Lipid Management & Familial Hypercholesterolaemia

IMpulse CVD

Improving outcomes for patients with Cardiovascular Disease in the West Midlands

Coventry and Warwickshire Training Hub

west midlands
ACADEMIC HEALTH SCIENCE NETWORK

Contributors

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West Midlands Academic Health Science Network CVD Prevention & Management Programme

Content delivered by:

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Declarations of interest

Nazish Khan – none to declare

Welcome & Agenda

Context: NHS LTP, CVD PCN DES

Aims of project: Detect, Protect, Perfect

Primary Prevention: CVD risk assessment & management

Secondary Prevention: CVD risk reduction & management

Familial Hypercholesterolaemia: Detection & management

National Guidance for Lipid Management: Outlining management in primary and secondary care

Clinical case studies: A practical guide to lipid management and the identification & management of FH (application of CG181 and CG71 recommendations)

Priority setting: Next steps & development of local networks

Learning objectives:

At the end of this workshop, attendees will be able to:

- Demonstrate an understanding of the priorities outlined in the **NHS Long Term Plan** with regards to the identification of people who may at risk of a cardiovascular event because of their lipid profile.
- Demonstrate an understanding of the different **risk stratification tools/resources** that can be used to identify people who are at risk of a cardiovascular event and in whom lipid lowering therapy should be initiated (e.g. QRISK2/3, JBS-3, NHS Health Checks, UCLPartners Proactive Care Frameworks).
- Understand **how to undertake searches** to identify people with possible familial hypercholesterolaemia and how they should be managed.
- **Analyse clinical** and **patient information** for people with hypercholesterolaemia and understand how to **apply this to their management** (pharmacological and non-pharmacological).

National drivers:
The NHS Long Term Plan
CVD PCN DES

27% of all CVD deaths are due to MIs/strokes
(1 death every 3 minutes)

7.4 million
people are living with heart and circulatory diseases in the UK

> 100,000 hospital admissions are due to MIs/strokes
(1 admission every 5 minutes)

Stroke is the 4th biggest killer in the UK
(36,000 deaths/year)

Health care costs related to CVD are estimated to be £9 billion/year

Cardiovascular Disease is PREVENTABLE

https://www.bhf.org.uk/what-we-do/our-research/heart-statistics (accessed 11/10/2020)

10 year cardiovascular disease ambitions for England

Atrial fibrillation (AF)

85%

of the expected number of **people with AF are detected by 2029**

90%

of patients with AF who are already known to be at high risk of a stroke **to be adequately anticoagulated by 2029**

High blood pressure

80%

of the expected number of **people with high blood pressure are diagnosed by 2029**

80%

of the total number of people already diagnosed with high blood pressure are **treated to target as per NICE guidelines by 2029**

High cholesterol

75%

of people **aged 40 to 74 have received a formal validated CVD risk assessment** and **cholesterol reading** recorded on a primary care data system in the last five years by 2029

45%

of people **aged 40 to 74 identified as having a 20% or greater 10-year risk** of developing CVD in primary care are treated with statins by 2029

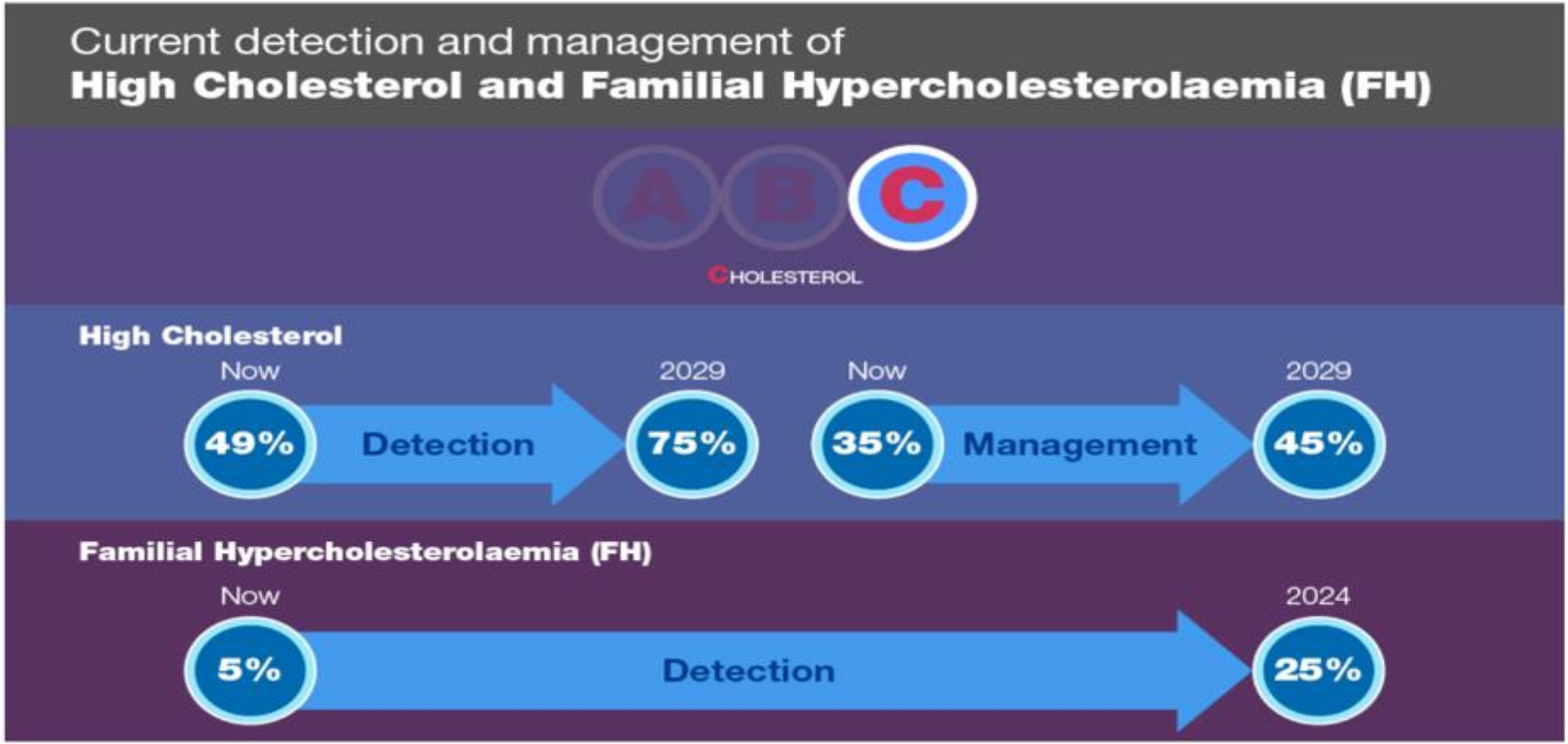
25%

of people with **Familial Hypercholesterolaemia (FH) are diagnosed and treated** optimally according to the NICE FH Guideline by 2024

The ambitions are underpinned by the need to do more to reduce health inequalities

Reduce the gap significantly in amenable CVD deaths between the most and least deprived areas by 2029

https://www.gov.uk/government/publications/health-matters-preventing-cardiovascular-disease/health-matters-preventing-cardiovascular-disease <accessed 12/09/2021>



https://www.gov.uk/government/publications/health-matters-preventing-cardiovascular-disease/health-matters-preventing-cardiovascular-disease <accessed 05/10/2021>

PCN DES 23/24 & IIF 23/24

DES Requirement:

- Offer statin treatment to patients with a QRISK2&3 score >= 10%, where clinically appropriate and in line with NICE guideline CG181
- Identify patients at high risk of Familial Hypercholesterolaemia (as defined in NICE guideline CG71, section 1.1), and make referrals for further assessment where clinically indicated. This should include systematic searches of primary care records to identify those aged 30+ with Chol > 9mmol/L or with Chol > 7.5mmol/L aged less than 30

IIF Indicator:

- Removed

https://www.england.nhs.uk/wp-content/uploads/2023/03/PRN00157-ncdes-cvd-prevention-and-diagnosis-supplementary-guidance.pdf < accessed 19.04.2023>

Cholesterol related QOF clinical indicators

Cholesterol control and lipid management (CHOL)	Points	Thresholds
Ongoing management		
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%

https://www.england.nhs.uk/wp-content/uploads/2023/03/PRN00289-quality-and-outcomes-framework-guidance-for-2023-24.pdf <accessed 19.04.2023>

Clinical Context

Hypercholesterolaemia: incidence and prevalence

- Significantly **increases** the risk of atherosclerotic cardiovascular disease (**heart disease** and **stroke**).

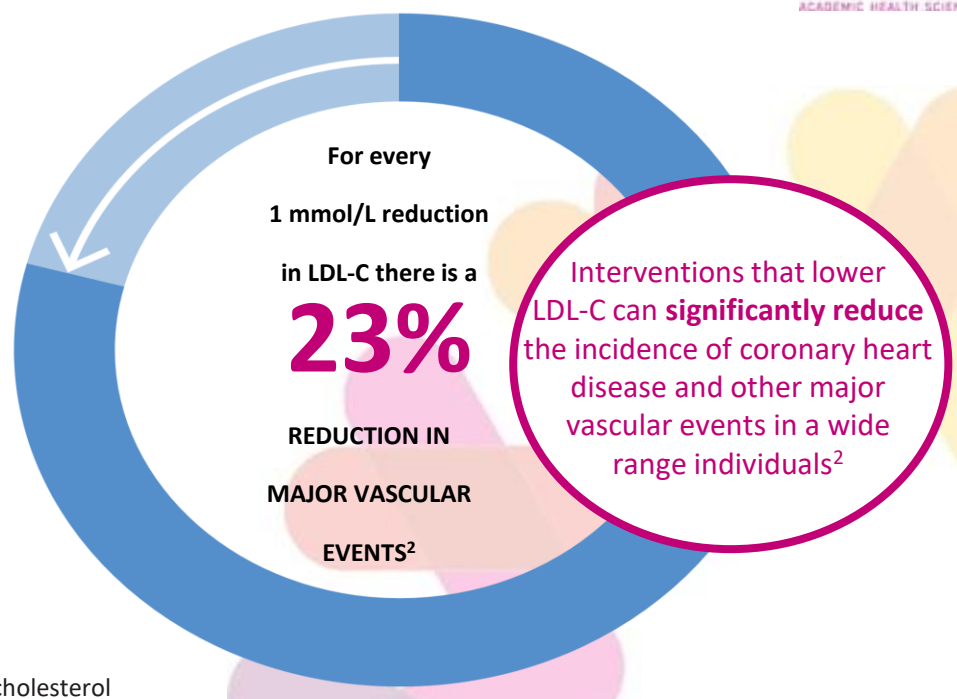
- It remains a **key modifiable risk factor** for **CVD**, yet despite advances in risk stratification and the availability of cost-effective treatment, identification and **management remains sub-optimal**.

