2026 ACC/AHA Dyslipidemia Guidelines

Key Updates for Clinical Practice

Published March 13, 2026 | JACC & Circulation

ACC/AHA/AACVPR/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA

The Lipid Hypothesis

Medical theory postulating that there is a link between serum cholesterol levels and cardiovascular disease.

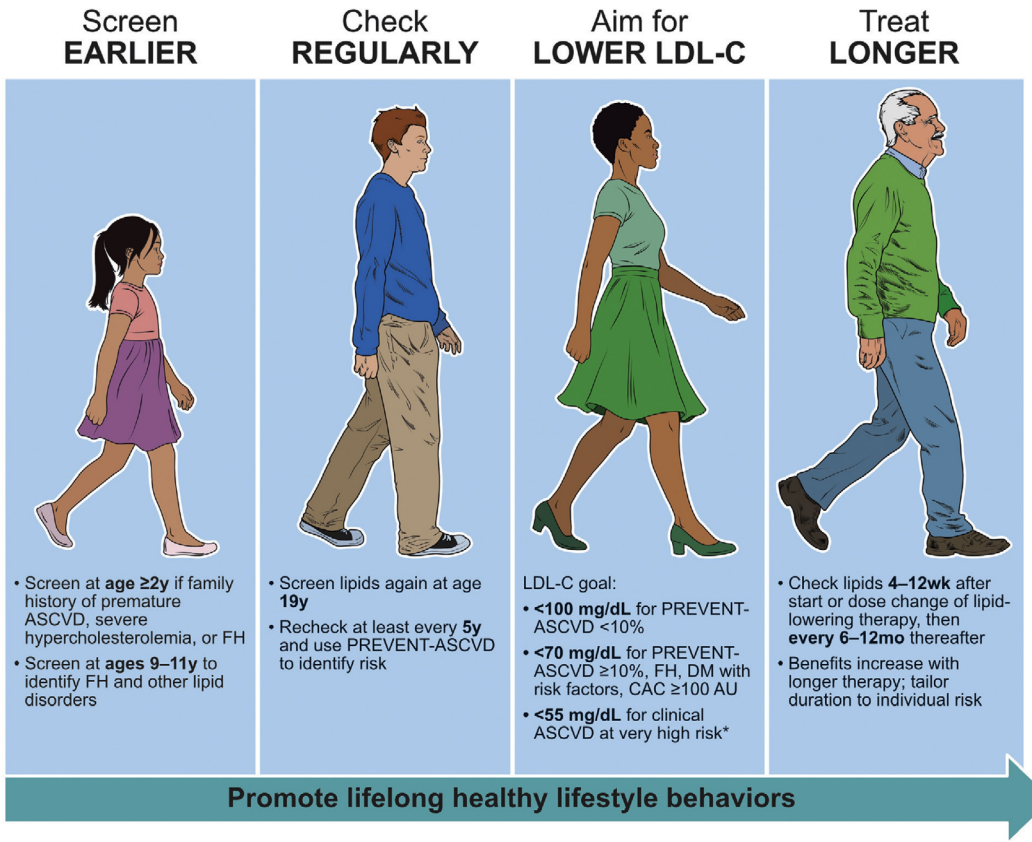
Has been debated since the 1850's.

Until the 1970's, there was debate as to whether elevated levels of serum cholesterol was a cause of coronary heart disease, or a physiological response to coronary heart disease.

These guidelines are not universal. Many sources still consider LDL 130-160 "borderline" and high cholesterol of LDL > 160 and total > 240.

CENTRAL ILLUSTRATION: 2026 Dyslipidemia Guideline-at-a-Glance

Lipid Lowering to Reduce ASCVD Risk



Wiggins BS, et al. JACC. 2026;10.1016/j.jacc.2026.02.4872

Lab Tests for Cholesterol Assessment

2026 guideline recommends universal Lp(a) screening and selective ApoB testing alongside the standard lipid panel

