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Tackling Cholesterol Together

Primary care challenges in lipid management and opportunities for improvement

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Intro & Declarations

MH

- GP with Special Interest in Cardiology, ESNEFT
- GP advisor, Health Innovation East
- Divisional Director, NEE community services

PA

- Partner, St James surgery, Clacton-on-sea
- GPPC – CVD Clinical lead
- ICB – Medicines Management

Learning Objectives

STRATEGIES TO ACHIEVE QOF INDICATORS

OPTIMISING LIPID MANAGEMENT IN PRIMARY AND SECONDARY CARDIOVASCULAR DISEASE PREVENTION

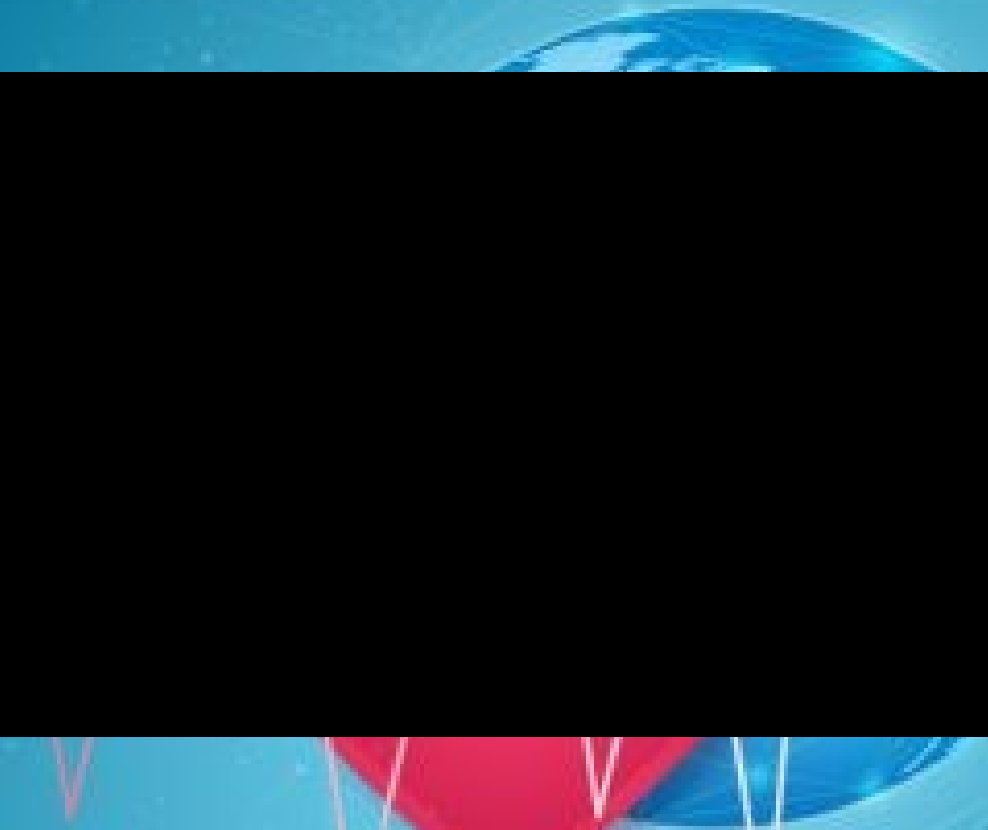
LEARNING ABOUT LATEST GUIDELINES AND THEIR APPLICATION TO PRIMARY CARE

LEARNING ABOUT INNOVATIVE NEW THERAPIES

OVERCOMING CHALLENGES SUCH AS STATIN INTOLERANCE

Scale of the problem

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

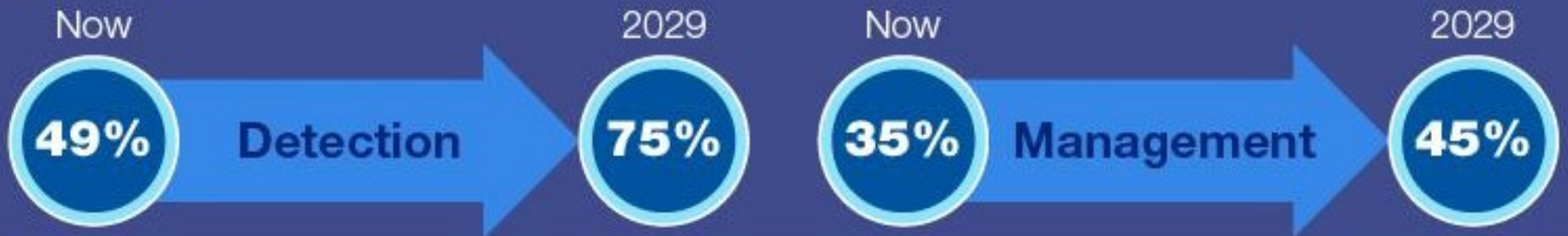


In England, CVD causes

Current detection and management of

High Cholesterol and Familial Hypercholesterolaemia (FH)

High Cholesterol



Familial Hypercholesterolaemia (FH)

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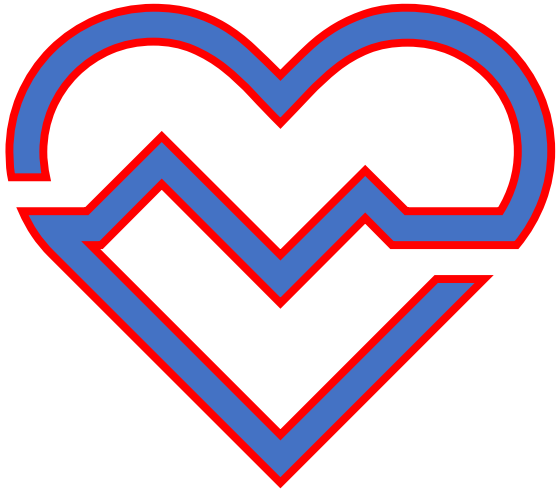
Let's think about how we can achieve best lipid outcomes for our patients

What is it we want to realistically achieve?

