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

<table>
<thead>
<tr>
<th>Fasting lipid panel (10 hr)</th>
<th>Normal range</th>
<th>Borderline</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol (TC)</td>
<td>&lt; 200</td>
<td>200 – 239</td>
<td>&gt; 240</td>
</tr>
<tr>
<td>LDL – C</td>
<td>&lt; 130</td>
<td>130 – 159</td>
<td>&gt; 160</td>
</tr>
<tr>
<td>HDL – C</td>
<td>&gt; 40 (men) &gt; 50 (women)</td>
<td>&lt; 40 (men) &lt; 50 (women)</td>
<td></td>
</tr>
<tr>
<td>Triglycerides (TG)</td>
<td>&lt; 150</td>
<td>150 – 199</td>
<td>&gt; 200</td>
</tr>
</tbody>
</table>

**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

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

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
<table>
<thead>
<tr>
<th>High intensity statin</th>
<th>Dose range</th>
<th>Characteristics</th>
<th>Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rosuvastatin (Crestor)</td>
<td>20 – 40 mg</td>
<td>Hydrophilic</td>
<td>Anytime</td>
</tr>
<tr>
<td>Atorvastatin (Lipitor)</td>
<td>40 – 80 mg</td>
<td>Lipophilic</td>
<td></td>
</tr>
</tbody>
</table>
# Pharmacology Management – Moderate Intensity Statins

<table>
<thead>
<tr>
<th>Moderate intensity statin</th>
<th>Dose range</th>
<th>Characteristics</th>
<th>Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rosuvastatin (Crestor)</td>
<td>10 – 20 mg</td>
<td>Hydrophilic</td>
<td>Anytime</td>
</tr>
<tr>
<td>Atorvastatin (Lipitor)</td>
<td>5 – 10 mg</td>
<td>Lipophilic</td>
<td>Anytime</td>
</tr>
<tr>
<td>Simvastatin (Zocor)</td>
<td>20 – 40 mg</td>
<td>Lipophilic</td>
<td>Night</td>
</tr>
<tr>
<td>Lovastatin (Mevacor)</td>
<td>40 mg</td>
<td>Lipophilic</td>
<td>Night</td>
</tr>
<tr>
<td>Pravastatin (Pravachol)</td>
<td>40 – 80 mg</td>
<td>Hydrophilic</td>
<td>Anytime</td>
</tr>
<tr>
<td>Fluvastatin (Lescol)</td>
<td>40 – 80 mg</td>
<td>Lipophilic</td>
<td>Night</td>
</tr>
<tr>
<td>Pitavastatin (Livalo)</td>
<td>2 – 4 mg</td>
<td>Lipophilic</td>
<td>Anytime</td>
</tr>
</tbody>
</table>
## Pharmacology Management – Low Intensity Statins

<table>
<thead>
<tr>
<th>Low intensity statin</th>
<th>Dose range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simvastatin (Zocor)</td>
<td>10 mg</td>
</tr>
<tr>
<td>Lovastatin (Mevacor)</td>
<td>20 mg</td>
</tr>
<tr>
<td>Pravastatin (Pravachol)</td>
<td>10 – 20 mg</td>
</tr>
<tr>
<td>Fluvastatin (Lescol)</td>
<td>20 – 40 mg</td>
</tr>
<tr>
<td>Pitavastatin (Livalo)</td>
<td>1 mg</td>
</tr>
</tbody>
</table>
# Monitoring Parameters - Statins

<table>
<thead>
<tr>
<th>Adverse Effects</th>
<th>Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Myalgia</td>
<td>• Fasting lipid panel</td>
</tr>
<tr>
<td>• Myopathy</td>
<td>• Liver function panel</td>
</tr>
<tr>
<td>• Rhabdomyolysis</td>
<td>• Creatinine kinase</td>
</tr>
<tr>
<td>• Hepatic dysfunction</td>
<td></td>
</tr>
<tr>
<td>• Renal dose adjustments</td>
<td></td>
</tr>
<tr>
<td>• Increase glucose</td>
<td></td>
</tr>
<tr>
<td>• Pregnancy category X</td>
<td></td>
</tr>
<tr>
<td>• Drug interactions</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>
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
- Lower LDL by 48 – 71 %
## Pharmacology Management – PCSK9 Inhibitors

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

**HeFH**: Heterozygous familial hypercholesterolemia  
**HoFH**: Homozygous Familial Hypercholesterolemia
### Pharmacology Management - Miscellaneous