Test	What It Measures	Desirable Level	2026 Guideline Notes
Total Cholesterol	Sum of LDL-C, HDL-C, VLDL-C, and Lp(a)	**<200 mg/dL**	Part of standard lipid panel; screen starting age 9–11
LDL-C	Primary atherogenic lipoprotein; direct or calculated (Friedewald)	**<100 mg/dL**	Primary treatment target; goals: <100, <70, or <55 based on risk
HDL-C	Protective lipoprotein; reverse cholesterol transport	**≥40 mg/dL (M)** **≥50 mg/dL (F)**	Low HDL-C is an ASCVD risk factor; included in PREVENT equations
Triglycerides	Blood fats from diet and liver; marker for TG-rich remnant particles	**<150 mg/dL**	≥150: consider icosapent ethyl if ASCVD/DM + risk factors
Non-HDL-C	Total cholesterol minus HDL-C; captures all atherogenic particles	**<130 mg/dL**	Co-primary target with LDL-C; goals: <130, <100, or <85 by risk
Lipoprotein(a)	Genetically determined atherogenic particle; pro-thrombotic and pro-inflammatory	**<125 nmol/L** **(<50 mg/dL)**	**NEW COR 1: Measure at least once in all adults**
Apolipoprotein B	One ApoB per atherogenic particle (LDL, VLDL, Lp(a)); reflects particle count	**<130 mg/dL** **(<90 if high risk)**	Selective use once LDL-C/non-HDL-C goals met; esp. with TG >200 or DM

Fasting not required for standard lipid panel (non-fasting acceptable); fasting preferred if TG ≥400 mg/dL | Lp(a) is stable over life and only needs to be measured once

LDL-C Treatment Goals: Primary Prevention

Treatment goals are back — absolute LDL-C targets now guide therapy alongside % reduction

Patient Group	LDL-C Goal	Details
Borderline/Intermediate Risk (LDL-C 70–189 mg/dL)	**<100 mg/dL**	PREVENT risk 3–<10%
High Risk (LDL-C 70–189 mg/dL)	**<70 mg/dL**	PREVENT risk ≥10%
LDL-C ≥190 mg/dL (no FH)	**<100 mg/dL**	High-intensity statin + ezetimibe if needed
Heterozygous FH	**<70 mg/dL**	With ≥1 risk factor or subclinical atherosclerosis
Subclinical Atherosclerosis (CAC ≥100 or ≥75th %ile)	**<70 mg/dL**	Intensify LLT based on CAC results
CAC ≥1000 AU	**<55 mg/dL**	Treat as very high-risk equivalent

Biomarkers: Lp(a) and ApoB

Lipoprotein(a)

COR 1: Measure at least once in all adults

- ≥125 nmol/L (50 mg/dL): ~1.4× risk
- ≥250 nmol/L (100 mg/dL): ≥2× risk
- Genetically determined, stable over time
- If elevated: intensify LDL-C lowering
- 1 in 5 people worldwide have elevated Lp(a)

Apolipoprotein B

Selective use for residual risk assessment

- Useful after LDL-C/non-HDL-C goals met
- Especially with elevated TG (>200 mg/dL)
- In diabetes or achieved LDL-C <70 mg/dL
- Confirms atherogenic lipoproteins treated
- Useful in ASCVD, CKD, metabolic conditions

Indications for CAC Scoring

COR 1 recommendation | Use the "R" in the CPR model to Reclassify risk when treatment decisions are uncertain

When to Order CAC

- **Borderline risk (PREVENT 3–<5%):** when clinician–patient discussion is uncertain about starting LLT
- **Intermediate risk (PREVENT 5–<10%):** to refine statin intensity and LDL-C goal
- **Low risk with risk enhancers:** family Hx of premature ASCVD, elevated Lp(a), South Asian ancestry, chronic inflammatory conditions
- **Statin hesitancy:** CAC >0 can motivate adherence; CAC = 0 may allow safe deferral
- **Incidental CAC on chest CT:** any coronary calcium on non-gated imaging should trigger lipid assessment
- **Eligible ages:** men ≥40 years and women ≥45 years

When NOT to Order CAC

- **Established ASCVD:** diagnosis already confirmed; statin therapy is indicated regardless
- **High risk (PREVENT ≥10%):** LLT is already recommended; CAC unlikely to change management
- **LDL-C ≥190 mg/dL or known FH:** high-intensity statin indicated based on LDL alone; CAC adds no decision value
- **Diabetes + age 40–75:** statin is COR 1 regardless; CAC may only help determine statin intensity
- **Serial/repeat CAC:** not recommended to monitor treatment response; CAC may progress despite effective LDL-C lowering
- **Age <40 (men) or <45 (women):** low prevalence of CAC; limited reclassification value in younger adults

