Woodlands Hospital
NHG Health

Hyperlipidemia Management:
What Every GP Needs to Know in 2026

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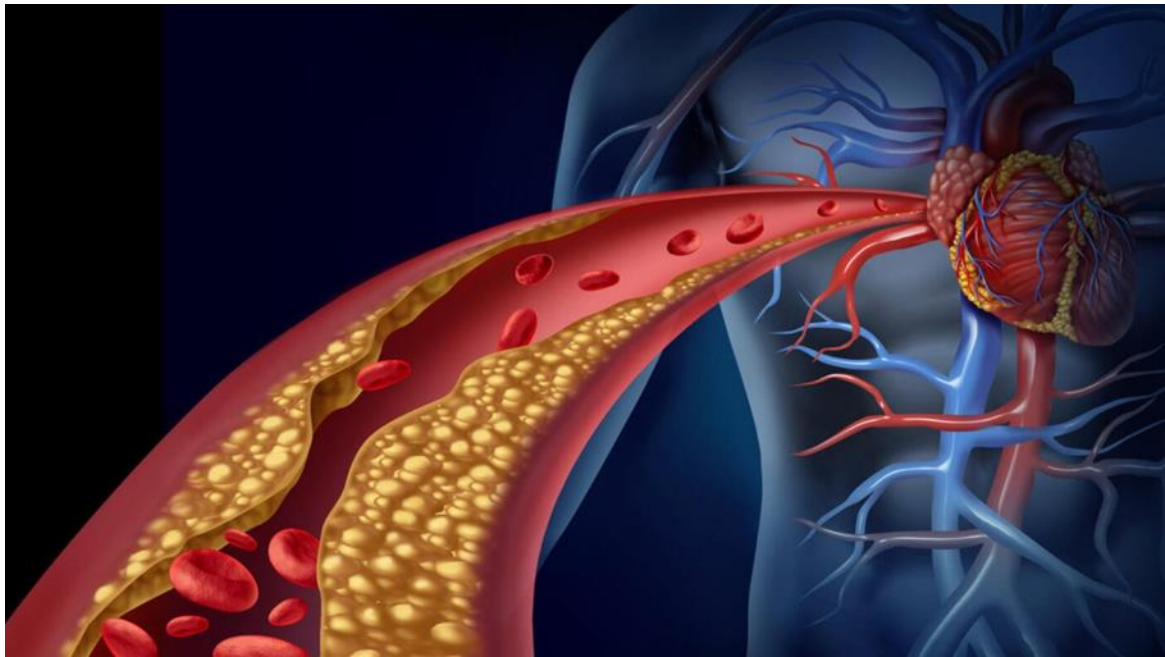
What We Will Cover

1. **Assess risk**
2. **Set the LDL-C goal**
3. **Choose & intensify therapy**
4. **Use ApoB & Lp(a) intelligently**
5. **Know when to refer**



References:

- 2026 ACC/AHA Dyslipidemia Guideline
- ESC/EAS 2025 Focused Update

What Has Changed in 2026?

1. **Lower earlier**
   - Cumulative LDL-C exposure matters
2. **Calculate risk differently**
   - **PREVENT** replaces Pooled Cohort Equations
   - 10- and **30-year risk estimation**
3. **LDL-C targets are back**
   - Treatment to both goal + % reduction
4. **Personalize risk**
   - **Risk enhancers → ApoB / Lp(a)**
   - Selective **CAC**
5. **Early Combination therapy**
   - Don't wait for prolonged statin monotherapy when the LDL-C gap is large

Lower LDL-C Earlier: “Lower for Longer”

Cumulative LDL-C exposure matters

- **Atherosclerosis is a cumulative-exposure disease — not a single LDL-C measurement.**

- Greater cumulative exposure to atherogenic lipoproteins → greater plaque burden
- Earlier and sustained LDL-C lowering may provide greater lifetime benefit than delayed treatment

1) Ference BA, et al. J Am Coll Cardiol. 2018 Sep 4;72(10):1141-1156.
2) Zhang Y, et al. JAMA Cardiol. 2021 Dec 1;6(12):1406-1413.
3) Domanski MJ, et al. J Am Coll Cardiol. 2020 Sep 29;76(13):1507-1516.

