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Empowering primary care to deliver
the best in cardiovascular health



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PCCS Lipid QI Programme

Patient identification and diagnosis

Prof. Raj Thakkar

Primary Care Cardiovascular Society President (and CKD representative), Oxford HIN primary care cardiology lead, UK Director - Healthy.io, Primary Care GP – Clinical Co-Lead with the National Cardiac Transformation Programme, Honorary Visiting Professor, Cardiff University Medical School

Dr Jim Moore

Immediate Past President of the Primary Care Cardiovascular Society, GP, GPSI Cardiology, Primary Care GP – Clinical Co-Lead with the National Cardiac Transformation Programme

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Prof. Raj Thakkar disclosures

- AstraZeneca
- Bayer
- Boehringer Ingelheim
- Novartis
- Amgen
- Medtronic
- Edwards
- Heathy.io
- Abbott

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Dr Jim Moore disclosures

- Amgen
- AstraZeneca
- Bayer
- Boehringer Ingelheim
- Cuviva
- Novartis
- Novo Nordisk
- VIFOR
- Amarin
- Medtronic
- Roche

PCCS Lipid QI Programme



Contents

- Pathological process of atherosclerosis
- Lipids and CVD risk
- Primary and secondary prevention of CVD
- National priorities around lipid management

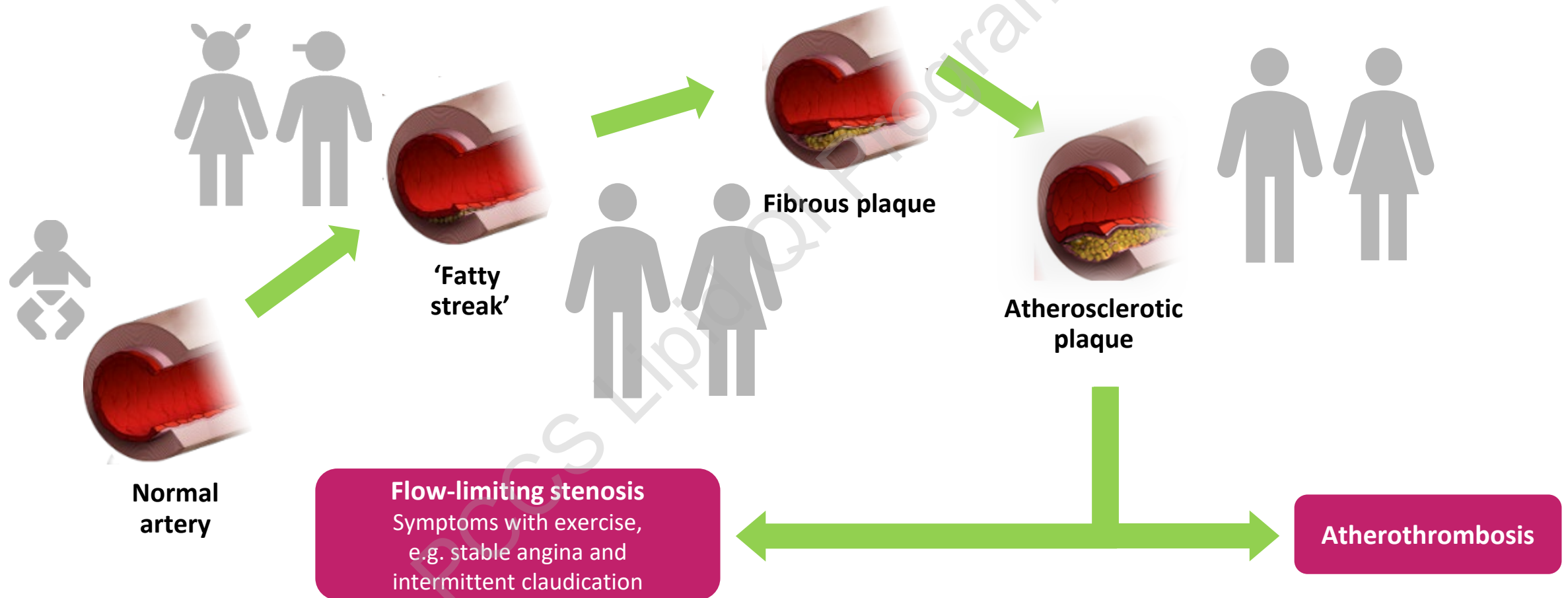
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Atherosclerosis, a progressive occlusive disease, potentially leading to atherothrombosis and ischaemia



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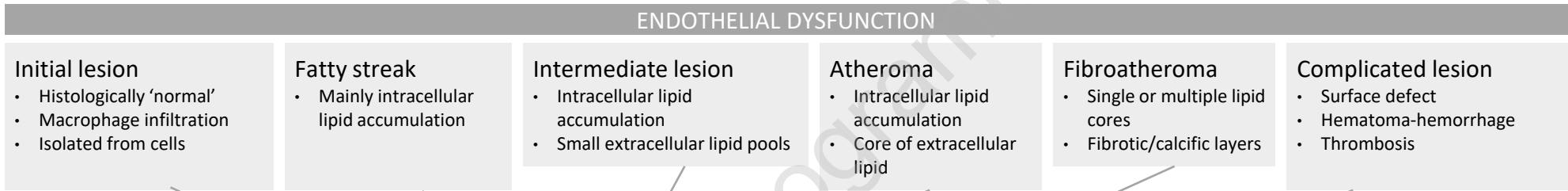
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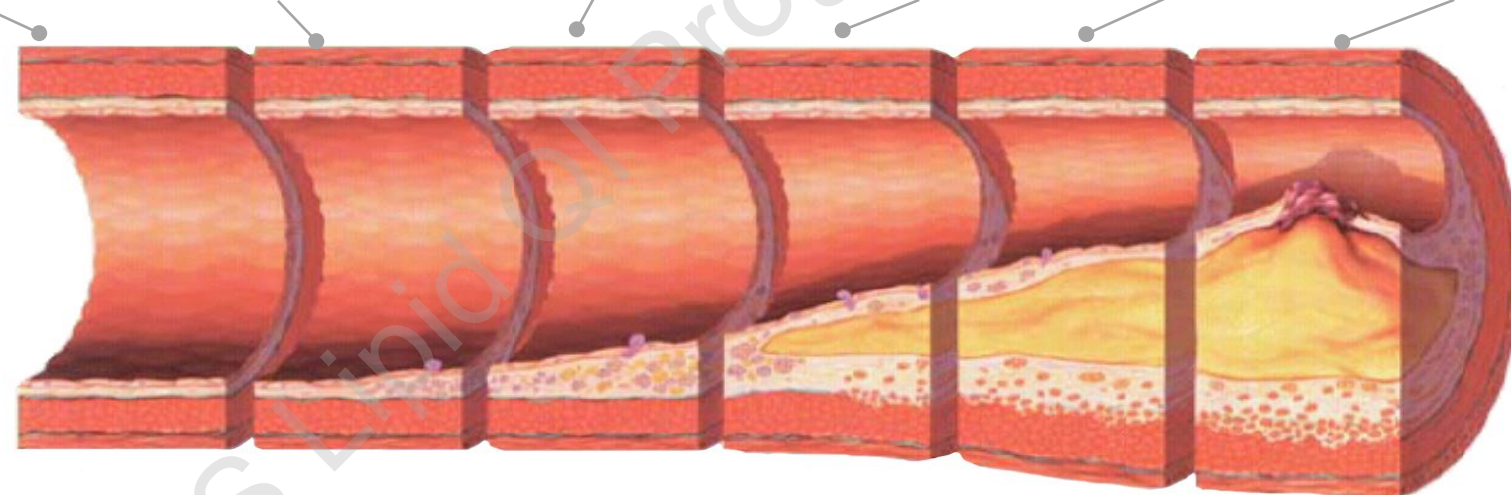


