Baptist Health
HEART INSTITUTE

Updates On The Guidelines For Hyperlipidemia

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Disclosures: None

Learning Objectives

- Review updated hyperlipidemia guidelines
- Compare statins and alternative lipid lowering therapies
- Develop individualized cholesterol treatment plans

Epidemiology & Burden

- Hyperlipidemia remains a leading modifiable risk factor for ASCVD
- Globally >4 million deaths annually linked to high cholesterol
- LDL reduction directly correlates with ASCVD risk reduction
- Earlier and aggressive management improves long-term outcomes

Epidemiology & Burden

- Cardiovascular disease (CVD) represents the leading cause of death worldwide.
- The role of low-density lipoprotein-cholesterol (LDL-C) in the pathophysiology of atherosclerosis and CVD has been well recognized.
- Statins are the standard of care for the management of hypercholesterolemia, and their effectiveness in lowering LDL-C and reducing CVD risk in both primary and secondary prevention has been well established.
- However, several patients fail to attain optimal LDL-C goals or are intolerant to statins, especially at high doses.

Motto for the new year

Lower is better & earlier is better

Four Statin Management Groups
Risk stratification

Risk Stratification

- Use ASCVD 10-year risk estimation in adults 40-75 yrs old
- Risk Enhancers:
  - Diabetes
  - Chronic kidney disease
  - Persistent hypertriglyceridemia
  - Elevated Lp(a) >50 mg/dL
  - Family history premature ASCVD
  - High hs-CRP

Established Therapies

- Statins remain first line.
- Ezetimibe as second line.
- Non-statins added based on LDL target gaps.

Risk stratification – Risk category determines LDL target

Risk Group	Who Is Included	LDL Goal	Treatment
Extreme risk	≥2 ASCVD events within 2 yrs despite optimal therapy	<40mg/dL - ESC	High-intensity statin → add ezetimibe → PCSK9
Very High Risk	ASCVD w multiple events or high-risk features; FH + ASCVD	<55 mg/dL (ESC <40-55) & ≥50% ↓	High-intensity statin → add ezetimibe → PCSK9
High Risk	LDL ≥190; Diabetes w complications; CKD 30–59; 10-yr risk ≥20%	<70 mg/dL (ESC <70)& ≥50% ↓	High-intensity statin ± add-on
Intermediate Risk	10-yr risk 7.5–19.9%; uncomplicated diabetes	<100 mg/dL, ≥30–49% ↓	Moderate–high statin
Moderate Risk	10-yr risk 5–7.4%	<100 mg/dL	Lifestyle ± statin if risk enhancers
Low Risk	10-yr risk <5%	—	Lifestyle only

Hypertriglyceridemia

Triglycerides (mg/dL)	Category	Primary Concern	Treatment Threshold
<150	Normal	None	No treatment
150–199	Mild	↑ ASCVD risk marker	Lifestyle ± statin if ASCVD risk
200–499	Moderate	↑ ASCVD risk	**Statin indicated**
500–999	Severe	**Pancreatitis risk begins**	**Lower TG urgently (consider fibrates)**
≥1000	Very severe	**High pancreatitis risk**	**Immediate TG lowering**

Hypertriglyceridemia

Therapy	TG ↓	CV Event ↓	Primary Use
Statins	10–30%	✅	First-line
Icosapent ethyl	15–25%	✅	High-risk ASCVD
Fenofibrate	30–50%	❌	TG ≥500
EPA+DHA (Omega-3 fatty acid)	20–45%	❌	TG ≥500
Niacin	20–30%	❌	Not recommended

Ezetimibe

- Class / Mechanism: Cholesterol absorption inhibitor (NPC1L1) at the intestinal brush border
- LDL-C Reduction: 15–25%
- Indication: Add-on to statin (primary & secondary prevention); statin intolerance
- Administration: Oral, 10 mg daily
- Key Advantage: First-line non-statin; inexpensive; excellent safety
- Adverse Effects: Rare GI upset, mild transaminase elevation
- Landmark Trial: IMPROVE-IT – ↓ CV events when added to statin

PCSK9 Inhibitors *(Alirocumab, Evolocumab)*

- Class / Mechanism: Monoclonal antibodies inhibiting PCSK9, increasing LDL receptor recycling
- LDL-C Reduction: 50–60%
- Indication: ASCVD or FH not at LDL goal on max statin ± ezetimibe
- Administration: Subcutaneous, every 2–4 weeks
- Key Advantage: Potent LDL lowering with proven outcome benefit
- Adverse Effects: Injection-site reactions, nasopharyngitis
- Landmark Trials: FOURIER, ODYSSEY OUTCOMES

