## LDL-C, Apo B and sdLDL targets: a guide for cardiologists and their patients

Most cholesterol in the blood travels inside protein-based particles called **lipoproteins**. These include chylomicrons, very low-density lipoproteins (VLDL), intermediate-density lipoproteins (IDL), low-density lipoproteins (LDL), LP(a) and high-density lipoproteins (HDL). All, except HDL, can contribute to atherosclerosis.

Traditional lipid tests measure **cholesterol mass**, but modern assays focus on **particle number and type**, which better reflect cardiovascular risk.

#### The NHS "Non-HDL Cholesterol"

The **non-HDL-cholesterol** value (total cholesterol minus HDL-cholesterol) represents the total amount of cholesterol carried by all potentially atherogenic particles — LDL (including sd-LDL), VLDL, IDL, and lipoprotein(a). It is a simple and practical marker available in every UK lipid profile.

Non-HDL-C correlates with ApoB and atherogenic particle burden but remains a cholesterol-mass estimate, not a particle count.

### **ApoB** — Counting the Particles That Matter

**Apolipoprotein B (ApoB)** is present as one molecule per atherogenic particle — including LDL, VLDL, IDL, and Lp(a). Measuring ApoB provides a **direct count of circulating atherogenic particles**, rather than their cholesterol content.

A high ApoB indicates **too many cholesterol-carrying particles**, even if the LDL-C result appears normal. This is particularly relevant in people with diabetes, insulin resistance, high VAT or metabolic syndrome, where particles tend to be small and cholesterol-depleted.

### Small Dense LDL — the Most Atherogenic Fraction

**Small dense LDL (sdLDL)** particles are smaller, denser, and more easily oxidised. They remain in circulation longer and are more likely to enter the arterial wall. Elevated sdLDL is

common in metabolic syndrome, type 2 diabetes, and high-triglyceride states linked to high VAT.

While sdLDL measurement requires specialised assays, ApoB and the **LDL-C / ApoB ratio** can indirectly estimate particle size predominance:

- Low LDL-C / ApoB ratio  $\rightarrow$  many small, dense LDL particles
- High LDL-C / ApoB ratio  $\rightarrow$  fewer, larger LDL particles

## **Comparing ApoB and sdLDL Measurements**

Feature	ApoB Assay	sdLDL Measurement
What it counts	Total number of atherogenic particles (LDL, sdLDL, VLDL, IDL, Lp(a)).	Cholesterol within only the small, dense LDL particles.
Particle size sensitivity	Not affected by size; gives a particle count.	Focuses on the smallest, densest, most atherogenic LDL.
Clinical value	More accurate predictor of cardiovascular risk than LDL-C alone.	Particularly valuable in metabolic syndrome, diabetes, and high triglycerides.
Testing method	Immunoassay or NMR spectroscopy.	Gel electrophoresis, ultracentrifugation, or automated sdLDL-C assays.
Relationship	High ApoB reflects high particle number, often driven by sdLDL excess.	High sdLDL and high ApoB frequently coexist but are not identical.