Pathological process¹

NOMENCLATURE AND MAIN HISTOLOGY



SEQUENCES IN PROGRESSION OF ATHEROSCLEROSIS



EARLIEST ONSET

From first decade	From third decade	From fourth decade	
Growth mainly by lipid addition		Increased smooth muscle and collagen increase	Thrombosis and/or haematoma
Clinically silent		Clinically silent or event	

MAIN GROWTH MECHANISM

CLINICAL CORRELATION

Adapted from: 1. Visentin S, et al. Infants Born with Intrauterine Growth Restriction: Renal and Cardiovascular Follow-Up, Contemporary Pediatrics. IntechOpen, March 2012. Available at: www.intechopen.com/books/contemporary-pediatrics/cardiovascular-changes-in-fetuses-and-infants-with-intrauterine-growth-restriction. Accessed February 2021.

Cholesterol circulates in the blood by forming lipoproteins¹

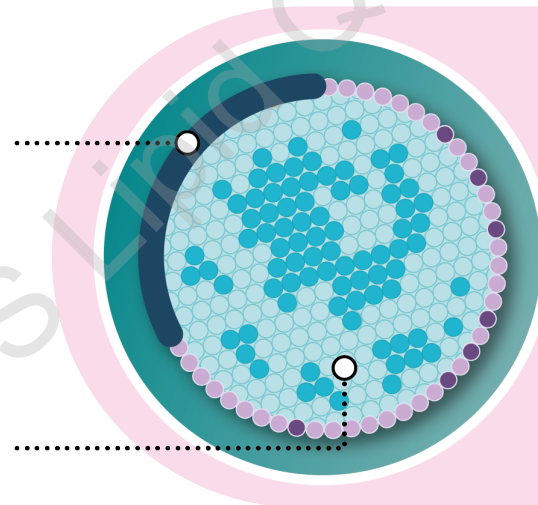


- Cholesterol is essential for life and can be absorbed via digestion, or synthesised within the body²
- Cholesterol plays a critical role in the structure and function of membrane bilayers²

As cholesterol is insoluble in water, it circulates in the blood by forming complexes known as lipoproteins which contain:¹

An outer layer of phospholipids, free cholesterol and proteins known as apolipoproteins, which are key regulators of lipid transport

An inner core of triglycerides and cholesterol



LIPOPROTEINS CONTAIN:

- Triglycerides
- Phospholipid
- Cholesteryl ester
- Free cholesterol
- Apolipoprotein

There are four main types of lipoprotein, defined by their density^{1,2}

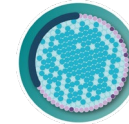
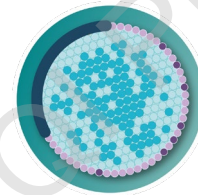
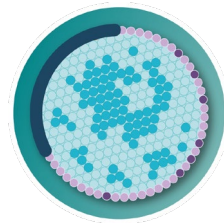
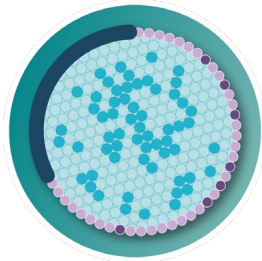


Very-low-density lipoprotein (VLDL)

Intermediate-density lipoprotein (IDL)

Low-density lipoprotein (LDL)

High-density lipoprotein (HDL)



Atherogenic lipoprotein^{1,2}

- Can be taken up and retained by arterial cell walls
- Associated with the development of atherosclerosis