Lipid Screening & Monitoring

Who Should Have a Lipid Profile?

Screen

- Adults **≥ 19 years**
- At least every **5 years**
- More frequently with increasing age or additional risk factors
- Earlier if FH / premature ASCVD is suspected

After starting / changing LLT

- Repeat in **4–12 weeks**
- Then **every 6–12 months**
- Annual testing is reasonable once stable

Fasting or Non-Fasting Lipids?

Non-fasting is appropriate for most patients

- Convenient
- Reflects usual physiology
- LDL-C generally changes little after meals
- LDL-C has similar prognostic value to fasting measurements

Consider fasting when:

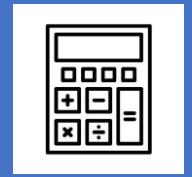
- Significant hypertriglyceridemia
- Assessing residual risk despite LLT
- Suspected genetic dyslipidaemia

Don't delay lipid assessment simply because the patient has not fasted.

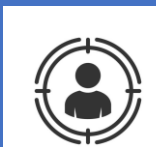
CPR Framework

The 2026 Cardiovascular Risk Assessment Framework

C **CALCULATE** baseline CV risk
- PREVENT-ASCVD
- 10-year + 30-year risk



P **PERSONALIZE**
- Risk enhancers



R **RECLASSIFY** when uncertain
- coronary artery calcium (CAC)

PREVENT-ASCVD: The New Risk Calculator

Replaces Pooled Cohort Equations

- Adults 30–79 years without known ASCVD
- 10-year and **30-year risk estimates**
- Derived from >3 million contemporary US adults
- Incorporates additional variables including HBa1C, UACR and social deprivation index

Risk Categories	10-year ASCVD Risk Estimates
Low	<3%
Borderline	3% to <5%
Intermediate	5% to <10%
High	≥10%

The 2026 ACC/AHA guideline uses PREVENT-ASCVD for primary prevention and emphasizes both 10- and 30-year assessment.

Personalize Risk: Risk Enhancers

When PREVENT Doesn't Tell the Whole Story

Clinical risk enhancers

- Premature ASCVD in first-degree relatives
- Higher risk ancestry (South Asian, Filipino)
- Chronic inflammatory disease (SLE, RA, advanced psoriasis)
- CKM syndrome
- Reproductive risk markers (premature menopause, preeclampsia, gestational diabetes, preterm delivery)

Lipid/biomarkers

- **Lp(a) ≥125 nmol/L (≥50mg/dL)**
- Persistent TG elevation
- LDL-C ≥4.1 mmol/L
- ApoB ≥120 mg/dL
- hsCRP ≥2 mg/L

Risk enhancers are most useful when the treatment decision is uncertain.

CAC: The Risk "Tie-Breaker"

Best supported in:

- **Men ≥40 years**
- **Women ≥45 years**
- Borderline/intermediate risk
- Uncertainty about starting or intensifying LLT

CAC	Practical implication
0	Selected patients may defer statin
1 - 99	LDL-C **<2.6mmol/L (<100 mg/dL)**
100 - 299	LDL-C **<1.8mmol/L (<70 mg/dL)**
300 - 999	LDL-C **<1.8mmol/L (<70 mg/dL)**; consider intensification toward **<1.4mmol/L(<55mg/dL)**
≥1000	LDL-C **<1.4mmol/L (55 mg/dL)**

CAC is not a screening test for everyone — use it when the result will change management.

