Hyperlipidemia: Past and Present

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Conflicts of Interest

- None to disclose

Learning Objectives for Pharmacist

- Describe the pathophysiology of hyperlipidemia
- Compare the 2013 ACC/AHA Blood Cholesterol guidelines and 2017 AACE Dyslipidemia and Prevention of CVD guidelines
- Analyze the literature that contributed to the 2018 ACC/AHA guideline on the Management of Blood Cholesterol
- Evaluate how these updated guidelines impact clinical practice

CVD: cardiovascular disease

Learning Objectives for Pharmacy Technicians

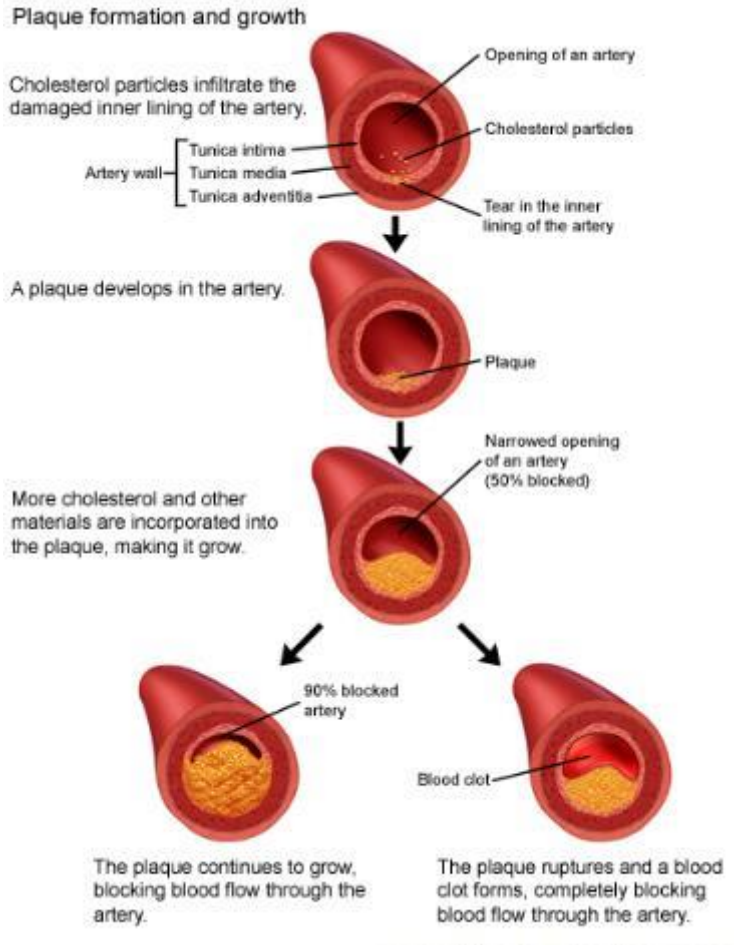
- Define dyslipidemia
- Describe the mechanism behind cholesterol
- Recognize the common treatments for lipid management

Introduction

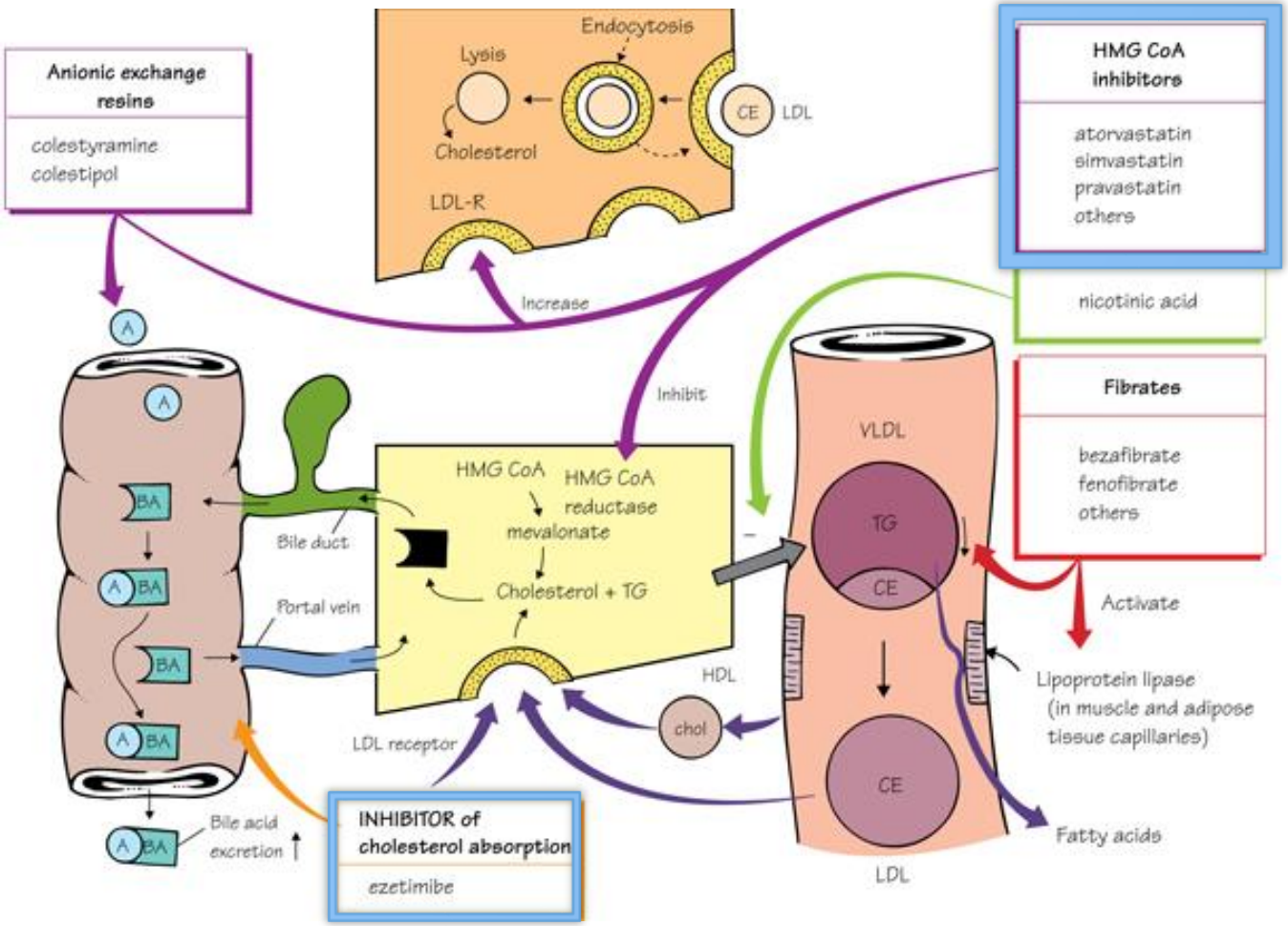
- 71 million American adults (33.5%) have high low-density lipoproteins (LDL)
- Only 1 out of every 3 adults with high LDL cholesterol have it under control
- Less than half of adults with high LDL cholesterol get treatment
- Hinds, et al. found only 40% of patients are appropriately prescribed a moderate – high intensity statin

Hyperlipidemia

- Hyperlipidemia is a disorder characterized by abnormally high levels of lipids
- Cholesterol and its lipoproteins are related to atherosclerotic cardiovascular disease (ASCVD)
  - People with high cholesterol have about twice the risk of having heart disease



Pathophysiology



Diagnostics

Fasting lipid panel (10 hr)	Normal range	Borderline	High
Total cholesterol (TC)	< 200	200 – 239	> 240
LDL – C	<130	130 – 159	> 160
HDL – C	> 40 (men) > 50 (women)	< 40 (men) < 50 (women)	
Triglycerides (TG)	< 150	150 – 199	> 200

Note: LDL – C calculated by: TC minus (HDL – C) minus (TG divided by 5)

- Not valid to calculate if TG are greater than 250 mg/dL

Risk Assessment

Variables	Framingham Risk Assessment Tool	10 – year Risk of Coronary Event (ASCVD risk)
Population	General population from Framingham Massachusetts	Based on cohort studies funded by the NHLBI
Age	30 – 74 years	40 – 79 years
Factors	• Sex • Age • Smoking status • Total cholesterol • HDL – C • Diabetes • Systolic blood pressure (SBP) • Hypertension treatment	• Sex • Age • Smoking status • Total cholesterol • HDL – C • Diabetes • SBP • Hypertension treatment (if SBP > 120 mmHg)
Target CVD Events	• Angina, myocardial infarction, CHD death, coronary insufficiency	• Myocardial infarction, CHD death, stroke