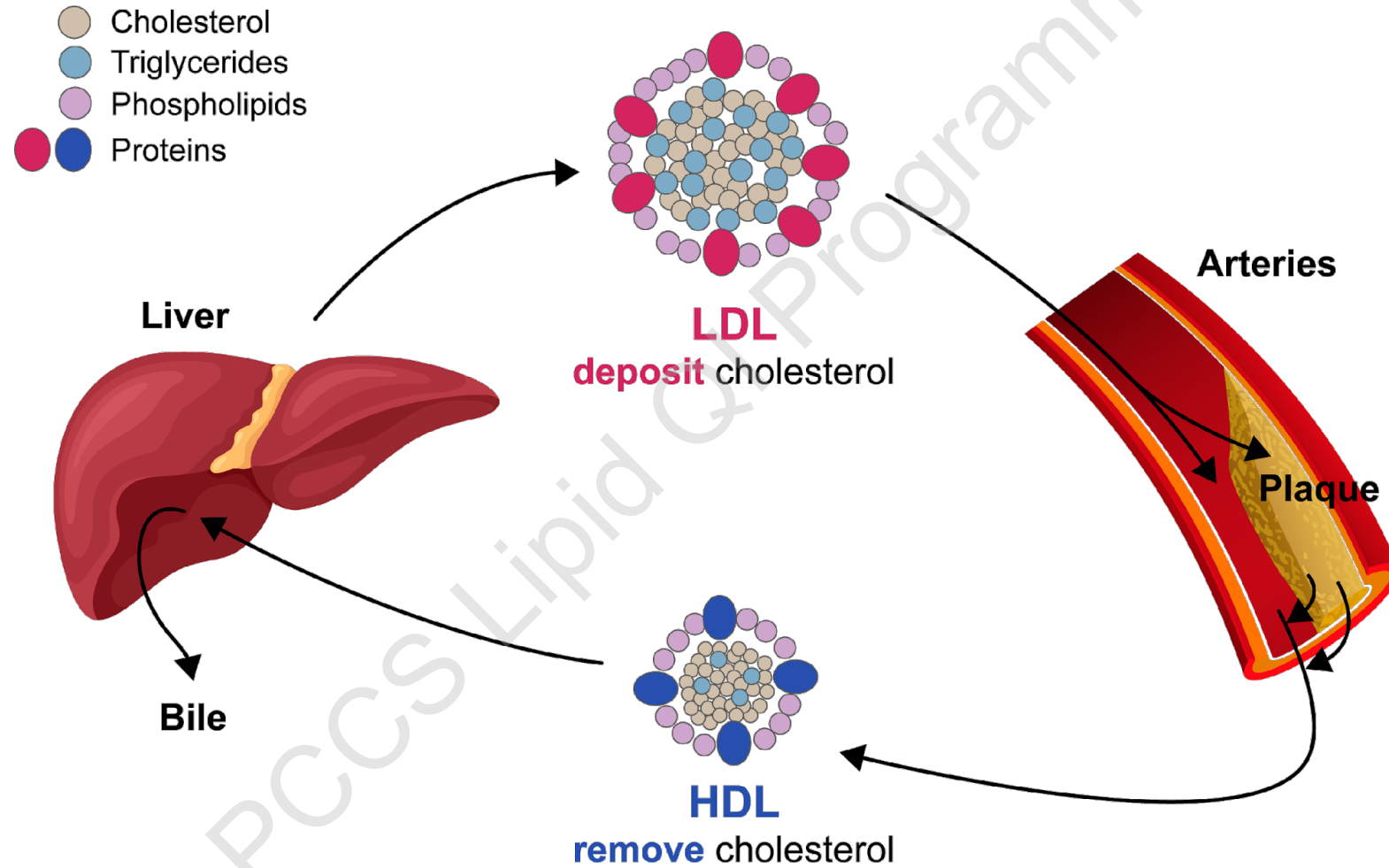
Anti-atherogenic lipoprotein²

- Plays an important role in reversing cholesterol transport

A high concentration of lipoproteins, in particular LDL-C, is implicated in the aetiology of atherosclerosis and increased incidence of CV events³



HDL vs LDL¹



PCCS Lipid Programme

HDL, high-density lipoprotein; LDL, low-density lipoprotein.

Adapted from 1. healthline. Why Is Cholesterol Needed by the Body? Available at: <https://www.healthline.com/health/high-cholesterol/why-is-cholesterol-needed>. Accessed May 2023.

CVD is responsible for 25% of all deaths in the UK¹



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CVD costs the UK economy*
an estimated

£19 BILLION

every year

*including premature death, disability
and informal costs



460 PEOPLE DIE

every day from CVD



7.6 MILLION

people are living with CVD
in the UK



CVD kills one person

EVERY 3 MINS

in the UK

CVD, cardiovascular disease; UK, United Kingdom.

1. British Heart Foundation. UK Factsheet April 2023. Available at: <https://www.bhf.org.uk/-/media/files/for-professionals/research/heart-statistics/bhf-cvd-statistics-uk-factsheet.pdf?rev=e771367bf0654a4dae85cbc9dbefae17&hash=76C0182379BB6EE118EC6F76FA35A158>. Accessed April 2023.



CVD and lipids¹⁻²

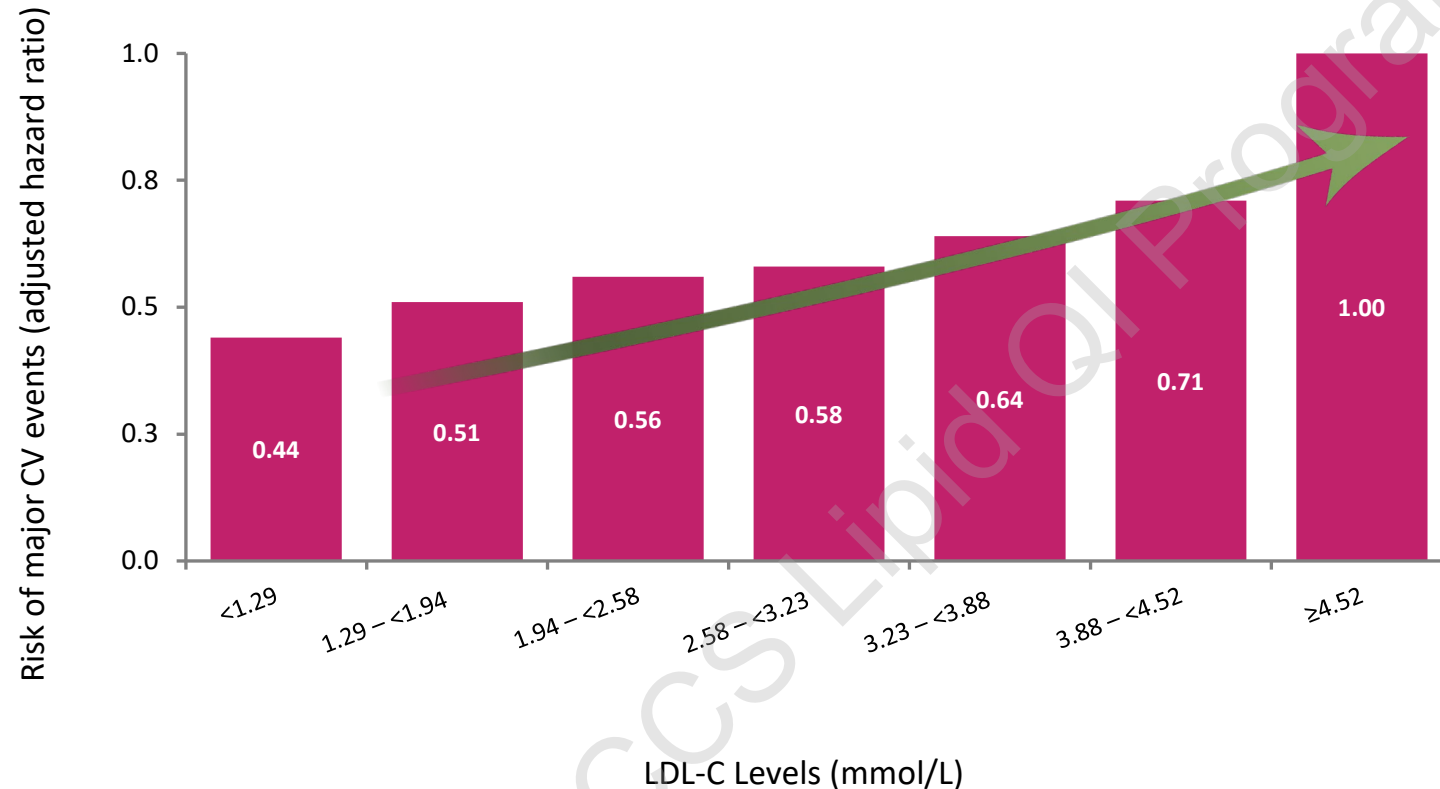
- CVD risk can be reduced by modifying the blood lipid profile
 - TC is an important predictor of CVD events
 - LDL-C is a powerful risk factor
 - Non-HDL-C constitutes atherogenic lipoprotein particles (LDL, VLDL, IDL and TG [20%])
 - Raised TG level is a risk factor for CVD and is independent of TC