Better patient outcomes?
Improved QOF achievement?



How will you develop a model for delivering this or achieving QOF?

- **Who?** What resources do we have in our PCNs/ practices? If any beyond QOF!
- **How?** PHM approach identifying cohorts to target? Opportunistic at medication reviews?

So what's stopping us achieving best outcomes?

- Virtual consultations hindering care?
- Covid hangover
- Competing priorities of a practice
- Confusion and uncertainty among the general public about statin therapy and lipids
- Lack of knowledge of all healthcare professionals managing lipids
- Inequality between practices in actively managing raised lipids in patients
- Lack of reference expertise – Lipidologists, PwSIs
- Restructuring of the NHS and ICBs

23/24 lipid QOF indicators

Table 1. Indicators related to lipid modification in the Quality and Outcomes Framework (QOF) of the General Medical Services (GMS) contract.

CHOL001 Percentage of patients on the QOF Coronary Heart Disease, Peripheral Arterial Disease, Stroke/TIA or Chronic Kidney Disease Register who are currently prescribed a statin, or where a statin is declined or clinically unsuitable, another lipid lowering therapy	14	70-95%
CHOL002 Percentage of patients on the QOF Coronary Heart Disease, Peripheral Arterial Disease, or Stroke/TIA Register, who have a recording of non HDL cholesterol in the preceding 12 months that is lower than 2.5 mmol/L, or where non HDL cholesterol is not recorded a recording of LDL cholesterol in the preceding 12 months that is lower than 1.8 mmol/L	16	20-35%
Data from: [NHS England, 2023]		

Hot off the press!

24/25 target changed to LDL <2mmol/l (non-HDL 2.8mmol/l)

23/24 lipid QOF indicators

Indicator	Points	Thresholds
MH011. The percentage of patients with schizophrenia, bipolar affective disorder and other psychoses who have a record of a lipid profile in the preceding 12 months (in those patients currently prescribed antipsychotics, and/or have pre-existing cardiovascular conditions, and/or smoke, and/or are overweight (BMI of ≥23 kg/m2 or ≥25 kg/m2 if ethnicity is recorded as White) or preceding 24 months for all other patients	7	50-90%

MH011 Rationale

NICE guidance (NICE CG178, NICE CG185) recommends annual blood lipid profiles for people with bipolar disorder, psychosis or schizophrenia.

Individuals with severe mental illness have five times the risk of dyslipidaemia than the general population (NHS England, 2016).

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

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INITIAL CONSIDERATIONS:

- Measure non-fasting ***full lipid profile*** (total cholesterol, HDL-C, non-HDL-C, triglycerides) and HbA1c as part of an initial baseline assessment.
- Consider secondary causes of hyperlipidaemia and manage as needed.
- Ensure appropriate baseline and follow up tests as detailed on page 2. Measure BMI.
- Identify and exclude people with contraindications/drug interactions
- If non-fasting triglyceride above 4.5mmol/L see page 2.

PRIMARY PREVENTION

Consider statin therapy for adults who do not have established CVD but fall into the categories below. Use QRISK risk assessment tool where appropriate (see page 2, *'Primary Prevention Risk Assessment'*)

- Age ≤84 & QRISK ≥10% over next 10 years
- Type 2 diabetes & QRISK ≥10% over next 10 years
- Type 1 diabetes, if they have one or more of the following:
  - Over 40 years
  - Had diabetes for >10 years
  - Have established nephropathy
  - Have other CVD risk factors
- CKD eGFR < 60 mL/min/1.73m² and/or albuminuria
- Age ≥85 years if appropriate consider comorbidities, frailty & life expectancy

Identify and address all modifiable risk factors - smoking, diet, obesity, alcohol intake, physical activity, blood pressure and HbA1c.

Consider additional risk factors, if present, together with QRISK score (treated for HIV, severe mental illness, taking medicines that cause dyslipidaemia, systemic inflammatory disorder (e.g. SLE), impaired fasting glycaemia, recent change in risk factors)

PRIMARY PREVENTION

If lifestyle modification is ineffective or inappropriate offer statin treatment.

Atorvastatin 20mg daily

- Measure full lipid profile again after 3 months (non-fasting).
- High intensity statin treatment should achieve reduction of non-HDL-C > 40% from baseline. If not achieved after 3 months;
  - discuss treatment adherence, timing of dose, diet and lifestyle
  - If at higher risk (based on comorbidities, risk score or clinical judgement – see page 2 *'Additional Risk Factors'*) consider increasing the dose every 2-3 months up to a maximum dose of atorvastatin 80mg daily.
  - For how to increase in people with CKD see *'Special Patient Populations'* (page 2).
- If patients on a high-intensity statin have side effects, offer a lower dose or an alternative statin (see page 2 *'Extent of lipid lowering with available therapies'*)
- If maximum tolerated dose of statin does not achieve non-HDL-C reduction > 40% of baseline value after 3 months consider adding Ezetimibe 10mg daily (NICE TA385)
- If statin treatment is contraindicated or not tolerated;
  - See AAC Statin Intolerance Algorithm for advice regarding adverse effects (click here)
  - Ezetimibe 10mg monotherapy may be considered. Assess response after 3 months.
  - Ezetimibe 10mg/bempedoic acid 180 mg combination may be considered when ezetimibe alone does not control non-HDL-C/LDL-C well enough (NICE TA694).

