Lipid Management and Cardiovascular Risk Reduction: The Evolving Treatment Paradigm

Faculty

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Disclosures

- Elizabeth Ofili, MD, MPH receives grant/research support from the National Institutes of Health. Dr. Ofili serves as a consultant and/or on the advisory board for Bristol-Myers Squibb, Novartis, Arbor, Eli-Lilly, Merck & Co., Janssen Research and Development.

- Anekwe Onwuanyi, MD has no relationships to disclose.

- Laurence O. Watkins, MD, MPH, FACC serves as a speaker/teacher for Arbor Pharmaceuticals and on the advisory committee for Boston Scientific.
Educational Objectives

1. Discuss the benefits of LDL-C lowering with pharmacologic therapies that improve cardiovascular outcomes
2. Recognize and understand the role of alternative or additional therapies in conjunction with statins
3. Recognize the strengths and limitations of the 2013 ACC/AHA cholesterol guidelines and how to optimally implement the recommendations
4. Recognize the potential role of emerging pharmacologic therapies to further lower LDL-C in those at high risk for cardiovascular disease
5. Recognize and develop appropriate treatment strategies for special populations (women, elderly, ethnic minorities) that would benefit from lipid lowering therapy

PRE-TEST QUESTIONS

Pre-test ARS Question 1

On a scale of 1 to 5, please rate how confident you would be in treating Hypercholesterolemia in patients that are not achieving optimal goals or are refractory to statin therapy?

1. Not at all confident
2. Slightly confident
3. Moderately confident
4. Pretty much confident
5. Very confident
Pre-test ARS Question 2

MR, a 61-year-old male with an LDL-C of 130 mg/dL and diabetes has an ASCVD risk of 6.6% based on the new risk-calculator. What therapy should MR be started on according to the ACC/AHA 2013 guidelines?

1. High-intensity statin
2. Moderate-intensity statin
3. Low-intensity statin
4. Non-statin therapy
5. None of the above

Pre-test ARS Question 3

SJ, a 62 year old BF is hospitalized in the Coronary care unit following a non-ST segment MI and stent placement in a 95% right coronary lesion. Her admission lipids are LDL-C=90 mg/dl, HDL=35 mg/dL, triglycerides=160 mg/dl.

In addition to being placed on a statin, which of the following treatments has been shown to reduce her risk of cardiovascular events.

1. Niacin
2. Fenofibrate
3. Cholestyramine
4. Ezetimibe
5. None of the above
Pre-test ARS Question 4

*Which of the following is NOT one of the 4 statin benefit groups according to the 2013 ACC/AHA Cholesterol Guideline to Reduce Atherosclerotic CV Disease?*

1. A patient with clinical ASCVD
2. A patient with an LDL-C > 190 mg/dL
3. A patient 56 years of age with diabetes and an LDL-C of 118 mg/dL
4. A patient 67 years of age without diabetes or ASCVD with an LDL-C of 125 mg/dL and an estimated 10-year ASCVD risk of 7.5% or greater.
5. A patient 28 years of age with an LDL-C of 145 mg/dL

Pre-test ARS Question 5

*Results to date with PCSK9 antibody use have demonstrated what effect?*

1. Comparable lowering of LDL-C to high-intensity statins
2. Significant reductions of LDL-C levels on top of statin therapy
3. Regression of atherosclerotic disease as measured by carotid intimal medial thickness studies
4. Hepatic fibrosis at the phase 3 doses studied
5. None of the above

Pre-test ARS Question 6

*According to the 2013 ACC AHA Cholesterol guidelines, which of the following is recommended therapy for a 78 year old male who suffers an NSTEMI?*

1. High intensity statin therapy
2. High intensity statin therapy plus Ezetimibe
3. Moderate Intensity statin therapy
4. Moderate Intensity statin therapy plus ezetimibe
5. Ezetimibe alone
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Burden of Atherosclerotic Cardiovascular Disease

- Annual rates in US
  - Myocardial infarction – 1.1 million
  - Strokes – 795,000
  - CVD Mortality – 1,344,185 (every 30 seconds a death)
  - Cardiac catheterization – 1.0 million
  - Percutaneous revascularization – 492,000
  - Surgical revascularization – 291,000
- Annual cost – >$315 billion


AHA/ACC Cholesterol Treatment Guidelines

AHA = American Heart Association; ACC = American College of Cardiology.

