Lipid Management in 2026: Modern Strategies for CAD & High-Risk Patients

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MISSION CARDIOLOGY | KVH CARDIOLOGY PROGRAM

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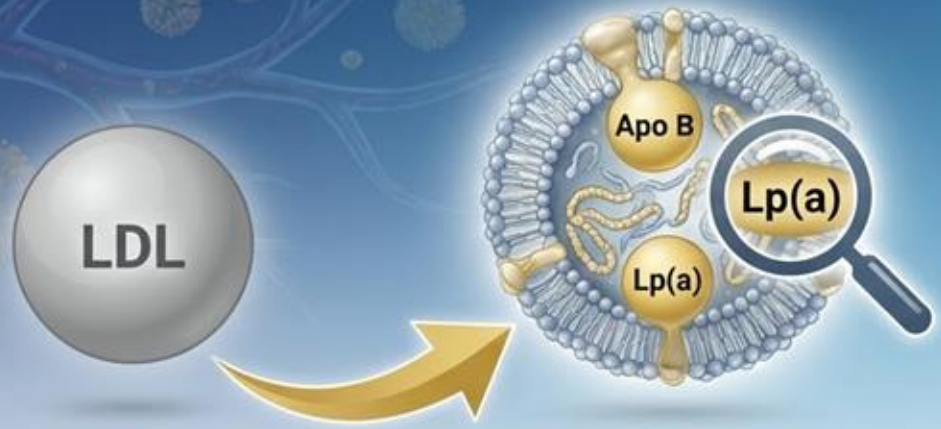
MISSION CARDIOLOGY

The New Era of Lipid Care

From Statins to Precision Lipidology...



The Past
(Statins & LDL)

The New Era
(Precision Lipidology)

Visualizing the shift to a more detailed, personalized understanding of lipid risks.

- Focus on residual risk beyond LDL...
- Personalized therapy with Apo B & Lp(a)
- 2025 AHA/ACC Dyslipidemia Guideline updates
- Triglyceride Management
- Identify Familial Lipid Disorders
- Nutrition, Lifestyle and Emerging therapies

WHY IT MATTERS

PREVALENCE & RISK

50% adults have elevated LDL-C

Every **40 seconds** someone has an MI

THE HIDDEN DANGER

25% CAD patients have elevated Lp(a)

<10% of FH cases diagnosed

THE SOLUTION & BENEFIT

1 mmol/L LDL reduction
(or 38 mg/dl)
= **22%-24%**
RRR↓ CV events

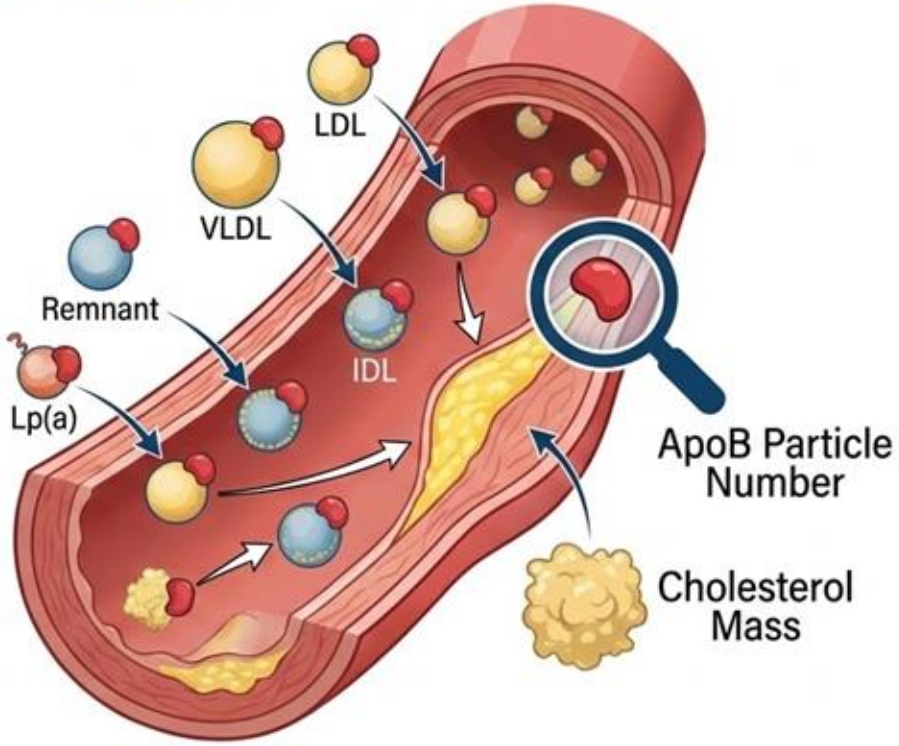
Every 10 mg/dl drop in Apo B cuts Heart Disease Risk by **9%**

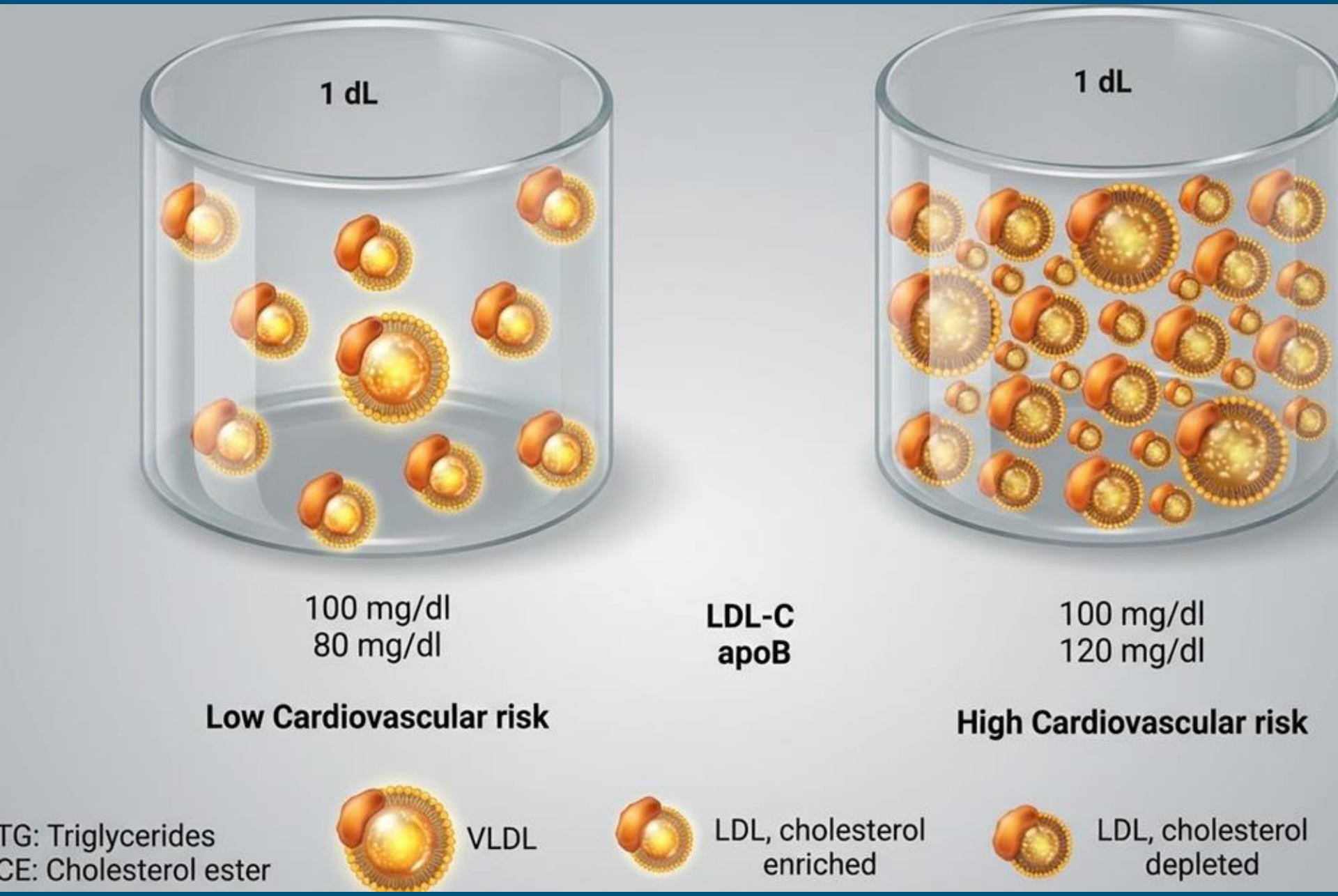
Apolipoprotein B (ApoB) Reflects the Number of Atherogenic Particles

A single ApoB molecule is present on each of the following particle types:

- Low-density lipoprotein (LDL)
- Very low-density lipoprotein (VLDL)
- Intermediate-density lipoprotein (IDL)
- Remnant lipoproteins
- Lipoprotein (a) [Lp(a)]

Key Concept:
ApoB is an established measure of the total number of cholesterol-carrying particles capable of entering the arterial wall. Particle number is considered a more accurate risk indicator than cholesterol mass alone.

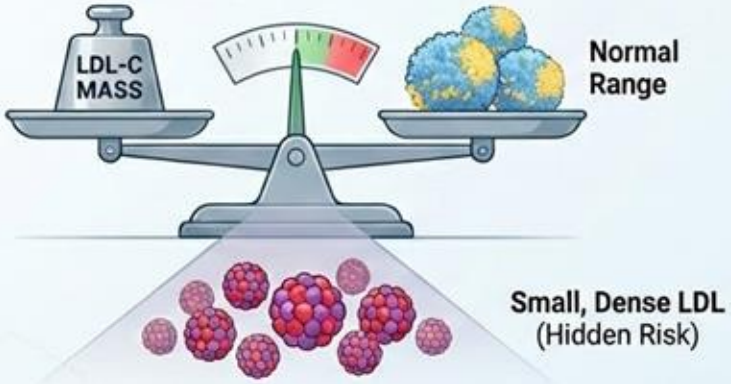



1 dL
1 dL
100 mg/dl
80 mg/dl
LDL-C
apoB
100 mg/dl
120 mg/dl
Low Cardiovascular risk
High Cardiovascular risk
TG: Triglycerides
CE: Cholesterol ester
VLDL
LDL, cholesterol enriched
LDL, cholesterol depleted

APOLIPOPROTEIN B (ApoB) REFLECTS THE NUMBER OF ATHEROGENIC PARTICLES

LIMITATIONS OF LDL-CHOLESTEROL (LDL-C) MEASUREMENT

THE LDL-C ILLUSION
(Measuring Mass, Not Number)



A **"normal"** LDL-C level may be associated with an **increased number of small, dense LDL particles**, thereby **underestimating risk.**

THE ApoB REALITY
(Counting Every Particle)

ApoB provides a direct measure of the **total number of atherogenic particles**, offering a more accurate assessment of cardiovascular risk.

CLINICAL CONTEXT

Metabolic Syndrome **Diabetes** **Hypertriglyceridemia**

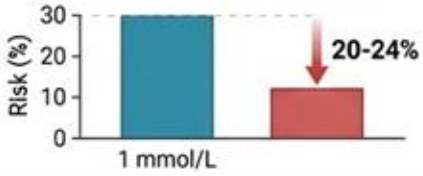
Underestimation of risk with LDL-C is frequently seen in conditions such as Metabolic Syndrome, Diabetes, and Hypertriglyceridemia.

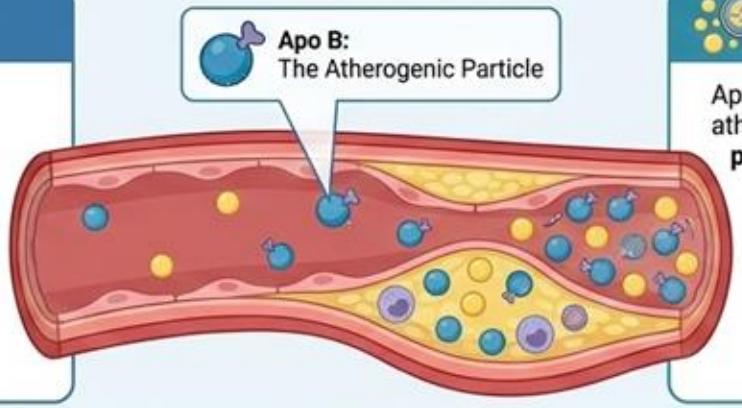
Apo B: Why It Matters

Apolipoprotein B (Apo B) - The Key to Cardiovascular Risk Assessment

Consistent Benefit

Research indicates that for every **1 mmol/L (≈38.7 mg/dL) drop** in LDL-C or Apo B, you get around a **20-24% lower risk** of major cardiovascular events.



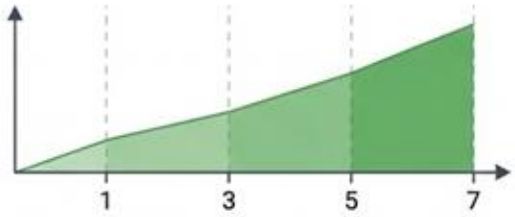


Apo B is a Stronger Predictor

Apo B directly measures the **number** of atherogenic particles (like LDL), making it a **more precise indicator** of CVD risk than LDL-C alone.

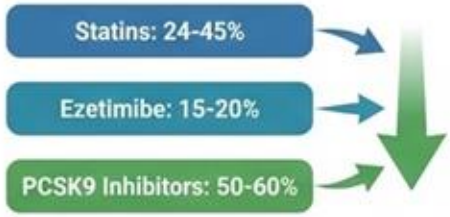
Time Matters

The longer the reduction is maintained, the **greater the cumulative benefit,** with significant risk reduction seen after **1, 3, 5, and 7 years**.