If non-HDL-C reduction remains < 40% of baseline despite maximal tolerated lipid lowering therapy (including people with intolerances and contraindications) consider referral to specialist lipid management clinic according to local arrangements

SEVERE HYPERLIPIDAEMIA

If TC>7.5mmol/L and/or LDL-C >4.9mmol/L and/or non-HDL-C >5.9mmol/L, a personal and/or family history of confirmed CHD (<60 years) and with no secondary causes: suspect familial hypercholesterolaemia (possible heterozygous FH)

Do not use QRISK risk assessment tool

DIAGNOSIS AND REFERRAL

Take fasting blood for repeat lipid profile to measure LDL-C.

Use the **Simon Broome** or **Dutch Lipid Clinic Network** (DLCN) criteria to make a **clinical diagnosis of FH**.

Refer to Lipid Clinic for further assessment if **clinical diagnosis of FH** or if TC>9.0mmol/L and/or LDL-C >6.5mmol/L and/or non-HDL-C >7.5mmol/L or Fasting triglycerides > 10mmol/L (regardless of family history) (page 2)

TREATMENT TARGETS IN FH

If clinical diagnosis of FH and/or other risk factors present follow the recommended treatment management pathway for primary or secondary prevention as for non-FH, ***BUT***

Aim to achieve at least a 50% reduction of LDL-C (or non-fasting non-HDL-C) from baseline.

Consider specialist referral for further treatment and/or consideration of PCSK9i therapy IF

- they are assessed to be at very high risk of a coronary event**
- OR therapy is not tolerated
- OR LDL-C remains >5mmol/L (primary prevention)
- OR LDL-C remains >3.5mmol/L (secondary prevention)

despite maximal tolerated statin and ezetimibe therapy.

**defined as any of the following:

- Established coronary heart disease
- Two or more other CVD risk factors

SECONDARY PREVENTION

Offer statin therapy to adults with CVD, this includes CHD, angina, Acute Coronary Syndrome (MI or unstable angina), revascularisation, stroke or TIA, or symptomatic peripheral arterial disease. Do not delay statin treatment if a person has acute coronary syndrome. Take a lipid sample on admission (within 24 hours).

Identify and address all modifiable risk factors - smoking, diet, obesity, alcohol intake, physical activity, blood pressure and HbA1c.

SECONDARY PREVENTION

Do not delay statin treatment in secondary prevention while managing modifiable risk factors.

Prescribe a high intensity statin:

Atorvastatin 80mg daily

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

Offer atorvastatin 20mg if CKD (people with GFR< 60 mL/min/1.73m²).

- Measure full lipid profile again after 3 months (non-fasting).
- High intensity statin treatment should achieve reduction of non-HDL-C > 40% from baseline. If not achieved after 3 months
  - discuss treatment adherence, timing of dose, diet and lifestyle measures
  - If started on less than atorvastatin 80mg and the person is judged to be at higher risk (based on comorbidities, risk score or clinical judgement - see page 2 *'Additional Risk Factors'*), consider increasing to 80mg atorvastatin. For how to increase in people with CKD see *'Special Patient Populations'* (page 2).
- If non-HDL-C baseline value is not available*, consider target non-HDL-C < 2.5mmol/L (approximately equivalent to LDL-C < 1.8mmol/L) as recommended by Joint British Societies (JBS3).
  **this scenario is not currently covered by NICE CG181. NICE will consider this as part of the guideline update with publication currently expected September 2023*
- If patients on a high-intensity statin have side effects, offer a lower dose or an alternative statin (see page 2 *'Extent of lipid lowering with available therapies'*)

If maximum tolerated dose of statin does not control non-HDL-C/LDL-C well enough after 3 months confirm statin adherence, then consider the following options based on shared decision making* with the patient

If recommended statin treatment is contraindicated or not tolerated - follow AAC Statin Intolerance Algorithm for advice regarding adverse effects (click here).

If statin intolerance is confirmed, consider:

- **Ezetimibe 10mg** monotherapy. Assess response after 3 months (TA385)
- **Ezetimibe 10mg/bempedoic acid 180 mg** combination when ezetimibe alone does not control non-HDL-C sufficiently. (NICE TA694)

If non HDL-C remains > 2.5mmol/L despite other lipid lowering therapies consider Injectable therapies - arrange a fasting blood test and assess eligibility criteria (TA393/394, TA733)

Ezetimibe 10mg daily (NICE TA385). Reassess after three months. If non-HDL-C remains > 2.5mmol/L; consider **injectable therapies** arrange a fasting blood test and assess eligibility

Injectable therapies**

If non-HDL-C > 2.5mmol/L; Arrange fasting blood test to measure LDL-C to assess eligibility:

- **Inclisiran** - if fasting LDL-C ≥ 2.6mmol/L despite maximum tolerated lipid lowering therapy (TA733)

OR

- **PCSK9i** - see overleaf for LDL-C thresholds. (TA393/4)

If eligibility criteria not met, consider **ezetimibe 10mg daily** (if not previously considered)

