Dyslipidemia

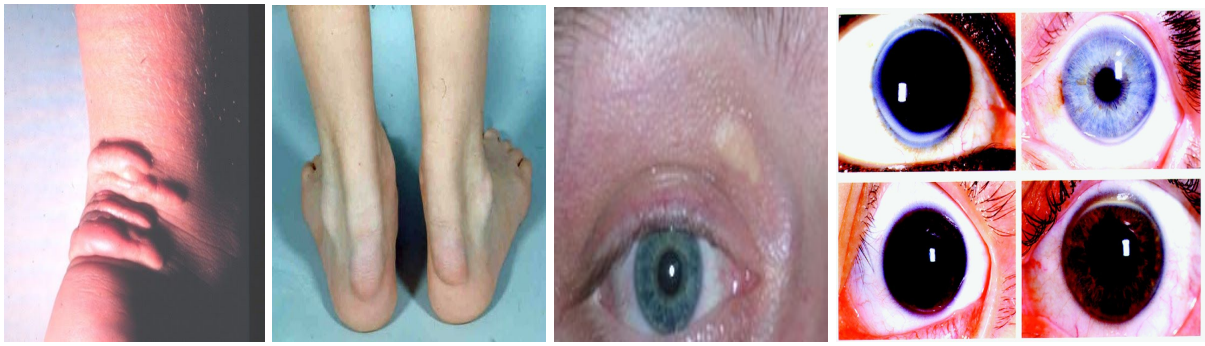
Dyslipidemia: A disorder of lipoprotein metabolism, including lipoprotein overproduction or deficiency. Dyslipidemia may be manifested by elevation of the total cholesterol, the "bad" low density lipoprotein (LDL) cholesterol and triglyceride concentrations, and a decrease in the “good" high-density lipoprotein (HDL) cholesterol concentration in the blood.

Values of Lipids:

- LDL
  - < 100 →Optimal
  - 100-129 → Near optimal
  - 130-159 → Borderline
  - 160-189→ High
  - ≥ 190 → Very High
- Total Cholesterol
  - < 200 → Desirable
  - 200-239 → Borderline
  - ≥240 → High
- HDL
  - < 40 → Low
  - ≥ 60 → High
- Serum Triglycerides
  - < 150 → normal
  - 150-199 → Borderline
  - 200-499 → High
  - ≥ 500 → Very High

Screen for Dyslipidemia：

- Men over 35 and woman 0ver 45.
- Anyone with atherosclerotic symptoms regardless of age
- Anyone with diabetes regardless of age
- Family history of premature CVD
- Inflammatory diseases (lupus, rheumatoid arthritis, psoroasis)
- Children of patients with severe dyslipidemia
- HIV infection with HAART therapy
- Clinical signs of hyperlipidemia; Xanthelasma, tendon xanthoma, corneal arcus.
- Erectile dysfunction
- Chronic renal disease
- Metabolic syndrome?



The goal for dyslipidemia treatment (primary prevention vs. secondary prevention) :

Primary prevention for:

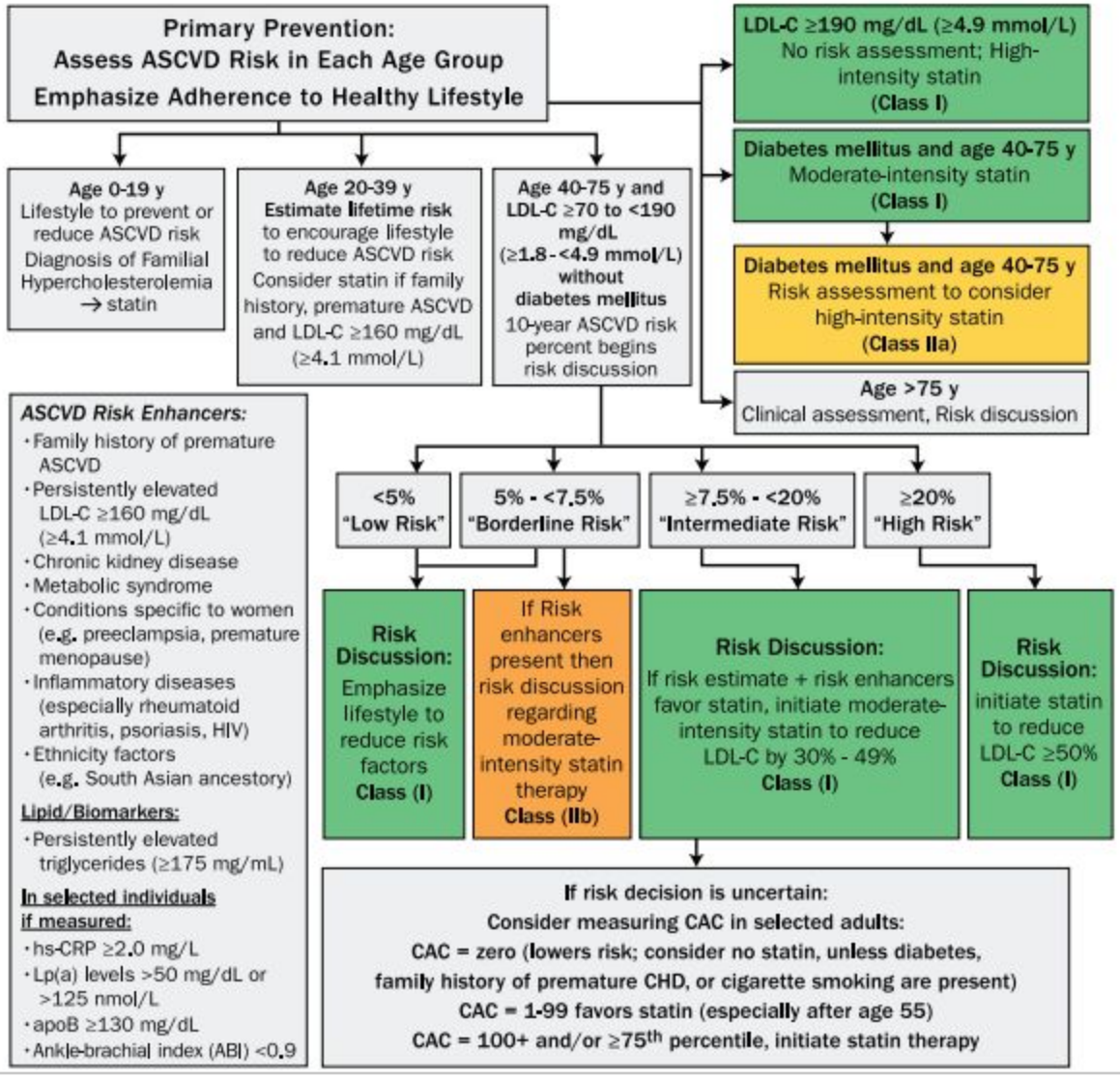
1- LDL-C >=190 mg/dl
2- Diabetes and aged 40-75 years with LDL-C between 70-189 mg/dl
3- No diabetes and estimated 10 year ASCVD risk of >= 7.5 % who are between 40 to 75 years of age with LDL-C between 70-189 mg/dl

Secondary prevention for:

1- Patients with known coronary heart disease (CHD; including myocardial infarction, angina, and prior coronary revascularization)
2- other cardiovascular disease (CVD; including stroke, transient ischemic attack, and peripheral arterial disease)
3- combinations of risk factors that result in a 10-year risk of ASCVD events of more than 20 percent
4- Chronic kidney disease with estimated GFR <45ml/min/1.73m^2
5- Risk equivalent for CV in diabetic patients:
Although some guidelines have considered all patients with diabetes mellitus (DM) to have a risk of CV events similar to patients with known CVD, this actually averages events across patients with widely differing risks of CHD. Issues that may affect risk with DM include patient age, sex, other CV risk factors, duration of DM, and whether the patient has type 1 or type 2 DM.
Given this, it is preferable to calculate patient-specific risks rather than to simply consider all patients with DM to require treatment for secondary prevention, particularly in patients who are under age 60 without multiple cardiovascular risk factors. A downloadable calculator for this purpose is available for patients with type 2 DM from the UK Prospective Diabetes Study (www.dtu.ox.ac.uk/riskengine)

