing CVD)

Healthcare assistants/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 One
One of:
• QRISK \geq 20%
• CKD
• Type 1 Diabetes
AND
• Not on statin

Priority Two
• QRISK 15-19%
AND
• Not on statin

Priority Three
• QRISK 10-14%
AND
• Not on statin

Priority Four
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

Resources to support management of high cholesterol and other long-term conditions

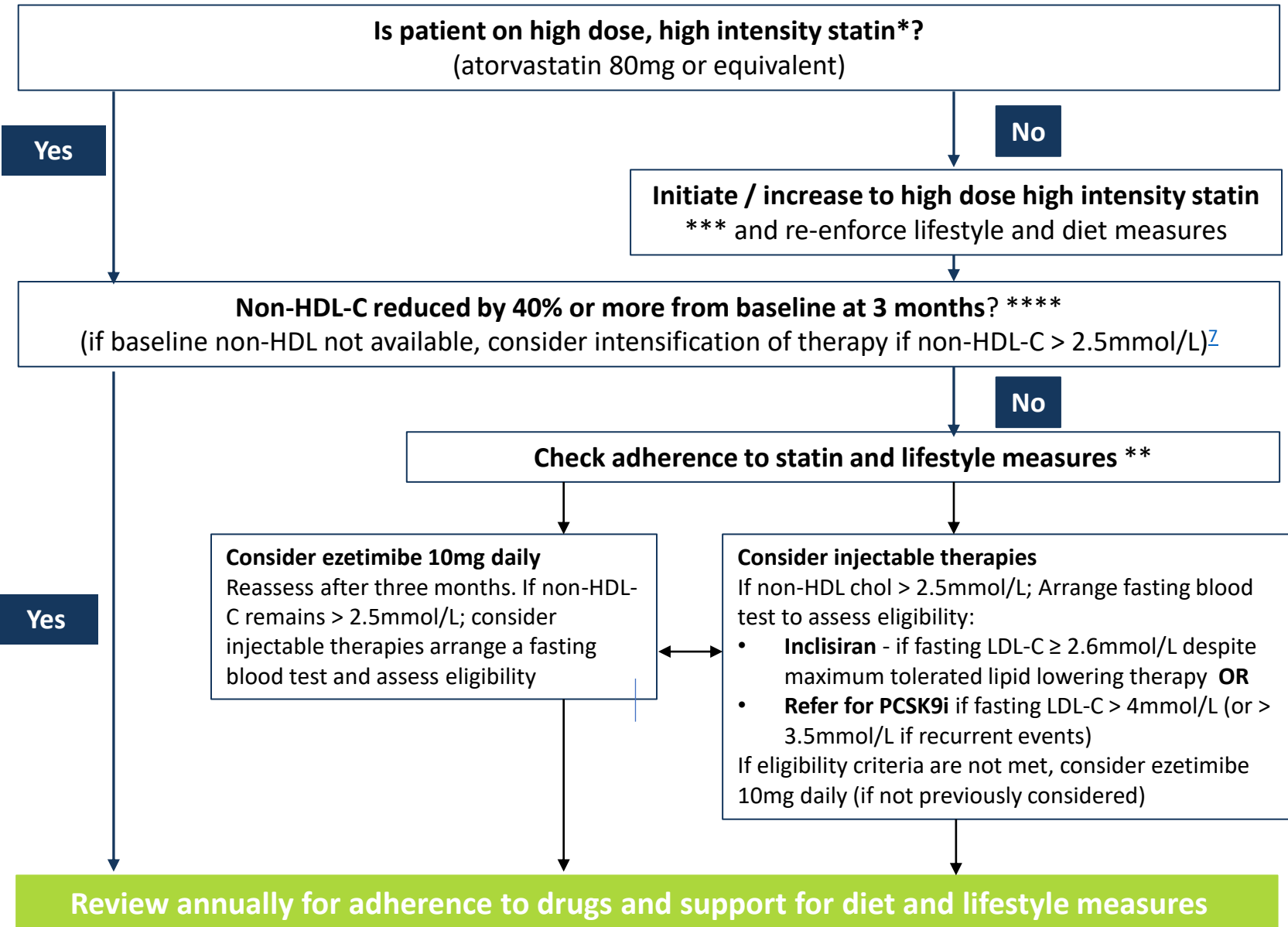
UCLP Resources – for local adaptation and integration