CHD: coronary artery disease

Additional Tests

Apolipoproteins

- Useful for individuals are at higher risk
- Assess success of LDL – C lowering therapy

Additional test to stratify ASCVD risk

- hsCRP
- Lipoprotein-associated phospholipase A2 (Lp-PLA2)
- Coronary artery calcification (CAC)
- Carotid intima media thickness (CIMT)

Non – Pharmacological Management

At least 30 minutes of moderate-intensity physical activity

- 4 – 6 times a week

Reduced calorie diet

- Lower intake of fats and cholesterol

Tobacco cessation

Pharmacology Management – High Intensity Statins

≥ 50%

High intensity statin	Dose range	Characteristics	Administration
Rosuvastatin (Crestor)	20 – 40 mg	Hydrophilic	Anytime
Atorvastatin (Lipitor)	40 – 80 mg	Lipophillic	

Pharmacology Management – Moderate Intensity Statins

30 - 49 %

Moderate intensity statin	Dose range	Characteristics	Administration
Rosuvastatin (Crestor)	10 – 20 mg	Hydrophilic	Anytime
Atorvastatin (Lipitor)	5 – 10 mg	Lipophillic	Anytime
Simvastatin (Zocor)	20 – 40 mg	Lipophillic	Night
Lovastatin (Mevacor)	40 mg	Lipophillic	Night
Pravastatin (Pravachol)	40 – 80 mg	Hydrophilic	Anytime
Fluvastatin (Lescol)	40 – 80 mg	Lipophillic	Night
Pitavastatin (Livalo)	2 – 4 mg	Lipophillic	Anytime

Pharmacology Management – Low Intensity Statins

< 30%

Low intensity statin	Dose range
Simvastatin (Zocor)	10 mg
Lovastatin (Mevacor)	20 mg
Pravastatin (Pravachol)	10 – 20 mg
Fluvastatin (Lescol)	20 – 40 mg
Pitavastatin (Livalo)	1 mg

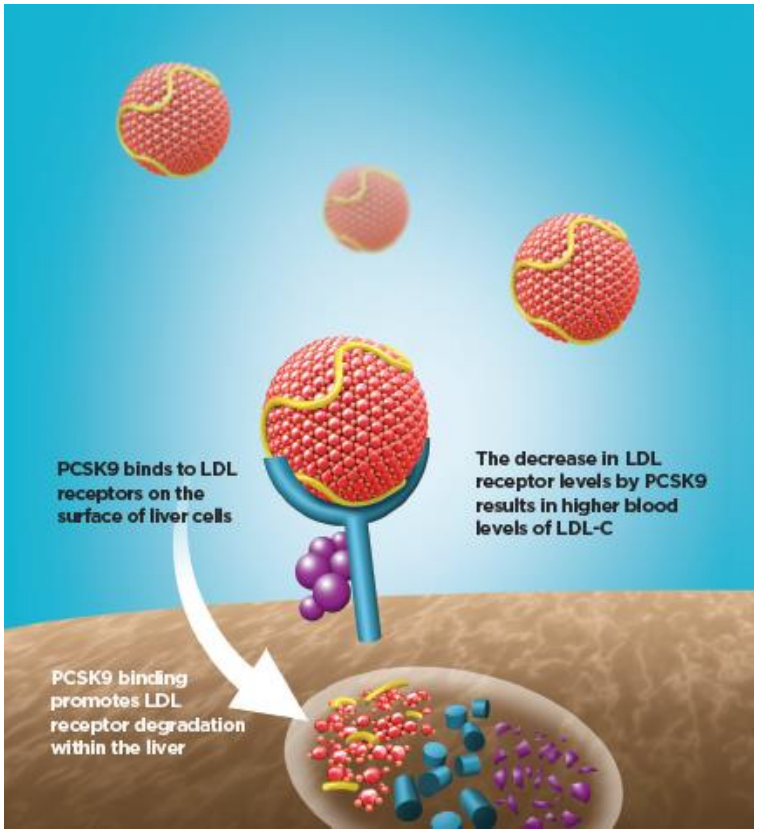
Monitoring Parameters - Statins

Adverse Effects	Monitoring
• Myalgia • Myopathy • Rhabdomyolysis • Hepatic dysfunction • Renal dose adjustments • Increase glucose • Pregnancy category X • Drug interactions	• Fasting lipid panel • Liver function panel • Creatinine kinase

Pharmacology Management – Cholesterol Absorption Inhibitors

- Zetia (ezetimibe) 10 mg PO once daily
- Lowers LDL 10 – 18 %
- With statins lowers LDL additional 25% (IMPROVE-IT trial)
  - Modest decrease in cardiovascular events
- Adverse effects
  - Increase liver function tests
  - Myopathy
  - Rhabdomyolysis
  - Upper respiratory infection
  - Diarrhea
  - Sinusitis

Pharmacology Management – PCSK9 Inhibitors



- Human monoclonal antibodies that bind to PCSK9 and inhibit them
- Lowers LDL by 48 – 71 %

Pharmacology Management – PCSK9 Inhibitors

Medications	Dose ranges	Adverse Effects
Alirocumab (Praluent)	HeFH/ASCVD: • 75 – 150 mg SC once every 2 weeks • 300 mg SC monthly	• Nasopharyngitis • Injection site actions • Influenza • Upper respiratory infections • Urinary tract infections • Back pain (evolocumab) • Increase liver function tests (alirocumab)
Evolocumab (Repatha)	HeFH/ASCVD: • 140 SC once every 2 weeks • 420 mg monthly	
	HoFH: • 420 mg SC monthly • 3 injections of 140 mg in 30 minute intervals SC monthly	

HeFH: Heterozygous familial hypercholesterolemia HoFH: Homozygous Familial Hypercholesterolemia

Pharmacology Management - Miscellaneous

Class	Medications	TG	LDL	Adverse Effects
Fibrates	Gemfibrozil	20 – 35%		• Myalgia • Increases liver function tests • GI symptoms • May increase SCr • Dyspepsia • Upper respiratory tract infections
	Fenofibrate		20 – 25%	
Fish – oil	Omega – 3 oil	27 – 45%	20 – 42%	• GI symptoms • May prolong bleeding • Increases in liver function tests • Increased incidence in A-fib or aflutter episodes • Avoid if hypersensitivity to fish and/or shellfish