**Table 1. UK Reference and Risk Ranges for Lipoprotein Markers (Dual Units)** 

Marker	Units (UK / US)	Healthy / Target Range	Moderate Risk Zone	High / Atherogenic Risk Zone	Clinical Notes / Sources
LDL-cholestero I (LDL-C)	mmol/L ( mg/dL )	< 3.0 (< 116) <sup>1</sup>	3.0–4.0 (116–155)	≥ 4.0 (≥ 155) or > 1.8 (> 70) if established CVD <sup>2 3</sup>	Primary target for lipid lowering. NICE secondary-preventi on goal ≤ 1.8 mmol/L (≤ 70 mg/dL).
Non-HDL-chole sterol (Non-HDL-C)	mmol/L ( mg/dL )	< 4.0 (< 155) <sup>1</sup>	4.0–5.0 (155–193)	> 5.0 (> 193) or > 2.6 (> 100) if CVD <sup>2</sup> <sup>3</sup>	Reflects cholesterol in all atherogenic particles (LDL, VLDL, IDL, Lp(a)). Practical NHS marker.
Apolipoprotein B (ApoB)	g/L ( mg/dL )	≤ 1.00 (≤ 100) <sup>4 6</sup>	0.90–1.10 (90–110)	> 1.10 (> 110) or > 0.80 (> 80) if CVD <sup>4</sup> - <sup>6</sup>	Measures <b>particle number</b> , not cholesterol mass. Superior risk predictor; aim ≤ 0.80 g/L in CVD.
Small Dense LDL-cholestero I (sdLDL-C)	mmol/L ( mg/dL )	< 1.0 (< 38.6) <sup>7</sup>	1.0–1.2 (38–46)	> 1.2 (> 46) or > 0.9 (> 35) if CVD 7 8	Identifies most atherogenic LDL fraction; elevated in metabolic syndrome, diabetes, and obesity.

#### **Interpretation Summary**

- Lower targets correspond to higher cardiovascular protection.
- For patients with known CVD, PAD, or CKD, NICE recommends non-HDL-C ≤ 2.6 mmol/L (≤ 100 mg/dL) and LDL-C ≤ 1.8 mmol/L (≤ 70 mg/dL).
- ApoB ≤ 0.80 g/L (≤ 80 mg/dL) is increasingly recognised as a superior marker of residual atherogenic risk.
- **sdLDL-C** is not yet part of routine NHS testing but may refine risk in patients with normal LDL-C and metabolic features.

#### References

- <sup>1</sup> Heart UK. Understanding your cholesterol test results.
- <sup>2</sup> NICE NG238 (2023). Cardiovascular disease: risk assessment and lipid modification.
- <sup>3</sup> RUH Bath PATH-018 (2023). Assessment and management of lipids in primary care.
- <sup>4</sup> Synnovis Labs (2024). *Apolipoprotein B test information*.
- <sup>5</sup> Medscape (2024). Apolipoprotein B: Overview.
- <sup>6</sup> Sniderman AD et al. Eur Heart J. 2023; 44(21):1930-1944.
- <sup>7</sup> Luo J et al. *Atherosclerosis*. 2024; 387:123-132.
- <sup>8</sup> Musunuru K et al. *J Am Coll Cardiol*. 2019; 73(12):1610-1623.

#### **Practical Summary**

- Non-HDL-C: easy, universally available NHS marker aim < 4 mmol/L; ≤ 2.6 mmol/L if existing CVD.</li>
- **ApoB**: best measure of *particle number*; aim ≤ 0.8 g/L for lower risk.
- **sdLDL-C**: identifies the most atherogenic particles; higher in metabolic or insulin-resistant states.
- Combining ApoB, LDL-C, and non-HDL-C gives a more complete picture of atherogenic burden than any single test.

## Table 2. LDL-C : ApoB Ratio — Surrogate Marker of LDL Particle Size and sdLDL Predominance

LDL-C : ApoB Ratio	Interpretation / Pattern	Typical LDL Particle Type	Clinical Significance	Key References
> 1.3	Favourable (Pattern A)	Large, buoyant LDL particles (cholesterol-rich)	Low sdLDL fraction; insulin-sensitive phenotype	Cromwell 2007 <sup>1</sup> , Musunuru 2019 <sup>4</sup>
1.0 <b>–</b> 1.3	Borderline / Mixed	Mixture of large and small LDL	Intermediate risk; mild insulin resistance or hypertriglyceridaemia	Mora 2009⁵
< 1.0	Unfavourable (Pattern B)	Predominantly small, dense LDL (sdLDL)	High atherogenic particle count and ASCVD risk	Boekholdt 2012², Sniderman 2023³
< 0.8	Severe Pattern B	Marked sdLDL predominance	Strongly associated with metabolic syndrome, diabetes, or residual risk despite normal LDL-C	Otvos 2011 <sup>6</sup>

#### Interpretation

- The LDL-C: ApoB ratio estimates how much cholesterol each LDL particle carries.
  - Higher ratio → larger, cholesterol-rich particles (less atherogenic)
  - Lower ratio → smaller, cholesterol-poor particles (more atherogenic)
- < 1.0 reliably indicates sdLDL predominance and heightened cardiometabolic risk.
- Simple to calculate from standard lipid and ApoB assays when advanced particle testing is unavailable. **NB** both must be in the same units to calculate the ratio.