1. Comprehensive search & stratification tools for EMIS and SystmOne
2. Protocols for HCA and similar roles to provide structured support for patient education, self management and behaviour change
3. Slide sets for clinicians – focus on the *how to* of optimising clinical management in real world primary care
4. Workforce training framework
5. Implementation guidance and support and case studies
6. Digital resources for staff and patients
 - Understanding your condition
 - How to check your BP, check your feet, identify red flags etc
 - New technologies eg Healthy.io, fibricheck
 - Brief interventions eg smoking, diet, activity
 - Videos – eg running the search tools

The UCLPartners Proactive Care Frameworks focus on
The HOW of doing things differently

Optimisation Pathway for Secondary Prevention



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
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Rosuvastatin	20mg
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* Dose may be limited if:

- eGFR<30ml/min
- Drug interactions
- Intolerance
- Older age / frailty

** **If statin not tolerated**, follow statin intolerance pathway and consider ezetimibe 10mg daily +/- [bempedoic acid](#) 180mg daily. If non HDL-C remains > 2.5mmol/L despite other lipid lowering therapies consider injectable therapies.

*** See [statin intensity table](#)

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

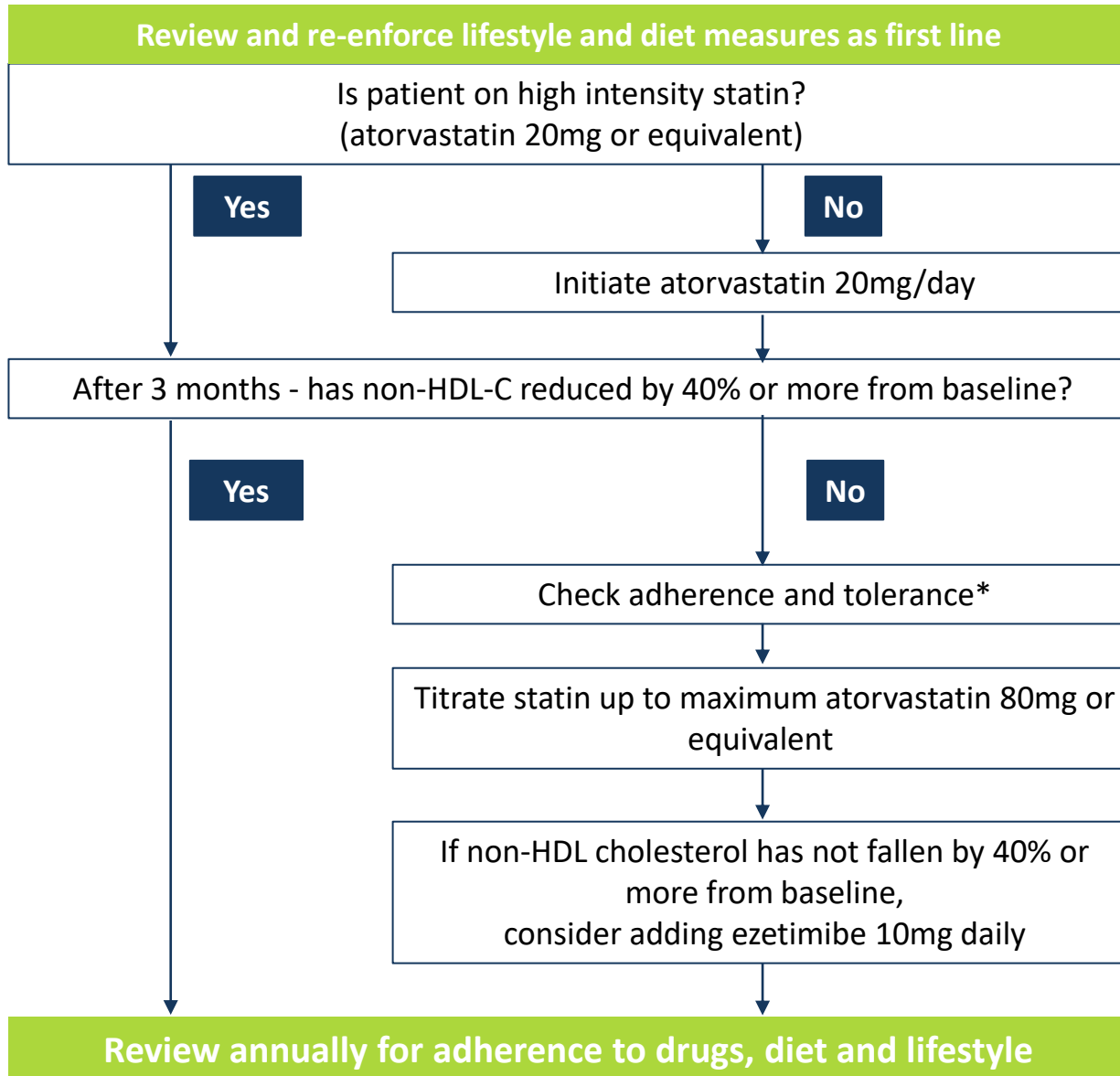
Inclisiran for secondary prevention

- 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 ≥ 2.6 mmol/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>

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 of Nilemdo 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, anemia, and elevated liver enzymes
- More information on bempedoic acid can be found at:
<https://www.medicines.org.uk/emc/product/11743/smpc#gref>

Optimisation Pathway for Primary Prevention



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

Shared Decision-Making Resources

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](#)

