Update on the Treatment of Hyperlipidemia

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Washington Metropolitan Society of Health Systems Pharmacists
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Please MUTE phones and do not put call on HOLD
Disclosure

• Nothing to disclose
Objectives

• Name the 4 Statin Benefit Groups for risk reduction of atherosclerotic cardiovascular disease (ASCVD)

• Discuss primary and secondary ASCVD risk reduction

• List risk factors that estimate the 10 year ASCVD risk

• Discuss the role of statins and other drug classes in ASCVD risk reduction
Terms and Definitions

- Atherosclerotic Cardiovascular Disease (ASCVD):
  - Coronary Heart Disease (CHD) or revascularization
  - Stroke or Transient Ischemic Attack (TIA)
  - Peripheral Arterial Disease or revascularization

- ASCVD events:
  - nonfatal MI
  - CHD death
  - Fatal or non-fatal Stroke
Terms and Definitions

• Low density lipoprotein cholesterol (LDL-C)
• Very low density lipoprotein cholesterol (VLDL)
• Triglyceride (TG)
• Total Cholesterol (TC)
• High density lipoprotein cholesterol (HDL-C)
• Non-HDL Cholesterol = VLDL+LDL = TC–HDL-C
  - Non-HDL-C includes atherogenic lipoproteins
Collaboration of Professional Organizations in Development of New Guidelines

• In 2013 The National Heart, Lung, and Blood Institute (NHLBI) collaborated with the American College of Cardiology and the American Heart Association (ACC/AHA) to develop clinical practice guidelines:
  - Assessment of Cardiovascular (CV) Risk
  - Lifestyle Modifications to Reduce CV Risk
  - Overweight and Obesity in Adults
  - Management of Blood Cholesterol

• Focus on highest quality evidence to develop recommendations for these 4 guidelines
Strategies to Reduce ASCVD Risk

Past Guidelines:
- Treat to Cholesterol Target
- Lower Cholesterol is better
- Risk based treatment approaches

Present Guideline (2013):
- Lifestyle modification remains a critical component in ASCVD risk reduction prior to and in conjunction with cholesterol-lowering therapy
- Focus on Statin RCTs (overwhelming evidence)
- Risk Factors (RFs) for ASCVD

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What’s New in the 2013 Blood Cholesterol Guideline?

1. Focus on Atherosclerotic Cardiovascular Disease (ASCVD) Risk Reduction: 4 Statin Benefit Groups
2. New Perspective on LDL-C and Non-HDL Treatment Goals
3. Global Risk Assessment for Primary Prevention: Use of the New Pooled Cohort Equations to estimate 10-Year ASCVD Risk
4. Safety Recommendations
What’s New in the 2013 Blood Cholesterol Guideline? (cont.)

5. Role of biomarkers and noninvasive tests

6. Future Updates to the Blood Cholesterol Guideline: RCTs comparing alternative treatment strategies (non-statins) are needed for future evidence based guidelines for optimum ASCVD risk reduction and for the management of complex lipid disorders
Features of 2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce ASCVD in Adults

• Treatment of Blood Cholesterol with Statin to reduce ASCVD events in adults based on RCTs
• Limited number of expert opinion recommendations only when RCT evidence is not present
• **Not** a comprehensive approach to the detection, evaluation, and treatment of lipid disorders as had been done in the ATPIII Report
• Not a source for questions regarding complex lipid disorders. This is beyond the scope of the systemic evidence review
Overview of the Guidelines

• Extensive and consistent evidence was found supporting use of statins for the prevention of ASCVD in many higher risk Primary and ALL Secondary Prevention individuals without NYHA class II-IV Heart Failure and who were not receiving Hemodialysis.

• The trials were not designed to evaluate the effect of titrated statin treatment to achieve pre-specified LDL-C or Non-HDL-C goals.

• Hence the Expert Panel was unable to find RCT evidence to support titrating cholesterol-lowering drug therapy to achieve target LDL-C and Non-HDL-C levels as recommended by ATPIII.
RCT Results found by Expert Panel

• Initiation of
  -Moderate Intensity Statin therapy: LDL-C reduction of approx. 30-<50%
  -High Intensity Statin therapy: LDL-C reduction ≥ 50%

is a critical factor in reducing ASCVD
Lifestyle Modification

• Remains an important component of ASCVD risk reduction
• Prospective cohort studies and RCTs suggest that healthier dietary patterns are associated with lower chronic disease risk, including CVD and risk factors such as type 2 Diabetes Mellitus (DMII) and Hypertension (HTN)
2013 ACC/AHA Lifestyle Management Guideline: Diet – Lowering LDL-C and BP

