Lowering Cholesterol.

Saving Lives.

Tackling Cholesterol Together

NICE CG181- what's in it for me- and my patients?

Welcome to the second in a series of webinars as part of the national education programme Tackling Cholesterol Together.

Delivered in partnership by The NHS Accelerated Access Collaborative (AAC), The AHSN Network and the cholesterol charity, HEART UK

The webinar will start at 1pm

August 2021

All programme content, recordings and next webinar bookings will be housed in the HEART UK pages. Visit the site for the **new** e-Learning modules on Statin Intolerance and Identifying FH in primary care https://www.heartuk.org.uk/tackling-cholesterol-together/home

This campaign is being funded by Novartis Pharmaceuticals UK Ltd. as part of a collaborative working agreement for lipid management, with NHS England & Improvement (NHSE&I) and Accelerated Access Collaborative (AAC). Novartis, NHSEI& and AAC contribute resources in the form of skills, expertise, project management and administrative activity. Novartis has approved the associated materials in line with the ABPI Code.

TheAHSNNetwork

ACCELERATED ACCESS COLLABORATIVE

HEART UK THE CHOLESTEROL CHARITY

NHS

NOVARTIS

PHASE 1 TACKLING CHOLESTEROL TOGETHER. PROVISIONAL PROGRAMME OF ACTIVITIES

Deliverable	Title	Date	Speakers
Webinars	1. Evaluating CVD risk	14th July	1. Shahed Ahmad, Dermot Neely, Peter Green
	2. NICE CG181: what's in it for me?	18th August	2. Dermot Neely, Helen Williams
	3. How to implement a cholesterol framework in real world primary care	15th Sept	4. Youssef Beaini, Helen Williams, Matt Kearney
	4. A Focus on FH	13th Oct	4. Jai Cegla, Steve Humphries and Nadeem Qureshi
	5. Diet and behaviour change	17th Nov	5. Lynn Garton & Motivational interviewing/ behavioural change expert (tbc)
	6. Post Cardiovascular event management of cholesterol	TBC	6. TBC
	7. Novel therapies- now and future	8th Dec	7. Kosh Ray, Yassir Javaid, Ameet Bakhai
	8. Statin hesitancy, health investment and benefits over time	19th Jan 2022	8. Derek Connolly, Terry McCormack and Handrean Soran
	9. Diabetes, obesity & lipids	16th Feb 2022	9. Derek Connolly, Jim Moore, Terry McCormack, Adie Viljoen
eLearning	1. Statin Intolerance – e-learning module (launched)	July	Content by Clinical Advisory Group and Primary Care Education Programme group
	2. Identifying FH in Primary Care (launched)	August	
	3. Lipid Management Pathway	September	
	4. Interpreting lipid profile results	October	
	5. Genetic conditions	November	
	6. Nutrition and Lipids (5x smaller modules)	November	
	7. Cardiometabolic conditions	December	

PHASE 1 TACKLING CHOLESTEROL TOGETHER. PROVISIONAL PROGRAMME OF ACTIVITIES

Deliverable	Title	Date	Speakers
Clinics: Booking required, limited numbers. Qs raised in webinars to be discussed in more detail with panel and small primary care teams. Case based deep dives.	1. Evaluating CVD risk and interpreting the national lipids guidance	8th Sept	All members of the Clinical Advisory Group may lead.
	2. Real world implementation of cholesterol	29th Sept	
	3. Familial Hypercholesterolaemia	27th Oct	
	4. Post CVD event management	1st Dec	
	5. Novel Therapies	5th Jan	
	6. Statin hesitancy and adherence	2nd Feb	
	7. Diabetes, obesity and cholesterol	2nd March	
Videos	1. CVD:COVID. Why cholesterol now?	Series to be launched end August	1. Shahed Ahmad
	2. Lipid guidance- what's new?		2. Dermot Neely
	3. Practical steps- applying the national lipid guidance		3. Youssef Beaini
	4. Statin intolerance		4. Youssef Beaini
	5. FH: why now?		5. Pete Green
	6. Therapies beyond statins		6. Ameet Bakhai
Podcasts: debate and discussion	1. Lipid management: secondary to primary care challenges.	Series to be recorded late summer and launched Autumn	1. Ameet Bakhai v Youssef Beaini & Gail Allsopp
	2. FH – late diagnosis, and its impact		2. Derek Connolly v Youssef Beaini and Pete Green
	3. What we can learn from patients.		3. Douglas Findlay v Matt Kearney v Rani Katib
	4. Referral pathways		4. Prof Kosh Ray, Dermot Neely Yassir Javaid and Ameet Bakhai v Youssef Beaini, Matt Kearney
	5. Words matter- how to have a behavioural change conversation		5. MI expert (tbc)

Housekeeping

- **This meeting will be recorded** and will be made available in the HEART UK Tackling Cholesterol Together pages
- **There will be time** to stop and ask questions at the end
- **Feel free to ask questions** or upvote questions in the chat function when it becomes available
- **Any questions that we are not able to cover in the Q&A** sections today will be addressed following the event
- **Any questions you provided** during registration will be covered during the session

Agenda

	Topic	Presenter
01	**Welcome and Introductions**	Christopher Allen
02	**Updates to the guidance- why they changed and what they mean**	Helen Williams
03	**Primary prevention- treatment guided by risk**	Helen Williams
04	**Secondary prevention- treatment guided by regression**	Dr Dermot Neely
05	**Close and next steps**	Christopher Allen

Objectives of today's Webinar

01

Review effective lipid management for patients in the context of national CVD priorities and as a modifiable CVD risk factor

02

Focus on the NICE guidance recommendations on non-HDL and achieving the benefits of high intensity statin therapy

03

Extend **knowledge** around primary prevention, cumulative risk and the product of long-term therapy

04

Apply the NICE endorsed national guidance for lipid management pathway for primary and secondary prevention

CVD Burden Remains a Significant Unmet Need; However, Recent UK Policy Reflects the Importance of Lipid Management

CVD in the UK[1]

- >7 million people have CVD
- CVD has an annual total healthcare cost of £9 billion
- CVD is one of the biggest cause of death despite the availability of medical interventions and strategies

The NHS Long-Term Plan:[2]

Up to 10 year outlook for a variety of healthcare topics

- Cholesterol was highlighted for the first time in a decade
- CV risk management is a combined approach: ABC (AF, Blood pressure, Cholesterol)

167,000 deaths/year from CVD; **44,000** are premature[1]

Improve early detection and treatment of CVD
NHS Long-Term Plan[2]

>100,000 hospital admissions/year for an MI[1]
>100,000 strokes/year[1]

Prevent 150,000 heart attacks, strokes and dementia cases
NHS Long-Term Plan[2]

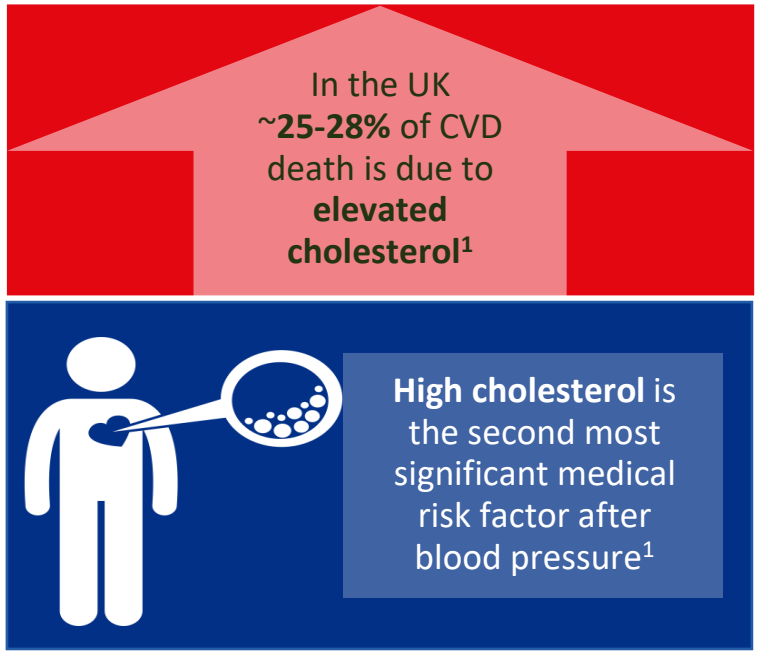
Up to **260,000** people in the UK have HeFH[3]