* See overleaf for information to support shared decision making

** Inclisiran and PCSK9i should not be prescribed concurrently

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

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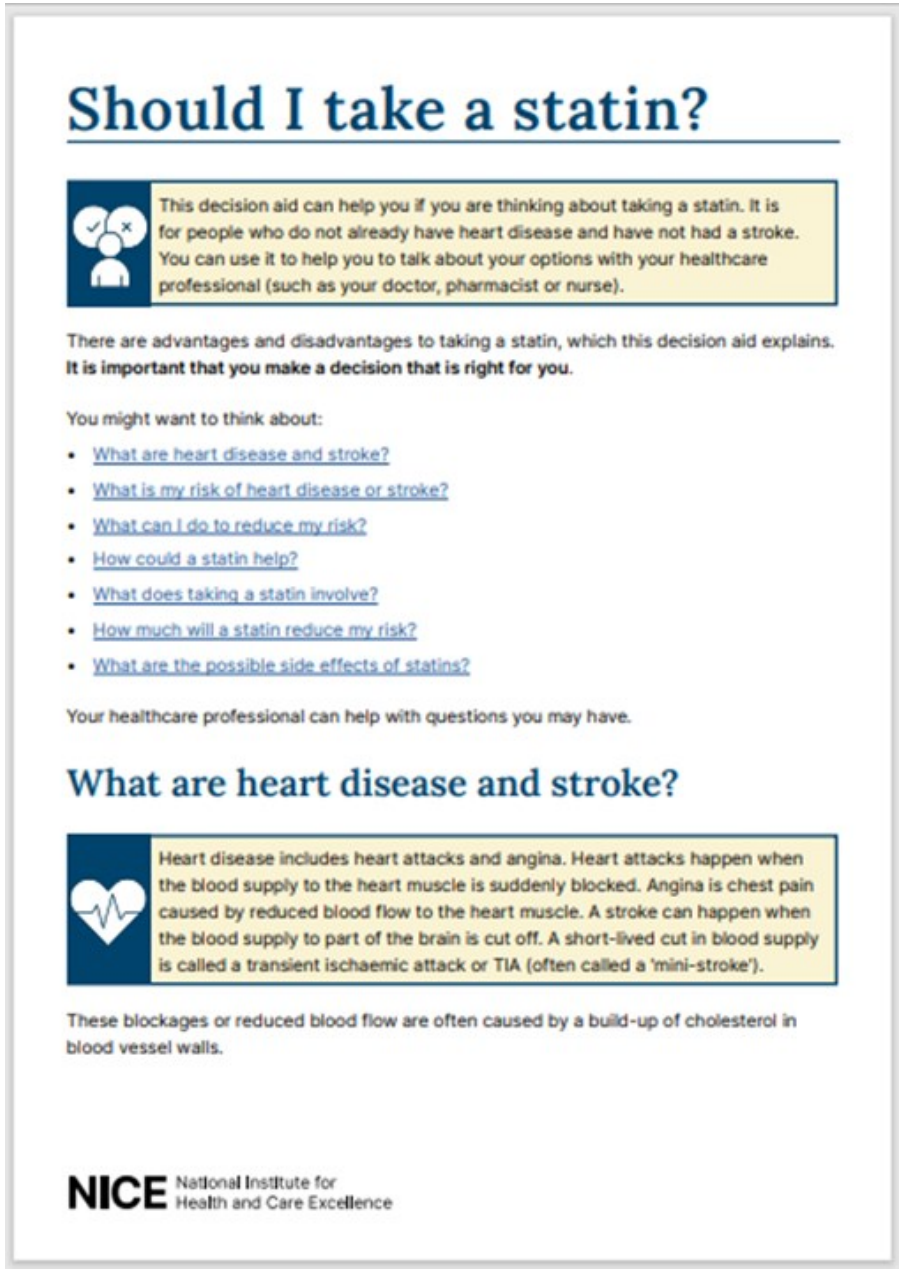
Patient Decision Aids

How do we get our patients on to the best therapy?

What is a Patient Decision Aid ?

Patient Decision Aids are tailored to a person's health status and help them to make specific, personal choices about their treatment. Importantly, they are intended to supplement or support the interaction between the person and their healthcare professional, rather than replace it.

The values and perceptions of individual people, and their attitudes to risk, may be different from those of their healthcare professional (Thornton 2003). Using PDAs in a consultation may help to improve a person's knowledge of the options and outcomes and give them more realistic expectations (Stacey et al. 2014).



Should I take a statin?

This decision aid can help you if you are thinking about taking a statin. It is for people who do not already have heart disease and have not had a stroke. You can use it to help you to talk about your options with your healthcare professional (such as your doctor, pharmacist or nurse).

There are advantages and disadvantages to taking a statin, which this decision aid explains. **It is important that you make a decision that is right for you.**

You might want to think about:

- What are heart disease and stroke?
- What is my risk of heart disease or stroke?
- What can I do to reduce my risk?
- How could a statin help?
- What does taking a statin involve?
- How much will a statin reduce my risk?
- What are the possible side effects of statins?

Your healthcare professional can help with questions you may have.

What are heart disease and stroke?

Heart disease includes heart attacks and angina. Heart attacks happen when the blood supply to the heart muscle is suddenly blocked. Angina is chest pain caused by reduced blood flow to the heart muscle. A stroke can happen when the blood supply to part of the brain is cut off. A short-lived cut in blood supply is called a transient ischaemic attack or TIA (often called a 'mini-stroke').

These blockages or reduced blood flow are often caused by a build-up of cholesterol in blood vessel walls.