Evidence-Based LDL-C Targets

- Treat to a goal — and achieve the appropriate percentage reduction

LDL-C Targets Are Back

The higher the ASCVD risk, the lower the LDL-C goal

2026 ACC/AHA: LDL-C Targets

Clinical setting	LDL-C goal
Borderline / Intermediate Risk Primary prevention	<2.6 mmol/L (<100 mg/dL)
High Risk Primary prevention	<1.8 mmol/L (<70 mg/dL)
ASCVD – not very high risk	<1.8 mmol/L (<70 mg/dL)
ASCVD – very high risk	<1.4 mmol/L (<55 mg/dL)

PLUS:

≥30% reduction when indicated

≥50% reduction in high-risk/ASCVD patients

The 2026 ACC/AHA guideline explicitly reinstates LDL-C and non-HDL-C goals.

Primary Prevention: Who Needs Treatment?

Primary Prevention: Turn Risk Into Action

- **Adults 30–79 years without ASCVD**

PREVENT-ASCVD 10-y risk	Approach
<3% Low	Lifestyle
3 – <5% Borderline	Consider LLT + risk enhancers
5 – <10% Intermediate	LLT generally recommended
≥10% High	High intensity statin → LDL-C <1.8 mmol/L (<70 mg/dL)

Borderline/intermediate risk?
Think: 30-year risk → risk enhancers → CAC if uncertain.

Special Populations

Patients Who May Need Treatment Regardless of PREVENT

Diabetes

- Age **40–75:** at least **moderate-intensity statin**
- Higher-risk diabetes → consider **high-intensity statin + lower LDL-C goal<1.8mmol/L**

CKD

- **Age ≥40 + CKD stage ≥3** → LLT recommended

HIV

- **Age ≥40** → LLT recommended

Severe hypercholesterolaemia

- **LDL-C ≥4.9 mmol/L** (≥190 mg/dL)
- Exclude secondary causes
- Assess for FH
- Treat aggressively

Young adults

- Consider earlier pharmacotherapy
  - LDL-C ≥4.1 mmol/L (≥160 mg/dL)
  - Strong family history of premature ASCVD
  - Other major risk enhancers

Secondary Prevention: How Low Should We Go?

Established ASCVD: Lower LDL-C, Lower Risk

Clinical ASCVD	LDL-C goal
ASCVD - Not very high risk	**<1.8 mmol/L (<70 mg/dL)**
ASCVD - very high risk	**<1.4 mmol/L (<55 mg/dL)**

Who is "Very High Risk"?

- ≥2 major ASCVD events

OR

- 1 major ASCVD event + ≥2 high-risk conditions

Major ASCVD Events:

- ACS within past 12 months
- MI
- Ischemic stroke
- Symptomatic PAD

- Age ≥ 65y
- Current smoker
- DM / HTN / CCF
- CABG / PCI

Treatment principle

- **High-intensity statin** → **add non-statin therapy early** when needed
- Do not wait for months of statin monotherapy if the required LDL-C reduction is unlikely to achieve goal.

Optimising Lipid-Lowering Therapy

- Selecting appropriate pharmacotherapy based on individual patient risk
- Practical approaches to treatment intensification and combination therapy

From LDL-C Goal to Treatment

Choose Treatment Based on the LDL-C Gap

Step 1 — Define the LDL-C goal

↓

Step 2 — Estimate the required % LDL-C reduction

↓

Step 3 — Choose therapy likely to achieve the goal

Expected LDL-C lowering

Treatment	Average LDL-C reduction
Moderate intensity statin	≈ 30-49%
High intensity statin	≈50%
High intensity statin + Ezetimibe	≈65%
High intensity statin + PCSK9 inhibitor	≈75%
High intensity statin + Ezetimibe + PCSK9 inhibitor	≈85%

The larger the LDL-C gap, the earlier combination therapy should be considered.

