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Lipid Management in 2025

Original Presenter: Molly Schoder, MSN, FNP-BC

Test Yourself!

Pre-Test Question 1

According to guideline recommendations, at what age should traditional risk factor screening begin?

a. Age 10
b. Age 20
c. Age 60
d. Age 70

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Pre-Test Question 2

Which drug class has been found to decrease LDL by ≥50%, when patients do not reach goal on maximized statin dose?

a. Bile Acid Sequestrants
b. Non-steroidal anti-inflammatory drug
c. Cholesterol absorption inhibitor
d. PCSK9i

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Objectives

1. Identify at risk populations with inherited and non-inherited hyperlipidemias highlighting testing guidelines
2. Summarize pharmacologic and non-pharmacologic approaches to lowering lipids
3. Using case studies, identify the appropriate lipid-lowering agent for specific patient scenarios
4. Discuss solutions to close the gap across social determinants of health in application of evidence-based lipid lowering guidelines

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Case Study - TR

- 52 y.o. male presents for routine cardiology follow up
- PMH: CAD with CABG x3 (age 46), dyslipidemia, hypertension, sleep apnea using CPAP nightly, ADHD
- Today he has no specific complaints
- Physical Exam:
  - BP 119/79, HR 62 bpm, BMI 28.1 kg/m2
  - A&Ox3. Regular rate and rhythm, no murmur, rub, gallop or click. Lungs clear. No edema.
- Labs:
  - CBC unremarkable
  - Na 137, K 4.4, Cr 1.01, BUN 15.9, GFR 86, ALT 35, AST 34
  - Lipid Panel: TC 158, HDL 65, LDL 82, TG 56

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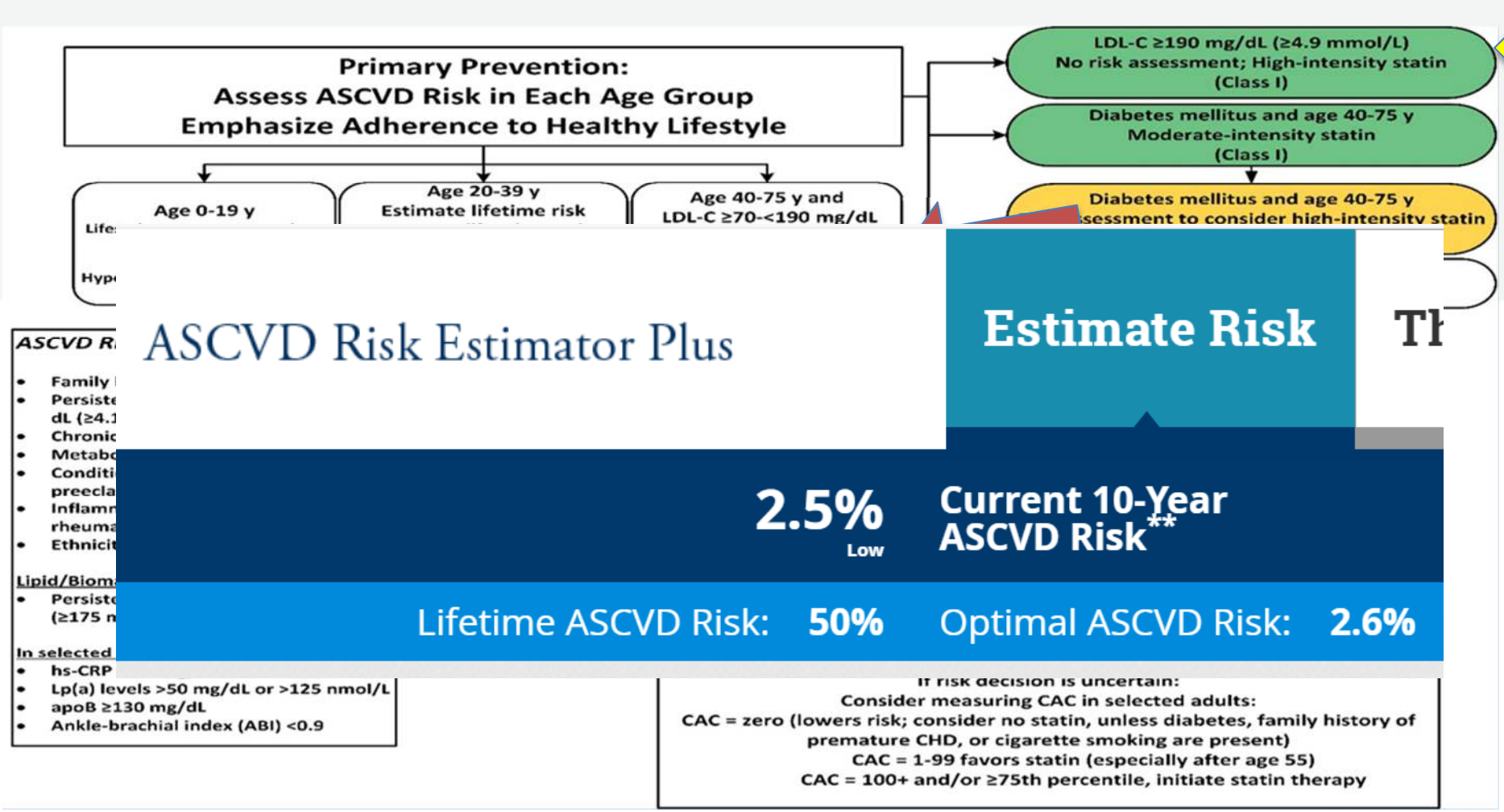