- **FH** is a common inherited disorder associated with elevated LDLC, affecting approx. **1 in 250 people**. Left untreated it can lead to **premature CHD**.

Hypercholesterolaemia increases CVD burden

In the UK
~25-28% of CVD death is due to **elevated cholesterol**[1]

High cholesterol is the second most significant medical risk factor after blood pressure[1]



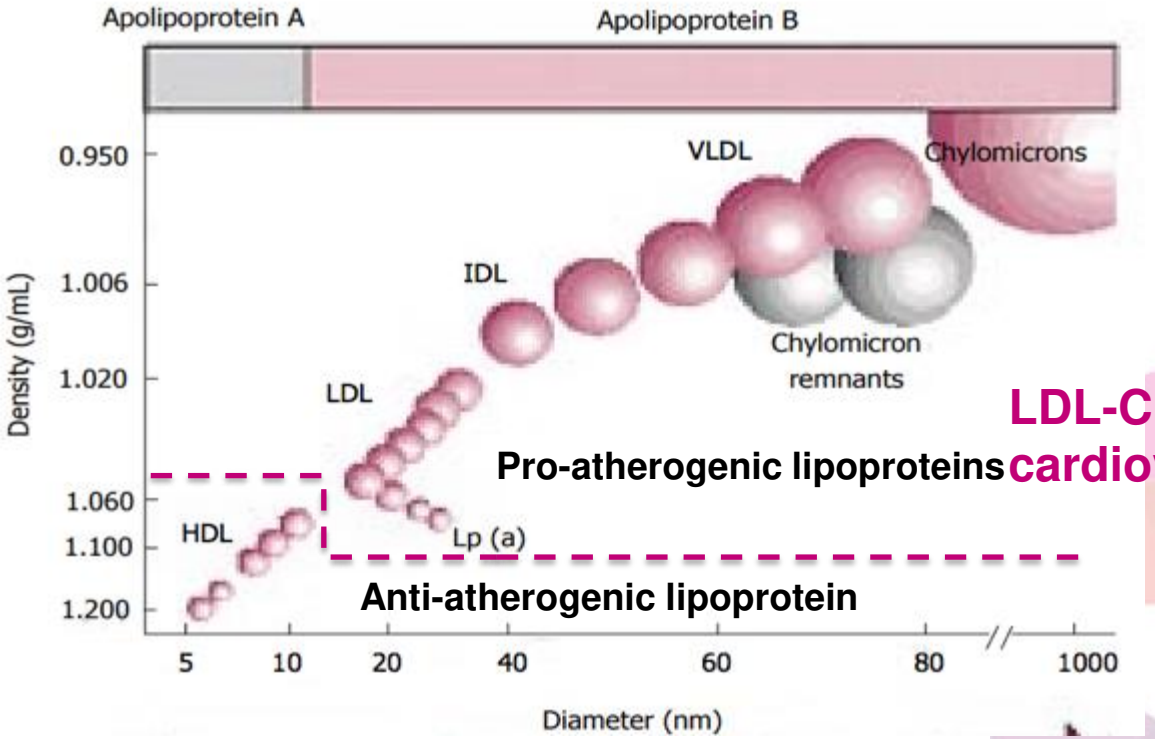
Interventions that lower LDL-C can **significantly reduce** the incidence of coronary heart disease and other major vascular events in a wide range individuals[2]

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

(1) . Wilkins E. et al. (2017). European Cardiovascular Disease Statistics 2017. (2). Silverman MG et al. JAMA. 2016;316:1289-97.

Pathophysiology & Clinical Consequences

Pathophysiology: Lipid and Lipoprotein Profile

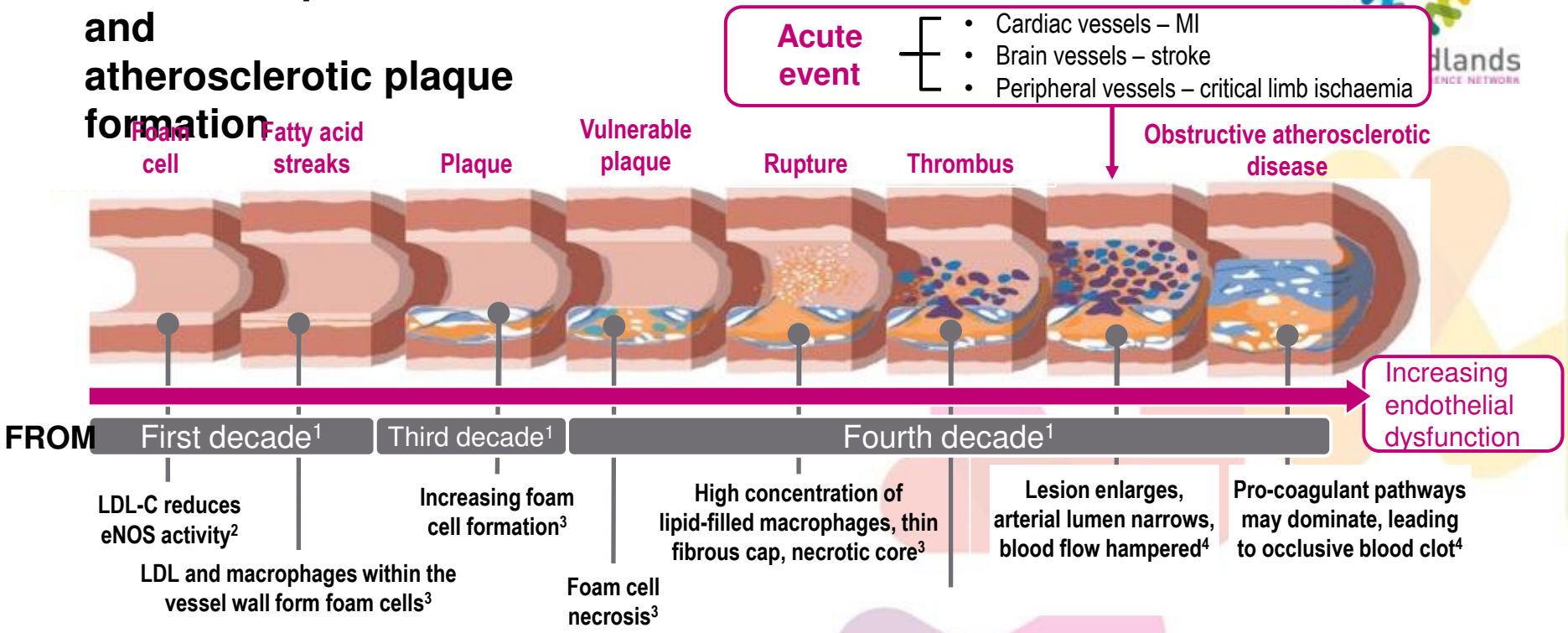


LDL-C exposure drives atherosclerotic cardiovascular disease (ASCVD)

Tabas I et al. Circulation. 2007;116:1832–1844;

Pathophysiology: Atherosclerotic Cardiovascular Disease (ASCVD)

Relationship between LDLC and atherosclerotic plaque formation



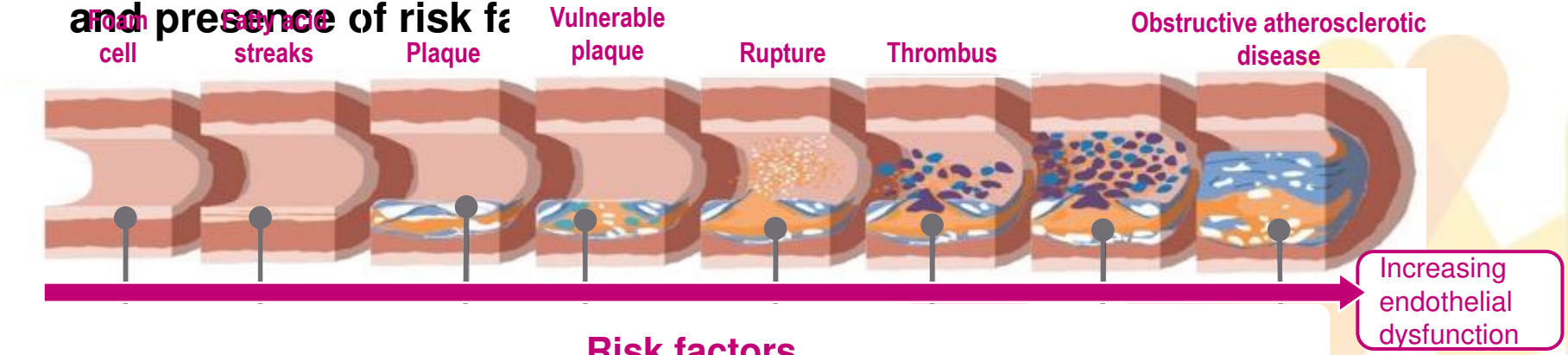
eNOS, endothelial nitric oxide synthase; LDL-C, low-density lipoprotein-cholesterol; MI, myocardial infarction.

1. Stary, et al. *Circulation*. 1995;92:1355–1374; 2. Davignon, et al. *Circulation*. 2004;109(23 Suppl 1):III27–II32; 3. Glass and Witztum. *Cell*. 2001;104:503–516; 4. Libby. *Nature*. 2002;420:868–874.