CAC = 0 allows safe deferral for ~5 years with lifestyle focus | CAC ≥1000 AU is treated as very high-risk equivalent (LDL-C goal <55 mg/dL)

CAC Scoring for Risk Reclassification

Recommended: Men ≥40 years, Women ≥45 years | COR 1 recommendation

CAC = 0	May defer statin for 5 years	LDL-C Goal **Reassess in 5 years**
CAC 1–99	Favors statin initiation	LDL-C Goal **<100 mg/dL**
CAC 100–299 or ≥75th %ile	Initiate high-intensity statin	LDL-C Goal **<70 mg/dL**
CAC ≥1000	Very high-risk equivalent	LDL-C Goal **<55 mg/dL**

Incidental CAC findings on chest CT should also be incorporated into risk assessment

Updated Risk Categories

Low

<3%

10-yr PREVENT risk

Lifestyle optimization

Borderline

3–<5%

10-yr PREVENT risk

LLT can be considered

Intermediate

5–<10%

10-yr PREVENT risk

LLT should be considered

High

≥10%

10-yr PREVENT risk

LLT recommended

Note: Thresholds recalibrated from PCE — PREVENT risk estimates are generally lower than PCE for the same patient

LDL-C Goals: Secondary Prevention

<55

mg/dL

Very High-Risk ASCVD

Non-HDL-C goal: <85 mg/dL

<70

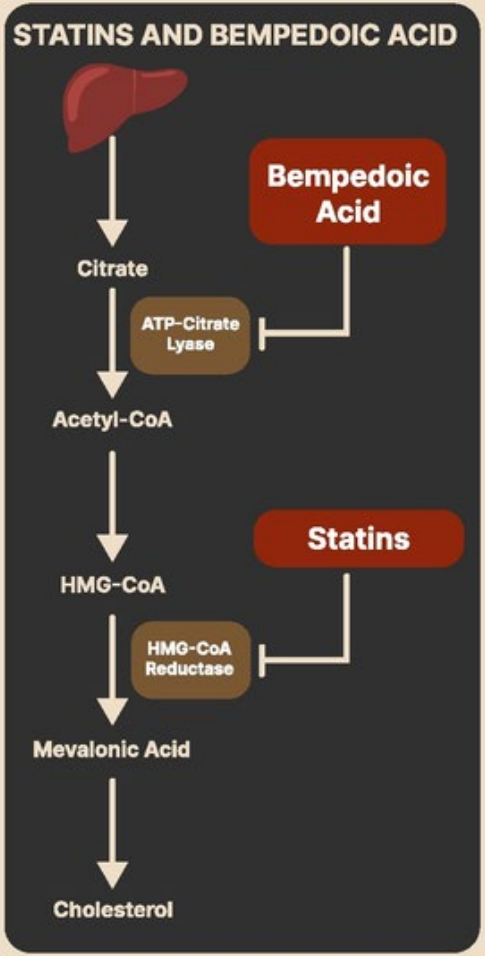
mg/dL

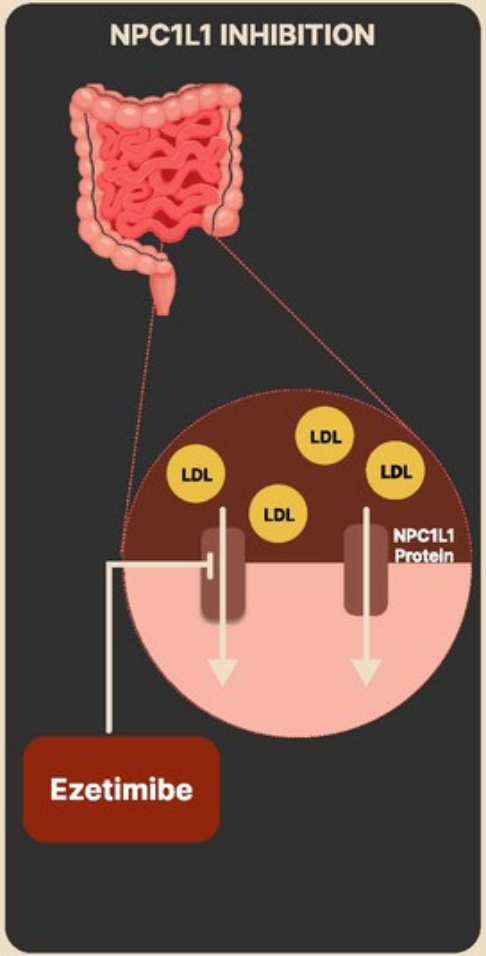
ASCVD Not at Very High Risk

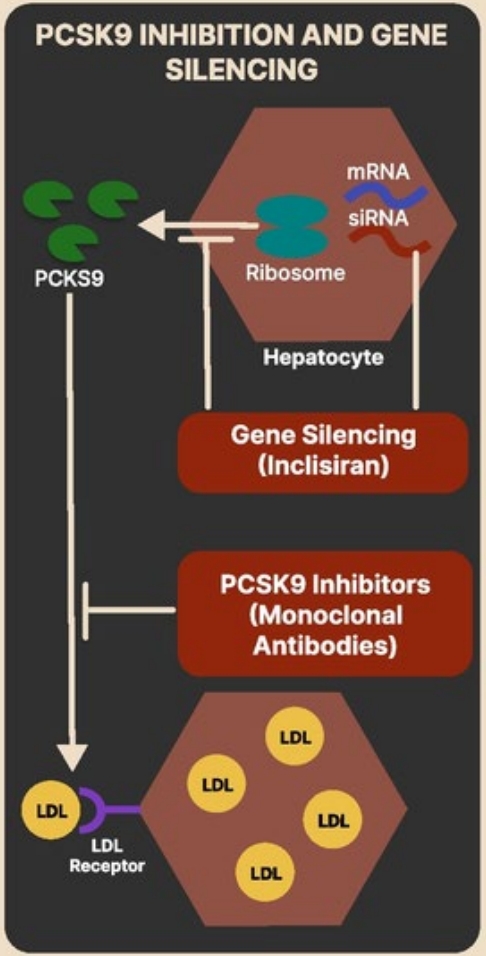
Non-HDL-C goal: <100 mg/dL

Key principle: *"Lower LDL-C for longer results in much greater protection against future heart attack and stroke risk." — Roger S. Blumenthal, MD*

THERAPEUTIC TARGETS FOR LDL-C REDUCTION







Statins

Discovered by Akira Endo in the 1970's.