Magnitude of Reduction

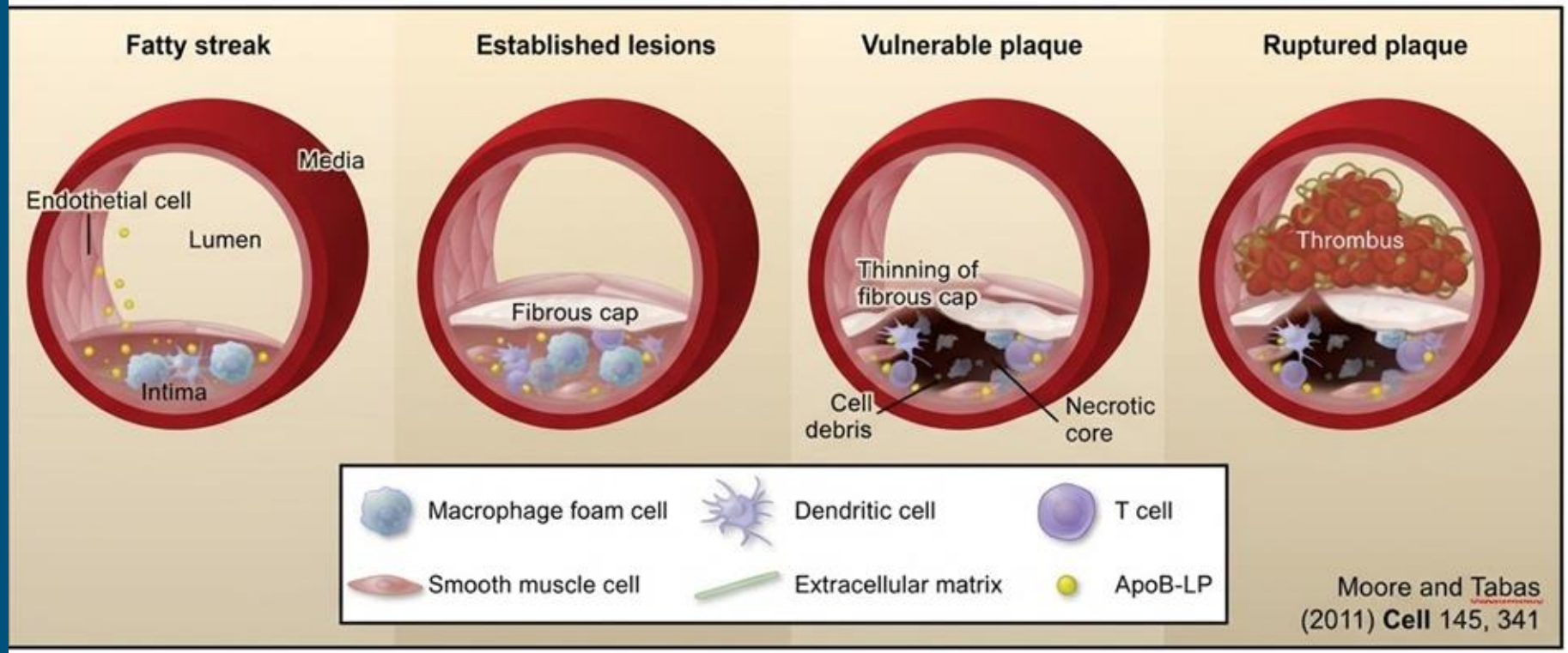
Effective therapies (statins, ezetimibe, PCSK9 inhibitors) can achieve these reductions, with statins often lowering Apo B by **24-45%** and non-statin agents adding further significant drops.



Apo B: A More Precise Measure of Cardiovascular Risk. Consult your doctor for more information.

Medical Organization

Plaque formation in CVD



- damaged endothelial cells provide sites for accumulation of fats
- fatty streaks signal for recruitment of immune cells

→

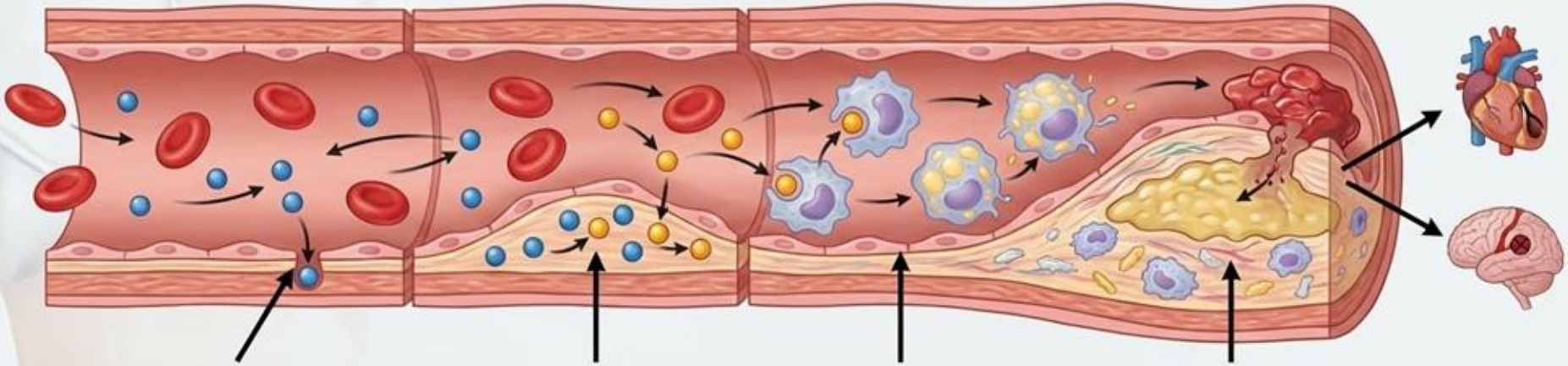
- macrophages eat cholesterol and turn into foam cells in plaque
- smooth muscle cells grow into the plaque generating fibrous cap

→

- plaque reduces blood flow
- necrosis at core can cause plaque rupture and thrombus formation, blocking arteries

Pathophysiology (Why It Causes Disease)

Stepwise Atherogenesis



Core Principle:

"No ApoB particles → No atherosclerosis"

(Ference et al., ESC / Mendelian data)

Clinical Importance: Why Treat It?

ApoB is the strongest predictor of ASCVD risk

Diabetes

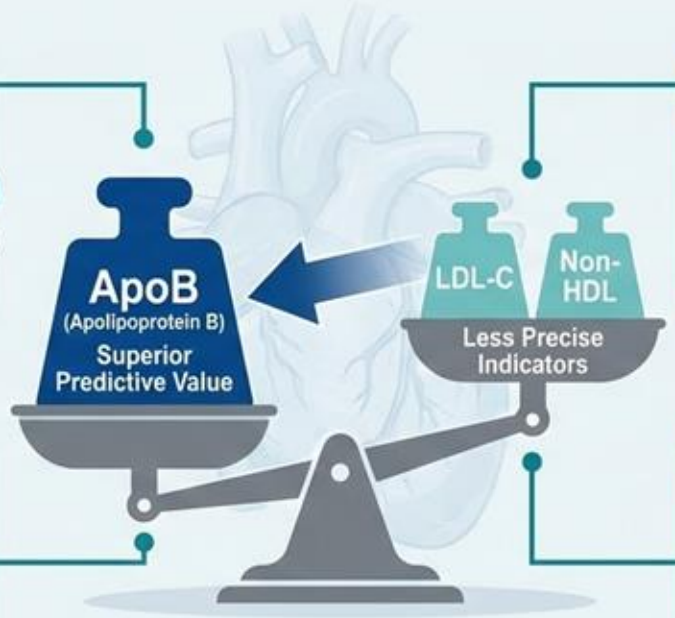
Outperforms LDL-C and non-HDL.

Accurately reflects high particle count despite "normal" LDL-C levels.

Hypertriglyceridemia

Outperforms LDL-C and non-HDL.

Reflects total burden of triglyceride-rich particles not fully captured by LDL-C.



Metabolic Syndrome

Outperforms LDL-C and non-HDL.

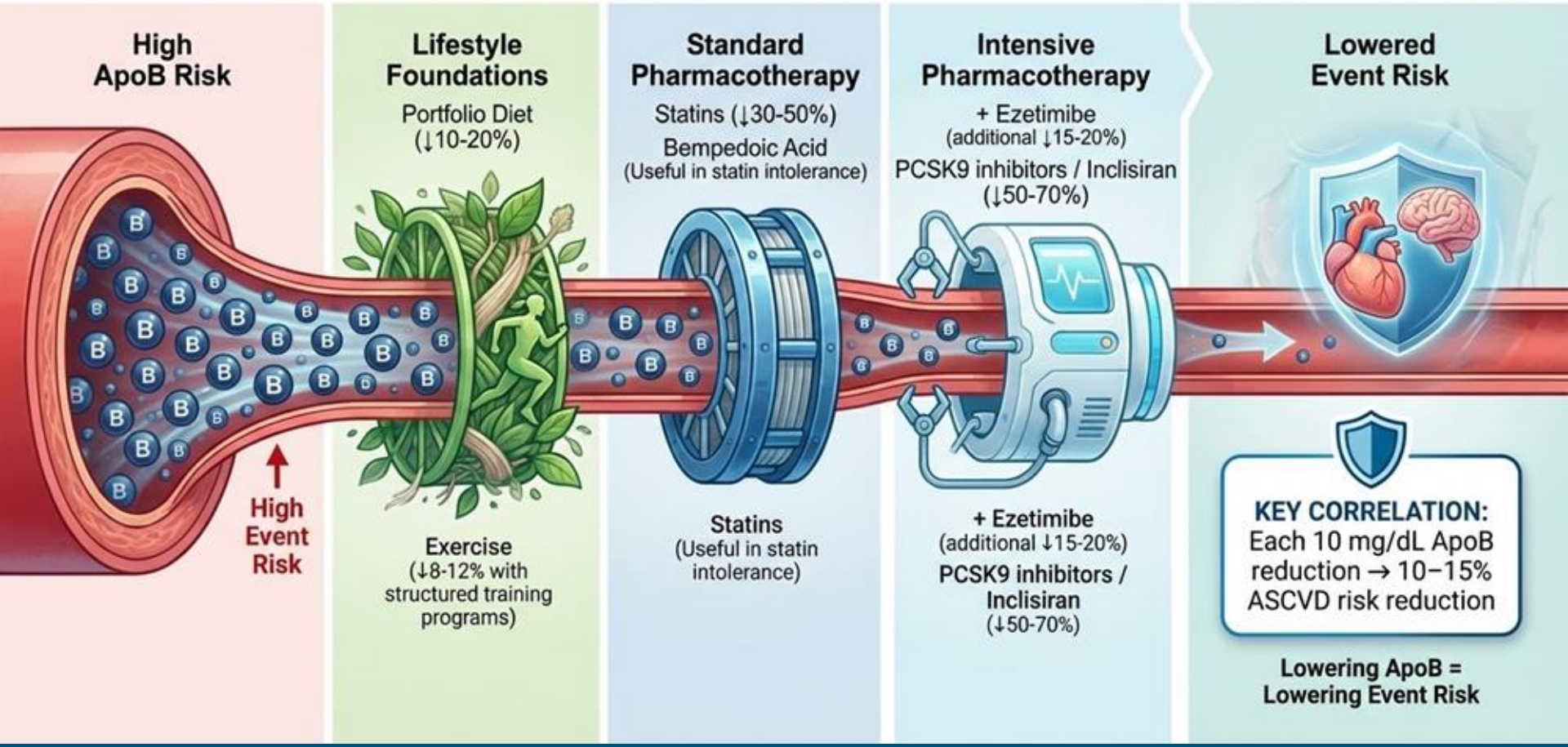
Captures all atherogenic particles, including small, dense LDL, often underestimated by LDL-C.

Statin-Treated Patients

Outperforms LDL-C and non-HDL.

Indicates residual risk even when LDL-C is controlled by statins.

Treatment Implications: Lowering ApoB = Lowering Event Risk



Guideline-supported targets

Guideline-supported target for ApoB by Risk Group

Risk Group	ApoB Goal
Very High Risk (CAD, MI, PAD, Stroke)	
High Risk (ASCVD, diabetes, LDL ≥190, FH)	
Primary Prevention (elevated risk)	

Risk Stratification

Very High Risk

- **CAD** (Coronary Artery Disease)
- **MI** (Myocardial Infarction) / **Stroke**
- **PAD** (Peripheral Artery Disease)
- **Stroke**

High Risk

- **LDL** ≥190 mg/dL
- **FH** (Familial Hypercholesterolemia)
- **Lp(a)** ≥125 nmol/L
- **CAC** (Coronary Artery Calcium) ≥100

→ Screen with a lipid panel, ApoB, Lp(a)

Clinical Pearl: Lp(a) one time test

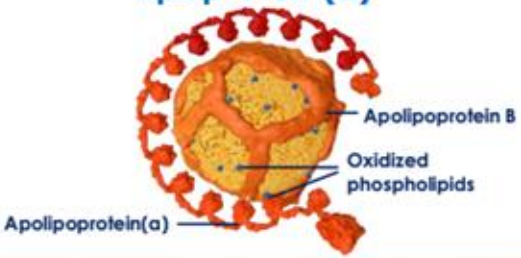
Elevated Lp(a) Is Independently Associated With ASCVD

DID YOU KNOW?