Adapted from Amgen slide deck

Clinical consequence of persistently elevated atherogenic lipoproteins: ASCVD

Disease progression is heavily influenced by exposure to LDLC (Lp[a])
and presence of risk fa



Risk factors

Non-modifiable

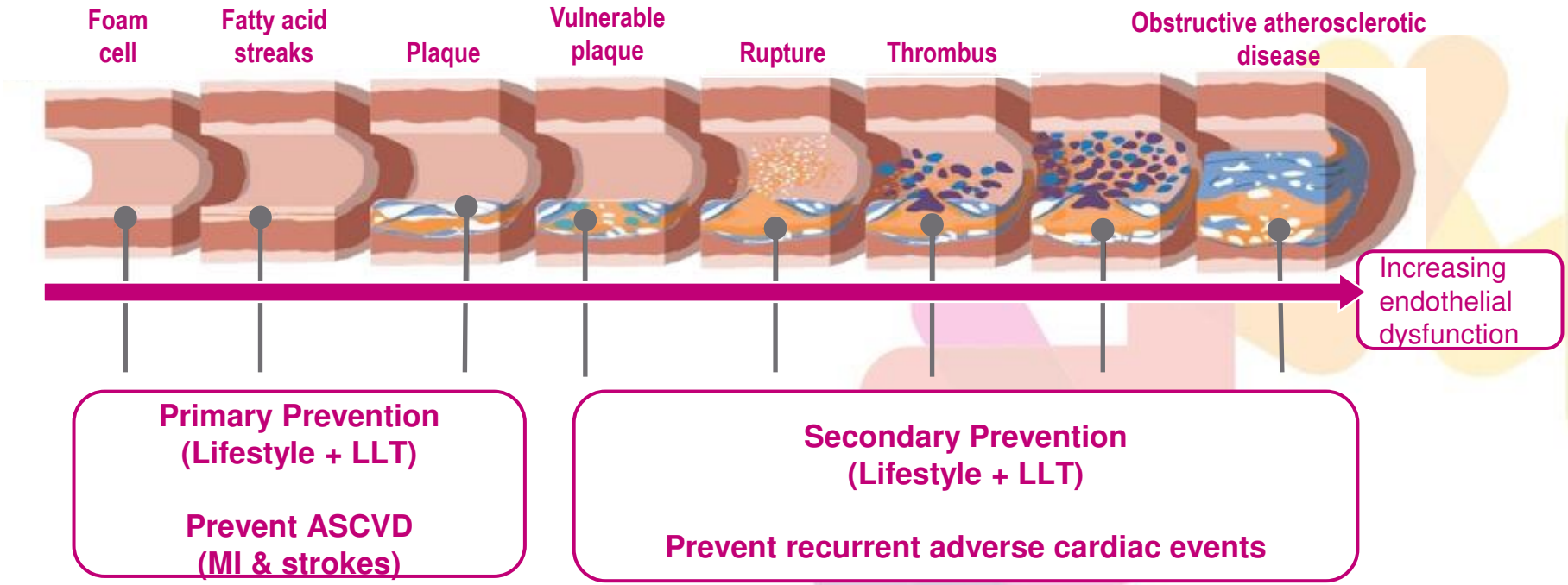
Increasing age
Male sex
Positive family history
Ethnic origin
Established CVD

Modifiable

Smoking
Hypertension
Dyslipidaemias
Diabetes mellitus
Obesity and metabolic syndrome
High calorie, high fat diet
Physical inactivity

Pathophysiology: Atherosclerotic Cardiovascular Disease (ASCVD)

Lipid lowering therapy (LLT) is the cornerstone of management



1. Stary, et al. *Circulation*. 1995;92:1355–1374; 2. Davignon, et al. *Circulation*. 2004;109(23 Suppl 1):III27–II32;
3. Glass and Witztum. *Cell*. 2001;104:503–516; 4. Libby. *Nature*. 2002;420:868–874.

Adapted from Amgen slide deck

Lipid lowering therapies: reduction in LDLC and

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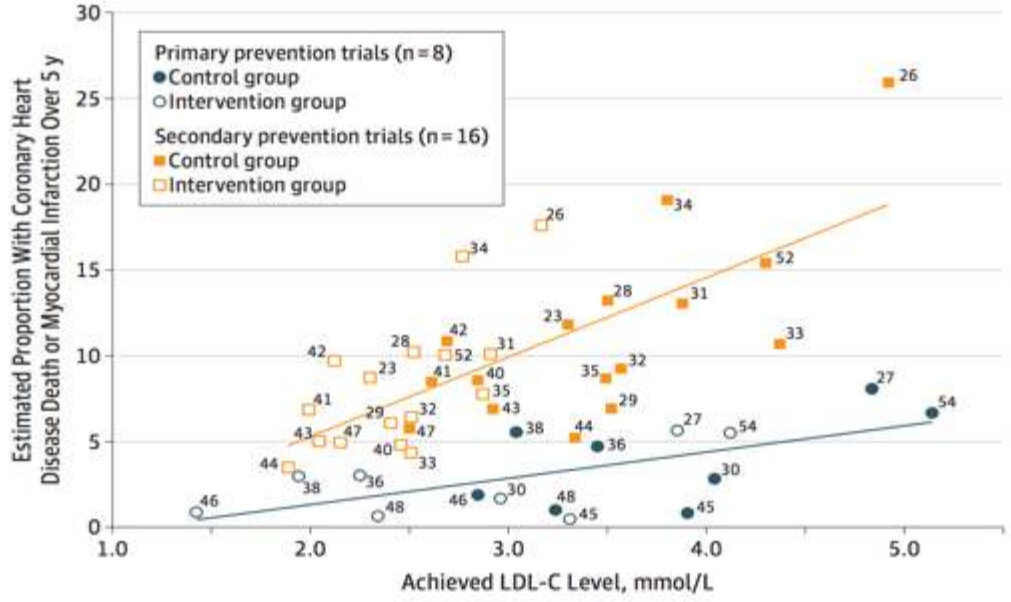
Figure 4. Association Between Achieved Low-Density Lipoprotein Cholesterol (LDL-C) and Major Coronary Event Rates From 24 Trials of Established Interventions That Lower LDL-C Predominantly Through Upregulation of LDL Receptor Expression



Primary & Secondary Preventio

Lower LDL-C levels are associate with lower rates of major adverse CV events (MACE)

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Silverman MG et al. JAMA. 2016;316(12):1289-1297. doi:10.1001/jama.2016.13985

Full Lipid Profile

Total Cholesterol includes pro-atherogenic (LDL-C, IDL-C, VLDL-C) and anti-atherogenic fractions (HDL-C)

- [LDL-C used to confirm lipid abnormalities and assess response to treatment]

HDL-Cholesterol anti-atherogenic fraction

- [HDL-C essential for risk assessment]

Non-HDL-Cholesterol pro -atherogenic fraction only

- [non-HDL-C essential to assess response to treatment]

Triglycerides not directly atherogenic, but considered a risk modifier (metabolic syndrome)

- [Fasting TG (<4.5mmol/L) required for calculation of LDL-C]

Calculated Lipid Variables

Non-HDL Cholesterol = Total Cholesterol – HDL-C

- **Non fasting** samples can be taken
- Total atherogenic lipoproteins, alternative to LDL-C and can be used when TG are likely to be elevated and patient is non-fasting
- NICE CG181 – allows for assessment of response to treatment

LDL-C = TC – (HDL-C + TG/2.2)*

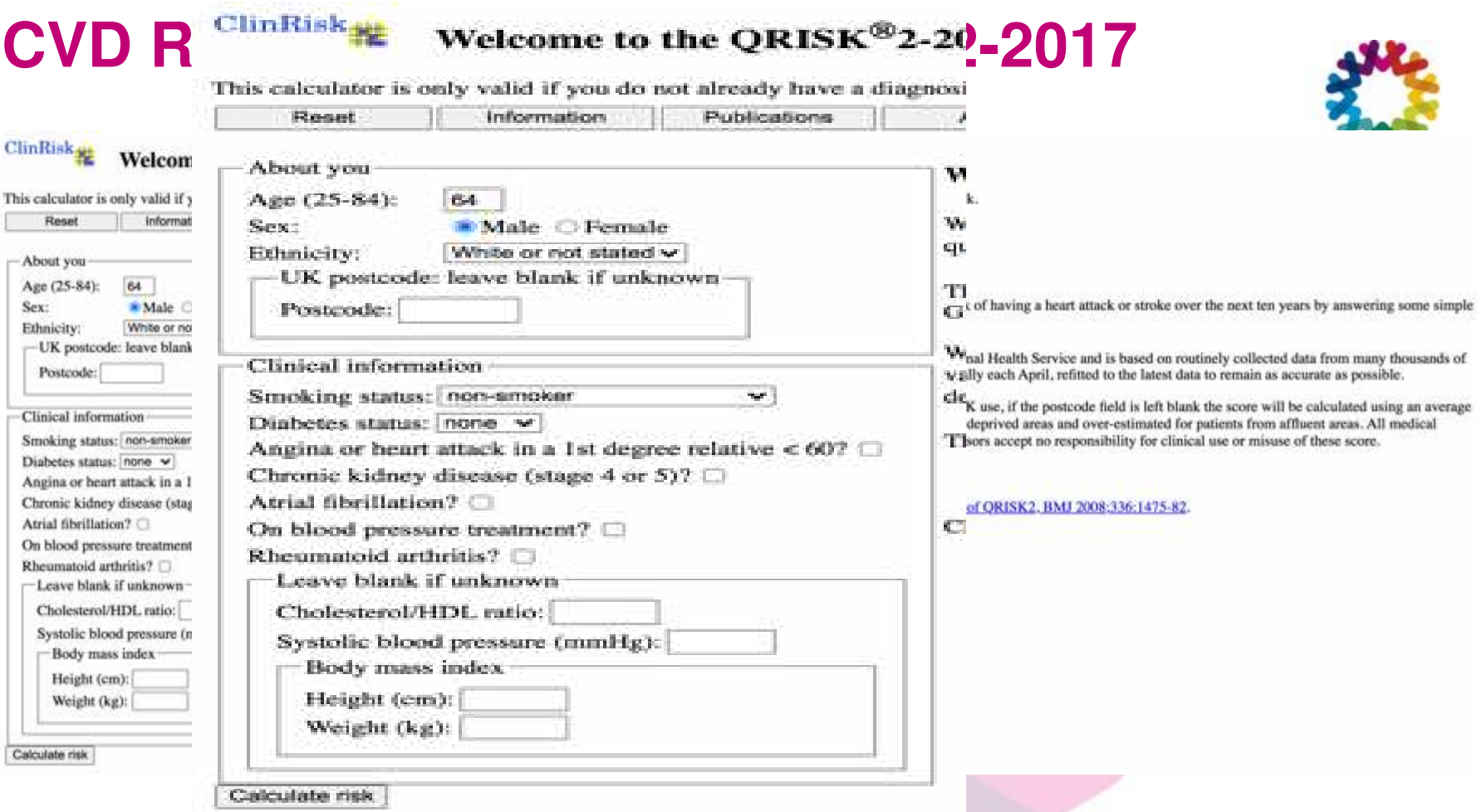
* (TG/2.2) = (TG x 0.45) = estimated VLDL-C

