Pharmacy Pearls

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Updates in Hyperlipidemia Management

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This issue summarizes the 2018 ACC/AHA Guideline on the Management of Blood Cholesterol on pages 1 and 2 of the document, medication classes used to treat hyperlipidemia on page 3. See also, AHP lipid screening and management guideline.

Primary Prevention

Relative to the 2013 release, the updated guideline offers a more individualized approach to identifying patients likely to benefit from primary prevention. Patients without ASCVD and an LDL 70 – 189 mg/dL are now divided into 4 risk categories based on their 10-year risk (use the *ASCVD Risk Estimator +* to calculate):

1) **Low risk:** 5% 2) **Borderline risk:** 5 - 7.4% 3) **Intermediate risk:** 7.5% - <20% 4) **High risk:** ≥20%

For patients classified as borderline or intermediate risk, the decision to initiate statins should be made based on the presence or absence of "risk enhancers" (see page 2) and willingness to manage risk with lifestyle changes alone. If risk status remains unclear, evidence now supports use of coronary artery calcium (CAC) scoring in ***select patients*** to further understand individualized risk:

- **CAC = 0:** Statin not necessary
- **CAC = 1 - 99:** Favors initiating statin
- **CAC ≥100 or ≥75th percentile:** Initiate statin

Patients who may benefit from CAC scoring include those reluctant to start or re-start statins, older patients with few risk factors, and middle-aged adults (40 – 55 years) classified as borderline risk. **CAC scoring is of no benefit to patients on statins** as statins elevate CAC.

Secondary Prevention

The new guidelines make a small return to "treat-to-target" for secondary prevention and offer guidance on the use of non-statin agents. The following is now recommended for high risk patients <75 years of age:

- Start high intensity statin with a **goal LDL ≤70 mg/dL**
- If LDL remains >70 mg/dL on max tolerated statin, start ezetimibe
- If LDL remains >70 mg/dL on max tolerated statin + ezetimibe, consider PCSK9 inhibitor

Special Populations

Recommendations for special populations are largely unchanged.

Adults <40 years

- Consider statin if LDL ≥160 mg/dL and/or presence of other risk factors.
- Insufficient evidence supporting CAC scoring in this population.

Adults >75 years

- For primary and secondary prevention, it is reasonable to continue or de-prescribe based on tolerance, life-expectancy and patient preference.

Diabetics

- Start moderate intensity statin and consider high intensity for patients ages 50 – 75 years and those with multiple diabetes-specific risk factors.*

*Diabetes-specific risk factors: disease duration (≥10 years for type II), CKD, retinopathy, neuropathy.

Severe HLD (LDL ≥190)

- For patients ages 20 – 75 years: start high intensity statin
- If patient's fail to achieve ≥50% reduction in LDL from baseline *or* LDL remains >100 on max tolerated statin, consider ezetimibe.
- If LDL remains above goal on max tolerated statin + ezetimibe, consider adding PCSK9 inhibitor.

Hyperlipidemia Management

Clinical ASCVD

ACS, MI, unstable angina, revascularization, stroke, TIA, PAD, AAA

Yes → **Secondary Prevention**

Multiple major ASCVD events *or* 1 major ASCVD event + multiple **high risk conditions**‡

- **Yes** → Very high ASCVD risk → Maximal tolerated statin
- **No** → Stable ASCVD → High or moderate intensity statin

No → **Primary Prevention (age 40 – 75 years)**

- LDL ≥190 mg/dL → Maximal tolerated statin
- LDL 70 – 189 mg/dL → Diabetes
  - **Yes** → Moderate or high intensity statin
  - **No** → **Assess 10-year ASCVD risk with the *ASCVD Risk Estimator +***
    - ≥20% High Risk → High intensity statin
    - 7.5 - <20% Intermediate Risk → Evaluate **risk enhancers**‡‡ and CAC score if uncertain → Moderate intensity statin based on risk enhancers
    - 5 - 7.4% Borderline Risk → Evaluate **risk enhancers**‡‡ and patient preference → Moderate intensity statin based on risk enhancers
    - <5% Low Risk → Lifestyle changes
- LDL <70 mg/dL → Assess lifetime risk

Treatment

Maximal tolerated statin | High or moderate intensity statin | Maximal tolerated statin | Moderate or high intensity statin | High intensity statin | Moderate intensity statin based on risk enhancers | Moderate intensity statin based on risk enhancers | Lifestyle changes | Assess lifetime risk