Statins: Still the Foundation

Statins: First-Line Therapy for Most Patients

High intensity	Moderate intensity
Atorvastatin 40-80mg Rosuvastatin 20-40mg	Atorvastatin 10-20mg Rosuvastatin 5-10mg Simvastatin 20-40mg
≥ 50% LDL-C reduction	**30-49% LDL-C reduction**

- Use the **maximally tolerated dose**
- Atorvastatin / rosuvastatin can be taken at any time of day
- Recheck LDL-C in 4–12 weeks
- Address adherence before assuming treatment failure

When Statin Alone Is Not Enough

Don't Just Increase the Statin—Close the LDL-C Gap

Maximally tolerated statin

↓

Is LDL-C still above goal?

↓

Add non-statin therapy

- Ezetimibe
- Bempedoic acid
- PCSK9 inhibitor

Consider combination therapy early when:

- Large LDL-C gap
- Very high-risk ASCVD
- Recent ACS
- Statin alone unlikely to reach target

The 2026 guideline specifically supports adding ezetimibe and/or bempedoic acid or a PCSK9 monoclonal antibody when LDL-C is not adequately controlled with lifestyle and statin therapy.

Non-Statin Therapies: What Can I Expect?

Therapy	Approximate LDL-C reduction	Practical point
Ezetimibe	15–25%	Oral, simple first add-on
Bempedoic acid	15–25%	Oral, useful in statin intolerance / additional lowering
PCSK9 mAb	50–60%	Potent + proven CV outcome benefit
Inclisiran	45–55%	Twice yearly maintenance dosing

Choose the drug based on the LDL-C gap, ASCVD risk, tolerability, cost/access and patient preference.

PCSK9 Inhibitors

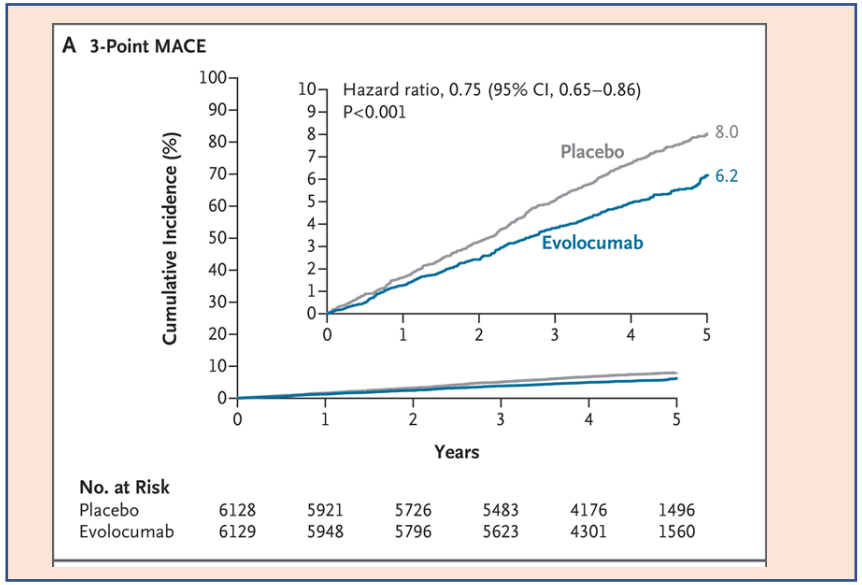
	PCSK9 monoclonal antibodies	Small interfering RNA (siRNA)
Examples	Evolocumab / Alirocumab	Inclisiran
Mechanism	Neutralise circulating PCSK9	siRNA suppresses hepatic PCSK9 production
LDL-C reduction	~50–60%	~50%
Dosing	SC every 2-4 weeks	SC Day 1 →3 months →**every 6 months**
CV outcomes	Proven	CVOT ongoing*
Best suited for	Patients needing large LDL-C reduction	Adherence/convenience considerations

**Inclisiran's LDL-lowering efficacy is established, but CV outcomes remain pending.*

Consider PCSK9-targeted therapy when LDL-C remains above goal despite maximally tolerated therapy, particularly in very-high-risk patients.

