Pharmacy Pearls

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2025 AACE Clinical Practice Guideline for the Pharmacologic Management of Adults with Dyslipidemia: Key Updates

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OVERVIEW

This 2025 clinical practice guideline serves as a **focused update** of the *2017 AACE Guidelines for Management of Dyslipidemia and Prevention of Cardiovascular Disease*. Its purpose is to provide practical evidence-based recommendations in adults 18 years of age and older who have dyslipidemia or hypertriglyceridemia *who are receiving standard of care treatment* (statin pharmacotherapies) **but who are not at goal and may consider additional medications.** Clinical topics such as screening, lipid panels, nutrition, physical activity, and statin use are not addressed.

DYSLIPIDEMIA: KEY CLINICAL QUESTIONS ADDRESSED

What are the benefits/harms of PCSK9 inhibitors compared with usual care?

- Patients on *maximally tolerated statins* **and** *have ASCVD* **or** *are at increased risk for ASCVD* but **who are not at goal (LDL-C <70 mg/dL)**, AACE suggests for the use of evolocumab or alirocumab in addition to usual care; either may be considered.
- AACE suggests **against** the use of evolocumab or alirocumab in patients **who do not have ASCVD** as most trial participants were at increased risk for ASCVD or were being treated for secondary prevention.

What are the benefits/harms of treating to a lower LDL-C goal (<70 mg/dL) compared with a higher LDL-C goal (≥70 mg/dL)?

- In adults on pharmacotherapy for dyslipidemia *who have ASCVD* **or** *are at increased risk for ASCVD*, AACE suggests for treatment to an LDL-C target of <70 mg/dL.
    - The 2017 recommendation for LDL-C treatment targets (<55 mg/dL) was informed by a single trial on statin plus ezetimibe. Subsequent meta-analyses of numerous trials did not show a difference in CV events or mortality.

What are the benefits/harms of bempedoic acid compared with usual care?

- Patients who are *statin intolerant* **and** *have ASCVD* **or** *are at increased risk for ASCVD*, AACE suggests for the use of bempedoic acid in addition to usual care.
- AACE suggests **against** the use of bempedoic acid in patients **who do not have ASCVD** and who may tolerate other lipid-lowering medications. While bempedoic acid may lead to a small reduction in myocardial infarction, there is a risk of potential harm in the form of gout, cholelithiasis and tendon rupture; shared decision-making should guide choice.

In adults with dyslipidemia *with CVD*, does the addition of risk enhancers such as calcium artery calcification (CAC) score, apolipoprotein B (ApoB), or lipoprotein a (Lp[a]) to traditional risk equations provide more accurate risk prediction of future cardiovascular events?

- For primary prevention, AACE recommends for the use of a validated tool or calculator to predict future risk of ASCVD events as part of shared decision-making around treatment.
- There is limited utility in **broad** application in adding CAC scores, ApoB, and Lp(a) measurements. Additional testing may be considered **for individuals at intermediate risk** who understand the potential additional costs of testing and still value the risk information ascertained from using CAC score, ApoB, and/or Lp(a) to inform a treatment decision.

As a companion to the guideline, AACE subsequently developed this algorithm as an update of the previous iteration published in 2020.

Risk Assessment and Testing for Dyslipidemia

- Emphasize life-long adoption of healthy lifestyle changes (diet, exercise, stress reduction, restful sleep, avoidance of tobacco, and a healthy body weight)
- Treat all cardiometabolic risk factors in an integrated manner

The following individuals should be considered at moderate to high risk for ASCVD events:
Presence of clinical ASCVD, FH, diabetes over 40 years of age (or younger if additional ASCVD risk factors), HIV, metabolic syndrome, MASLD, and chronic inflammatory disease.

For primary prevention, use a validated risk assessment calculator to determine risk of future ASCVD risk.
Emphasize healthy life-style modifications to all.

Low risk (‹7.5%)

Focus on lifestyle interventions

Example Risk Assessment Tools or Calculators [a]

1. PCE 10-year risk calculator - https://tools.acc.org/ascvd-risk-estimator-plus/#!/calculate/estimate/
2. PREVENT risk calculator - https://professional.heart.org/en/guidelines-and-statements/prevent-calculator
3. Framingham risk score - https://www.mdcalc.com/calc/38/framingham-risk-score-hard-coronary-heart-disease
4. SCORE2 & SCORE2-OP - https://www.escardio.org/Education/Practice-Tools/CVD-prevention-toolbox/SCORE-Risk-Charts
5. PAHO HEARTS Cardiovascular Risk Calculator https://www.paho.org/en/hearts-americas/cardiovascular-risk-calculator-app
6. QRISK - https://qrisk.org/