CVD is one of the biggest health challenges in the US[1]

Elevated **Lp(a)** is independently associated with ASCVD[2]

Lipoprotein(a)[3]



10 Facts About Lp(a)

1. Elevated Lp(a) (≥ 100–125 nmol/L) affects **~1 in 5** people globally[4,*]

2. Lp(a) levels are predominantly **genetically determined**[5]

3. **Lifestyle modifications**, including diet and exercise, have a minimal impact on Lp(a) levels[6,7]

4. Lp(a) is associated with **atherosclerosis, thrombosis, inflammation, and valvular calcification**[8]

5. Elevated Lp(a) is associated with an **increased risk of CV events**, independent of LDL-C[2]

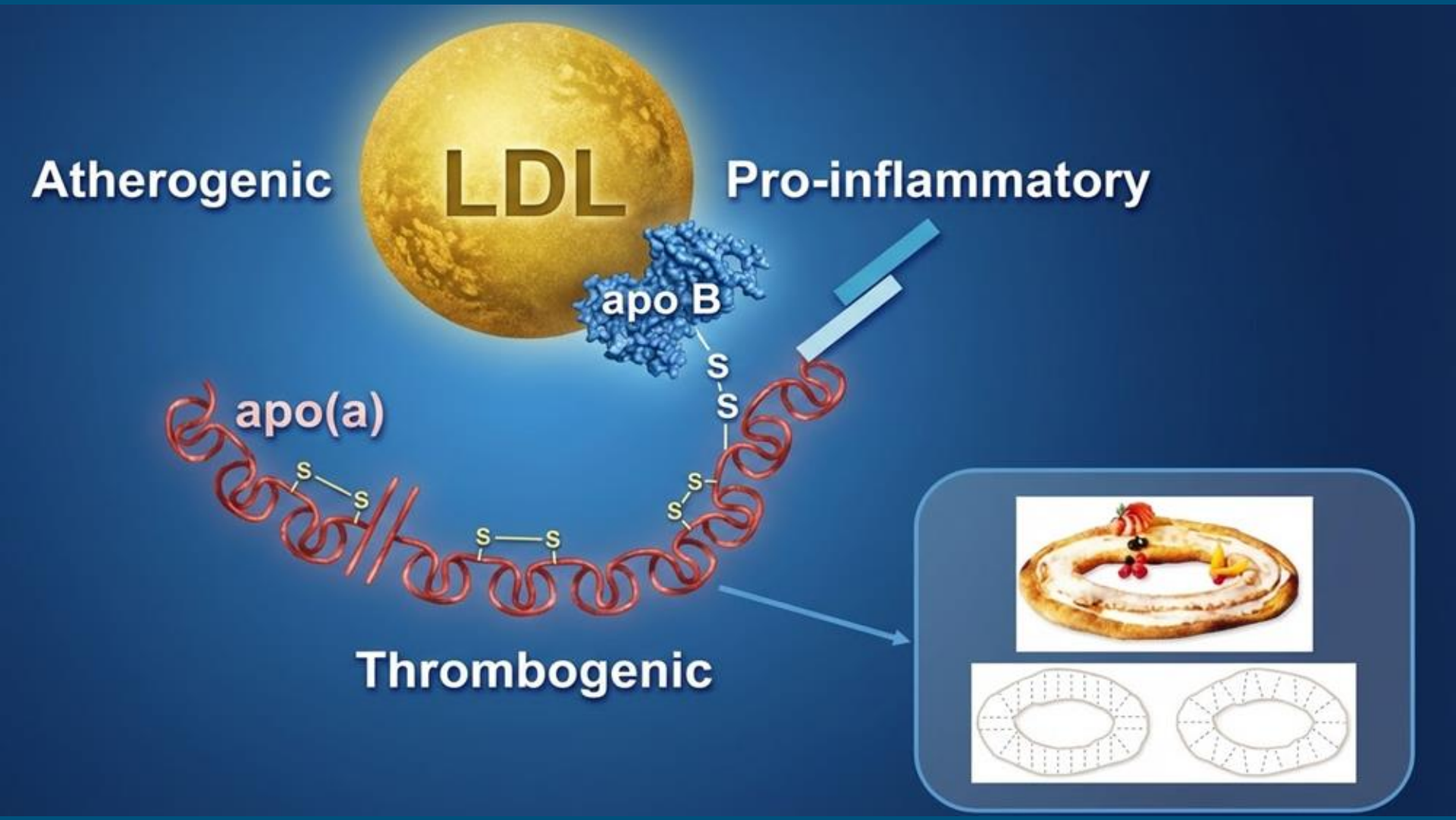
6. Clinical Guidelines/Statements recommend **Lp(a) testing** at least once in a lifetime as part of CV risk assessment[7,9,10]

7. International Guidelines/Statements recommend measuring Lp(a) levels ideally using isoform-insensitive molar assays (nmol/L)[5,10-12]

8. Lp(a) can be assessed via a **nonfasting blood test**, which can be performed in addition to a routine lipid panel[13-15]

9. Elevated Lp(a)† is associated with a residual risk of ASCVD even when LDL-C is lower[2]

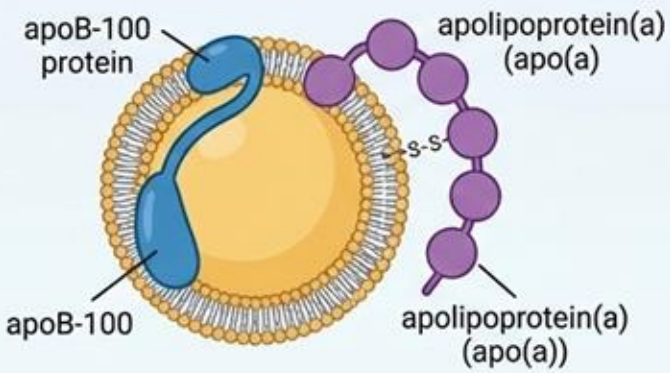
10. Despite its clinical significance, **Lp(a) testing rates are low**, even in patients with established ASCVD[2,16]


Atherogenic
LDL
Pro-inflammatory
apo B
apo(a)
Thrombogenic

Lipoprotein(a): Physiology & Why It Matters

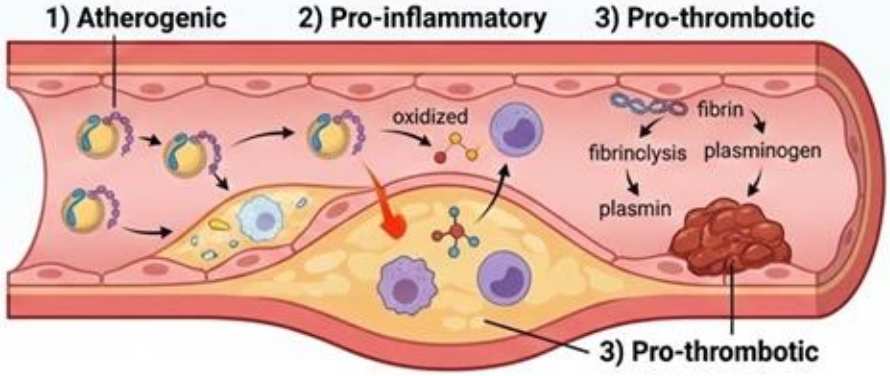
What is Lp(a)?

- LDL-like particle with an attached apolipoprotein(a) moiety
- Entirely genetically determined (90%+), stable over lifetime
- Independent of diet, exercise, and most lipid therapies



Pathophysiology

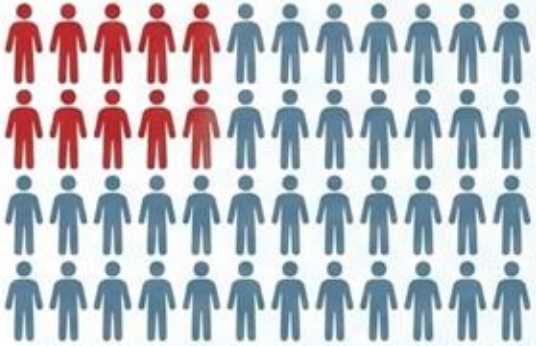
- **Atherogenic** → delivers cholesterol into arterial wall
- **Pro-inflammatory** → oxidized phospholipids accelerate plaque formation
- **Pro-thrombotic** → apo(a) mimics plasminogen → impairs fibrinolysis



Lipoprotein(a): Physiology & Why It Matters

Prevalence

~20–25%



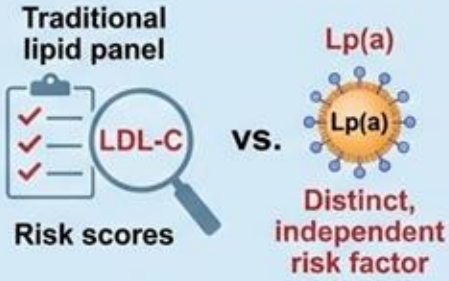
of population has elevated Lp(a)

Common in:

- Premature CAD / stroke
- Strong family history of CAD/Premature CAD
- Recurrent events despite "normal" LDL
- Aortic Stenosis (non bicuspid)

Key Takeaway

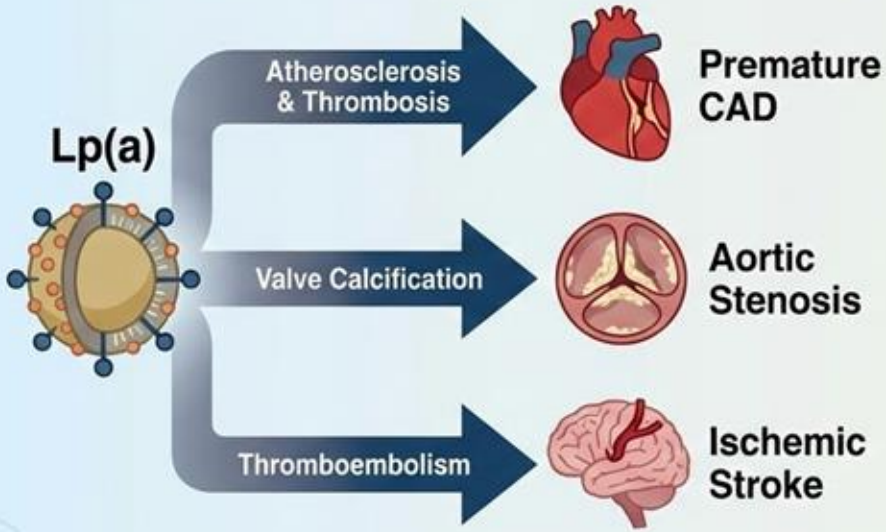
Lp(a) identifies inherited cardiovascular risk not captured by LDL-C or traditional risk scores.



Clinical Importance: Testing, Risk & Management

Why Test Lp(a)?

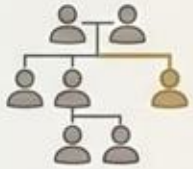
Strong, Causal Risk Factor For:



Explains "residual risk" in optimally treated patients.

Who Should Be Tested?

(Once in a lifetime)



Family history of premature ASCVD

Personal history of early CAD or stroke

Recurrent events despite LDL control

Familial hypercholesterolemia

Borderline / intermediate risk patients

Clinical Importance: Testing, Risk & Management

Risk Thresholds

Normal:
<30 mg/dL
(<75 nmol/L)

Elevated:
≥50 mg/dL
(≥125 nmol/L) → high ASCVD risk

Management Today

- No approved Lp(a)-lowering therapy (yet)
- Aggressive LDL-C / ApoB lowering
- Earlier combination therapy
- Consider PCSK9 inhibitors (↓ Lp(a) ~20–30%)

Clinical Importance: Testing, Risk & Management

What's Coming: RNA-Based Therapies

Therapies
pelacarsen, olpasiran, SLN360

Trial Results
↓ Lp(a) by 80–90% in trials

Outcome Trials
Underway (2025–2027)

Key Takeaway

1x

Measure Lp(a) once — it changes:

- ☑ Risk Stratification
- ☑ Intensity of Therapy
- ☑ Family Screening

Familial Hypercholesterolemia

Prevalence & Burden

- **~1 in 250** people have heterozygous FH (≈**1.3 million** in the U.S.)
- **90%** remain undiagnosed
- Lifetime exposure to very high LDL-C → **accelerated atherosclerosis**
- Untreated FH → **10–20x higher risk** of **premature CAD**

Natural History

- LDL-C elevated from birth
- MI often occurs:
  Men: **30s–40s**
  Women: **40s–50s**
- Homozygous FH: **childhood ASCVD** if untreated

Familial Hypercholesterolemia Strong Red Flags

LDL-C Thresholds

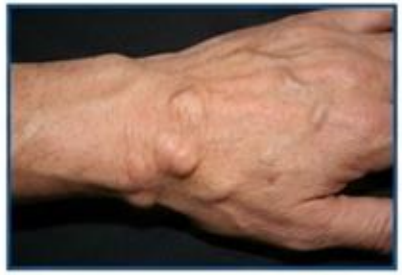
- [x] LDL-C Threshold <10- LDL
  - Lower than LDL <30 yrs
- [ ] LDL-C Versus Premature ASCVD
  - Mover than LDL <35 yrs
- [ ] Clinical LDL-C History

Premature ASCVD History

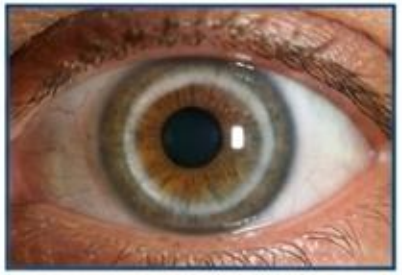
- [x] Premature ASCVD History <45 yrs
  - Lowertion agens <40 yrs
  - Peptile ASCVD history
  - Premature ASCVD history
- [ ] Premature ASCVD Premature ASCVD History

Family History & Clinical Signs

- [x] First-degree relative with early MI / stroke
- [x] Known FH or very high cholesterol



Tendon xanthomas



Corneal arcus <45 yrs

- [x] Poor LDL response to statins
- [x] Family history of “cholesterol problems” or sudden cardiac death

Familial Hypercholesterolemia: The Primary Care & Specialty Connection

Primary Care: The First Line

- Most FH patients first present in **primary care**
- **Early identification + early treatment =** dramatic **risk reduction**
- **Cascade screening**
  Cascade screening identifies affected family members