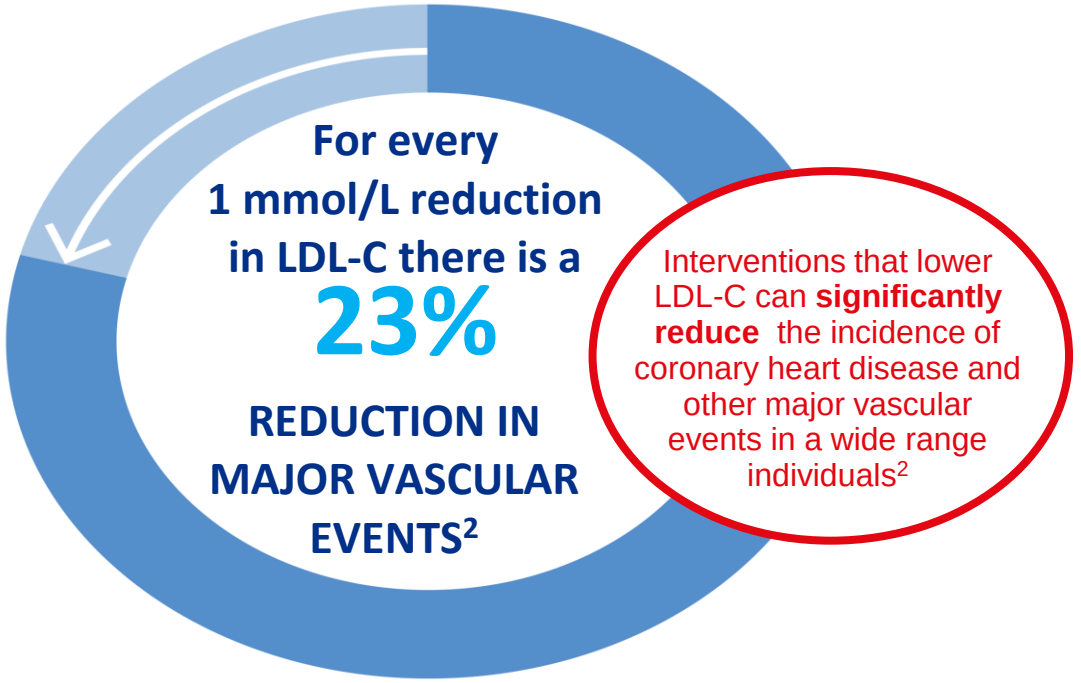
Expand access to genetic testing for identification of FH cases to at least 25% in 5 years
NHS Long-Term Plan[2]

- AF, atrial fibrillation; CV, cardiovascular; CVD, cardiovascular disease; FH, familial hypercholesterolaemia; HeFH, heterozygous familial hypercholesterolaemia; MI, myocardial infarction.

- 1. BHF. UK Factsheet, August 2019. Available at: https://www.bhf.org.uk/what-we-do/our-research/heart-statistics. Accessed November 2019;
  2. NHS Long-Term Plan. Available at: https://www.longtermplan.nhs.uk/wp-content/uploads/2019/08/nhs-long-term-plan-version-1.2.pdf;
  3. NICE Clinical Guidance [CG71]. Available at: https://www.nice.org.uk/guidance/cg71/. Accessed December 2019.

Why is cholesterol management so important in CVD prevention?





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

02

Updates to the guidance- why they changed and what they mean

Helen Williams

National Specialty Adviser for Cardiovascular Disease Prevention at NHS England and Improvement

We will cover:

- Why establishing CVD risk is the basis of good communication
- The relevance of non-HDL-C and its practical application
- High intensity therapy v High dose statin

NICE strategy 2021 to 2026

NICE's core purpose

Improving health and wellbeing by putting science and evidence at the heart of health and care decision making

Pillar 1

Rapid, robust and responsive technology evaluation

Pillar 2

Dynamic, living guideline recommendations

Pillar 3

Effective guidance uptake to maximise our impact

Pillar 4

Leadership in data, research and science

Recommendations and Tools for Effectively Screening Patients for High-Risk and Very-High-Risk CVD, and FH

NICE recommendations[1]

- Use a systematic strategy to screen patients
- Prioritise people on the basis of an estimate of their CVD risk before a full formal risk assessment
- Use CVD risk factors recorded in primary care electronic medical records to estimate risk
- Prioritise people for a full formal risk assessment if their estimated 10-year CVD risk is ≥10%
- People >40 years old should have their CVD risk reviewed on an ongoing basis

QRISK®2 online tool

- Tool to assess CVD risk for the primary prevention of CVD in people aged ≤84 years[1,2]
- **NOT** to be used in patients with:[2]
  - Suspected/confirmed FH
  - Type 1 diabetes
  - Pre-existing CVD
  - eGFR <60 mL/min/1.73 m^2 and/or albuminuria
- Available at:[3] https://qrisk.org/2017/

Primary Care FH Identification and Lipid Optimisation tools[4]

- Comprehensive search tools to select and risk stratify patients
- Integrate with EMIS and SystmOne
- Allow GP practices to prioritise patients for FH, primary and secondary prevention screening
- Example tools: CDRC Precision; PRIMIS FAMCAT; UCLP Proactive Care Frameworks

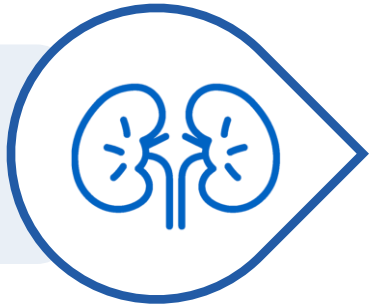
Secondary causes of hyperlipidaemia should be excluded before considering lipid lowering therapy

Key secondary causes of hyperlipidaemia should be excluded prior to treatment with any LLT. These include…[1]

- Type 2 diabetes

- Medication (e.g. steroids, beta-blockers)

