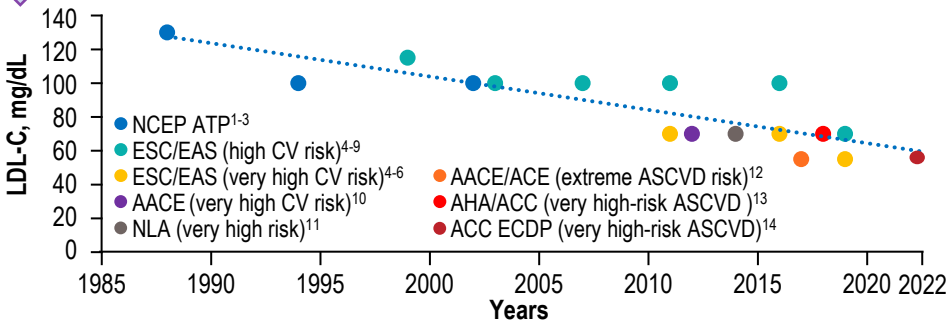
What Do Clinical Guidelines and Pathways Recommend for LDL-C Management of High-Risk ASCVD Patients?

LDL-C Recommendations for Patients with High CV Risk Have Been Lowered Through the Years to Reduce the Risk for CV Events[1-14]



Many ASCVD Patients Do Not Achieve Recommended LDL-C Levels[15]

Among ASCVD patients on lipid-lowering therapy followed over a 2-year period in GOULD registry (N = 5,006):

- **Only 32% of patients** achieved LDL-C < 70 mg/dL; only **15% achieved** LDL-C < 55 mg/dL
- Lipid-lowering therapy intensification occurred in **17% of patients**
- **21% of patients** had only one lipid panel in 2 years, and **11% did not have** a lipid panel

Clinical Guidelines and Pathways Define Patients with ASCVD Who Are at Increased CV Risk and Recommend Intensive LDL-C Lowering With Nonstatin Therapies[6,12,13,16]

2018 AHA/ACC Guideline[13]

Very High-Risk ASCVD:

Multiple major ASCVD events

ACS < 12 months, history of MI (other than ACS event) or IS, symptomatic PAD

OR

One major ASCVD event and multiple high-risk conditions

Age ≥ 65, HeFH, a history of CABG or PCI outside of major ASCVD events, DM, HTN, CKD, current smoker, persistently elevated LDL-C despite maximally tolerated statin therapy and ezetimibe, history of congestive HF

2019 ESC/EAS Guidelines[6]

Very High-Risk ASCVD:[a]

Documented ASCVD, including previous ACS (MI or UA), stable angina, coronary revascularization (PCI, CABG, and other arterial revascularization procedures), stroke, TIA, and PAD.

2017 AACE Guidelines[12,16]

Extreme Risk ASCVD:[a]

Progressive ASCVD, including UA, established clinical ASCVD plus diabetes or CKD ≥ 3 or HeFH, history of premature ASCVD (< 55 years, male; < 65 years, female)

Very High-Risk ASCVD:[a]

Established clinical ASCVD or recent hospitalization for ACS, carotid, or peripheral vascular disease.

Statins are universally recommended as first-line therapy, followed by addition of nonstatin therapies[6,12,13,16]

LDL-C THRESHOLD of **≥ 70 mg/dL**[13]

Threshold = trigger to intensify therapy by using non-statin medications

LDL-C GOAL of **< 55 mg/dL** AND **≥ 50% reduction** from baseline[6]

For patients with ASCVD, who have recurrent events within 2 years, a lower LDL-C goal of < 40 mg/dL may be considered

LDL-C GOAL of **< 55 mg/dL** (extreme risk) AND **< 70 mg/dL** (very high risk)[12,16]

2022 ACC Expert Consensus Decision Pathway (ECDP)[14,*]

Very High-Risk ASCVD:[b]

LDL-C THRESHOLD of **≥ 55 mg/dL** AND **< 50% reduction** from baseline[14]

Consider initiating nonstatin therapies in very high-risk patients[b] with LDL-C of ≥ 55 mg/dL OR < 50% LDL-C reduction from baseline on maximally tolerated statin therapy

Not Very High-Risk ASCVD:

LDL-C THRESHOLD of **≥ 70 mg/dL** AND **< 50% reduction** from baseline[14]

