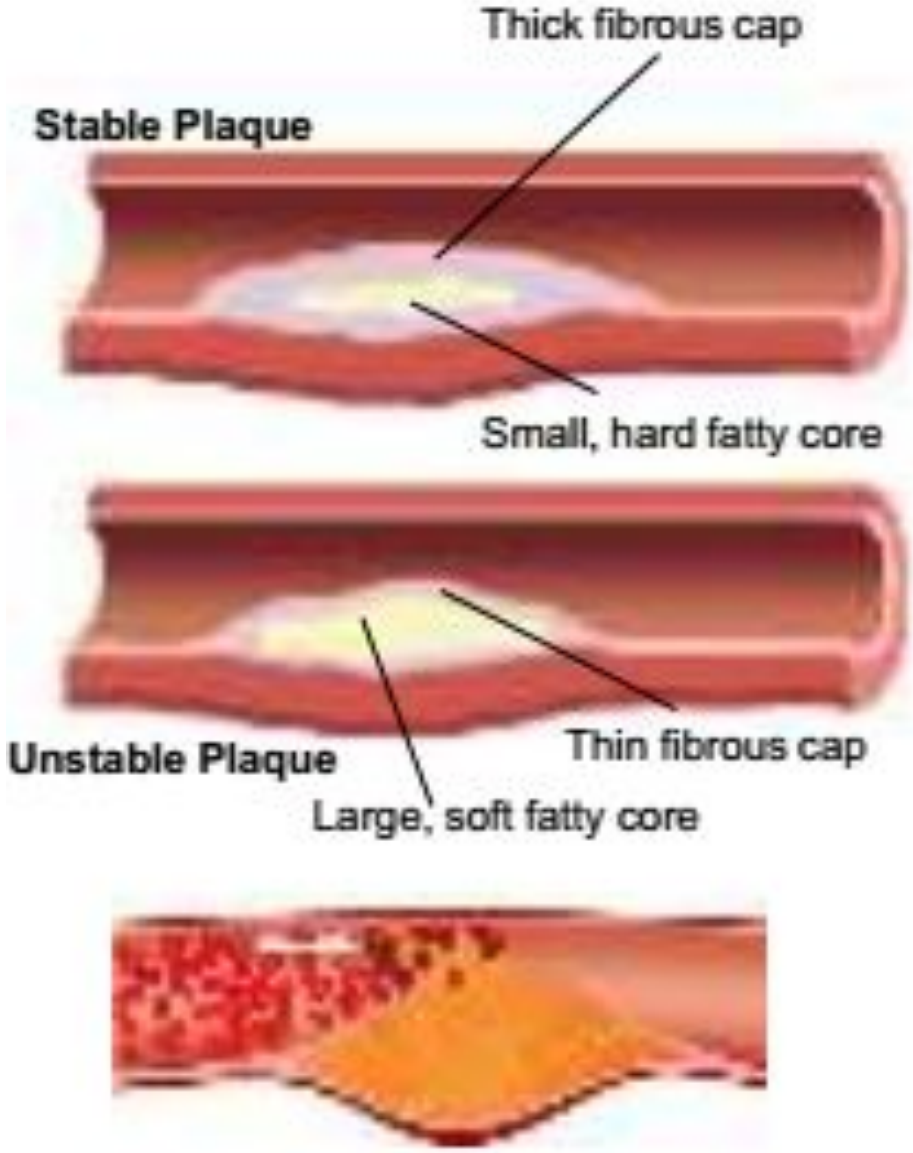
Dyslipidemia

Learning Objectives

- Definition and Classification of Dyslipidemia
  - Hypercholesterolemia
  - Familial hypercholesterolemia
  - Hypertriglyceridemia
- Atherosclerotic Cardiovascular Disease-ASCVD
- Review the updated guidelines for statin therapy in preventing ASCVD.
- Common Anti-lipid Medications.