Important considerations

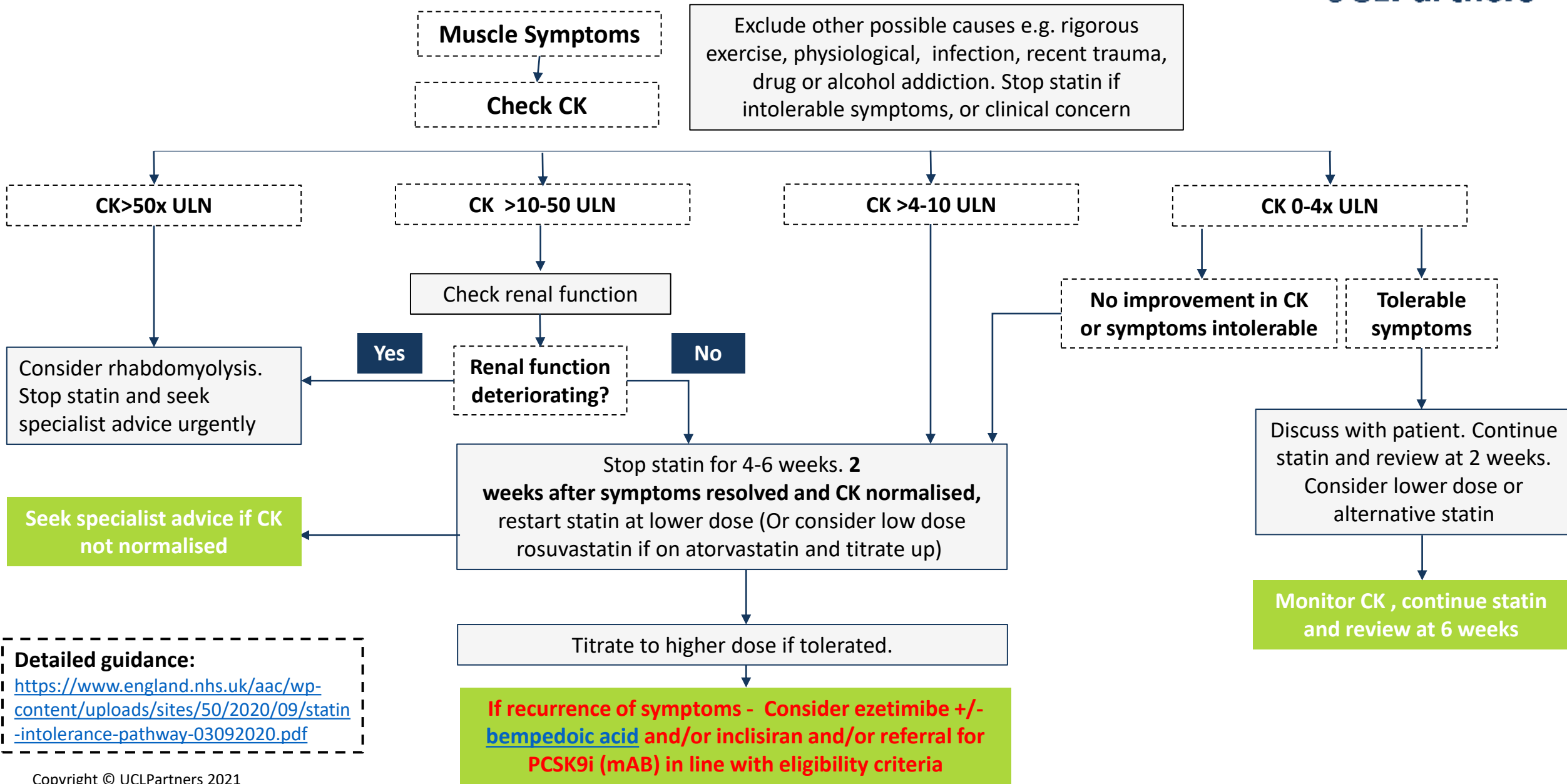
- Most adverse events attributed to statins are no more common than placebo*
- Stopping statin therapy is associated with an increased risk of major CV events. It is important not to label patients as 'statin intolerant' without structured assessment
- If a person is not able to tolerate a high-intensity statin, aim to treat with the maximum tolerated dose
- A statin at any dose reduces CVD risk – consider annual review for patients not taking statins to review cardiovascular risk and interventions