<table>
<thead>
<tr>
<th>Class</th>
<th>Medications</th>
<th>TG</th>
<th>LDL</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibrates</td>
<td>Gemfibrozil</td>
<td>20 – 35%</td>
<td></td>
<td>• Myalgia&lt;br&gt;• Increases liver function tests&lt;br&gt;• GI symptoms&lt;br&gt;• May increase SCr&lt;br&gt;• Dyspepsia&lt;br&gt;• Upper respiratory tract infections</td>
</tr>
<tr>
<td></td>
<td>Fenofibrate</td>
<td>20 – 25%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fish – oil</td>
<td>Omega – 3 oil</td>
<td>27 – 45%</td>
<td>20 – 42%</td>
<td>• GI symptoms&lt;br&gt;• May prolong bleeding&lt;br&gt;• Increases in liver function tests&lt;br&gt;• Increased incidence in A-fib or aflutter episodes&lt;br&gt;• Avoid if hypersensitivity to fish and/or shellfish</td>
</tr>
</tbody>
</table>
## Pharmacology Management - Miscellaneous

<table>
<thead>
<tr>
<th>Class</th>
<th>Medications</th>
<th>TG</th>
<th>LDL</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Niacin</td>
<td>Niacin IR</td>
<td>20 – 30%</td>
<td>10 – 25%</td>
<td>• Flushing&lt;br&gt;• Nausea/vomiting/diarrhea&lt;br&gt;• Increases uric acid levels&lt;br&gt;• Increase glucose&lt;br&gt;• Increase liver functions test</td>
</tr>
<tr>
<td></td>
<td>Niaspan ER</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Slo - Niacin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bile acid sequestrants</td>
<td>Cholestyramine</td>
<td>15 – 25%</td>
<td></td>
<td>• GI symptoms&lt;br&gt;• Increase liver functions tests&lt;br&gt;• May increase TG</td>
</tr>
<tr>
<td></td>
<td>Colestipol</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Colesevelam</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
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 Blood Cholesterol Guidelines
- 2017 AACE Dyslipidemia and Prevention of CVD Guidelines
- 2018 ACC/AHA guideline on the Management of Blood Cholesterol
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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METHODOLOGY MEMBERS
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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

- Age ≥ 21 and a candidate for statin therapy
- Clinical ASCVD
  - Stroke, acute coronary syndrome, peripheral arterial disease
- LDL − C ≥ 190 mg/dl
- Diabetic
  - LDL − C 70 – 189 mg/dl and Age 40 – 75 years
- Primary prevention
  - No diabetes, LDL − C 70 – 189 mg/dl, and not receiving statin therapy
2013 ACC/AHA Guidelines – Group 1

Clinical ASCVD

- Age ≤ 75 years
  - High intensity statin (if tolerated)
- Age > 75 years or if not candidate for high intensity statin
  - Moderate intensity statin
2013 ACC/AHA Guidelines – Group 2

LDL – C ≥ 190 mg/dl

- High intensity statin
  - Moderate intensity if high intensity not tolerated
2013 ACC/AHA Guidelines – Group 3

Diabetes (LDL-C 70-189 mg/dl and Age 40-75 years)

- Moderate intensity statin
- High intensity statin if 10-year ASCVD risk ≥ 7.5 %
Primary Prevention

- Age < 40 or > 75 years and LDL-C < 190 mg/dl
  - Select patients

- ASCVD < 5%
  - Select patients

- ASCVD 5 to <7.5%
  - Moderate intensity statin

- ASCVD ≥ 7.5%
  - Moderate or high intensity statin

**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

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

Paul S. Jellinger, MD, MACE, Chair; Yehuda Handelsman MD, FACP, FACE, FNLA, Co-Chair; Paul D. Rosenblit, MD, PhD, FNLA, FACE; Zachary T. Bloomgarden, MD, MACE; Vivian A. Fonseca, MD, FACE; Alan J. Garber, MD, PhD, FACE; George Grunberger, MD, FACP, FACE; Chris K. Guerin, MD, FNLA, FACE; David S. H. Bell, MD, FACP, FACE; Jeffrey I. Mechanick, MD, FACP, FACE, FACN, ECNU; Rachel Pessah-Pollack, MD, FACE; Kathleen Wyne, MD, PhD, FNLA, FACE; Donald Smith, MD, MPH, FACE; Eliot A. Brinton, MD, FAHA, FNLA; Sergio Fazio, MD, PhD and Michael Davidson, MD, FACC, FACP, FNLA
## 2017 AACE Guidelines

### PATIENTS WILL BENEFIT FROM LDL – C TARGET GOALS

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>Risk factors</th>
<th>LDL – C (mg/dl)</th>
<th>Non-HDL – C (mg/dl)</th>
<th>Apo B (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low Risk</td>
<td>• 0 risk factors</td>
<td>&lt; 130</td>
<td>&lt; 160</td>
<td>Not recommended</td>
</tr>
<tr>
<td>Moderate Risk</td>
<td>• ≤ 2 risk factors and <strong>10 – year risk &lt; 10%</strong></td>
<td>&lt; 100</td>
<td>&lt; 130</td>
<td>&lt; 90</td>
</tr>
<tr>
<td>High Risk</td>
<td>• ≥ 2 risk factors and 10 year risk 10 – 20 %</td>
<td>&lt; 100</td>
<td>&lt; 130</td>
<td>&lt; 90</td>
</tr>
<tr>
<td></td>
<td>• Diabetes or CKD stage 3 or 4 with no other risk factors</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### 2017 AACE Guidelines cont.