Plaque Rupture

Most common cause of ACS

- Coronary atherosclerotic plaque rupture occurs when the fibrous cap ruptures
  - Nearly 50% at sites with <50% luminal narrowing
- Thrombus develops on top of the disrupted plaque
- Statins, exercise and ACE inhibitors stabilize the fibrous cap of a coronary atheroma, reducing the likelihood of rupture

The four Statin Benefit Groups

1. Atherosclerotic cardiovascular disease (acute coronary syndrome, past myocardial infarction, angina, coronary or other arterial revascularization, past stroke, TIA, or peripheral artery disease)
2. Primary elevations of LDL ≥190 mg/dL (usually familial)
3. Diabetes age 40-75 yrs and LDL ≥70 mg/dl
4. Without clinical ASCVD or diabetes, age 40-75, LDL 70-189, *and* estimated 10-year ASCVD risk of ≥7.5%

Types of Statin

High-intensity Statins

(≥50% LDL-C reduction)

Atorvastatin 40-80 mg

Rosuvastatin 20 mg

Moderate-intensity Statins

(30% to <50% LDL-C reduction)

Atorvastatin 10-20 mg

Rosuvastatin 5-10 mg

Simvastatin 20-40 mg

Pravastatin 40-80 mg

Lovastatin 40 mg

Fluvastatin 40 mg bid

Selecting Statin Intensity

1. Individuals with clinical ASCVD
   High-intensity or maximally tolerated statin. Goal: lower LDL by ≥50%

2. Primary elevations of LDL ≥190 mg/dL (usually familial)
   High-intensity statin

3. 40-75 yrs with diabetes and LDL ≥70 mg/dl
   Moderate or high-intensity statin. Goal: lower LDL by ≥50%

4. 40-75 yrs without clinical ASCVD or diabetes and LDL ≥70, *and* estimated 10-year ASCVD risk of ≥7.5%
   Moderate intensity statin if a ***discussion of options*** favors statins

ASCVD Risk Calculators

(use to calculate the 10-year risk for atherosclerotic cardiovascular disease in patients without clinical ASCVD, diabetes, or familial hyperlipidemia)

http://tools.acc.org/ASCVD-Risk-Estimator/
http://my.americanheart.org/cvriskcalculator

Information used in ASCVD risk calculators		
Age Gender Race	Total cholesterol HDL cholesterol Diabetes status	Systolic blood pressure Blood pressure lowering medication use Smoking status

For Patients Without Clinical ASCVD

Cholesterol Treatment Guideline vs. **USPTSF Guideline**

CTG 2018: *calculate 10 yr CV risk and if >7.5%, have a statin discussion*

USPSTF: for ages 40-75 with *one risk factor...*

[Dyslipidemia (LDL > 130 or HDL < 40), Diabetes, Smoking, Hypertension]

...calculate 10 yr CV risk and
if ≥10% start statin (low-moderate dose)
if 7.5-10% selectively start statin (low-moderate dose)

Insufficient evidence re: benefits and harms of initiating statin use in adults >75 years.

Statin Use for Primary Prevention of Cardiovascular Disease in Adults. USPSTF Recommendation. JAMA 16;316(19)

Risk-enhancing Factors in Statin Decision

- Family history of premature ASCVD (male <55, female <65)
- Persistently elevated LDL levels ≥ 160 mg/dl
- Metabolic Syndrome
- Chronic kidney disease
- History of preeclampsia or early menopause (age ≤40)
- Chronic inflammatory disorders
- High-risk ethnic groups (South Asian)
- Triglycerides ≥175 mg/dl
- Highly sensitive C-reactive protein >2.0 mg/L.
- Ankle-brachial index (ABI) <0.9
- Lipoprotein (a) ≥50 mg/dl
- Apolipoprotein B ≥130 mg/dl

- Also consider lifestyle changes, side effects, cost, and patient preference

Coronary Artery Calcium (CAC) Testing

New in 2018 Guidelines

In select adults 40-75 yo without diabetes and with LDL ≥70 mg/dl and 10-year ASCVD risk of ≥7.5% to 19.9%, consider measuring CAC to add to the decision discussion.