Effects on MAJOR VASCULAR EVENTS

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Events (%)</th>
<th>Rate Ratio (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-fatal MI</td>
<td>2031 (4.4)</td>
<td>0.74 (0.70 – 0.79)</td>
</tr>
<tr>
<td>CHD death</td>
<td>1548 (3.4)</td>
<td>0.81 (0.75 – 0.87)</td>
</tr>
<tr>
<td>Any major coronary event</td>
<td>3337 (7.4)</td>
<td>0.77 (0.74 – 0.80)</td>
</tr>
<tr>
<td>CABG</td>
<td>713 (3.3)</td>
<td>0.75 (0.69 – 0.82)</td>
</tr>
<tr>
<td>PTCA</td>
<td>510 (2.4)</td>
<td>0.70 (0.69 – 0.90)</td>
</tr>
<tr>
<td>Unspecified</td>
<td>1397 (3.1)</td>
<td>0.76 (0.69 – 0.84)</td>
</tr>
<tr>
<td>Any coronary revascularisation</td>
<td>2620 (5.8)</td>
<td>0.76 (0.73 – 0.80)</td>
</tr>
<tr>
<td>Haemorrhagic stroke</td>
<td>105 (0.2)</td>
<td>1.05 (0.78 – 1.41)</td>
</tr>
<tr>
<td>Presumed ischaemic stroke</td>
<td>1225 (2.8)</td>
<td>0.81 (0.74 – 0.88)</td>
</tr>
<tr>
<td>Any stroke</td>
<td>1340 (3.0)</td>
<td>0.83 (0.78 – 0.88)</td>
</tr>
<tr>
<td>Any major vascular event</td>
<td>6354 (14.1)</td>
<td>0.79 (0.77 – 0.81)</td>
</tr>
</tbody>
</table>

CTT. Lancet 2008 371: 117-125
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**Similar Benefits on Vascular Events Regardless of Baseline LDL-C, More vs Less, or Statin vs No Statin**

<table>
<thead>
<tr>
<th>Baseline LDL-C (mg/dL)</th>
<th>Events (per year)</th>
<th>30-day or 3-month mortality vs LDL-C Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 80</td>
<td>1.96 (1.73)</td>
<td>1.97 (1.74)</td>
</tr>
<tr>
<td>80 - &lt; 100</td>
<td>1.53 (1.39)</td>
<td>1.69 (1.54)</td>
</tr>
<tr>
<td>100 - &lt; 120</td>
<td>1.53 (1.39)</td>
<td>1.69 (1.54)</td>
</tr>
<tr>
<td>120 - &lt; 140</td>
<td>2.17 (2.06)</td>
<td>2.37 (2.25)</td>
</tr>
<tr>
<td>&gt; 140</td>
<td>2.50 (2.38)</td>
<td>2.67 (2.55)</td>
</tr>
</tbody>
</table>

Similar Benefits on Vascular Events Regardless of Baseline LDL-C, More vs Less, or Statin vs No Statin

**ASCVD Statin Benefit Groups**

- Adults >20 years of age and a candidate for statin therapy
- LDL-C ≥190 mg/dL
- Diabetes type 1 or 2 and age 40-75
- Estimate 10-year ASCVD RISK
- ≥7.5% 10-year ASCVD risk and age 40 to 75

[Diagram showing the flow of decision-making process for statin benefit groups]

LDL-C values converted to non-SI units, and rounded to nearest 20 mg/dL. Adapted from Lancet. 2010 Nov 13;376(9753):1670-81.
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Nonadherence to Statin Treatment begins early

Adherence continues to drop over time, particularly when treating the asymptomatic patient

Adapted from cohort study using linked population-based administration data from Ontario, Canada (N=85,020). Jackevicius et al.