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(Grundy, Stone et al. 2019)

Familial (inherited) Hyperlipidemia

Underrecognized & Underdiagnosed

- Affects 1 in 250 US adults
- Equal prevalence between males and females
- Characterized by lifelong elevated LDL
- Individuals with FH have a 90-fold increased risk of ASCVD during their lifetime
- FH is caused by pathogenic variants in one of three genes, *LDLR, APOB, and PCSK9*
- Can be heterozygous (1 pathogenic variant) or homozygous (2 pathogenic variants)

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(de Ferranti, Rodday et al. 2016, Balla, Ekpo et al. 2020, Beheshti, Madsen et al. 2020)

When to test?

General Recommendations

- Based on the 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease
  - Screen for traditional risk factors every 4-6 years starting at age 20 including a lipid panel
- Selective screening in children with a family history of cardiovascular disease, dyslipidemia, or other risk factors as early as age 2
  - Recommendations on screening children vary among different organizations
  - *Of note, less than 3% of children are screened for lipids*

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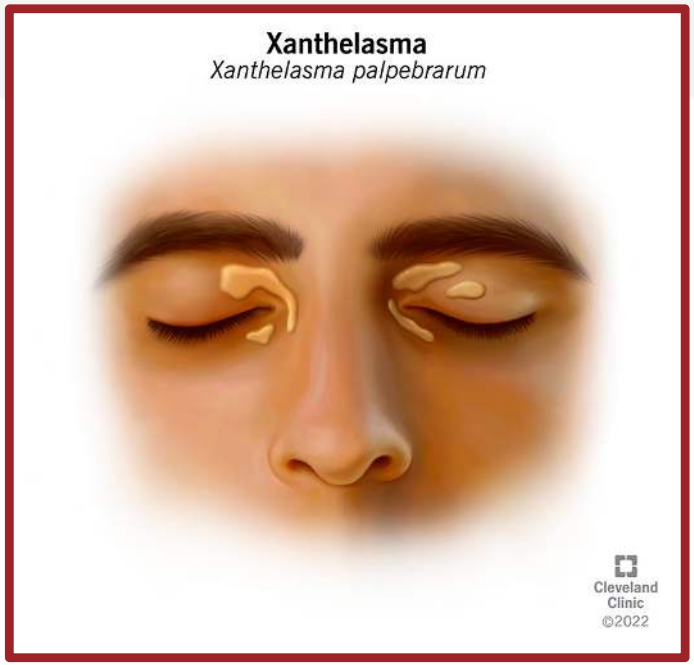
(Arnett, Blumenthal et al. 2019, Grundy, Stone et al. 2019, Balla, Ekpo et al. 2020)

