CME OUTFITTERS

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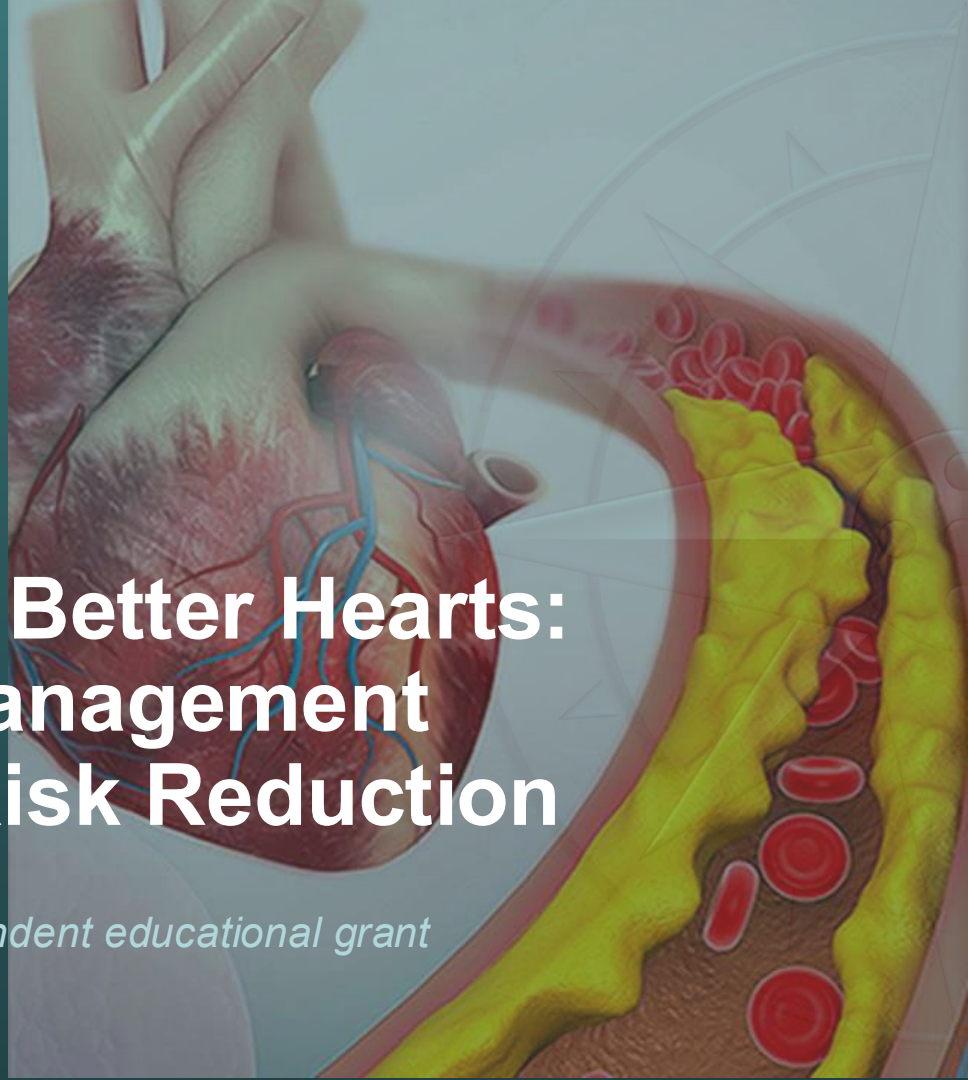
Breaking Barriers to Better Hearts: Optimizing LDL-C Management for Cardiovascular Risk Reduction



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Nisha D’Souza, MD, MPH

Assistant Professor
Department of General Internal Medicine
University of Florida College of Medicine
Gainesville, FL

Eric Dietrich, PharmD, BCACP

Clinical Associate Professor
University of Florida College of Pharmacy
Gainesville, FL

Dhaval Naik, DO

Assistant Professor
Department of Medicine, Division of Cardiovascular Medicine
University of Florida (UF) Health
Gainesville, FL

CME OUTFITTERS

LEARNING OBJECTIVE 1

Apply current guideline recommendations for ASCVD risk assessment to appropriate patients

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LEARNING OBJECTIVE 2

Identify the importance of achieving recommended LDL-C targets as a means of managing ASCVD in intermediate- and high-risk patients

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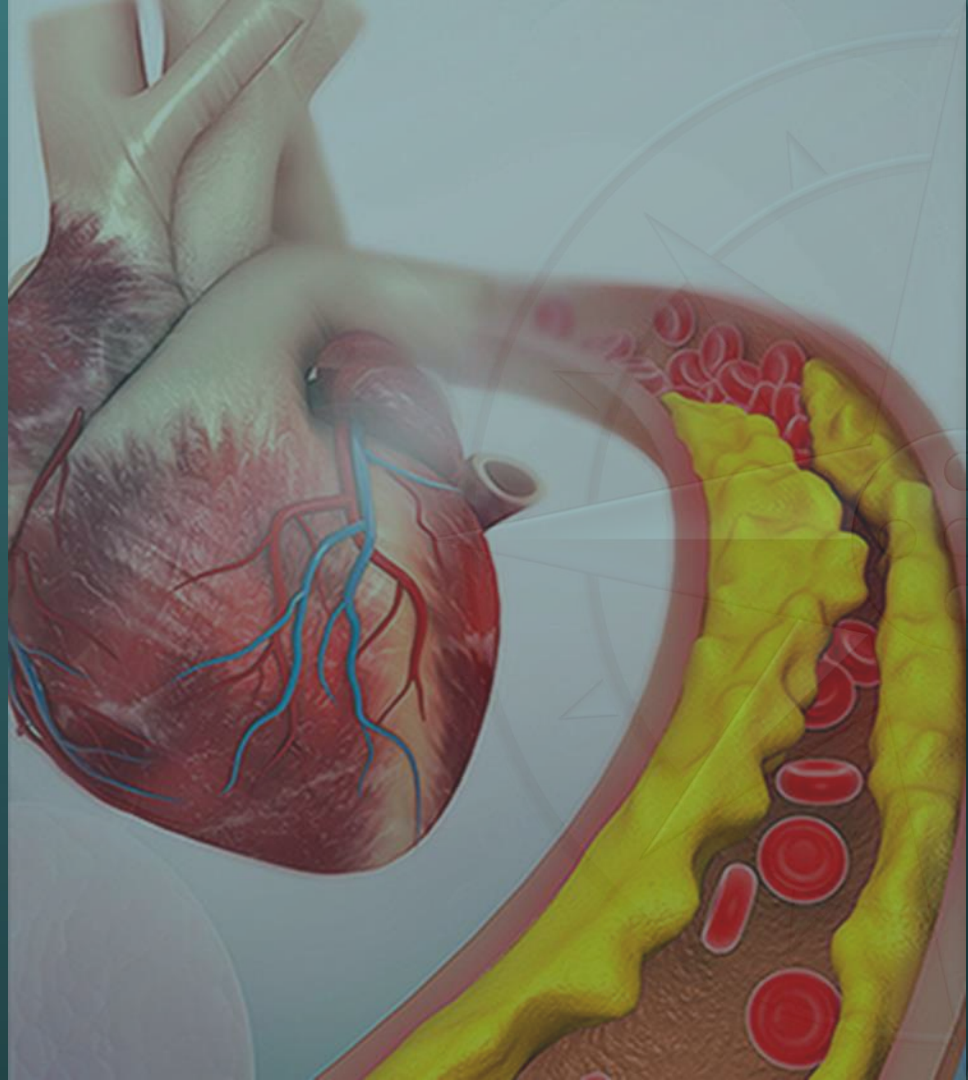
LEARNING OBJECTIVE 3

Implement strategies designed to optimize therapeutic decision-making among intermediate- and high-risk patients who may require add-on therapy to achieve LDL-C treatment goals

PART 1

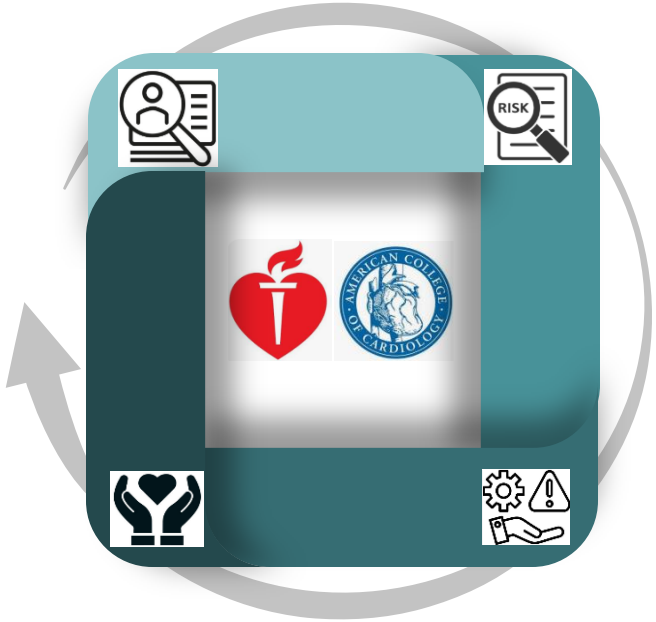
ASCVD Risk Assessment



ASCVD = atherosclerotic cardiovascular disease.

