Cholesterol Management Guidelines

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Cholesterol Guidelines

• Million Hearts Campaign
  ○ Improving quality of care for the ABCS
    • C = Cholesterol Management
  ○ Improving prescription of and adherence to appropriate medications for the ABCS
  ○ Focusing clinical attention on the prevention of heart attack and stroke
  ○ Improving access to effective care
  ○ Activating the public to lead a heart-healthy lifestyle

• Screening

• Treatment
Screening – Adults

U.S. Preventive Services Task Force (USPSTF), currently revising

- Latest from USPSTF 2008 for adults:
  - Screen men age 35 and older for lipid disorders (Grade A)
  - Screen men age 20-35 at increased risk for coronary heart disease (CHD) (Grade B)
  - Screen women age 45 and older at increased risk for CHD (Grade A)
  - Screen women age 20-45 at increased risk for CHD (Grade B)
  - No recommendation for or against routine screening for lipid disorders in men age 20 to 35, or in women age 20 and older who are not at increased risk for CHD. (Grade C)
Treatment – Adults

“2013 American College of Cardiology (ACC)/American Heart Association (AHA) Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular (ASCVD) Risk in Adults”
- *Journal of American College of Cardiology*

- Goals:
  - Prevent cardiovascular disease (CVD)
  - Improve management of those with CVD
  - Accomplish this with guidelines based on high quality evidence
  - Utilize guidance from 2011 Institute of Medicine’s report regarding developing trustworthy clinical guidelines
Treatment – Adults: Inclusion Criteria

Inclusion criteria:

- Studies January 1, 1995 to July 2013
- Randomized controlled studies (RCTs) with ASCVD outcomes
- Systematic reviews of RCTs with ASCVD outcomes
- Meta-analyses of RCTs with ASCVD outcomes
- ASCVD
  - Defined as CHD, stroke, peripheral artery disease believed to be of atherosclerotic origin
- “Clinical ASCVD”
  - Used for the secondary prevention statin RCTs
  - Defined as ACS, stable angina, history of MI, coronary or other arterial revascularization, stroke, TIA, peripheral artery disease believed to be of atherosclerotic origin
Treatment – Adults: Exclusion Criteria

Exclusion criteria:

• Observational studies
• Studies with less than 12 or 18 months (depending on which critical question was being addressed)
• Individuals with secondary causes of hyperlipidemia were excluded from the RCTs reviewed
• Individuals with triglycerides greater than 500 were an exclusion criteria for almost all of the RCTs utilized
Treatment – Adults: 3 CQs

Three Critical Questions:

1. What is the evidence for LDL-C and non-HDL-C goals for secondary prevention of ASCVD?
   - 19 RCTs
   - Panel did not find any RCTs that:
     - evaluated titration to specific LDL-C goals of less than 100 or less than 70
     - compared two LDL-C treatment targets
     - reported on treatment of non-HDL-C levels
Treatment – Adults: 3 CQs

Three Critical Questions:

2. What is the evidence for LDL-C and non-HDL-C goals for primary prevention of ASCVD?
   • 6 RCTs
   • Panel did not find any RCTs that:
     o evaluated titration to specific LDL-C goals of less than 100 or less than 70
     o compared two LDL-C treatment targets
     o reported on treatment of non-HDL-C levels
Treatment – Adults: 3 CQs

Three Critical Questions:

3. Efficacy and safety of cholesterol lowering drugs
   • Identify groups of patients who will benefit from pharmacological treatment
   • Define pharmacological treatments for which there is the best evidence of net benefit
   • Provide guidance on the appropriate intensity of pharmacological treatment to lower LDL-C
Treatment – Adults: Recommendations

• First and foremost this is a guideline
• This will likely apply to the majority of patients
• It is not meant to replace clinical judgment in the setting of other clinical circumstances in a particular patient
Treatment – Adults: Recommendations

• “LIFESTYLE is the foundation for ASCVD Risk Reduction efforts!”