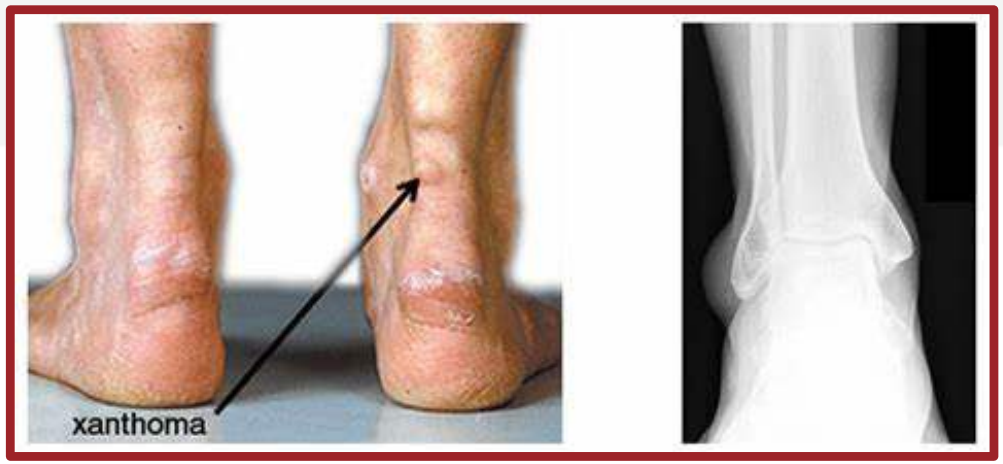
When to suspect FH?

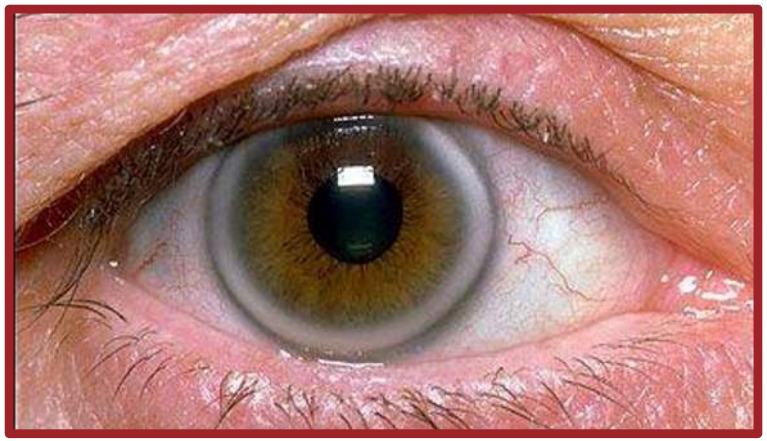
Assessment Components	Indicators of possible FH
LDL levels	• Persistently ≥ 160 mg/dL in children • Persistently ≥ 190 mg/dL in adults • Of note, individuals can have FH with LDL levels below 160 and 190 mg/dL, respectively. • LDL-C > 95th percentile in a first degree relative
Personal and family history	• Premature ASCVD (males age <55 years; females age <65 years)
Physical manifestations	• Xanthelasmas (yellowish deposit of cholesterol under the skin) • Extensor tendon xanthomas (typically Achilles, subpatellar, and hand extensor tendons) • Corneal arcus (white arc near the iris of the eye)

(McGowan, Hosseini Dehkordi et al. 2019)

Physical Manifestations of elevated cholesterol







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Does TR have familial hyperlipidemia?

- 52 y.o. male
- PMH: CAD with CABG x3 (age 46), dyslipidemia, hypertension, sleep apnea using CPAP, ADHD
- Lipids: TC 158, HDL 65, LDL 82, TG 56

1. Yes
2. No

3. Why?
4. What if I told you TR's baseline LDL prior to his CABG was 200?

What factors make you think TR may have FH?

A. First ASCVD event at age 46
B. Baseline LDL cholesterol of 200
C. Hypertension
D. Sleep Apnea
E. A & B
F. A, B, & C
G. All of the above