Specialty Referral

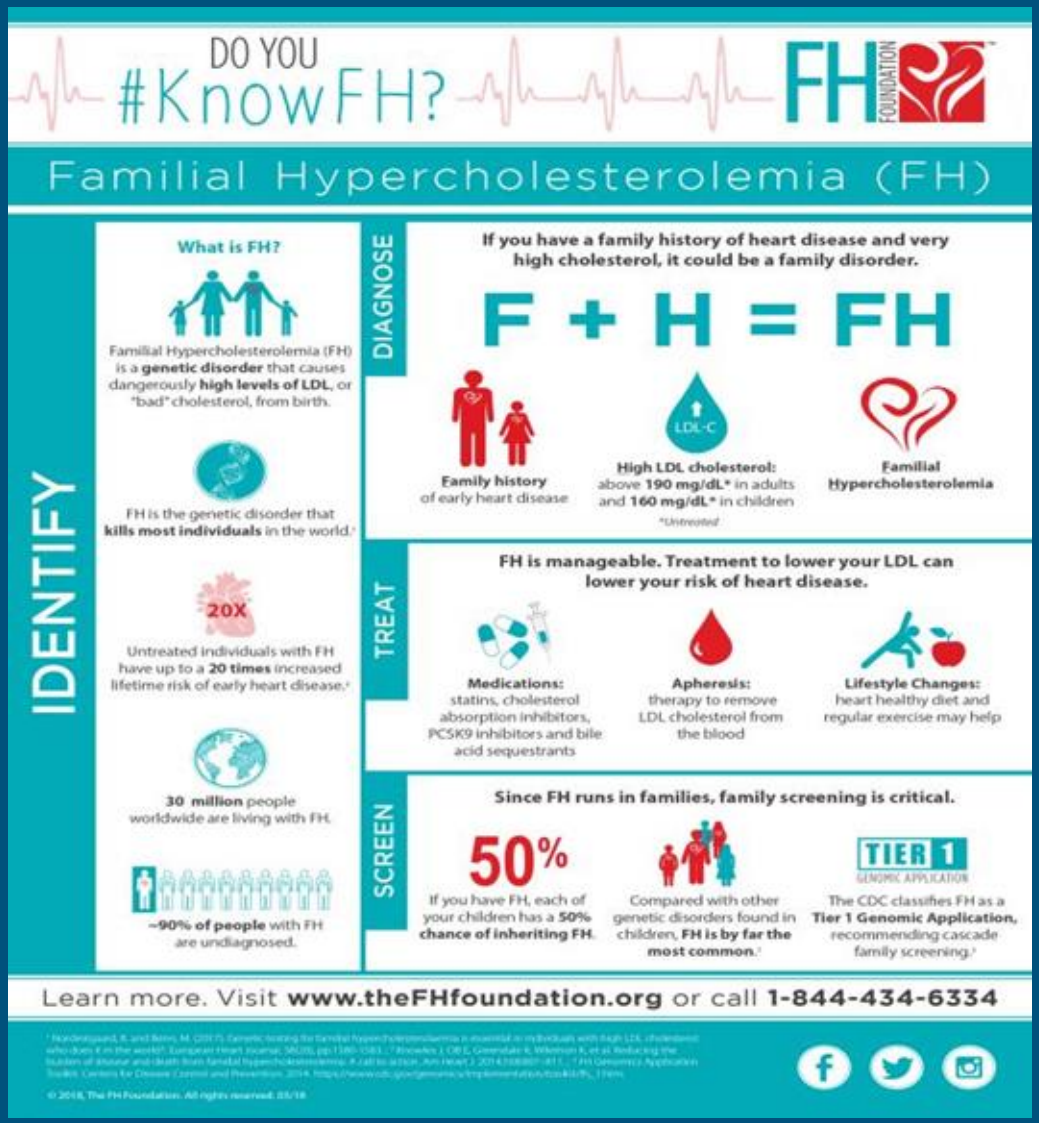
Specialty Referral: The Path to Optimal Management

- **Confirm diagnosis** (Dutch Lipid Score / genetic testing)
- **Advanced lipid therapy initiation**
- **Family screening coordination**
- **Long-term ASCVD risk reduction**

Bottom Line: Critical Insights

"An LDL ≥190 mg/dL is FH until proven otherwise."

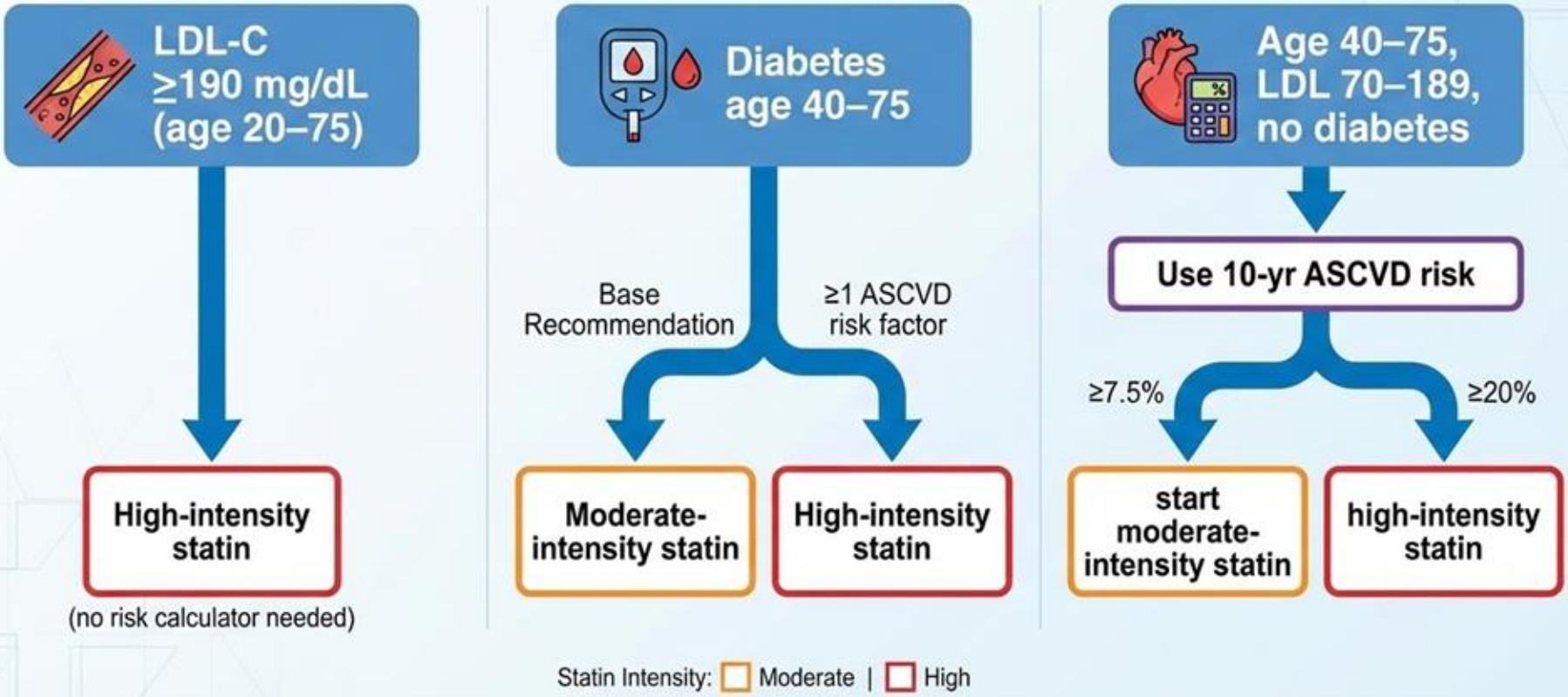
"FH is one of the **most common life-threatening genetic disorders — and one of the most under-diagnosed."**



CardioSmart.org/FH

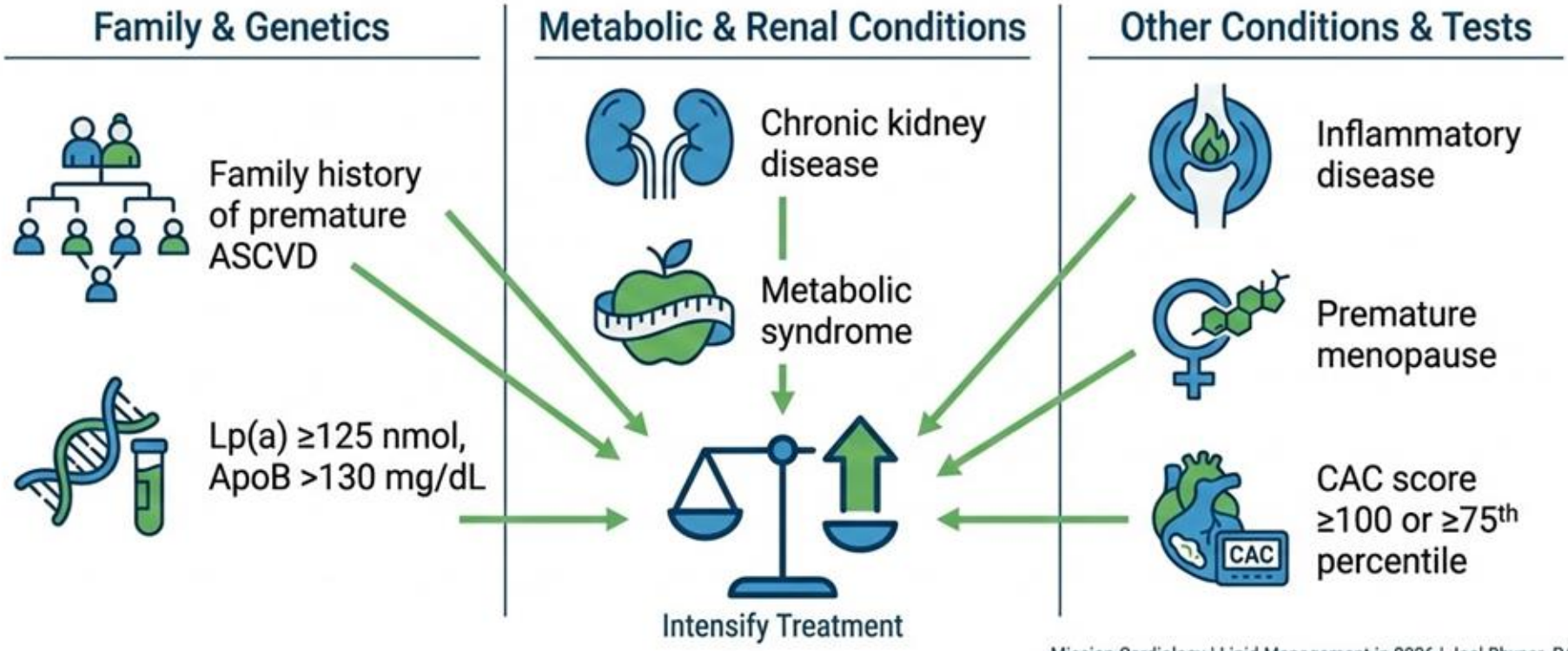
www.theFHfoundation.org

ACC/AHA Dyslipidemia Management (2026): Who should be on a statin



ACC/AHA Dyslipidemia Management (2026): Who should be on a statin

Risk enhancers (push you toward treatment/intensification)



LDL-C Management Simplified in Adults: Guidance from the National Lipid Association

A three-step guide to simplifying measurement & management of low-density lipoprotein cholesterol in the blood

Step 1: Measure LDL-C

Universal Lipid Screening: Guideline-Directed Intervals

Children 9-11 Years Old	Young Adults 17-21 Years Old	Adults 21+ Years Old
		

Additional Lipid Screening Intervals

4-12 Weeks	4-12 weeks after initiating lipid-lowering therapy or dose change to assess response & adherence.
3-12 Months	Every 3-12 months thereafter to monitor response & adherence to lipid-lowering therapy.
Annually	Individuals (1) at increased risk for heart disease, stroke, and other CVD risk or (2) on lipid-lowering therapy.
Young Children	Children with a family history of (1) hypercholesterolemia or (2) early CVD should have lipids tested as early as 2 years of age.

Step 2: Assess Risk

Adult LDL-C Levels Requiring Immediate Action

LDL-C ≥ 190 mg/dL	Severe hypercholesterolemia & may identify familial hypercholesterolemia (FH). FH is a genetic disorder causing elevated LDL-C, which can result in major ASCVD events at a young age. FH is common, impacting ~1 in 300 people.	Lower LDL-C & refer to Lipid Specialist

*The threshold for children is typically ≥ 160 mg/dL.

Very High-Risk Individuals

Major ASCVD Events

- ☐ ACS (< last 12 months)
- ☐ MI history (other than ACS above)
- ☐ Ischemic stroke history
- ☐ Symptomatic PAD*

High-Risk Conditions

- ☐ Age ≥ 65 years
- ☐ Diabetes mellitus
- ☐ Hypertension
- ☐ Smoker (current)
- ☐ LDL-C ≥ 100 mg/dL despite maximally tolerated statin & ezetimibe
- ☐ CHF history
- ☐ Heterozygous FH (LDL-C ≥ 190 mg/dL)
- ☐ CKD (eGFR 15-59 mL/min/1.73m^2)
- ☐ Prior coronary artery bypass surgery^
- ☐ Prior percutaneous coronary intervention^

Risk Assessment	LDL-C Objective
2+ Major ASCVD Events or 1 Major ASCVD Event & 2+ High-Risk Conditions	**< 55 mg/dL**

*History of claudification with ABI <0.85 or previous revascularization or amputation ^Outside of the major ASCVD event(s)

High-Risk Individuals

Patients with 1+ of the Following:

- ☐ Type 2 diabetes mellitus
- ☐ Familial Hypercholesterolemia, without a prior event
- ☐ CAC score > 100 AU or ≥ 75th percentile of the CAC score distribution for a particular age and sex
- ☐ Clinical ASCVD without other high-risk features
- ☐ Primary prevention patient with an estimated 10-year event risk of ≥ 20% in a pooled cohort risk calculation

LDL-C Objective: **< 70 mg/dL**

Patients with 1+ of the Following:

- ☐ No clinical ASCVD and baseline LDL-C ≥ 190 mg/dL
- ☐ Calculated 10-year ASCVD risk of 7.5-19.9% by AHA/ACC pooled cohort equation

LDL-C Objective: **< 100 mg/dL**

Optimal LDL-C for healthy adults — **< 100 mg/dL**

ACS: acute coronary syndrome; ACC: American College of Cardiology; AHA: American Heart Association; ABI: ankle-brachial index; ASCVD: atherosclerotic cardiovascular disease; AU: Agatston Units; CAC: coronary artery

Step 3: Manage LDL-C (Adults)

Date: _____ **My LDL-C:** _____ **LDL-C Objective:** _____

How Low Can You Go? Low LDL-C Safety

Healthy infants are generally born with LDL-C levels between 30-70 mg/dL. Evidence suggests LDL-C levels between 10-40 mg/dL are safe & that there is an incrementally lower risk of ASCVD events with LDL-C levels below 30 mg/dL. — **10-40 mg/dL**

Diet & Lifestyle

Guidelines & best practices emphasize the importance of a heart healthy diet and lifestyle habits for the management of LDL-C. Reduction in LDL-C from healthy diet and lifestyle is usually limited to 5-15%. — **5-15% LDL ↓**

Statin Medicines

Medicine	Anticipated* % LDL-C Reduction
Low-Intensity Statins	
☐ Pravastatin 10-20 mg	**< 30%**
☐ Other: _____	
Moderate-Intensity Statins	
☐ Atorvastatin 10-20 mg	**30-49%**
☐ Rosuvastatin 5-10 mg	
☐ Other: _____	
High-Intensity Statins	
☐ Atorvastatin 40-80 mg	**≥ 50%**
☐ Rosuvastatin 20-40 mg	

Non-Statin Medicines

to Add to Statin Therapy for Further LDL-C Lowering

Medicine	Anticipated* % LDL-C Reduction
Ezetimibe	
☐ Ezetimibe	**15-25%**
Bempedoic Acid	
☐ Bempedoic acid	**14-21%**
☐ Bempedoic acid + ezetimibe	**30-47%**
PCSK9 Inhibitor	
☐ Alirocumab 75 mg Q2W^	**47%**
☐ Alirocumab 150 mg Q2W^	**58%**
☐ Evolocumab 140 mg Q2W^	**60%**
☐ Inclisiran	**50%**

*Real world evidence suggests individual patient responses may vary. ^ Every 2 weeks.