- Chronic kidney disease



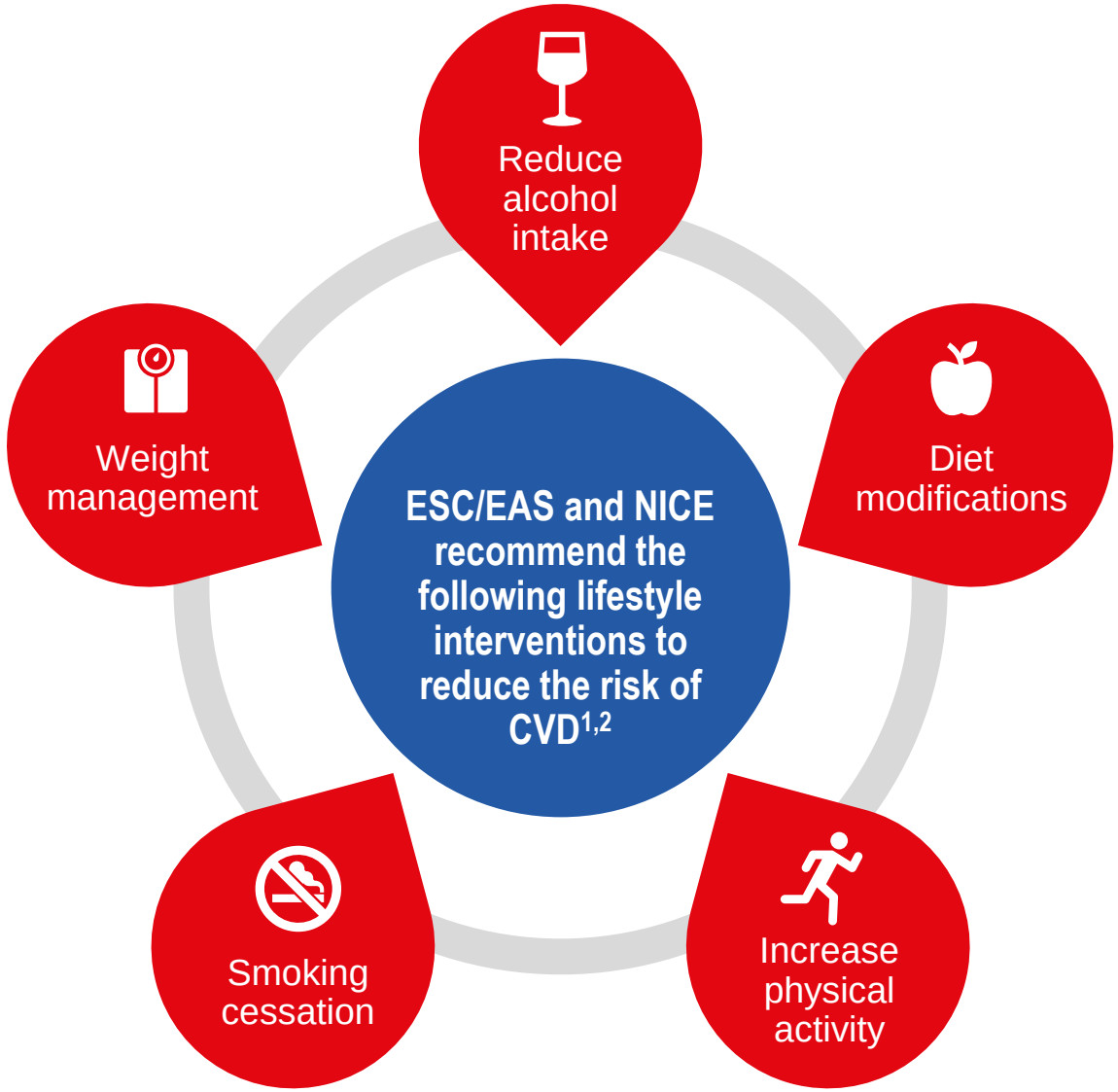
- Obesity

- Hypothyroidism

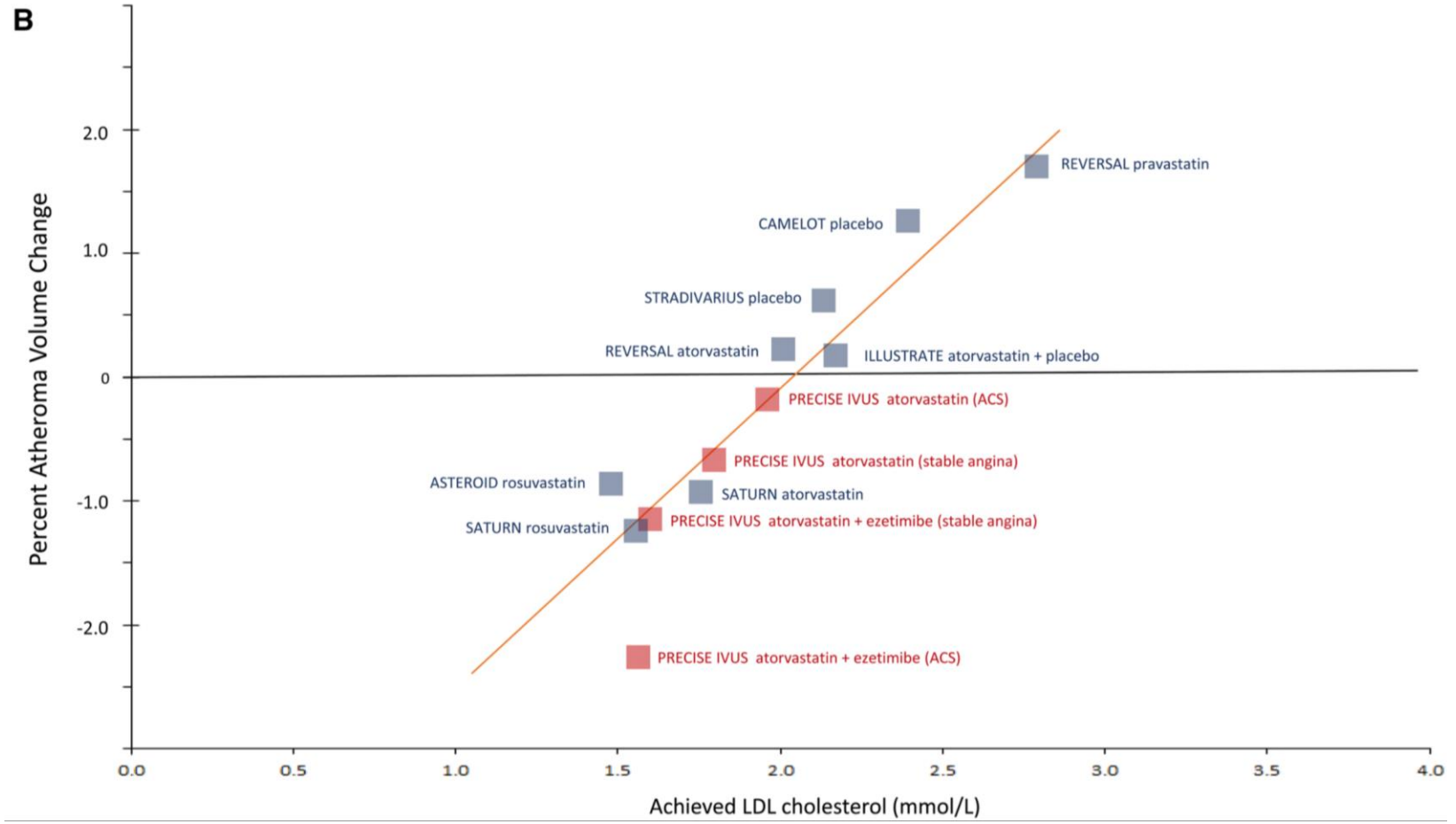
- Excessive alcohol consumption

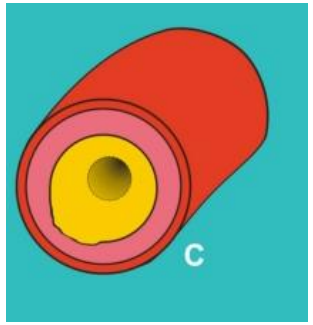
- LLT, lipid-lowering therapy.
- 1. Stone NJ. *Med Clin North Am* 1994;78:117–141.

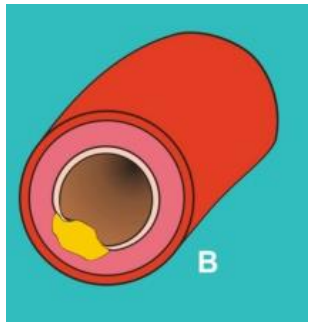
Lifestyle Changes Are Recommended for Patients at High-Risk of CVD



Lower LDL-C promotes regression







From: Low-density lipoproteins cause atherosclerotic cardiovascular disease. 1. Evidence from genetic, epidemiologic, and clinical studies. A consensus statement from the European Atherosclerosis Society Consensus Panel
Eur Heart J. 2017;38(32):2459-2472. doi:10.1093/eurheartj/ehx144

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%

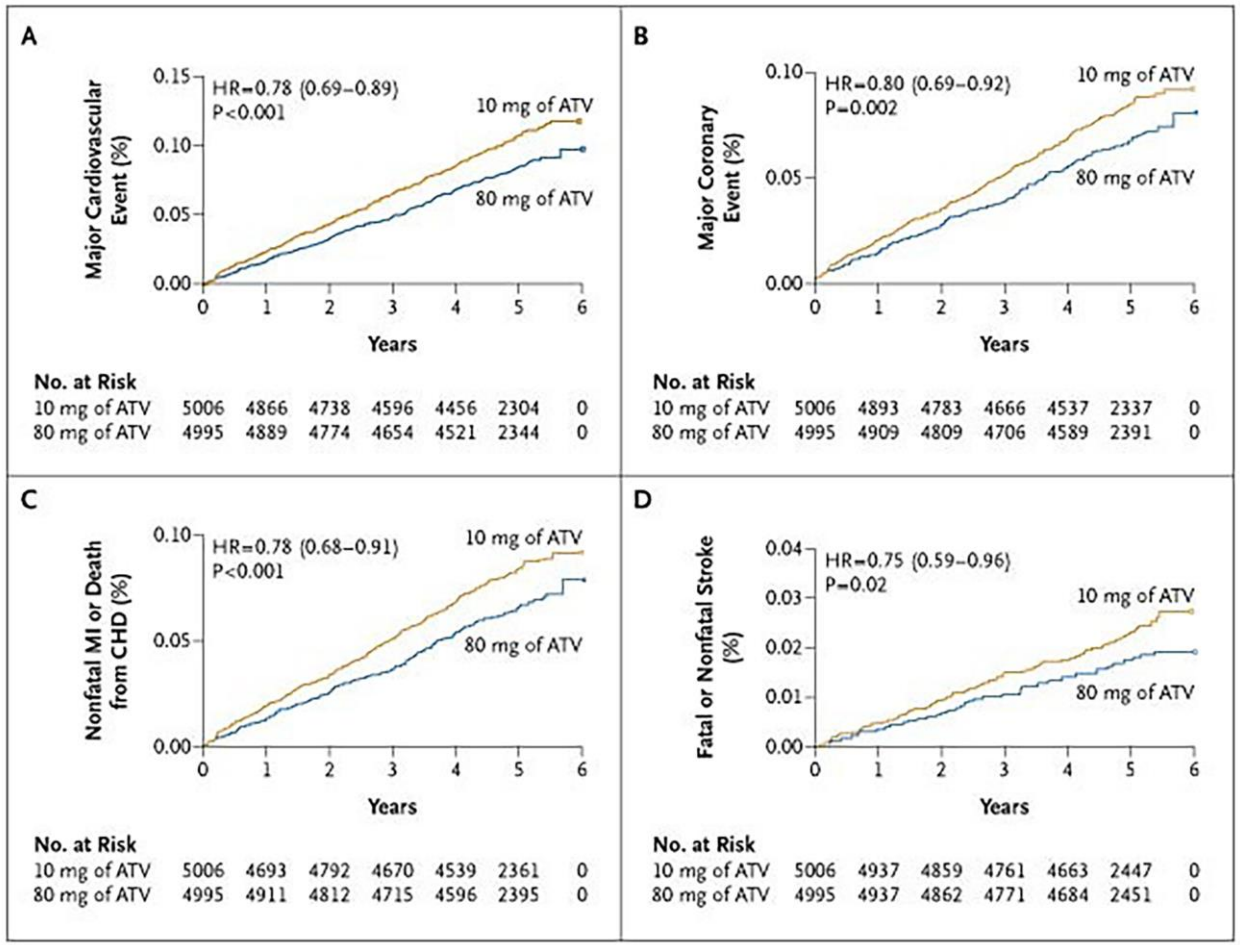
Low/moderate intensity statins will produce an LDL-C reduction of 20-30%