Patients Non-adherent to Statin Therapy Are Twice as Likely to Experience Subsequent MI

Adherent Nonadherent

Patients Non-adherent to Statin Therapy Are Twice as Likely to Experience Subsequent MI

High Risk Patients with the Greatest Unmet Needs

- Statin-resistant patients
- Statin-intolerant patients
- Familial hypercholesterolemia (FH)
- Low HDL patients


Adherence defined as fill frequency ≥ 80% (n=661).
Nonadherence defined as fill frequency ≤ 60% (n=395).

Patients with MI (%)

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Patients &lt;65 Years</th>
<th>Patients ≥65 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adherent</td>
<td>P=0.047</td>
<td>4.1</td>
<td>4.1</td>
</tr>
<tr>
<td>Nonadherent</td>
<td>P=0.001</td>
<td>2.1</td>
<td>1.5</td>
</tr>
<tr>
<td></td>
<td>P=0.73</td>
<td>3.5</td>
<td>4.0</td>
</tr>
</tbody>
</table>


Inter-individual Variability in Response to Statins

The graph below shows dramatic interindividual variability in response to Atorvastatin 10 mg daily. This has also been observed with other statins.

Inter-individual Variability in Response to Statins

CLINICAL PEARL # 1

Even though statins are robust LDL-C lowering drugs, there is significant inter-patient variability in statin response.

Poor response to statins linked to CAD progression

- Data from 7 prospective trials was obtained (647 patients)
  - One-fifth of the patients were statin hyporesponders.
- Except for LDL-C, risk factors did not differ between groups.
- Even after adjustment, hypo-responders showed greater progression in percent atheroma volume than responders.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hyporesponder</th>
<th>Responder</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percent Atheroma Volume</td>
<td>2.23 ± 1.62</td>
<td>1.95 ± 1.55</td>
<td>0.06</td>
</tr>
<tr>
<td>Intima-media intima thickness</td>
<td>-1.66 ± 1.16</td>
<td>-1.21 ± 0.92</td>
<td>0.02</td>
</tr>
<tr>
<td>Lipid volume, mm3</td>
<td>-12.9 ± 0.9</td>
<td>-13.3 ± 0.95</td>
<td>0.004</td>
</tr>
<tr>
<td>Plasma lipids, mg/dL</td>
<td>-15.1 ± 1.7</td>
<td>-13.3 ± 1.87</td>
<td>0.001</td>
</tr>
<tr>
<td>Substantial Regression</td>
<td>22.5%</td>
<td>37.7%</td>
<td>0.001</td>
</tr>
</tbody>
</table>

*Adjustment for differences in clinical characteristics and adherence to dietary and lifestyle changes.

High Risk Patients with the Greatest Unmet Needs

- Statin-resistant patients
- Statin-intolerant patients
- Familial hypercholesterolemia (FH)
- Low HDL patients

Statin Intolerance

- An estimated 5–20% cannot tolerate statin treatment
- Statin intolerance (most commonly muscle pain, aching, and weakness) commonly leads to discontinuation
- Most statin-intolerant patients can be successfully re-challenged
  - Intolerance may be the result of perception or expectation
  - Muscle adverse events without significant elevation of creatine kinase levels are unlikely to be related to statin
- There is a subset of patients who are truly statin intolerant

77 year old woman 2 years S/P NSTEMI who complains of muscle aches

- 77 yo female
- very functional
- Normal BP; glucose; nonsmoker
- Suffered NSTEMI 2 years ago and begun on multiple medications, including a statin
- Has tried several statins at several doses over the past 2 years but she states “I ache all over”
Which of the following strategies is least likely to decrease her muscular side effects from statins?