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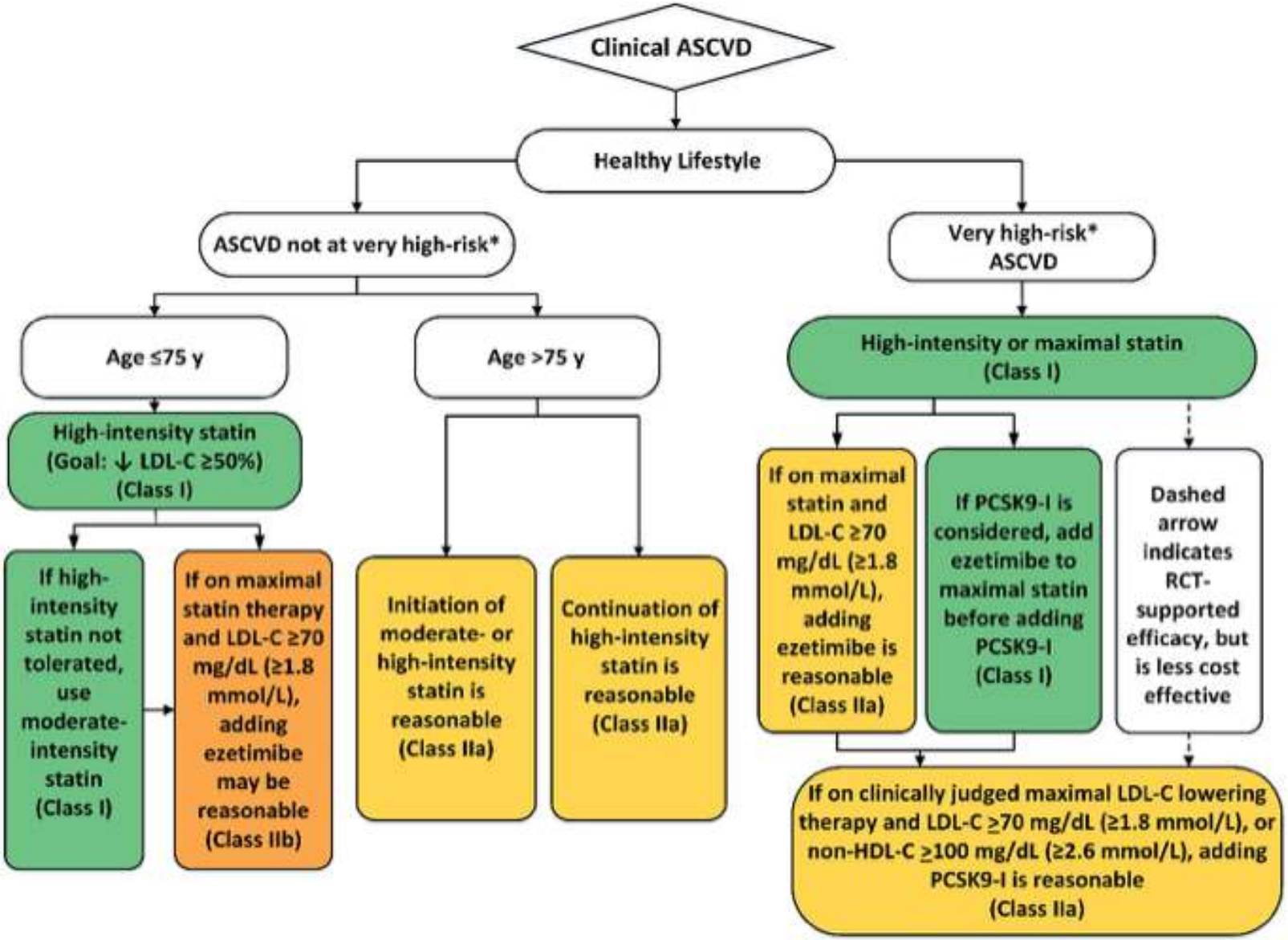