VESALIUS-CV

Evolocumab in high risk patients without previous MI or stroke



- 12,257 high risk patients
- **Atherosclerosis or diabetes**
- **No previous MI or stroke**
- Evolocumab vs placebo

3-Point MACE → 25% lower risk

- Evolocumab led to a **25% lower risk of first CV events** than placebo among patients without a previous MI or stroke.
- No evidence of a between-group difference was seen in the incidence of safety events

Bohula EA, et al. N Engl J Med 2026;394:117-127

Bempedoic Acid

An Oral Option When Statins Are Not Enough or Not Tolerated

Mechanism
- ATP-citrate lyase inhibitor
- Acts upstream of HMG-CoA reductase

LDL-C reduction

≈ 20–25%

Useful for
- Statin intolerance
- Additional LDL-C lowering
- Combination therapy

Watch for
- Hyperuricemia / gout
- Tendon problems
- Cholelithiasis

CLEAR Outcomes Trial
- Statin-intolerant/high-risk patients
- **13% reduction in 4-point MACE**
- Benefit demonstrated in both primary- and secondary-prevention populations

Hypertriglyceridaemia: A Practical Approach

TG ≥1.7 mmol/L (150 mg/dL)

1. **Look for secondary causes**
   - Diabetes / poor glycaemic control
   - Obesity
   - CKD / Nephrotic syndrome
   - Liver disease
   - Hypothyroidism
   - Alcohol
   - Medications
2. **Lifestyle first**
   - Weight reduction
   - Reduce refined carbohydrate / added sugar
   - Reduce saturated fat
   - Limit alcohol
   - Regular exercise
3. **Assess ASCVD risk**
   - Optimize LDL-C-lowering therapy
   - **Statin** remains **first-line pharmacotherapy**
4. **If persistent TG elevation**
   - Consider risk-based TG-lowering therapy

Icosapent ethyl

- **Consider in selected high-risk statin-treated patients with persistent TG elevation**
- **REDUCE-IT demonstrated CV event reduction**

Treat the patient's overall atherogenic risk—not the TG number alone.

Severe Hypertriglyceridaemia: Prevent Pancreatitis

TG ≥5.6 mmol/L (500 mg/dL)
Especially ≥11.3 mmol/L (1000 mg/dL)

1. Identify and treat secondary causes

2. Intensive lifestyle intervention

- Very low-fat diet
- Glycaemic control
- Weight loss
- No alcohol when TG is markedly elevated

3. Pharmacotherapy

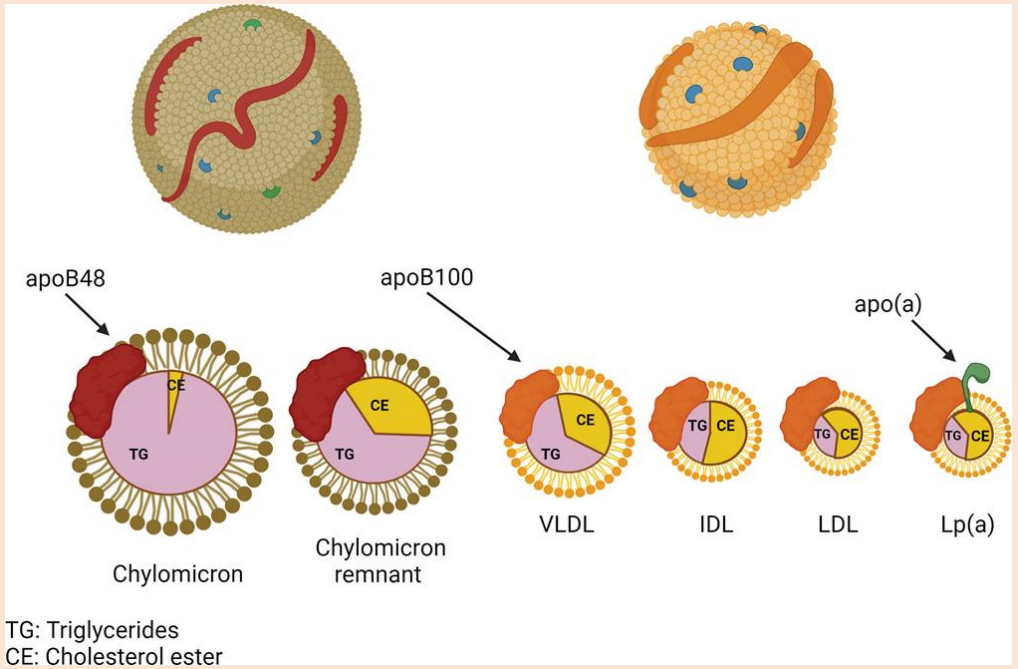
- **Fenofibrate**
- Prescription omega-3 fatty acids
- Olezarsen for familial chylomicronaemia syndrome