Statin Safety & Tolerability

Statins are safe & generally well-tolerated. Most patients can tolerate some of statin therapy (agent, dose, and/or regimen).

Partial Statin Intolerance

Partial statin intolerance is the ability to tolerate a dose of statin that is lower than that required to reach the LDL-C objective.

Complete Statin Intolerance

Complete statin intolerance is the inability to take any statin dose or regimen. *It is estimated that < 5% of people are completely statin intolerant.*

Clinical Judgement for Statin Prescribing

Clinical judgement to personalize statin therapy (agent, dose, and/or regimen) may be appropriate to meet the needs of the individual patient.

High & Very High-Risk Individuals

Individuals at high-risk or very high-risk experiencing statin intolerance should consider non-statin therapy while finding a tolerable statin dose or regimen.

Initiating Non-Statin Therapy

Non-statin therapy may be required for patients who cannot reach their LDL-C objective with diet, lifestyle, and maximally tolerated statin therapy.

Lipid Specialists - Support & Referral

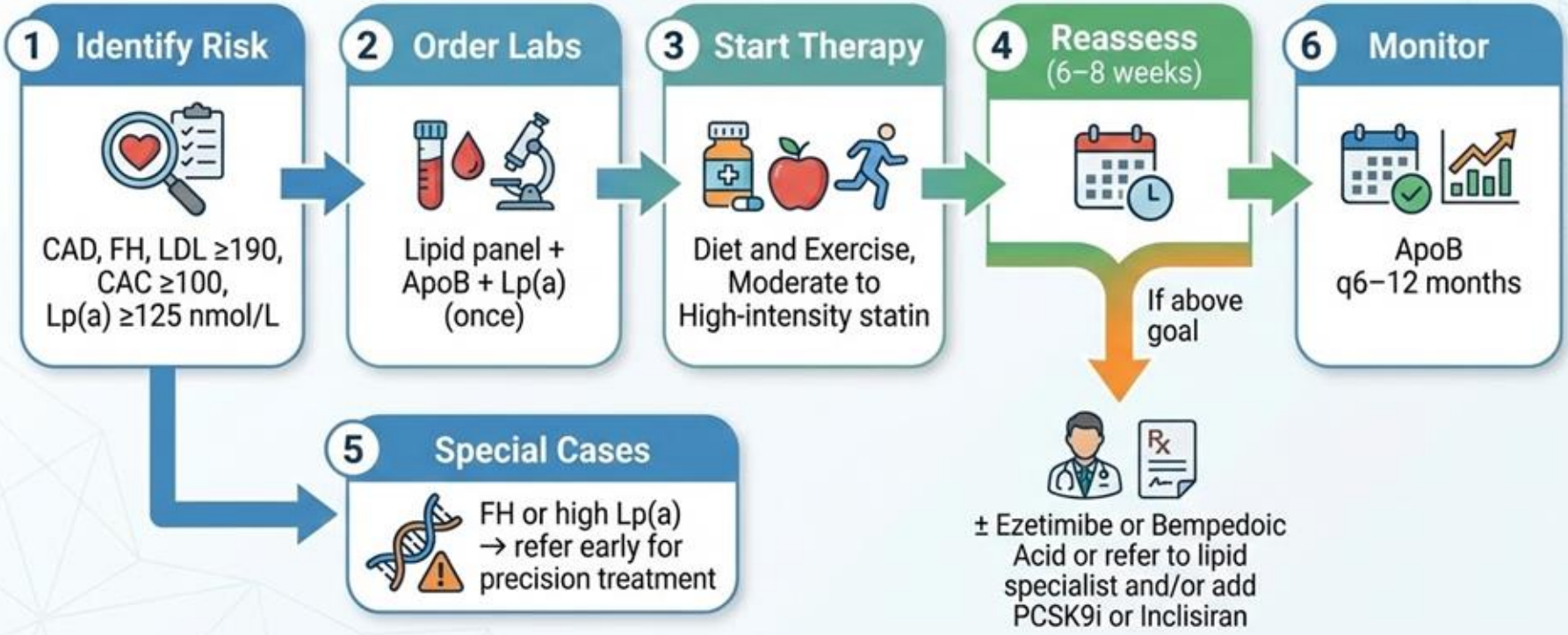
A Lipid Specialist is a clinician with advanced expertise in lipid management, certified by the American Board of Clinical Lipidology. Find a Lipid Specialist at learnyourlipids.com/find-a-clinician/.

Key Points

1. LDL-C must be measured regularly
2. LDL-C is managed based on ASCVD risk
3. Low LDL-C is generally safe
4. Lipid lowering medicines are safe
5. Lipid Specialists are available for support & referral

WWW.lipid.org

PCP Quick Algorithm – Lipid Management 2026



Treatment Targets (2026 Consensus)

Coronary Artery Disease (CAD)

Achieve LDL-C levels

< 55 mg/dL

Target ApoB levels

< 60 mg/dL

Maintain **Non-HDL** cholesterol

< 85 mg/dL

Emphasize the importance of **EARLY** and **SUSTAINED** reduction of **Low-Density Lipoprotein cholesterol (LDL-C).**

Consistent lowering prevents cumulative plaque buildup.

High Risk

Achieve LDL-C levels

< 70 mg/dL

Target ApoB levels

< 80 mg/dL

Maintain **Non-HDL** cholesterol

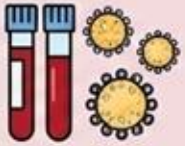
< 100 mg/dL

Hypertriglyceridemia & Chylomicronemia: Management Steps

STEP 1 — Identify Severity

TG 150–499
→ lifestyle
± statin
(ASCVD focus)

TG ≥500
→ pancreatitis prevention pathway



TG ≥1,000
→ evaluate for chylomicro-nemia/FCS

Genetics

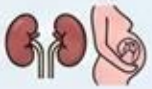
Specialized referral

STEP 2 — Address Secondary Causes (ALL PATIENTS)

- Diabetes control

- Alcohol cessation

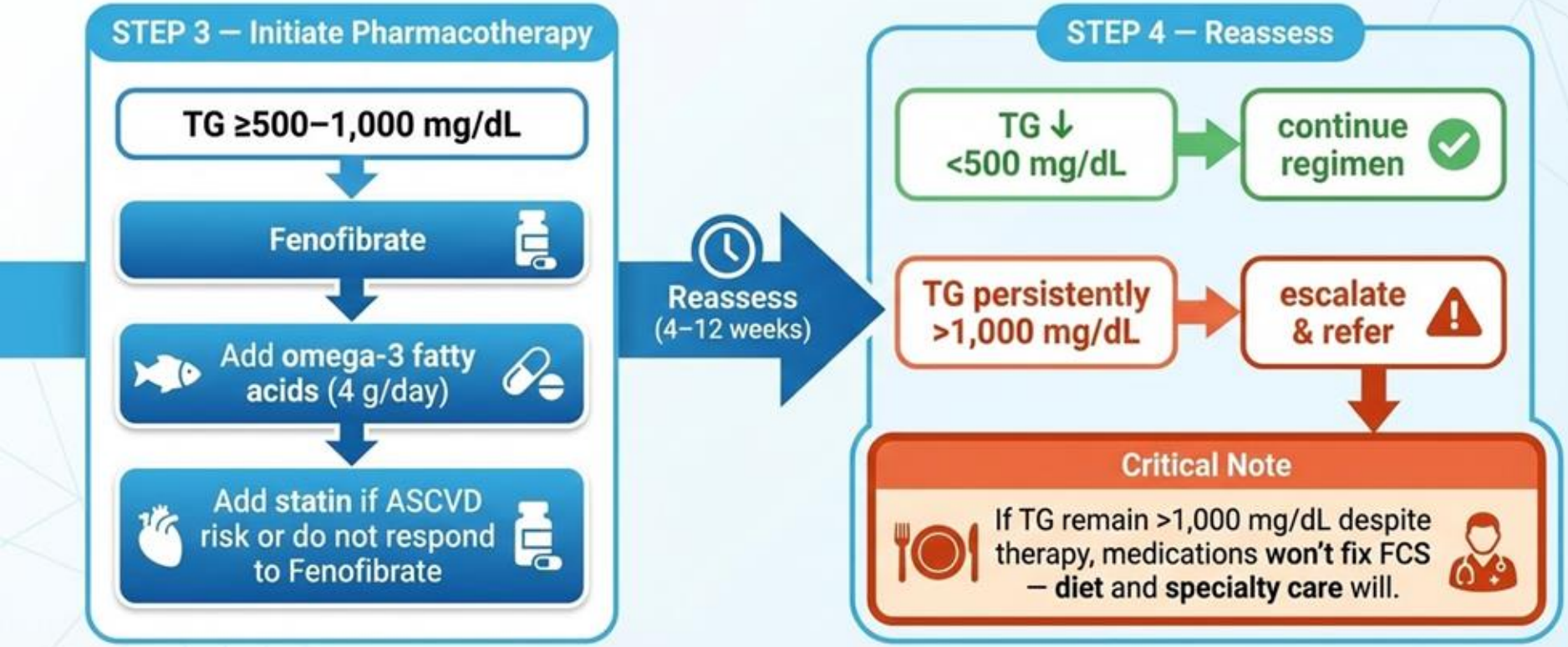
- Hypothyroidism



- CKD, pregnancy

- Medications (estrogen, steroids, beta-blockers, thiazides)

Hypertriglyceridemia & Chylomicronemia: Pharmacotherapy & Reassessment Steps



Familial Chylomicronemia Syndrome (FCS): Management Pathway

Key Point: LPL pathway failure

→ Standard TG-lowering drugs are ineffective

- Fibrates
- Omega-3 fatty acids
- Statins

TRUE FIRST-LINE

- Very-low-fat diet (≤10–15% total calories)
- Absolute alcohol avoidance
- Aggressive secondary cause control

NEXT STEP

→ Early lipid specialist referral

→ Consider ApoC-III / ANGPTL3–targeted therapies

Key Takeaways

Diet and alcohol cessation are non-negotiable.

Use fibrate (Fenofibrate) and Omega-3 FA early.

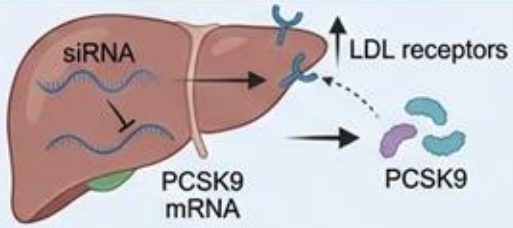
Treat pancreatitis risk first, ASCVD second.

Early referral prevents complications.

Emerging RNA-Based Therapies: Targeting LDL and Lp(a)

Investigational Agents and Their Impact on Lipid Parameters

Inclisiran (siRNA)

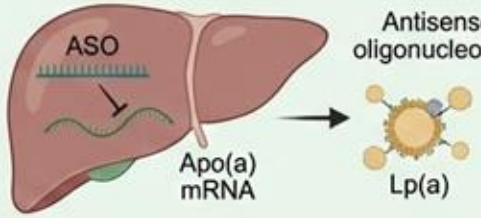


Outcome: ↓ LDL-C 50%

Mechanism: Inhibits PCSK9 production, increasing LDL receptor expression.

Target: PCSK9

Pelacarsen (ASO)

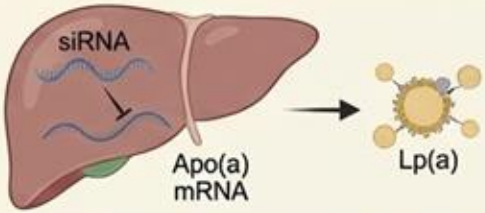


Outcome: ↓ Lp(a) 80–90%

Mechanism: Inhibits Apo(a) production, preventing Lp(a) assembly.

Target: Lp(a)

Olpasiran (siRNA)

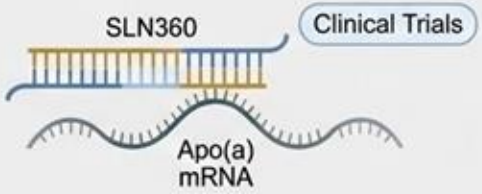


Outcome: ↓ Lp(a) 80–90%

Mechanism: Silences Apo(a) mRNA, blocking Lp(a) formation.