Established Approaches to ASCVD Risk Assessment: 2019 ACC/AHA Guidelines

1 IDENTIFY ELIGIBLE PATIENTS
- Age 40-75
- LDL-C 70-189 mg/dL
- No clinical ASCVD



2 ESTIMATED 10-YEAR ASCVD RISK
- Low Risk: <5%
- Borderline Risk: 5%-<7.5%
- **Intermediate Risk*: ≥7.5%-<20%**
- High Risk: ≥20%

3 REFINE RISK (IF UNCERTAIN)
- Risk-enhancing factors: CKD, inflammatory disease, family history
- Consider CAC in borderline/intermediate risk

4 MATCH THERAPY TO RISK
- Lifestyle therapy
- Moderate-intensity statin
- High-intensity statin
- Escalate based on LDL-C response

***Intermediate risk** is where risk enhancers and CAC matter most.

ACC = American College of Cardiology; AHA = American Heart Association; CAC = coronary artery calcium; CKD = chronic kidney disease; LDL-C = low-density lipoprotein cholesterol.

Arnett DK, et al. *Circulation*. 2019;140(11):e596-e646.

How Prior ACC/AHA Risk Categories Inform Clinical Decisions

Low Risk: <5%

- Emphasize lifestyle optimization
- Routine pharmacologic therapy typically not recommended
- Reassess risk periodically

Borderline Risk: 5%-<7.5%

- Consider risk-enhancing factors during clinician–patient discussion
- Statin therapy may be appropriate in selected patients

Intermediate Risk: >7.5%-<20%

- Moderate-intensity statin therapy is generally recommended
- Risk enhancers and CAC scoring can refine treatment decisions

High Risk: ≥20%

- Treat aggressively with high-intensity statin therapy
- Goal: ≥50% LDL-C reduction

Arnett DK, et al. *Circulation*. 2019;140(11):e596-e646.

Established ASCVD Risk-Enhancing Factors

Risk-Enhancing Factors That Inform Treatment Decisions

Clinical Factors

- Family history of premature ASCVD (<55 men, <65 women)
- Persistently elevated LDL-C ≥160 mg/dL
- Chronic kidney disease
- Chronic inflammatory conditions (RA, psoriasis, lupus, HIV)
- Pregnancy-related conditions (preeclampsia, premature menopause)
- High-risk ethnicity (e.g., South Asian ancestry)

Lipids/Biomarkers

- Triglycerides ≥175 mg/dL
- Elevated Lipoprotein(a)
- Elevated apoB
- Elevated hs-CRP
- ABI <0.9

ABI = ankle-brachial index; apoB = apolipoprotein B; HIV = human immunodeficiency virus; hs-CRP = high-sensitivity C-reactive protein; RA = rheumatoid arthritis.

Arnett DK, et al. *Circulation*. 2019;140(11):e596-e646.

Beyond Traditional Risk Assessment: Emerging Contributors to ASCVD Risk

Established and Emerging Biologic Risk Factors

- Lipoprotein(a) and apolipoprotein B
- Chronic inflammatory conditions
- Metabolic dysfunction and insulin resistance

Non-traditional and Environmental Risk Contributors

- Sedentary lifestyle
- Psychosocial stress
- Environmental exposures (e.g., air pollution)
- Social drivers of health (SDoH)

Clinical Implications

- Traditional risk models may underestimate total ASCVD risk
- Risk assessment is increasingly multidimensional and individualized

Bredehorst M, et al. *Front Med (Lausanne)*. 2025;11:1494234. Blumenthal RS, et al. *Circulation*. 2026 Mar 13. [Epub ahead of print].

ASCVD Risk Assessment in Women: Recognizing Female-Specific Risk Enhancers

Female-Specific Risk Enhancers

History of preeclampsia or gestational hypertension

Premature menopause (age <40)

Gestational diabetes or adverse pregnancy outcomes

Implications for Lipid Management

ASCVD risk is often underestimated in women

LDL-C remains a major driver of CV risk in women

Recognition should prompt earlier initiation of lipid-lowering therapy

Arnett DK, et al. *Circulation.* 2019;140(11):e596-e646.

2026 ACC/AHA Updates: Evolving ASCVD Risk Assessment Framework

Updated **2026 ACC/AHA** guidelines

Transition from PCE to **PREVENT™** risk model

Earlier and more precise risk identification

Greater integration of **biomarkers and imaging**

PCE = pooled cohort equations; PREVENT™ = Predicting Risk of cardiovascular disease EVENTs.

Blumenthal RS, et al. *Circulation.* 2026 Mar 13. [Epub ahead of print].

2026 ACC/AHA Guidelines: Implications for ASCVD Risk Assessment

Risk Assessment

- PREVENT™ score replaces PCE
- Risk assessment **starts at age 30 instead of age 40**

New Risk Categories

- Low: <3%
- Borderline: 3%-<5%
- Intermediate: 5%-<10%
- **High: ≥10% (previously ≥20%!)**

New or Emphasized Risk Enhancers

- Lipoprotein(a) measurement at least once in all adults
- hs-CRP recognized as a risk enhancer

Lower thresholds and earlier assessment expand the population eligible for preventive therapy

Blumenthal RS, et al. *Circulation.* 2026 Mar 13. [Epub ahead of print].

2026 ACC/AHA Guidelines: Implications for ASCVD Risk Assessment (cont.)

Primary Prevention: LDL-C Targets by Risk

Borderline/intermediate risk (3%-<10%)

- LDL-C <100 mg/dL
- Non–HDL-C <130 mg/dL

High risk (≥10%)

- LDL-C <70 mg/dL
- Non–HDL-C <100 mg/dL

Imaging

- CAC scoring *SHOULD* be used to guide treatment decisions in intermediate-risk patients
  - Refines risk and guides statin initiation/intensification

Lower thresholds and CAC-guided decision-making expand opportunities for earlier intervention

Blumenthal RS, et al. *Circulation.* 2026 Mar 13. [Epub ahead of print].

Why This Matters

Earlier identification of at-risk patients

Improved risk discrimination (race-agnostic model)

Greater emphasis on:
- Subclinical disease (CAC)
- Biomarkers (lipoprotein[a], hs-CRP)

Greater opportunity to reduce lifetime ASCVD risk

What This Means in Practice

- Initiate risk assessment earlier (age ≥30 with PREVENT™)
- Use risk enhancers and CAC more proactively
- Do not rely on LDL-C alone for risk decisions
- Consider earlier initiation of therapy in at-risk patients

Lloyd-Jones DM, et al. *J Am Coll Cardiol*. 2022;80(14):1366-1418.

Why ASCVD Risk Assessment Falls Short in Clinical Practice

Consequences of Unrecognized or Undocumented Risk

Missed Opportunities for Timely Therapy

- Eligible patients remain untreated
- Delayed treatment → prolonged LDL-C exposure
- Earlier LDL-C reduction = greater lifetime risk reduction

Under-recognition of Risk Enhancers

- CKD, inflammatory disease, metabolic syndrome overlooked
- Elevated Lp(a) or family history missed
- Borderline and/or intermediate risk often undertreated

Inconsistent Implementation

- Variability in applying guideline recommendations
- Overreliance on individual risk factors
- Leads to therapeutic inertia

Documentation Gaps

- Risk scores calculated but not recorded
- Lack of standardized EHR workflows
- Limits decision support and population management

EHR = electronic health record; Lp(a) = lipoprotein(a).

Bredehorst M, et al. *Front Med (Lausanne)*. 2025;11:1494234.