CV, cardiovascular; CVD, cardiovascular disease; HDL-C, high-density lipoprotein cholesterol; IDL, intermediate-density lipoprotein; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglycerides; VLDL, very-low-density lipoprotein.

1. NICE CKS. Lipid modification – CVD prevention. Available at: <https://cks.nice.org.uk/topics/lipid-modification-cvd-prevention/>. Accessed June 2023; 2. Bhatt DL. What is non-HDL cholesterol? Available at: <https://www.health.harvard.edu/heart-health/what-is-non-hdl-cholesterol#:~:text=A%20non%2DHDL%20cholesterol%20value,are%20eventually%20transformed%20into%20LDL..> Accessed June 2023.



Increased LDL-C levels are a proven, direct cause of ASCVD and CV events¹⁻⁴



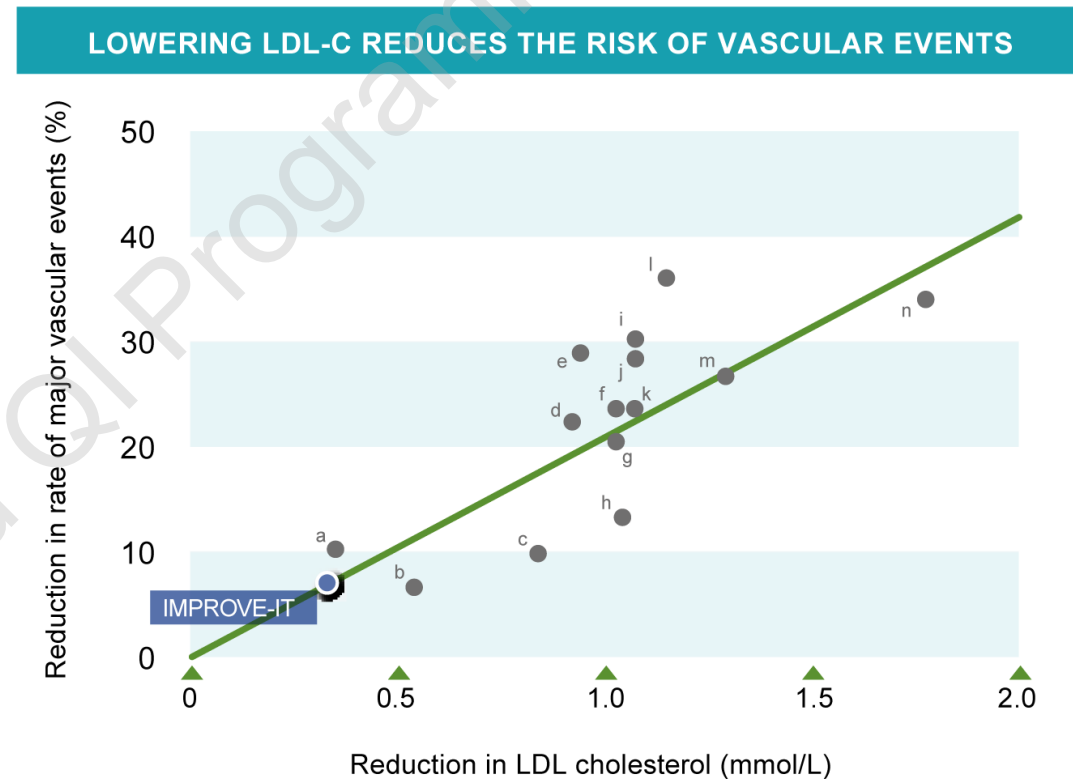
- The cumulative arterial burden of LDL-C drives the development and progression of ASCVD²
- Patients who achieve very low LDL-C levels have a lower risk of major CV events than those who achieve moderately low levels⁴

Figure adapted from Boekholdt M, et al. JACC 2014.



Reducing LDL-C can have a clinically relevant treatment effect¹

- The IMPROVE-IT study provides strong evidence that lowering LDL-C through the reduction of cholesterol absorption from the digestive tract results in an expected reduction in the risk of major vascular events
- There is a linear relationship between the magnitude of LDL-C reduction and the risk of major cardiovascular events