The first statin (Mevastatin) was developed by Sankyo. Research studies showed the drug caused lymphoma in animal studies. However, data review later showed the animals had received 200x the therapeutic dose.

Merck developed lovastatin (the active ingredient in red yeast rice). Trials stopped when reports came out about mevastatin. They were later restarted, and no increase in cancer was seen. Lovastatin was then approved by the FDA in 1987.

Statin Therapy Recommendations

Primary Prevention

- PREVENT risk 3–<5%: consider LLT
- PREVENT risk 5–<10%: recommend LLT
- PREVENT risk ≥10%: high-intensity statin
- Young adults with LDL-C ≥160: early Rx
- Lifestyle counseling from youth

COR 1 Populations

- Diabetes, ages 40–75: statin therapy
- CKD stage 3–4: statin regardless of LDL
- HIV: statin regardless of LDL-C
- After age 75: shared decision-making
- FH: early aggressive treatment

Secondary Prevention

- High-intensity statin for all ASCVD
- Maximize tolerated statin dose first
- Add non-statin if goal not achieved
- Very high-risk: target <55 mg/dL
- Earlier combination therapy approach

Non-Statin Lipid-Lowering Therapies

Agent	Mechanism	LDL-C ↓	Key Points
Ezetimibe	Cholesterol absorption inhibitor	**~18–25%**	First-line add-on; oral, well-tolerated
Bempedoic Acid	ACL inhibitor (liver-specific)	**~21%**	CLEAR Outcomes: 13% MACE reduction; COR I for statin intolerance
Inclisiran	siRNA targeting PCSK9	**~50%**	Twice-yearly injection; VICTORION trials confirm efficacy
Icosapent Ethyl	Omega-3 (EPA)	**—**	For elevated TG ≥150 mg/dL with ASCVD or diabetes + risk factors