1. Adding Coenzyme Q 10
2. Decreasing the statin dose
3. Switching to nighttime dosing
4. Switching to alternate day dosing
5. Substituting red yeast rice

Statin Muscle Adverse Effects

<table>
<thead>
<tr>
<th>Muscle AE</th>
<th>Incidence above placebo (per 100,000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myalgias</td>
<td>1,500 to 10,000</td>
</tr>
<tr>
<td>Myopathy (Sx + CK)</td>
<td>5</td>
</tr>
<tr>
<td>Rhabdomyolysis</td>
<td>1.6</td>
</tr>
</tbody>
</table>

Factors That Increase the Risk of Statin-Induced Myopathy

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Statin Properties</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increasing age</td>
<td>High systemic exposure</td>
</tr>
<tr>
<td>Female sex</td>
<td>Increased dose</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>High bioavailability</td>
</tr>
<tr>
<td>Hepatic dysfunction</td>
<td>Limited protein binding</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>Potential for drug-drug interactions metabolized by CYP pathways (particularly CYP450 3A4)</td>
</tr>
<tr>
<td>Diet or Meds</td>
<td></td>
</tr>
<tr>
<td>Polypharmacy</td>
<td></td>
</tr>
</tbody>
</table>

Adapted from Law M, Rudnicka AR. Am J Cardiol. 2006;97:52C-60C.

Management of Muscle Symptoms on Statin Therapy (con’t)

If unexplained severe muscle symptoms or fatigue develop during statin therapy:

• promptly discontinue the statin
• address possibility of rhabdomyolysis with:
  • CK
  • Creatinine
  • urine analysis for myoglobinuria

If mild-to-moderate muscle symptoms develop during statin therapy:

• Discontinue the statin until the Sx are evaluated
• Evaluate the patient for other conditions that might increase the risk for muscle symptoms
• If after 2 months without statin Rx, muscle Sx or elevated CK levels do not resolve completely, consider other causes of muscle symptoms

*Hypothyroidism, reduced renal or hepatic function, rheumatologic disorders such as polymyalgia rheumatica, steroid myopathy, Vitamin D deficiency or primary muscle diseases

77 year old woman 2 years S/P NSTEMI who complains of muscle aches

• Statin held until symptoms disappeared
• Re-challenged with very low dose rosuvastatin every other day
• Able to tolerate new statin regimen
• NOTE: No outcome studies have evaluated this dosing scheme
Many patients labelled as statin intolerance can be re-challenged with a statin; however, there is a real subgroup of patients who are truly statin intolerant.

**44 year old woman with recent NSTEMI**

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol</td>
<td>489 mg/dL</td>
</tr>
<tr>
<td>– HDL-C</td>
<td>39 mg/dL</td>
</tr>
<tr>
<td>– LDL-C</td>
<td>377 mg/dL</td>
</tr>
<tr>
<td>– Triglycerides</td>
<td>367 mg/dL</td>
</tr>
<tr>
<td>Fasting Blood Sugar</td>
<td>176 mg/dl</td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.9 mg/dl</td>
</tr>
</tbody>
</table>

No significant past medical history

Family history: Mother has hypertension but is otherwise well. She has no siblings and never knew her father.

1. Poor diet
2. Diabetes
3. Obesity
4. Hypothyroidism
5. Familial Hypercholesterolemia

What is the most likely cause for her hypercholesterolemia?
High Risk Patients with the Greatest Unmet Needs

- Statin-resistant patients
- Statin-intolerant patients
- Familial hypercholesterolemia (FH)
- Low HDL patients


FH: Most Common Inherited Disorder

FH: Most Common Inherited Disorder

CLINICAL PEARL # 3

Heterozygous FH occurs in about 1:500 patients
Familial Hypercholesterolemia (FH)

- Heritable, autosomal dominant disorder
- Due to mutations that cause decreased clearance of LDL
  - Usually LDL receptor gene
  - Other mutations include Apo B and PCSK9 genes
- Clinical manifestations include:
  - Severe hypercholesterolemia
  - CVD early in life: Men 42–46 yrs; Women 50–52 yrs
- FH is underdiagnosed and undertreated
  - > 600,000 people in the US with FH
  - But only 10% diagnosed
- FH is difficult to treat
  - High potency statin is often not enough

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CLINICAL PEARL # 4

Consider Familial Hypercholesterolemia whenever the LDL-C is > 190 mg / dL

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FH: Why is it important?