- Recommendations for lowering LDL-C & BP (A: strong):
  - Consume a dietary pattern that emphasizes
    - intake of vegetables, fruits and whole grain
    - includes low-fat dairy products
    - Poultry, fish, legumes
    - Non-tropical vegetable oils and nuts
    - Limits intake of sweets, sugary beverages & red meat
- Adapt dietary pattern based on appropriate calorie requirements, food preferences and nutrition therapy for other medical conditions e.g. DM.
- Achieve this pattern by following plans such as DASH, USDA food pattern, or the AHA diet.
Diet – Lowering LDL-C (A)

• Aim for a dietary pattern that achieves
  - 5% to 6% of Calories from saturated fat
  - 26-27% of Calories from fat
• Reduce % Calories from trans fat
Diet: Lowering Blood Pressure

- Lower Sodium intake (A: strong)
- Consume no more than 2,400 mg sodium/day
- Further reduction of sodium intake to 1,500 mg/day is associated with even greater reduction in BP (B: moderate)
- Combine DASH diet with lower sodium intake (A: strong)
Lifestyle Modification: Physical Activity

- Reduce LDL-C, Non-HDL-C and BP:
  - Advise moderate to vigorous intensity aerobic physical activity 3-4 times weekly for an average of 40 minutes
  (B: moderate)
<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Defining Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal Obesity</td>
<td>Waist Circumference: &gt;102 cm (&gt; 40 inches)</td>
</tr>
<tr>
<td></td>
<td>&gt; 88 cm (&gt; 35 inches)</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>≥ 150 mg/dl</td>
</tr>
<tr>
<td>HDL-Cholesterol (HDL-C)</td>
<td>&lt; 40 mg/dl</td>
</tr>
<tr>
<td></td>
<td>&lt; 50 mg/dl</td>
</tr>
<tr>
<td>Blood Pressure (BP)</td>
<td>≥ 130/85 mmHg</td>
</tr>
<tr>
<td>Fasting Glucose (Glc)</td>
<td>110-125 mg/dl</td>
</tr>
</tbody>
</table>

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# Classification of Overweight and Obesity

• Disease risk for DMII, HTN and CVD

<table>
<thead>
<tr>
<th></th>
<th>BMI (kg/m²)</th>
<th>Disease Risk ♂ ≤ 102cm (≤40”)</th>
<th>Disease Risk ♂ ≥ 102cm (≥40”)</th>
<th>Disease Risk ♀ ≤ 88 cm (≤35”)</th>
<th>Disease Risk ♂ ≥ 88 cm (≥35”)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>&lt; 18.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>18.5-24.9</td>
<td>Increased</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overweight</td>
<td>25.0-29.9</td>
<td></td>
<td>High</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obesity</td>
<td>30.0-34.9</td>
<td></td>
<td>Very high</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>35.0-39.9</td>
<td></td>
<td>Very High</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extreme Obesity</td>
<td>≥ 40</td>
<td>Extremely high</td>
<td></td>
<td>Extremely high</td>
<td></td>
</tr>
</tbody>
</table>
Major Risk Factors for CVD (NCEP/ATPIII guideline)

- Age (♂>45, ♀>55 yrs)
- FH of premature CHD: MI or sudden death in ♂ relatives <55, ♀ relatives <45 yr
- Cigarette smoking
- HTN or on drugs for HTN
- Low HDL-C (< 40 mg/dl) and high LDL-C
- DM: CHD risk equivalent (in ATP III)
- Also referred to in the 2013 Guidelines along with DM as Traditional Risk Factors
Emerging Risk Factors for CVD (NCEP/ATPIII guideline)

- Triglycerides/non-HDL-C
- Subclinical atherosclerotic disease
- High VLDL
- Lipoprotein a
- Homocysteine
- Thrombogenic/ Hemostatic factors
- Inflammatory markers/ CRP
- Impaired Fasting Glc
Additional Risk Factors

- Primary LDL ≥ 160 mg/dl or other evidence of genetic hyperlipidemia
- CAC score ≥ 300 Agatston or > 75\textsuperscript{th} % for age, sex, ethnicity
- Ankle-Brachial Index (ABI) < 0.9
- Carotid Intima-media thickness (CIMT)
- Other Traditional RFs: HDL, SBP, tobacco
- Elevated lifetime risk of ASCVD
Risk Assessment Tools in Primary Prevention