A structured approach to reported adverse effects of statins

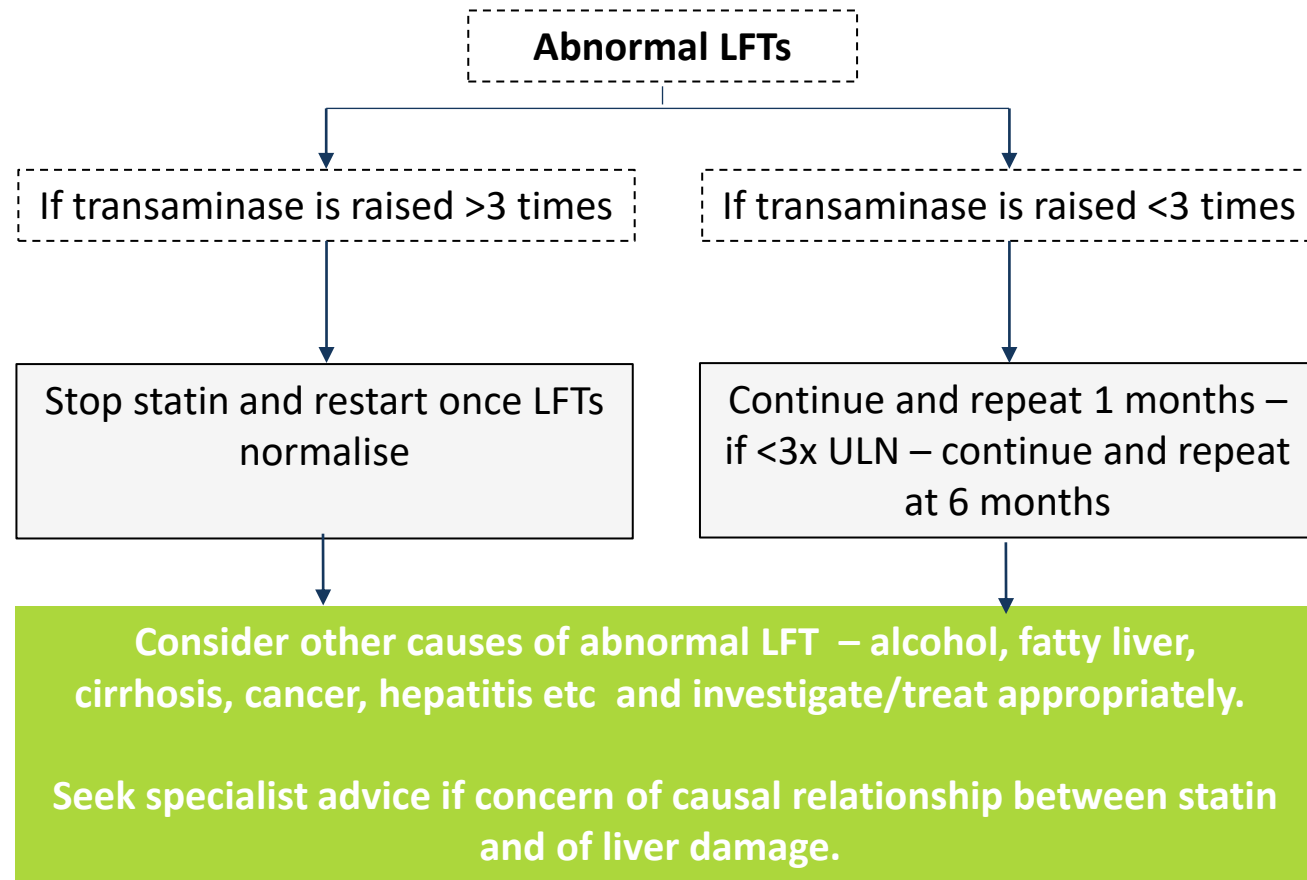
1. Stop for 4-6 weeks.
2. If symptoms persist, they are unlikely to be due to statin
3. Restart and consider lower initial dose
4. If symptoms recur, consider trial with alternative statin
5. If symptoms persist, consider ezetimibe +/- [bempedoic acid](#)

*(Collins et al systematic review, Lancet 2016)

Muscle Symptoms Pathway



Abnormal Liver Function Test Pathway



- 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.

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](#)

Familial hypercholesterolaemia

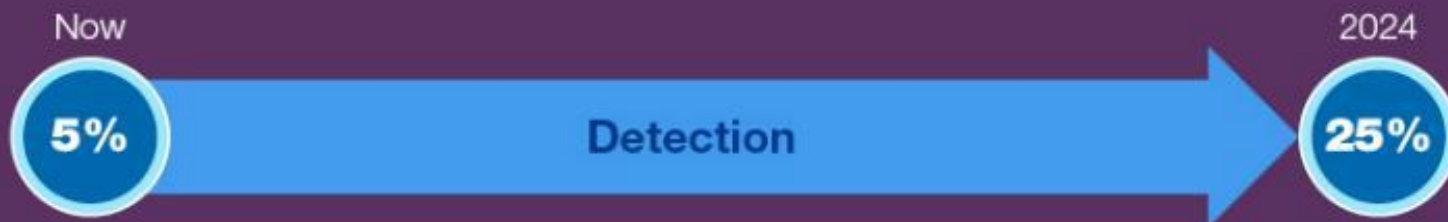
Current detection and management of High Cholesterol and Familial Hypercholesterolaemia (FH)