![Graph showing cumulative probability of clinical CAD over age]

- Non-FH Women
- Non-FH Men
- FH Women
- FH Men

MED-PED Registry 2001
The Phenotype of FH May Reflect LDL-R, Apo B, or PCSK9 Mutations

- LDLR gene codes for the LDL Receptor, which clears LDL particles from the circulation by binding to surface Apo B
- PCSK9 induces degradation of LDLR
- FH may be caused by mutations in Apo B, LDL-R, or PCSK9


44 year old woman with recent NSTEMI

No significant past medical history
Family history: Mother has hypertension but is otherwise well. She has no siblings and never knew her father.

Atorvastatin 80 mg po qd started

44 year old woman s/p NSTEMI

3 months later... Follow-up laboratory tests

- Total cholesterol: 323 mg/dL
  - HDL-C: 39 mg/dL
  - LDL-C: 238 mg/dL
  - Triglycerides: 220 mg/dL
- Fasting Blood Sugar: 136 mg/dl
- Creatinine: 0.9 mg/dl

What should we do?
According to the 2013 ACC-AHA Cholesterol guidelines, which of the following statements is true?

1. A non-statin agent must be added to her regimen
2. Advanced lipid testing should be performed
3. An LDL goal of < 70 mg/dL is optimal
4. An LDL goal of < 100 mg/dL is optimal
5. Her current treatment is consistent with these guidelines

ASCVD Statin Benefit Groups

Intensity of Statin Therapy

Drugs/doses highlighted in yellow have demonstrated reduction in major CVD events in clinical trials
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**Insufficient Response to Statin Therapy**

- Use the maximum tolerated intensity of statin
- Consider addition of a nonstatin cholesterol-lowering drug(s)
  - If a less-than-anticipated therapeutic response
  - Only if ASCVD risk-reduction benefits outweigh the potential for adverse effects in higher-risk persons:
    - Clinical ASCVD <75 years of age
    - Baseline LDL-C ≥190 mg/dL
    - Diabetes mellitus 40 to 75 years of age
- Nonstatin cholesterol-lowering drugs shown to reduce ASCVD events in RCTs are preferred

**IMPROVE-IT Study Design**

**Patients < 10 days post ACS LDL < 125mg/dL**

N=18,144  
ASA + Standard Medical Therapy

- Simvastatin 40 mg
- Eze/Simva 10/40 mg

Uptitrated to Simva 80 mg if LDL >79  
(adapted per FDA label 2011)

Duration: Minimum 2 1/2 year follow-up (5250 events)

Primary Endpoint: CV Death, MI, Hospital Admission for UA, revascularization (> 30 days after randomization), or Stroke

Presented by Dr. Christopher Cannon at AHA 2014

- Primary endpoint:
  - CV death
  - MI
  - UA
  - coronary revascularization
  - Stroke
  - moderate-severe bleeding

www.cardiosource.org
44 year old woman s/p NSTEMI

We decided to add ezetimibe

3 months later...Follow-up laboratory tests

- Total cholesterol 261 mg/dL
  - HDL-C 39 mg/dL
  - LDL-C 178 mg/dL
  - Triglycerides 220 mg/dL
- Fasting Blood Sugar 176 mg/dL
- Creatinine 0.9 mg/dL

CLINICAL PEARL # 4

Addition of non-statin cholesterol-lowering drug(s) may be considered if the ASCVD risk-reduction benefits outweigh the potential for adverse effects
New drugs for treatment of hypercholesterolemia

PCSK9
- A secreted protein which targets the LDL receptor for degradation
- Up-regulated by statin therapy
- Gain of function mutations cause high LDL-C
- Loss of function mutations cause low LDL-C
- Inhibition lowers LDL-C levels