At very high TG levels, the immediate priority shifts from ASCVD prevention to prevention of acute pancreatitis.

Emerging Lipid Biomarkers: ApoB & Lipoprotein(a)

- Reclassify risk.
- Personalize treatment.

ApoB: Counting Atherogenic Particles



LDL-C tells us:

- **"How much cholesterolmass inside LDL particles?"**

ApoB tells us:

- **"How many atherogenic particles are circulating?"**

Why this matters ?

1 ApoB molecule ≈ 1 atherogenic particle

- Includes: LDL / IDL / VLDL / Lp(a)
- ApoB significantly associated with CV events, independent of LDL-C.
- More accurate risk prediction
- Detect residual CVD risk in statin-treated populations
  - Discordant: Normal/Low LDL-C + High ApoB

ApoB can reveal residual atherogenic risk when LDL-C appears reassuring.

When should GPs measure ApoB?

Consider ApoB when LDL-C may underestimate risk:

- **Diabetes Mellitus**
- Obesity
- CKM syndrome
- **TG ≥1.7** mmol/L (≥150mg/dL)
- LDL-C/ApoB**discordance**
- Very low LDL-C on intensive LLT

Example:

LDL-C 1.8 mmol/L + ApoB 120 mg/dL

→ LDL-C looks good

→ atherogenic particle burden may still be high

ApoB is particularly useful when LDL-C and the clinical picture do not "match."

ApoB Targets

ApoB: A Secondary Target When Discordance Is Suspected

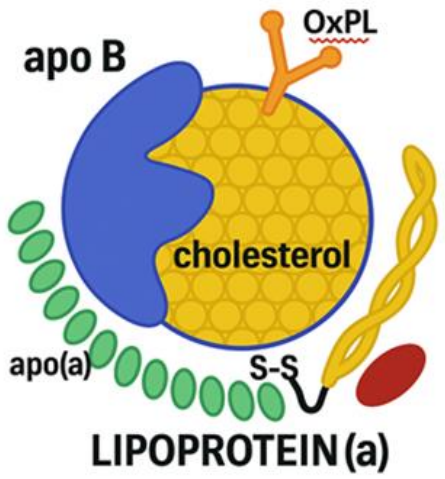
ASCVD risk	ApoB goal	LDL-C targets
Moderate	< 90mg/dL	<2.6 mmol/L (100mg/dL)
High	< 70mg/dL	<1.8 mmol/L (70mg/dL)
Very high	< 55mg/dL	<1.4 mmol/L (55mg/dL)

Use ApoB to refine treatment—not to replace LDL-C.