NICE National Institute for Health and Care Excellence

Examples of PDAs

- **The NICE guideline recommends that, before offering statin treatment for primary prevention, the benefits of lifestyle modification should be discussed with the person after initial CVD risk assessment.**
- **Management of all other modifiable CVD risk factors should be prioritised with the person. If, after a reasonable time period, lifestyle modification has been ineffective, statin treatment should be offered to people who have a 10% or greater 10-year risk of developing CVD using the QRISK assessment tool**

NICE. Patient decision aid: user guide for healthcare professionals Implementing the NICE guideline on lipid modification (CG181) www.nice.org.uk/guidance/cg181/resources/patient-decision-aid-user-guide-pdf-243780158
NICE. Patient Decision Aid: Taking a statin to reduce the risk of coronary heart disease and stroke www.nice.org.uk/guidance/cg181/resources/patient-decision-aid-pdf-243780159
CG181 Patient decision aid on should I take a statin? (nice.org.uk)

Shifting sands…
What targets should I be aiming for?

NICE /AAC algorithm- Aiming for a reduction in non-HDL-cholesterol Or LDL concentration of greater than 40% is recommended (50% in FH).
If this is not achieved, adherence to drug treatment should be checked and lifestyle modifications optimised.

QOF – Specific targets in secondary prevention ie LDL <1.8 (soon 2) and /or non HDL <2.5 (soon 2.6)

ESC- At least a 50% reduction! Secondary prevention and very high risk primary prevention LDL <1.4. High risk patients LDL <1.8.

THE LOWER THE BETTER!
Especially in very high-risk patients

Why LDL-C ?
Lipid profiles… the BIGGER picture

Patient A	Patient B
• Total cholesterol 5.5 HDL-C: 2.4 LDL-C: 2.6 Non-HDL-C: 3.1 TG: 1.9 TC/HDL-C: 2.3	• Total cholesterol 5.5 HDL-C: 0.7 LDL-C: 4.0 Non-HDL: 3.8 TG: 4.9 TC/HDL-C: 7.8

95% confidence limits on a single cholesterol measurement are around ±14% of the true value[1]

- HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglycerides.

- **1.** Glasziou PP et al. Ann Intern Med 2008;148(9):656–661.

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Key slide re effectiveness of different lipid lowering therapies

EXTENT OF LIPID LOWERING WITH AVAILABLE THERAPIES

Approximate reduction in LDL-C					
Statin dose mg/day	5	10	20	**40**	**80**
Fluvastatin			21%	27%	33%
Pravastatin		20%	24%	29%	
Simvastatin		27%	32%	37%	42%
Atorvastatin		37%	43%	49%	55%
Rosuvastatin	38%	43%	48%	53%	
Atorvastatin + Ezetimibe 10mg		52%	54%	57%	61%

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

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

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

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

- **Rosuvastatin** may be used as an alternative to atorvastatin if compatible with other drug therapy. Some people may need a lower starting dose (see BNF).
- Low/medium intensity statins should only be used if intolerance or drug interactions.
- **Ezetimibe** when combined with any statin is likely to give greater reduction in non-HDL-C or LDL-C than doubling the dose of the statin.
- **PCSK9i** (NICE TA393, TA394) alone or in combination with statins or ezetimibe produce an additional LDL-C reduction of approximately 50% (range 25-70%).
- **Bempedoic acid** when combined with ezetimibe (TA694) produces an additional LDL-C reduction of approximately 28% (range 22-33%) but no clinical outcome evidence is currently available.
- **Inclisiran** (TA733) alone or in combination with statins or ezetimibe produces an additional LDL-C reduction of approximately 50% (range 48-52%) but no clinical outcome evidence is currently available.

Managing patient resistance to statins

If a person is not able to tolerate a high-intensity statin aim to treat with the maximum tolerated dose.

Inform the patient that any statin at any dose reduces CVD risk.

If someone reports adverse effects when taking high-intensity statin discuss the following possible strategies with them :

1) stopping the statin and trying again when the symptoms have resolved to check if the symptoms are related to the statin
2) reducing the dose within the same intensity group
3) changing the statin to a lower intensity group

Statins are stopped when CK>10x ULN

(Check Renal function stable/normal eGFR)

(Seek specialist advice about options for treating people at high risk of CVD such as those with CKD, type 1 diabetes, type 2 diabetes or genetic dyslipidaemias, and those with CVD, who are intolerant to 3 different statins)

Practice case study in NEE

- ***<u>Data from St James</u>***
- 252 / 320 patients have been identified as per new QOF rules (M 115; F 137)
- In the past years they had ‘statin declined’ code was added…when patient refused statins (gold standard in the past) due to side effects
- With the change in guidelines an alternative lipid lowering therapy needs to be offered
- CHOL001 we are currently 78% (from 12th March 24 data) and our target is 95%
- For CHOL002 we are currently 42% (from 12th March 24 data) and our target is 35% - **We have achieved this target already!!**

- **A search for statin decline coded within 2023/2024** - *within this spreadsheet, another code to identify if they have had "Lipid lowering therapy declined" code too was added.*
- *If they have, they have been excluded from the CHOL001 QOF search*
- **-41 patients have been identified (M 22; F 19)**
- **A search for lipid lower therapy decline code within 2023/2024** - *These patients have been excluded from the CHOL001 QOF search.*
- **-27 patients have been identified (M 11; F 16)**

Patient case study- statin intolerance

THE PATIENT

- 42-year-old male civil engineer
- Married with one son aged 12 years
- Never smoked
- Drinks one glass of wine with meals during the week, three to four glasses on weekend nights when socialising
- Jogs for 45 minutes five days of the week
- Admits to 'not paying any attention to his diet' and 'eating what he likes'. He is particularly fond of cheese, bacon and pork ribs

- He recently moved to a new town , Cambridge in East of England

following a promotion, seeking new medical care

- MEDICAL HISTORY
- Hypertension controlled
- Raised BMI :29
- Hypercholesterolaemia:LDL cholesterol 8.6 He first became aware of high cholesterol at the age of 40. Although his previous doctor advised him to take lipid-lowering medication he only did so briefly for a few months. His main reasons for not taking lipid-lowering medication at the moment are that he felt the medication 'did not agree with him' and he thought it not necessary because he was a non-smoker and exercised regularly.
- Target reduction in cholesterol 40% or 50 % if FH confirmed
- Treatment initiated with a HIS not previously trialled (rosuvastatin) .Patient developed muscle aches and we considered other causes . Checked CK, Vit D , CRP and bone profile. Low Vit D corrected , CK less than 4x ULN. Symptoms resolved within 6 weeks and patients was happy to continue with his statin treatment he could tolerate which was Rosuvastatin 10mg .
- Target reduction not achieved and patient was initiated on a combination with ezetimibe 10mg which achieved a greater than 50 % reduction in LDL-C.