Pharmacology Management - Miscellaneous

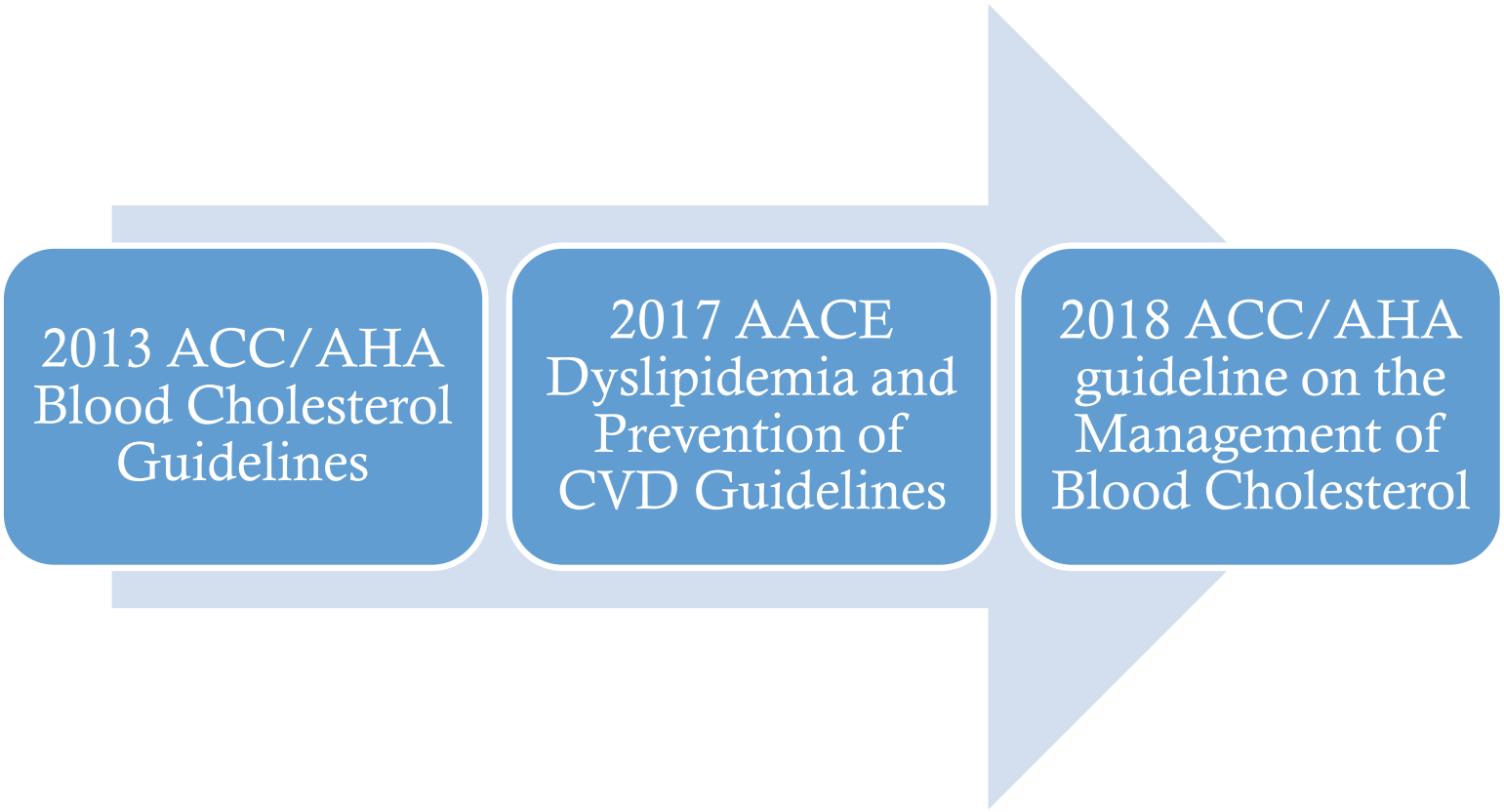
Class	Medications	TG	LDL	Adverse Effects
Niacin	Niacin IR	20 – 30%	10 – 25%	• Flushing • Nausea/vomiting/diarrhea • Increases uric acid levels • Increase glucose • Increase liver functions test
	Niaspan ER			
	Slo - Niacin			
Bile acid sequestrants	Cholestyramine		15 – 25%	• GI symptoms • Increase liver functions tests • May increase TG
	Colestipol			
	Colesevelam			

Assessment Question 1

Which of the following is a first – line option for lipid management?

A. Lifestyle modifications
B. Statin therapy
C. Niacin
D. Ezetimibe

Timeline of Hyperlipidemia Guidelines



2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

Endorsed by the American Academy of Physician Assistants, American Association of Cardiovascular and Pulmonary Rehabilitation, American Pharmacists Association, American Society for Preventive Cardiology, Association of Black Cardiologists, Preventive Cardiovascular Nurses Association, and WomenHeart: The National Coalition for Women With Heart Disease

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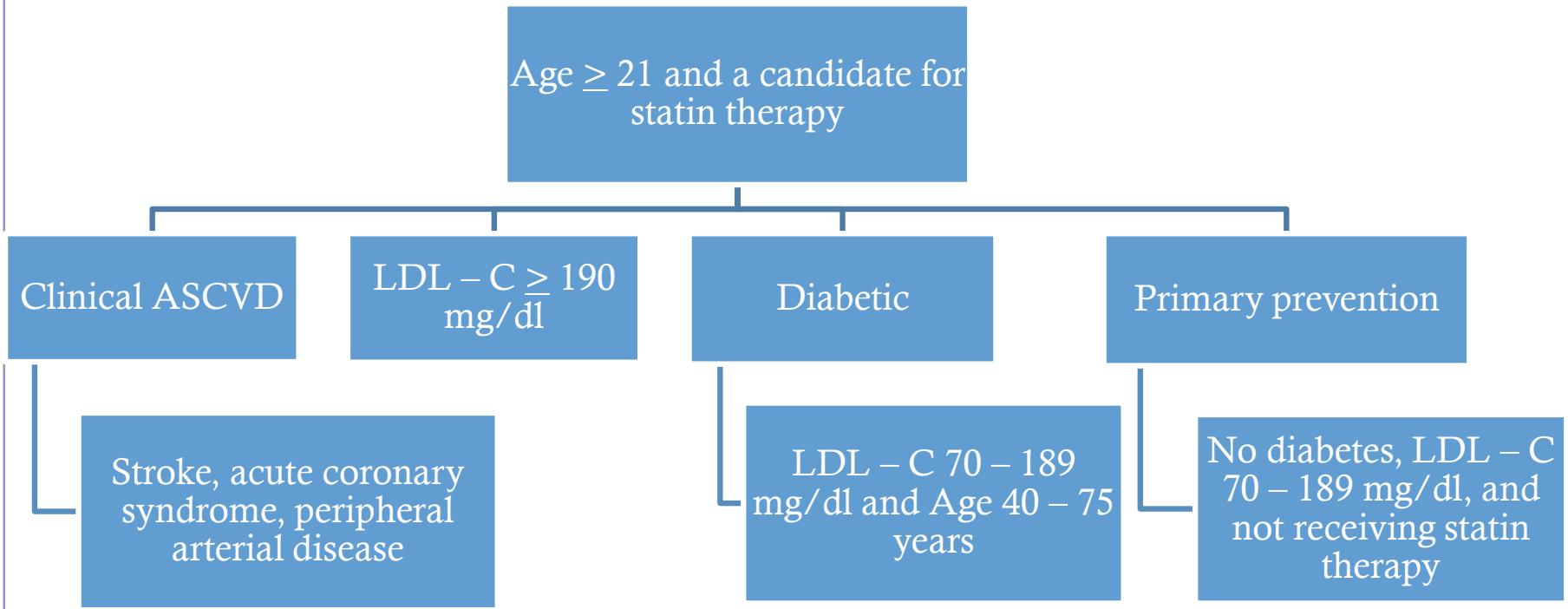
Right Patient, Right Statin, Right Dosage

- Many people at high risk for CVD events, were not receiving statins
- **ONLY** 58.2% of individuals with CHD and 52% of individuals with diabetes who are 40 years of age and older were taking statin

2013 ACC/AHA Guidelines

FOUR GROUPS THAT BENEFIT FROM STATIN THERAPY



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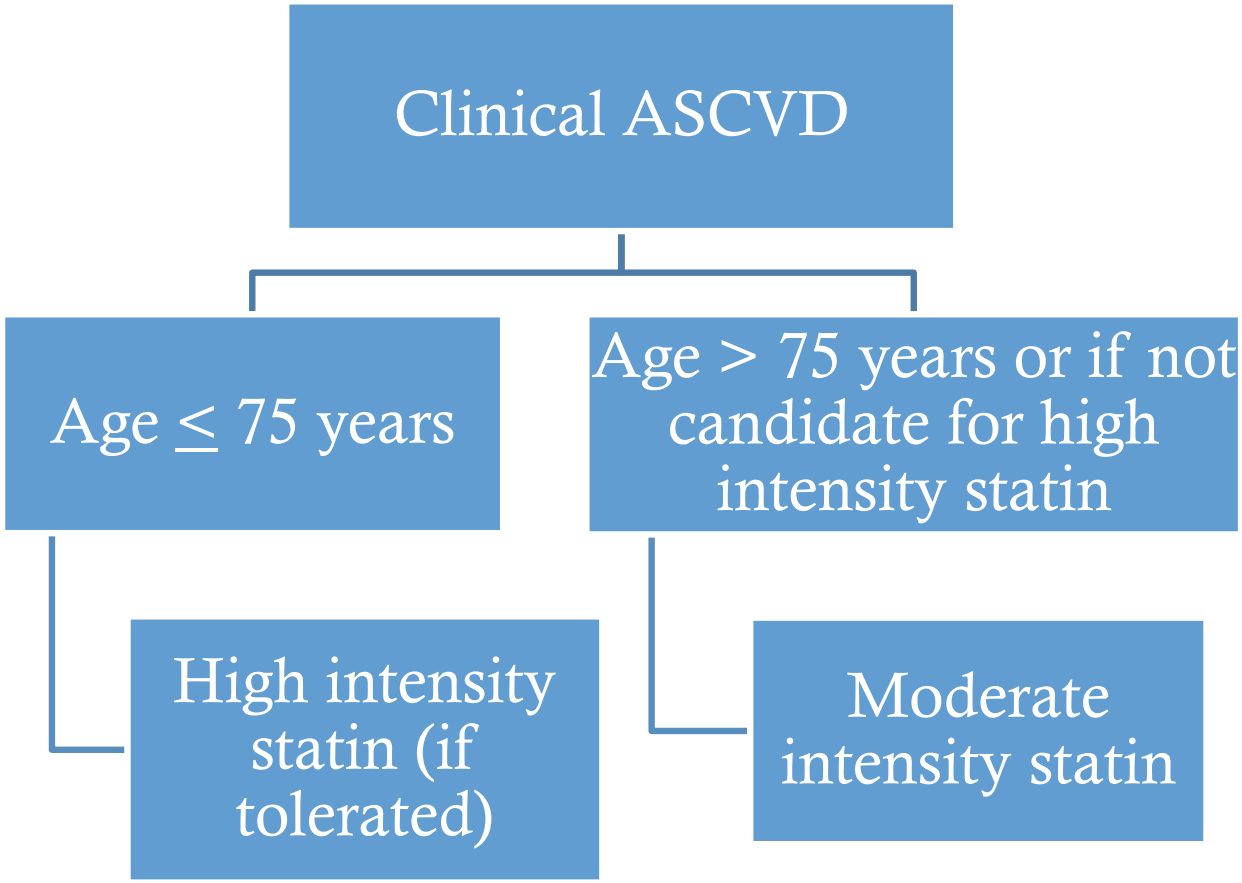