- CAC = 0, may withhold statins
- CAC 1-99 and age ≥55, reasonable to start statin
- CAC ≥100 or ≥75th percentile, reasonable to start statin

Indications for Non-Statin Therapy

- Severe hypercholesterolemia-unlikely to respond to statin
- Severe adverse effect, myositis, Hepatitis
- Pregnancy

Statin-related Myopathy

- Myalgia (muscle complaints without CK elevations)
- Myositis (muscle complaints with CK elevations)
- Rhabdomyolysis (elevated CK levels, elevated creatinine)

- Risk increased in liver or renal failure, hypothyroidism, diabetes mellitus
- Risk increased with macrolides, azoles, cyclosporine, gemfibrozil, niacin, HIV protease inhibitors, nefazodone, verapamil, diltiazem, and amiodarone.
- Risk increased with drinking more than a quart of grapefruit juice a day.

- Routine monitoring of CK not required.
- Discontinue statin if CK more than 10 times upper limit of normal (ULN)

Non-statin Therapies

New in 2018 Guidelines

- In very high-risk ASCVD and LDL still ≥70 mg/dl on maximally tolerated statin, consider adding ezetimibe.

- If LDL still ≥70 mg/dl, consider adding a PCSK9 inhibitor.

PCSK9 Inhibitors

- Proprotein convertase subtilisin/kexin type 9 (PCSK9) is a natural protein that binds/destroys LDL receptors in liver, preventing them from removing LDL-C.
- Loss-of-function mutation in the PCSK9 gene is associated with significantly reduced levels of LDL-C and a lower lifetime risk for cardiovascular disease.

- Mutations of PCSK9 gene identified with familial hypercholesterolemia.
- Injectable monoclonal antibodies bind to PCSK9 allowing the receptors to continue clearing LDL-C: evolocumab (Repatha), alirocumab (Praluent).

- 2018 Guidelines: “these drugs are of low value due to their high cost”

CASE NO. 1

A 67-year-old woman returns to discuss the results of her recent lipid panel. She had a transient ischemic attack 2 years ago, and her only medications are aspirin, vitamin D, and calcium supplements. She does not smoke and has no history of angina or heart disease. She has a sister with hypothyroidism and a brother who was diagnosed with type 2 diabetes at age 65.

The patient's blood pressure is 122/82 mm Hg, her heart rate is 76 beats per minute, and her BMI is 22.7.

Laboratory testing yields a glycated hemoglobin value of 5.6% (reference range, 3.8–5.6) and the following lipid results:

	Patient value
Total cholesterol (mg/dL)	233
LDL cholesterol (mg/dL)	156
HDL cholesterol (mg/dL)	62
Triglycerides (mg/dL)	75

What type of prevention does this patient need?

How are you going to provide such prevention?

- Age <75Clinical-ASCVD (TIA)-**Secondary prevention**.
- Female
- Not Diabetic.
- Non-Smoker ..
- LDL-C is 156mg/dl

10-year ASCVD risk estimation is not required

- Four groups most likely to benefit from statin therapy are identified:
  1. Patients with any form of clinical ASCVD
  2. Patients with primary LDL-C levels of 190 mg per dL or greater
  3. Patients with diabetes mellitus, 40 to 75 years of age, with LDL-C levels of 70 to 189 mg per dL
  4. Patients without diabetes, 40 to 75 years of age, with an estimated 10-year ASCVD risk $\geq$ 7.5%
- Risk assessment for 10-year and lifetime risk is recommended using an updated ASCVD risk calculator: http://my.americanheart.org/cvriskcalculator.