Role of Ancillary Testing in Patients with Intermediate-Risk ASCVD

When to consider CAC

- Adults (age ≥30) with borderline or intermediate ASCVD risk
  - Particularly when treatment decisions are uncertain or discretionary
- LDL-C 70-189 mg/dL
- Consider in younger patients with unclear risk

CAC Score Interpretation

CAC = 0
Low short-term risk; may defer statin (unless high-risk features)

CAC = 1-99
Supports statin therapy (particularly age ≥55)

CAC ≥100 or >75th percentile
high risk; statin therapy recommended

CAC is a guideline-supported tool to guide treatment decisions, particularly in intermediate-risk patients

Kippax Medical Imaging (KMI). 2026. https://kippaxmedicalimaging.com.au/coronary-artery-calcium-score/.
Arnett DK, et al. *Circulation*. 2019;140(11):e596-e646. Arnett DK, et al. *Circulation*. 2019;140(11):e596-e646.

Audience Response

According to the updated 2026 ACC/AHA risk categories, which of the following represents the lowest threshold for what is now considered HIGH 10-year ASCVD risk?

A. 5%
B. 7%
C. 10%
D. 20%
E. I don’t know

Audience Response

According to the updated 2026 ACC/AHA risk categories, which of the following represents the lowest threshold for what is now considered HIGH 10-year ASCVD risk?

A. 5%
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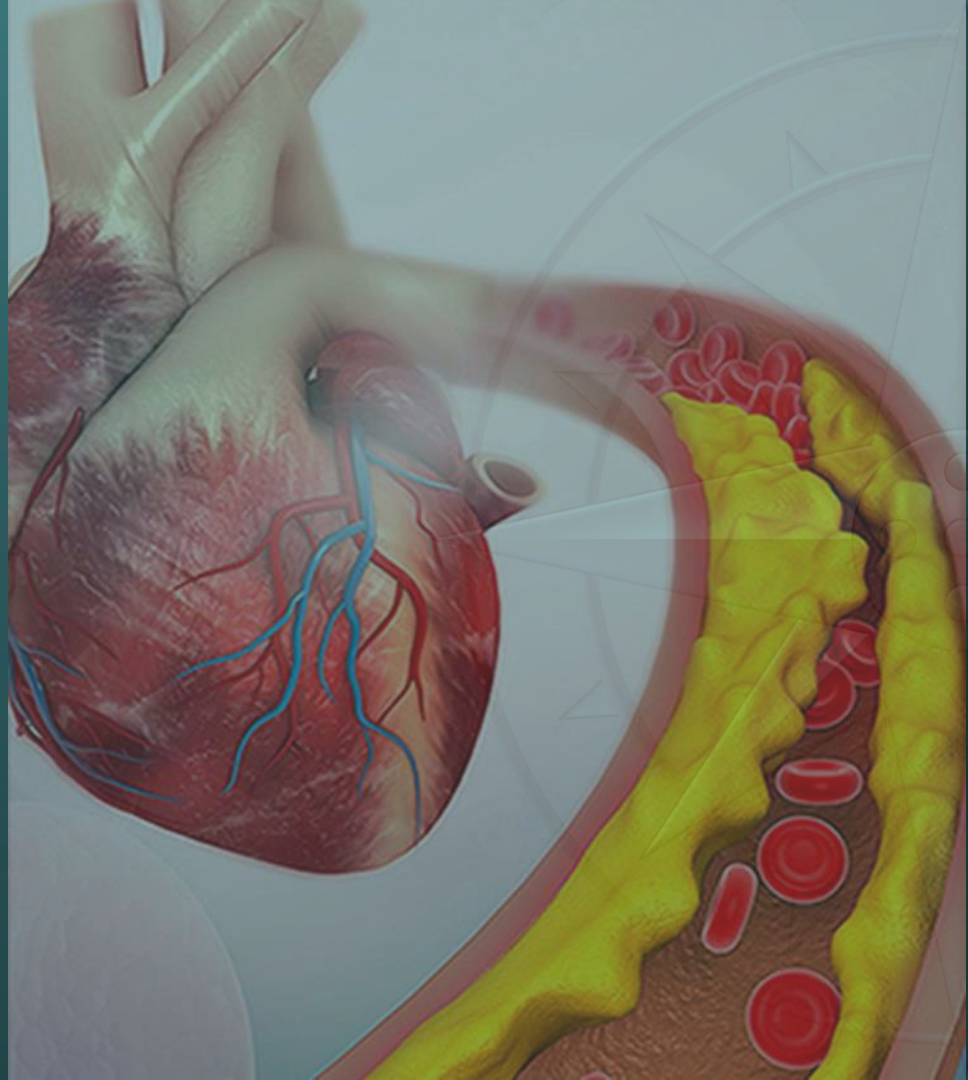
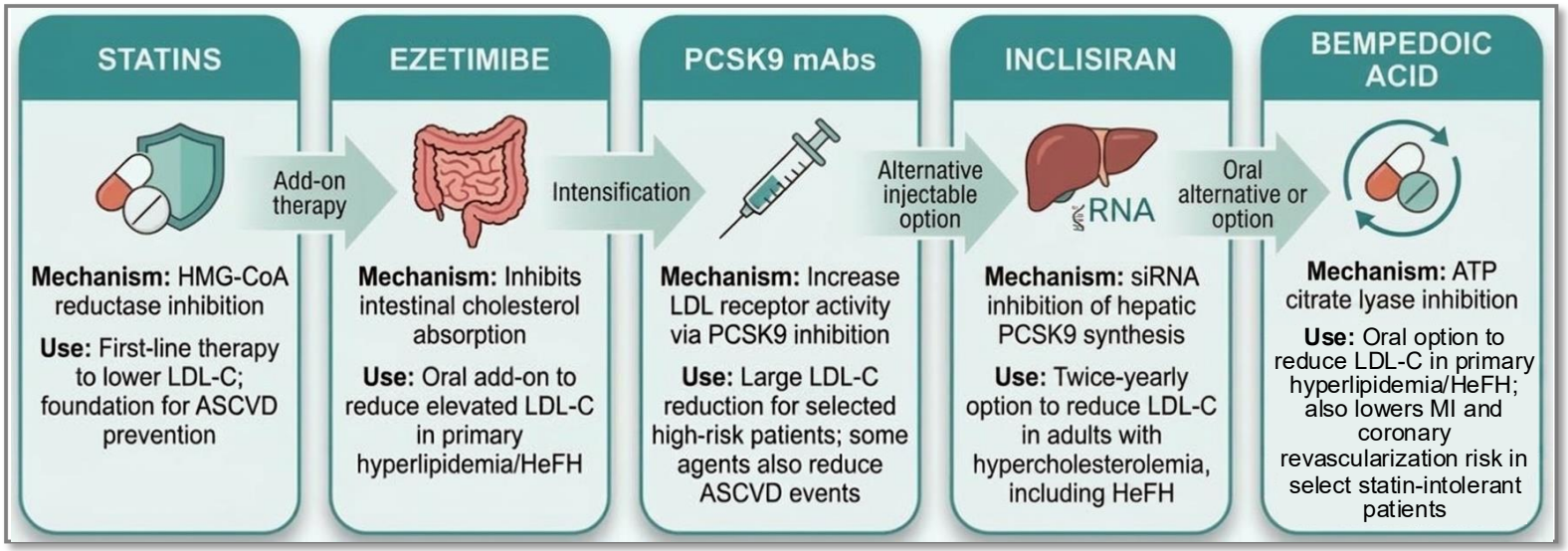
PART 2

Setting LDL-C Goals in ASCVD



The Evolving ASCVD Treatment Landscape: More Options, Better Patient Targeting

Multiple effective therapies now enable deeper LDL-C reduction with options tailored to patient profile and treatment goals



Clinical Implication

Improved risk stratification ensures the right patients receive the right therapy in an increasingly complex treatment landscape

ATP = adenosine triphosphate; HeFH = heterozygous familial hypercholesterolemia; HMG-CoA = 3-hydroxy-3-methylglutaryl coenzyme A; mAbs = monoclonal antibodies; MI = myocardial infarction; siRNA = small interfering RNA.

Blumenthal RS, et al. *Circulation.* 2026 Mar 13. [Epub ahead of print]. Sabatine MS, et al. *N Engl J Med.* 2017;376(18):1713-1722. Cannon CP, et al. *N Engl J Med.* 2015;372(25):2387-2397. Nissen SE, et al. *N Engl J Med.* 2023;388(15):1353-1364.