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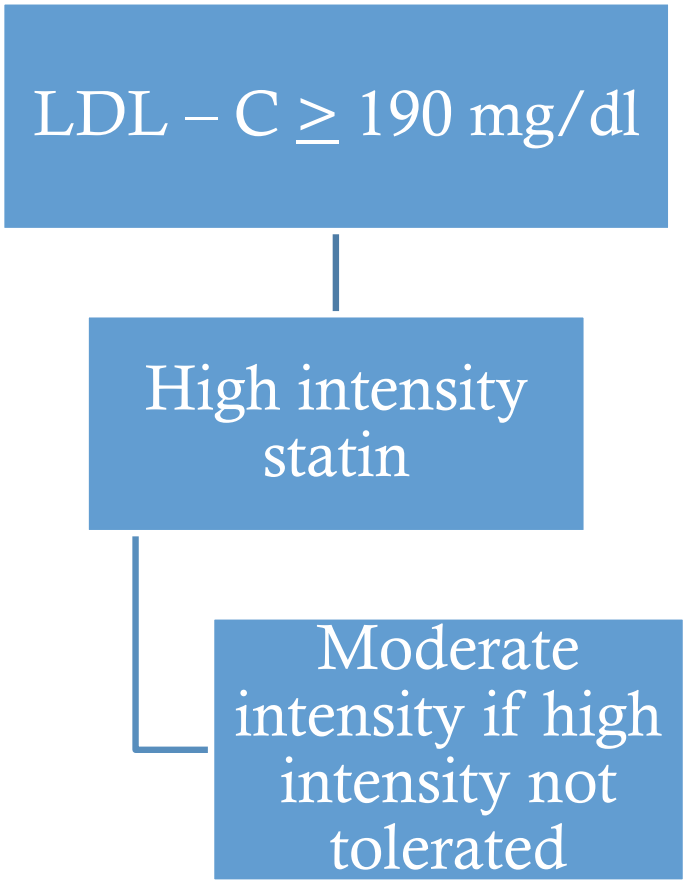
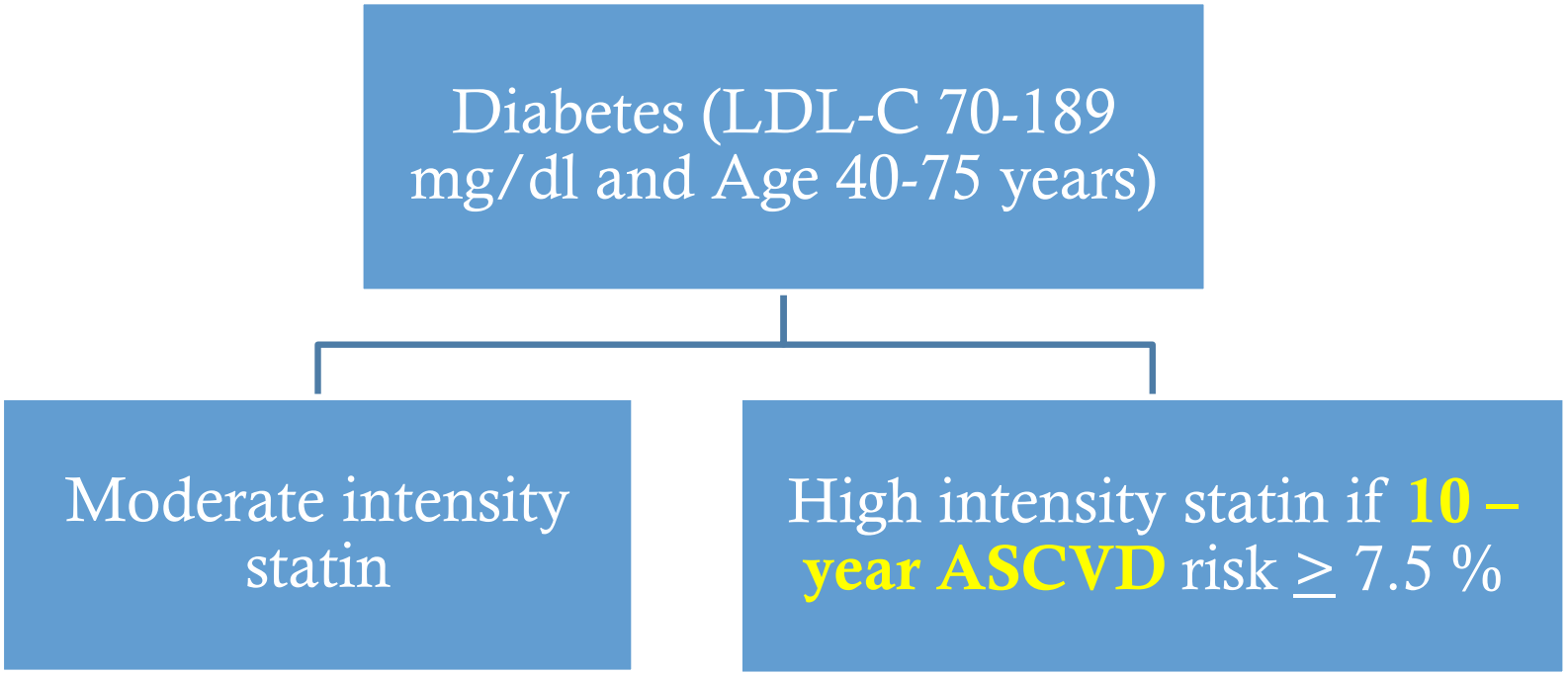
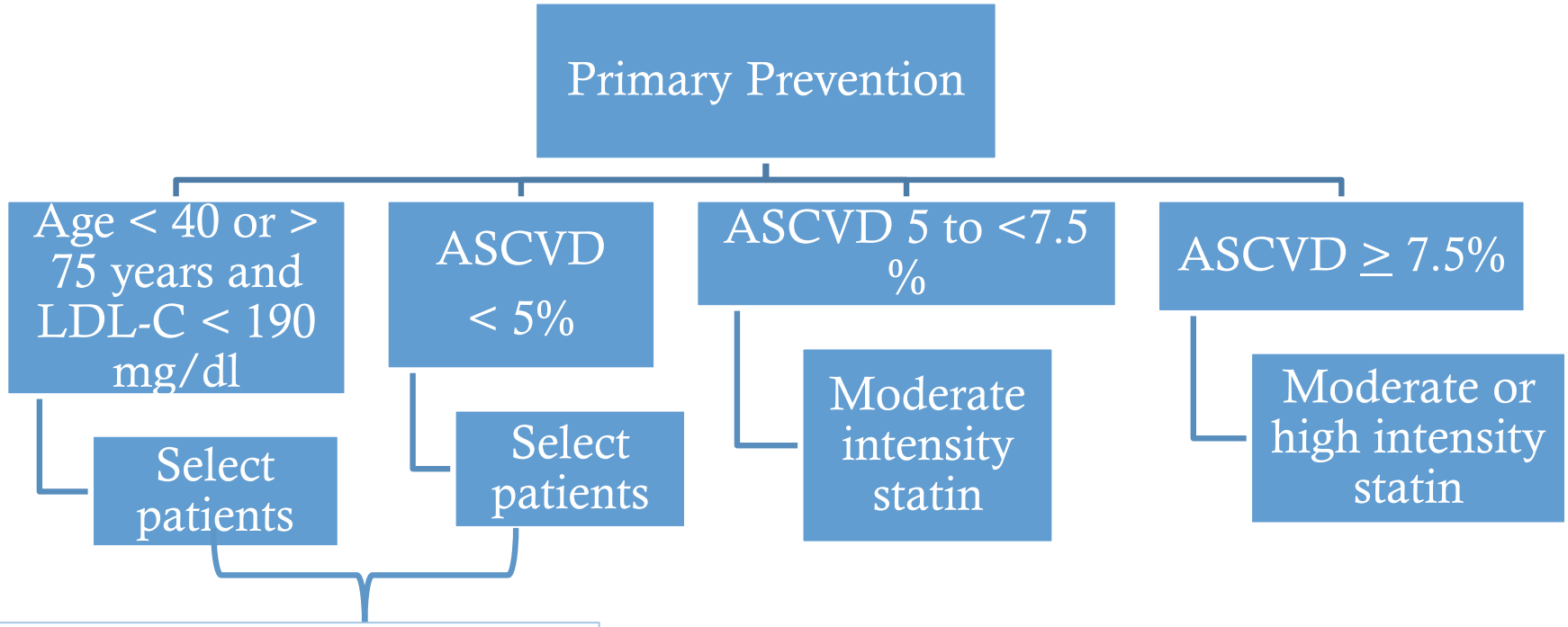