- LDL-C most atherogenic lipoprotein [calculated using Friedewald equation]
- **Fasting** sample recommended
  - TG < 4.5mmol/l for calculation of LDL-C
  - LDL-C required for diagnosis of Familial Hypercholesterolaemia

https://www.nice.org.uk/guidance/cg181

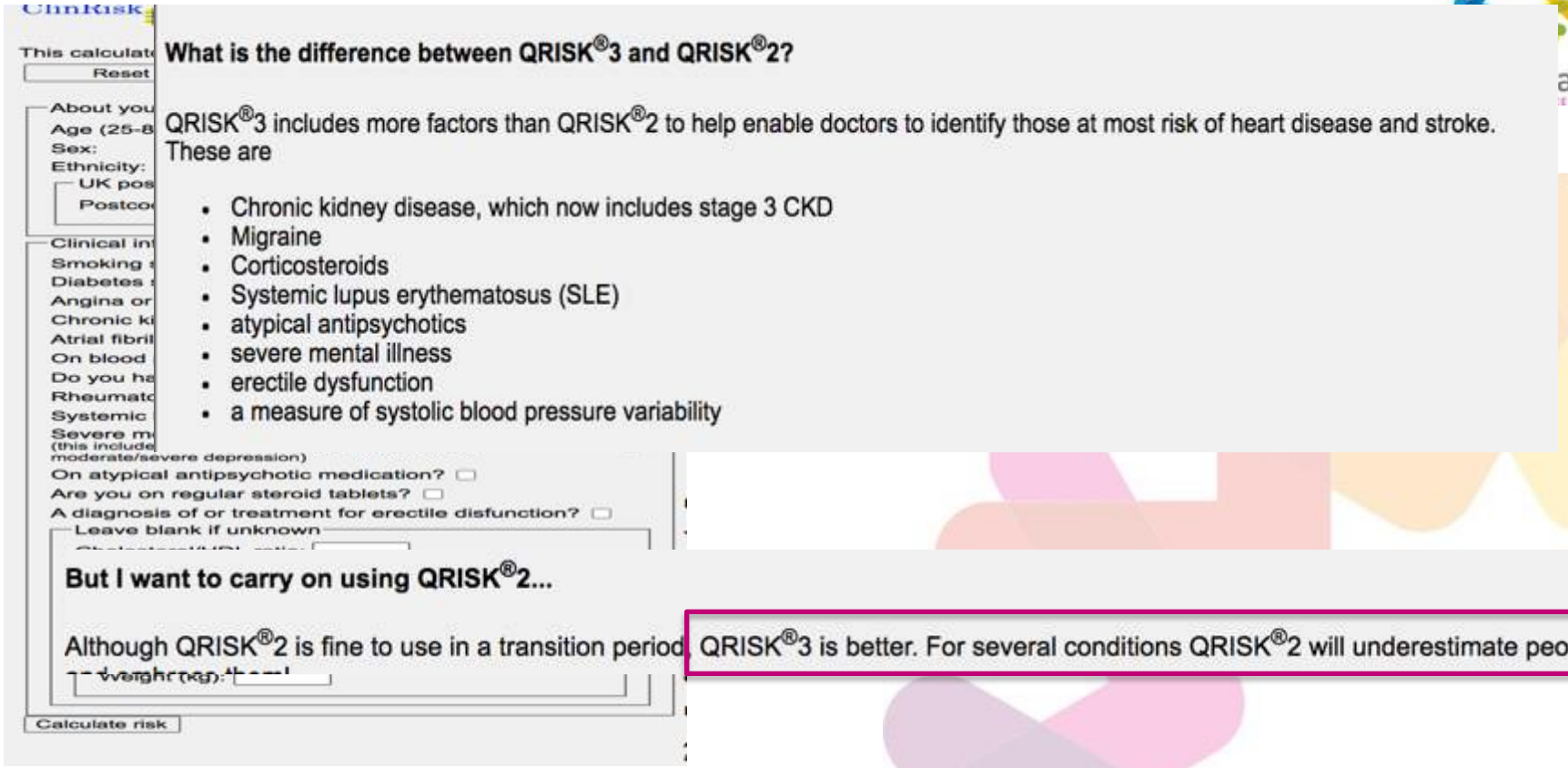
Primary Prevention

CVD R :-2017



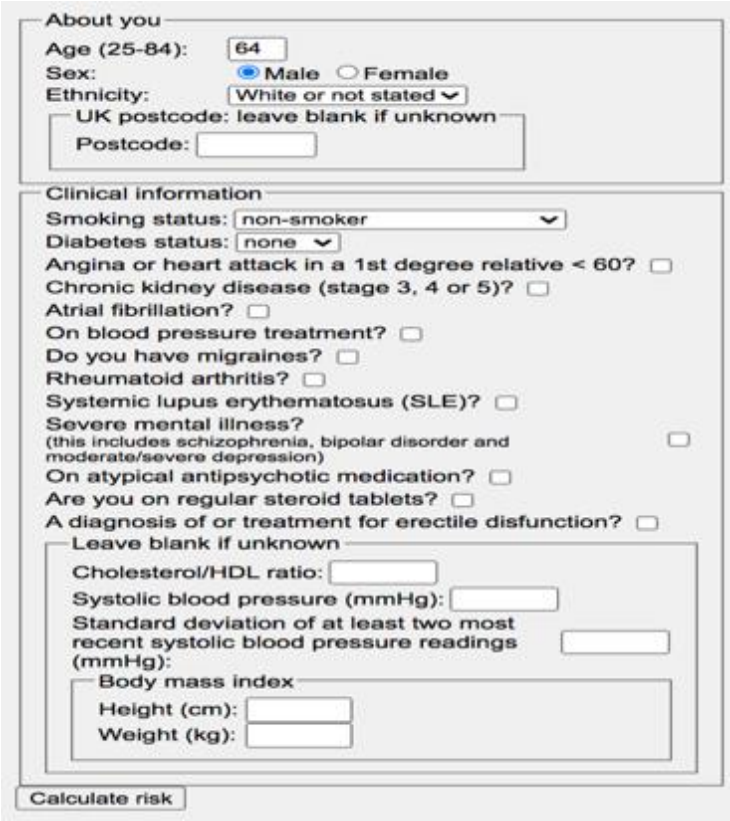
https://www.nice.org.uk/guidance/cg181; https://www.qrisk.org/2017/ <accessed 16/10/2021>

CVD Risk Assessment: QRISK®3-2018



https://qrisk.org/three/ <accessed 16/10/2021>

CVD Risk Assessment: QRISK®3-2018



- Assess an individuals risk of experiencing a heart attack or stroke over the next 10 years
- Based on presence and identification of modifiable & non-modifiable CVD risk factors
    - Low risk < 10%
    - Moderate risk 10-20%
    - High risk > 20%

https://qrisk.org/three/ <accessed 16/10/2021>

CVD Risk Assessment: Q-RISK 3-2018

About you

Age (25-84): 52
Sex: (•) Male ( ) Female
Ethnicity: White or not stated

UK postcode: leave blank if unknown
Postcode:

Clinical information

Smoking status: non-smoker
Diabetes status: none
Angina or heart attack in a 1st degree relative < 60? ☐
Chronic kidney disease (stage 3, 4 or 5)? ☐
Atrial fibrillation? ☐
On blood pressure treatment? ☐
Do you have migraines? ☐
Rheumatoid arthritis? ☐
Systemic lupus erythematosus (SLE)? ☐
Severe mental illness? ☐
(this includes schizophrenia, bipolar disorder and moderate/severe depression)
On atypical antipsychotic medication? ☐
Are you on regular steroid tablets? ☐
A diagnosis of or treatment for erectile disfunction? ☐

Leave blank if unknown

Cholesterol/HDL ratio:
Systolic blood pressure (mmHg): 148
Standard deviation of at least two most recent systolic blood pressure readings (mmHg):

Body mass index

Height (cm): 165
Weight (kg): 68

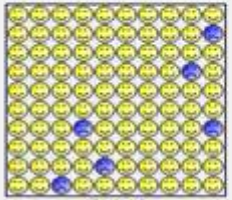
Calculate risk

Your results

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

6.1%

In other words, in a crowd of 100 people with the same risk factors as you, 6 are likely to have a heart attack or stroke within the next 10 years.



Risk of a heart attack or stroke

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

Your body mass index was calculated as 24.98 kg/m^2.

How does your 10-year score compare?

Your score	
Your 10-year QRISK®3 score	6.1%
The score of a healthy person with the same age, sex, and ethnicity*	4.5%
Relative risk**	1.3
Your QRISK®3 Healthy Heart Age***	56

* This is the score of a healthy person of your age, sex and ethnic group, i.e. with no adverse clinical indicators and a cholesterol ratio of 4.0, a stable systolic blood pressure of 125, and BMI of 25.
** Your relative risk is your risk divided by the healthy person's risk.
*** Your QRISK®3 Healthy Heart Age is the age at which a healthy person of your sex and ethnicity has your 10-year QRISK®3 score.

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https://qrisk.org/three/ <accessed 16/10/2021>

CVD Risk Assessment: QRISK®3-2018

About you

Age (25-84): 52
Sex: Male / Female
Ethnicity: White or not stated

UK postcode: leave blank if unknown
Postcode:

Clinical information

Smoking status: non-smoker
Diabetes status: type 2
Angina or heart attack in a 1st degree relative < 60?
Chronic kidney disease (stage 3, 4 or 5)?
Atrial fibrillation?
On blood pressure treatment?
Do you have migraines?
Rheumatoid arthritis?
Systemic lupus erythematosus (SLE)?
Severe mental illness?
(this includes schizophrenia, bipolar disorder and moderate/severe depression)
On atypical antipsychotic medication?
Are you on regular steroid tablets?
A diagnosis of or treatment for erectile disfunction?

Leave blank if unknown
Cholesterol/HDL ratio:
Systolic blood pressure (mmHg): 148
Standard deviation of at least two most recent systolic blood pressure readings (mmHg):

Body mass index
Height (cm): 165
Weight (kg): 68

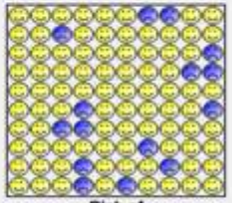
Calculate risk

Your results

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

14.9%

In other words, in a crowd of 100 people with the same risk factors as you, 15 are likely to have a heart attack or stroke within the next 10 years.



Risk of
a heart attack or stroke

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

Your body mass index was calculated as 24.98 kg/m^2.

How does your 10-year score compare?