Inherited Syndromes of Extremes of LDL-C: Story of PCSK9

Frequency (%)

Helen Hobbs et al.
PCSK9 Loss Of Function Mutations Are Associated With Decreased Plasma LDL-C Concentrations

81% of PCSK9 Y142X and PCSK9 C679X subjects had mean plasma LDL-C below 50th percentile

Moderate mean plasma LDL-C lowering effect in PCSK9 R46L allele carriers


PCSK9 Regulates LDLR Turnover Through Increased Intracellular Degradation

Blocking PCSK9 Activity Inhibits Intracellular Degradation of LDLR
% LDL-C Change with Once Every 2 Week PCSK9 Inhibitor On Top of Statin-based Rx

ODYSSEY LONG TERM Trial
2341 Patients with LDL-C at least 70 mg/dl Despite Maximum Tolerated Statin W or W/O other Lipid-Lowering Drugs Randomized to Alirocumab or Placebo

In a post-Hoc safety analysis, the rate of major adverse CV events* was 48% lower among alirocumab patients than among those receiving placebo during 80 weeks of f/up (nominal p=0.02)


*Primary end point: CHD death, nonfatal MI, fatal and nonfatal ischemic stroke, unstable angina
OSLER 1 & 2 Studies
Long Term Extension Studies Use of Evolocumab Or Standard Therapy
(Standard therapy in some cases included statin or ezetimibe)

Adverse Event rates similar in both groups except for neurocognitive complaints which were more frequent with evolocumab


OSLER 1 & 2 Studies
Effect on CV Events
(Pre-specified Exploratory Analysis)


PCSK9 Monoclonal Antibodies Have Been Studied in...

- Monotherapy
- Add on to Statin +/- Ezetimibe
- Statin Intolerance
- Familial Heterozygote Hypercholesterolemia
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### PCSK9 Inhibitors Furthest along in Development

<table>
<thead>
<tr>
<th>Molecule</th>
<th>Description</th>
<th>Clinical Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alirocumab</td>
<td>Fully human IgG1 mAb</td>
<td>3*</td>
</tr>
<tr>
<td>Evolocumab</td>
<td>Fully human IgG1 mAb</td>
<td>3*</td>
</tr>
<tr>
<td>Bococizumab</td>
<td>Humanized IgG1 mAb</td>
<td>3</td>
</tr>
</tbody>
</table>

* application for approval already submitted to FDA

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### Heterozygous Familial Hypercholesterolemia

**Frequency:** 1/500

USA: 600,000 patients

**FINAL OPTION - LDL apheresis**

↓ LDL 75-80% acutely (50% over 2-week average)

**FDA APPROVAL (HELP, LIPOSORBER)**

- LDL > 200 mg/dL (with CHD)
- LDL > 300 mg/dL (no CHD)

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### Future Updates to the Blood Cholesterol Guideline

- This is a comprehensive guideline for the evidence-based treatment of blood cholesterol to reduce ASCVD risk
- These guidelines represent a change from previous guidelines that aligns recommendations closely to the evidence
- For primary prevention, they are “patient-centered”
- Guidelines will change in the future as high-quality data will improve future cholesterol treatment guidelines

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Percentage of the Population by Race/Ethnicity: 2000 and 2025

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>2000</th>
<th>2025</th>
</tr>
</thead>
<tbody>
<tr>
<td>White*</td>
<td>71.4</td>
<td>61.9</td>
</tr>
<tr>
<td>AA*</td>
<td>12.2</td>
<td>12.9</td>
</tr>
<tr>
<td>American Indian, Eskimo, Asian*</td>
<td>9.7</td>
<td>8.8</td>
</tr>
<tr>
<td>Asian and Pacific Islander*</td>
<td>3.9</td>
<td>6.2</td>
</tr>
<tr>
<td>Hispanic Origin (of any race)</td>
<td>11.8</td>
<td>18.2</td>
</tr>
</tbody>
</table>

*Indicates non-Hispanic.
AA = African American.