- **The guideline specifically positions ApoB as an adjunctive marker, particularly after LDL-C/non-HDL-C goal attainment in selected higher-risk groups.**

Lipoprotein(a): The Inherited Risk Factor

- LDL-like particle containing:
  - **ApoB-100 + apolipoprotein(a)**
  - Rich in oxidized phospholipids → **atherogenic + inflammatory + prothrombotic effects**
- **~80–90% genetically determined**
- Present in approximately **1 in 5 people**
- Independent risk factor for:
  - ASCVD
  - Calcific aortic valve stenosis
- **Risk rises continuously with increasing Lp(a)**



Lp(a) is a lifelong inherited CV risk factor that is largely independent of LDL-C.

Lp(a): Measure Once, Think Lifelong

Measure Lp(a) at least once in every adult

Why?

- Detect inherited risk
- Refine ASCVD risk
- Inform treatment intensity
- Identify relatives at risk

Testing pearls

- Fasting not required
- Relatively stable throughout life
- Repeat testing usually unnecessary

Family screening

- Consider first-degree relatives, particularly with:
  - Premature ASCVD / AS
  - Familial hypercholesterolaemia
  - Markedly elevated Lp(a)

ASCVD Risk Increases with Lp(a) Concentration

Lp(a) Level	Relative ASCVD Risk
125 nmol/L (50 mg/dL)	↑ ~40% (≈1.4-fold)
250 nmol/L (100 mg/dL)	≥2-fold
430 nmol/L	≥4-fold

One Lp(a) measurement can identify a lifelong risk—and potentially an entire family at risk.

High Lp(a): What Should GPs Do?

Don’t try to “treat the number”

Treat the risk.

1. Optimise all modifiable CV risk factors

- BP control
- Diabetes management
- Smoking cessation
- Lifestyle optimization

2. Lower LDL-C / ApoB more intensively

- Optimize statin therapy
- Add non-statin therapy when indicated

3. Consider family screening

What lowers Lp(a)?

Therapy	Effect on Lp(a)
Statins	↔ / may ↑ slightly
PCSK9 mAbs	↓ ~20–30%
Inclisiran	↓ ~20–30%

Lp(a) is currently a risk enhancer—not the primary treatment target.
High Lp(a) → think “lower LDL-C harder”

JUPITER: Elevated Lp(a) and Residual Cardiovascular Risk

Secondary analysis | 9,612 participants

Rosuvastatin 20 mg/day

- **Key Findings:**

🔴 **Lp(a) identifies residual CV risk**

- Even with very low LDL-C and reduced inflammation, patients with higher Lp(a) remained at significantly increased risk of cardiovascular events.

🔵 **Statins do not meaningfully lower Lp(a)**

- Rosuvastatin had minimal effect on Lp(a).

🟢 **Lower LDL-C still matters**

- Rosuvastatin reduced CV risk regardless of baseline Lp(a)

In patients with elevated Lp(a), aggressive LDL-C lowering and reduction of overall atherogenic burden remain highly beneficial.

PCSK9 Inhibitors Modestly Lower Lp(a)

	FOURIER	ODYSSEY OUTCOMES
PCSK9 inhibitor	Evolocumab	Alirocumab
Population	Established ASCVD	Recent ACS
Lp(a) reduction	26.9% at 48 weeks	~23–25%
Key finding	Greater absolute reduction with higher baseline Lp(a)	Same
Clinical implication	Lp(a) reduction may contribute to residual risk reduction	Lp(a) reduction independently associated with lower MACE risk

PCSK9 inhibitors lower Lp(a) modestly, but their proven CV benefit is primarily driven by LDL-C lowering.

When to Refer?

- Recognising patients who need specialist assessment
- FH • Severe dyslipidaemia • Complex lipid disorders • Persistent treatment failure

When Should GP Refer?

GP management	• Most uncomplicated hyperlipidemia • Statin initiation / titration • Addition of ezetimibe • Routine monitoring
Consider referral	• LDL-C persistently above goal despite optimized therapy • Statin intolerance • Severe hypertriglyceridaemia • Markedly elevated Lp(a) + premature/established ASCVD • Young patient with severe dyslipidaemia
Refer	• Suspected / confirmed FH • Complex / inherited dyslipidaemia • Premature ASCVD • Pregnancy with severe hypercholesterolemia • Need for advanced lipid-lowering therapy

When Should You Think Genetics?