Your score	
Your 10-year QRISK®3 score	14.9%
The score of a healthy person with the same age, sex, and ethnicity*	4.5%
Relative risk**	3.3
Your QRISK®3 Healthy Heart Age***	69

* This is the score of a healthy person of your age, sex and ethnic group, i.e. with no adverse clinical indicators and a cholesterol ratio of 4.0, a stable systolic blood pressure of 125, and BMI of 25.
** Your relative risk is your risk divided by the healthy person's risk.
*** Your QRISK®3 Healthy Heart Age is the age at which a healthy person of your sex and ethnicity has your 10-year QRISK®3 score.

Does this person warrant any intervention?

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https://qrisk.org/three/ <accessed 16/10/2021>

CVD Risk Assessment: JBS-3

JBS3

Joint British Societies for the prevention of cardiovascular disease

HOME | WHO WE ARE | LIFETIME RISK | JBS3 REPORT | RISK CALCULATOR | CONTACT US

Welcome to the website for the Joint British Societies recommendations on the prevention of Cardiovascular Disease (JBS3). On this site you can access the JBS3 Risk Calculator and download the JBS3 report, with its recommendations.

The proposals published in the **JBS3 report** are consensus recommendations, and are a collaborative effort from the British cardiovascular societies who deal with cardiovascular disease prevention. The report was written for GPs and practitioners to help guide their work with patients, in preventing CVD.

The **JBS3 risk calculator** is a tool to help communicate the risk of CVD and the benefits of interventions, whether they are lifestyle or pharmacological. Although the JBS3 risk calculator is openly available on this website, it has been designed for use by Doctors and Practitioners with their patients.

http://www.jbs3risk.com <accessed 17/10/2021>

JBS-3 – Concept of Heart Age

Mr MD

- 51 years old
- Currently unemployed – but did work as a taxi driver

SHx
- Alcohol 5-6 pints/day
- Smokes 20/day
- Sedentary lifestyle

FHx
- Nil significant

PMHx
- Diabetes
- Hypertension
- Hypercholesterolaemia

- Weight – 102kg
- Height 5'10"
- BMI – 32
- Tc 6.2
- BP 174/98

What are Mr MD's RF for CHD??

What is Mr MD's heart age??

Risk Factors

Modifiable

- Smoking
- Hypertension
- Dyslipidaemia
- Diabetes Mellitus
- Obesity/metabolic syndrome
- High calorie, high fat diet
- Physical inactivity

Non-modifiable

- Increasing age
- Male sex
- Family history
- Ethnic origin
- Established CVD

Risk Factors

Modifiable

- Smoking
- Hypertension
- Dyslipidaemia
- Diabetes Mellitus
- Obesity/metabolic syndrome
- High calorie, high fat diet
- Physical inactivity

Non-modifiable

- Increasing age
- Male sex
- Family history
- Ethnic origin
- Established CVD

JBS-3 Heart Age

http://www.jbs3risk.com <accessed 17/10/2021>

Mr MD - Heart Age = 85 years

Your heart age is about

85

compared to a person of the same age, gender and ethnicity with optimal risk factors

Interventions

Future smoking category

20+/day

Systolic Blood Pressure

174 → 174

Total Cholesterol

6.4 → 6.4

HDL Cholesterol

1.2 → 1.2

NonHDL Cholesterol: 5.2

BMI: 32.2

Reset

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http://www.jbs3risk.com <accessed 17/10/2021>

Reduced life expectancy

On average, expect
to survive to age 65
without a heart attack or stroke

55 60 65 70 75 80 85 90 95 100

expected life without a heart attack or stroke

Your risk of a heart attack or stroke
in the next 10 years is

29%

assuming you don't die of anything else

Interventions

Future smoking category
20+/day

Systolic Blood Pressure
174 → 174

Total Cholesterol
6.4 → 6.4

HDL Cholesterol
1.2 → 1.2

NonHDL Cholesterol: 5.2

BMI: 32.2

Reset

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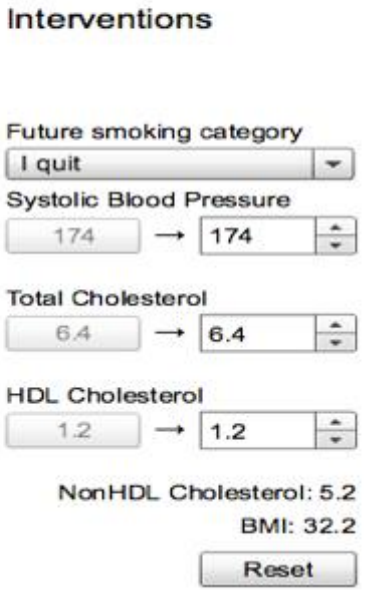
http://www.jbs3risk.com <accessed 17/10/2021>

Modification of risk factors: smoking

Your heart age is about

76

compared to a person of the same age, gender and ethnicity with optimal risk factors



http://www.jbs3risk.com <accessed 17/10/2021>

Modification of risk factors: ↓ BP

Your heart age is about

57

compared to a person of the same age, gender and ethnicity with optimal risk factors

Interventions

Future smoking category

I quit

Systolic Blood Pressure

174 → 140

Total Cholesterol

6.4 → 6.4

HDL Cholesterol

1.2 → 1.2

NonHDL Cholesterol: 5.2

BMI: 32.2

Reset

http://www.jbs3risk.com <accessed 17/10/2021>

Modification of risk factors: ↓TC (non-HDL-

JBS3 Cardiovascular Risk Assessment

Profile | Heart Age | Healthy Years | Outlook | more

Your heart age is about

52

compared to a person of the same age, gender and ethnicity with optimal risk factors

Interventions

Future smoking category: I quit

Systolic Blood Pressure: 174 → 140

Total Cholesterol: 6.4 → 4.0

HDL Cholesterol: 1.2 → 1.2

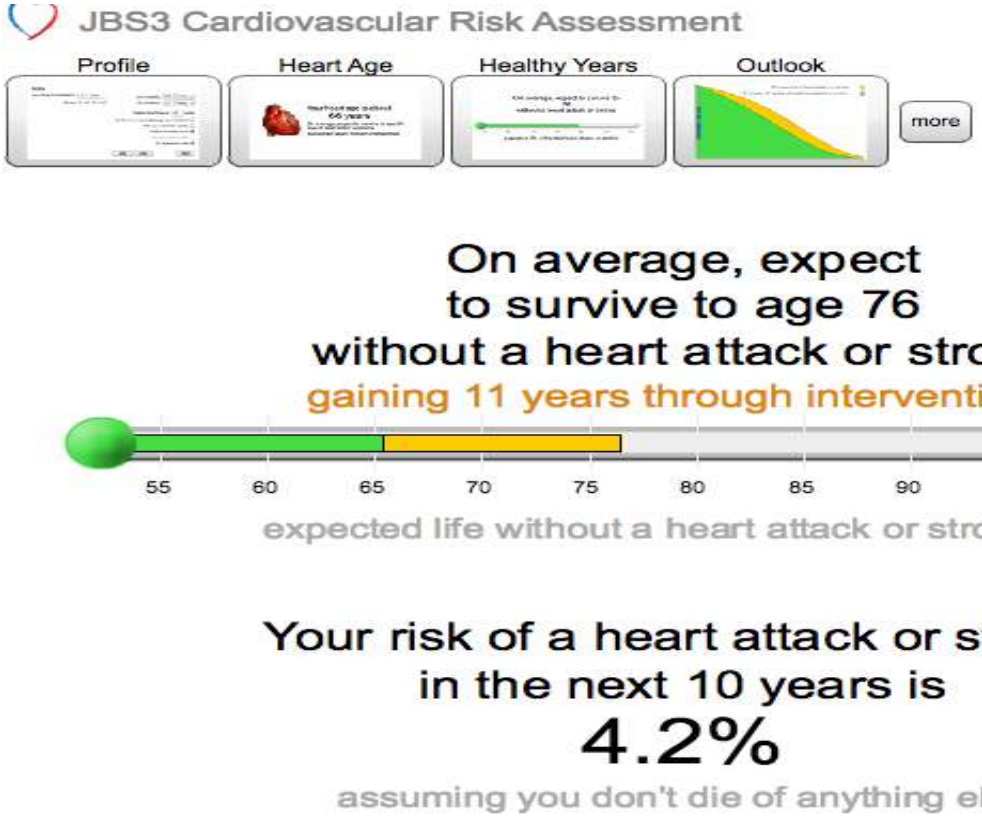
NonHDL Cholesterol: 2.8

BMI: 32.2

Reset

http://www.jbs3risk.com <accessed 17/10/2021>

Improved life expectancy



http://www.jbs3risk.com <accessed 17/10/2021>

QRISK®2-2017 or QRISK®3-2018 or JBS3??

QRISK®2-2017

- NICE CG181
- 10 year risk
- Validated for use in the NHS
- Underestimate risk in younger people & females

QRISK®3-2018

- 10 year risk
- Additional risk factors to identify those most at risk
- Underestimate risk in younger people & females

JBS-3

- Lifetime risk
- Identification of those at risk when overt disease is not present

Not appropriate for use in:

- established CVD,
- T1DM, CKD, FH → individuals are at a high risk of CVD

Lifestyle advice and behaviourial modifications to reduce CVD risk
- exercise, healthy eating, smoking cessation, alcohol

Optimise management of co-morbidities e.g. diabetes, hypertension

NICE CG181: Lipid modification for primary prevention

Key priorities for implementation

- When a decision is made to prescribe a statin use a statin of **high intensity** and low acquisition cost

[1.3.2]

- Offer **atorvastatin 20 mg** for the primary prevention of CVD to people who have a **10% or greater 10-year risk** of developing CVD.
- Estimate the level of risk using the **QRISK2** assessment tool.

[1.3.18]

- Measure total cholesterol, HDL cholesterol and non-HDL cholesterol in all people who have been started on **high-intensity statin treatment** (both primary and secondary prevention, including atorvastatin 20 mg for primary prevention) **at 3 months of treatment and aim for a greater than 40% reduction in non-HDL cholesterol**.

[1.3.28]

NICE CG181: High intensity statin treatment

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%	

- **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

https://www.nice.org.uk/guidance/cg181

https://www.england.nhs.uk/aac/wp-content/uploads/sites/50/2020/04/Lipid-Management-Pathway-NEW.pdf <accessed 17/10/2021>

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

ACCELERATED ACCESS COLLABORATIVE

NHS

INITIAL CONSIDERATIONS:

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

PRIMARY PREVENTION

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

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

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

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

PRIMARY PREVENTION

If lifestyle modification is ineffective or inappropriate offer statin treatment

Atorvastatin 20mg daily

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

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

SEVERE HYPERLIPIDAEMIA

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

Do not use QRISK risk assessment tool

DIAGNOSIS AND REFERRAL

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

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

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

TREATMENT TARGETS IN FH

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

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

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

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

despite maximal tolerated statin and ezetimibe therapy.