Striking Differences in CVD Mortality Rates by Race/Ethnicity

<table>
<thead>
<tr>
<th></th>
<th>CHD</th>
<th>Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Hispanic Black</td>
<td>186.8</td>
<td>81.6</td>
</tr>
<tr>
<td>Non-Hispanic White</td>
<td>182.8</td>
<td>60.3</td>
</tr>
<tr>
<td>Hispanic</td>
<td>124.2</td>
<td>40.0</td>
</tr>
<tr>
<td>Native American</td>
<td>112.7</td>
<td>39.2</td>
</tr>
<tr>
<td>Asian</td>
<td>100.1</td>
<td>54.6</td>
</tr>
</tbody>
</table>

Data are expressed as mortality per 100,000 population and are based on rates age-adjusted to the 2000 standard; they are from the National Center for Health Statistics (personal communication, August 2000).

In which racial-ethnic group is cardiovascular disease the leading cause of death?

1. Hispanic Americans
2. South Asians
3. African Americans
4. White Americans
5. All of the above
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Leading Causes of Death by Race

<table>
<thead>
<tr>
<th>Race</th>
<th>CVD</th>
<th>Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>38.2%</td>
<td>23.1%</td>
</tr>
<tr>
<td>Black</td>
<td>33.6%</td>
<td>21.6%</td>
</tr>
<tr>
<td>Hispanic</td>
<td>39.6%</td>
<td>18.7%</td>
</tr>
<tr>
<td>Asian</td>
<td>34.8%</td>
<td>26.4%</td>
</tr>
<tr>
<td>Hispanic</td>
<td>29.6%</td>
<td>19.7%</td>
</tr>
</tbody>
</table>


Clinical Pearl #5

Cardiovascular disease is the leading cause of death in all racial/ethnic groups in the United States.

CHD Death Rates Among African Americans and Whites

[Graph showing CHD death rates among African Americans and Whites]
US Adults ≥20 Years Cholesterol Checked, Aware, Receiving Cholesterol-Lowering Medication

<table>
<thead>
<tr>
<th></th>
<th>Checked, %</th>
<th>Aware, %</th>
<th>Treated, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>72.4 (2.4)</td>
<td>36.3 (1.8)</td>
<td>12.1 (1.2)</td>
</tr>
<tr>
<td>Black</td>
<td>63.5 (2.7)</td>
<td>30.9 (2.1)</td>
<td>10.9 (1.2)</td>
</tr>
<tr>
<td>Mexican-American</td>
<td>53.1 (2.9)</td>
<td>23.3 (1.9)</td>
<td>6.9 (1.1)</td>
</tr>
</tbody>
</table>

Ford, E.S. et al Circulation 2003; 107: 2185-2189

Heart Disease & Stroke Mortality Disparities

- Black men & women much more likely to die of heart disease & stroke vs. whites
- CHD & stroke not only leading U.S. causes of death, but also account for largest proportion of inequality in life expectancy between whites and blacks
- Despite existence of low-cost, highly effective preventive treatment


Suboptimal Lipid Management

- Despite less than optimal treatment, identification of known CV risk increases chance of treatment for dyslipidemia.
- Optimal levels rarely attained in African-American adults under treatment with prescribed medication.

Taylor et al. The American Journal of Medicine, Vol 122, No 5, May 2009
**Statin Therapy Background**

- Few statin clinical trials involve non-whites
- Possible variability exists in statin drug response among various races, with slightly diminished response in blacks
- African-Americans under represented in statin efficacy and outcome clinical trials

**CHD as Cause of Death in Asians**

<table>
<thead>
<tr>
<th>Vietnamese</th>
<th>Korean</th>
<th>Chinese*</th>
<th>Japanese*</th>
<th>Samoan*</th>
<th>Filipinos*</th>
<th>Guamanians*</th>
<th>Hawaiian*</th>
<th>Other Asians</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tbody>
</table>