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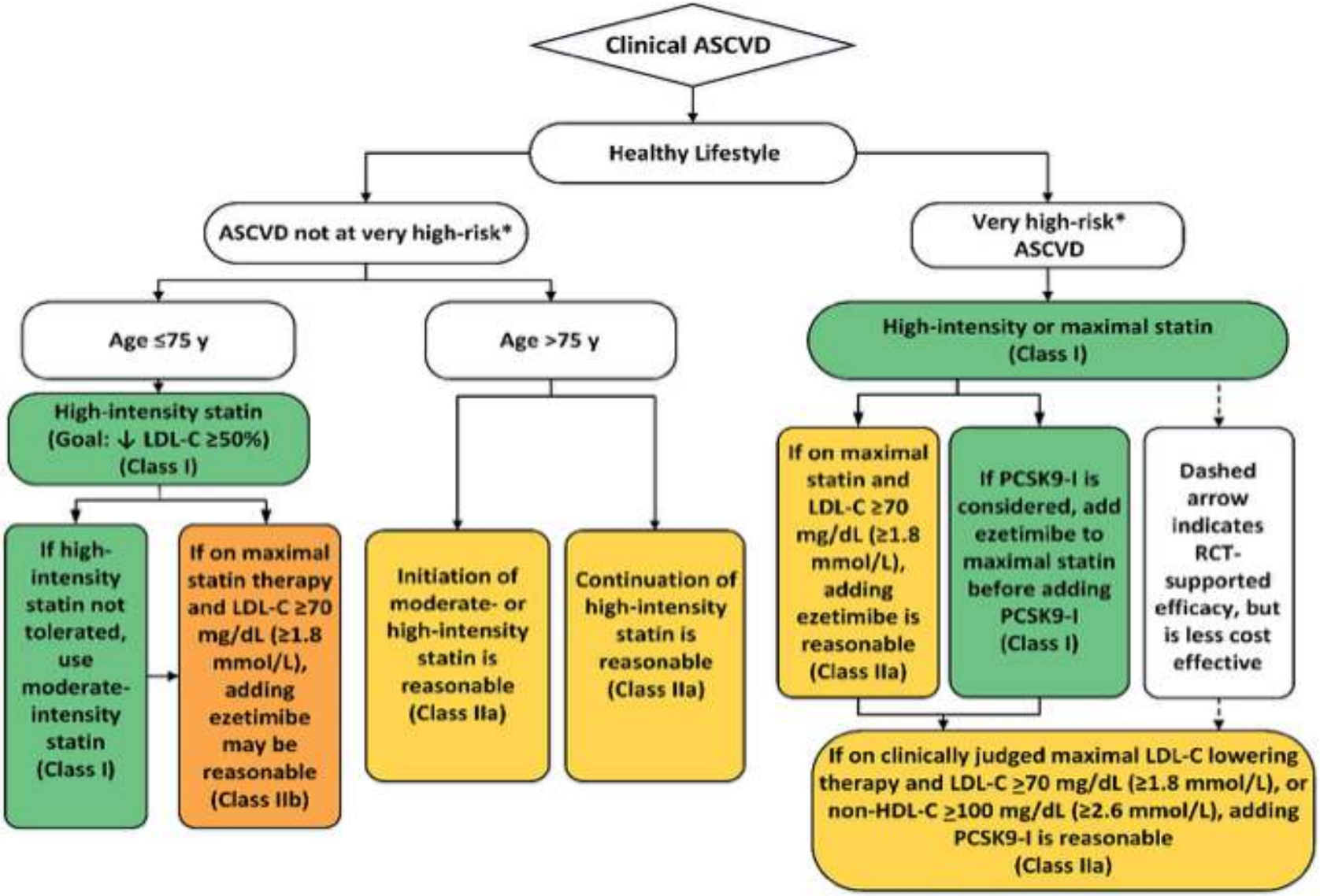
(Grundy, Stone et al. 2019)



(Grundy, Stone et al. 2019)

Lifestyle Interventions:

Nutrition & Diet

- A diet emphasizing intake of vegetables, fruits, legumes, nuts, whole grains, and fish
- Replacement of saturated fat with dietary monounsaturated and polyunsaturated fats
- A diet containing reduced amounts of cholesterol and sodium
- Minimize the intake of processed meats, refined carbohydrates, and sweetened beverages
- Intake of *trans* fats should be avoided

Exercise & Physical Activity

- Adults should be routinely counseled in healthcare visits to optimize a physically active lifestyle
- Engage in at least 150 minutes per week of accumulated moderate-intensity or 75 minutes per week of vigorous-intensity aerobic physical activity (or an equivalent combination of moderate and vigorous activity)
- If unable to meet the above, engaging in some moderate- or vigorous-intensity physical activity, even if less than this recommended amount, can be beneficial
- Decreasing sedentary behavior

(Arnett, Blumenthal et al. 2019)

Statin dosing:

Table 3. High-, Moderate-, and Low-Intensity Statin Therapy*

	High Intensity	Moderate Intensity	Low Intensity
LDL-C lowering†	≥50%	30%–49%	<30%
Statins	Atorvastatin (40 mg‡) 80 mg Rosuvastatin 20 mg (*40 mg*	Atorvastatin 10 mg (20 mg) Rosuvastatin (5 mg) 10 mg Simvastatin 20–40 mg§	Simvastatin 10 mg
	…	Pravastatin 40 mg (80 mg) Lovastatin 40 mg (80 mg) Fluvastatin XL 80 mg Fluvastatin 40 mg BID Pitavastatin 1–4 mg	Pravastatin 10–20 mg Lovastatin 20 mg Fluvastatin 20–40 mg

*Percent reductions are estimates from data across large populations. Individual responses to statin therapy varied in the RCTs and should be expected to vary in clinical practice (S3.2.1-2).