**defined as any of the following:

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

SECONDARY PREVENTION

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

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

SECONDARY PREVENTION

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

Prescribe a high intensity statin:

Atorvastatin 80mg daily

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

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

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

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

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

If statin intolerance is confirmed, consider:

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

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

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

Injectable therapies**

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

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

OR

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

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

* See overleaf for information to support shared decision making

** Inclisiran and PCSK9i should not be prescribed concurrently

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

https://www.england.nhs.uk/aac/wp-content/uploads/sites/50/2020/04/National-Guidance-for-Lipid-Management-Prevention-Dec-2022.pdf <accessed 19.01.2023>

Primary Prevention: Key Learning Points

- Estimate the level of risk using the **QRISK** assessment tool.
- **> 10% 10-year risk** - offer **atorvastatin 20 mg od**
- Offer lifestyle advice to supplement pharmacological management with HIST
- Repeat full lipid profile at 3 months of treatment and aim for a greater than **40% reduction** in **non-HDL cholesterol**.
  - But, **the lower the better!**

Secondary Prevention

NICE CG181: Lipid modification for secondary prevention

Key priorities for implementation

- Start statin treatment in people with CVD with atorvastatin 80 mg.
- Use a lower dose of atorvastatin if any of the following apply:
  - potential drug interactions
  - high risk of adverse effects
  - patient preference

[1.3.20]

- Measure total cholesterol, HDL cholesterol and non-HDL cholesterol in all people who have been started on **high-intensity statin treatment** (both primary and secondary prevention, including atorvastatin 20 mg for primary prevention) **at 3 months of treatment and aim for a greater than 40% reduction in non-HDL cholesterol**.

[1.3.28]

Does your local hospital request a full lipid profile and are these results available to y
How often is full lipid profile repeated 3/12 post-discharge?

https://www.nice.org.uk/guidance/cg181

Cholesterol related QOF clinical indicators

Cholesterol control and lipid management (CHOL)	Points	Thresholds
Ongoing management		
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%

NICE CG181 – currently put for consultation - ? Alignment with QOF?

https://www.england.nhs.uk/wp-content/uploads/2023/03/PRN00289-quality-and-outcomes-framework-guidance-for-2023-24.pdf <accessed 19.04.2023>

Andrew – 51 year old accountant

- Usually fit and well, no past medical history of note, non-smoker
- 2020 – at a dancing class, experienced chest pain, not relieved by rest, ambulance crew – ECG showed anterior ST elevation MI, transferred to nearest heart attack centre
    - PPCI to LAD

- Commenced on usual secondary prevention medication regime
    - Aspirin 75mg od + ~~Ticagrelor 90mg bd~~ HIST
    - Bisoprolol 1.25mg od + Ramipril 2.5mg od
    - Atorvastatin 80mg od
    - S/L GTN

- **Baseline full lipid profile**

Non fasting sample

Total cholesterol = 5.7mmol/L
HDL cholesterol = 1.2mmol/L
Non-HDL cholesterol = 4.5mmol/L
Triglycerides = 1.1mmol/L

- **3/12 full lipid profile**

Non fasting sample

Total cholesterol = 5.0mmol/L
HDL cholesterol = 1.2mmol/L
Non-HDL cholesterol = 3.8mmol/L
Triglycerides = 1.1mmol/L

west midlands
ACADEMIC HEALTH SCIENCE NETWORK

Cardiovascular disease: risk assessment and reduction, including lipid modification

Clinical guideline
Published: 18 July 2014
www.nice.org.uk/guidance/cg181

- Baseline full lipid profile
- Commenced on atorvastatin 80mg od
- 3/12 full lipid profile
- non-HDL C < 2.5mmol/L
(= LDL-C <1.8mmol/L)
(or > 40% reduction from baseline)

Coventry and Warwickshire Training Hub

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

ACCELERATED ACCESS COLLABORATIVE

NHS

INITIAL CONSIDERATIONS:

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

PRIMARY PREVENTION

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

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

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

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

PRIMARY PREVENTION

If lifestyle modification is ineffective or inappropriate offer statin treatment

Atorvastatin 20mg daily

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

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

SEVERE HYPERLIPIDAEMIA

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

Do not use QRISK risk assessment tool

DIAGNOSIS AND REFERRAL

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

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

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

TREATMENT TARGETS IN FH

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

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

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

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

despite maximal tolerated statin and ezetimibe therapy.

**defined as any of the following:

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

SECONDARY PREVENTION

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

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

SECONDARY PREVENTION

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

Prescribe a high intensity statin:

Atorvastatin 80mg daily

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

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

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

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

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

If statin intolerance is confirmed, consider:

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

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

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

Injectable therapies**

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

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

OR

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

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

* See overleaf for information to support shared decision making

** Inclisiran and PCSK9i should not be prescribed concurrently

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

https://www.england.nhs.uk/aac/wp-content/uploads/sites/50/2020/04/National-Guidance-for-Lipid-Management-Prevention-Dec-2022.pdf <accessed 19.01.2023>

NICE CG181: HIST + Ezetimibe

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%

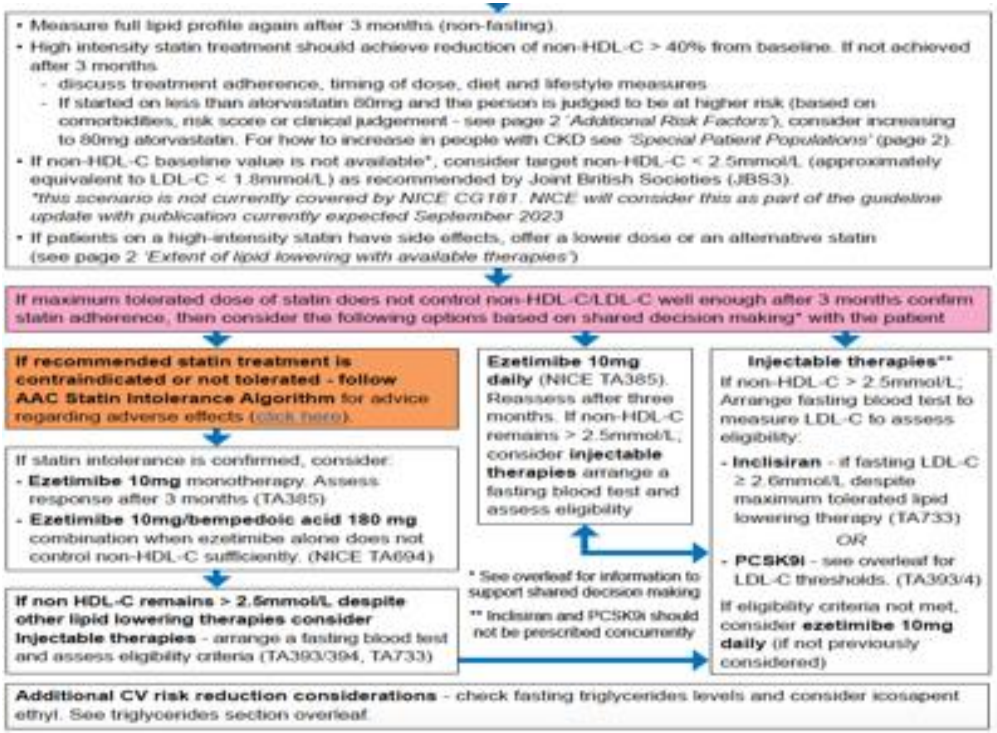
- **Low intensity statins** will produce an LDL-C reduction of 20-30%
- **Medium intensity statins** will produce an LDL-C reduction of 31-40%
- **High intensity statins** will produce an LDL-C reduction above 40%
- **Simvastatin** 80mg is not recommended due to risk of muscle toxicity

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.

HIST – pleiotropic benefits

- Plaque stabilisation
- Plaque regression

https://www.nice.org.uk/guidance/cg181
https://www.england.nhs.uk/aac/wp-content/uploads/sites/50/2020/04/Lipid-Management-Pathway-NEW.pdf <accessed 17/10/2021>



Atorvastatin 80mg OD

+

Ezetimibe 10mg OD

↓ 3/12

Non-HDL-C = 3.4mmol/L

↓

LDL-C = 2.8mmol/L

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How to manage those not at target with ezetimibe??

Bempedoic acid/ezetimibe eligibility criteria

If HIST is contra-indicated/not tolerated

Inclisiran eligibility criteria

Maximum tolerated statin

LDL-C > 2.6mmol/L

PCSK9i Eligibility Criteria (established CVD)

High risk = LDL-C > 4.0mmol/L

Very High Risk = LDL-C >3.5mmol/L

Coventry and Warwickshire Training Hub

https://www.england.nhs.uk/aac/wp-content/uploads/sites/50/2020/04/Lipid-Management-Pathway-NEW.pdf <accessed 17/10/2021>