#### References

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   Available from: https://doi.org/10.1373/clinchem.2006.071068
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## **▲ SCVC Target Table 3 (Dual Units, 2025)**

Risk Category	LDL-C Target	Non-HDL -C Target	ApoB Target	sdLDL-C (if measured)	Clinical Context / Notes
Low / Primary Prevention	< 3.0 mmol/L (< 116 mg/dL) <sup>1</sup>	< 4.0 mmol/L (< 155 mg/dL) <sup>1</sup>	≤ 1.00 g/L (≤ 100 mg/dL) <sup>4 6</sup>	< 1.2 mmol/L (< 46 mg/dL) <sup>7</sup>	Healthy adults without major risk factors; focus on diet and exercise.
Moderate Risk	< 2.6 mmol/L (< 100 mg/dL) <sup>2</sup>	< 3.4 mmol/L (< 130 mg/dL) <sup>2</sup>	≤ 0.90 g/L (≤ 90 mg/dL) <sup>4 6</sup>	< 1.0 mmol/L (< 38 mg/dL) <sup>7</sup>	Diabetes without CVD, subclinical atheroma, or family history of premature CAD.
High / Secondary Prevention	≤ 1.6 mmol/L (≤ 70 mg/dL) <sup>2 3</sup>	≤ 2.6 mmol/L (≤ 100 mg/dL) <sup>2 3</sup>	≤ 0.80 g/L (≤ 80 mg/dL) <sup>4 6</sup>	< 0.9 mmol/L (< 35 mg/dL) <sup>7 8</sup>	Established CVD, PAD, or CKD; aligns with NICE and ESC intensive targets.
Very High / Recurrent Events / Progressive Disease	≤ 1.4 mmol/L (≤ 55 mg/dL) <sup>2</sup>	≤ 2.0 mmol/L (≤ 77 mg/dL) <sup>2</sup>	≤ 0.70 g/L (≤ 70 mg/dL) <sup>4 6</sup>	< 0.8 mmol/L (< 31 mg/dL) <sup>7 8</sup>	Post-ACS, progressive CAD, or multiple recurrent events despite therapy.

### ✓ Clinical Rationale (Simplified)

Marker	What It Reflects	Why Target Falls with Risk
LDL-C	Cholesterol mass in LDL particles	Core measure for statin response and treatment escalation
Non-HDL -C	Total cholesterol in all ApoB-containing particles	Captures remnant cholesterol and Lp(a) contribution
АроВ	Number of atherogenic particles	Lower particle count = fewer opportunities for arterial entry
sdLDL-C	Cholesterol content of the smallest, most atherogenic LDL	Strong link to plaque instability and metabolic risk; should fall with treatment

### Summary of ApoB and sdLDL Targets

Risk Level	ApoB (g/L / mg/dL)	sdLDL-C (mmol/L / mg/dL)
Low / Primary	≤ 1.00 / ≤ 100	< 1.2 / < 46
Moderate	≤ 0.90 / ≤ 90	< 1.0 / < 38
High	≤ 0.80 / ≤ 80	< 0.9 / < 35
Very High	≤ 0.70 / ≤ 70	< 0.8 / < 31

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## How to Represent Variance Across Various International Guidelines

#### 1. ApoB

Different bodies define slightly different thresholds:

- NICE / UK consensus (lab references): desirable < 1.00 g/L; high risk > 1.20 g/L.
- **ESC/EAS 2023**: < 0.80 g/L for high risk; < 0.70 g/L for very high risk.
- Canadian and ACC/AHA: 0.90 g/L (high risk); 0.70 g/L (very high risk).
   → This gives an approximate IQR (inter-guideline range) of ± 0.10–0.15 g/L at each tier.