Target: Lp(a)

SLN360 (siRNA)

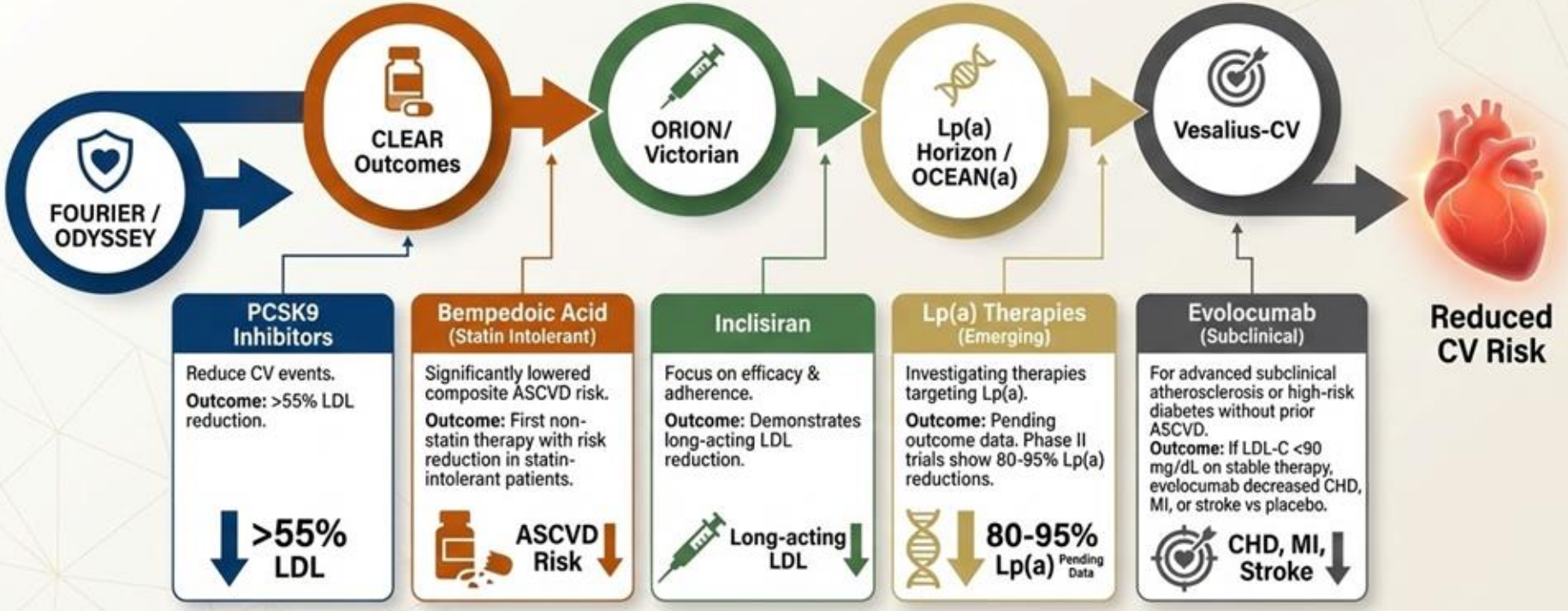


Outcome: In trials

Mechanism: siRNA targeting Apo(a) mRNA for Lp(a) reduction.

Target: Lp(a)

Key Lipid Trials & Their Cardiovascular Impact

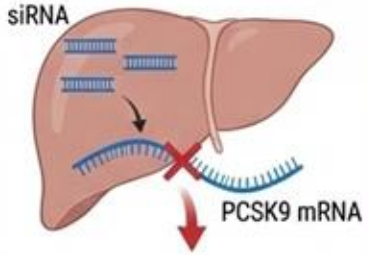


Next Generation Lipid Agents

RNA-Based & Precision Lipid Therapies

> "We can now silence PCSK9 — and soon, we may be able to silence Lp(a). The next era of lipid care is precision-based."

Inclisiran

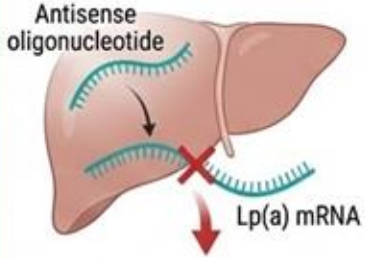


Target / Mechanism:
siRNA → PCSK9 silencing

Primary Effect: ↓ LDL ~50%

Clinical Status (2025–26):
FDA-approved
(twice-yearly dosing)

Pelacarsen

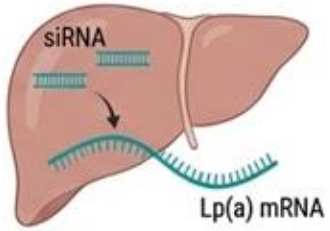


Target / Mechanism:
Antisense oligonucleotide → Lp(a)

Primary Effect: ↓ Lp(a) 80–90%

Clinical Status (2025–26):
Phase 3 outcomes trials
(Lp(a) HORIZON)

Olpasiran

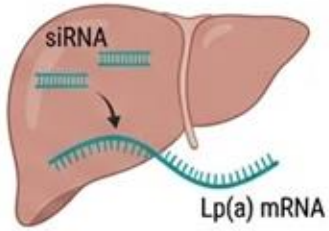


Target / Mechanism:
siRNA → Lp(a)

Primary Effect: ↓ Lp(a) 80–90%

Clinical Status (2025–26):
Phase 3 outcomes trials
(OCEAN(a))

SLN360



Target / Mechanism:
siRNA → Lp(a)

Primary Effect: ↓ Lp(a) 70–90%

Clinical Status (2025–26):
Phase 2 (dose-finding / safety)

Pharmacologic Agents to Lower ApoB (2026 Clinical Summary)

Medication Class	Examples	Mechanism	Typical ApoB ↓	Key Clinical Notes
High-Intensity Statins	Atorva 40–80 mg | Rosuva 20–40 mg	↓ Hepatic cholesterol synthesis → ↑ LDL receptor	30–50%	First-line therapy; strongest outcome data; dose dependent
Moderate-Intensity Statins	Atorva 10–20 | Rosuva 5–10 | Simva, Prava	Same as above	20–35%	Often insufficient alone for secondary prevention targets
Ezetimibe	Zetia	↓ Intestinal cholesterol absorption	10–20%	Excellent add-on; minimal side effects; synergistic with statins
PCSK9 monoclonal antibodies	Evolocumab (Repatha) | Alirocumab (Praluent)	↑ LDL receptor recycling	50–65%	Rapid, potent; proven ↓ MACE; injectable q2–4 weeks
Inclisiran (siRNA)	Leqvio	Silences PCSK9 synthesis	50–65%	Twice yearly dosing; ideal for adherence; growing outcomes data
Bempedoic Acid	Nexletol	Inhibits ATP-citrate lyase (upstream of statins)	15–25%	Useful in statin intolerance; CLEAR Outcomes benefit
Statin + Ezetimibe Combo	Fixed dose combos	Dual synthesis + absorption blockade	40–60%	Best initial combo strategy per ACC/ESC consensus
Statin + PCSK9 / Inclisiran	—	Max LDL receptor up-regulation	60–75%	Standard for very high-risk / CAD patients
Fibrates	Fenofibrate, Gemfibrozil	↓ VLDL production, ↑ TG clearance	5–15%	Modest ApoB effect; best for hypertriglyceridemia
Omega-3 EPA (icosapent ethyl)	Vascepa	↓ VLDL synthesis; plaque stabilization	Minimal (0–5%)	Event reduction independent of ApoB lowering
Niacin (rarely used)	Niaspan	↓ Hepatic ApoB secretion	10–25%	No outcome benefit; poor tolerability; generally not recommended
Lomitapide (HoFH only)	Juxtapid	MTP inhibition → ↓ ApoB assembly	40–50%	Specialized FH therapy; hepatotoxicity risk
Mipomersen (HoFH, limited use)	Kynamro	ApoB antisense oligo	25–40%	Rarely used now; replaced by newer agents

LIFESTYLE FOUNDATIONS

MEDITERRANEAN / PORTFOLIO DIET

Plant-based, healthy fats, fiber-rich. Focuses on fruits, vegetables, legumes, nuts, seeds, fish, and olive oil. Reduces LDL-C and CV risk.

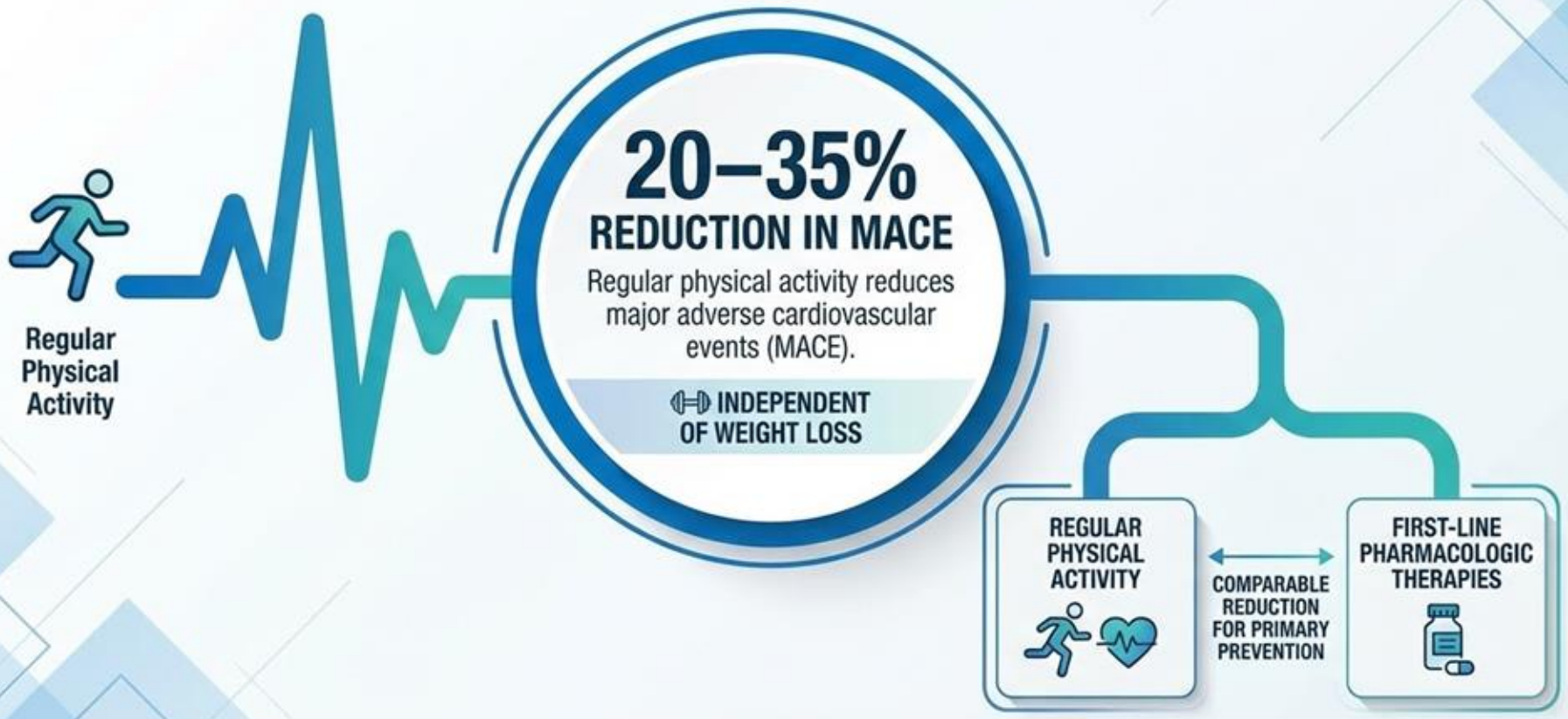
EXERCISE

Boosts HDL, lowers TG and Apo B, and reduces CV events. Regular moderate-to-vigorous physical activity improves lipid profile and cardiovascular health.

MANAGE STRESS, SLEEP, REDUCE/ELIMINATE ALCOHOL

Adequate sleep (7-9 hours), stress reduction techniques, and minimizing alcohol intake support overall heart health.

EXERCISE IS MEDICINE



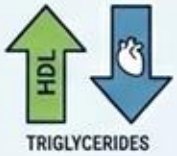
EXERCISE IS MEDICINE...

Relative CV Risk Reduction Comparison

BIG PICTURE...
SET EXPECTATIONS EARLY

The Role of Exercise in Lipid Management
& Cardiovascular Health

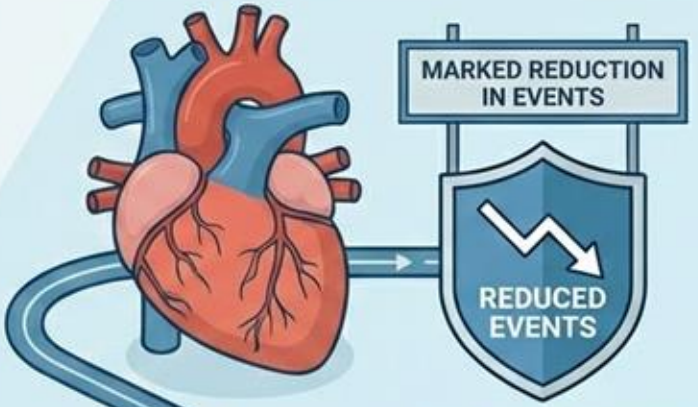
Exercise is **NOT** a strong LDL-lowering therapy alone.



Meaningfully lowers **triglycerides** and **raises HDL**.

Reduces **ApoB particle atherogenicity.**

Best lipid results come from
exercise + diet + pharmacotherapy.



Even if LDL changes are modest, **marked reduction in events** can occur.

CARDIAC REHAB

Cardiac Rehab is essential.