Secondary Prevention: Key Learning Points

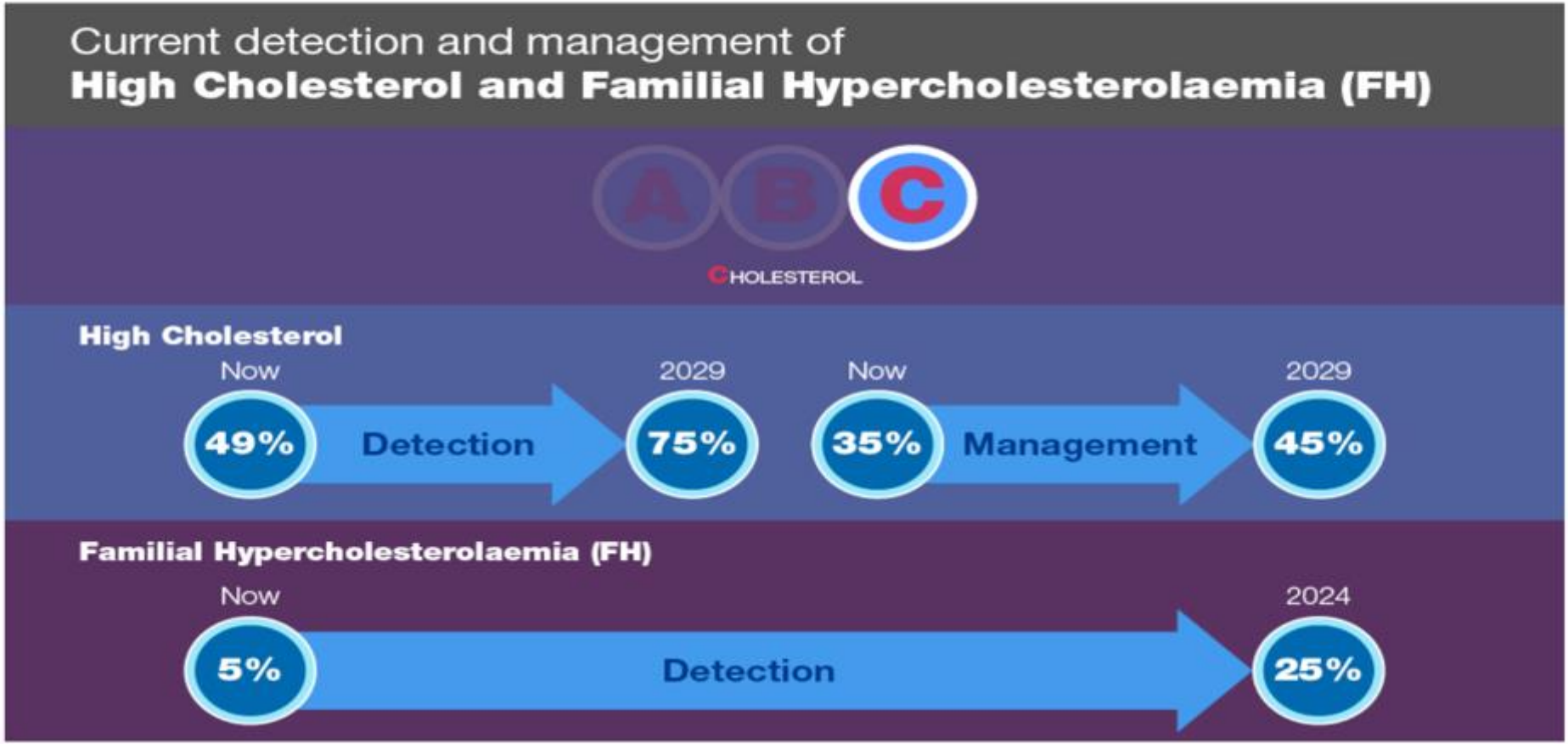
- People with **established cardiovascular disease** should be treated with high intensity statin therapy (usually **atorvastatin 80mg od**)
- Not “fire and forget” – **3/12** full lipid profile is important
    - **non HDLC > 2.5mmol/L** (LDLC >1.8mmol/L) at risk of recurrent events
    - opportunity to optimise lipid lowering therapy
        - **lower LDL-C is better**
    - reinforce lifestyle advice

- For people who still don’t attain secondary prevention target (LDL-C < 1.8mmol/L)
    - Ezetemibe
    - PCSK9i (but thresholds for treatment are high)
    - Bempedoic acid +/- ezetimibe (if unable to tolerate max dose HIST)
    - Inclisiran
    - Icosapent ethyl

Familial Hypercholesterolaemia

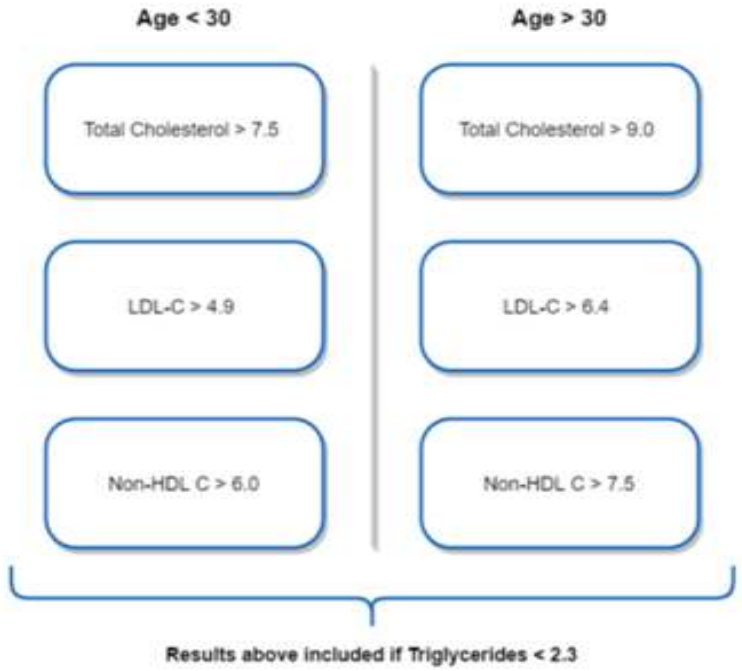
Incidence and prevalence of FH

- **FH** is a common inherited disorder associated with elevated LDLC, affecting approx. **1 in 250 people**.
  - autosomal dominant disorder
  - genetic mutations in LDLR, APOB, PCSK9 or APOE genes
- If left untreated it can lead to **premature CHD**.
- It is estimated that approx. **80%** of people with HeFH remain **undiagnosed**.
- **Primary care** is an ideal setting to **identify** people with possible FH



https://www.gov.uk/government/publications/health-matters-preventing-cardiovascular-disease/health-matters-preventing-cardiovascular-disease <accessed 05/10/2021>

CDRC tool to support case finding (EMIS & SystmOne) [cdrc.nhs.uk]



Exclude secondary causes of dyslipidaemia

Use **Simon Broome** Criteria **or** **Dutch Lipid Clinic Network** criteria to make clinical diagnosis

Referral to the **West Midlands Familial Hypercholesterolaemia Service***

(Genetic confirmation followed by cascade testing for family members)

* westmidlands.fhnurses@nhs.net

https://www.nice.org.uk/guidance/cg71 <accessed 17/10/2021>

https://cdrc.nhs.uk/resources/fh/lipids-familial-hypercholesterolaemia-fh-and-pcsk9i-guide-for-emis/ <accessed 17/10/2021>

FH Diagnostic Criteria

Both are available on-line via MDCalc

Simon Broome Criteria

SIMON BROOME DIAGNOSTIC CRITERIA FOR FAMILIAL HYPERCHOLESTEROLEMIA[1]	
Point	Criteria
1	Total cholesterol levels > 290mg/dL (7.5 mmol/L) or LDL-C > 190 mg/dL (4.9 mmol/L) in adults. Total cholesterol levels > 260 mg/dL (6.7 mmol/L) or LDL-C > 155 mg/dL (4.0 mmol/L)
2	Tendon xanthomas in the patient or tendon xanthomas in a first or second degree relative.
3	DNA-based evidence of an LDL-receptor mutation, familial defective apo B-100, or a PCSK9 mutation.
4	Family history of myocardial infarction before age 50 years in a second degree relative or before age 60 years in a first degree relative.
5	Family history of elevated total cholesterol > 290 mg/dL (7.5 mmol/L) in an adult first or second-degree relative. Family history of elevated totacl cholesterol > 260 mg/dL (6.7 mmol/L) in a child, brother, or sister 16 years or younger.
DIAGNOSIS	
Definite familial hypercholesterolemia = 1+2 or 3 Possible familial hypercholesterolemia = 1+4 or 5	

1. Austin MA, Hutter CM, Zimmern RL, Humphries SE. Genetic causes of monogenic heterozygous familial hypercholesterolemia: a HuGE prevalence review. *American journal of epidemiology*. 2004;160:407-420.

WMFHS for DNA testing (application of Welsh Score: improved diagnostic yield & improved targeting of genetic testing**)**

Dutch Lipid Clinic Network Criteria

DUTCH LIPID CLINIC NETWORK DIAGNOSTIC CRITERIA FOR FAMILIAL HYPERCHOLESTEROLEMIA[1,2]	
Criteria	Point
Family History	
First-degree relative with known premature* coronary and vascular disease OR First-degree relative with known LDL-C level above the 95th percentile.	1
First-degree relative with tendinous xanthomata and/or arcus cornealis OR Children aged less than 18 years with LDL-C level above the 95th percentile.	2
Clinical History	
Patient with premature* coronary artery disease.	2
Patient with premature* cerebral or peripheral vascular disease.	1
Physical Examination	
Tendinous xanthomata	6
Arcus cornealis prior to age 45 years	4
Cholesterol levels mg/dl (mmol/liter)	
LDL-C >= 330 mg/dL (≈8.5)	8
LDL-C 250 – 329 mg/dL (6.5–8.4)	5
LDL-C 190 – 249 mg/dL (5.0–6.4)	3
LDL-C 155 – 189 mg/dL (4.0–4.9)	1
DNA Analysis	
Functional mutation in the LDLR, apo B or PCSK9 gene	8
Diagnosis (diagnosis is based on the total number of points obtained)	
Definite familial hypercholesterolemia	>8
Probable familial hypercholesterolemia	6 – 8
Possible familial hypercholesterolemia	3 – 5
Unlikely familial hypercholesterolemia	<3

* Premature = < 55 years in men; < 60 years in women
LDL-C = low density lipoprotein cholesterol; FH, familial hypercholesterolemia.
LDLR = low density lipoprotein receptor
Apo B = apolipoprotein B
PCSK9 = Proprotein convertase subtilisin/kexin type 9

1. Austin MA, Hutter CM, Zimmern RL, Humphries SE. Genetic causes of monogenic heterozygous familial hypercholesterolemia: a HuGE prevalence review. *American journal of epidemiology*. 2004;160:407-420.