It’s not all about the statins

QOF Personalised Care Adjustment changed from just statins to……

They decline or are clinically unsuitable for both statin treatment and all available alternative lipid-lowering therapies within the current fiscal year.

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3 relatively recent (primary care) therapeutic interventions in primary familial or non-familial hypercholesterolaemia or mixed dyslipidaemia- all supported by NICE

Ezetimibe for treating primary heterozygous-familial and non-familial hypercholesterolaemia

Technology appraisal guidance | TA385 | Published: 24 February 2016

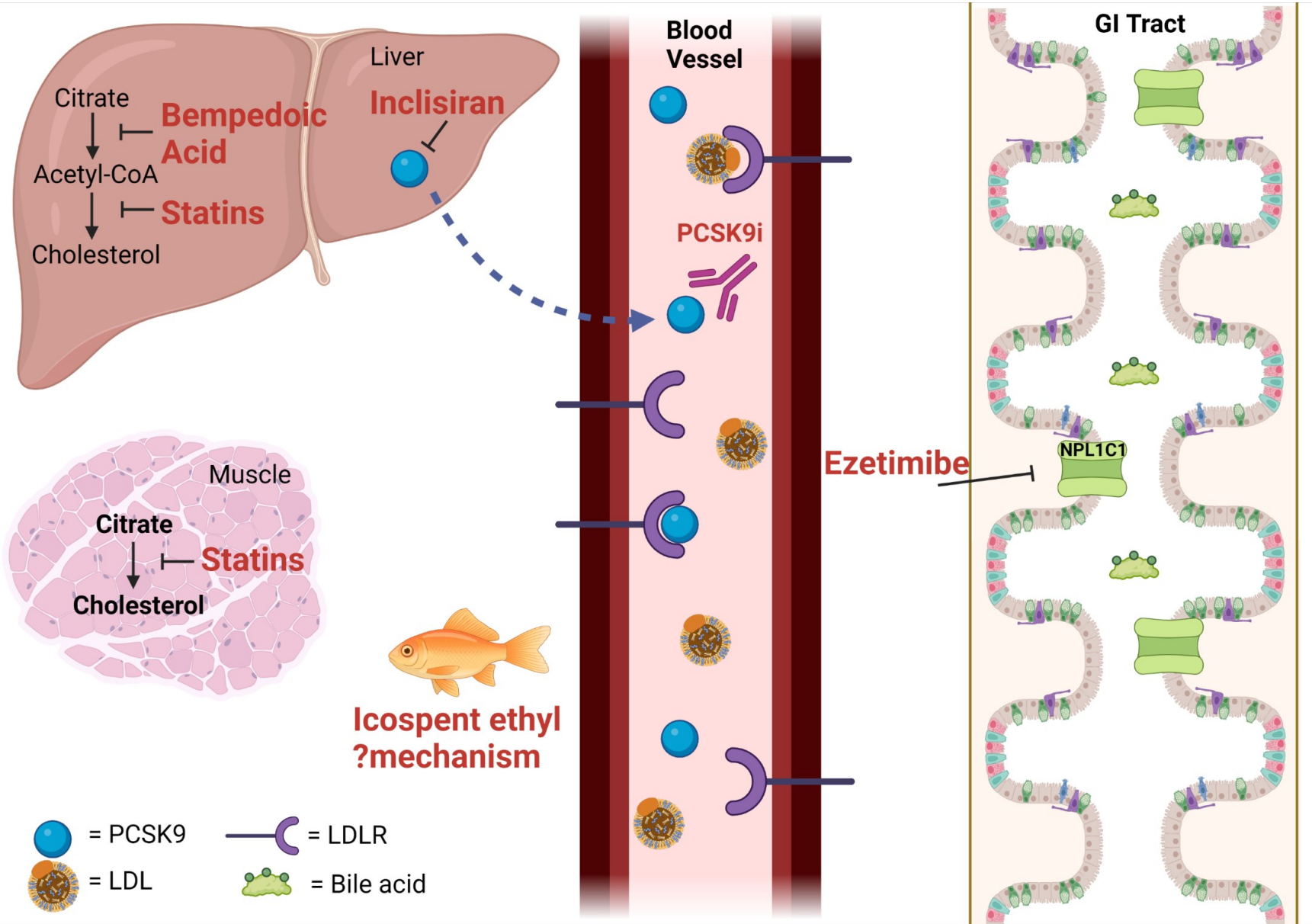
Bempedoic acid with ezetimibe for treating primary hypercholesterolaemia or mixed dyslipidaemia

Technology appraisal guidance | TA694 | Published: 28 April 2021

Inclisiran for treating primary hypercholesterolaemia or mixed dyslipidaemia

Technology appraisal guidance | TA733 | Published: 06 October 2021

Lipid treatments and modes of action



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When should I introduce ezetimibe?