Exercise Prescription for Lipid Management

EXPECTED EFFECT

LDL-C: ↓ ~3–10% (modest)

ApoB: ↓ modestly, improves particle quality

Greatest benefit via weight loss + visceral fat reduction

COMBINATION TRAINING

BEST EXERCISE PRESCRIPTION

Aerobic: 150–300 min/week moderate **OR** 75–150 min/week vigorous

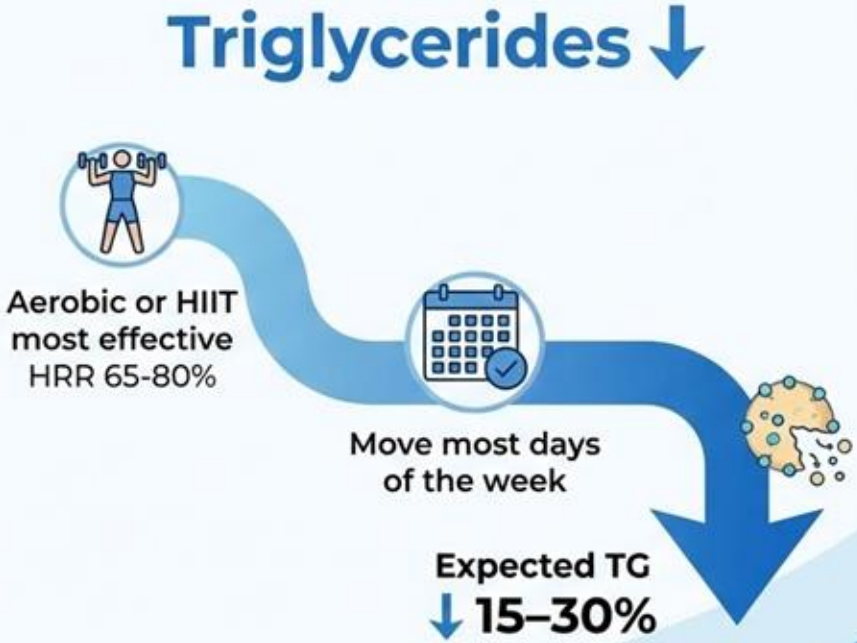
Resistance training: ≥2 days/week (major muscle groups)

EXERCISE TYPES

- Brisk walking/ hiking/rucking
- Cycling
- Rowing
- Swimming
- Circuit-based resistance training/HIIT

Exercise Prescription for Lipid Management

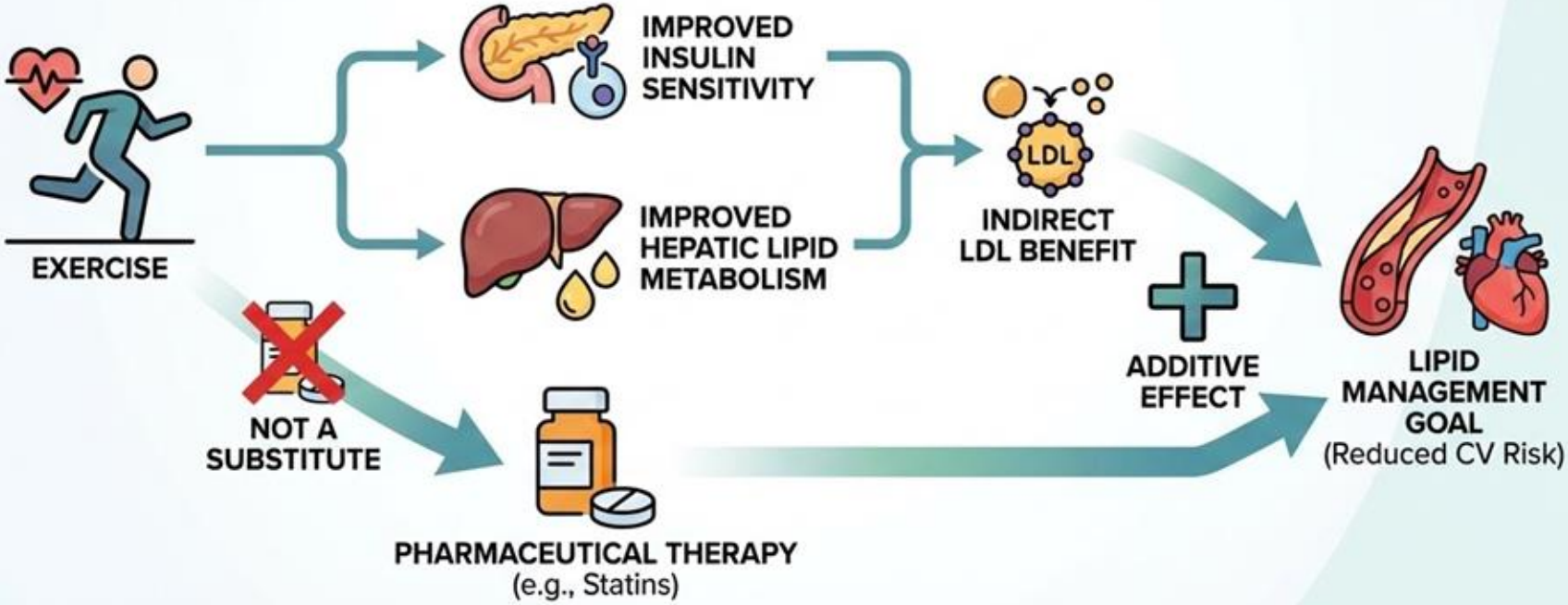
Targeting HDL-C and Triglycerides for Cardiovascular Health

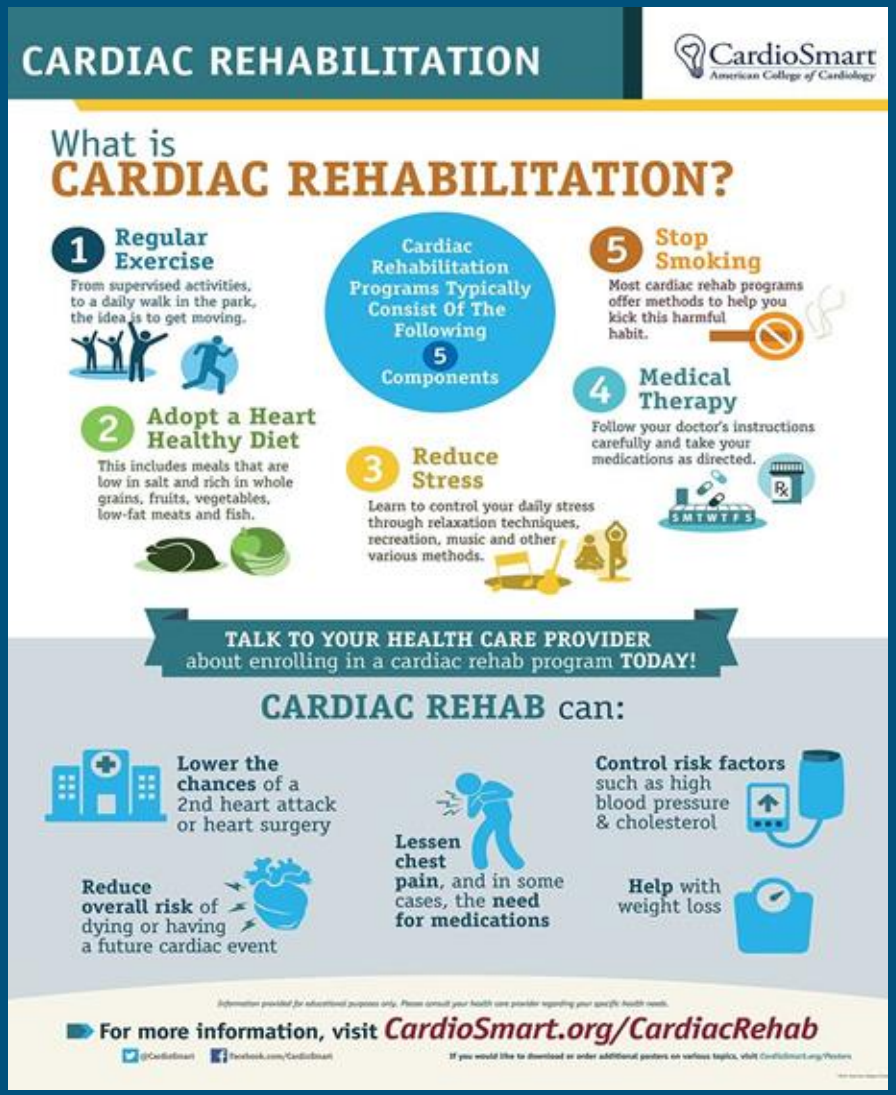


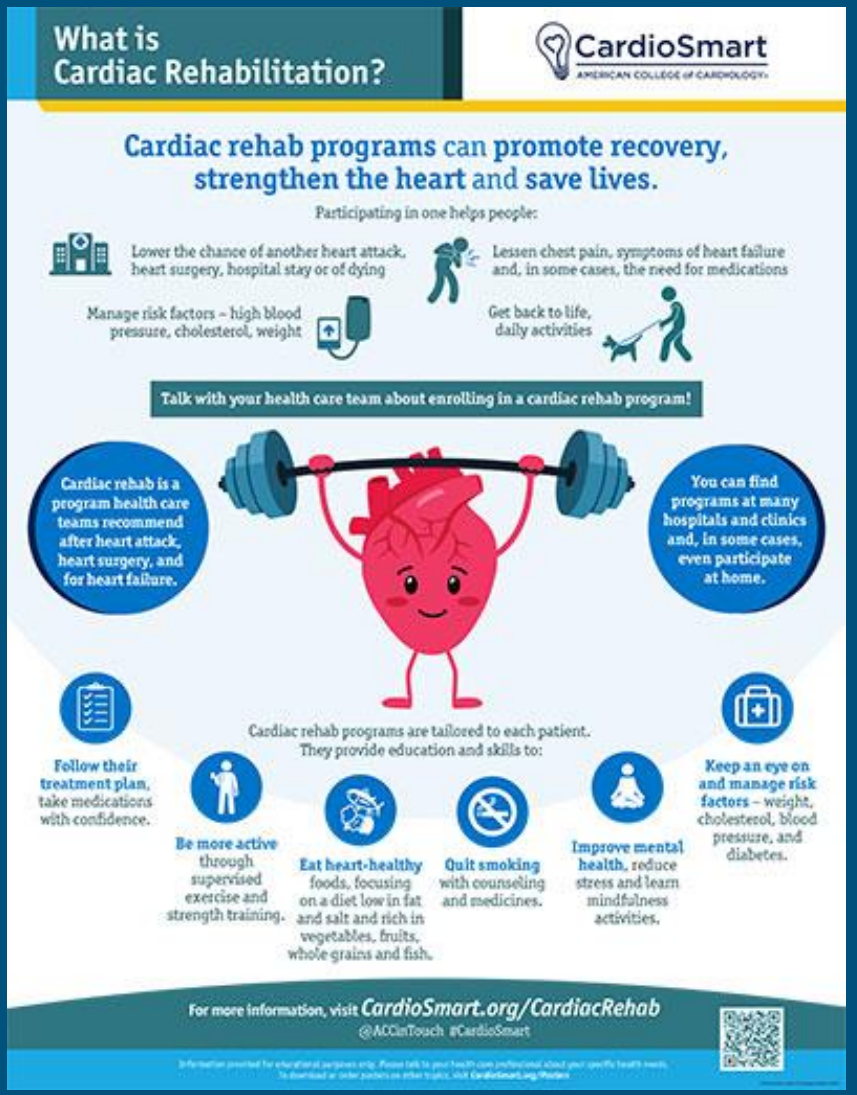
Exercise Prescription for Lipid Management

CLINICAL PEARL

Exercise helps LDL indirectly by improving insulin sensitivity and hepatic lipid metabolism — **it is additive**, not substitutive, to statins and other pharmaceutical therapy.







CardioSmart.org/FH

WORLD HEART FEDERATION

PHYSICAL ACTIVITY & CVD

Each year, physical inactivity contributes to more than **1 MILLION** preventable deaths

Regular physical activity helps prevent and treat

Heart disease · Stroke · Diabetes · Hypertension · Overweight and obesity

It can also improve mental health, quality of life and well-being!

It only takes **30 MINUTES** of moderate-intensity physical activity **5 DAYS** per week to improve and maintain your health.

Steps you can take on the road to a healthy heart

CHILDREN & ADOLESCENTS
5-17 years

At least **60 MINUTES** of moderate to vigorous-intensity physical activity **EVERY DAY**

Vigorous-intensity aerobic activities, as well as those that strengthen muscle and bone, should be incorporated at least **3 DAYS A WEEK**

ADULTS & SENIORS
18+ years

At least **150-300 MINUTES** of moderate-intensity or 75-150 minutes of vigorous-intensity aerobic physical activity **THROUGHOUT THE WEEK**

Adults should also do muscle strengthening activities at moderate or greater intensity that involve all major muscle groups on **2 OR MORE DAYS A WEEK**

Limit the amount of time spent being sedentary, particularly recreational screen time, and replace it with more physical activity of any intensity (even light intensity).

If you are not active, **start with small amounts of physical activity and gradually increase the duration,** frequency and intensity over time.

YOU DON'T NEED TO GO TO THE GYM TO BE PHYSICALLY ACTIVE!

Take the stairs instead of the elevator. If you can, walk or cycle to work – even if it's just part of the way. Take breaks during the day to move around and do simple exercises.

In order to be beneficial for your cardiorespiratory health, all activity should be performed in bouts of at least **10 MINUTES**

10 min

EXAMPLES OF MODERATE INTENSITY PHYSICAL ACTIVITY

- Brisk walking
- Cycling
- Gardening
- Housework
- Ballroom dancing
- Skateboarding

EXAMPLES OF VIGOROUS INTENSITY PHYSICAL ACTIVITY

- Jogging/running
- Hiking
- Fast cycling
- Fast swimming
- Aerobics
- Playing competitive sports

AND DON'T FORGET... SOME PHYSICAL ACTIVITY IS BETTER THAN NONE AT ALL!