Framingham Risk Score
NCEP/ATPIII

- Age
- Sex
- Total Cholesterol (TC)
- Smoker/non-smoker
- HDL-C
- Systolic Blood Pressure (SBP) un-treated/treated
- Total number of points were added to calculate the 10-yr risk of a CHD event (%)

Pooled Cohort Equations
ACC/AHA 2013

- Sex
- Race: AA, White, Hispanic, other
- If Risk-based treatment decision still unsure, ≥ 1 of the following may be considered: FH, CRP, CAC score, ABI
- Reasonable to assess Traditional RFs (left) including DM every 4-6 yr
Intensity of Risk Reduction Therapy

- Risk Assessment is a prerequisite to risk reduction therapy
- Intensity of risk reduction therapy is based on Absolute Risk (both Guidelines)
- NCEP/ATPIII: risk assessment based on Framingham Scoring System. Outcome of interest was CHD
- ACC/AHA 2013 guideline uses Pooled Cohort Equations from the community
- Outcome of interest is focused on estimation of first hard ASCVD events—first occurrence of non-fatal MI or CHD death, or fatal or non-fatal stroke
Focus of 2013 Guideline  ASCVD Risk Reduction: 4 Statin Benefit Groups

• Clinical ASCVD
• Primary Elevations of LDL-C ≥ 190 mg/dl
• 40-75 yrs of age with DM & LDL-C 70-189 mg/dl
• Without clinical ASCVD or DM who are 40-70 yrs of age with LDL-C 70-189 mg/dl
Figure 2. Major recommendations for statin therapy for ASCVD prevention

ASCVD Statin Benefit Groups

Heart healthy lifestyle habits are the foundation of ASCVD prevention. In individuals not receiving cholesterol-lowering drug therapy, recalculate estimated 10-y ASCVD risk every 4-6 y in individuals aged 40-75 y without clinical ASCVD or diabetes and with LDL-C ≥ 180 mg/dL.

Adults age ≥ 21 y and a candidate for statin therapy

Clinical ASCVD

NO

LDL-C ≥ 180 mg/dL

NO

Diabetes Type 1 or 2

Age ≥ 40-75 y

Yes

Yes

Yes

NO


Definitions of High- and Moderate-Intensity Statin Therapy (See Table 5)

High Daily dose lowers LDL-C by approx. ≥ 50%

Moderate Daily dose lowers LDL-C by approx. 30% to <50%

Yes

High-Intensity statin (Moderate-Intensity statin if not candidate for high-intensity statin)

High-Intensity statin

Moderate-Intensity statin

Moderate-Intensity statin

High-Intensity statin

Estimate 10-y ASCVD Risk with Pooled Cohort Equations*

≥ 27.5% estimated 10-y ASCVD risk and age ≥ 40-75 y

Yes

No

ASCVD prevention benefit of statin therapy may be less clear in other groups. In selected individuals, consider additional factors influencing ASCVD risk and potential ASCVD risk benefits and adverse effects, drug-drug interactions, and patient preferences for statin treatment.
Pharmacotherapy

- Statin Treatment is recommended for primary and secondary prevention of ASCVD based on evidence from RCTs, reviews and meta-analyses of RCTs.
- If Age ≥ 21 yrs and LDL ≥ 190 mg/dl after Maximum Intensity Statin achieved, consider addition of a NON-STATIN to further reduce LDL
- Treatment Targets: No recommendation for or against specific LDL or Non-HDL targets for the primary or secondary prevention of ASCVD
## High- Moderate- and Low-Intensity Statin Therapy Reviewed by the Expert Panel in RCTs

<table>
<thead>
<tr>
<th>High-Intensity Statin Therapy</th>
<th>Moderate-Intensity Statin therapy</th>
<th>Low-Intensity Statin Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily dose lowers LDL on average by approx. ≥50%</td>
<td>Daily dose lowers LDL on average by approx. 30% to &lt; 50%</td>
<td>Daily dose lowers LDL on average by &lt; 30%</td>
</tr>
</tbody>
</table>

**Atorvastatin** (40mg-1 trial: if unable to tolerate 80mg) 80mg
**Rosuvastatin** 20 (40mg)

**Atorvastatin** 10 (20)mg
**Rosuvastatin** (5) 10 mg
**Simvastatin** 20-40 mg
**Pravastatin** 40 (80) mg
**Lovastatin** 40 mg
**Fluvastatin XL** 80 mg
**Fluvastatin** 40 mg BID
**Pitavastatin** 2-4 mg