(Grundy, Stone et al. 2019)

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TR is taking rosuvastatin 20 mg daily and has tried 40 mg in the past and developed muscle symptoms. As a reminder, his LDL is currently 82, what would you do as a next step?

A. Re-attempt rosuvastatin 40 mg daily
B. Switch rosuvastatin to atorvastatin at 20 mg daily
C. Add ezetimibe (Zetia) 10 mg daily
D. Discuss lifestyle changes
E. Consider all of the above
F. I'm not sure!

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FDA- Approved Nonstatin LDL-C lowering agents

When patients do not achieve adequate LDL-C levels with maximized statin dose

Class or Agent	LDL-C ↓
Cholesterol absorption inhibitor (ezetimibe – Zetia) (Grundy, Stone et al. 2019)	13-20%
PSCK9 inhibitors: Monoclonal antibodies (evolocumab – Repatha and alirocumab - Praluent) (Schwartz, Steg et al. 2018; Sabatine, Giugliano et al. 2017)	55-59%
PCSK9 inhibitor: siRNA (inclisiran - Leqvio) (Leqvio. 2024)	50-52%
Bile Acid Sequestrants (cholestyramine, colesevelam, colestipol) (Grundy, Stone et al. 2019)	15-30%
ATP citrate lyase inhibitor (bempedoic acid - Nexletol) (Banach, Duell et al. 2020, Ray, Wright et al. 2020)	13-17%
Bempedoic acid + ezetimibe, fixed combination (Nexlizet) (Ballantyne, Laufs et al. 2020)	36%

Agent	LDL-C ↓
Lomitapide – Juxtapid (Cuchel, Meagher et al. 2013)	50%
Evinacumab – Evkeeza (Raal, Kallend et al. 2020)	47%

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Case Study - Lena R

- CC: 55 y.o. F following up today on her cholesterol panel
- PMH: CAD s/p MI with stent 2 years ago, HTN, HLD, Type 2 DM
- Lifestyle Hx: non-smoker, 1 alcoholic beverage a week
- FH: father with MI age 50, 1 brother age 48 with HLD
- Current Medications: rosuvastatin 10 mg daily, Zetia 10 mg daily, aspirin 81 mg daily, atenolol 100 mg daily, lisinopril 5 mg daily, HCTZ 12.5 mg daily, dapagliflozin-metformin 5-1000 mg daily

Physical Examination

Height: 5'6"
Wt: 150 lbs
BMI:24.2 kg/m2
BP: 126/78
HR: 66

Laboratory Results

TC: 240 mg/dl
TG: 267 md/dl
HDL: 55 mg/dl
LDL: 137 mg/dl
Non-HDL: 185 mg/dl

Cr: 0.88 mg/dl
ALT: 16 U/L
TSH – WN
GFR: 73 mL/min
HgA1c: 6.0

Thinking about Lena, what is her cholesterol goal and what next step(s) would you consider?