Resistance Training (Often Underused)

A key component for metabolic health and lipid management

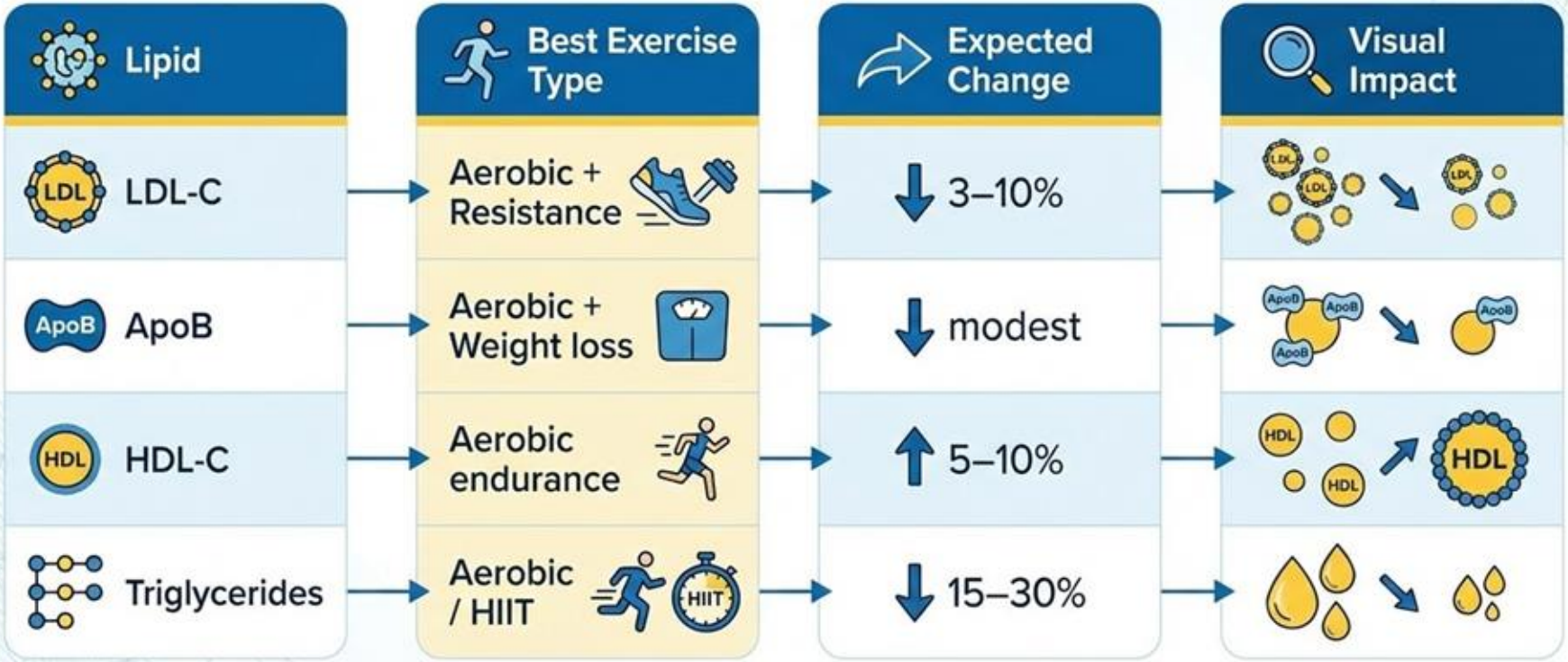
BENEFITS

- Improves insulin sensitivity and lean body mass
- Reduces visceral fat
- Modest HDL ↑
- TG ↓ when combined with aerobic training

PRESCRIPTION

- ≥2–3 days/week
- 8–10 exercises
- 2–3 sets per movement
- Moderate–heavy loads

Lipid Specific Summary Table



Dietary Strategies to Lower Estimated LDL-C (↓)

Implementing these evidence-based changes can significantly reduce your LDL cholesterol levels.

SFAs Replacement

Replace 5% of total daily energy (TDE) from saturated fatty acids with unsaturated fatty acids.

↓ 5–10%
LDL-C Reduction

Viscous Fiber

Consume 7.5 g/day of viscous (soluble) fiber.

↓ 6–9%
LDL-C Reduction

Plant Sterols/Stanols

Incorporate 2 g/day of plant sterols/stanols.

↓ 5–8%
LDL-C Reduction

Plant Protein

Replace animal protein or carbohydrates with 30 g/day of plant protein.

↓ 3–5%
LDL-C Reduction

Weight Loss

Achieve a 5% loss of body weight (if excess adiposity is present).

↓ 3–5%
LDL-C Reduction

Combined Effect: Significant Reduction in Estimated LDL-C

Portfolio Diet vs Mediterranean Diet (Clinical)

MEDITERRANEAN DIET

(The Foundation)

Goal: CV event reduction

LDL reduction: 5–15%

Best for: Secondary prevention, diabetes, adherence

PORTFOLIO DIET

(The Targeted Add-on)

Goal: LDL-C & ApoB lowering

LDL reduction: 15–30%

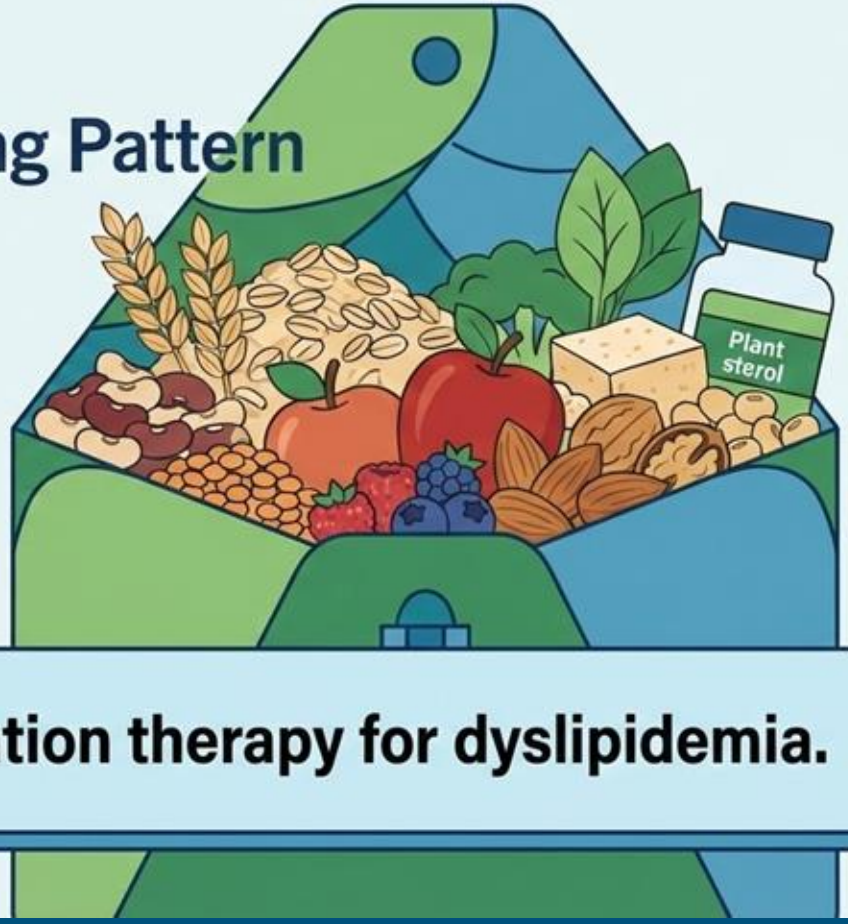
Best for: FH, statin intolerance, LDL above goal

Best Practice

Mediterranean base + Portfolio components

The Portfolio Diet:
An Evidence-Based, Cholesterol-Lowering Eating Pattern

The Portfolio Diet is a plant-forward dietary pattern specifically designed to lower LDL-C and ApoB by combining several foods with independent lipid-lowering effects into one "portfolio."



Think of it as dietary combination therapy for dyslipidemia.

HOW TO FOLLOW THE PORTFOLIO DIET

A 4-Part Dietary Strategy for Lowering Cholesterol (LDL-C & ApoB)

1. VISCOUS FIBER

Target: ≥10–20 g/day

Oats, Beans, Lentils, Apples, Berries

Reduces absorption.

2. PLANT STEROLS/STANOLS

Target: 2 g/day

Fortified Foods, Supplements

Blocks absorption.

3. SOY & PLANT PROTEIN

Target: 50 g/day (Substitute)

Tofu, Soy Milk, Edamame, Legumes

Replaces animal protein.

4. NUTS & SEEDS

Target: 42 g/day (A Handful)

Almonds, Walnuts, Pistachios, Chia Seeds

Healthy fats & fiber.

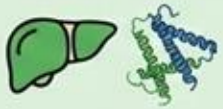
BEST PRACTICE: Combine all 4 components for an additive effect, like a 'dietary combination therapy'. 1 + 2 + 3 + 4 = **MAX LDL REDUCTION**.

The Portfolio Diet: Why it Clinically Matters

SIGNIFICANT LDL-C REDUCTION

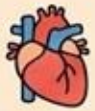
Can lower LDL-C by 20-30%, comparable to starting dose of statins.

REDUCES ApoB



Lowers Apolipoprotein B, a key marker for cardiovascular risk.

IMPROVES CV HEALTH



Lowers blood pressure and reduces inflammation (CRP).

FLEXIBLE & PLANT-FORWARD

Based on combining four cholesterol-lowering food groups.

CLINICAL RELEVANCE, IMPLEMENTATION & PATIENT TALKING POINTS

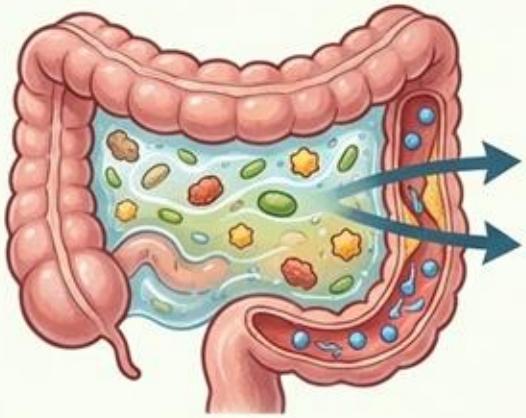
ADDITIVE THERAPY & IMPLEMENTATION

- Effective dietary strategy for dyslipidemia management.
- Can be used as a standalone therapy or additive to medication.
- Additive to statins, ezetimibe & PCSK9 inhibitor therapy.
- Supported by numerous clinical trials and guidelines.
- Addresses residual risk beyond statin therapy.

KEY PATIENT TALKING POINTS

- Primary prevention.
- FH (adjunctive).
- Statin intolerant patients.
- Patients motivated for lifestyle-based risk reduction.

The 4 Components (The Portfolio)



Viscous (Soluble) Fiber

Mechanism:
Reduces cholesterol absorption and bile acid reuptake

Target:
≥10–20 g/day

Best sources:

Oats, barley	Beans, lentils, chickpeas	**Psyllium**	Apples, berries, citrus
			
Oats, barley	Beans, lentils, chickpeas	Psyllium	Apples, berries, citrus

Plant Stanol/Sterols

Target: 2 g/day

Mechanism: Competes with cholesterol for absorption in the gut

Best sources:
Fortified margarines
Fortified orange juice
Fortified yogurt

LDL reduction: 5–10%

Soy and Plant Protein

Target: ~25-50 g/day

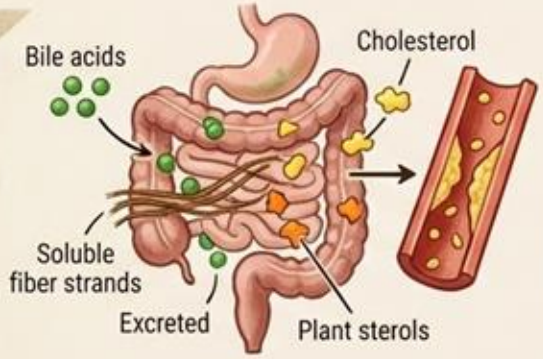
Mechanism:
Replaces animal fat,
Modest LDL receptor upregulation

Sources: Tofu, tempeh, edamame, soy milk, soy yogurt, beans, lentils, pea protein

LDL reduction: 3–5%

Nuts & Seeds: The Power of Plant-Based Fats for Lipid Management

HOW THEY WORK (Mechanism)



Fiber binds bile acids; Sterols block cholesterol absorption. Reduces LDL.

LIPID PROFILE IMPACT

Favorable effects on non-HDL & apoB.

NUTRIENT POWERHOUSE

- **HEALTHY FATS** (MUFA, PUFA, ALA Omega-3)
- **FIBER** (Soluble)
- **PLANT STEROLS**
- **ANTIOXIDANTS** (Vit E, Polyphenols)

Rich in heart-healthy compounds that improve endothelial function & reduce inflammation.

INCORPORATION & SERVING

Enjoy a daily serving.
Add to meals or as a snack.

Key Takeaways

- Lower LDL early
- Measure ApoB and Lower
- Screen Lp(a)
- Manage FH
- Combine lifestyle + medical therapy

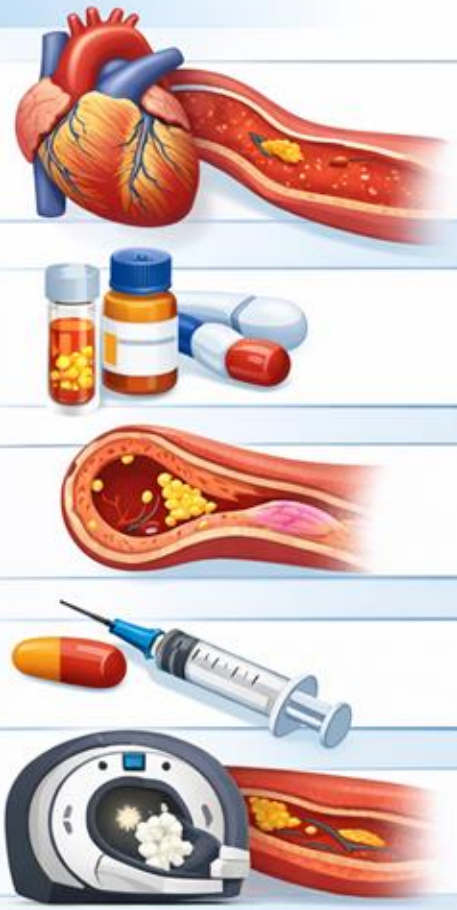
"The Mediterranean diet lowers events; the Portfolio diet lowers LDL. Together, they close the residual risk gap."

- Exercise is Medicine

When to Refer to Preventive Cardiology / Lipid Clinic

Refer patients with ANY of the following:

- **Established ASCVD/CAD** not at **LDL-C or ApoB goal** despite statin ± ezetimibe
- **LDL-C ≥190 mg/dL OR** Family History of FH
- **Statin intolerance** limiting lipid targets
- **Elevated Lp(a) ≥100 nmol/L OR** Family History of Elevated Lp(a)
- **Need for advanced lipid therapy** *(PCSK9 inhibitor, Inclisiran, etc.)*
- **Strong Family History of Premature ASCVD**
- **Severely Elevated** Triglycerides **> 500 mg/dL**
- **CAC Score > 100**



Early referral enables rapid goal attainment, combination therapy, and ASCVD risk reduction.

MISSION CARDIOLOGY

Coltrain

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