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

Treat to New Targets

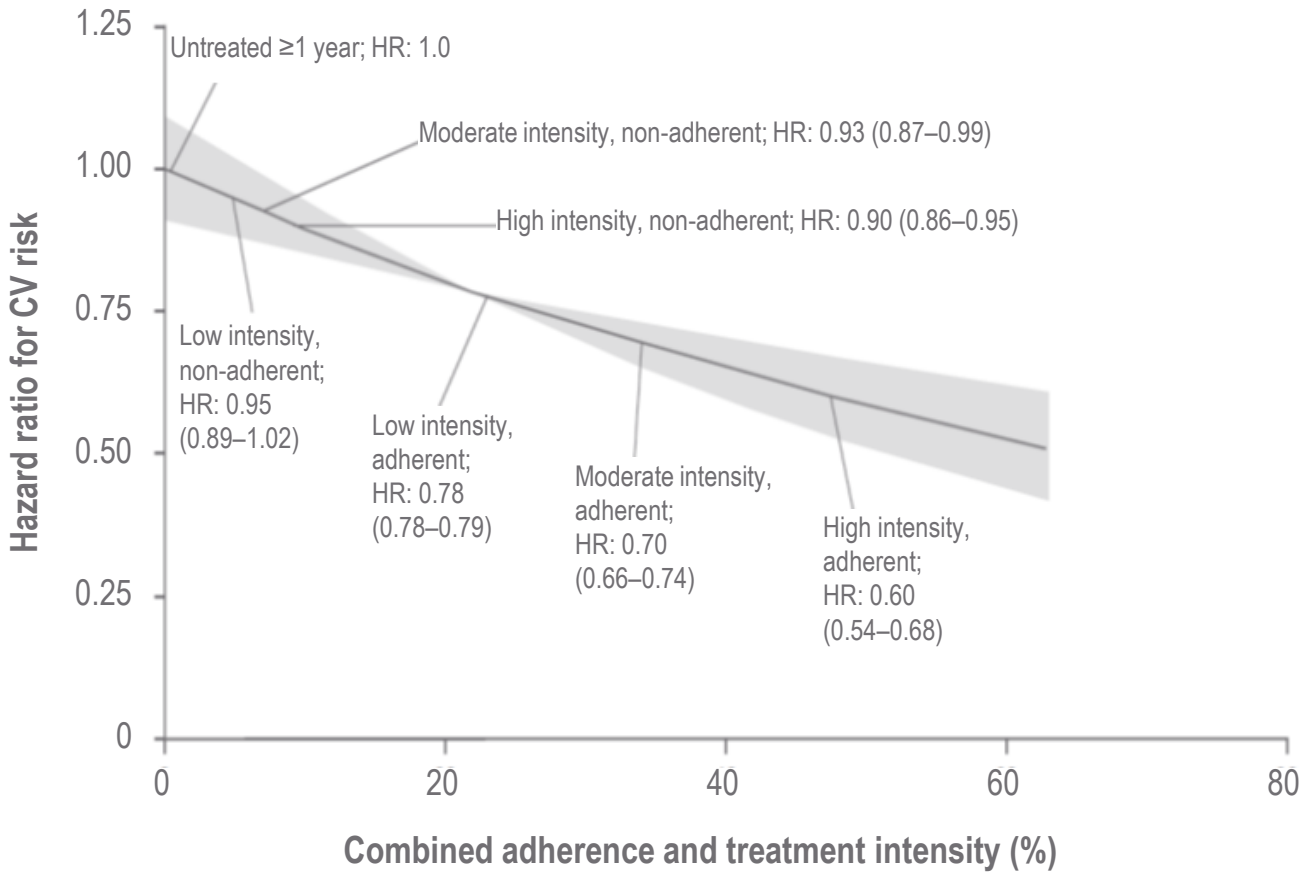


10mg vs 80mg atorvastatin in patients with stable coronary heart disease

N Engl J Med 2005; 352:1425-1435

High Treatment Intensity and Adherence Reduces CV Risk

- **Retrospective cohort study evaluating the association of adherence and treatment intensity with CV outcomes in the UK primary care setting**
  - Newly treated patients who received first statin and/or ezetimibe dose January 2010–December 2013
  - 16,701 patients with documented CVD were assessed
- **Compared to untreated patients:**
  - Adherent patients on a high-intensity regimen had a 40% lower CV risk
  - Non-adherent patients on a low-intensity regimen had a 5% lower CV risk



CV, cardiovascular; CVD, cardiovascular disease; HR, hazard ratio.

Khunti, et al. *JAMA Netw Open*. 2018;1:e185554.

NICE guidelines (NG197)

Shared decision making

- Shared decision making is a joint process in which a healthcare professional works together with a person to reach a decision about care.
- It involves choosing tests and treatments based both on evidence and on the person's individual preferences, beliefs and values.
- It makes sure the person understands the risks, benefits and possible consequences of different options through discussion and information sharing.

Benefits

- It allows people to discuss and share information. This makes sure people have a good understanding of the benefits, harms and possible outcomes of different options.
- It empowers people to make decisions about the treatment and care that is right for them at that time. This includes choosing to continue with their current treatment or choosing no treatment at all.
- It allows people the opportunity to choose to what degree they want to engage in decision making. Some people prefer not to take an active role in making decisions with their healthcare professionals.