Novel and Emerging Lipid-Lowering Agents

Drug	Primary and Secondary Lipid Targets	LDL-C Lowering (key late-phase/near-late data)	Non-HDL-C, apoB, Lp(a)
Enlicitide (MK-0616)* Daily oral pill *(oral PCSK9 inhibitor)*	**Primary:** LDL-C **Secondary:** non–HDL-C, apoB, Lp(a)	Phase III CORALreef Lipids: LDL-C reduced **~57%** vs. placebo at 24 weeks; additional Phase III data showed greater LDL-C lowering than bempedoic acid, ezetimibe, or the combination at 8 weeks	Phase III: Significant reductions in non–HDL-C **(~53%),** apoB **(~50%),** and Lp(a) **(~28%)** at 24 weeks
Lerodalcibep monthly SC injection *(PCSK9-binding adnectin fusion)*	**Primary:** LDL-C, non–HDL-C, apoB **Secondary:** Lp(a)	FDA approved in 2025; Phase III LIBerate-HR showed **~56%** placebo-adjusted LDL-C reduction at 52 weeks, with broader LIBerate program data showing ≥**60%** LDL-C reduction in high-risk patients and ≥**50%** in HeFH	Phase III and extension data: clinically meaningful reductions in non–HDL-C, apoB, and Lp(a), with sustained effects through long term
Obicetrapib* Daily oral pill *(CETP inhibitor)*	**Primary:** LDL-C **Secondary:** Reduction in non–HDL-C, apoB, increase in HDL-C	Phase III BROADWAY: **~33%** LDL-C reduction vs placebo at 12 weeks on top of maximally tolerated therapy; Plus ezetimibe (TANDEM): **~48.6%** vs. placebo at 12 weeks	Phase III and pooled RCTs: significant reductions in non–HDL-C, apoB, and Lp(a), with marked HDL-C increase and no excess adverse events

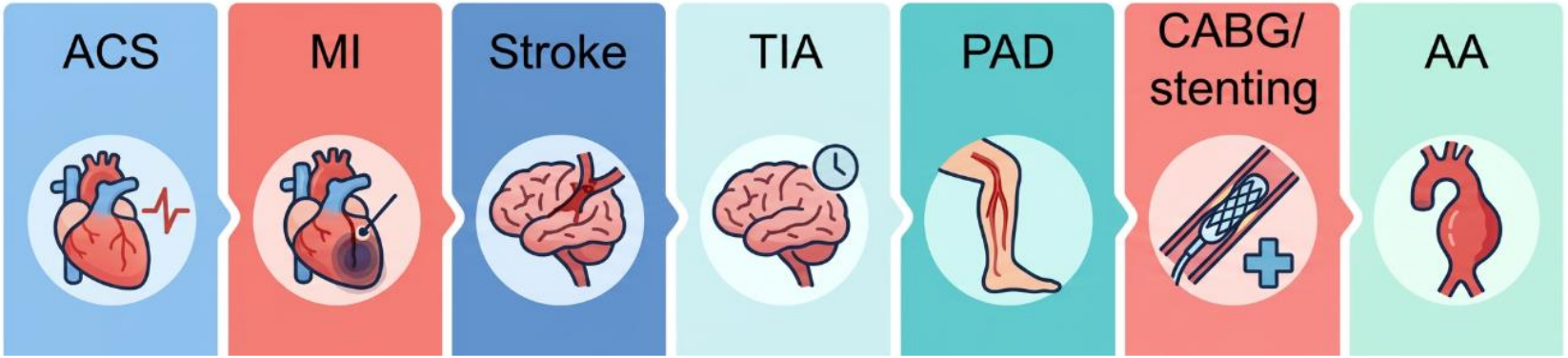
*Not FDA-approved for use in ASCVD.

PCSK9 = proprotein convertase subtilisin/kexin type 9; RCTs = randomized controlled trials; SC = subcutaneous.

Ballantyne CM, et al. *JAMA*. 2026;335(2):129-139. Nicholls SJ, et al. *N Engl J Med*. 2025;393(1):51-61.
Sarraju A, et al. *Lancet*. 2025;405(10491):1757-1768. Klug EQ, et al. *JAMA Cardiol*. 2024;9(9):800-807.

Why LDL-C Reduction Matters Across the Risk Spectrum

Cumulative exposure to atherogenic lipoproteins drives ASCVD risk over time



LDL-C reduction reduces ASCVD events across risk groups

Lower earlier; lower longer; lower risk

AA = aortic aneurysm; ACS = acute coronary syndromes; CABG = coronary artery bypass grafting; PAD = peripheral arterial disease; TIA = transient ischemic attack.

Arnett DK, et al. *Circulation*. 2019;140(11):e596-e646. Blumenthal RS, et al. *Circulation*. 2026 Mar 13. [Epub ahead of print].

Evidence That Lowering LDL-C Reduces ASCVD Risk

Therapy	Typical Clinical Use	Approximate LDL-C Reduction	Evidence for ASCVD Risk Reduction
Statins	First-line for ASCVD, high risk, LDL-C ≥190	~30%-50%	Robust randomized-trial and meta-analysis evidence demonstrating reduction in MACE per mmol/L LDL-C reduction (Cholesterol Treatment Trialists' [CTT] Collaboration)
Ezetimibe	First add-on to statin; statin intolerance	~15%-25% (additional)	Incremental reduction in ASCVD events when added to statin therapy (IMPROVE-IT)
PCSK9 (mAbs)	High/very high risk not at goal; large LDL-C gap	~50%-60%	Significant reduction in MACE in patients with high-risk ASCVD (FOURIER, ODYSSEY OUTCOMES); robust LDL-C lowering in Phase III studies (LIBerate-HR, LIBerate program)
Bempedoic acid	Statin intolerance; oral add-on	~15%-25%	Reduced MACE in statin-intolerant patients (CLEAR Outcomes)
Inclisiran (siRNA)	Adherence-friendly injectable; LDL-C above goal	~50%	Sustained LDL-C reduction; CV outcomes trials ongoing (no completed outcomes data to date)

Greater LDL-C reduction → greater ASCVD risk reduction

MACE = major adverse cardiovascular events.

Blumenthal RS et al. *Circulation*. 2026 Mar 13. [Epub ahead of print]. Cannon CP, et al. *N Engl J Med*. 2015;372(25):2387-2397.
Nissen SE, et al. *N Engl J Med*. 2023;388(15):1353-1364. Sabatine MS, et al. *N Engl J Med*. 2017;376(18):1713-1722.
Klug EQ, et al. *JAMA Cardiol*. 2024;9(9):800-807.

Audience Response

A 62-year-old man with established ASCVD is on high-intensity statin therapy. His LDL-C remains 78 mg/dL. Based on current evidence and guidelines, what is the most appropriate next step?

A. Continue current therapy and reassess in 1 year
B. Reduce statin dose due to diminishing returns
C. Add ezetimibe to further lower LDL-C
D. Discontinue statin and initiate non-statin therapy
E. I don’t know

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LDL-C Targets and Treatment Intensity by Risk (2026 ACC/AHA)

Risk Category	LDL-C Goal	Treatment Approach
Very high risk (ASCVD)	<55 mg/dL	High-intensity statin; add ezetimibe; → add PCSK9 inhibitor if needed; consider additional non-statin therapies
Secondary prevention	<70 mg/dL	High-intensity statin; add ezetimibe and/or PCSK9 inhibitor as needed to reach goal
Primary prevention: high risk	<70 mg/dL	High-intensity statin; add ezetimibe or PCSK9 inhibitor if LDL-C remains ≥70 mg/dL despite statin therapy
Primary prevention: intermediate risk	**<100 mg/dL**	**Moderate-intensity statin; use CAC and risk enhancers to guide statin initiation and intensification**
Severe hypercholesterolemia (LDL ≥190)	≥50% LDL-C reduction and <100 mg/dL	High-intensity statin; add ezetimibe and/or PCSK9 inhibitor as needed

Intermediate risk is where risk enhancers and CAC most influence treatment decisions

Blumenthal RS, et al. *Circulation.* 2026 Mar 13. [Epub ahead of print].

Translating ASCVD Risk Into Treatment Decisions

Low-Risk	Intermediate-Risk	High/Very High-Risk

• Emphasize lifestyle therapy
• Reassess risk over time
	• **Clinical decision point**
	  • Consider statin initiation based on overall risk
	  • Use risk enhancers and CAC to refine decision
	  • Reclassify risk to guide treatment vs. deferral
		• Treat early and intensively
		• Add non-stain early therapy if needed
		  • Aim for rapid LDL-C reduction

Intermediate risk is where individualized decision-making has the greatest impact

Blumenthal RS, et al. *Circulation*. 2026 Mar 13. [Epub ahead of print].