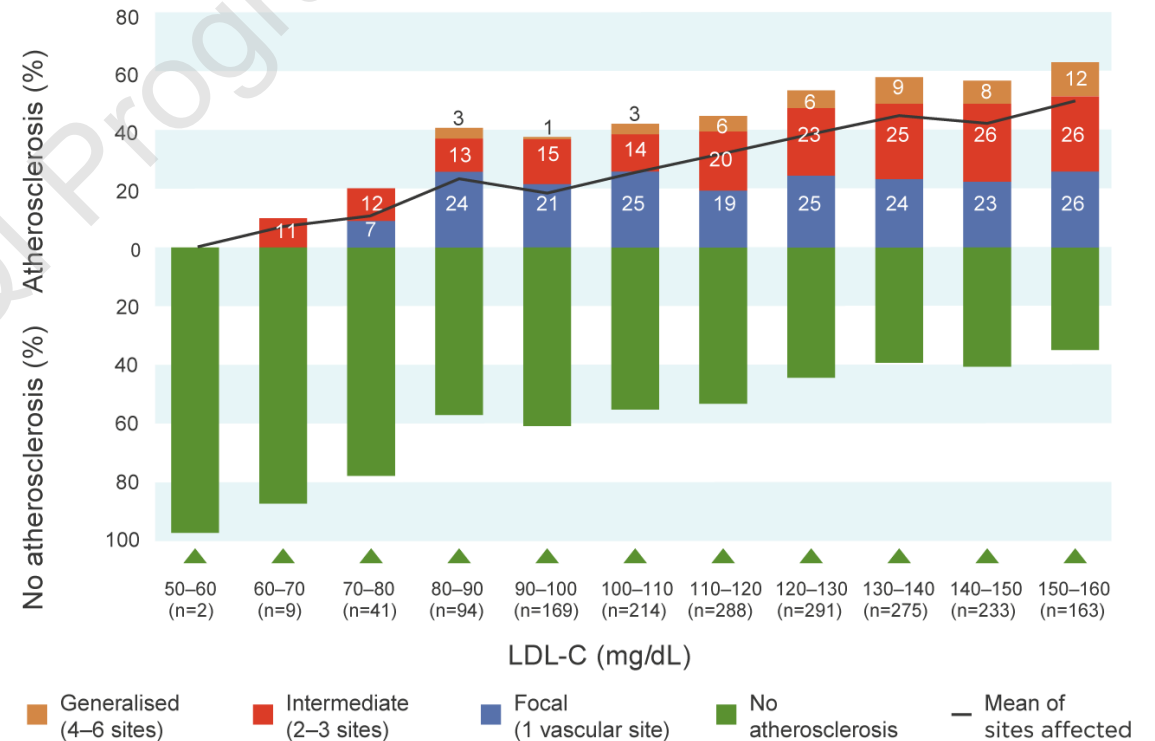
a: Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico (GISSI Prevenzione); b: Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial-Lipid Lowering Trial (ALLHAT-LLT); c: Assessment of Lescol in Renal Transplantation (ALERT); d: Lescol Intervention Prevention Study (LIPS); e: Air Force/Texas Coronary Atherosclerosis Prevention Study (AFCAPS/TexCAPS); f: Cholesterol and Recurrent Events (CARE); g: Long-term Intervention with Pravastatin in Ischaemic Disease (LIPID); h: Prospective Study of Pravastatin in the Elderly at Risk (PROSPER); i: Anglo-Scandinavian Cardiac Outcomes Trial-Lipid Lowering Arm (ASCOT-LLA); j: West of Scotland Coronary Prevention Study (WOSCOPS); k: Post-Coronary Artery Bypass Graft (Post CABG); l: Collaborative Atorvastatin Diabetes Study (CARDS); m: Heart Protection Study (HPS); n: Scandinavian Simvastatin Survival Study (4S). Adapted from Cannon et al. 2015.



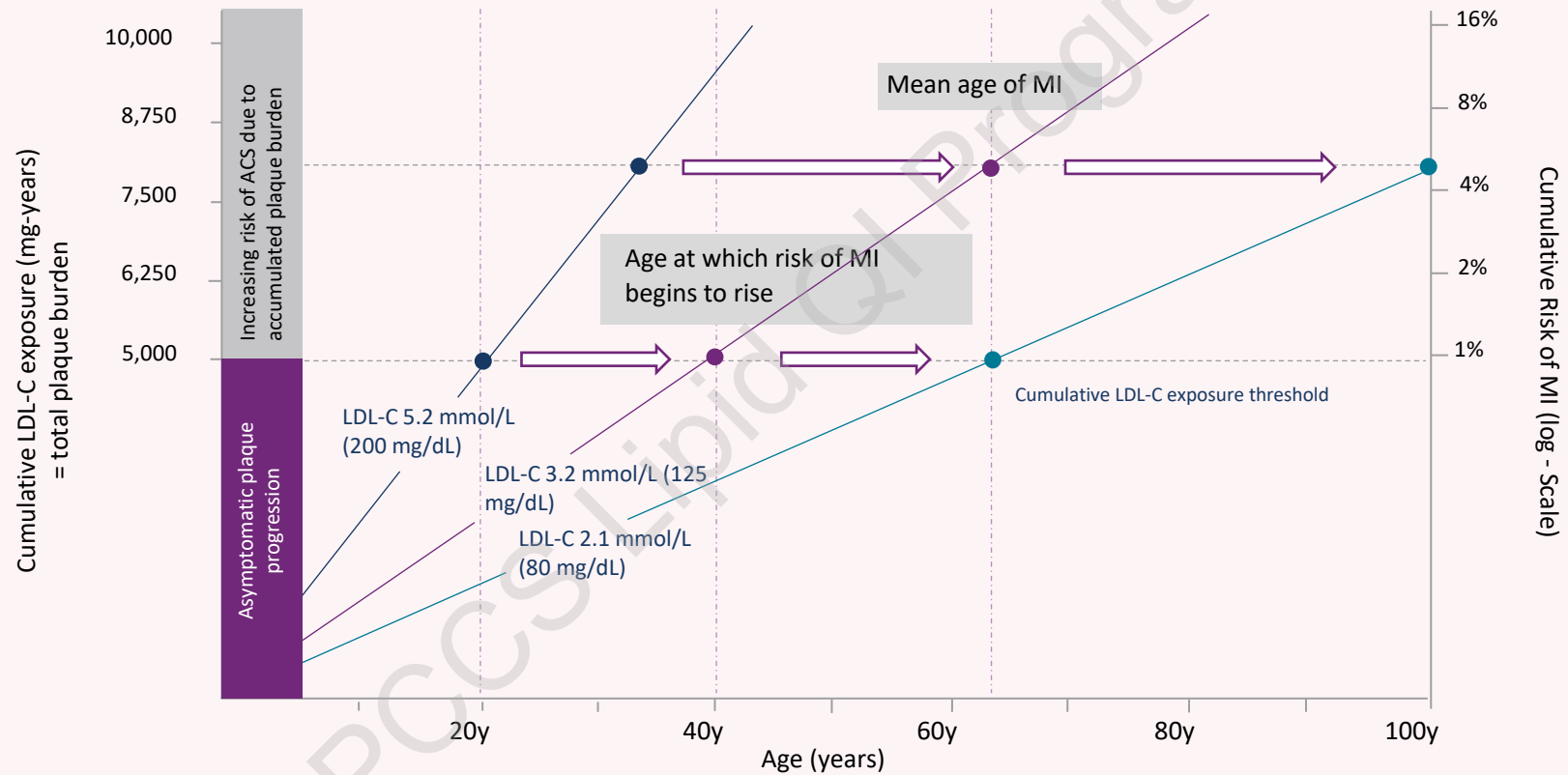
LDL cholesterol: the earlier, the better; the lower, the better¹

- Plaque or coronary artery calcification was present in 49.7% of people without CVD risk factors
- As blood LDL-C levels rise, there is a linear and significant increase in the prevalence of atherosclerosis, ranging from
 - 11% in the 60–70 mg/dL subgroup to
 - 64% in the 150–160 mg/dL subgroup (P<0.001)
- **Many middle-aged individuals with an LDL-C concentration of greater than 50–60 mg/dL (1.3–1.6 mmol/L) are likely to have clinically manifested atherosclerosis**

RELATIONSHIP BETWEEN LDL-C LEVELS AND ATHEROSCLEROSIS



Magnitude and duration of LDL-C exposure impact ASCVD risk¹



ASCVD, atherosclerotic cardiovascular disease; LDL-C, low-density lipoprotein cholesterol; MI, myocardial infarction.
1. Ference BA et al. J Am Coll Cardiol 2018;72(10):1141-1156.