Consider initiating nonstatin therapies in ASCVD patients not at very high risk with LDL-C of ≥ 70 mg/dL OR < 50% reduction from baseline on maximally tolerated statin therapy

- Threshold = level of LDL-C, in terms of both absolute on-treatment LDL-C and percentage of LDL-C reduction from baseline (level of LDL-C before initiation of any LLT), which if not achieved by adherent patients, would serve as factors to consider in decision making regarding further therapy.
- Recommended LDL-C thresholds are not firm triggers for adding medication, but they are factors that may be considered within the broader context of an individual patient's clinical situation.
- Nonstatin therapies are recommended to be considered after evaluating and optimizing lifestyle, adherence to guideline-recommended statin therapy, risk factor control, and statin-associated side effects.
- Preference given to therapies demonstrating reduction in ASCVD events in randomized controlled trials.
- *Note that this process did not involve formal systematic reviews, grading of evidence, or synthesis of evidence. The goal was to provide practical guidance in situations not covered by the 2018 AHA/ACC/Multi-Society cholesterol guideline until the next round of guidelines has the opportunity to formally review recent scientific evidence.

Guidelines and Pathways Recommend "Lower is Better" for LDL-C in Patients with ASCVD[6,13]

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Factors to Consider in the Clinician-Patient Discussion for the Addition of Nonstatin Therapy in ASCVD Patients, According to the 2022 ACC ECDP[14]

Potential for additional ASCVD risk reduction

- Patient's status as very high-risk or not very high-risk
- Percentage LDL-C reduction achieved with statin therapy and whether patient is above LDL-C threshold
- Additional desired percentage LDL-C lowering beyond that achieved on statin therapy
- Mean percentage LDL-C lowering expected with proposed nonstatin therapy
- Available scientific evidence of ASCVD risk reduction (and magnitude of benefit) when nonstatin therapy is added to evidence-based statin therapy)

Patient preferences and considerations

- Patient's perception of benefit from addition of nonstatin therapy
- Convenience of nonstatin therapy (eg, route, setting [home or medical office], and frequency of administration, pill burden, storage)
- Potential of nonstatin therapy to jeopardize adherence to other evidence-based therapies
- Cost of nonstatin therapy
- Anticipated life expectancy, comorbidities, and impact of therapy on quality of life

Adverse reactions

Potential for adverse events or drug-drug interactions from addition of nonstatin therapy

Assessment of Response[6,13,14]

Patients With ASCVD[6,13,14]	Assess lipid levels 4–12 weeks after treatment initiation or modification	Repeat lipid measurements every 3–12 months as needed
Patients With ACS[6]	Assess lipid levels at admission	Reassess lipid levels at week 4–6 and adjust treatment as necessary

[a]Patients fall into the respective designation if they have one or more of the listed criteria. [b]Very high-risk patients have a history of multiple major ASCVD events or 1 major ASCVD event and multiple high-risk conditions, as previously defined in the 2018 AHA/ACC/Multi-Society Cholesterol guidelines.

AACE = American Association of Clinical Endocrinologists; **ACC** = American College of Cardiology; **ACE** = American College of Endocrinology; **ACS** = acute coronary syndrome; **AHA** = American Heart Association; **ASCVD** = atherosclerotic cardiovascular disease; **ATP** = adult treatment panel; **CABG** = coronary artery bypass graft; **CKD** = chronic kidney disease; **CV** = cardiovascular; **DM** = diabetes mellitus; **EAS** = European Atherosclerosis Society; **ECDP** = Expert Consensus Decision Pathway; **eGFR** = estimated glomerular filtration rate; **ESC** = European Society of Cardiology; **FH** = familial hypercholesterolemia; **GOULD** = Getting to an Improved Understanding of Low-Density Lipoprotein Cholesterol and Dyslipidemia Management; **HeFH** = heterozygous familial hypercholesterolemia; **HF** = heart failure; **HTN** = hypertension; **IS** = ischemic stroke; **LDL-C** = low-density lipoprotein cholesterol; **LLT** = lipid-lowering therapy; **MI** = myocardial infarction; **NCEP** = National Cholesterol Education Program; **NLA** = National Lipid Association; **PAD** = peripheral artery disease; **PCI** = percutaneous coronary intervention; **TIA** = transient ischemic attack; **UA** = unstable angina.

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