Secondary Prevention in Patients with Clinical ASCVD

Very high-risk includes a history of multiple major ASCVD events or 1 major ASCVD event and multiple high-risk conditions

High risk conditions includes:

- Age >65
- Familial hypercholesterolemia
- Prior CABGE or PCI
- CKD with eGFR<60
- High LDL despite of max. Rx
- Current smoking
- DM
- History of CHF

Major Events includes:

- Recent ACS within 12 mo
- History of MI
- History of Ischemic stroke
- Peripheral Arterial Disease

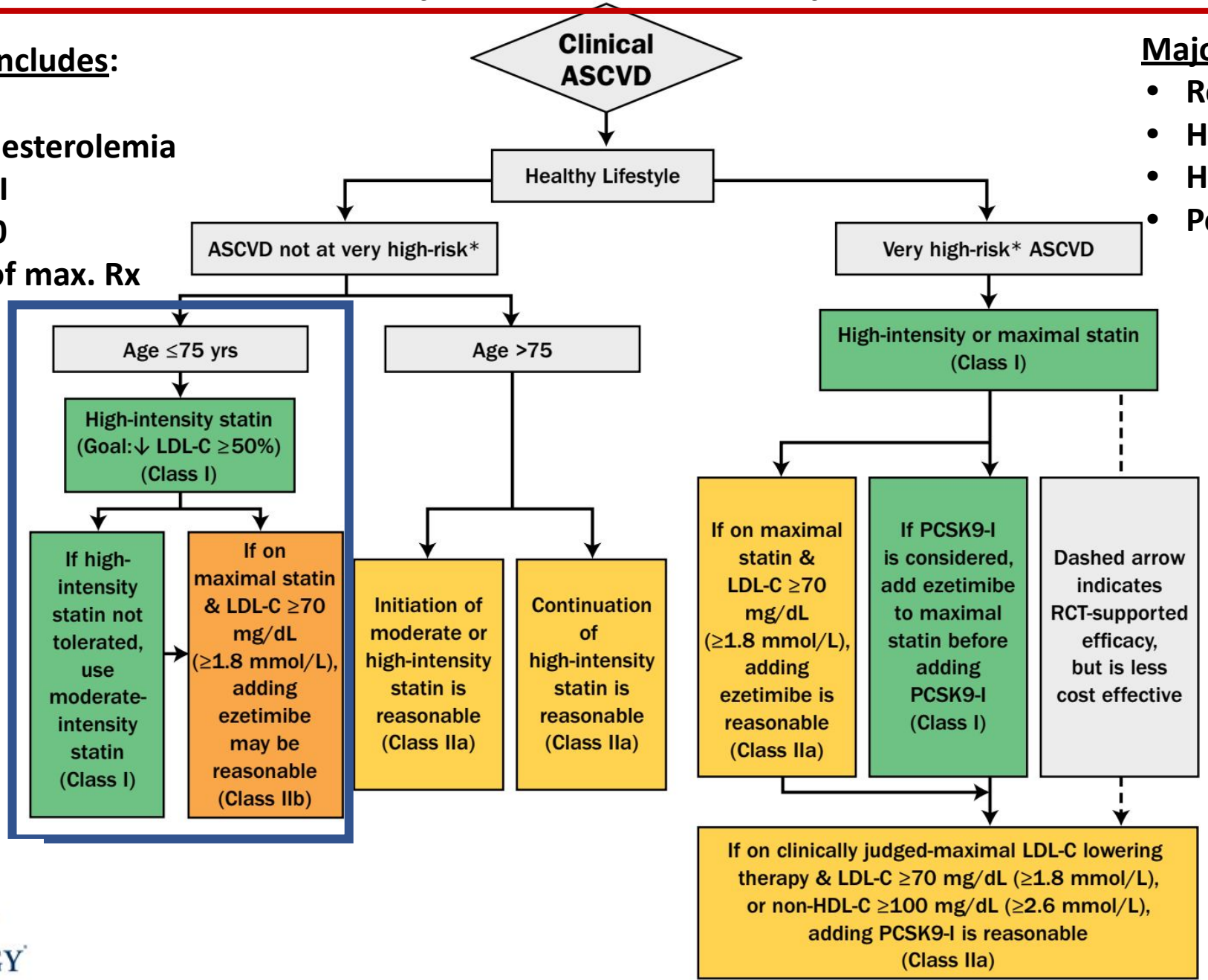


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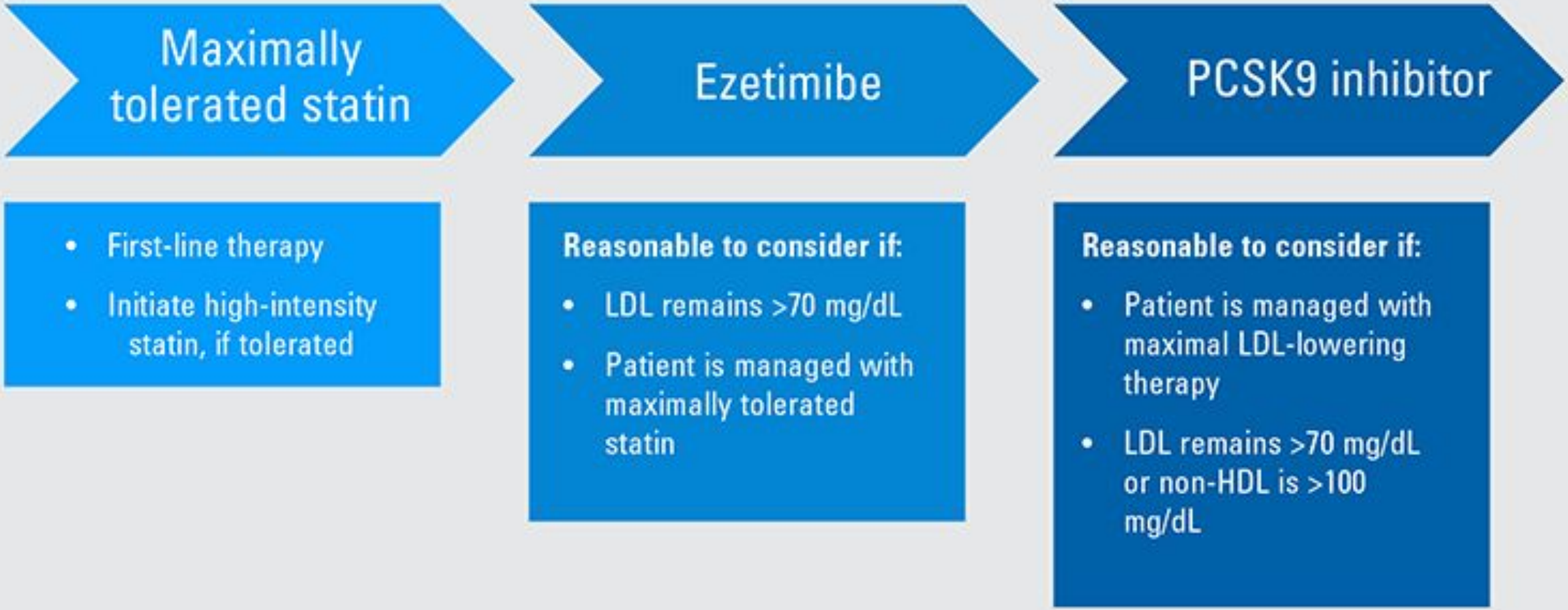
Figure 1

Updated Treatment Based on ACC/AHA Cholesterol Risk Guideline for Very-High-Risk ASCVD



ACC/AHA: American College of Cardiology/American Heart Association; ASCVD: atherosclerotic cardiovascular disease; PCSK9: proprotein convertase subtilisin/kexin type 9. Source: Reference 2.