Source: NICE guidelines (NG197) Shared Decision Making

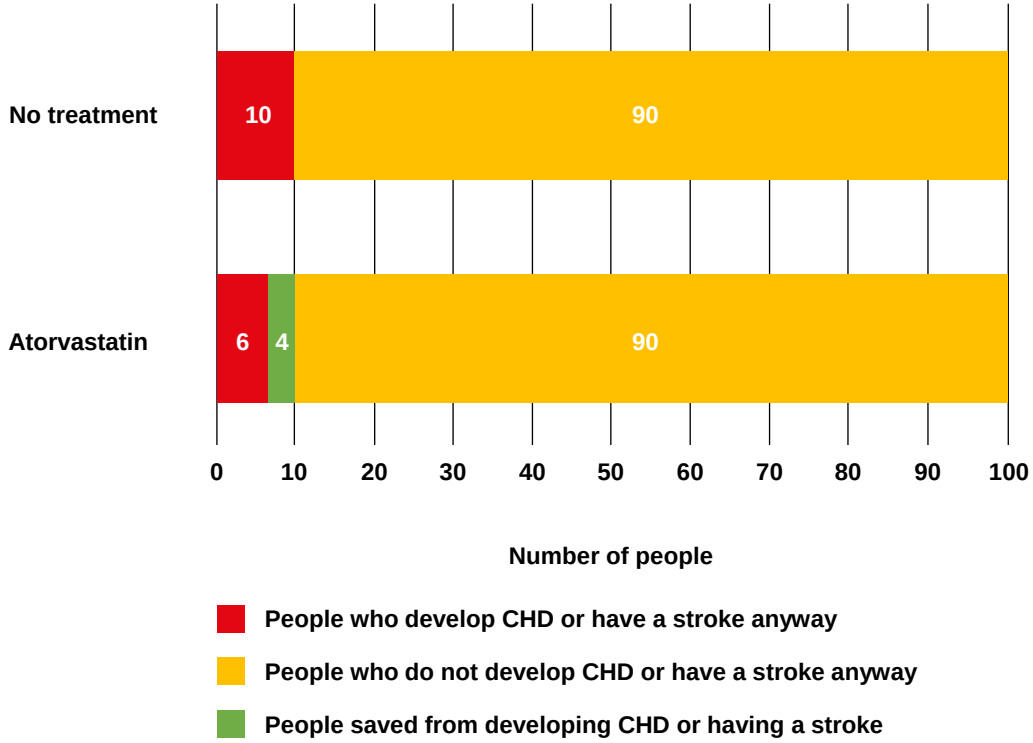
Shared decision making

These graphics show 2 different ways of looking at the risk of coronary heart disease (CHD) and stroke **over 10 years** in a group of 100 people. If none of those people take atorvastatin, over the next 10 years 10 people would develop CHD or have a stroke and 90 people would not.

If all 100 people take atorvastatin at the usual recommended dose for 10 years, over that time on average:

- **4 people** will be saved from developing CHD or having a stroke
- **90 people** will not develop CHD or have a stroke, but would not have done anyway
- **6 people** will still develop CHD or have a stroke.

It is not possible to tell what will happen to an individual person.



Shared decision making

Cardiovascular risk 10% over 10 years: no treatment

If 100 people at this level of risk take no statin, over 10 years on average:

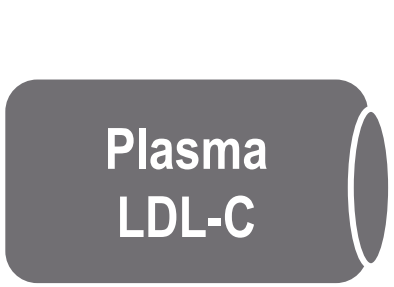
- 90 people will develop CHD or have a stroke (the green faces)
- 10 people will develop CHD or have a stroke (the red faces)

If 100 people take atorvastatin for 10 years, over that time on average:

- 4 people will be saved from developing CHD or having a stroke (the yellow faces)
- 90 people will not develop CHD or have a stroke, but would not have done anyway (the green faces)
- 6 people will stll develop CHD or have a stroke (the red faces).

Non-HDL-C vs LDL-C

- **Non-HDL-C levels can be used in the UK to assess and monitor CV risk; *however*:**[1]
  - Most evidence for reducing CV risk is based on LDL-C levels[2–6]
  - Access to some treatments require a measurement of LDL-C levels[7–9]



MEASURED

PREPARATIVE ULTRACENTRIFUGATION[10,11]

- **Gold standard** that provides a direct measurement of LDL-C
- **Expensive** technique that is often used in **research** settings

CALCULATED

FRIEDEWALD FORMULA[10–13]

- TC and HDL-C are directly measured: *LDL-C = TC – HDL-C – (TG/2.2 mmol/L)**
- **Fasting blood samples** are required for the calculation
- Can underestimate LDL-C at low levels
- Marked deviations in hypertriglyceridemia have been observed

*Only applicable if TG measure is <4.5 mmol/L, as higher values can distort LDL-C value.
CV, cardiovascular; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglycerides.

Advantages of using non-HDL cholesterol

- Non-HDL comprises all the atherogenic lipoproteins
- Can be calculated from a *non-fasted* sample
- A *simple* calculation:

Non-HDL cholesterol = Total Cholesterol – HDL cholesterol

- Widely available
- *No* additional cost to provide
- Avoids the variable influence of measured triglycerides
- Avoids imprecision and inaccuracy of LDL calculation
- Superior to LDL-C as a predictor of outcomes on statin treatment

Tackling Cholesterol Together

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03

Primary prevention- treatment guided by risk

Helen Williams

National Specialty Adviser for Cardiovascular Disease Prevention at NHS England and Improvement

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 yearsif 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 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 OD.
  - 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 'Statin Intensity Table')
- If maximum tolerated dose of statin does not achieve non-HDL-C reduction > 40% of baseline value after 3 months consider adding Ezetimibe 10mg OD (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

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 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 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 'Statin Intensity Table')

- If maximum tolerated dose of statin does not achieve non-HDL-C reduction > 40% of baseline value and/or non-HDL-C < 2.5mmol/L after 3 months consider adding Ezetimibe 10mg OD **(NICE TA385)**
- If recommended statin therapy is contraindicated or not tolerated
  - See AAC Statin Intolerance Algorithm for advice regarding adverse effects
  - Ezetimibe 10mg monotherapy may be considered. Assess response after 3 months
  - Ezetimibe 10mg/Bempedoic acid 180mg combination may be considered Ezetimibe alone does not control non-HDL-C/LDL-C well enough. (NICE TA694)

If non-HDL-C > 4.0mmol/L despite maximal tolerated lipid lowering therapy (including people with intolerances and contraindications), arrange a **fasting blood test** for LDL-C measurement and if **PCSK9i eligibility criteria** (see page 2 'Specialist Services') are met, refer for confirmation and initiation of PCSK9i (NICE TA 393, 394) according to local arrangements.

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.

If statin therapy is contraindicated, not tolerated or not effective, consider first ezetimibe, then ezetimibe/bempedoic acid, then PCSK9 inhibitor. Use of ezetimibe/bempedoic acid is not precluded when prior low dose statin is used due to intolerance to higher-intensity statin (check SPC for interactions). 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

CVD: Cardiovascular Disease
CKD: Chronic Kidney Disease
FH: Familial Hypercholesterolaemia
TC: Total Cholesterol
ALT: Alanine Aminotransferase
AST: aspartate aminotransferase
Non-HDL-C: Non-High Density Lipoprotein Cholesterol
OD: Once Daily
LDL-C: Low Density Lipoprotein Cholesterol
PCSK9i: Proprotein Convertase Subtilisin 9 Inhibitor

Authors: Dr Rani Khatib & Dr Dermot Neely on behalf of the AAC Clinical Subgroup. March 2020. Review date: March 2021. Pathway endorsed by NICE April 2020.

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

- **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 the long-term treatment effect of Bempedoic acid is uncertain. TA694 does not preclude use of a low dose statin (check SPC for interactions)

MONITORING

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.
If statin therapy is contraindicated, not tolerated or not effective, consider ezetimibe. 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		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 triglyceridesa/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).

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)

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NICE. 2014. CG181 www.nice.org.uk/guidance/CG181
NICE. 2008. CG71 www.nice.org.uk/guidance/cg71

ACCELERATED ACCESS COLLABORATIVE

NHS

Endorsed by the National Institute for Health and Care Excellence (NICE), April 2020.

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.

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.