2013 ACC/AHA Guidelines – Group 3



2013 ACC/AHA Guidelines – Group 4



Note: Also consider for diabetics age < 40 or > 75 years or LDL-C < 70 mg/dl

2013 ACC/AHA Guidelines – Risk versus benefits

- Potential for ASCVD risk-reduction benefits
- Potential for ADR and interactions
- Heart-healthy lifestyle
- Patient preferences
- Consider LDL-C $\geq$ 160 mg/dl, family history, lifetime ASVD risk, abnormal CAC score or ABI or hs-CRP $\geq$ 2 mg/dl

2013 ACC/AHA Guidelines

- LDL – C monitoring is recommended for adherence and efficacy, but NOT for treatment goals
- Found no supporting evidence for the routine use of non-statin drugs in combination with statins

Benefits of Statins

Rosuvastatin to prevent vascular events in men and women with elevated C-reactive protein	**Efficacy of high intensity atorvastatin versus moderate intensity statin for acute coronary syndrome**
• Rosuvastatin versus placebo • Population: patients with normal LDL and elevated hs-CRP • Outcome: reduction in incidence of major CV events • Statin reduced LDL and hs-CRP, and also reduced major CV events *(NNT= 25)*	• High-intensity or moderate-intensity atorvastatin • Population: diabetics with acute coronary syndrome • Outcome: cardiovascular benefit • High-intensity had an additional 44.5% decrease in major cardiovascular events *(P = 0.018)*

Assessment Question 2

The 2013 ACC/AHA Blood Cholesterol guidelines identifies which group(s) should receive a high – intensity statin [SELECT ALL THAT APPLY]?

A. 40 year old patient that had a stroke
B. 65 year old male with a LDL level of 50 mg/dl
C. 31 year old diabetic with a LDL level of 82 mg/dl
D. 29 year old diabetic with a LDL level of 200 mg/dl

AACE 2017 Guidelines

AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS AND AMERICAN COLLEGE OF ENDOCRINOLOGY GUIDELINES FOR MANAGEMENT OF DYSLIPIDEMIA AND PREVENTION OF CARDIOVASCULAR DISEASE

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2017 AACE Guidelines

PATIENTS WILL BENEFIT FROM LDL – C TARGET GOALS

Risk Category	Risk factors	LDL – C (mg/dl)	Non-HDL – C (mg/dl)	Apo B (mg/dl)
Low Risk	• 0 risk factors	< 130	< 160	Not recommended
Moderate Risk	• ≤ 2 risk factors and **10 – year risk < 10%**	< 100	< 130	< 90
High Risk	• ≥ 2 risk factors and 10 year risk 10 – 20 % • Diabetes or CKD stage 3 or 4 with no other risk factors	< 100	< 130	< 90

2017 AACE Guidelines cont.

Risk Category	Risk factors	LDL – C (mg/dl)	Non-HDL – C (mg/dl)	Apo B (mg/dl)
Very High Risk	• Established or recent ASCVD, 10 year risk > 20% • Diabetes or CKD stage 3 or 4 with 1 or more risk factor(s) • Heart failure	< 70	< 100	< 80
Extreme Risk	• ASCVD in patient after achieving an LDL – C < 70 • Clinical cardiovascular disease in patients with diabetes, CKD stage 3/4 , or heart failure	< 55	< 80	< 70

Major Risk Factors

- High LDL – C
- Polycystic ovary syndrome (PCOS)
- Cigarette smoking
- Hypertension (BP $\geq$ 140/90 or on BP medication)
- Low HDL – C (< 40 mg/dl)
- Family history of CHD
- Chronic renal disease (CKD) stage 3 or 4
- Evidence of coronary artery calcification
- Age (men $\geq$ 45; women $\geq$ 55 years)

Note: subtract risk factor if high HDL – C

2017 AACE Guidelines cont.

- Used Framingham risk score assessment
- Ezetimibe may be considered for:
  - Monotherapy for statin intolerant individuals
  - In combination with statins to further reduce LDL – C and ASCVD risk
- PCSK9 inhibitors can be considered for:
  - In combination with statin therapy for LDL – C lowering in individuals with FH
  - Individuals with clinical CV disease who are unable to reach LDL – C with maximum tolerated statin

Targeting LDL Levels

- Studies showing LDL levels are associated with decreased CVD event rate
- Meta – analysis of eight randomized controlled statin trial
  - 38,153 diabetic patients
  - Achieved very low LDL – C levels (< 50 mg/dl or 50 – 70 mg/dl) had a lower risk for major CVD events > moderately low levels (75 – 100 mg/dl)

IMPROVE – IT Trial

- Evaluated addition of ezetimibe 10 mg to **moderate**-intensity statin (simvastatin)
- Population: high risk patients with recent acute coronary syndrome who has one additional high risk characteristic
- Outcome: ASCVD event reduction
- Results: ASCVD events were reduced by 10% in the ezetimibe group *(NNT = 50)*
  - Addition of ezetimibe reduced LDL – C to a mean of 54 mg/dl compared to 70 mg/dl in simvastatin monotherapy group

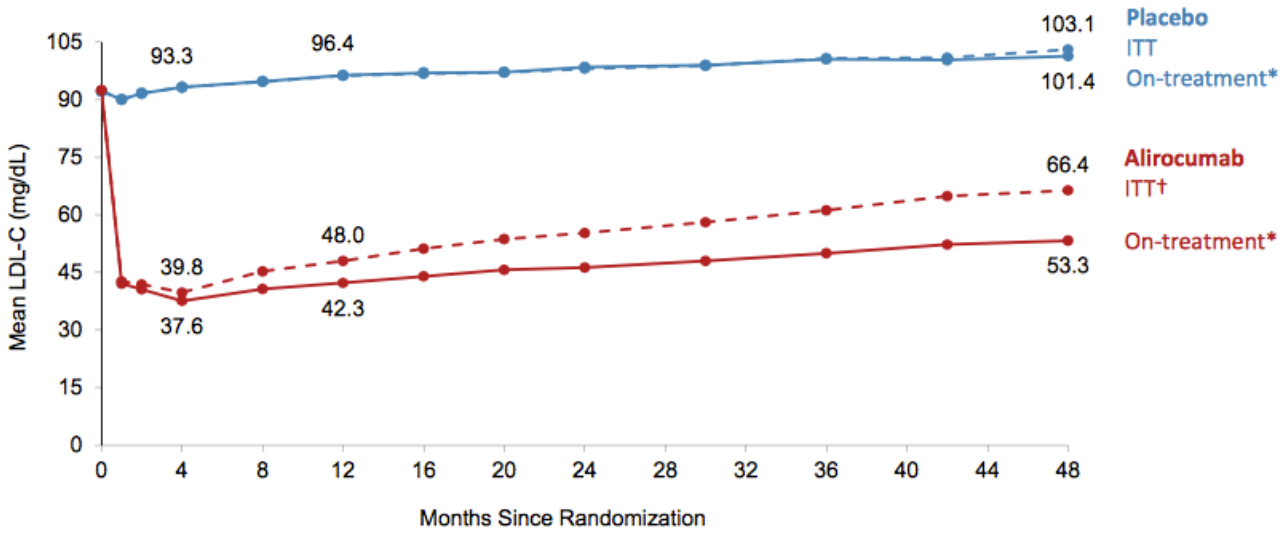
	Simvastatin	Ezetimibe	P Value
Goal of LDL < 70 and hs-CRP < 2 at one month	30.5 %	50.6 %	< 0.001