CASE NO. 3

A 54-year-old woman with a history of obesity and impaired fasting glucose presents for a regularly scheduled visit. She has no specific concerns but is newly motivated to improve her health because her first grandchild was recently born, and she would like to see him grow up.

She has no personal or family history of cardiovascular disease or cancer. Her only medication is a daily multivitamin. She has smoked half a pack of cigarettes per day since age 22. She walks for 30 minutes three times per week but does not engage in any other formal exercise.

Her blood pressure is 118/76 mm Hg, her heart rate is 62 beats per minute, and her BMI is 33. Her physical examination is unremarkable.

Her laboratory results are as follows:

	Patient value	Reference range
Glycated hemoglobin (%)	5.9	3.8–5.6
Total cholesterol (mg/dL)	198	125–200
HDL cholesterol (mg/dL)	36	≥46
LDL cholesterol (mg/dL)	140	<130
Triglycerides (mg/dL)	111	<150
Fasting glucose (mg/dL)	110	70–100

How do you approach this patient? Explain

- **Primary prevention**-No clinical ASCVD
- Age > 40 years
- Female
- Not Diabetic. Although she has an impaired FBS
- Smoker ..
- LDL-C is 140mg/dl

10-year ASCVD risk estimation is:

5.8%

- Four groups most likely to benefit from statin therapy are identified:
  1. Patients with any form of clinical ASCVD
  2. Patients with primary LDL-C levels of 190 mg per dL or greater
  3. Patients with diabetes mellitus, 40 to 75 years of age, with LDL-C levels of 70 to 189 mg per dL
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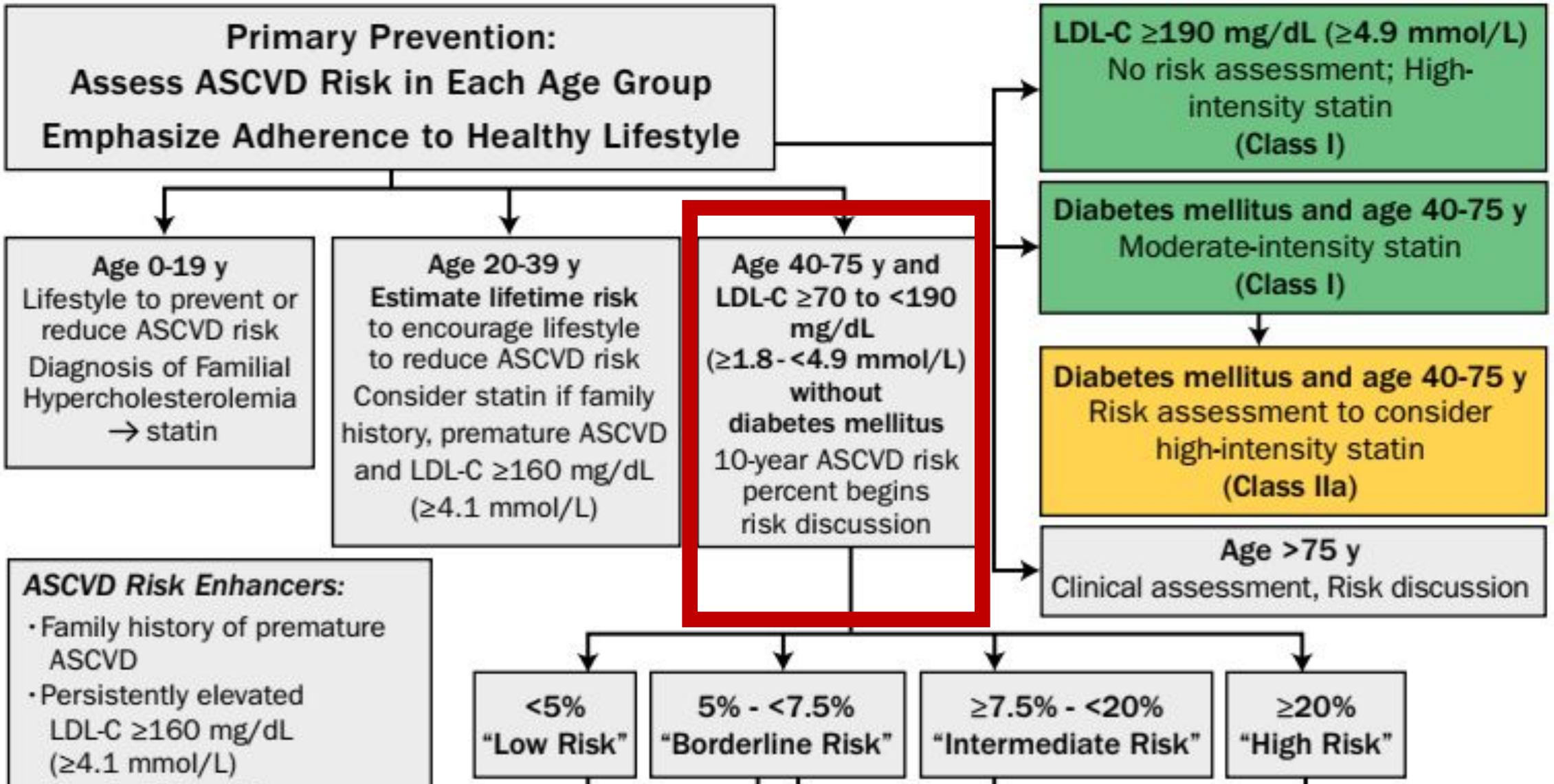
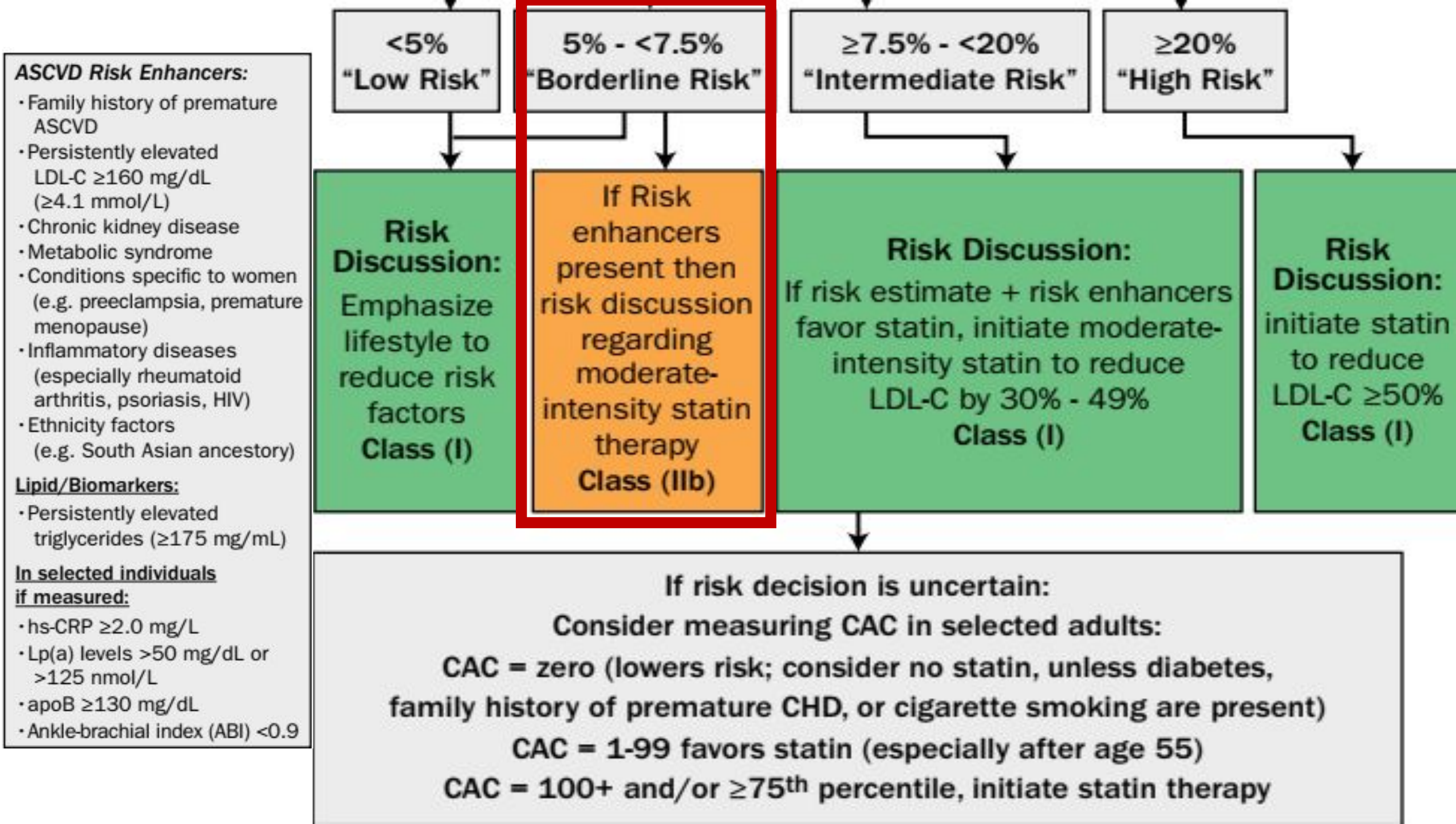
Primary Prevention