EZETIMIBE

Ezetimibe is a cholesterol-absorption inhibitor that blocks the intestinal absorption of dietary and biliary cholesterol and related plant sterols, without affecting the uptake of triglycerides or fat-soluble vitamins. Because of this mechanism of action, **ezetimibe can be combined with a statin to provide either a complementary or an alternative mode of cholesterol reduction**

Ezetimibe monotherapy was recommended as an option for treating primary hypercholesterolaemia in adults who:

1)Are unable to start statin therapy because it is contraindicated

2)Cannot tolerate statin therapy

Ezetimibe, co-administered with initial statin therapy, is recommended as an option for treating primary (heterozygous-familial or non-familial) hypercholesterolaemia in adults who have started statin therapy when:

1) serum total or low-density lipoprotein (LDL) cholesterol concentration is not appropriately controlled either after appropriate dose titration of initial statin therapy or because dose titration is limited by intolerance to the initial statin therapy and

2)a change from initial statin therapy to an alternative statin is being considered.

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When should I consider ezetimibe/ Bempedoic acid ?

Recommendations

It is 'indicated in adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, as an adjunct to diet:

1. in combination with a statin in patients unable to reach LDL-C goals with the maximum tolerated dose of a statin in addition to ezetimibe. Works through the same pathway as a statin so less effective as a combination with statin.
2. in patients who are either statin intolerant or for whom a statin is contraindicated, and are unable to reach LDL-C goals with ezetimibe alone,

Bempedoic acid with ezetimibe can be used as separate tablets or a fixed-dose combination (Dose 180/10 mg daily)

- Common side effects include anaemia; gout; hyperuricaemia; pain in extremity
- Manufacturer advise discontinue if transaminases at least 3x ULN or if hyperuricaemia with gout symptoms

PCSK9 inhibitors

Gene silencers and monoclonal antibodies

INCLISIRAN

Inclisiran is a novel potent therapy that reduces LDL-C and, after an initial dose and another at 3 months, is maintained by two doses a year by subcutaneous injection.

Inclisiran has been identified by NHS England and Improvement as a medicine that it wishes to adopt systematically and at scale to help address sub-optimal lipid management in high-risk patient populations

The introduction of inclisiran into the lipid management pathway is seen as an opportunity to address a current gap in the range of treatment options available for people with ASCVD in whom lipid targets cannot be met on maximum tolerated statins alone or with ezetimibe.

ALIROCUMAB

(Binds to a pro-protein involved in the regulation of LDL receptors on liver cells; receptor numbers are increased, which results in increased uptake of LDL-cholesterol from the blood.)

EVOLOCUMAB

(Binds to a pro-protein involved in the regulation of LDL receptors on liver cells; receptor numbers are increased, which results in increased uptake of LDL-cholesterol from the blood.)

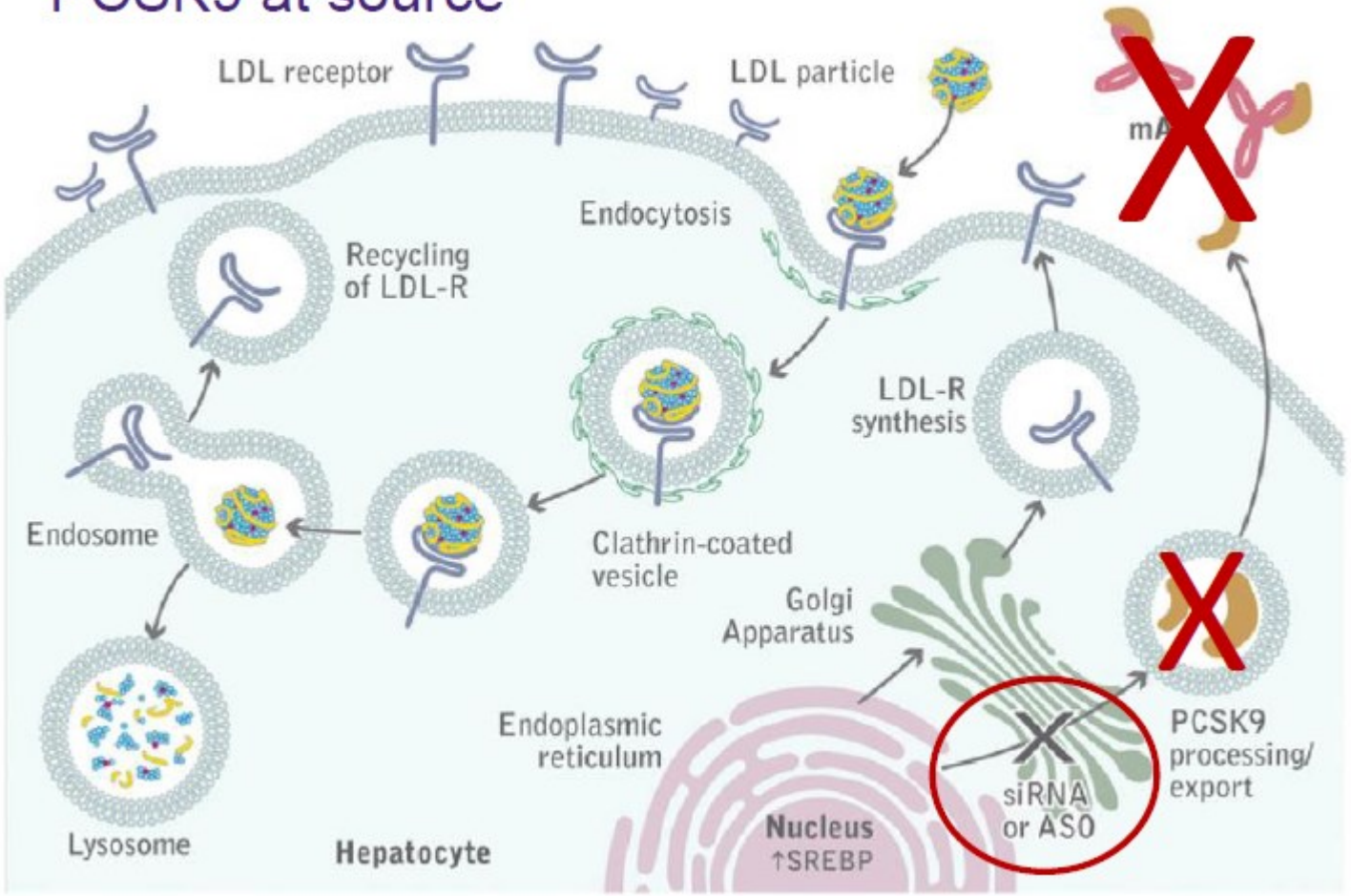
	Without CVD	With CVD	
		High risk of CVD [1]	Very high risk of CVD [2]
Primary non-familial hypercholesterolaemia or mixed dyslipidaemia	Not recommended at any LDL-C concentration	Recommended only if LDL-C concentration is persistently above 4.0 mmol/l	Recommended only if LDL-C concentration is persistently above 3.5 mmol/l
Primary heterozygous-familial hypercholesterolaemia	Recommended only if LDL-C concentration is persistently above 5.0 mmol/l	Recommended only if LDL-C concentration is persistently above 3.5 mmol/l	