*Simvastatin* 10 mg
**Pravastatin** 10-20mg
**Lovastatin** 20 mg
**Fluvastatin** 20-40mg
**Pitavastatin** 1 mg

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## Secondary Prevention

### Recommendations for Secondary Prevention

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>NHLBI Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. High-Intensity Statin Therapy should be initiated or continued as First-line therapy in ♀ and ♂ Age ≤ 75 yrs who have Clinical ASCVD</td>
<td>A</td>
</tr>
<tr>
<td>2. In individuals with Clinical ASCVD in whom High-Intensity Statin therapy is contraindicated or adverse effects are present, Moderate-Intensity Statin can be used if tolerated.</td>
<td>A</td>
</tr>
<tr>
<td>3. In individuals with Clinical ASCVD &gt; 75 yrs of Age. Evaluate potential for ASCVD Risk Reduction and adverse effects, drug-drug interactions, and consider patient preference when initiating a Moderate- or High-Intensity Statin. It is reasonable to continue statin therapy when tolerated.</td>
<td>E expert opin.</td>
</tr>
</tbody>
</table>
## Primary Prevention: ≥ 21 Yrs with LDL ≥190 mg/dl

<table>
<thead>
<tr>
<th>≥ 21 Yrs, LDL ≥190 mg/dl</th>
<th>NHLBI Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. LDL ≥190 mg/dl or Triglycride (TG) ≥ 500 mg/dl, evaluate for Secondary causes of Hyperlipidemia</td>
<td>B</td>
</tr>
<tr>
<td>2. Age ≥ 21 Yrs with Primary LDL ≥190 mg/dl: treat with a Statin --10-Yr ASCVD Risk Estimate not required High-Intensity Statin if tolerated. If not, use maximum tolerated statin.</td>
<td>B</td>
</tr>
<tr>
<td>3. ≥ 21 Yrs and Untreated LDL ≥190 mg/dl, reasonable to use High-Intensity Statin to achieve at least 50% LDL reduction</td>
<td>E</td>
</tr>
<tr>
<td>4. ≥ 21 Yrs and Untreated LDL ≥190 mg/dl, after Maximum Intensity Statin achieved, consider addition of a NON-STATIN to further reduce LDL</td>
<td>E</td>
</tr>
</tbody>
</table>

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Knowledge and Compassion *Focused on You*
Primary Prevention: Adults ≥ 21yrs, LDL ≥190 mg/dl

- Adults ≥ 21yrs with Primary LDL ≥190 mg/dl have a high lifetime risk for ASCVD events due to lifetime exposure to elevated LDL (genetics)
- Extensive evidence shows a ↓ LDL of 39mg/dl by Statin therapy → ↓ ASCVD Risk by 20%
- High-Intensity Statin therapy recommended to achieve at least a 50% ↓ in LDL.
- In addition to maximally tolerated Statin Dose, Non-Statin Cholesterol-lowering drug is needed
### Primary Prevention: DM and LDL 70-189 mg/dl

<table>
<thead>
<tr>
<th>Primary Prevention in DM and LDL 70-189 mg/dl</th>
<th>NHLBI Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Moderate-Intensity Statin therapy should be initiated or continued for adults 40-75 Yrs of Age with DM</td>
<td>A</td>
</tr>
<tr>
<td>2. High-Intensity Statin Therapy is reasonable for adults 40-75 Yrs of Age with DM with a ≥ 7.5% estimated 10-Yr</td>
<td>E</td>
</tr>
<tr>
<td>ASCVD risk unless contraindicated</td>
<td></td>
</tr>
<tr>
<td>3. Adults with DM and Age &lt;40 or &gt; 75, it is reasonable to evaluate the potential for ASCVD benefits, and for</td>
<td>E</td>
</tr>
<tr>
<td>adverse effects, drug-drug interactions, and patient preference when deciding to initiate, continue or intensify</td>
<td></td>
</tr>
<tr>
<td>Statin therapy</td>
<td></td>
</tr>
</tbody>
</table>
Primary Prevention in Diabetes