ASCVD Risk Enhancers:
• Family history of premature ASCVD
• Persistently elevated LDL-C ≥160 mg/dL (≥4.1 mmol/L)
• Chronic kidney disease
• Metabolic syndrome
• Conditions specific to women (e.g. preeclampsia, premature menopause)
• Inflammatory diseases (especially rheumatoid arthritis, psoriasis, HIV)
• Ethnicity factors (e.g. South Asian ancestory)
Lipid/Biomarkers:
• Persistently elevated triglycerides (≥175 mg/mL)
In selected individuals if measured:
• hs-CRP ≥2.0 mg/L
• Lp(a) levels >50 mg/dL or >125 nmol/L
• apoB ≥130 mg/dL
• Ankle-brachial index (ABI) <0.9
<5% "Low Risk"
5% - <7.5% "Borderline Risk"
≥7.5% - <20% "Intermediate Risk"
≥20% "High Risk"
Risk Discussion: Emphasize lifestyle to reduce risk factors Class (I)
If Risk enhancers present then risk discussion regarding moderate-intensity statin therapy Class (IIb)
Risk Discussion: If risk estimate + risk enhancers favor statin, initiate moderate-intensity statin to reduce LDL-C by 30% - 49% Class (I)
Risk Discussion: initiate statin to reduce LDL-C ≥50% Class (I)
If risk decision is uncertain:
Consider measuring CAC in selected adults:
CAC = zero (lowers risk; consider no statin, unless diabetes, family history of premature CHD, or cigarette smoking are present)
CAC = 1-99 favors statin (especially after age 55)
CAC = 100+ and/or ≥75th percentile, initiate statin therapy

Discussion …

- This patient has relatively low risk for ASCVD
- Motivated to reduce her risk
  - Smoking cessation
  - Life style intervention-diaetary changes , weight loss, and increase in aerobic exercise
  - 5-8Kg body weight loss. 5mg/dl reduction in LDL and 2 -3 mg/dl increase in HDL
- Since the patient has no risk enhancer statin could be offered electively to these patient but <u>lifestyle remains the foundation for such patient without the need for statin therapy.</u>