[1]High risk of cardiovascular disease is defined as a history of any of the following: acute coronary syndrome (such as myocardial infarction or unstable angina requiring hospitalisation), coronary or other arterial revascularisation procedures, coronary heart disease, ischaemic stroke, peripheral arterial disease.

[2]Very high risk of cardiovascular disease is defined as recurrent cardiovascular events or cardiovascular events in more than 1 vascular bed (that is, polyvascular disease).

Abbreviations: CVD, cardiovascular disease; LDL-C, low-density lipoprotein cholesterol.

Inclisiran blocks production of PCSK9 at source



J Lipid Res 2012;**53:**2515

Summary of lipid lowering therapies

Drug class	NICE approved Recommendation	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
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
Bempedoic acid	For use where statins are not tolerated 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]	No CV outcomes data. On-going studies due to report in 2022.	Short term safety data from trials of up to 2 years.
Inclisiran	Secondary prevention in patients who meet eligibility criteria	S/C injection administered by a healthcare professional 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.

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.

CASE STUDY Male 70

- Male, 70 years

Medical history:

- Angina and hypertension 2016

Current medication:

- Atorvastatin 80mgs
- Aspirin 75mgs
- Bisoprolol 5mgs
- Ramipril 10mgs
- GTN spray prn
- Citalopram 20mgs
- Fostair inhaler
- Lansoprazole 15mgs
- Sildenafil 100mgs prn

Please refer to the respective SmPCs of these therapies for full information.

✓ **Discussed results – good diet, BMI 24.2 K/m2**

✓ **Agreed to be initiated on novel oral therapy Bembedoic acid/ezetimibe**

Lab results: 10th Feb 2023
LDL-C 2.6 HDL-C 1.1

25th April
LDL-C 1.8 HDL-C 1.3

Additional 28% reduction achieved in LDL-C .

How Can You Maximize Lipid Management for Optimal Cardiovascular Health?

1. What are the key steps in maximizing lipid management for optimal cardiovascular health?
2. How can interactions be optimised to enhance lipid health?
3. Why is collaboration with local experts crucial for successful lipid management?
4. What strategies can be implemented to execute an effective action plan for lipid management?
5. How can patient cohorts be efficiently targeted for lipid management purposes?
6. Why is it important to understand national lipid pathways and guidelines in lipid management?
7. What alternative strategies exist for managing statin intolerance?
8. Why is it crucial to stay updated on emerging therapies such as Inclisiran in lipid management?
9. How can data gathering and templates be utilized to streamline lipid management processes?
10. What is the significance of focusing on lowering lipids for achieving better cardiovascular outcomes?
11. How does teamwork contribute to the effectiveness of lipid management strategies?

Take home messages

- There is no evidence for the J curve! The lower the better whatever the case scenario !
- Most lipid management tools are available in primary care.
- Statin resistance can be dealt with.
- Decide which lipid targets you are going to aim for.
- Focus on LDL cholesterol on non-HDL cholesterol.
- QOF recognises that patients with SMI have particularly poor outcomes (The homeless population is a similar group).
- Know the effectiveness of different LLTs eg what are the high intensity statins?
- Use a stepwise approach to intensify therapy. Use all the tools!

References

e.g.

- NHS England- Quality and Outcomes Framework guidance for 2023/24 (please provide links and ‘accessed on’ if available)
- Sampson M, Ling C, Sun Q, et al. A New Equation for Calculation of Low-Density Lipoprotein Cholesterol in Patients With Normolipidemia and/or Hypertriglyceridemia. JAMA Cardiol. 2020;5(5):540–548. doi:10.1001/jamacardio.2020.0013
- NHS England- Business Rules for Quality and Outcomes Framework (QOF) 2023/24- CHOLESTEROL
- 1. Gov.uk. Blog. Public health matters: The 10-year CVD ambitions for England – one year on. February 2020. Available at: publichealthmatters.blog.gov.uk/2020/02/06/the-10-year-cvd-ambitions-for-england-one-year-on/ (accessed February 2021).

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Thank you !
Discussion

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