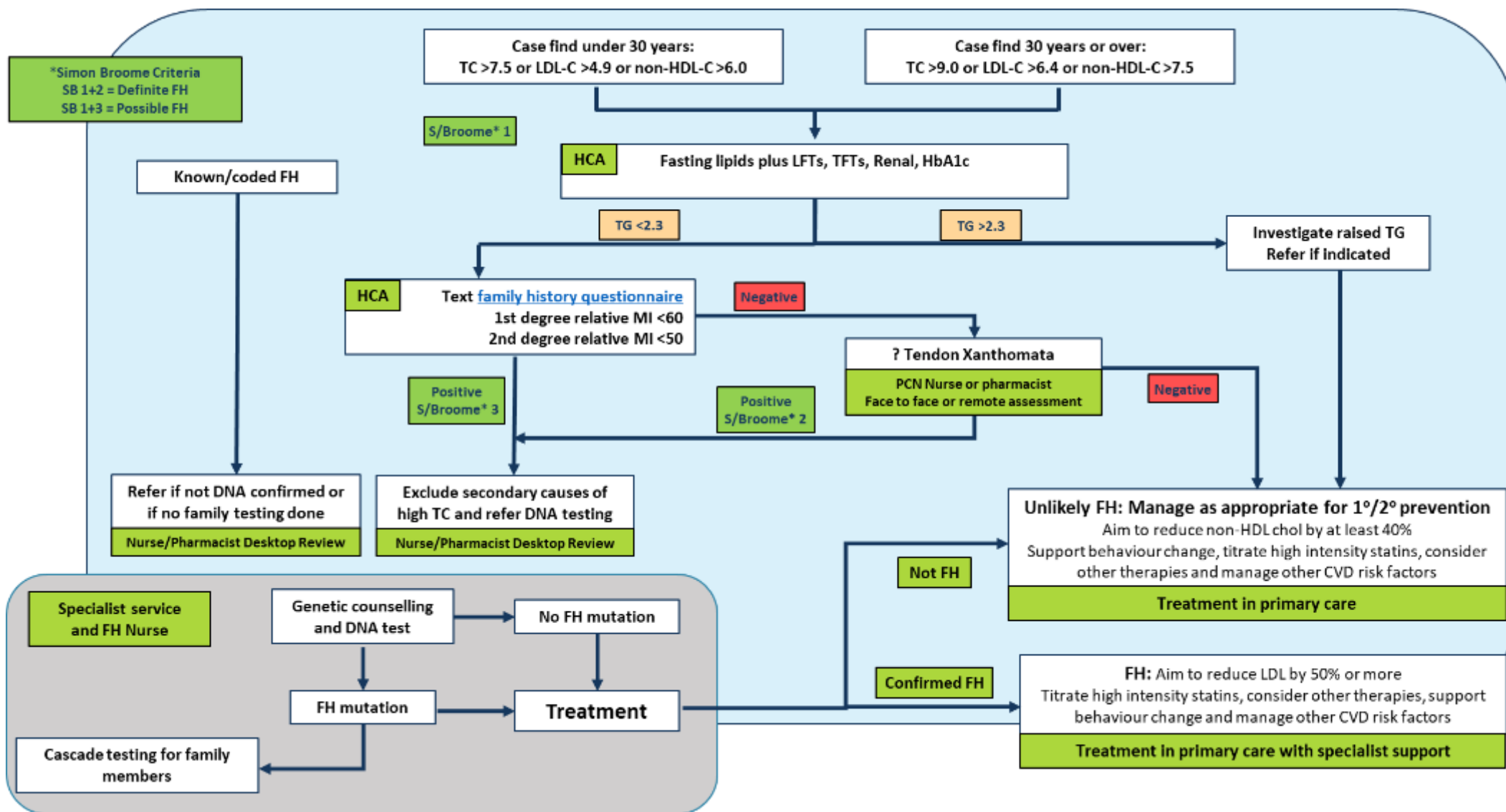
High Cholesterol



Familial Hypercholesterolaemia (FH)



FH Pathway – automating the process



Familial Hypercholesterolaemia Family History Questionnaire

We have reviewed your cholesterol results and would like some information on your family history to help inform your treatment. Please answer the following questions:

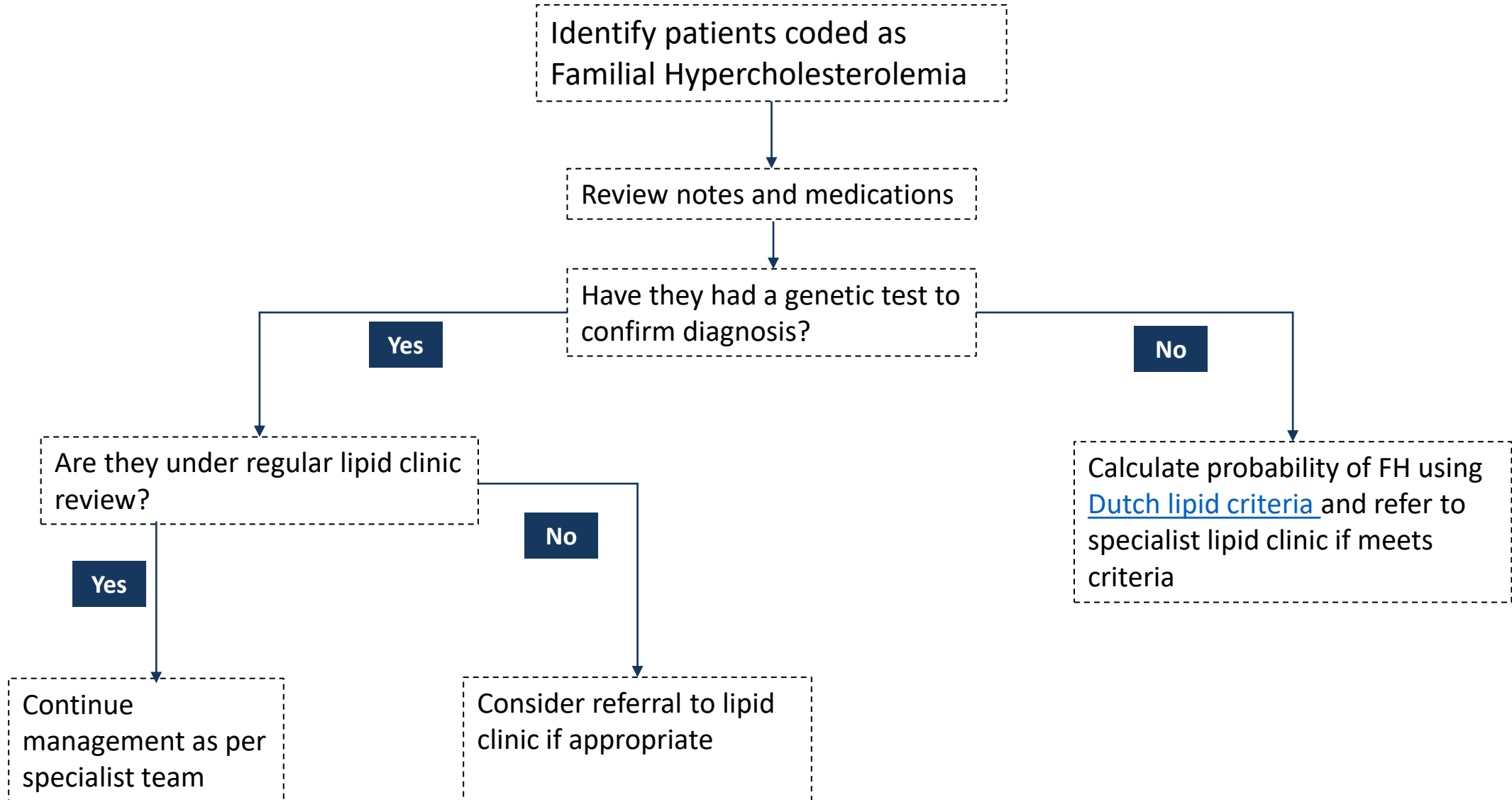
- 1 Have any of your first-degree blood relatives (mother, father, brother or sister) had a heart attack under the age of 60? **Yes/ No**

If Yes, which relative (mention how they are related to you) and how old were they when they had the heart attack?

