CHOLESTEROL MANAGEMENT GUIDELINES (Part 1 of 2)

SECONDARY PREVENTION IN PATIENTS WITH ASCVD

Clinical ASCVD[1]

Healthy lifestyle

ASCVD not at very high-risk

- **Age ≤75yrs**
  - High-intensity statin[2] (Goal: reduce LDL-C by ≥50%)
    - If on maximal statin and LDL-C ≥70mg/dL, can add ezetimibe
- **Age >75yrs**
  - Initiate moderate- or high-intensity statin or continue high-intensity statin

ASCVD at very high-risk[3]

- High-intensity or maximal statin
  - If on maximal statin and LDL-C ≥70mg/dL, can add ezetimibe. If PCSK9-I is considered, add ezetimibe to maximal statin first before adding
    - If on clinically judged maximal LDL-C lowering therapy and LDL-C ≥70mg/dL or non-HDL-C ≥100mg/dL, can add PCSK9-I

PRIMARY PREVENTION OF ASCVD

Assess ASCVD risk in each age group
Emphasize adherence to healthy lifestyle

- **Age 0–19yrs**
  - Lifestyle modification to prevent or reduce ASCVD risk
  - FH diagnosis: start statin
- **Age 20–39yrs[7]**
  - Assess risk factors at least every 4–6yrs or estimate 30-year/lifetime ASCVD risk
  - Family history of premature ASCVD and LDL-C ≥160mg/dL: consider statin
- **Age 40–75yrs**
  - **WITHOUT diabetes and with LDL-C ≥70–<190mg/dL**
    Estimate 10-year ASCVD risk (PCE-calculated)
    - **<5% "Low risk"**
      - Risk discussion[6]
        - Emphasize lifestyle to reduce risk factors
        - Age 40–59yrs: consider estimating 30-year/lifetime ASCVD risk
    - **5–<7.5% "Borderline risk"**
      - Risk discussion[6]
        - If risk enhancers[8] present, then risk discussion regarding moderate-intensity statin
        - Age 40–59yrs: consider estimating 30-year/lifetime ASCVD risk
    - **≥7.5–<20% "Intermediate risk"**
      - Risk discussion[6]
        If risk estimate + risk enhancers[8] favor statin, start moderate-intensity statin to reduce LDL-C by 30–49%[9]
    - **≥20% "High risk"**
      - Risk discussion[6]
        Start statin to reduce LDL-C ≥50%
    - Select patients
      - **If risk decision is uncertain:**
        Consider measuring CAC
        CAC = 0: lowers risk; consider no statin unless diabetes, family history of premature CHD, cigarette smoking present
        CAC = 1–99: favors statin (esp. after age 55)
        CAC = 100+ and/or ≥75th percentile: start statin
  - **WITH diabetes**
    Moderate-intensity statin
    Risk assessment to consider high-intensity statin[5]
- **Age >75yrs**
  - Clinical assessment
    Risk discussion[6]
- **LDL-C ≥190mg/dL**
  - No risk assessment
    High-intensity statin[4]

(continued)

CHOLESTEROL MANAGEMENT GUIDELINES (Part 2 of 2)

STATIN THERAPY

High-Intensity	Moderate-Intensity	Low-Intensity
Daily dose lowers LDL-C by approx. ≥50%[10]	Daily dose lowers LDL-C by approx. 30–49%[10]	Daily dose lowers LDL-C by approx. <30%[10]
• atorvastatin 40–80mg • rosuvastatin 20–40mg	• atorvastatin 10–20mg • rosuvastatin 5–10mg • simvastatin 20–40mg • pravastatin 40–80mg • lovastatin 40–80mg • fluvastatin XL 80mg • fluvastatin 40mg twice daily • pitavastatin 1–4 mg	• simvastatin 10mg • pravastatin 10–20mg • lovastatin 20mg • fluvastatin 20–40mg

NONSTATIN THERAPY

- Bile acid sequestrants: cholestyramine, colesevelam, colestipol
- Ezetimibe
- PCSK9 inhibitors: alirocumab, evolocumab