Adapted from Ference BA et al. J Am Coll Cardiol 2018.¹



Lipid profiles... the BIGGER picture

Patient A

- Total cholesterol 5.5
- HDL-C: 2.4
- LDL-C: 2.4
- Non-HDL-C: 3.1
- TG: 1.9
- TC/HDL-C: 2.3

Patient B

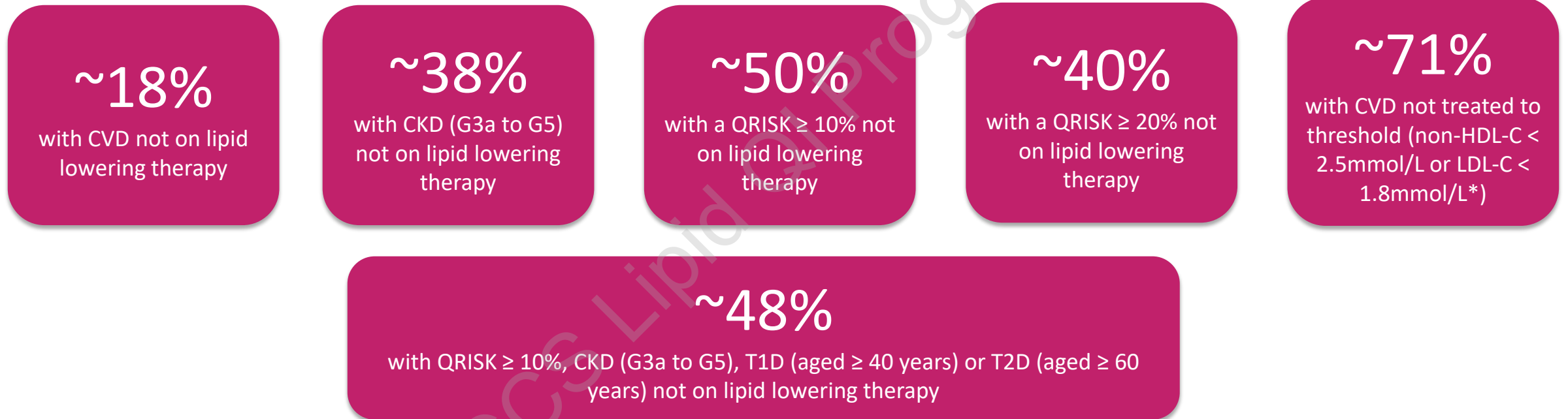
- Total cholesterol 5.5
- HDL-C: 0.7
- LDL-C: 4.1
- Non-HDL-C: 4.8
- TG: 4.9
- TC/HDL-C: 7.8

95% confidence limits on a single cholesterol measurement are around $\pm 14\%$ of the true value¹



Detection and management

In England, in patients ≥ 18 years:



To June 2023

*most recent blood cholesterol level, measured in the preceding 12 months.

CKD, chronic kidney disease; CVD, cardiovascular disease; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; T1D, type 1 diabetes; T2D, type 2 diabetes. CVDPREVENT. Data & Improvement Tool. Available at: <https://www.cvdprevent.nhs.uk/home>. Accessed November 2023.



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NICE National Institute for Health and Care Excellence

**Cardiovascular disease: risk assessment and reduction, including lipid modification (CG181)
July 2014 (updated May 2023)**

*NICE guidance in development: Cardiovascular disease: risk assessment and
reduction, including lipid modification - Escalation of Therapy.
(expected publication date: September 2023)*



Primary prevention – risk assessment

- NICE CG181 provides guidance for risk assessment and reduction (including lipid modification) in cardiovascular disease¹
- Use a systematic strategy to identify those likely to be at high risk of CVD:¹
 - Estimate CVD risk and prioritise those with a 10-year CVD risk of 10% or more for a full formal risk assessment
 - Review risk in over 40s on an ongoing basis

Opportunistic assessment should not be used as the main strategy to identify CVD in unselected people.¹



Primary prevention – formal risk assessment

- Use QRISK3 risk calculator:¹
 - Up to 84 years old
 - Type 2 diabetes
 - Consider other factors not included in formal risk score
- Do not risk assess:¹
 - Existing CVD or familial lipid disorder
 - Type 1 diabetes
 - CKD (eGFR less than 60 and/or albuminuria)
 - 85 years or older (assume they are at increased risk of CVD)

NICE (CG181)