Statins as First-Line Therapy: Foundation of LDL-C Lowering

Core Role

- First-line therapy for **primary and secondary prevention**
- Foundation of therapy before adding non-statin agents

How to Use Statins in Practice

- Select **intensity based on ASCVD risk**
- Aim for:
- **≥50% LDL-C reduction** in high/very high risk
- Reassess LDL-C in **4-12 weeks** after initiation or dose adjustment

When Statins Are Not Enough

- LDL-C remains above goal despite **maximally tolerated statin**
- High or very high-risk patients → consider **early combination therapy**

Clinical Considerations

- Use **maximally tolerated statin dose**
- Address **adherence and statin intolerance**
- Do not delay escalation in **higher-risk patients**

Statins are the foundation of therapy—
but are often insufficient alone to achieve LDL-C goals

Blumenthal RS, et al. *Circulation*. 2026 Mar 13. [Epub ahead of print].

When and Why to Add Non-statin Therapy

Clinical Role of Non-statin Therapy

- **Add-on therapy** to achieve LDL-C targets
- Initiate when statin alone is insufficient
- Use as **alternative in statin intolerance**

Evolving Treatment Paradigm (2026 perspective)

- Greater emphasis on **earlier combination therapy**
- Movement away from prolonged stepwise escalation
- Focus on achieving **LDL-C targets efficiently**

How to Use Non-Statin Therapies in Practice

- **Ezetimibe**
  - First-line add-on to statin
  - Modest additional LDL-C reduction
- **PCSK9 mAbs**
  - For patients requiring substantial LDL-C reduction
  - Appropriate in high/very high risk
- **Inclisiran (siRNA)**
  - Injectable LDL-C–lowering option, especially when infrequent dosing may help adherence
- **Bempedoic acid**
  - Oral option for additional LDL-C lowering or for statin intolerance

Non-statin therapies are essential to achieving lower LDL-C targets in higher-risk patients

Blumenthal RS, et al. *Circulation.* 2026 Mar 13. [Epub ahead of print]. Cannon CP, et al. *N Engl J Med.* 2015;372(25):2387-2397.
Nissen SE, et al. *N Engl J Med.* 2023;388(15):1353-1364. Sabatine MS, et al. *N Engl J Med.* 2017;376(18):1713-1722.

Addressing Residual ASCVD Risk Beyond LDL-C

Icosapent ethyl

- Targets triglyceride-related residual risk beyond LDL-C

Who to Consider

Established ASCVD or high-risk patients

On maximally tolerated statin

Triglycerides ≥150 mg/dL

Implications for Lipid Evidence: REDUCE-IT

~25% relative risk reduction in MACE; reduced CV death (4.3% vs. 5.2%)

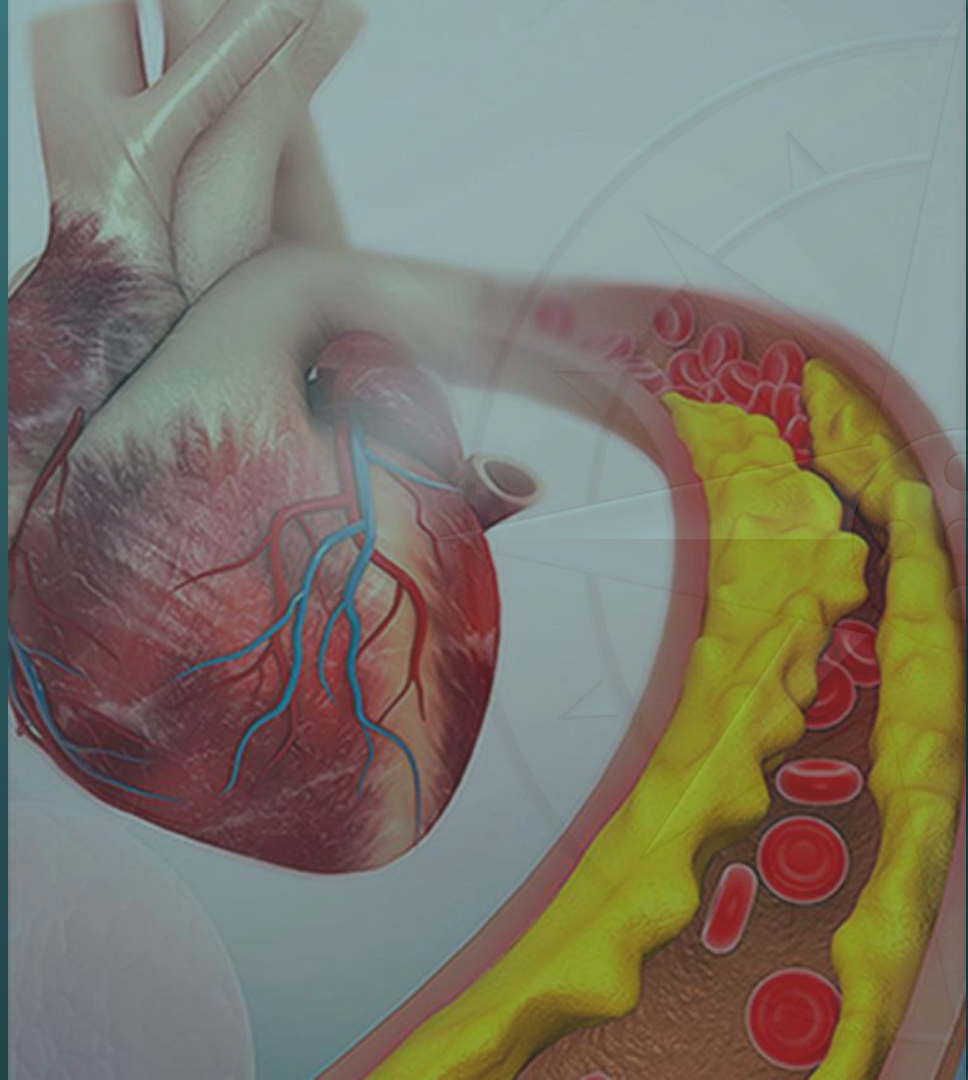
Benefit on top of statin therapy

Not driven by LDL-C lowering → targets residual risk

Bhatt DL, et al. *N Engl J Med.* 2019;380(1):11-22.
Icosapent ethyl [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/202057s035lbl.pdf.

PART 3

Achieving LDL-C Goals in ASCVD



Commonly Used Statins for ASCVD Risk Reduction

Statin	Intensity	FDA-Labeled Use	Key Safety Considerations	Practical Notes
Atorvastatin	Moderate-High	LDL-C lowering; CV risk reduction in adults with CHD or multiple CHD risk factors	Myalgia **3.5%**; persistent transaminase elevations $> 3 \times$ ULN **0.7%** overall	Preferred high-intensity statin
Rosuvastatin	Moderate-High	LDL-C lowering; CV risk reduction in selected higher-risk adults without established CHD	Myalgia **2.8%**; transaminase elevations $> 3 \times$ ULN **1.1% vs. 0.5% placebo**	High potency; fewer drug interactions
Simvastatin	Low-Moderate	LDL-C lowering; CHD mortality/event risk reduction in selected high-risk patients	Label highlights myopathy/rhabdomyolysis risk, especially with interacting drugs and 80 mg dosing; myalgia led to discontinuation in **0.1%**	Less favored when drug interaction risk is high
Pravastatin	Low-Moderate	LDL-C lowering; MI/revascularization/CV mortality risk reduction in selected patients	Myalgia **2.3% vs. 1.2% placebo**; ALT increased **2.9% vs. 1.2% placebo**	Useful with polypharmacy or interaction concerns
Pitavastatin	Moderate	LDL-C lowering in primary hyperlipidemia or mixed dyslipidemia	Myalgia **1.9%-3.1% by dose vs. 1.4% placebo**	Alternative when interactions or intolerance occur

CHD = coronary heart disease.

Atorvastatin [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/020702s081lbl.pdf.
Rosuvastatin [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/021366s046lbl.pdf.
Simvastatin [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/019766s102lbl.pdf.
Pravastatin [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/019898s070lbl.pdf.
Pitavastatin [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/022363s022lbl.pdf.