Goals of Therapy

- Goal LDL <70 mg/dL. If not met, add ezetimibe and then consider PCSK9 inhibitor
- High intensity goal: LDL ↓ ≥50%
Moderate intensity goal: LDL ↓30 – 49%
- If LDL ≥100 mg/dL, consider ezetimibe and then PCSK9 inhibitor
- High intensity goal: LDL ↓ ≥50%
Moderate intensity goal: LDL ↓30 – 49%
- Goal: LDL ↓ ≥50% from baseline
- Goal: LDL ↓ 30 - 49% from baseline
- Goal: LDL ↓ 30 - 49% from baseline

High Risk Conditions‡

- Age ≥65 years
- Heart failure
- Smoker
- Diabetes
- Prior CABG or PCI
- Hypertension
- Chronic kidney disease
- LDL persistently ≥100 mg/dL
- Heterozygous familial hyperlipidemia

Risk Enhancers‡‡

- Family history of early ASCVD
- LDL persistently ≥160 mg/dL or TG ≥175 mg/dL
- Chronic kidney disease
- Metabolic syndrome
- Inflammatory conditions (RA, psoriasis, HIV)

Ethnicity (South Asian)

Conditions in women that increase CV risk (e.g, menopause <40)

Adapted from Grundy SM et al. JACC. 2018 Nov 10.
http://www.onlinejacc.org/guidelines/cholesterol

Hyperlipidemia Medication Table

Therapy	LDL Reduction*	Additional Considerations
Statins *$4-355^* Moderate: 30 – 49% High: ≥50%	• **Consider poor adherence as a reason for treatment failure** • Refer to AHP Lipid Guideline for Statin Intensity Table here
Ezetimibe *added to statin* *$134^*	13 – 20%	• Well tolerated, established safety, low cost • IMPROVE-IT: After 6 years, patients with ACS and LDL ≥50 mg/dL on moderate intensity statin had reduced risk of ACS with ezetimibe vs. placebo (NNT =50) • Greatest benefit observed in patients with ≥3 risk factors (NNT = 16); no added benefit in low risk patients • **Role in therapy**: adjunct to max tolerated statin dose; reasonable option for those who refuse statins
Bile Acid Sequestrants *added to statin*	15 – 30%	• Low cost, established safety, poor GI tolerance • Must take 1 hour before or 4 hours after other meds • May increase triglycerides, particularly in those with TG ≥300 • **Role in therapy:** alternative for those who refuse statins **Judge efficacy by percent reduction in LDL. Max effect should occur in 4 – 12 weeks.**
PCSK9 Inhibitors *added to statin* *$660^*	46 – 64%	• Well tolerated, costly, safety >3 years not established • FOURIER trial: After 2 years, patients with ASCVD and LDL ≥70 mg/dL on statin + ezetimibe + PCSK9 had 15% reduced risk of ASCVD relative to those on statin + ezetimibe alone (ARR = 1.5%, NNT = 67) • ODYSSEY trial: Patients with ACS on max tolerated statin + ezetimibe randomized to receive PCSK9 or placebo. After 2.8 years, PCSK9 patients had a 15% reduced risk of ASCVD (ARR = 1.6%, NNT = 66) • **Role in therapy**: adjunct to max tolerated statin + ezetimibe for high risk patients unable to achieve adequate LDL reduction
Fibrates	• Multiple Meta-analyses have shown trends towards harm when fibrates are used for ASCVD prevention • **Role in therapy:** Consider if TG ≥500 for prevention of acute pancreatitis. Fenofibrate is preferred over gemfibrozil as it has less potential for drug interactions. In the absence of significant hypertriglyceridemia, *evidence no longer supports use of fibrates as add on to statins* for primary or secondary ASCVD prevention.

*LDL reductions when added to statin therapy ^*Average monthly cash prices from www.goodrx.com as of April 2019; prices vary based on pharmacy*

Hyperlipidemia in Children

Unlike prior releases, the new guidelines include recommendations for managing hyperlipidemia in children. These recommendations are in line with other society guidelines and include:

- It is reasonable to screen lipids at 9 – 11 years and then again at 17 – 21 years or in children with metabolic syndrome or other risk factors.
- Consider statins in children ≥10 years with LDL ≥190 mg/dL who do not respond 3 – 6 months of lifestyle changes. Statins may also be considered in children ≥8 years with family history of extremely high LDL.