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

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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)

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 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 OD.
- For how to increase in people with CKD see 'Special Patient Populations' (page 2)

STATIN INTENSITY TABLE					
Approximate reduction in LDL-C					
Statin dose mg/day	5	10	20	**40**	**80**
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Atorvastatin		37%	43%	49%	55%
Rosuvastatin	38%	43%	48%	53%	
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Low/moderate intensity statins will produce an LDL-C reduction of 20-30%

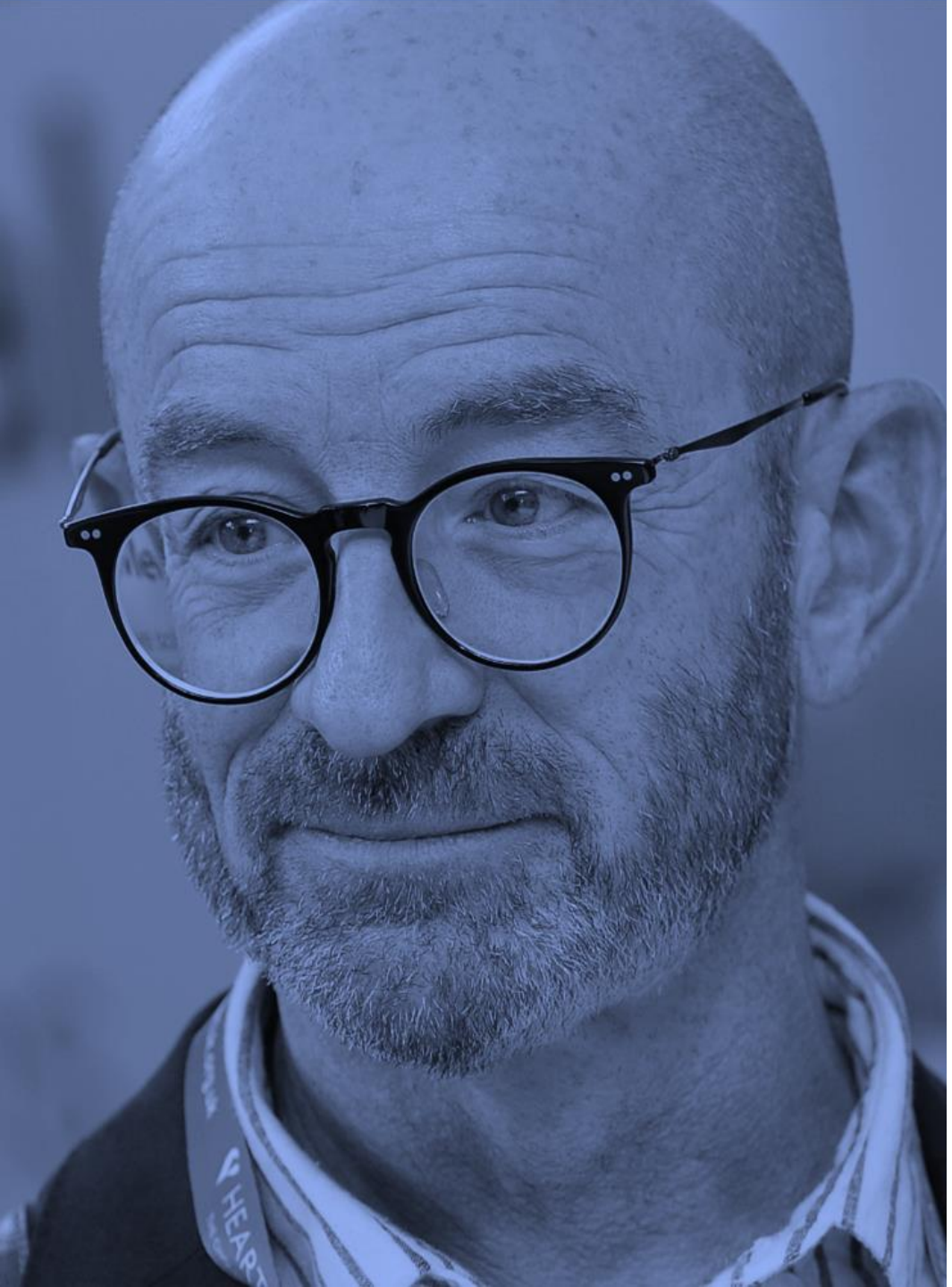
Medium intensity statins will produce an LDL-C reduction of 31-40%

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

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

• If patients on a high-intensity statin have side effects, offer a lower dose or an alternative statin (see page 2 ‘Statin Intensity Table’)
• If maximum tolerated dose of statin does not achieve non-HDL-C reduction > 40% of baseline value after 3 months consider adding Ezetimibe 10mg OD (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

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.



04

Secondary prevention- treatment guided by regression

Dr Dermot Neely

Consultant Lipidologist and Specialist Adviser on Lipids to the AHSNs.

We will cover:

- Scope of the national guidance for lipid management for Primary and secondary prevention
- Management, monitoring and titration
- A brief introduction to the statin intolerance pathway

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 yearsif 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 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 OD.
  - 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 'Statin Intensity Table')
- If maximum tolerated dose of statin does not achieve non-HDL-C reduction > 40% of baseline value after 3 months consider adding Ezetimibe 10mg OD (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

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 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 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

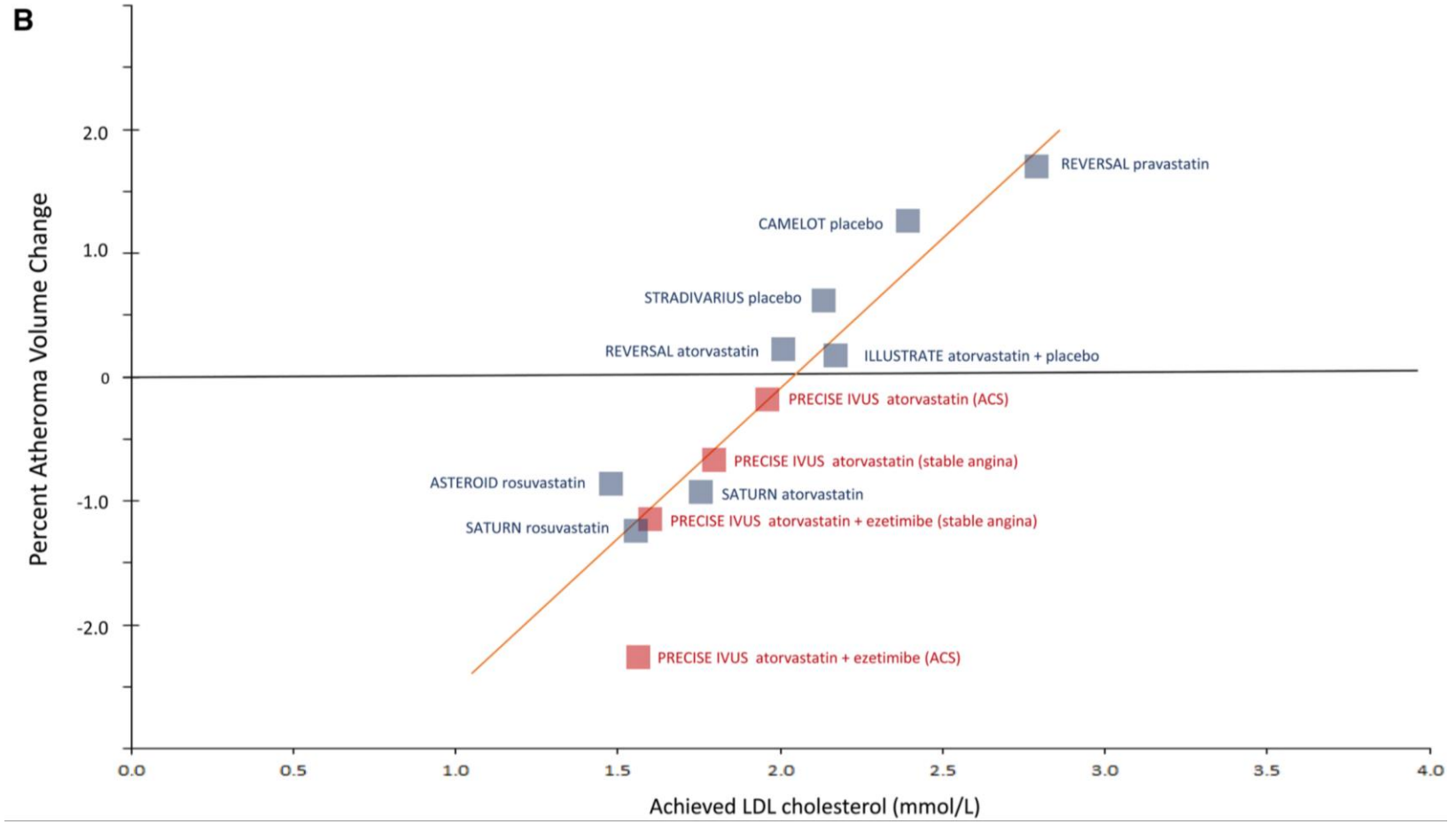
Do not delay statin treatment in secondary prevention while managing modifiable risk factors.
Prescibe a high intensity statin:
Atorvastatin 80mg OD
Use a lower dose of Atorvastatin if there is a potential drug interaction, high risk of or experiencing adverse effects, or patient preference.
Offer Atorvastatin 20mg if CKD (people with GFR< 60 mL/min/1.73m2).