• High level of evidence supports use of Moderate-Intensity Statin in DM, Ages 40-75yr
• High-Intensity Statins recommended in Ages 40-75 yr with or without DM + ≥ 7.5% 10-Yr ASCVD Risk
• Individuals with Diabetes, Age 40-75 yr are at an ↑ lifetime risk ASCVD events and death
<table>
<thead>
<tr>
<th>Primary Prevention: No DM; With LDL 70-189 mg/dl</th>
<th>NHLBI Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Use Pooled Cohort Equations to Estimate 10-Yr ASCVD Risk for LDL 70-189 mg/dl without Clinical ASCVD to guide initiation of Statin therapy for the Primary Prevention of ASCVD</td>
<td>E</td>
</tr>
<tr>
<td>2. Adults 40-75 Yrs and LDL 70-189 mg/dl without Clinical ASCVD or DM &amp; estim. 10-Yr ASCVD Risk ≥ 7.5% should be treated with Moderate- to High-Intensity Statin</td>
<td>A</td>
</tr>
<tr>
<td>3. Reasonable to offer Treatment with Moderate-Intensity Statin to Adults Ages 40-75 Yrs, with LDL 70-189 mg/dl without Clinical ASCVD or DM and an estimated 10-Yr ASCVD Risk of 5% to &lt;7%</td>
<td>C</td>
</tr>
<tr>
<td>4. Statin for Primary Prevention with LDL 70-189 mg/dl, without Clinical ASCVD or DM discuss benefits, ADR, pref.</td>
<td>E</td>
</tr>
<tr>
<td>5. Adults with LDL &lt; 190 mg/dl not in a Statin Benefit Gp, may consider additional RFs to decide on Statin therapy</td>
<td>E</td>
</tr>
</tbody>
</table>
Primary Prevention: Selected Individuals

• Additional factors may be considered for treatment decisions in adults with LDL-C < 190 mg/dl not identified in a Statin Benefit Group:
  • Primary LDL ≥ 160 mg/dl or other evidence of genetic hyperlipidemia
  • FH of premature ASCVD
  • hs-CRP
  • CAC score
  • ABI
  • Elevated lifetime risk of ASCVD
• Consideration of Traditional RFs
• Additional factors may be identified in the future
Heart Failure and Hemodialysis

• The Expert Panel makes no recommendations regarding initiation or continuation of statins in patients with NYHA Classes II-IV ischemic systolic heart failure or in patients on maintenance hemodialysis.

• The potential for ASCVD risk reduction benefit, adverse effects, drug-drug interactions using Statin therapy and choice of Statin must be considered by the treating clinician.
Age in Global risk Assessment for Primary Prevention

• Most ASCVD events occur after age 70 yrs
• Age represents cumulative RF exposure
• Individuals ≥ 70 yrs with no other RFs still have an estimated 10-yr risk ≥ 7.5%
• This age group hence has the greatest potential for Absolute Risk Reduction
Figure 3. Initiating statin therapy in individuals with clinical ASCVD

Clinical ASCVD
Not currently on statin therapy
Initial evaluation prior to statin initiation
- Fasting lipid panel*
- ALT
- CK (if indicated)
- Consider evaluation for other secondary causes (Table 6) or conditions that may influence statin safety (Table 8, Rec 1).

Evaluate and Treat Laboratory Abnormalities
1. Triglycerides ≥500 mg/dL
2. LDL-C ≥190 mg/dL
   - Secondary causes (Table 6)
   - If primary, screen family for FH
3. Unexplained ALT >3X ULN

Aged <75 y without contraindications, conditions or drug-drug interactions influencing statin safety, or a history of statin intolerance
Initiate high-intensity statin therapy
Counsel on healthy lifestyle habits

Aged >75 y† OR with conditions or drug-drug interactions influencing statin safety, or a history of statin intolerance
Initiate moderate-intensity statin therapy
Counsel on healthy lifestyle habits

Monitor statin therapy (Figure 5)

Colors correspond to the class of recommendations in the ACC/AHA Table 1.
*Fasting lipid panel preferred. In a nonfasting individual, a nonfasting non-HDL-C ≥220 mg/dL may indicate genetic hypercholesterolemia that requires further evaluation or a secondary etiology. If nonfasting triglycerides are >500 mg/dL, a fasting lipid panel is required.
†It is reasonable to evaluate the potential for ASCVD benefits and for adverse effects, and to consider patient preferences, in initiating or continuing a moderate- or high-intensity statin, in individuals with ASCVD >75 years of age.
Figure 4. Initiating statin therapy in individuals without clinical ASCVD

- No Clinical ASCVD
  - Not currently on cholesterol-lowering drugs
  - Initial evaluation prior to statin initiation
    - Fasting lipid panel
    - ALT
    - Hemoglobin A1c (if diabetes status unknown)
    - CK (if indicated)
    - Consider evaluation for other secondary causes (Table 6) or conditions that may influence statin safety (Table 8, Rec 1)