- 2 Have any of your second-degree blood relatives (grandparents, aunts, uncles, nephews, nieces and half brothers and half sisters) had a heart attack aged 50 or under? **Yes/ No**

If Yes, which relative (mention how they are related to you) and how old were they when they had the heart attack?

Desktop Review for People with Coded FH



Dutch Lipid Clinic Criteria

Family history		
First-degree relative with known premature coronary and/or vascular disease (men aged <55 years and women aged <60 years)		1
or		
First-degree relative with known low-density lipoprotein-cholesterol (LDL-C) above the 95th percentile for age and sex		
First-degree relative with tendinous xanthomata and/or arcus cornealis or		2
Children aged <18 years with LDL-C above the 95th percentile for age and sex		
Clinical history		
Patient with premature coronary artery disease (ages as above)		2
Patient with premature cerebral or peripheral vascular disease (as above)		1
Physical examination		
Tendon xanthomas		6
Arcus cornealis prior to 45 years of age		4
LDL-C (mmol/L)		
	LDL-C ≥8.5	8
	LDL-C 6.5–8.4	5
	LDL-C 5.0–6.4	3
	LDL-C 4.0–4.9	1
Deoxyribonucleic acid (DNA) analysis: Functional mutation in the low-density lipoprotein receptor (LDLR), apolipoprotein B (APOB) or proprotein convertase subtilisin/kexin type 9 (PCSK9) gene		8
Stratification		Total score
Definite familial hypercholesterolaemia (FH)		≥8
Probable FH		6–7
Possible FH		3–5
Unlikely FH		<3
<i>ApoB</i> , apolipoprotein B; DNA, deoxyribonucleic acid; FH, familial hypercholesterolaemia; LDL-C, low-density lipoprotein-cholesterol; <i>LDLR</i> , low-density lipoprotein receptor; <i>PCSK9</i> , proprotein convertase subtilisin/kexin type 9		

Overview of Medicines Optimisation in FH

- 1 Offer a high-intensity statin to all adults with FH
- 2 Aim for at least a 50% reduction in LDL-C concentration
- 3 Increase the dose of statin after 3 months if not achieving a 50% reduction in LDL-C and not already prescribed maximum dose
- 4 Use ezetimibe in patients with FH who have contraindications to or cannot tolerate statin therapy **and consider adding [bempedoic acid](#)**
- 5 Add ezetimibe to statin therapy in patients who are not achieving a 50% reduction in LDL-C concentration despite maximum dose high intensity statin OR where statin dose is limited by side effects. Consider inclisiran in patients with CVD, who are not achieving an LDL-C < 2.6mmol/L despite optimal oral lipid lowering therapy (high intensity statins with or without ezetimibe)
- 6 Refer patients to a specialist:
 - if treatment with the maximum tolerated dose of a high-intensity statin and ezetimibe is inadequate
 - if they are assessed to be at very high risk of a coronary event:
 - Established coronary heart disease
 - A family history of premature coronary heart disease
 - Two or more other cardiovascular risk factors (for example, they are male, they smoke, or they have hypertension or diabetes)
- 7 Specialists may initiate PCSK9i (alirocumab or evolocumab), bile acid binders (resins) or fibrates in patients with an inadequate response to first line lipid lowering therapies.
- 8 PCSK9i are recommended for use in people with FH:
 - For primary prevention when LDL remains > 5mmol/L despite optimal statin / ezetimibe therapy
 - For secondary prevention when LDL remains > 3.5mmol/L despite optimal statin / ezetimibe therapy

Proactive care frameworks

We have developed a series of proactive care frameworks to support primary care teams to manage patients with cardiovascular and respiratory long-term conditions.



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

www.uclpartners.com/proactive-care

Thank you

For more information please contact:

primarycare@uclpartners.com

www.uclpartners.com
[@uclpartners](#)