ODYSSEY trial

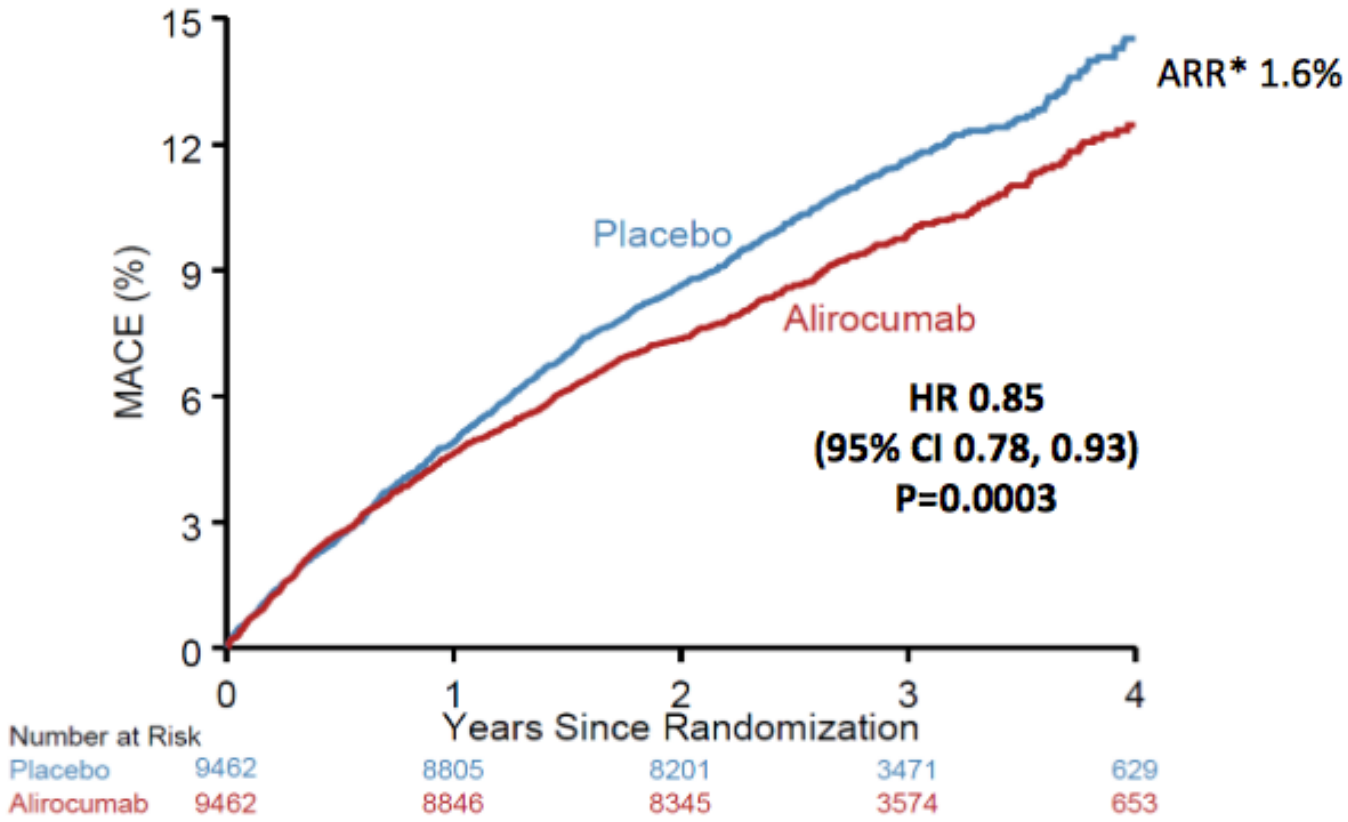
- Evaluated alirocumab versus placebo
- Population: high risk for cardiovascular events, LDL cholesterol $\geq$ 70 mg/dl, and on maximum tolerated statin
- Outcome: percent change in LDL cholesterol from baseline to week 24

ODYSSEY trial

- Results (alirocumab versus placebo):
  - Change in LDL: -74.2 mg/dl versus -3.6 mg/dl *(P < 0.001)*
  - LDL < 70 mg/dl: 79.3% versus 8.0% *(P < 0.001)*



Endpoint: MACE



Assessment Question 3

The 2017 AACE Dyslipidemia and Prevention of CVD guidelines targets a goal LDL level < 70 mg/dl for which patient(s) [SELECT ALL THAT APPLY]?

A. Diabetic patient with a history of a NSTEMI
B. Diabetic patient with an ASCVD = 11.5%
C. Female patient that smokes with an ASCVD = 25%
D. Male patient with an ASCVD = 5.1%

2018 ACC/AHA Guidelines

2018

AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

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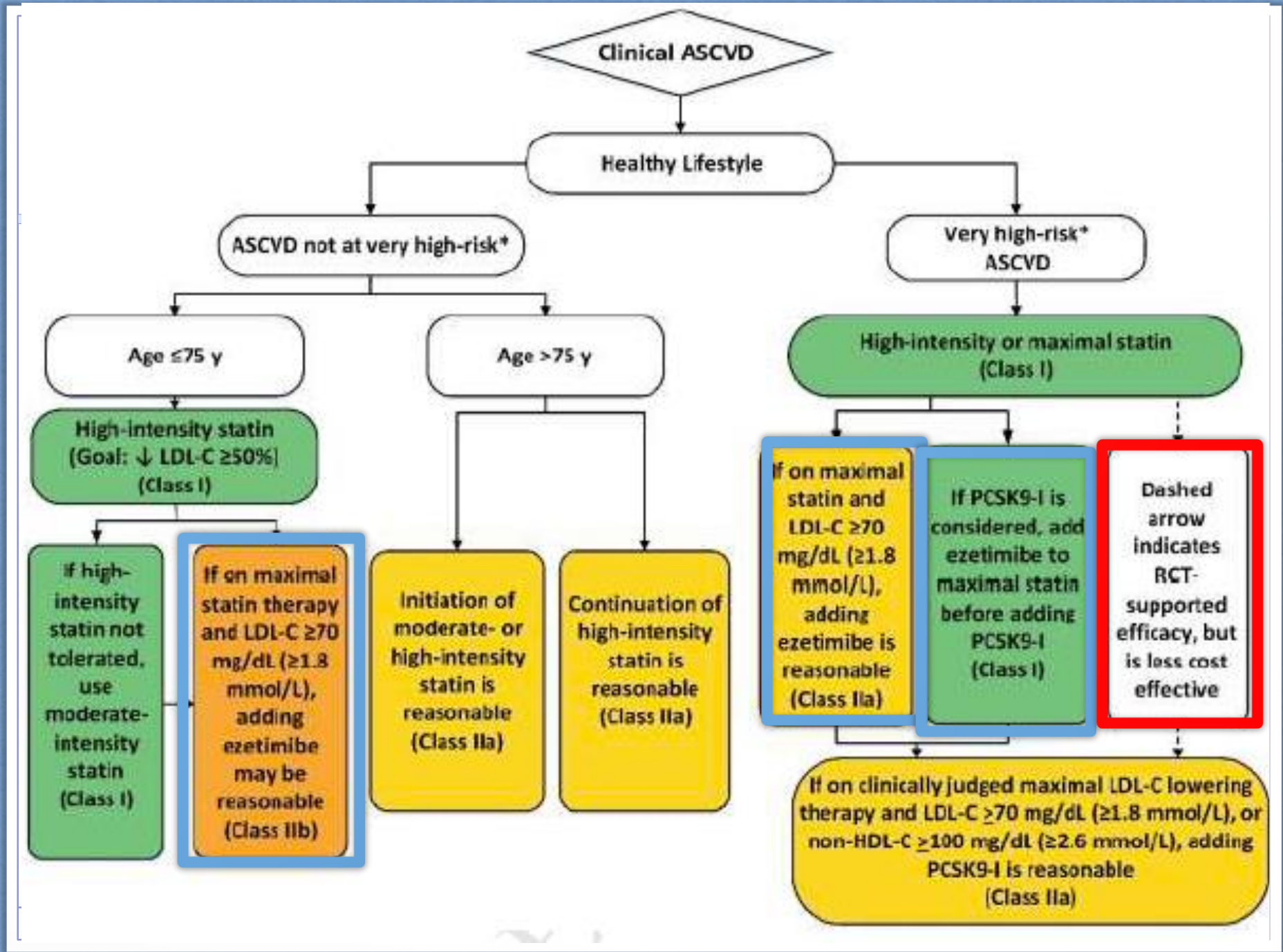