- Assign to statin benefit group
  - (Figure 2)
  - Counsel on healthy lifestyle habits

- Diabetes and age 40-75 y
  - OR
  - LDL-C ≥190 mg/dL

- Estimate 10-y ASCVD risk with Pooled Cohort Equations

- >7.5% 10-y ASCVD risk
  - Clinicians and patients should engage in a discussion of the potential for:
    - 1. ASCVD risk reduction benefits
    - 2. Adverse effects
    - 3. Drug-drug interactions
    - 4. Patient preferences

- Initiate statin therapy
  - (Figure 2)
  - Re-emphasize healthy lifestyle habits

- <5% 10-y ASCVD risk
  - Age <40 or >75 y
  - LDL-C <190 mg/dL

- <5% 10-y ASCVD risk
  - In selected individuals, additional factors may be considered to inform treatment decision making

MedStar Washington Hospital Center

Knowledge and Compassion Focused on You
# Secondary Causes of Hyperlipidemia
Most Commonly Seen in Clinical Practice

<table>
<thead>
<tr>
<th>Secondary Cause</th>
<th>Elevated LDL-C</th>
<th>Elevated Triglyceride</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diet</td>
<td>Saturated or trans fats, weight gain, anorexia</td>
<td>Wt gain, very low-fat diets, high intake of refined CHO, excessive Alcohol intake</td>
</tr>
<tr>
<td>Drugs</td>
<td>Diuretics, CSA, glucocorticoids (GC), amiodarone</td>
<td>PO estrogens, GCs, BA seq, PIs, sirolimus, tamoxifen, bbs(not Coreg), thiazides</td>
</tr>
<tr>
<td>Diseases</td>
<td>Biliary obstruction, nephrotic syndrome</td>
<td>Lipodystrophies, CRF, nephrotic syndrome</td>
</tr>
<tr>
<td>Disorders &amp; Δ States of Metabolism</td>
<td>Hypothyroidism, Obesity, Pregnancy</td>
<td>DM (poorly controlled), Hypothyroidism, Obesity, Pregnancy</td>
</tr>
</tbody>
</table>

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## Statin Safety Recommendations

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>CK</td>
<td>Not routinely measured. Obtain a Hx of current/previous muscle Sxs baseline. Measure if at ↑ risk for adverse muscle event.</td>
</tr>
<tr>
<td>ALT</td>
<td>Measure baseline ALT before initiating statin.</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Evaluate for new-onset DM. Continue statin, recommend lifestyle changes.</td>
</tr>
<tr>
<td>Age &gt; 75yr, Hepatic or Renal Dis.</td>
<td>If High-intensity statin not tolerated, use Moderate intensity statin.</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>Category X, also avoid during lactation.</td>
</tr>
</tbody>
</table>

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PHARMACOTHERAPY: Drug Classes

• Statins
• Non-Statins:
  - Niacin
  - Bile Acid sequestrants
  - Cholesterol absorption inhibitor
  - Fibrates
  - Omega 3 Fatty Acids
## Drug Classes in Hyperlipidemia Treatment