NOTES

Key: **ACS** = acute coronary syndrome;
ASCVD = atherosclerotic cardiovascular disease;
CAC = coronary artery calcium;
CHD = coronary heart disease;
CKD = chronic kidney disease;
FH = Familial Hypercholesterolemia
LDL-C = low-density lipoprotein cholesterol;
HDL-C = high-density lipoprotein cholesterol;
MI = myocardial infarction;
PCE = pooled cohort equations;
PCSK9-I = proprotein convertase subtilisin kexin type 9 inhibitor

Assess adherence and percentage response to LDL-C lowering medications and lifestyle changes with repeat lipid measurement 4–12wks after statin initiation or dose adjustment, repeated every 3–12mos as needed.

[1] Clinical ASCVD consists of ACS, history of MI, stable or unstable angina, coronary other arterial revascularization, stroke, transient ischemic attack (TIA), or peripheral artery disease (PAD) including aortic aneurysm, all of atherosclerotic origin.

[2] If high-intensity statin contraindicated or not tolerated, use moderate-intensity statin (Goal: reduce LDL-C by 30–49%).

[3] Very high-risk includes a history of multiple major ASCVD events or 1 major ASCVD event and multiple high-risk conditions (eg, ≥65yrs, diabetes, hypertension, CKD [eGFR 15–59 mL/min/1.73m^2], smoking, CHF, heterozygous familial hypercholesterolemia, prior CABG or PCI outside of major ASCVD event, persistently elevated LDL-C ≥100mg/dL).

[4] If <50% reduction in LDL-C and/or LDL-C remains ≥100mg/dL on maximally tolerated statin, can add ezetimibe. If <50% reduction in LDL-C and fasting triglycerides ≤300mg/dL on statin and ezetimibe, may add bile acid sequestrant. If heterozygous FH and LDL-C remains ≥100mg/dL on statin and ezetimibe, may add PCSK9-I.

[5] In adults with multiple ASCVD risk factors, initiate high-intensity statin to reduce LCL-C by ≥50%. In adults with 10-year ASCVD risk ≥20% who are on maximally tolerated statin therapy, may add ezetimibe to reduce LDL-C by ≥50%.

[6] Risk discussion should include a review of major risk factors (eg, cigarette smoking, elevated blood pressure, LDL-C, hemoglobin A1C [if indicated], and calculated 10-yr risk of ASCVD); the presence of risk-enhancing factors (see note #8); the potential benefits of lifestyle and statin therapies; the potential for adverse effects and drug-drug interactions; consideration of costs of statin therapy; and patient preferences and values in shared decision making.

[7] If diabetes mellitus present in this age group, consider diabetes-specific risk enhancers (eg, long duration [≥10yrs for T2DM or ≥20yrs for T1DM], albuminuria ≥30mcg albumin/mg creatinine, eGFR <60mL/min/1.73m^2, retinopathy, neuropathy, ankle-brachial index [ABI] <0.9) to determine if initiation of statin therapy is appropriate.

[8] ASCVD risk enhancers: family history of premature ASCVD, persistently elevated LDL-C ≥160mg/dL, CKD, metabolic syndrome, conditions specific to women (eg, preeclampsia, premature menopause), inflammatory disease (esp. rheumatoid arthritis, psoriasis, HIV), ethnicity (eg, South Asian ancestry). Lipid/biomarkers: persistently elevated triglycerides (≥175mg/dL). In selected individuals if measured: hs-CRP ≥2mg/L, Lp(a) >50mg/dL or >125nmol/L, apoB ≥130mg/dL, ABI <0.9.

[9] In patients who would benefit from more aggressive LDL-C lowering and in whom high intensity statins are advisable but not acceptable or tolerated, it may be reasonable to add nonstatin drug therapy (eg, ezetimibe or bile acid sequestrant) to a moderate-intensity statin.

[10] Percent reductions are estimates from data across large populations and reductions should be expected to vary in clinical practice.

REFERENCES

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