Commonly Used Non-statin LDL-C–Lowering Therapies

Therapy	Route	FDA-Labeled Use	Key Safety Considerations	Practical Notes
Ezetimibe	Oral	LDL-C lowering alone or with statin when additional lowering is needed	URTI **4.3%**, diarrhea **4.1%**, arthralgia **3.0%**, sinusitis **2.8%**, pain in extremity **2.7%**, fatigue **2.4%**	First-line add-on; oral and well tolerated
Alirocumab	SC	LDL-C lowering in primary hyperlipidemia; CV risk reduction in adults with established CVD	Myalgia **6.0% vs. 5.6% placebo**; hypersensitivity **8.6% vs. 7.8% placebo**; allergic discontinuation **0.6% vs. 0.2% placebo**	Substantial LDL-C reduction
Evolocumab	SC	LDL-C lowering in primary hyperlipidemia; CV risk reduction in adults with established CVD	Nasopharyngitis **10.5%**, URTI **9.3%**, influenza **7.5%**, back pain **6.2%**, injection-site reactions **5.7%**	Potent LDL-C lowering; useful when LDL-C gap to goal is large
Inclisiran	SC	LDL-C lowering in adults with ASCVD or HeFH needing additional LDL-C reduction	Injection-site reactions **8% vs. 2% placebo**; arthralgia **5% vs. 4% placebo**; bronchitis **4% vs. 3% placebo**	Twice-yearly maintenance dosing may help adherence
Bempedoic acid	Oral	Adjunct to diet and other LDL-C–lowering therapy to reduce LDL-C in indicated adults	Common label-reported AEs: hyperuricemia, renal impairment, anemia, elevated liver enzymes, muscle spasms, gout, cholelithiasis	Oral option for additional LDL lowering

AEs = adverse events; HeHF = heterozygous familial hypercholesterolemia; URTI = upper respiratory tract infection.

Alirocumab [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/125559s039lbl.pdf.
Evolocumab [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/125522s043lbl.pdf.
Inclisiran [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/214012s016lbl.pdf.
Bempedoic acid [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2026/211616s026lbl.pdf.
Ezetimibe [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/021445s042lbl.pdf.

From Goals to Achievement: Closing the Gap

Many patients fail to reach LDL-C targets

Treatment gaps are driven by:

Under-treatment

Perceived statin intolerance

Delayed intensification

System-level barriers

Setting goals is not enough—active management is required

Blumenthal RS, et al. *Circulation*. 2026 Mar 13. [Epub ahead of print]. Virani SS, et al. *Circulation*. 2023;148(9):e9-e119.

LDL-C Monitoring and When to Intensify Therapy

LDL-C Screening

- Every 4-6 years in adults age ≥20
  - More frequently with risk factors, family history, or borderline/intermediate risk
- 4-12 weeks after therapy initiation or change
- Every 3-12 months thereafter

Monitor

- Adherence
- Response to therapy
- Need for intensification
- Adverse effects/tolerability

When to Intensify Therapy

- LDL-C above goal despite maximally tolerated therapy
- High- or very high-risk patients not at target
- **≥30%-50% LDL-C reduction not achieved**
- Risk enhancers or CAC support escalation

Blumenthal RS, et al. *Circulation*. 2026 Mar 13. [Epub ahead of print].

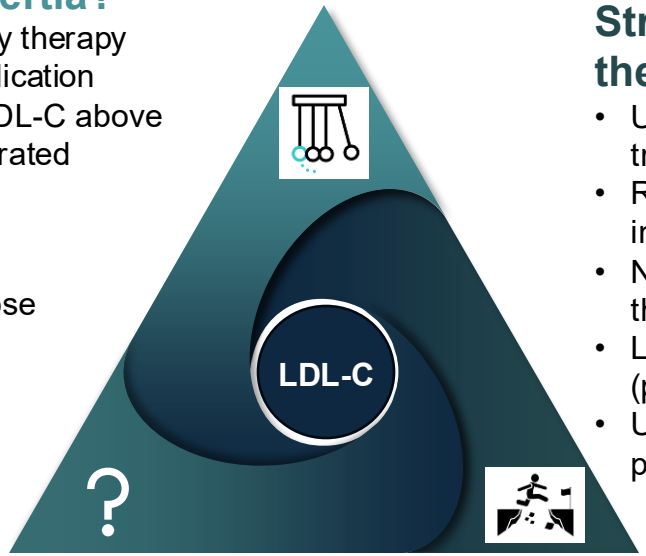
Overcoming Therapeutic Inertia in LDL-C Management

What is therapeutic inertia?

- Failure to initiate or intensify therapy despite guideline-based indication
- Common in patients with LDL-C above goal despite maximally tolerated therapy

Why does it happen?

- Perception that LDL-C is “close enough”
- Concerns about AEs or tolerability
- Time constraints / competing priorities
- Lack of follow-up or monitoring systems



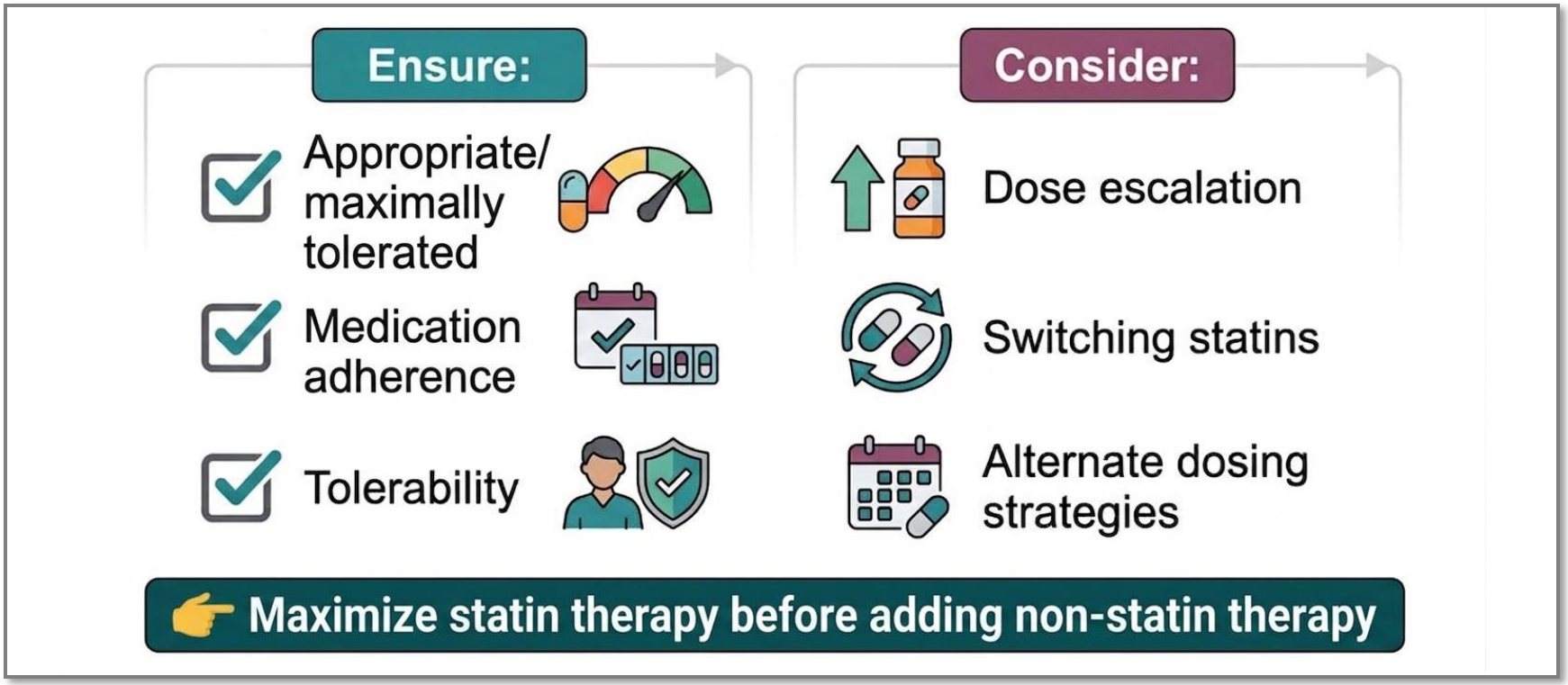
Strategies to overcome therapeutic inertia

- Use risk-based thresholds to trigger action
- Reassess LDL-C at defined intervals (4-12 weeks)
- Normalize early combination therapy in higher-risk patients
- Leverage team-based care (pharmacists, APPs)
- Use EHR prompts / treatment pathways

APPs = advanced practice providers.