Clinical ASCVD
Healthy Lifestyle
ASCVD not at very high-risk*
Very high-risk* ASCVD
Age ≤75 y
Age >75 y
High-intensity or maximal statin (Class I)
High-intensity statin (Goal: ↓ LDL-C ≥50%) (Class I)
If high-intensity statin not tolerated, use moderate-intensity statin (Class I)
If on maximal statin therapy and LDL-C ≥70 mg/dL (≥1.8 mmol/L), adding ezetimibe may be reasonable (Class IIb)
Initiation of moderate- or high-intensity statin is reasonable (Class IIa)
Continuation of high-intensity statin is reasonable (Class IIa)
If on maximal statin and LDL-C ≥70 mg/dL (≥1.8 mmol/L), adding ezetimibe is reasonable (Class IIa)
If PCSK9-I is considered, add ezetimibe to maximal statin before adding PCSK9-I (Class I)
Dashed arrow indicates RCT-supported efficacy, but is less cost effective
If on clinically judged maximal LDL-C lowering therapy and LDL-C ≥70 mg/dL (≥1.8 mmol/L), or non-HDL-C ≥100 mg/dL (≥2.6 mmol/L), adding PCSK9-I is reasonable (Class IIa)

Very High – Risk for Future ASCVD Events

Major ASCVD Events

- Recent ACS (within past 12 months)
- History of MI (other than recent ACS)
- History of ischemic stroke
- Symptomatic peripheral arterial disease

High – Risk Conditions

- Age ≥ 65 years
- Heterozygous familial hypercholesterolemia
- History of prior coronary artery bypass surgery ior percutaneous coronary intervention outside of major ASCVD event(s)
- Diabetes
- Hypertension
- CKD (eGFR 15 -59 mL/min)
- Current smoking
- Persistently elevated LDL – c despite maximally tolerated statin and ezetimibe
- History of congestive HF

2018 ACC/AHA Guidelines Key Updates

Severe primary hypercholesterolemia (LDL – C ≥ 190 mg/dl)

- Without calculating 10 – year ASCVD start high – intensity statin
- If LDL – C remains ≥ 100 mg/dl **consider** adding ezetimibe
- If LDL – C > 100 mg/dl with statin and ezetimibe then **consider adding** PCSK9 inhibitor

Patients 40 – 75 years with diabetes and LDL-C ≥ 70 mg/dl

- Start moderate intensity statin **without** calculating 10 – year ASCVD risk
- If at higher risk (multiple risk factors or 50 – 75 years) reasonable to start high – intensity statin

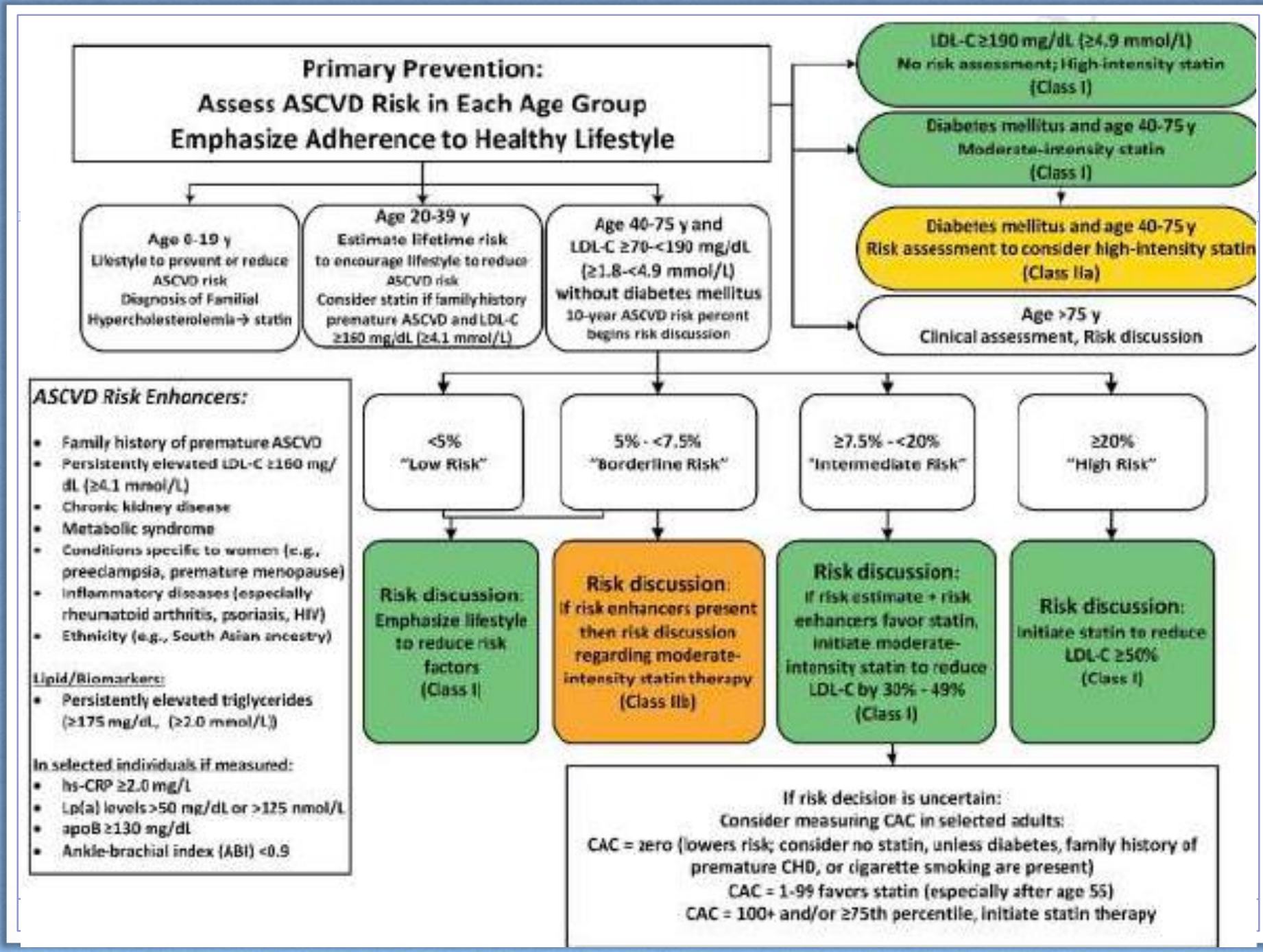
Diabetic Risk Enhancers

Risk Enhancers

- Long duration (≥10 years of type 2 diabetes or ≥ 20 years of type 1 diabetes)
- Albuminuria ≥ 30 mcg of albumin/mg creatinine
- eGFR < 60 mL/min
- Retinopathy
- Neuropathy
- Ankle-brachial index < 0.9

2018 ACC/AHA Guidelines Key Updates Cont.

Adults 40 – 75 years without diabetes and with LDL – C level ≥ 70 mg/dl at 10 – year ASCVD risk ≥ 7.5 %	• Start moderate intensity statin • **Consider CAC (coronary artery calcium) test**
Adults 40 – 75 years without diabetes and 10 – year ASCVD risk is 7.5 – 19.9 %	• Risk-enhancing factors favor initiation of statin therapy
Adults 40 – 75 years without diabetes and with LDL – C levels ≥ 70 – 189 mg/dl at a 10 – year ASCVD risk of ≥ 7.5 – 19.9 %	• If unsure then consider measuring CAC