Primary Prevention: Lifestyle Changes and Team-Based Care

Primary Prevention



Assessment of Cardiovascular Risk

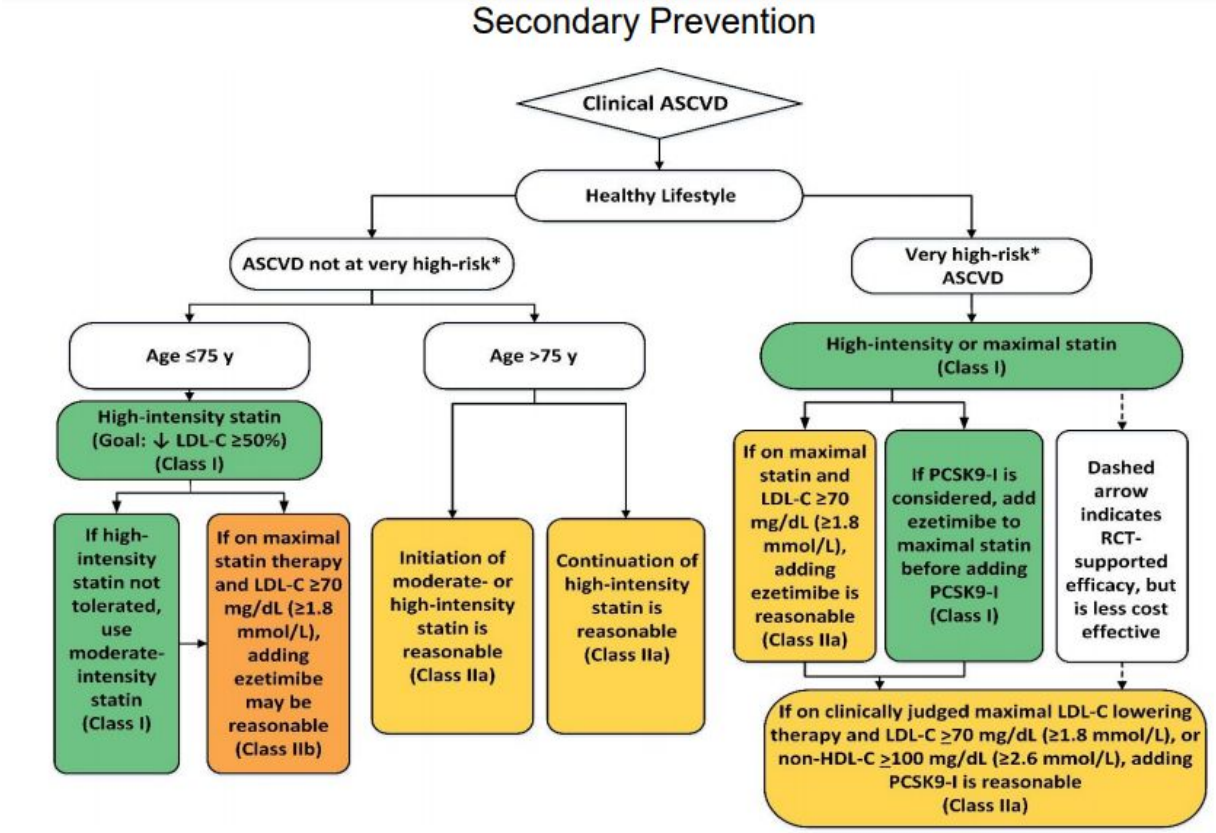
Risk-Enhancing Factors for Clinician-Patient Risk Discussion

- **Family history of premature ASCVD** (males, age <55 y; females, age <65 y)
- **Primary hypercholesterolemia** (LDL-C, 160–189 mg/dL [4.1–4.8 mmol/L]; non–HDL-C 190–219 mg/dL [4.9–5.6 mmol/L])*
- **Metabolic syndrome** (increased waist circumference [by ethnically appropriate cutpoints], elevated triglycerides [>150 mg/dL, nonfasting], elevated blood pressure, elevated glucose, and low HDL-C [<40 mg/dL in men; <50 mg/dL in women] are factors; a tally of 3 makes the diagnosis)
- **Chronic kidney disease** (eGFR 15–59 mL/min/1.73 m2 with or without albuminuria; not treated with dialysis or kidney transplantation)
- **Chronic inflammatory conditions**, such as psoriasis, RA, lupus, or HIV/AIDS
- **History of premature menopause (before age 40 y) and history of pregnancy-associated conditions that increase later ASCVD risk, such as preeclampsia**
- **High-risk race/ethnicity** (e.g., South Asian ancestry)
- **Lipids/biomarkers**: associated with increased ASCVD risk
  - Persistently elevated,* primary hypertriglyceridemia (≥175 mg/dL, nonfasting)
  - If measured:
    - **Elevated high-sensitivity C-reactive protein** (≥2.0 mg/L)
    - **Elevated Lp(a)**: A relative indication for its measurement is family history of premature ASCVD. An Lp(a) ≥50 mg/dL or ≥125 nmol/L constitutes a risk-enhancing factor, especially at higher levels of Lp(a).
    - **Elevated apoB** (≥130 mg/dL): A relative indication for its measurement would be triglyceride ≥200 mg/dL. A level ≥130 mg/dL corresponds to an LDL-C >160 mg/dL and constitutes a risk-enhancing factor
    - **ABI** (<0.9)

Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol, Journal of the American College of Cardiology (2018), doi: https://doi.org/10.1016/j.jacc.2018.11.003.