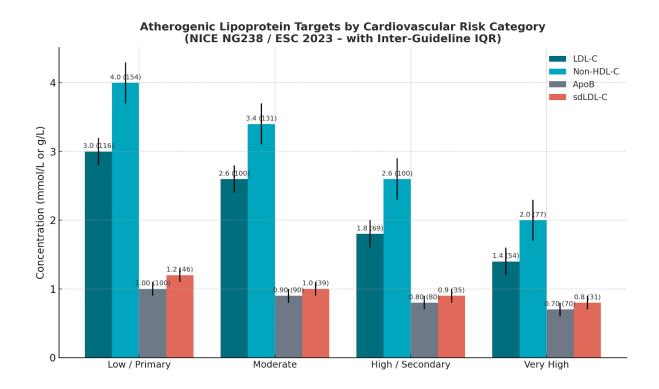
#### 2. sdLDL-C

Not formally standardised, but UK Biobank and US datasets suggest thresholds roughly:

- Low risk: < 1.0–1.2 mmol/L
- High risk: < 0.8–1.0 mmol/L
  - → Reasonable IQR ≈ ± 0.1 mmol/L to capture analytic and definitional variance.

#### 3. LDL-C and Non-HDL-C

NICE and ESC values overlap tightly; differences are usually ± 0.2 mmol/L.



#### Figure Key - Understanding the Lipoprotein Target Chart

#### What the figure shows:

Each group of bars represents the recommended target levels for different blood lipoproteins that carry cholesterol.

As cardiovascular risk increases (from  $Low \rightarrow Very High$ ), the targets for these particles become progressively lower.

Lower values mean fewer cholesterol-carrying particles in the blood and lower risk of artery blockage.

Colour / Label	What It Represents	Why It Matters
LDL-C (Low-Density Lipoprotein Cholesterol)	The amount of cholesterol contained in LDL particles — often called "bad cholesterol".	High levels drive cholesterol into artery walls. Lowering LDL-C remains the main goal of treatment.

	Non-HDL-C
(No	n-High-Density
Lip	oprotein
Ch	olesterol)

Total cholesterol in *all* potentially harmful particles — includes LDL, VLDL, IDL and Lp(a).

A broader marker than LDL-C that captures all atherogenic cholesterol.

ApoB (Apolipoprotein B)

The **number** of cholesterol-carrying particles (each particle has one ApoB).

More particles mean more opportunities for cholesterol to enter artery walls, even when cholesterol levels seem "normal".

sdLDL-C (Small Dense LDL-Cholesterol)

The cholesterol carried in the smallest, densest LDL particles.

These particles are the most dangerous — they linger in blood longer and more easily penetrate artery walls.

#### Error bars (thin lines above bars):

Show the **range of target values** found across major international guidelines (NICE UK 2023, ESC 2023, AHA 2023, and Canadian 2021).

These reflect small variations (the "inter-guideline IQR") rather than measurement uncertainty.

#### Units:

- mmol/L or g/L are the **UK/European** laboratory units.
- mg/dL (shown in brackets) are the **US** equivalents.

#### Take-home message:

- All four markers fall as cardiovascular risk rises.
- ApoB gives the most accurate single measure of harmful particle number.
- sdLDL-C provides extra insight in metabolic or insulin-resistant states.
- For people with heart disease or diabetes, aiming for the lower targets markedly reduces event risk.