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Lipid/ Lipoprotein Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HMG-CoA reductase Inhibitors</strong></td>
<td>↓LDL: 18-55%</td>
</tr>
<tr>
<td><em>(Statins)</em></td>
<td>↓63% (rosuvastatin)</td>
</tr>
<tr>
<td></td>
<td>↑HDL: 5-15%</td>
</tr>
<tr>
<td></td>
<td>↓TG: 7-30%</td>
</tr>
<tr>
<td><strong>Bile Acid Sequestrants</strong></td>
<td>↓LDL: 15-30%</td>
</tr>
<tr>
<td></td>
<td>↑HDL: 3-5%</td>
</tr>
<tr>
<td><strong>Nicotinic Acid Niacin</strong></td>
<td>↓LDL: 5-25%</td>
</tr>
<tr>
<td></td>
<td>↑HDL: 15-35%</td>
</tr>
<tr>
<td></td>
<td>↓TG: 20-50%</td>
</tr>
<tr>
<td><strong>Fibric Acids</strong></td>
<td>↓LDL: 5-20%</td>
</tr>
<tr>
<td></td>
<td>↑HDL: 15-35%</td>
</tr>
<tr>
<td></td>
<td>↓TG: 20-50%</td>
</tr>
<tr>
<td><strong>Ezetimibe</strong></td>
<td>↓cholesterol absorption</td>
</tr>
</tbody>
</table>
## HMG-CoA Reductase Inhibitors (Statins)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose (mg)</th>
<th>↓ LDL%</th>
<th>↓ TC%</th>
<th>↓ TG%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atorvastatin (Lipitor)</td>
<td>Initial: 10</td>
<td>35-40%</td>
<td>5-45%</td>
<td>19-37%</td>
</tr>
<tr>
<td></td>
<td>Maximum: 80</td>
<td>50-60%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluvastatin (Lescol)</td>
<td>Initial: 20</td>
<td>20-25%</td>
<td>13%</td>
<td>8.6%</td>
</tr>
<tr>
<td></td>
<td>Maximum: 40</td>
<td>30-35%</td>
<td>17%</td>
<td>11%</td>
</tr>
<tr>
<td>Lovastatin (Mevacor)</td>
<td>Initial: 20</td>
<td>25-30%</td>
<td>6.6%</td>
<td>10%</td>
</tr>
<tr>
<td></td>
<td>Maximum: 80</td>
<td>35-40%</td>
<td>9.5%</td>
<td>19%</td>
</tr>
<tr>
<td>Pravastatin (Pravachol)</td>
<td>Initial: 20</td>
<td>25-32%</td>
<td>24%</td>
<td>11%</td>
</tr>
<tr>
<td></td>
<td>Maximum: 40</td>
<td>30-35%</td>
<td>25%</td>
<td>24%</td>
</tr>
<tr>
<td>Simvastatin (Zocor)</td>
<td>Initial: 20</td>
<td>35-40%</td>
<td>24%</td>
<td>10%</td>
</tr>
<tr>
<td></td>
<td>Maximum: 40</td>
<td>45-50%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rosuvastatin (Crestor)</td>
<td>Initial: 10</td>
<td>45-52%</td>
<td>36-40%</td>
<td>10-37%</td>
</tr>
<tr>
<td></td>
<td>Maximum: 40</td>
<td>43-63%</td>
<td>40-46%</td>
<td>28-43%</td>
</tr>
<tr>
<td>Pitavastatin</td>
<td>Initial: 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Maximum: 4</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

May 19, 2015
Monitoring Statin Therapy

• Initial fasting lipid panel: TC, TG, HDL-C and calculated LDL-C
• 4-12 weeks later: second lipid panel to determine adherence
• Every 3-12 months thereafter
• Adherence to both medication and lifestyle regimens are required to reduce ASCVD risk
• High-Intensity Statin therapy reduces ASCVD risk more than Moderate-Intensity Statin therapy
• If patient requiring High-Intensity Statin is intolerant to it, start Moderate-Intensity Statin
Selected Drug Interactions with Statins

- Amiodarone ↑risk of myopathy with lovast & simvast
- Azoles ↑lovastatin levels by 20%; pravastatin and rosuvastatin are least altered
- Macrolides ↑risk of severe myopathy with Statins with a 40% ↑with atorvastatin. ↓pitavastatin dose
- Protease Inhibitors ↑risk of myopathy
- Protease Inhibitors ↓pravastatin levels
- Rifampin ↓simvastatin and fluvastatin levels
- Verapamil ↑risk of myopathy with atorvastatin, simvastatin, lovastatin
- Digoxin levels may ↑by 20% with atorvastatin
- Warfarin causes ↑INR with lova, simva, rosvu, fluva
- Oral Contraceptives: atorvast. & rosvu. can ↑AUC
# Niacin

<table>
<thead>
<tr>
<th>Niacin</th>
<th>Dose (gm/day)</th>
<th>↓ LDL</th>
<th>↓ TG</th>
<th>↑ HDL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crystalline form (OTC)</td>
<td>1.5-3 gm (Max. 4.5)</td>
<td>5-25%</td>
<td>20-50%</td>
<td>15-35%</td>
</tr>
<tr>
<td>Sustained Release (OTC)</td>
<td>1-2 gm (Max. 2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extended Release (Niaspan)</td>
<td>1-2 gm (Max. 2)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

May 19, 2015
Niacin Safety Recommendations

• Before initiation, up-titration, then q6 months: obtain baseline hepatic transaminases, HgbA1c or fasting Glc, uric acid

• Avoid if LFTs > 2-3 X ULN, persistent severe cutaneous Sxs, persistent hyperglycemia, acute gout, unexplained GI Sxs