• Lifestyle Management Work Group Guideline
  - Heart-healthy diet (Grade A, COR I, LOE A)
    • DASH, AHA, USDA food pattern
    • Reduce percentage of calories from trans and saturated fats
  - Regular exercise habits (Grade B, COR IIa, LOE A)
    • Moderate to vigorous
    • 40 minutes, 3 to 4 times per week
  - Avoid tobacco products
  - Maintain healthy weight
Treatment – Adults: Recommendations

Four Major Statin Benefit Groups:

1. Individuals with clinical ASCVD (for secondary prevention)
2. Primary elevations of LDL-C greater than or equal to 190mg/dL
3. Diabetes, aged 40 to 75 years, with LDL-C 70-189 mg/dL and without clinical ASCVD
4. No clinical ASCVD, no DM but with LDL-C 70 to 189 mg/dL AND estimated 10-year ASCVD risk of greater than 7.5%
Treatment – Adults: Recommendations

First Major Statin Benefit Groups:

Individuals with clinical ASCVD:

- Moderate-intensity statin for whom high-intensity statin would otherwise be used but is contraindicated or have characteristics predisposing to statin-associated adverse events (Grade A = strong, COR I, LOE A)
- High-intensity statin as first line for men and women younger than 75 years old unless contraindicated (Grade A = strong, COR I, LOE A)
- Evaluate risks/benefits and patient preference when starting moderate to high-intensity statin for individuals 75 years and older. Reasonable to continue statin if tolerated (Grade E, COR IIa, LOE B).
Treatment – Adults: Recommendations

Second Major Statin Benefit Groups:

Primary elevations of LDL-C greater than or equal to 190:

• Should be evaluated for secondary causes of hyperlipidemia (Grade B = moderate, COR I, LOE B)

• Age 21 and older:
  o High-intensity statin unless contraindicated (Grade B = moderate, COR I, LOE B)
  o If unable to tolerate high intensity, use maximum tolerated statin intensity (Grade B = moderate, COR I, LOE B)
  o Reasonable to intensify statin therapy to achieve at least a 50% LDL-C reduction (Grade E = expert, COR IIa, LOE B)
  o After maximum statin intensity achieved, reasonable to add non-statin drug to further lower LDL-C after evaluating risk/benefits and patient preference (E, IIb, LOE C)
Treatment – Adults: Recommendations

Third Major Statin Benefit Groups:

Diabetes aged 40 to 75 years with LDL-C 70-189 mg/dL and without clinical ASCVD:

• Initiate or continue moderate-intensity statin therapy (Grade A, COR I, LOE A)
• If ASCVD risk score for an event in 10 years is greater than or equal to 7.5%, it is reasonable to treat with high-intensity statin, unless contraindicated (Grade E, COR IIa, LOE B)
• If age less than 40 or greater than 75, it is reasonable to evaluate risks/benefits and patient preference when deciding to initiate, continue, or intensify statin therapy (Grade E, COR IIa, LOE C)
Treatment – Adults: Recommendations

Fourth Major Statin Benefit Groups:
Age 40 to 75, with no clinical ASCVD, no DM but with LDL-C 70 to 189 mg/dL AND estimated 10-year ASCVD risk of greater than 7.5%:

- Use the ASCVD risk calculator to guide initiation of statin therapy for primary prevention of ASCVD (Grade E, COR I, LOE B)
- If 10-year ASCVD risk is greater than or equal to 7.5%, treat with moderate to high-intensity statin therapy (Grade A, COR I, LOE A)
- If 10-year ASCVD risk is between 5 to 7.5%, it is reasonable to treat with a moderate intensity statin (Grade C, COR IIa, LOE B)
Treatment – Adults: Recommendations

Fourth Major Statin Benefit Groups:
No clinical ASCVD, no DM but with LDL-C 70 to 189 mg/dL AND estimated 10-year ASCVD risk of greater than 75%:

• Reasonable for clinician and patient to discuss risks/benefits and preference for treatment with statin (Grade E, COR IIa, LOE C)

• If not in an identified statin benefit group, or for whom a risk-based treatment is uncertain after using the ASCVD risk calculator, additional factors can be utilized to decide. Then discuss risks/benefits and patient preference. (Grade E, COR IIb, LOE C)
Treatment – Adults: Recommendations

• The panel makes no recommendations for or against specific LDL-C or non HDL-C targets for the primary or secondary prevention of ASCVD

• The panel makes no recommendation regarding the initiation or discontinuation of statins in patients with NYHA class II-IV ischemic systolic heart failure or in those requiring maintenance hemodialysis
Treatment – Adults: Recommendations