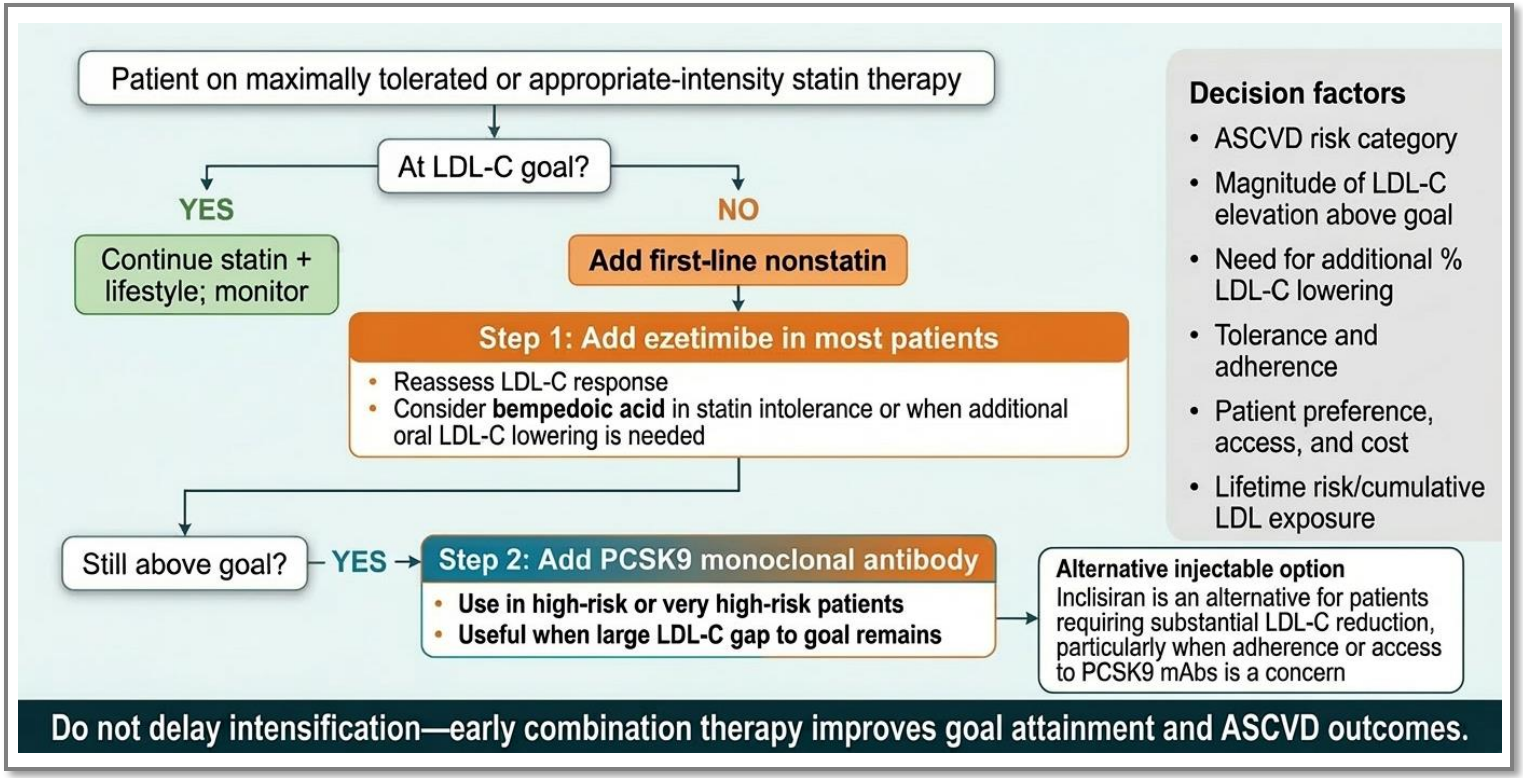
Virani SS, et al. *Circulation*. 2023;147(8):e93-e621. Bredhorts M, et al. *Front Med (Lausanne)*. 2025;11:1494234.
Lloyd-Jones DM, et al. *J Am Coll Cardiol*. 2022;80(14):1366-1418.

Optimizing Statin Therapy Before Escalation



Blumenthal RS, et al. *Circulation*. 2026 Mar 13. [Epub ahead of print]. Lloyd-Jones DM, et al. *J Am Coll Cardiol*. 2022;80(14):1366-1418.

When to Add Non-statin Therapy: 2026 ACC/AHA Risk-Based Approach



In high- and very high-risk patients, consider earlier combination therapy rather than prolonged stepwise escalation

Blumenthal RS, et al. *Circulation.* 2026 Mar 13. [Epub ahead of print]. Lloyd-Jones DM, et al. *J Am Coll Cardiol.* 2022;80(14):1366-1418.

Audience Response

A 68-year-old woman with ASCVD is on maximally tolerated statin therapy and ezetimibe. Her LDL-C remains above goal. What is the most appropriate next step?

A. Continue current therapy and reassess in 6 months
B. Add a PCSK9 inhibitor
C. Discontinue statin due to lack of goal attainment
D. Focus on lifestyle modification alone
E. I don’t know

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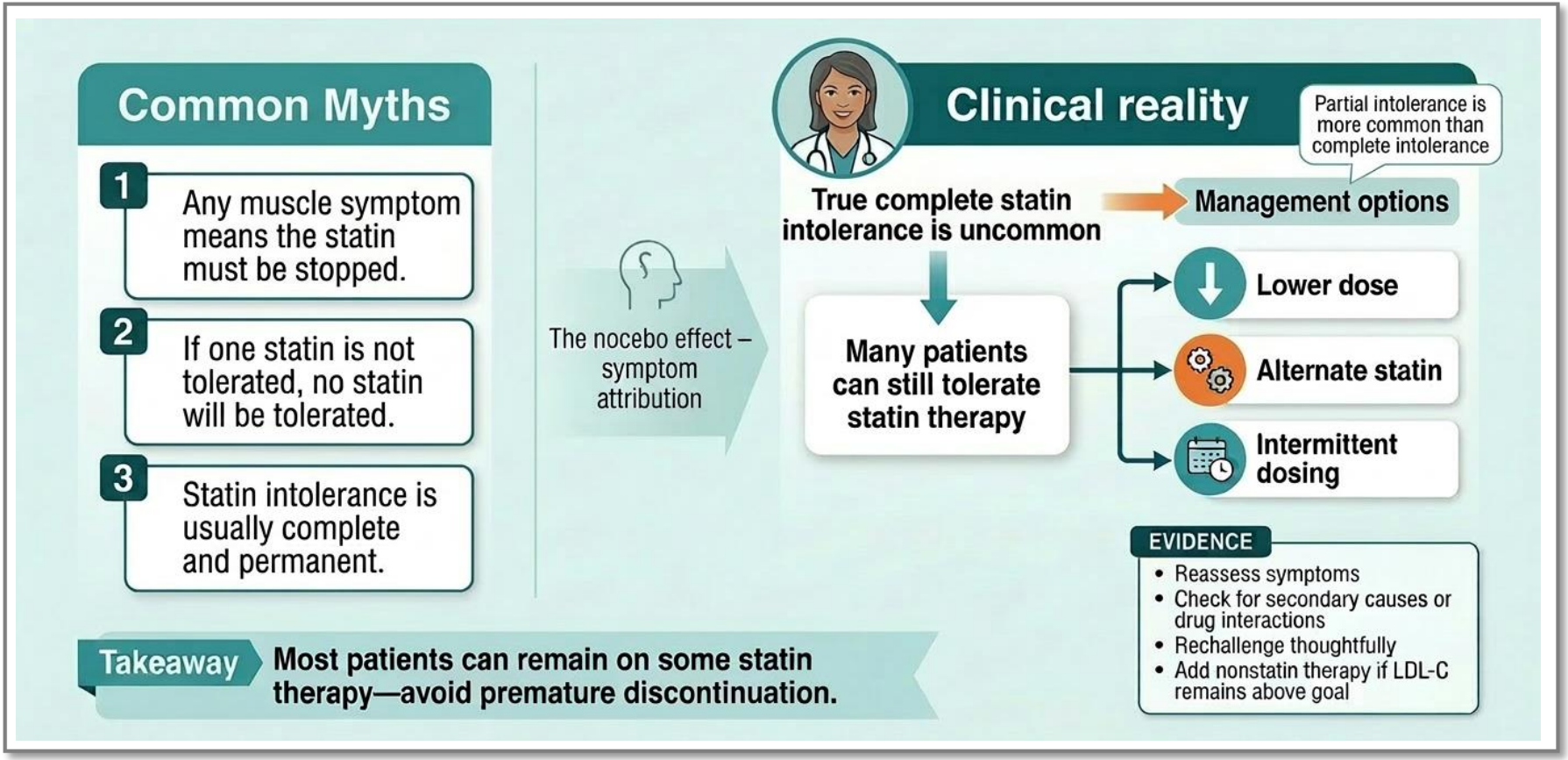
Statin Intolerance: Myths vs. Clinical Reality



Stroes ES, et al. *Eur Heart J*. 2015;36(17):1012-1022. Newman CB, et al. *Arterioscler Thromb Vasc Biol*. 2019;39(2):e38-e81.
Nissen SE, et al. *N Engl J Med*. 2016;375(22):2159-2160.