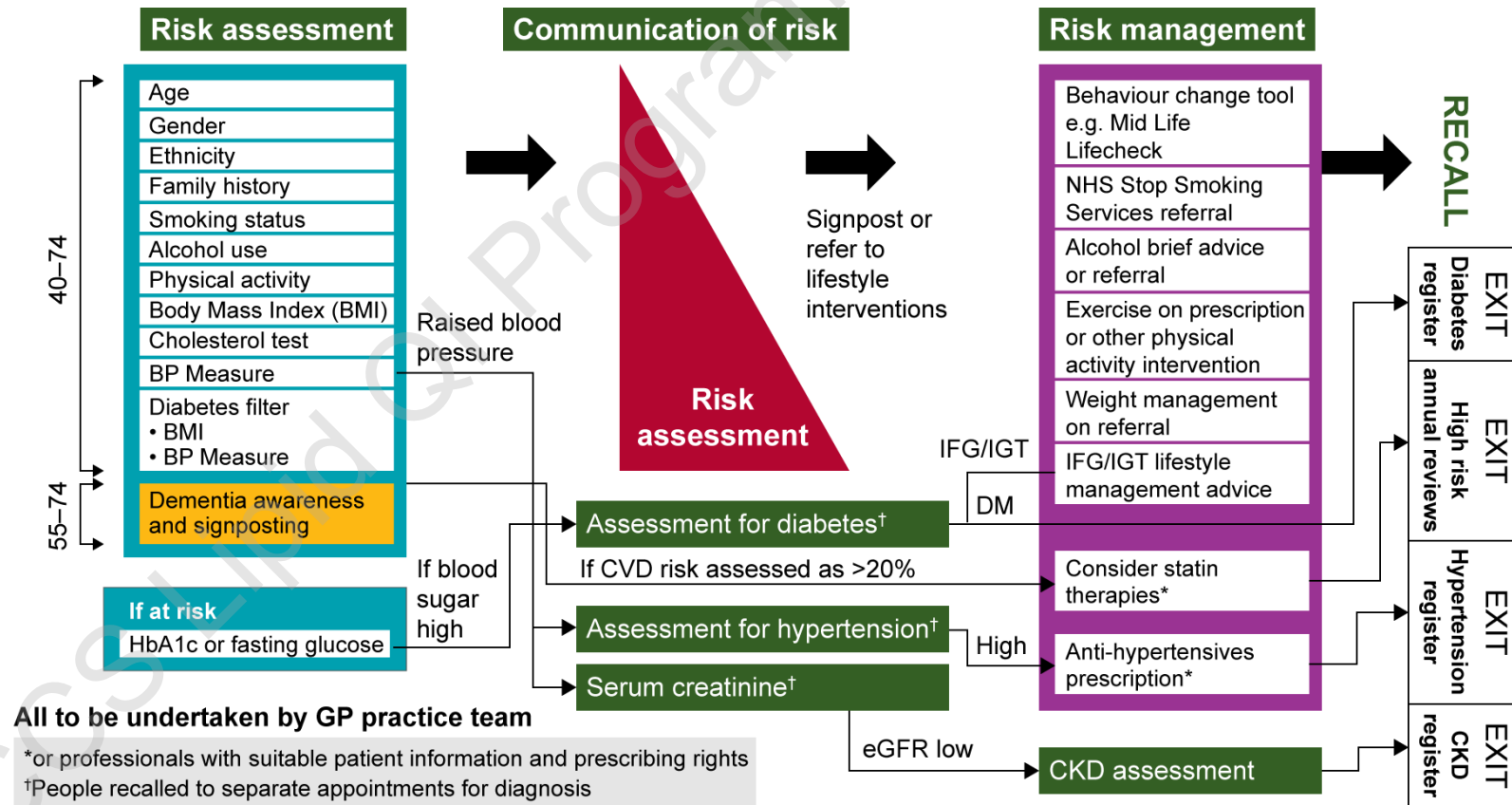
Do not rule out treatment with a statin for primary prevention of CVD just because a person's QRISK3 score is < 10% if the person has an informed preference for taking a statin or there is concern that risk may be underestimated.

Discuss absolute risk of CVD including benefits and harms of treatment over a 10-year period.¹



NHS Health Check programme¹

- Over half of all adults in the UK have raised cholesterol (>5mmol/L)²
- One in every 250-500 people in the UK and Ireland may have FH, but less than 10% of these people have been diagnosed^{2,3}
- It is estimated that 59,000 children in the UK have FH; fewer than 600 of these are known²



BP, blood pressure; CKD, chronic kidney disease; CVD, cardiovascular disease; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; FH, familial hypercholesterolaemia; GP, general practice; HbA1c, haemoglobin A1c; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; NHS, National Health Service; UK, United Kingdom. 1. GOV.UK. Guidance: NHS Health Check implementation review and action plan. Available at: <https://www.gov.uk/government/publications/nhs-health-check-implementation-review-and-action-plan>. Accessed April 2023; 2. Heart UK. Facts and figures. Available at: <https://www.heartuk.org.uk/>. Accessed April 2023; 3. Irish Heart Foundation. Heart & Stroke Conditions Explained: Familial Hypercholesterolemia (FH). Available at: <https://irishheart.ie/heart-and-stroke-conditions-a-z/familial-hypercholesterolaemia-fh/>. Accessed April 2023.



Targeting young adults for early intervention in lowering high cholesterol levels

- NHS Health Checks¹ (offered to adults aged 40–74 in England) include finger-prick test for checking cholesterol
- *Should adults in their 20s and 30s have cholesterol levels checked, so they can take steps to manage high cholesterol levels?*
- Family history of early onset ASCVD could help identify some young adults at elevated risk²
- Important to raise awareness of the risks of high cholesterol and CVD risk in young people as they have more time to develop CVD compared with older people
- Younger patients may have a low 10-year CVD risk, but which is still higher than others of their age. Calculating lifetime risk in this cohort of patients can help to identify these high-risk younger patients, to allow early intervention and modification of risk factors³
- LDL-C lowering beginning earlier in life is associated with a greater CHD risk reduction than lowering only later in life⁴

ASCVD, atherosclerotic cardiovascular disease; CHD, coronary heart disease; CVD, cardiovascular disease; LDL-C, low-density lipoprotein cholesterol; NHS, National Health Service.

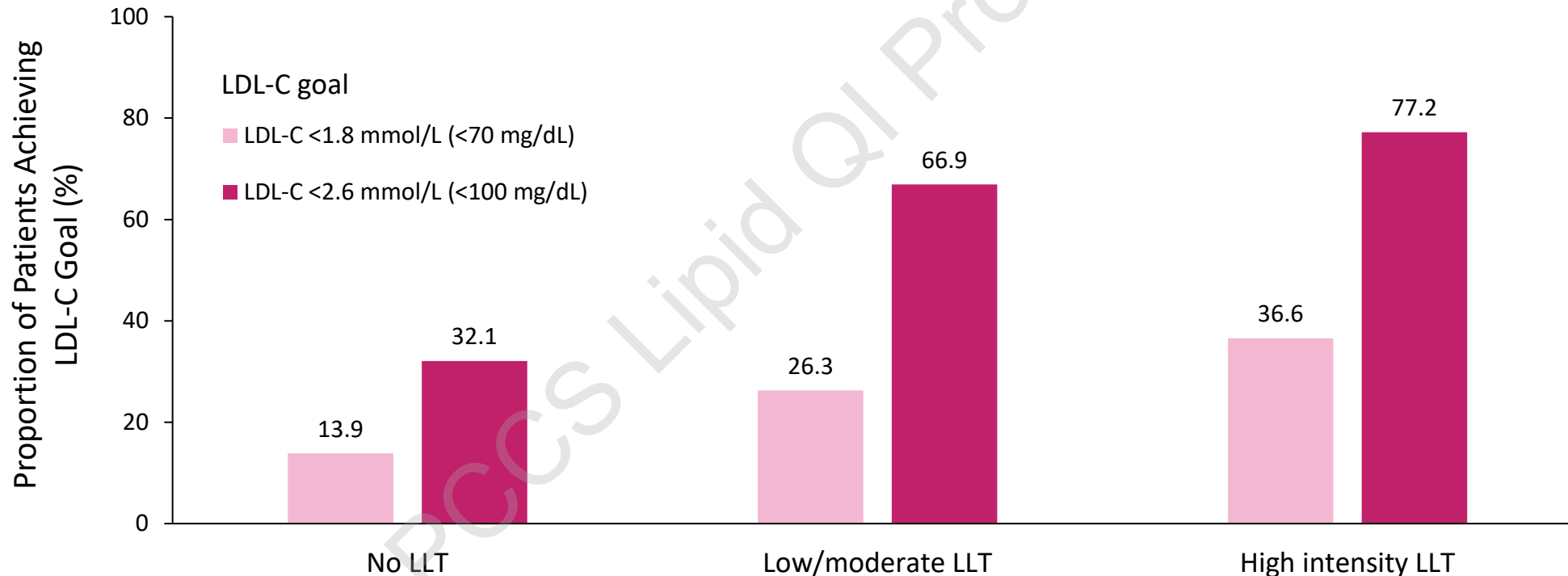
1. NHS. NHS Health Check. Available at: <https://www.nhs.uk/conditions/nhs-health-check/>. Accessed April 2023; 2. Moonesinghe R, et al. J Am Heart Assoc 2019;8(14):e012364; 3. Keele University: Centre for Medicines Optimisation. NPC Archive Item: Estimating lifetime cardiovascular risk – we can, but should we? Available at: <https://www.centreformedicinesoptimisation.co.uk/estimating-lifetime-cardiovascular-risk-we-can-but-should-we/>. Accessed June 2023; 4. Ference BA, et al. Eur Heart J 2017;38(32):2459–2472.