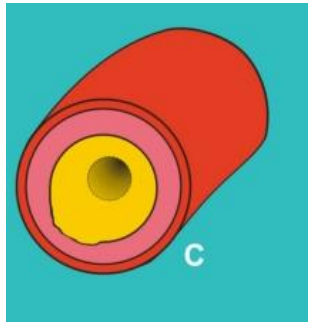
- Measure full lipid profile again after 3 months (non-fasting).
- High intensity statin treatment should achieve reduction of non-HDL-C > 40% from baseline. If not achieved after 3 months
  - Discuss treatment adherence, timing of dose, diet and lifestyle measures
  - If started on less than atorvastatin 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 'Statin Intensity Table')

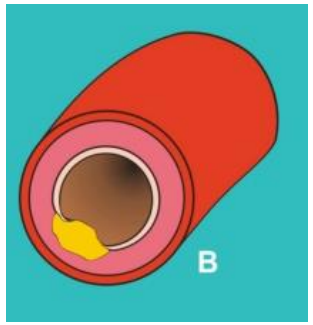
- If maximum tolerated dose of statin does not achieve non-HDL-C reduction > 40% of baseline value and/or non-HDL-C < 2.5mmol/L after 3 months consider adding Ezetimibe 10mg OD **(NICE TA385)**
- If recommended statin therapy is contraindicated or not tolerated
  - See AAC Statin Intolerance Algorithm for advice regarding adverse effects
  - Ezetimibe 10mg monotherapy may be considered. Assess response after 3 months
  - Ezetimibe 10mg/Bempedoic acid 180mg combination may be considered Ezetimibe alone does not control non-HDL-C/LDL-C well enough. (NICE TA694)

If non-HDL-C > 4.0mmol/L despite maximal tolerated lipid lowering therapy (including people with intolerances and contraindications), arrange a **fasting blood test** for LDL-C measurement and if **PCSK9i eligibility criteria** (see page 2 'Specialist Services') are met, refer for confirmation and initiation of PCSK9i (NICE TA 393, 394) according to local arrangements.

Lower LDL-C promotes regression







From: Low-density lipoproteins cause atherosclerotic cardiovascular disease. 1. Evidence from genetic, epidemiologic, and clinical studies. A consensus statement from the European Atherosclerosis Society Consensus Panel
Eur Heart J. 2017;38(32):2459-2472. doi:10.1093/eurheartj/ehx144

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).
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• If patients on a high-intensity statin have side effects, offer a lower dose or an alternative statin (see page 2 ‘Statin Intensity Table’)

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

ACCELERATED ACCESS COLLABORATIVE

NHS

INITIAL CONSIDERATIONS:

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

PRIMARY PREVENTION

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

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

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- High intensity statin treatment should achieve reduction of non-HDL-C > 40% from baseline. If not achieved after 3 months;
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  - 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 OD.
  - For how to increase in people with CKD see 'Special Patient Populations' (page 2)

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

Despite maximal tolerated statin and Ezetimibe therapy.
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- 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 'Statin Intensity Table')

- If maximum tolerated dose of statin does not achieve non-HDL-C reduction > 40% of baseline value and/or non-HDL-C < 2.5mmol/L after 3 months consider adding Ezetimibe 10mg OD **(NICE TA385)**
- If recommended statin therapy is contraindicated or not tolerated
  - See AAC Statin Intolerance Algorithm for advice regarding adverse effects
  - Ezetimibe 10mg monotherapy may be considered. Assess response after 3 months
  - Ezetimibe 10mg/Bempedoic acid 180mg combination may be considered Ezetimibe alone does not control non-HDL-C/LDL-C well enough. (NICE TA694)

If non-HDL-C > 4.0mmol/L despite maximal tolerated lipid lowering therapy (including people with intolerances and contraindications), arrange a **fasting blood test** for LDL-C measurement and if **PCSK9i eligibility criteria** (see page 2 'Specialist Services') are met, refer for confirmation and initiation of PCSK9i (NICE TA 393, 394) according to local arrangements.

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.

If statin therapy is contraindicated, not tolerated or not effective, consider first ezetimibe, then ezetimibe/bempedoic acid, then PCSK9 inhibitor. Use of ezetimibe/bempedoic acid is not precluded when prior low dose statin is used due to intolerance to higher-intensity statin (check SPC for interactions). 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

CVD: Cardiovascular Disease
CKD: Chronic Kidney Disease
FH: Familial Hypercholesterolaemia
TC: Total Cholesterol
ALT: Alanine Aminotransferase
AST: aspartate aminotransferase
Non-HDL-C: Non-High Density Lipoprotein Cholesterol
OD: Once Daily
LDL-C: Low Density Lipoprotein Cholesterol
PCSK9i: Proprotein Convertase Subtilisin 9 Inhibitor

Authors: Dr Rani Khatib & Dr Dermot Neely on behalf of the AAC Clinical Subgroup. March 2020. Review date: March 2021. Pathway endorsed by NICE April 2020.

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

- **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 the long-term treatment effect of Bempedoic acid is uncertain. TA694 does not preclude use of a low dose statin (check SPC for interactions)

MONITORING

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.
If statin therapy is contraindicated, not tolerated or not effective, consider ezetimibe. 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		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 triglyceridesa/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).

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. 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

ACCELERATED ACCESS COLLABORATIVE

NHS

Endorsed by the National Institute for Health and Care Excellence (NICE), April 2020.

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

non HDL-C = Total Cholesterol (TC) minus HDL-C

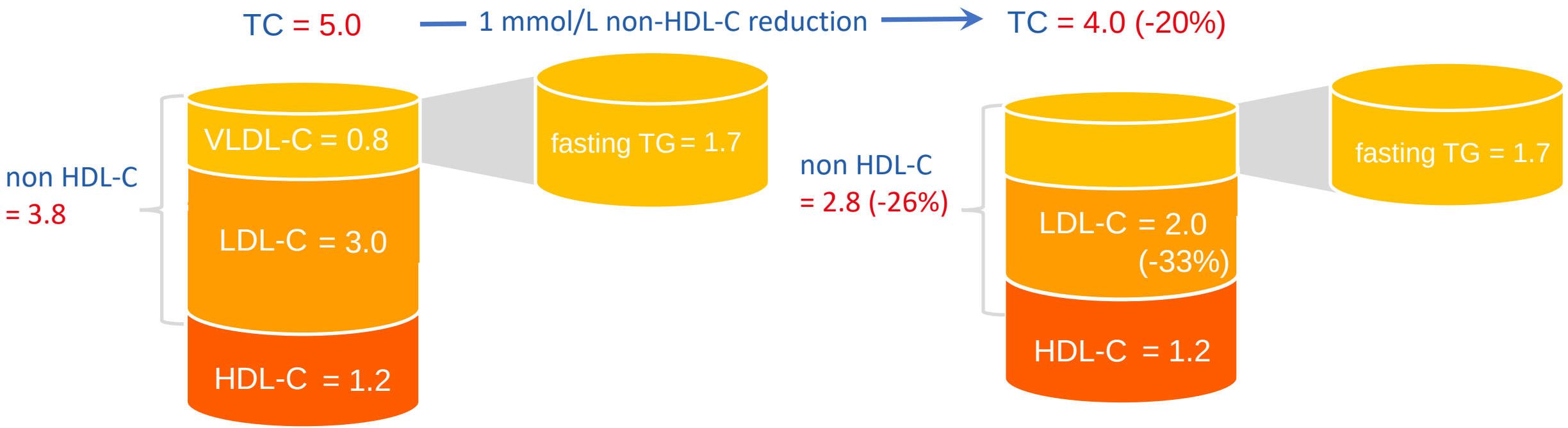
(easy to calculate and does not require fasting)

TC = HDL-C + LDL-C + VLDL-C

LDL-C= non-HDL-C minus VLDL-C (fasting triglycerides */2.2)
*Valid only when fasting triglycerides less than 4.5mmol/L

When HDL-C remains the same, the reduction non-HDL-C = reduction in LDL -C

When HDL-C AND triglycerides (TG) remain the same, the reduction in TC ≈ reduction in non-HDL-C = reduction in LDL -C