• Flushing: start low and titrate slowly over weeks, take with food or Aspirin 325 mg ½ hr before dose
# Bile Acid Sequestrants (Resins)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose (gm/day)</th>
<th>Preparations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholestyramine</td>
<td>Usual: 4-16</td>
<td>9 gm packets (4 gm drug)</td>
</tr>
<tr>
<td>(Questran)</td>
<td>Maximum: 24</td>
<td>378 gm bulk</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Light: 210 gm bulk</td>
</tr>
<tr>
<td></td>
<td></td>
<td>378 gm bulk</td>
</tr>
<tr>
<td>Colestipol (Colestid)</td>
<td>Usual: 5-20</td>
<td>5 gm packets (5 gm drug)</td>
</tr>
<tr>
<td></td>
<td>Maximum: 30</td>
<td>450 gm bulk</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 gm tablets</td>
</tr>
<tr>
<td>Colesevelam (WelChol)</td>
<td>Usual: 2.6-3.8</td>
<td>625 mg tablet</td>
</tr>
<tr>
<td></td>
<td>Maximum: 4.4</td>
<td></td>
</tr>
</tbody>
</table>

May 19, 2015

Knowledge and Compassion **Focused on You**

MedStar Washington Hospital Center
Bile Acid Sequestrants (BSA)

- MOA: bind to cholesterol and bile acids in GI tract inhibiting re-absorption and enterohepatic cycling
- ADRs: bloating, gas, constipation
- Avoid if baseline TG ≥ 300 mg/dl
- Decreases absorption of Vitamins A,D,E,K
- Monitoring: Fasting Lipid Panel before BSA initiated, 3 months after, then every 6-12 months
Cholesterol absorption Inhibitor: Ezetimibe (Zetia)

• MOA: Inhibits absorption of dietary and biliary cholesterol.
• Dose: 10 mg po daily
• Drug-Drug Interaction: can ↑ cyclosporine level up to 15%
## Fibric acids

<table>
<thead>
<tr>
<th>Fibric Acid</th>
<th>Dose (mg/day)</th>
<th>Forms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gemfibrozil (Lopid)</td>
<td>600mg twice /day</td>
<td>600 mg tab</td>
</tr>
</tbody>
</table>
| Fenofibrate (Tricor) | 145 mg/day  
ClCr 30-80 ml/min: start at 48 mg/d  
ClCr <15ml/min: contraindicated | 48 mg tab  
145 mg tab |
Fibrates Safety Recommendations

- **Gemfibrozil** should not be initiated in patients on Statins because of increased risk of myopathy and rhabdomyelosis
- **Fenofibrate** may be given with a low- or moderate-intensity Statin if the benefits from ASCVD risk reduction or Triglyceride lowering (TG > 500 mg/dl) outweighs risk
- Fenofibrate is renally dosed:
  - eGFR 30-59 ml/min/1.73m²: Max. = 54mg/d
  - eGFR < 15 ml/min: Avoid
Evidence Gaps and Need for Future Research: High Priority Research Areas

- Outcomes of RCTs to evaluate statins for primary prevention of ASCVD in adults > 75 yrs
- Outcomes of RCTs to evaluate alternative treatment strategies for ASCVD risk reduction—titration to specific cholesterol goals versus fixed-dose statin therapy in high risk pt
- RCTs to determine whether submaximal statin doses, combined with non-statins, reduce ASCVD risk in statin-intolerant patients
- Evaluation of new-onset diabetes associated with statin therapy
- Outcomes of RCTs of new lipid-modifying agents to determine ASCVD event reduction benefits when added to evidence-based statin therapy
Summary

• New ACC/AHA blood cholesterol guideline arose from a review of RCTs, reviews and meta-analyses of RCT.
• Lifestyle modification remains a critical component in ASCVD risk reduction prior to and in conjunction with cholesterol-lowering therapy.
• Overwhelming evidence from RCTs demonstrated that statins provide a reduction in ASCVD events.
• Focus on Atherosclerotic Cardiovascular Disease (ASCVD) Risk Reduction: 4 Statin Benefit Groups.
• Focus on Percentage Reduction in LDL of ≥ 50% in High-Intensity Statin therapy and 30-< 50% in Moderate-Intensity Statin therapy required to achieve ASCVD risk reduction in Primary and Secondary Prevention.
• After Maximum Intensity Statin achieved, may consider addition of a Non-Statin to further reduce LDL.
• Not a comprehensive approach to the detection, evaluation and treatment of lipid disorders.
References


- Online version for blood cholesterol guidelines:
  - [http://circ.ahajournals.org/content/early/2013/11/11/01.cir.0000437738.63853.7a.citation](http://circ.ahajournals.org/content/early/2013/11/11/01.cir.0000437738.63853.7a.citation)


References


References