Many very high-risk patients on low/moderate- or high-intensity statin therapy do not achieve their treatment goal



EUROASPIRE V: a survey of secondary prevention patients from 27 European countries (n=7,632)

- 34.1% (2603) of patients on low/moderate lipid-lowering therapy (LLT)
- 49.9% (3811) of patients on high intensity LLT





Effective LDL-C reduction remains a challenge

The situation in England (to June 2023):

Recent national **CVDPREVENT** data showed that

- **Over 71% of patients with CVD have non-HDL-C levels above 2.5 mmol/L or LDL-C above 1.8 mmol/L¹**
- **Over 17% of patients with CVD are not on any lipid-lowering therapy²**



In a **European study** of patients prescribed lipid-lowering therapy for primary or secondary prevention:^{3*}

Just 33% of patients achieved
2019 ESC/EAS LDL-C goals
(95% CI: 32–35)

The likelihood of goal attainment
fell with increasing risk (i.e., a lower
LDL-C goal)

OVER 80% of very high-risk patients
were **UNABLE TO REACH 2019
ESC/EAS LDL-C GOALS** on statins
alone[†]

Greater utilisation of adjunctive therapies is needed to help patients at highest risk reach guideline-recommended LDL-C goals

*Data from an 18-country, European-wide, cross-sectional, observational study of patients prescribed lipid-lowering therapy for primary or secondary prevention in primary or secondary care across Europe, including the UK (N=5,888).³ †Treatment goals for very high-risk patients: LDL-C <1.4 mmol/L (<55 mg/dL) and ≥50% LDL-C reduction from baseline.⁴ As untreated lipid levels were not available, the authors could not quantify to what extent the ≥50% LDL-C reduction from baseline was achieved.³ All patients with documented ASCVD, either clinical or unequivocal on imaging, are considered very high risk.⁴ ASCVD, atherosclerotic cardiovascular disease; CI, confidence interval; CVD, cardiovascular disease; ESC/EAS, European Society of Cardiology/European Atherosclerosis Society; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol. 1. CVDPREVENT. Data Explorer: Cholesterol: CVD treated to threshold (CVDP007CHOL). Available at: <https://www.cvdprevent.nhs.uk/data-explorer?period=9&area=1&indicator=30>. Accessed October 2023; 2. CVDPREVENT. Data Explorer: Cholesterol: CVD treated with LLT (CVDP009CHOL). Available at: <https://www.cvdprevent.nhs.uk/data-explorer?period=9&area=1&indicator=34>. Accessed October 2023; 3. Ray KK, et al. Eur J Prev Cardiol 2021;28(11):1279-1289; 4. Mach F, et al. Eur Heart J 2020;41(1):111-188.



National priorities

The NHS Long Term Plan:¹

- Outlined aims to prevent up to 150,000 heart attacks, strokes and dementia cases over a ten-year period through
 - Early CVD detection and treatment by tackling high-risk conditions which are often undetected
 - AF, raised BP and cholesterol - ABC
- CVDPREVENT:²
 - National primary care audit for QI across GP practices and PCNs which will provide data to highlight gaps, identify inequalities and opportunities for improvement across CVD. In the longer term this will be updated every quarter
 - Recognises six high-risk conditions which may cause CVD
 - AF, hypertension, high cholesterol, diabetes, non-diabetic hyperglycaemia and CKD



National priorities (cont.)

- Core20PLUS5 (adults):¹
 - NHS England’s approach to reduce health inequalities by identifying five clinical areas requiring accelerated improvement
 - One of the five: hypertension case-finding and optimal management and lipid optimal management
- QOF 2023/24:²
 - Cholesterol Control and Lipid Management

! NICE lipid targets are currently under review and the new recommendations will impact on QOF targets

Indicator	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%

HDL, high-density lipoprotein; LDL, low-density lipoprotein; NHS, National Health Service; QOF, Quality and Outcomes Framework; TIA, transient ischaemic attack.

1. NHS England. Core20PLUS5 (adults) – an approach to reducing healthcare inequalities. Available at: <https://www.england.nhs.uk/about/equality/equality-hub/national-healthcare-inequalities-improvement-programme/core20plus5/>. Accessed June 2023; 2.

NHS England. Quality and Outcomes Framework guidance for 2023/24. Available at: <https://www.england.nhs.uk/wp-content/uploads/2023/03/PRN00289-quality-and-outcomes-framework-guidance-for-2023-24.pdf>. Accessed June 2023.



Summary

- Atherosclerosis is a progressive condition that may result in CVD^{1,2}
- CVD is associated with high morbidity and mortality and can place a huge burden on the health economy³
- CVD risk can be reduced through modification of blood lipids⁴
 - By targeting non-HDL-C
 - Raised LDL-C levels are associated with atherosclerotic CVD⁵⁻⁸
- NICE have guidance on primary and secondary prevention of CVD⁹
- Currently, there are national priorities for CVD and lipid management¹⁰⁻¹³
 - The NHS Long Term Plan, CVDPREVENT, Core20PLUS5 and new QOF cholesterol indicators (2023/24)