Impact of Social Drivers of Health on LDL-C Goal Attainment

Key Barriers

- Medication cost and insurance coverage
- Limited access to specialty therapies (e.g., PCSK9 inhibitors)
- Low health literacy and patient understanding
- Transportation and follow-up limitations
- Structural inequities in care delivery

Clinical Implications

- Reduced medication adherence
- Delayed therapy initiation or intensification
- Lower likelihood of achieving LDL-C goals
- Persistent disparities in ASCVD outcomes

Addressing SDoH is essential to improving LDL-C goal attainment and reducing ASCVD risk

Havranek EP, et al. *Circulation*. 2015;132(9):873-898. Khan SU, et al. *J Am Coll Cardiol*. 2022;79(12):1205-1213.

Optimizing LDL-C Management Requires Shared Decision-Making

- Recognize barriers to care, including cost, access, and health literacy
- Avoid labeling patients as “noncompliant”
- Review prior therapy use, tolerability, and concerns
- Address patient questions about statins and non-statin options
- Incorporate patient preferences through open, bidirectional communication

Effective LDL-C management depends on evidence-based therapy, patient preferences, and sustained team-based care

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Put information into action!

Takeaways from this program can be implemented into your practice to improve patient care.

- **Improve clinician confidence by ≥20%** in applying 2026 ACC/AHA guideline recommendations and clinical trial evidence to individualized ASCVD risk and LDL-C management.
- **Increase appropriate LDL-C monitoring and follow-up by ≥25%**, including reassessment within 4-12 weeks after therapy initiation or intensification.
- **Increase appropriate use of non-statin therapy by ≥20%** in patients not at LDL-C goal despite maximally tolerated statin therapy.
- **Increase achievement of guideline-recommended LDL-C targets by ≥15%-20%** in intermediate-, high-, and very high-risk patients.
- **Reduce therapeutic inertia by ≥20%** by promoting timely treatment intensification and use of combination therapy when indicated.

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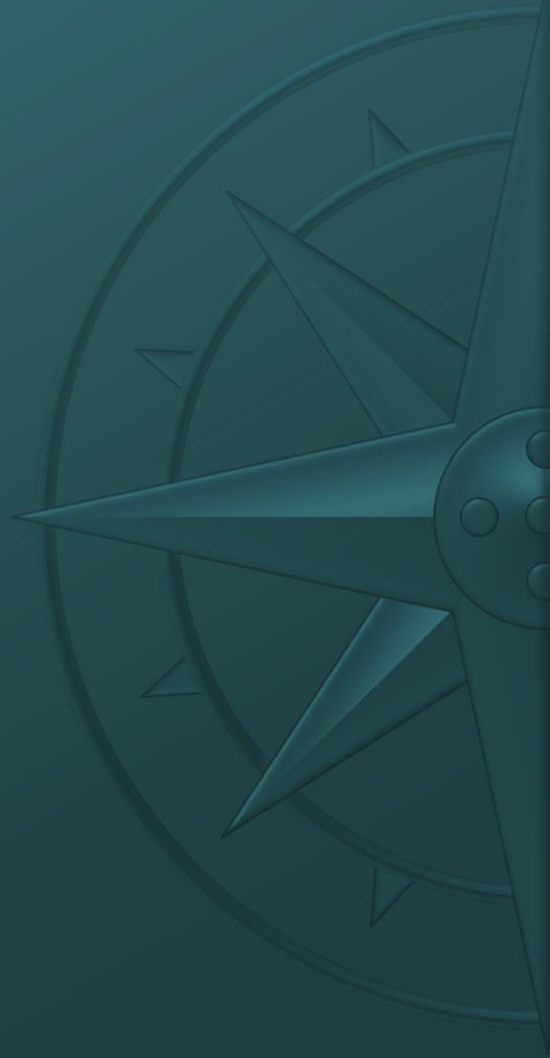
Additional Resources

Visit www.cmeoutfitters.com for clinical information and certified educational activities



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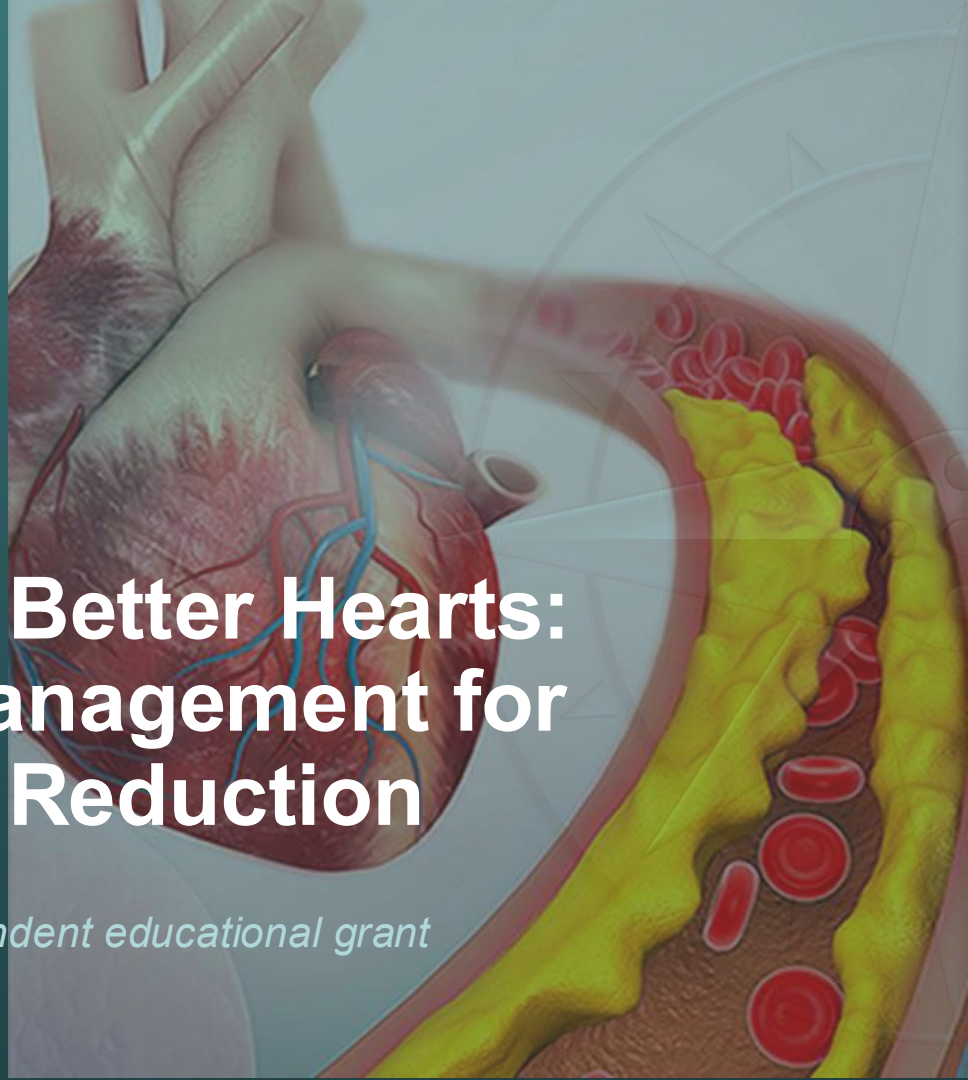
Breaking Barriers to Better Hearts: Optimizing LDL-C Management for Cardiovascular Risk Reduction



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