## Table 4. LDL-C : ApoB Ratio Targets by Cardiovascular Risk Category

Risk Category	LDL-C : ApoB Ratio (unitless)	Interpret ation / LDL Particle Profile	Associated Phenotype	Clinical Guidance / Implication	Key Referenc es
Low / Primary Prevention	> 1.3	Large, buoyant LDL (Pattern A)	Insulin-sensitive, metabolically healthy	Optimal particle profile; low sdLDL fraction. Lifestyle maintenance recommended.	Cromwell 2007 <sup>1</sup> ; Sniderma n 2023 <sup>3</sup>
Moderate Risk	1.0 – 1.3	Mixed populatio n (Pattern A/B)	Emerging insulin resistance, mild hypertriglyceridaem ia	Intermediate risk; consider intensifying lifestyle and statin therapy if ApoB > 1.0 g/L.	Mora 2009 <sup>5</sup> ; Boekholdt 2012 <sup>2</sup>
High Risk / Secondary Prevention	0.9 – 1.0	Small, dense LDL predomin ance (Pattern B)	Insulin-resistant, metabolic syndrome, or diabetes	High atherogenic risk even when LDL-C appears normal; monitor ApoB and triglycerides.	Musunuru 2019 <sup>4</sup> ; Otvos 2011 <sup>6</sup>
Very High Risk / Recurrent Events	< 0.9	Severe small-den se LDL predomin ance	Marked insulin resistance or type 2 diabetes	Indicates residual sdLDL risk despite low LDL-C; consider combination lipid therapy or GLP-1/PCSK9 use.	Sniderma n 2023³; Otvos 2011 <sup>6</sup>

#### **Interpretation Notes**

- The LDL-C: ApoB ratio estimates the cholesterol load per LDL particle.
  - $\circ \quad \text{High ratio} \rightarrow \text{large cholesterol-rich particles} \rightarrow \text{lower risk}$
  - $\circ \quad \text{Low ratio} \rightarrow \text{small dense cholesterol-poor particles} \rightarrow \text{higher risk}$
- Ratios < 1.0 indicate sdLDL predominance, a powerful independent marker of atherogenic dyslipidaemia.
- The ratio complements **ApoB concentration** (particle count) together they describe **quantity and quality** of LDL particles.
- This measure is especially helpful in **metabolic syndrome**, **raised VAT**, **type 2 diabetes**, **and hypertriglyceridaemia**, where LDL-C alone may underestimate risk.

#### References

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LDL-C : ApoB Ratio — Surrogate for LDL Particle Size and sdLDL Predominance

Large, buoyant LDL Mixed particles Small dense LDL (Pattern A) (Pattern A/B) (Pattern B)
Low risk Moderate risk High risk
LDL-C:ApoB > 1.3 1.0-1.3 < 1.0
Insulin sensitive Insulin resistant

## Quick rule (UK labs)

Use this to compare with published cut-offs:

literature\_ratio = LDL-C (mmol/L) / [ApoB (g/L) × 2.59]

(equivalently, convert LDL-C to mg/dL and ApoB to mg/dL, then divide)

#### **Examples:**

- 3.0 mmol/L  $\div$  (1.0 × 2.59) = **1.16**  $\rightarrow$  mixed/normal
- 5.0 mmol/L ÷ (1.2 × 2.59) = **1.61** → large LDL (Pattern A)

# Table 5. LDL-C : ApoB ratio targets by risk (dimensionless)

(with quick SI "mmol/L ÷ g/L" equivalents so you can read it straight off UK reports)

Risk category	LDL-C:ApoB (dimensionless)	Quick SI band (LDL-C/ApoB using mmol/L ÷ g/L)	Interpretation
Low / Primary prevention	> 1.3	> 3.37	Large, buoyant LDL (Pattern A) – low sdLDL fraction
Moderate risk	1.0 – 1.3	2.59 – 3.37	Mixed particle size (Pattern A/B)
High / Secondary prevention	0.9 – 1.0	2.33 – 2.59	Small, dense LDL predominance (Pattern B)
Very high / Recurrent events	< 0.9	< 2.33	Marked sdLDL predominance