Suspected Familial Hypercholesterolaemia

Red flags:

- Markedly elevated LDL-C
- Premature ASCVD
- Family history of premature ASCVD
- Suggestive physical findings - Tendon xanthomas, Xanthelasmas/corneal arcus in young adults
- LDL-C remains very high despite therapy

National FH Genetic Testing Programme

Referral To Genomic Assessment Centre (GAC):

- LDL-C level ≥ 5.5 mmol/L (≥212 mg/dL)
- Singapore Citizen / PR
- Age ≥ 18

Case 1: Primary Prevention

Mr. A, **45-year-old** gentleman with **hypertension** and **type 2 diabetes mellitus**. He is currently on Metformin and Losartan. He came for a routine follow-up. On physical examination, vital signs are normal. **BMI is 26.**
Lipid panel: Total cholesterol 5.51mmol/L, **LDL 3.68 mmol/L**, HDL 0.98 mmol/L, and **TG 1.86 mmol/L.**
What would you do?

Calculate PREVENT-ASCVD 10-year risk: 7.6% (Intermediate risk)
Personalize risk: Any risk enhancers? Eg. family history of premature ASCVD, consider Lipoprotein (a) and apolipoprotein B.

Which medication would you start?
A. High-intensity atorvastatin
B. Moderate-intensity atorvastatin
C. Ezetimibe
D. Omega-3 supplement

Answer: Moderate-intensity statin.
Why?
- Intermediate PREVENT risk. Diabetes, LDL-C above optimal range
- Initial therapy should be statin-based
- Target LDL: ≥30% LDL-C reduction, LDL-C goal < 2.6mmol/L, with intensification according to response/risk

In primary prevention, start with risk assessment → personalize → treat to LDL-C reduction and goal.

Case 2: Secondary Prevention

Mdm B, **72-year-old** female, has a **stable coronary artery disease** with previous coronary artery bypass surgery more than 10 years ago. Past medical history also includes **diabetes**,**hypertension**, and **obesity**. She has been adhering to **Atorvastatin 40mg OM**. Other medications are aspirin, bisoprolol, enalapril, metformin, and empagliflozin.

- On physical examination, vital signs are normal. **BMI is 36**.
- Total cholesterol 5.57 mmol/L, **LDL 2.20 mmol/L**, HDL 1.24 mmol/L, TG 1.45 mmol/L

What would you do?

A. Add evolocumab

B. Add ezetimibe

C. Add icosapent ethyl

D. Switch atorvastatin to rosuvastatin

Case 2: Secondary Prevention

Answer: For this patient, **ezetimibe** is the most appropriate next step.

Why?

- Established ASCVD
- LDL-C above goal of <1.8 mmol/L (70 mg/dL)
- LDL-C gap is modest → Required reduction is modest
- Ezetimibe is a simple oral add-on

- **If LDL-C remains above target, don't simply wait—intensify therapy.**
- **Early combination therapy** is increasingly favored, particularly when the required LDL-C reduction is large. The 2026 guideline explicitly emphasizes timely intensification and combination therapy.

Take-Home Messages

5 Things Every GP Should Know in 2026

1. **Calculate risk**
   - Use **PREVENT-ASCVD**
2. **Personalize**
   - Think **risk enhancers + Lp(a) + ApoB**
3. **Reclassify**
   - Use **CAC when treatment remains uncertain**
4. **Treat & Intensify**
   - **Lower LDL-C earlier, lower further, and treat to goal**
5. **Refer**
   - Think **FH, severe/complex dyslipidaemia and persistent failure to reach target**

CALCULATE → PERSONALIZE →RECLASSIFY → TREAT → INTENSIFY → REFER

Thank You

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