Inclisiran

- Class / Mechanism: siRNA that inhibits hepatic PCSK9 synthesis
- LDL-C Reduction: ~50%
- Indication: ASCVD or FH needing additional LDL lowering
- Administration: Subcutaneous at 0, 3 months, then every 6 months
- Key Advantage: Twice-yearly dosing → improved adherence
- Adverse Effects: Injection-site reactions
- Outcome Data: LDL-lowering proven; CV outcomes trials ongoing

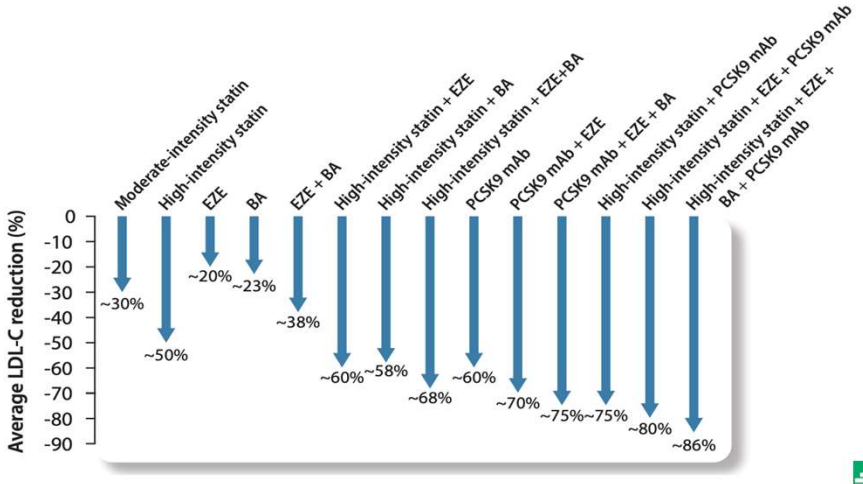
Bempedoic acid

- Class / Mechanism: ATP-citrate lyase inhibitor (upstream of HMG-CoA reductase); activated only in liver
- LDL-C Reduction: 15–25% (up to 35% with ezetimibe combo)
- Indication: ASCVD or high-risk patients, especially statin intolerance
- Administration: Oral, daily
- Key Advantage: No muscle activation → useful in statin-associated myalgias
- Adverse Effects: ↑ Uric acid/gout, tendon rupture (rare)
- Landmark Trial: CLEAR Outcomes – ↓ CV events in statin-intolerant patients

Inclisiran vs PCSK9mAbs

- There are no head-to-head comparisons of the PCSK9mAbs and inclisiran, although when comparing similarly designed trials, the LDL-C–lowering response to inclisiran appears to be approximately 10% less than that seen with the PCSK9 mAbs. The twice-yearly administration by subcutaneous injection after the initial 2 doses at baseline and 3 months is a potentially attractive aspect of this therapy, particularly in patients with adherence concerns.
- A second lipid panel 4 to 12 weeks following initiation of statin therapy, to determine a patient's adherence and response to statin therapy. Thereafter, assessments should be performed every 3 to 12 months as clinically indicated.

Treatment Algorithm



Evinacumab

- Class / Mechanism: Fully human monoclonal antibody against ANGPTL3, leading to lipoprotein lipase activation and LDL-C reduction independent of LDL receptor function
- Indication: Homozygous familial hypercholesterolemia (HoFH) in adults and children ≥12 years
- LDL-C Reduction: ~45–55% reduction, effective even when LDL receptors are nonfunctional
- Administration: IV infusion, 15 mg/kg every 4 weeks
- Key Advantage: Works in patients refractory to statins, ezetimibe, and PCSK9 inhibitors
- Adverse Effects: Nasopharyngitis, influenza-like symptoms, infusion reactions
- Landmark Trial: ELIPSE HoFH trial – significant LDL-C lowering vs placebo

Newer Evolving Therapies

Drug	Primary Target	Main Lipid Effect	FDA Approved?
Lomitapide	LDL (HoFH)	↓ LDL 40–50%	✅
Evinacumab	LDL (HoFH)	↓ LDL 45–55%	✅
Pelacarsen	Lp(a)	↓ Lp(a) 70–80%	❌
Olpasiran	Lp(a)	↓ Lp(a) >90%	❌
Olezarsen	TG	↓ TG	✅
Obicetrapib	LDL & Lp(a)	↓ LDL & Lp(a)	❌

Take Away Points

- **LDL-C is causal** → "Lower is better, earlier is better"
- **Statins remain first-line**
- **Non-statins added based on residual LDL-C & risk**
- **Risk stratification drives LDL-C targets and therapy intensity**

References

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Thank You