Treatment Escalation Algorithm

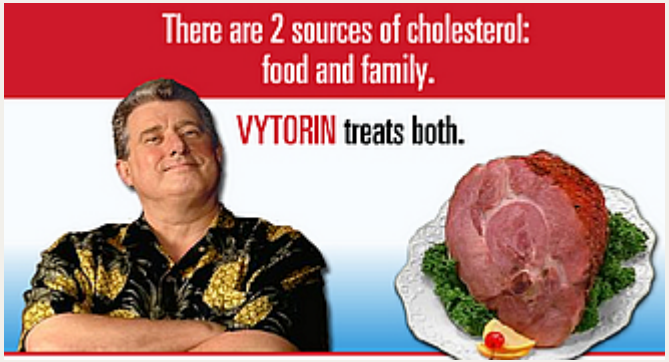
Step 1: Maximize tolerated statin dose → **Step 2:** Add ezetimibe → **Step 3:** Add bempedoic acid or PCSK9i/inclisiran

For statin-intolerant patients: Bempedoic acid (COR I) is now a first-line alternative with proven CV outcomes benefit (CLEAR Outcomes trial)

Ezetimibe (Zetia)

Approved in 2002, inhibits cholesterol absorption in the small intestine.

Lowers cholesterol, and potentially non fatal MI. Limited data that is has any mortality benefit.



Bempedoic Acid (Nexletol)

Approved in 2020, inhibits adenosine triphosphate citrate lyase, an upstream enzyme from HMG Co-A.

Decreased rate of MI, coronary revasc, non fatal MI and stroke to placebo. Similar rates of call cause mortality and overall stroke to placebo.

Main side effects are gout and tendon rupture.

Inclisiran(Leqvio)

Approved in 2020, small interfering RNA (siRNA) that interferes with the translation of the protein for PCSK9.

Available at Valley Infusion Center

Twice yearly infusion.

PCSK9 Inhibitors
Evolocumab (Repath) and Alirocumab (Praulent)

Monoclonal antibodies to PCSK9.

PCSK9 degrades the LDL receptor on hepatocytes. By interfering with PCSK9, there is higher LDL receptor expression and lower serum LDL.

PCSK9 is upregulated in the presence of statin therapy. This would indicate a complimentary effect of PCSK9 inhibitor with statin.

Reduction in MI and mortality vs placebo, as well as suggested additive benefit with statin.

Development of PCSK9 inhibitors was driven by Amgen, Pfizer, and Regenron/Sanofi. Pfizer dropped their research, thinking this was a non-viable pathway for drug development.

Regenron/Sanofi purchased a priority review voucher from a small biotech in 2014. These vouchers are meant for drugs that can have a great impact on health but have limited market/profitability (tropical disease, rare pediatric disease, etc.). These vouchers can reduce the review time and development costs of the drugs.

Regenron/Sanofi hoped that acquiring a priority review voucher would lead to their produce (alirocumab / Praulent) coming to market first. It did, but only by four months.

Amgen (evolobumab / Repatha) had a patent to antibodies to PCSK9, and sued for patent infringement. The Supreme Court ruled unanimously in May, 2023, that an entire biological process cannot be patented. Amgen can maintain the patent to their drug, but patents for any antibody to PCSK9 (of which there are potentially millions) were invalidated.

Key Takeaways

1. Treat earlier — lifestyle counseling from youth, pharmacotherapy for young adults with LDL-C ≥160 mg/dL or FH
2. Use PREVENT equations (not PCE) for 10-year and 30-year risk; apply the CPR model to personalize decisions
3. Absolute LDL-C goals are restored: <100, <70, or <55 mg/dL based on risk category
4. Measure Lp(a) at least once in all adults (COR 1); use ApoB selectively for residual risk
5. Leverage new therapies — bempedoic acid, inclisiran, alirocumab, evolobumab
6. CAC scoring reclassifies risk when treatment decisions are uncertain (COR 1 for eligible adults)

Source: 2026 ACC/AHA/Multisociety Guideline on the Management of Dyslipidemia | JACC, March 2026