*CHD is the leading cause of death

Percent of Deaths

National Vital Statistics System, CDC, NCHS

**South Asians and CAD**

- Rapidly growing segment of US population
- Elevated CAD incidence in young adults
- High CAD risk vs. whites, with equivalent risk factors
  - higher prevalence insulin resistance, metabolic syndrome, DM
  - elevated CRP
  - lipoprotein (a) levels

Racial and Ethnic Groups

• Cardiovascular disease is the leading cause of death for African Americans, Latinos, Asian Americans, Pacific Islanders, and American Indians

• African American women are at the highest risk for death from heart disease among all racial, ethnic, and gender groups

Source: American Heart Association

Take Home Points

• Despite improvements in cardiovascular care, coronary heart disease (CHD) rates remain unacceptably high

• Response to statins is variable and influenced by many factors including genetic factors

• New therapies are emerging for treatment of dyslipidemia

• Patient populations at highest CHD risk may potentially benefit greatly from such therapies

• Cardiovascular disease is the leading cause of death for all races

POST-TEST QUESTIONS
Post-test ARS Question 1

MR, a 61-year-old male with an LDL-C of 130 mg/dL and diabetes has an ASCVD risk of 6.6% based on the new risk-calculator. What therapy should MR be started on according to the ACC/AHA 2013 guidelines?

1. High-intensity statin
2. Moderate-intensity statin
3. Low-intensity statin
4. Non-statin therapy
5. None of the above

Post-test ARS Question 2

SJ, a 62 year old BF is hospitalized in the Coronary care unit following a non-ST segment MI and stent placement in a 95% right coronary lesion. Her admission lipids are LDL-C=90 mg/dl, HDL=35 mg/dL, triglycerides=160 mg/dl.

In addition to being placed on a statin, which of the following treatments has been shown to reduce her risk of cardiovascular events.

1. Niacin
2. Fenofibrate
3. Cholestyramine
4. Ezetimibe
5. None of the above
Post-test ARS Question 3

Which of the following is NOT one of the 4 statin benefit groups according to the 2013 ACC/AHA Cholesterol Guideline to Reduce Atherosclerotic CV Disease?

1. A patient with clinical ASCVD
2. A patient with an LDL-C > 190 mg/dL
3. A patient 56 years of age with diabetes and an LDL-C of 118 mg/dL
4. A patient 67 years of age without diabetes or ASCVD with an LDL-C of 125 mg/dL and an estimated 10-year ASCVD risk of 7.5% or greater.
5. A patient 28 years of age with an LDL-C of 145 mg/dL

Post-test ARS Question 4

Results to date with PCSK9 antibody use have demonstrated what effect?

1. Comparable lowering of LDL-C to high-intensity statins
2. Significant reductions of LDL-C levels on top of statin therapy
3. Regression of atherosclerotic disease as measured by carotid intimal medial thickness studies
4. Hepatic fibrosis at the phase 3 doses studied
5. None of the above

Post-test ARS Question 5

According to the 2013 ACC AHA Cholesterol guidelines, which of the following is recommended therapy for a 78 year old male who suffers an NSTEMI?

1. High intensity statin therapy
2. High intensity statin therapy plus Ezetimibe
3. Moderate Intensity statin therapy
4. Moderate Intensity statin therapy plus ezetimibe
5. Ezetimibe alone
Post-test ARS Question 6

On a scale of 1 to 5, please rate how confident you would be in treating Hypercholesterolemia in patients that are not achieving optimal goals or are refractory to statin therapy?

1. Not at all confident
2. Slightly confident
3. Moderately confident
4. Pretty much confident
5. Very confident

Post-test ARS Question 7

Which of the statements below describes your approach to treating Hypercholesterolemia?

1. I do not treat Hypercholesterolemia, nor do I plan to this year.
2. I did not treat Hypercholesterolemia, but as a result of attending this course I’m thinking of doing this now.
3. I do treat Hypercholesterolemia and this course helped me change my methods.
4. I do treat Hypercholesterolemia and this course confirmed that I don’t need to change my methods.