A. LDL goal <100. Increase rosuvastatin to 20 mg per day and reassess in 3 months

B. LDL goal <70. Increase rosuvastatin to 20 mg per day and reassess in 3 months

C. LDL goal <70. Start PCSK9 inhibitor such as Repatha or Praluent and reassess in 3 months

D. LDL goal <70. Review and encourage lifestyle interventions

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European Guidelines

Recommendations for treatment goals for low-density lipoprotein cholesterol

Recommendations	Class[a]	Level[b]
In secondary prevention for patients at very-high risk,[c] an LDL-C reduction of ≥50% from baseline[d] and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) are recommended.[33–35,119,120]	I	A
In primary prevention for individuals at very-high risk but without FH,[c] an LDL-C reduction of ≥50% from baseline[d] and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) are recommended.[34–36]	I	C
In primary prevention for individuals with FH at very-high risk, an LDL-C reduction of ≥50% from baseline and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) should be considered.	IIa	C
For patients with ASCVD who experience a second vascular event within 2 years (not necessarily of the same type as the first event) while taking maximally tolerated statin-based therapy, an LDL-C goal of <1.0 mmol/L (<40 mg/dL) may be considered.[119,120]	IIb	B
In patients at high risk,[c] an LDL-C reduction of ≥50% from baseline[d] and an LDL-C goal of <1.8 mmol/L (<70 mg/dL) are recommended.[34,35]	I	A
In individuals at moderate risk,[c] an LDL-C goal of <2.6 mmol/L (<100 mg/dL) should be considered.[34]	IIa	A
In individuals at low risk,[c] an LDL-C goal <3.0 mmol/L (<116 mg/dL) may be considered.[36]	IIb	A

ASCVD = atherosclerotic cardiovascular disease; FH = familial hypercholesterolaemia; LDL-C = low-density lipoprotein cholesterol.
[a]Class of recommendation.
[b]Level of evidence.
[c]For definitions see *Table 4*.
[d]The term 'baseline' refers to the LDL-C level in a person not taking any LDL-C-lowering medication. In people who are taking LDL-C-lowering medication(s), the projected baseline (untreated) LDL-C levels should be estimated, based on the average LDL-C-lowering efficacy of the given medication or combination of medications.

(Mach, Baigent et al. 2020)

ESC Risk Categories

- Very-high-risk:
  - Documented ASCVD
  - DM with target organ damage
  - Severe CKD
  - Calculated SCORE ≥ 10% for 10-year risk of fatal CVD
  - FH with ASCVD or with another major risk factor

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(Mach, Baigent et al. 2020)

Racial/Ethnic Considerations

Asian Americans

- ASCVD risk varies by country of origin
- ↑ LDL-C among Asian Indians, Filipinos, Japanese and Vietnamese than whites
- ↑ TG in all Asian subgroups
- ↑ Metabolic syndrome seen with lower waist circumference than in whites
- Japanese patients may be sensitive to statin dosing
- Higher plasma concentrations of rosuvastatin are seen in Japanese, Chinese, Malay, and Asian Indians as compared to whites

➢ Based on this, the FDA recommends starting a low dose of 5 mg per day and caution urged with increasing the dose

(Grundy, Stone et al. 2019)

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Racial/Ethnic Considerations

Hispanic/Latino

- ASCVD risk varies by country of origin together with socioeconomic status and acculturation level may explain risk factor burden more precisely
- DM is disproportionately present compared with whites and blacks
- ↑ metabolic syndrome and DM in Mexican Americans compared with whites and Puerto Ricans
- No sensitivity to statin dosing is seen and no specific safety considerations

Blacks/African Americans

- ASCVD risk assessment in black women higher than otherwise similar white counterparts
- ↑ DM and HTN
- No sensitivity to statin dosing is seen and no specific safety considerations
- Of note, baseline CK values are higher in blacks than whites

(Grundy, Stone et al. 2019)

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Social Determinates of Health

- Socioeconomic and education status
- Cultural, work and home environment
- Centers for Medicare & Medicaid Screening tool assess the 5 domains of non-health related measures that affect health outcomes:
  - Housing instability
  - Food insecurity
  - Transportation difficulties
  - Utility assistance needs
  - Interpersonal safety

(Arnett, Blumenthal et al. 2019)

(CDC, 2025)

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Summary:

- We reviewed characteristics of patients with inherited and non-inherited hyperlipidemias highlighting testing guidelines
- We Summarize pharmacologic and non-pharmacologic approaches to lowering lipids
- We used case studies to identify the appropriate lipid-lowering agent for specific patient scenarios
- We discuss solutions to close the gap across social determinants of health in application of evidence-based lipid lowering guidelines

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Post-Test Question 1

According to guideline recommendations, at what age should traditional risk factor screening begin?

a. Age 10
b. Age 20
c. Age 60
d. Age 70

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Post-Test Question 2

Which drug class has been found to decrease LDL by ≥50%, when patients do not reach goal on maximized statin dose?

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b. Non-steroidal anti-inflammatory drug
c. Cholesterol absorption inhibitor
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