Coventry and Warwickshire Training Hub

Secondary causes of dyslipidaemia

Table 3: Drugs and disease conditions that may cause secondary dyslipidemia

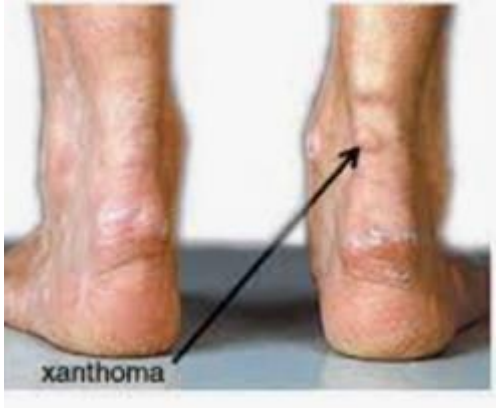
Drugs and diseases that increase LDL-C levels		Drugs and diseases that increase TG levels	
Drugs	**Diseases**	**Drugs**	**Diseases**
Amiodarone	Hypothyroidism	Beta-blockers (especially nonbeta 1-selective)	Diabetes mellitus
Thiazide diuretics	CKD	Thiazide diuretics	Metabolic syndrome
Glucocorticoids	Nephrotic syndrome	Glucocorticoids	Hypothyroidism
Thiazolidinediones	Obstructive airway disease	Rosiglitazone	CKD
Fibrates (in severe hypertriglyceridemia)	Human immunodeficiency virus infection	Bile acid sequestrants	Nephrotic syndrome
Long chain omega-3 fatty acids (in severe hypertriglyceridemia)	Autoimmune disorders	Oral estrogens	Human immunodeficiency virus infection
Anabolic steroids	Pregnancy	Tamoxifen, raloxifene	Autoimmune disorders
Some progestins	Polycystic ovary disease	Retinoids	Pregnancy
Danazol		Immunosuppressive drugs (cyclosporine, sirolimus)	Polycystic ovary disease
Isotretinoin		Cyclophosphamide	
Immunosuppressive drugs (cyclosporine)		Interferons	
		Atypical antipsychotic drugs (fluperlapine, clozapine, olanzapine)	
		Protease inhibitors	
		L-asparaginase	

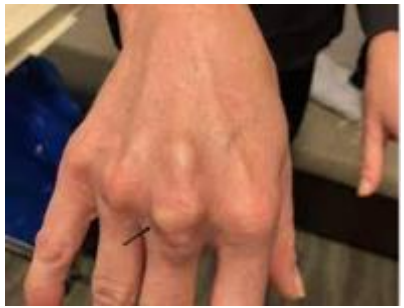
CKD=Chronic kidney disease, LDL-C=Low-density lipoprotein cholesterol, TG=Triglycerides

https://www.jcpconline.org/viewimage.asp?img=JClinPrevCardiol_2016_5_2_51_186492_t5.jpg <accessed 19/10/2021>

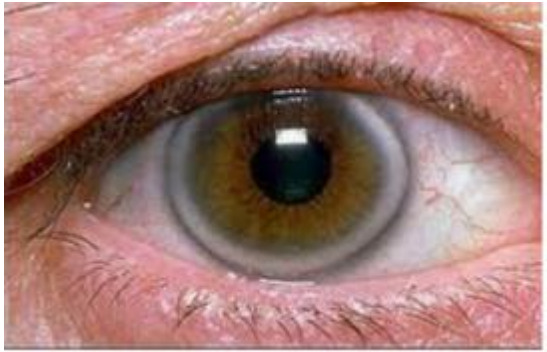
Clinical Signs

Tendon xanthomata

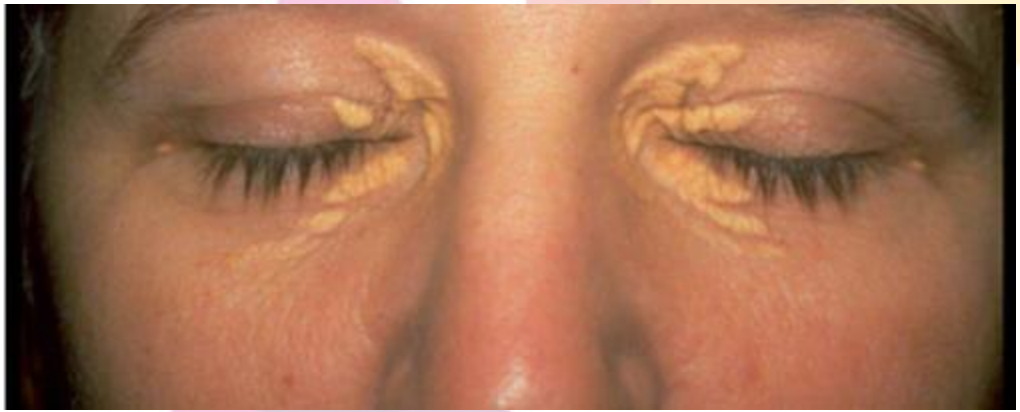




Corneal arcus



Xanthelasma



Peter – 44yr old paramedic

- NSTEMI 08/07/2019
    - PCI to LAD
- Premature FHx – father MI at age of 48yrs
- Commenced on secondary prevention treatment
- (atorvastatin 80mg od)

- Baseline full lipid profile (non-fasting)
    - Total cholesterol = 8.1mmol/L
    - HDL cholesterol = 1.1mmol/L
    - Non-HDL cholesterol = 6.7mmol/L
    - Triglycerides = 1.3mmol/L

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

ACCELERATED ACCESS COLLABORATIVE

NHS

INITIAL CONSIDERATIONS:

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

PRIMARY PREVENTION

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

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

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

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

PRIMARY PREVENTION

If lifestyle modification is ineffective or inappropriate offer statin treatment.

Atorvastatin 20mg 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 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

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 angina, previous MI, revascularisation,stroke or TIA or symptomatic peripheral arterial disease. Do not delay statin treatment if a person has acute coronary syndrome. Take a lipid sample on admission (within 24 hours)

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

SECONDARY PREVENTION

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

Prescribe a high intensity statin:

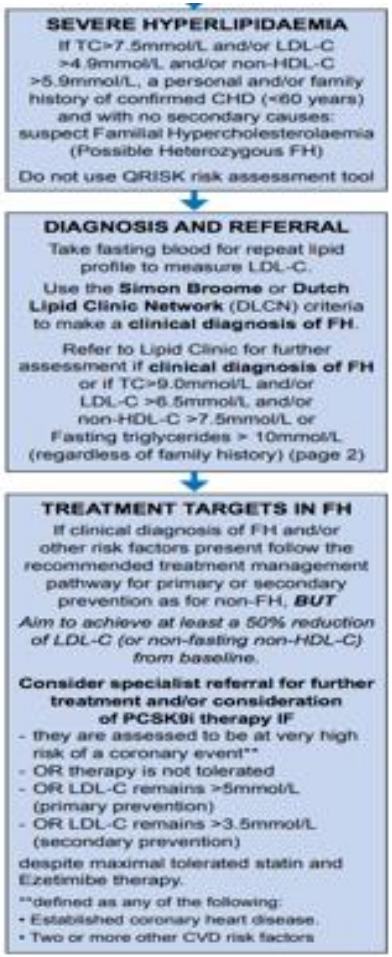
Atorvastatin 80mg OD

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

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

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



Baseline full lipid profile

Non fasting sample

Total cholesterol = 8.1mmol/L

HDL cholesterol = 1.1mmol/L

Non-HDL cholesterol = 6.7mmol/L

Triglycerides = 1.3mmol/L

Fasting LDL cholesterol = 5.8mmol/L

Referral to local lipidologist

Commenced on ezetimibe 10mg od

Referral to local regional FH service
Genetic confirmation of HeFH
(LDLR mutation)

Fasting LDL cholesterol = 4.0mmol/L

Commenced on evolocumab 140mg every 2/52

Current full lipid profile

Fasting sample

Total cholesterol = 4.4mmol/L

HDL cholesterol = 1.4mmol/L

Non-HDL cholesterol = 3.0mmol/L

Triglycerides = 1.1mmol/L

LDL cholesterol = 2.3mmol/L

west midlands
ACADEMIC HEALTH SCIENCE NETWORK

Coventry and Warwickshire Training Hub

https://www.england.nhs.uk/aac/wp-content/uploads/sites/50/2020/04/Lipid-Management-Pathway-NEW.pdf <accessed 17/10/2021>

Familial Hypercholesterolaemia: Key Learning Points

- FH is common
  - **Underdiagnosed** and **undertreated**

- Risk **assessment tools** should not be used in people with FH
  - **underestimate risk**

- **High clinical suspicion** if TC> 7.5mmol/l and premature cardiovascular event +/- positive family history
  - **Referral to** regional **FH service**
  - **Process: 1.** clinical diagnosis, **2**. genetic diagnosis, **3**. initiation of LLT

- **Aggressive lipid management** to reduce likelihood of index/recurrent adverse cardiovascular event(s)

Useful Resources

Heart UK: Tackling Cholesterol Together

Tackling Cholesterol Together

HEART UK has partnered with the **NHS Accelerated Access Collaborative (AAC)** and the **Academic Health Science (AHSN) Network** to provide a comprehensive and varied education programme for healthcare professionals.

Post CV-Event Management

Sign up to our HCP e-news to be the first to hear when we schedule new webinars

Novel Therapies

Sign up to our HCP e-news to be the first to hear when we schedule new webinars

Statin Hesitancy

Sign up to our HCP e-news to be the first to hear when we schedule new webinars

Coventry and Warwickshire Training Hub

https://www.heartuk.org.uk/tackling-cholesterol-together/home <accessed 17/10/2021>

Proactive Care Framework: Lipid Management & FH

https://uclpartners.com/proactive-care/cvd-resources/ <accessed 17/10/2021>

Cholesterol –Primary Prevention (no pre-existing CVD)

UCLPartners

Healthcare assistants/other appropriately trained staff

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

Stratification

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

AND
- Not on statin

Priority Two
- QRISK 15-19%

AND
- Not on statin

Priority Three
- QRISK 10-14%

AND
- Not on statin

Priority Four
- On statin for primary prevention but not high intensity

Prescribing clinician

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

*QRISK 3 score is recommended to assess CV risk for patients with Severe Mental Illness, Rheumatoid Arthritis , Systemic Lupus Erythematosus, those taking antipsychotics or oral steroids

https://uclpartners.com/proactive-care/cvd-resources/ <accessed 17/10/2021>

Cholesterol – Secondary Prevention (pre-existing CVD)

UCLPartners

Healthcare assistants/other appropriately trained staff

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

Stratification

Priority One	Priority Two (A)	Priority Two (B)	Priority Three – routine follow up
Not on statin therapy	On suboptimal intensity statin*	On suboptimal statin dose**	Sub-optimal non-HDL (>2.5mmol/l) levels despite maximal statin therapy

Prescribing clinician

Optimise lipid modification therapy and CVD risk reduction

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

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

Coventry and Warwickshire Training Hub

https://uclpartners.com/proactive-care/cvd-resources/ <accessed 17/10/2021>

Key take home messages

Primary prevention:

- Undertake CVD risk assessment
- Offer **Atorvastatin 20mg od** (+ lifestyle advice)

Secondary prevention:

- Offer **Atorvastatin 80mg od** (+/- ezetimibe + lifestyle advice)
- 3/12 full lipid profile
- intensification with inclisiran or bempedoic acid/ezetimibe
- aim for non-HDL < 2.5mmol/l (or LDL-C < 1.8mmol/L)
- the **lower the LDL-C the better**!

Familial Hypercholesterolaemia:

- Underdiagnosed (prevalence 1 in 250)
- Undertreated – commence treatment with HIST

Detection & management – can be undertaken in primary ca

Thank you for listening

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