High-Intensity Statin Therapy

• Daily dose lowers LDL-C on average, by approximately ≥50%
• Atorvastatin 80 mg – only reduce titrate to 40 if 80 is not tolerated
• Rosuvastatin 20 (40) mg
Treatment – Adults: Recommendations

Moderate-Intensity Statin Therapy

• Daily dose lowers LDL-C on average, by approximately 30% to <50%
  - 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
Treatment – Adults: Recommendations

Low-Intensity Statin Therapy

- Daily dose lowers LDL-C on average, by <30%
  - Simvastatin 10 mg
  - Pravastatin 10–20 mg
  - Lovastatin 20 mg
  - Fluvastatin 20–40 mg
  - Pitavastatin 1 mg
Treatment – Adults: ASCVD Risk Calculator

Based on Pooled Cohort Risk Assessment Equations

- Estimate 10-year ASCVD risk defined as
  - First occurrence of non fatal and fatal MI
  - First occurrence of non fatal and fatal stroke
- Used to determine candidates for statin therapy
  - Treat if 10-year risk for event is >7.5%

Utilizes

- Gender, age, race
- HDL (optimal if 50 or higher)
- Total Cholesterol (optimal if less than 170)
- Diabetes (optimal if “no”)
- Systolic BP (optimal if 110 or less)
- Treatment for HTN (optimal if “no”)
- Tobacco use (optimal if “no”)

http://my.Americanheart.org/cvriskcalculator
http://tools.cardiosource.org/ASCVD-Risk-Estimator/
Treatment – Adults: ASCVD Risk Calculator

ASCVD Risk Estimator

*Intended for use if there is not ASCVD and the LDL-cholesterol is <190 mg/dL

**Optimal risk factors include: Total cholesterol of 170 mg/dL, HDL-cholesterol of 50 mg/dL, Systolic BP of 110 mm Hg, Not taking medications for hypertension, Not a diabetic, Not a smoker
Treatment – Adults: ASCVD Risk Calculator

Controversy regarding overestimation of risk leading to inappropriate statin treatment:

- MESA (Multi-Ethnic Study of Atherosclerosis)
  - Funded by NHLBI, 50-70 years old, no DM at baseline
  - Multiple sites (6), community-based, 10.2 year follow-up
  - 4 of the 5 risk calculators overestimated ASCVD risk
    - FRS-CHD: 53% in males, 48% in females
    - ATP 3 – FRS – CHD (2001): 154% in m, 46% in f
    - FRS – CVD (includes stroke) (2008): 37% in m, 8% in f
    - AHA/ACC ASCVD risk score (2013): 86% in m, 67% in f
  - Reynolds risk score (2007) underestimated female risk by 21%
Treatment – Adults: ASCVD Risk Calculator

Probable reasons for over-estimation:

- Selection bias
  - Those who participate in these studies are often healthier
- Older cohorts used
  - Significant differences over time regarding:
    - Dietary guidelines, food regulations (trans fats)
    - Environmental exposures (second-hand smoke)
    - Content of tobacco products
    - Improved quality/effectiveness of therapies
Summary

Grade A recommendations:

• First statin benefit group: Individuals with clinical ASCVD:
  o High-intensity statin as first line in men and women younger than 75 years old unless contraindicated
    (Grade A = strong, COR I, LOE A)
  o Moderate-intensity statin in whom high-intensity statin would otherwise be used but is contraindicated or have characteristics predisposing to statin-associated adverse events
    (Grade A = strong, COR I, LOE A)
Summary

Grade A recommendations:

• Third Major Statin Benefit Group: Diabetes aged 40 to 75 years with LDL-C 70-189 mg/dL and without clinical ASCVD:
  ○ Initiate or continue moderate-intensity statin therapy (Grade A, COR I, LOE A)

• Fourth Major Statin Benefit Group: Age 40 to 75, with no clinical ASCVD, no DM but with LDL-C 70 to 189 mg/dL AND estimated 10-year ASCVD risk of greater than 7.5:
  ○ If 10-year ASCVD risk is greater than or equal to 7.5%, treat with moderate to high-intensity statin therapy (Grade A, COR I, LOE A)
Bibliography