Intermediate risk (7.5-20%)

- Consider additional risk enhancers
- Engage in shared decision-making regarding treatment

Additional risk enhancers:
- Family history
- Cardiometabolic disease
- TG/Non-HDL
- CKD

Additional Testing: [b]
- CAC score / or 2D-3D carotid and femoral ultrasound
- Lp(a)
- ApoB
- hsCRP

High risk (›20%)

Recommend pharmacotherapy

a Percent risk refers to risk of future ASCVD-related events. Risk cutoff points vary across assessment tools. Currently there is no evidence to support the preferential use of any particular risk calculator.

b Current evidence does not show meaningful improvement in prediction of ASCVD risk with the addition of non-traditional risk factors (i.e, CAC score, ApoB, or Lp[a]) to the risk model for most individuals. May be considered to reclassify risk for individuals at intermediate risk (2025 AACE Dyslipidemia Guideline).

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Algorithm Figure 2-Risk Assessment AACE

Algorithm Fig. 2. Risk assessment and testing for dyslipidemia.

Targeting LDL-Cholesterol with Pharmacologic Therapy for ASCVD Prevention in Adults

Primary Prevention

Counsel on lifestyle modifications that reduce ASCVD risk

Assess ASCVD risk [a]

- Low risk → Focus on lifestyle modifications
- Intermediate risk → Consider moderate-intensity statin
- High risk → High-intensity statin

T1D [b]/T2D [b] | Metabolic syndrome/ MASLD | CKD, Chronic inflammatory diseases | Persistent LDL-C ≥ 190 mg/dL (≥4.9 mmol/L) [c]

→ Consider moderate- to high-intensity statin

If LDL-C above goal on maximally tolerated statin, add ezetimibe

Secondary Prevention (Clinical ASCVD)

High-intensity statin [d]

If LDL-C above goal or continues to have CV events, add ezetimibe

Consider add-on therapy: bempedoic acid, PCSK9-based therapy, or bile acid resins

Note: Not all add-on agents have evidence for reducing ASCVD risk. Use shared decision-making to discuss benefits and harms of the individual therapies. [e]

AACE suggests treating individuals with ASCVD or increased risk of ASCVD to an LDL-C target of ‹70 mg/dL. Potential impacts from polypharmacy and the increased costs with certain medications should be considered when determining appropriate treatment goals. [e]

High Intensity Statin	Moderate-intensity Statin			
Atorvastatin 40-80 mg	Rosuvastatin 5-10 mg	Atorvastatin 10-20 mg	Simvastatin 20-40 mg	Pitavastatin 2-4 mg
Rosuvastatin 20-40 mg	Fluvastatin XL 80 mg	Fluvastatin 40 mg BID	Pravastatin 40-80 mg	Lovastatin 40 mg

a Use a validated risk tool (see full list in text). Family history of premature coronary disease carries increased ASCVD risk; individuals will fall in the intermediate or high-risk categories depending on overall risk. Current evidence does not show meaningful improvement in prediction of ASCVD risk with the addition of non-traditional risk factors (i.e. hsCRP, CAC score, ApoB, or Lp(a)) to the risk model (see 2025 AACE Dyslipidemia Guideline)
b Individuals with diabetes and age ›40 or younger if ASCVD risk factors are present
c Confirm whether the elevated LDL-C trend is genetic or acquired, and exclude secondary causes, including dietary factors. See the narrative for additional details on familial hypercholesterolemia (FH).
d Combination therapy may be of benefit after an acute CV event. (see narrative)
e See GRADE evidence frameworks in 2025 AACE Dyslipidemia Guideline

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Algorithm Figure 5-LDL Pharmacologic Therapy AACE