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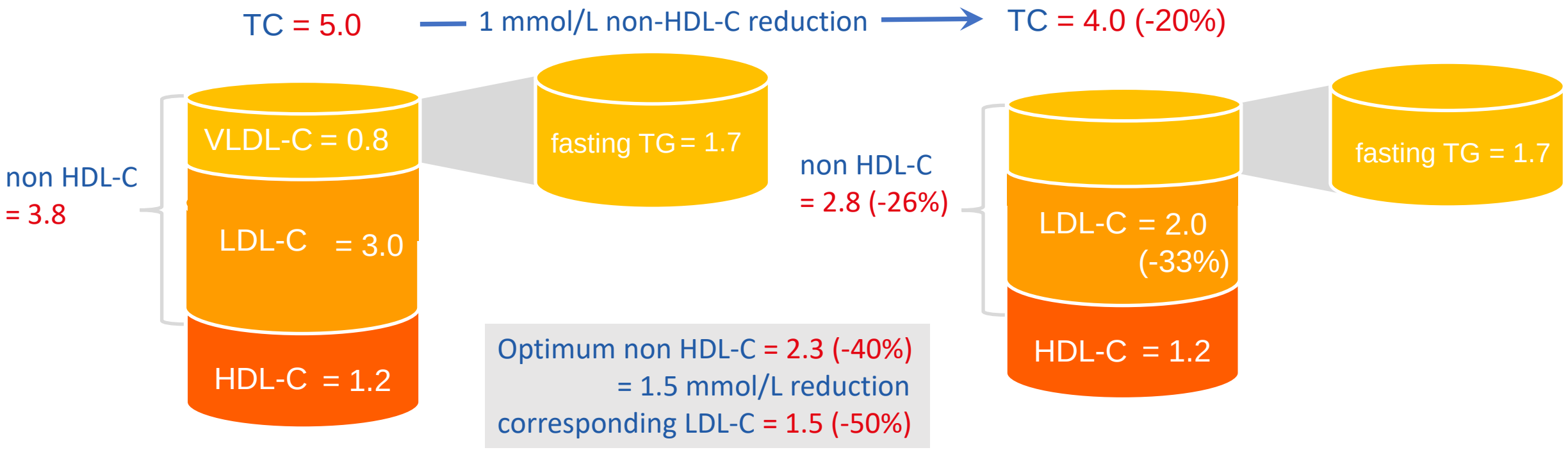

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Yearly	✓ (where needed)		✓ (where needed)	

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

STATIN INTOLERANCE

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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)

Statin Intolerance Pathway

ACCELERATED ACCESS COLLABORATIVE

NHS

This resource relates to NICE guidance:
CG181, CG71, TA385, TA393/394, QS100

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

New onset or worsening of muscle symptoms since starting statins? (pain, tenderness or weakness)

NO → Consider other potential side effects for statins
- Be aware of **Statin Reluctance** and **Nocebo Effect**
- See **'Person Centred Care'** box at page 2

YES

Symptoms typical for Statin Related Muscle toxicity (SRM)*?

NO → Muscular symptoms not related to statins

*Symmetrical pain and/or weakness in large proximal muscle groups, worsened by exercise

YES

Measure Creatinine Kinase (CK)
Assess severity of symptoms
+/- repeat baseline assessment**

Non SRM: Consider other causes e.g. PMR, Vit D deficiency. Check bone profile, Vit D, CRP.

**Consider other causes if new onset of muscle symptoms of > 2 weeks duration in a person previously tolerant of statin therapy for > 3 months

Tolerable symptoms
No clinical concern
CK < 4x ULN

Intolerable symptoms
and/or clinical concern and/or CK > 4x and < 10x ULN

CK > 10x and < 50x ULN

CK > 50x ULN

Improvement within 2 weeks
Resolved within 6 weeks
Patient happy to continue

NO → **Stop statin for 4-6 weeks**
Document time to symptom onset and time to resolution

YES ← **Renal function** stable/normal eGFR

NO → Stop statin and consider **Rhabdomyolysis**

Has CK normalised?

Consider **Statin induced necrotising autoimmune myopathy** (SINAM)

YES

Have symptoms resolved?

NO → Non-SRM. **Consider other causes**

YES

Has the patient been **symptom free for at least 2 weeks?**

NO → Wait for 2 weeks before **rechallenge**

YES

Seek specialist advice and consider PCSK9i
(NICE TA 393, 394)

Urgently seek specialist advice and inpatient assessment

Reassess and **restart** with lower dose/alternative statin (see page 2 - **'Statin-based Approaches'**)
Offer low or moderate dose of a higher intensity statin (Atorvastatin 10 or 20 mg OD, or Rosuvastatin 5 or 10mg OD)

No recurrence of muscle symptoms
Titrate at 8 weeks intervals to achieve appropriate targets

Recurrence of muscle symptoms
Short time to onset
Symptoms intolerable

Symptoms tolerable
Treatment goals achieved
Patient happy to continue

NO → **Consider further options**
(For example co-administering ezetimibe or as monotherapy)
see page 2 - **'Statin-based Approaches'**

IF NOT EFFECTIVE

Abbreviations

CK = Creatinine Kinase
CRP = C-Reactive Protein
eGFR = Estimated Glomerular Filtration Rate
PMR = Polymyalgia Rheumatica
SINAM = Statin Induced Necrotising Autoimmune Myopathy
SRM = Statin Related Muscle Toxicity
ULN = Upper Limit of Normal Range
Vit D = Vitamin D

Please refer to page 2 for more details

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 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

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

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- 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

Practical Guidance for Patients Whose Cholesterol Levels Are Not at Target

OPTIMISE

01 Optimise treatment (if possible)

- Consider increasing statin dose if not already prescribing maximum recommended dose
- Consider adding additional lipid-lowering-therapy, such as ezetimibe

02 Investigate tolerance (if applicable)

- Investigate for known symptoms of statin intolerance and consider:
  - Alternative statin
  - Reduced dose
- Aim to treat with maximum tolerated dose

03 Assess adherence

- Explore adherence and timing of dose
- Discuss the impact of treatment adherence on CVD risk and suggest patient resources
- Consider adherence to diet and lifestyle measures as well as pharmacological interventions

- CVD, cardiovascular disease.
- NICE Clinical Guidance [CG181]. Available at: https://www.nice.org.uk/guidance/cg181/. Accessed November 2019

Take Home Messages

Lipid management of high risk patients in the UK remains suboptimal despite effective treatment recommended by NICE. Recommended High Intensity Statins (HIST) and ezetimibe are underused. Many high risk patients are on no lipid lowering therapy at all

Shared decision making includes communication about the expanding choice of medicines and regimes in the context of what is important to an individual and what benefit may be achieved

It is our job to take a holistic approach and communicate with a range of tools. We need to translate the evidence base for treatments and cumulative benefits over time, which ultimately lead to event free survival

NICE endorsed pathways summarising Lipid Management and Statin Intolerance are now available to guide lipid optimisation in practice

Non-fasting non-HDL-cholesterol replaces fasting LDL-cholesterol for monitoring and assessment of adequacy of response to therapy- with HIST we should achieve at least 40% reduction; if not consider adding ezetimibe

Where baseline lipid measurements are unavailable for setting secondary prevention targets, non-HDL-C <2.5 mmol/L can be used

Consider specialist referral for people at high risk of CVD who are statin intolerant or who remain poorly controlled despite maximum tolerated doses of statins and ezetimibe

Consider specialist referral for people with a clinical diagnosis of FH or who have severe hyperlipidaemia (as defined in CG181) regardless of family history

05 Q&A

Next steps: Join us for the next webinar: How to implement a cholesterol framework in real world primary care: Wednesday 15th September 1-2pm

Dr Youssef Beaini
Clinical lead for education for The NHS Accelerated Access Collaborative (AAC) and The AHSN Network national lipids programme in England. Practising GP Bradford
Dr Matt Kearney
Programme Director for Primary Care Innovation at UCL Partners: to effectively manage patients with long term conditions. National Clinical Director for Cardiovascular Disease Prevention, 2016-2019
Helen Williams
National Specialty Adviser for Cardiovascular Disease Prevention at NHS England and NHS Improvement

All programme content, recordings and next webinar bookings will be housed in the HEART UK pages. Visit the site for the new e-Learning module on Statin Intolerance and Identifying FH in primary care.

Lowering Cholesterol.

Saving Lives.

TheAHSNNetwork ACCELERATED ACCESS COLLABORATIVE HEART UK THE CHOLESTEROL CHARITY NHS

Tackling Cholesterol Together

Thank you

This webinar has now finished.

Today's slides and recording will be available after the webinar on the HEART UK pages. Visit the site for the **new** e-Learning module on Statin Intolerance and Identifying FH in primary care

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Some content in this deck is based on slides created and provided by Amgen UK in scientific exchange to our speakers, which have been adapted for this talk