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>Risk factors</th>
<th>LDL – C (mg/dl)</th>
<th>Non-HDL – C (mg/dl)</th>
<th>Apo B (mg/dl)</th>
</tr>
</thead>
</table>
| 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 ≥ 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 ≥ 45; women ≥ 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

<table>
<thead>
<tr>
<th>Goal of LDL &lt; 70 and hs-CRP &lt; 2 at one month</th>
<th>Simvastatin</th>
<th>Ezetimibe</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>30.5 %</td>
<td>50.6 %</td>
<td>&lt; 0.001</td>
<td></td>
</tr>
</tbody>
</table>
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

- **HR 0.85**
- **(95% CI 0.78, 0.93)**
- **P=0.0003**

Number at Risk:
- Placebo: 9462
- Alirocumab: 9462

Years Since Randomization:
- 0: Placebo 9462, Alirocumab 9462
- 1: 8805, 8846
- 2: 8201, 8345
- 3: 3471, 3574
- 4: 629, 653

ARR* 1.6%
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

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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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 or 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.

- Start moderate intensity statin
- Consider CAC (coronary artery calcium) test

Adults 40 – 75 years without diabetes and with LDL – C level ≥ 70 mg/dl at 10 – year ASCVD risk ≥ 7.5 %

- Risk-enhancing factors favor initiation of statin therapy

Adults 40 – 75 years without diabetes and 10 – year ASCVD risk is 7.5 – 19.9 %

- If unsure then consider measuring CAC

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 %
Primary Prevention: 
Assess ASCVD Risk in Each Age Group
Emphasize Adherence to Healthy Lifestyle

- Age 6-19 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

- 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

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

Risk discussion:
- <5% “Low Risk”
- 5% - <7.5% “Borderline Risk”
- ≥7.5% - <20% “Intermediate Risk”
- ≥20% “High Risk”

Risk discussion:
- If risk factors present then risk discussion regarding moderate-intensity statin therapy (Class IIb)
- 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

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Criteria</th>
</tr>
</thead>
</table>
| **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

A Primary Efficacy End Point

Hazard ratio, 0.85 (95% CI, 0.79–0.92)
P<0.001

No. at Risk
Placebo 13,780 13,278 12,825 11,871 7610 3690 686
Evolocumab 13,784 13,351 12,939 12,070 7771 3746 689
### FOURIER Trial

**Table 2. Primary and Secondary End Points.**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Evolocumab (N=13,784)</th>
<th>Placebo (N=13,780)</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary end point: cardiovascular death, myocardial infarction, stroke, hospitalization for unstable angina, or coronary revascularization</td>
<td>1344 (9.8)</td>
<td>1563 (11.3)</td>
<td>0.85 (0.79–0.92)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Key secondary end point: cardiovascular death, myocardial infarction, or stroke</td>
<td>816 (5.9)</td>
<td>1013 (7.4)</td>
<td>0.80 (0.73–0.88)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Other end points</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular death</td>
<td>251 (1.8)</td>
<td>240 (1.7)</td>
<td>1.05 (0.88–1.25)</td>
<td>0.62</td>
</tr>
<tr>
<td>Due to acute myocardial infarction</td>
<td>25 (0.18)</td>
<td>30 (0.22)</td>
<td>0.84 (0.49–1.42)</td>
<td></td>
</tr>
<tr>
<td>Due to stroke</td>
<td>31 (0.22)</td>
<td>33 (0.24)</td>
<td>0.94 (0.58–1.54)</td>
<td></td>
</tr>
<tr>
<td>Other cardiovascular death</td>
<td>195 (1.4)</td>
<td>177 (1.3)</td>
<td>1.10 (0.90–1.35)</td>
<td></td>
</tr>
<tr>
<td>Death from any cause</td>
<td>444 (3.2)</td>
<td>426 (3.1)</td>
<td>1.04 (0.91–1.19)</td>
<td>0.54</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>468 (3.4)</td>
<td>639 (4.6)</td>
<td>0.73 (0.65–0.82)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hospitalization for unstable angina</td>
<td>236 (1.7)</td>
<td>239 (1.7)</td>
<td>0.99 (0.82–1.18)</td>
<td>0.89</td>
</tr>
<tr>
<td>Stroke</td>
<td>207 (1.5)</td>
<td>262 (1.9)</td>
<td>0.79 (0.66–0.95)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

*P Values for evolocumab vs placebo.
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 ≥ 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 ≥ 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?

“IT'S A GREAT IDEA AND REALLY WELL DRAWN, BRADLEY, BUT I'M NOT SURE THAT TODAY'S KIDS WILL LATCH ON TO 'LOW - CHOLESTEROL MAN' AS A NEW SUPER HERO.”
Hyperlipidemia: Past and Present

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