Primary Prevention:
Assess ASCVD Risk in Each Age Group
Emphasize Adherence to Healthy Lifestyle
LDL-C ≥190 mg/dL (≥4.9 mmol/L)
No risk assessment; High-intensity statin
(Class I)
Diabetes mellitus and age 40-75 y
Moderate-intensity statin
(Class I)
Diabetes mellitus and age 40-75 y
Risk assessment to consider high-intensity statin
(Class IIa)
Age >75 y
Clinical assessment, Risk discussion
Age 0-19 y
Lifestyle to prevent or reduce ASCVD risk
Diagnosis of Familial Hypercholesterolemia→ statin
Age 20-39 y
Estimate lifetime risk to encourage lifestyle to reduce ASCVD risk
Consider statin if family history premature ASCVD and LDL-C ≥160 mg/dL (≥4.1 mmol/L)
Age 40-75 y and LDL-C ≥70-<190 mg/dL (≥1.8-<4.9 mmol/L) without diabetes mellitus
10-year ASCVD risk percent begins risk discussion
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 (e.g., South Asian ancestry)
Lipid/Biomarkers:
Persistently elevated triglycerides (≥175 mg/dL, (≥2.0 mmol/L))
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)
Risk discussion
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

Risk – Enhancing Factors

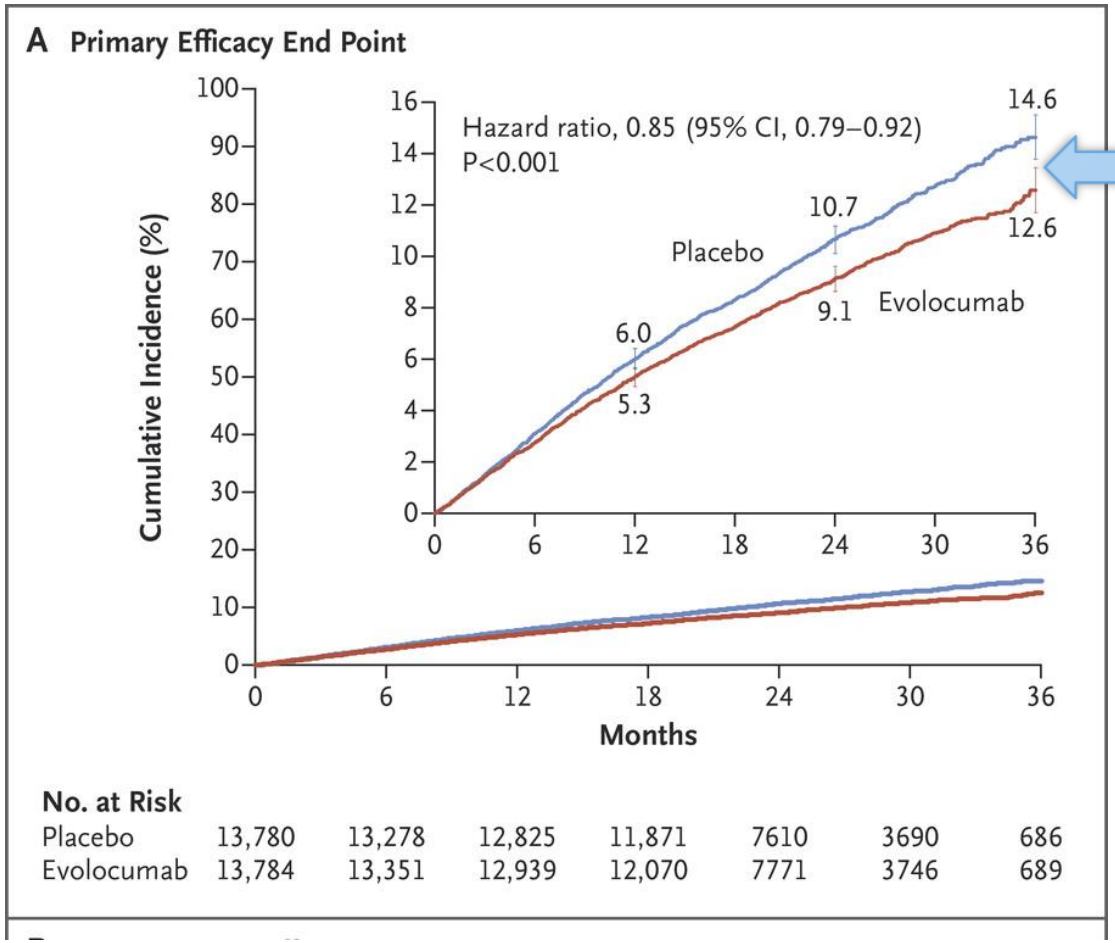
Family history of premature ASCVD	Males: age < 55 years Females: age < 65 years
Primary hypercholesterolemia	LDL: 160 – 189 mg/dl Non – HDL: 190 – 219 mg/dl
Metabolic syndrome	Waist circumference Elevated triglycerides, BP, glucose Low HDL – C (at least 3)
Chronic kidney disease	eGFR 15 – 59 mL/min Not treated with dialysis or kidney transplant
Chronic inflammation conditions	Psoriasis, RA, HIV/AIDS
History of premature menopause, pregnancy – associated conditions (preeclampsia)	
High – risk race/ethnicities	South Asian ancestry
Lipid/biomarkers	Elevated CRP, apoB, triglycerides

FOURIER Trial

- Evaluated addition of evolocumab compared to placebo
- Population: patient with clinical atherosclerotic disease and LDL > 70 despite moderate or high intensity statin therapy
- Outcome: Reduction of major cardiovascular (CVD) events
- Results: The addition of evolocumab resulted in an absolute 1.5% reduction in major CVD events
  - Overall **no CV – specific mortality** benefit with evolocumab

Duration: 2 years

FOURIER Trial



FOURIER Trial

Table 2. Primary and Secondary End Points.

Outcome	Evolocumab (N = 13,784)	Placebo (N = 13,780)	Hazard Ratio (95% CI)	P Value*
	no. of patients (%)			
Primary end point: cardiovascular death, myocardial infarction, stroke, hospitalization for unstable angina, or coronary revascularization	1344 (9.8)	1563 (11.3)	0.85 (0.79–0.92)	<0.001
Key secondary end point: cardiovascular death, myocardial infarction, or stroke	816 (5.9)	1013 (7.4)	0.80 (0.73–0.88)	<0.001
Other end points				
Cardiovascular death	251 (1.8)	240 (1.7)	1.05 (0.88–1.25)	0.62
Due to acute myocardial infarction	25 (0.18)	30 (0.22)	0.84 (0.49–1.42)	
Due to stroke	31 (0.22)	33 (0.24)	0.94 (0.58–1.54)	
Other cardiovascular death	195 (1.4)	177 (1.3)	1.10 (0.90–1.35)	
Death from any cause	444 (3.2)	426 (3.1)	1.04 (0.91–1.19)	0.54
Myocardial infarction	468 (3.4)	639 (4.6)	0.73 (0.65–0.82)	<0.001
Hospitalization for unstable angina	236 (1.7)	239 (1.7)	0.99 (0.82–1.18)	0.89
Stroke	207 (1.5)	262 (1.9)	0.79 (0.66–0.95)	0.01

Assessment Question 4

Which patient's treatment is not influenced by a 10 – year ASCVD risk score?

A. Patient with a history of a STEMI
B. Non – diabetic patient with a LDL level of 83 mg/dl
C. Diabetic patient with a LDL level of 83 mg/dl
D. All of the above

Assessment Question 5

Which patients can we consider adding ezetimibe?

A. 40 year old female patient without diabetes and LDL $\geq$ 70 mg/dl and ASCVD = 8.7%
B. 55 year old male patient without diabetes and ASCVD = 10.3%
C. Very high-risk ASCVD patients on maximally tolerated statin and LDL remains $\geq$ 70 mg/dl

Role of a Pharmacist

- Optimizing therapy
  - Identifying patients that should be on statin therapy
  - Follow up with lipid panel
    - Recommend titration of dose
- Educate about CV benefits of lipid management

Conclusion

- Statins are efficacious LDL – C lowering agents that also have cardiovascular benefit
- Statin doses should be optimized to target LDL – C level
- Ezetimibe can be considered in addition to statins when LDL – C level are not at goal
- PCSK9 inhibitors can potentially be considered if statins and ezetimibe are not sufficient
- Can consider utilizing CAC in addition to ASCVD risk score when the benefit of statin therapy is unknown
- Pharmacist can play an important role optimizing hyperlipidemia therapy

Questions?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Hyperlipidemia: Past and Present

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