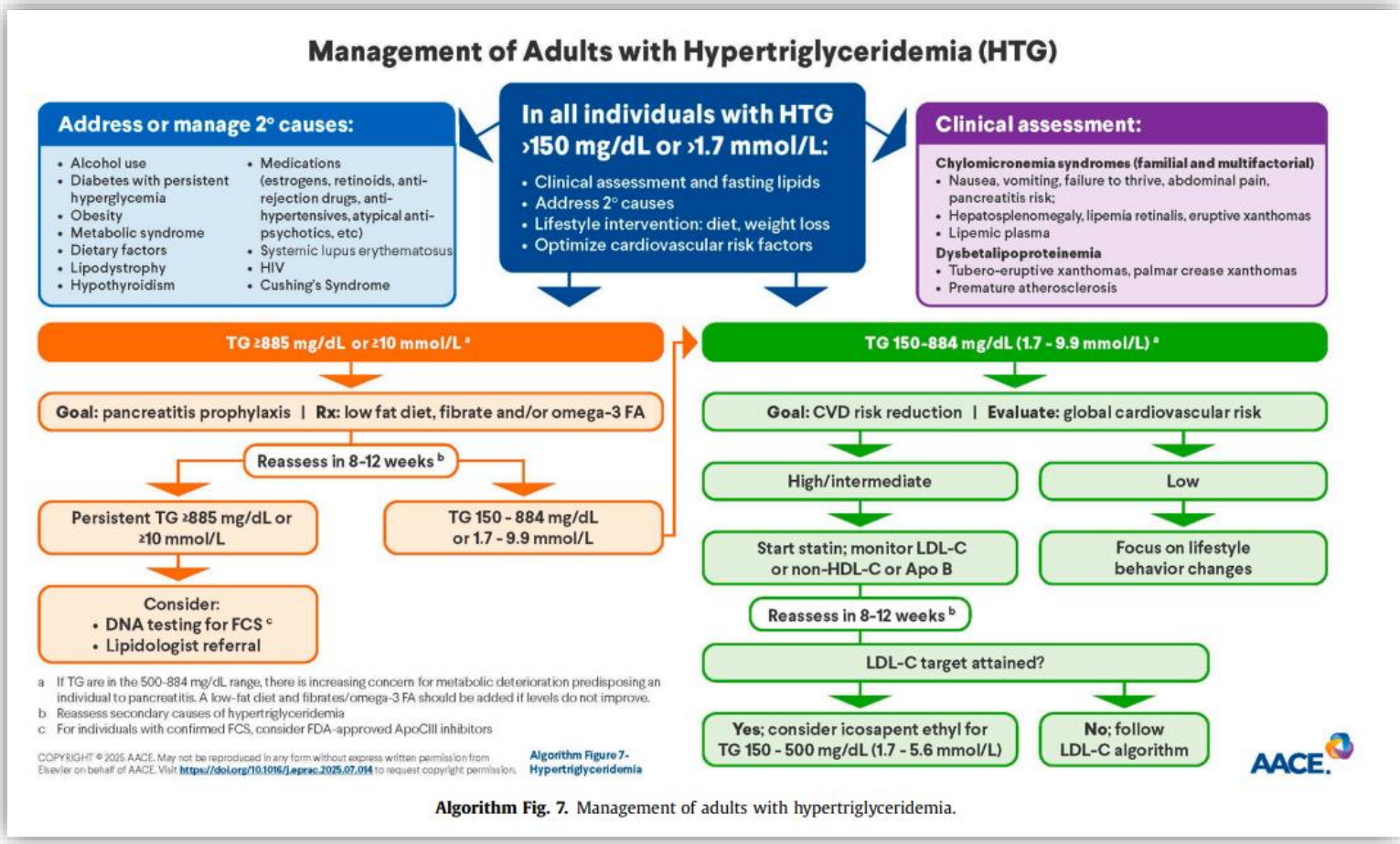
HYPERTRIGLYCERIDEMIA: KEY CLINICAL QUESTIONS ADDRESSED

What are the benefits and harms of eicosapentaenoic acid (EPA) compared with EPA plus docosahexaenoic acid (DHA)?

- In patients with hypertriglyceridemia (150-499 mg/dL) *with ASCVD* **or** who are *at increased risk for ASCVD*, AACE suggests for the use of EPA in addition to statins. They suggest **against** the use of EPA plus DHA in addition to statin therapy in this population.
- In patients with severe hypertriglyceridemia (≥500 mg/dL), there is insufficient evidence to recommend for or against the use of EPA or EPA plus DHA.

What are the benefits/harms of extended-release niacin compared with non-statin treatments such as fibrates and EPA?

- In patients with hypertriglyceridemia (150-499 mg/dL) *with ASCVD* **or** who are *at increased risk for ASCVD*, AACE recommends **against** the use of niacin in addition to usual care.
- In patients with severe hypertriglyceridemia (≥500 mg/dL), there is insufficient evidence to recommend for or against the use of niacin.



Algorithm Fig. 7. Management of adults with hypertriglyceridemia.

SUMMARY

- **PCSK9 inhibitors** are recommended for high-risk or ASCVD patients not at LDL-C goal despite statins; not recommended for patients without ASCVD.
- **LDL-C target <70 mg/dL** is suggested for ASCVD or high-risk patients, with no clear added benefit for targets below this level.
- **Bempedoic acid** may be used in statin-intolerant high-risk or ASCVD patients but has limited benefit.
- **Risk enhancers (CAC, ApoB, Lp[a])** are not *routinely* recommended and may be used selectively in intermediate-risk patients.
- **Triglyceride therapies:** EPA is recommended with statins for moderate hypertriglyceridemia; EPA+DHA and niacin are not recommended.