**Optimally, 3 determinations.*

AIDS indicates acquired immunodeficiency syndrome; ABI, ankle-brachial index; apoB, apolipoprotein B; ASCVD, atherosclerotic cardiovascular disease; eGFR, estimated glomerular filtration rate; HDL-C, high-density lipoprotein cholesterol; HIV, human immunodeficiency virus; LDL-C, low-density lipoprotein cholesterol; Lp(a), lipoprotein (a); and RA, rheumatoid arthritis.



Pharmacological treatment:

- When a pharmacologic agent is required for treatment in primary prevention, a statin is the preferred medication.
- If a statin is not tolerated or a particular LDL-C goal is not achieved on a statin alone, we suggest administering or adding a non-statin lipid-lowering medication; Ezetimibe.
- Cardiovascular risk should be calculated by Pooled Cohort Equations CV risk calculator (ACC/AHA Calculator) to determine 10 year risk factor for CV events.
-10 year ASCVD risk: a quantitative estimation of absolute risk based upon data from representative population samples. Example: if 10 year ASCVD risk estimates is 10%, this indicates that among 100 patients with the entered risk factor profile, 10 would be expected to have a heart attack or stroke in the next 10 years.

STATIN Therapy:

High-Intensity Statin Daily dose lowers LDL-C, on average by approximately ≥50%:
Atorvastatin 40-80 mg
Rosuvastatin 20-(40) mg

Moderate-Intensity Statin Daily dose lowers LDL-C, on average by approximately 30% to <50%:
Atorvastatin 10-(20) mg
Rosuvastatin (5)-10 mg
Simvastatin 20-40 mg

Low-Intensity Statin Daily dose lowers LDL-C, on average by approximately <30%:
Fluvastatin 20-40 mg
Simvastatin 10 mg

Statin Safety Recommendations

- Characteristics predisposing individuals to statin adverse effects include, but are not limited to:
1. Multiple or serious comorbidities, including impaired renal or hepatic function.
2. History of previous statin intolerance or muscle disorders. It is reasonable to evaluate and treat muscle symptoms, including pain, tenderness, stiffness, cramping, weakness, or fatigue, in statin-treated patients according to the following management algorithm: (IIa B)

1. If unexplained severe muscle symptoms or fatigue develop during statin therapy, promptly discontinue the statin and address the possibility of rhabdomyolysis by evaluating CK, creatinine, and urinalysis for myoglobinuria.
2. If mild to moderate muscle symptoms develop during statin therapy:

A- Discontinue the statin until the symptoms can be evaluated.
B- Evaluate the patient for other conditions that might increase the risk for muscle symptoms (e.g., hypothyroidism, reduced renal or hepatic function, rheumatologic disorders such as polymyalgia rheumatica, steroid myopathy, vitamin D deficiency, or primary muscle diseases).
C- If muscle symptoms resolve, and if no contraindication exists, give the patient the original or a lower dose of the same statin to establish a causal relationship between the muscle symptoms and statin therapy.
D- Once a low dose of a statin is tolerated, gradually increase the dose as tolerated.
E- If, after 2 months without statin treatment, muscle symptoms or elevated CK levels do not resolve completely, consider other causes of muscle symptoms listed above.
F- If persistent muscle symptoms are determined to arise from a condition unrelated to statin therapy, or if the predisposing condition has been treated, resume statin therapy at the original dose.

3. Unexplained ALT elevations >3 times ULN.

1. Baseline measurement of hepatic transaminase levels (ALT) should be performed before initiating statin therapy. (I B)

2. During statin therapy, it is reasonable to measure hepatic function if symptoms suggesting hepatotoxicity arise (e.g., unusual fatigue or weakness, loss of appetite, abdominal pain, dark colored urine or yellowing of the skin or sclera). (IIa C)

4. Patient characteristics or concomitant use of drugs affecting statin metabolism.

5. >75 years of age - For individuals taking any dose of statins, it is reasonable to use caution in individuals >75 years of age, as well as in individuals that are taking concomitant medications that alter drug metabolism; cyclosporine, macrolides, various antifungals, cytochrome p-450 inhibitors, can cause drug interaction leads to high incidence of myositis., taking multiple drugs, or taking drugs for conditions that require complex medication regimens (e.g., those who have undergone solid organ transplantation or are receiving treatment for HIV). A review of the manufacturer's prescribing information may be useful before initiating any cholesterol-lowering drug. (IIa C)

NON-STATIN Therapy:

Ezetimibe — modestly lowers the LDL-C when used alone and may be helpful for avoiding high doses of statins (and potentially increased susceptibility to muscle injury) in patients who do not meet cholesterol goals on statin therapy alone. However, the clinical benefits of either ezetimibe monotherapy or combining ezetimibe with statin therapy remain to be proven.

Fibrates — the major effects of the fibrates are to lower plasma triglyceride and raise HDL-C levels. They are effective for the treatment of hypertriglyceridemia and combined hyperlipidemia with or without hypoalphalipoproteinemia. There is an increased risk of muscle toxicity in patients taking some fibrates and a statin.

PCSK9 inhibitors--- are a class of injectable monoclonal antibodies approved in 2015 that have been shown to dramatically lower LDL cholesterol levels -- by up to 60% in some cases when combined with a statin.

Nicotinic acid — Nicotinic acid (niacin) is effective in improving lipid parameters in patients who have hypercholesterolemia or combined hyperlipidemia associated with normal and low levels of HDL-C (hypoalphalipoproteinemia). The HDL raising properties of nicotinic acid occur with dosages as low as 1 to 1.5 g/day.The use of nicotinic acid is often limited by poor tolerability, and there are concerns about the safety of nicotinic acid as well as its efficacy for clinical endpoints.

Bile acid sequestrants — Bile acid sequestrants are effective in patients with mild to moderate elevations of LDL-C. Bile acid sequestrants are also effective when used in combination with a statin or nicotinic acid in patients with markedly elevated plasma levels of LDL-C . The use of a bile acid sequestrant is often limited by side effects.

Take-Home Messages for the Primary Prevention of Cardiovascular Disease

1 The most important way to prevent atherosclerotic vascular disease, heart failure, and atrial fibrillation is to promote a healthy lifestyle throughout life.

2 A team-based care approach is an effective strategy for the prevention of cardiovascular disease. Clinicians should evaluate the social determinants of health that affect individuals to inform treatment decisions.

3 Adults who are 40 to 75 years of age and are being evaluated for cardiovascular disease prevention should undergo 10-year atherosclerotic cardiovascular disease (ASCVD) risk estimation and have a clinician–patient risk discussion before starting on pharmacological therapy, such as antihypertensive therapy, a statin, or aspirin. In addition, assessing for other risk-enhancing factors can help guide decisions about preventive interventions in select individuals, as can coronary artery calcium scanning.

4 All adults should consume a healthy diet that emphasizes the intake of vegetables, fruits, nuts, whole grains, lean vegetable or animal protein, and fish and minimizes the intake of trans fats, red meat and processed meats, refined carbohydrates, and sugar-sweetened beverages. For adults with overweight/obesity, counseling and caloric restriction are recommended for achieving and maintaining weight loss.

5 Adults should engage in at least 150 minutes per week of accumulated moderate-intensity physical activity or 75 minutes per week of vigorous-intensity physical activity.

6 For adults with type 2 diabetes mellitus, lifestyle changes, such as improving dietary habits and achieving exercise recommendations, are crucial. If medication is indicated, metformin is first-line therapy, followed by consideration of a sodium-glucose cotransporter 2 inhibitor or a glucagon-like peptide-1 receptor agonist.

7 All adults should be assessed at every healthcare visit for tobacco use, and those who use tobacco should be assisted and strongly advised to quit.

8 Aspirin should be used infrequently in the routine primary prevention of ASCVD because of lack of net benefit.

9 Statin therapy is first-line treatment for primary prevention of ASCVD in patients with elevated low-density lipoprotein cholesterol levels (≥190 mg/dL), those with diabetes mellitus, who are 40 to 75 years of age, and those determined to be at sufficient ASCVD risk after a clinician–patient risk discussion.

ACC/AHA 2019