New guideline for management of blood cholesterol: Focuses on lifestyle, statin therapy for patients who most benefit

The American College of Cardiology (ACC) and the American Heart Association (AHA) recently established new standards for treating blood cholesterol.[1] These recommendations are based on a thorough and careful review of the very latest, highest quality clinical trial research. They help doctors deliver the best care possible. The guideline identifies four major groups of patients for whom cholesterol-lowering HMG-CoA reductase inhibitors, or statins, have the greatest chance of preventing stroke and heart attacks. The guideline also emphasizes the importance of adopting a heart-healthy lifestyle to prevent and control high blood cholesterol. For the first time, these guideline panels and work groups took an approach that was based almost solely on systematic reviews of the medical literature and synthesis of high-quality evidence.[2]

Highpoints of 2013 guidelines

New Pooled Cohort Equations for atherosclerotic cardiovascular disease (ASCVD) risk assessment

For the first time, a major guideline focuses on estimation of risk for both heart attacks and strokes and provides estimates applicable to non-white people. As a result, they are much better at representing overall, or global, cardiovascular disease risk, especially in women and African Americans, in whom risk for stroke increases earlier in life than does risk for heart attacks.[2]

- Stroke now included in ASCVD risk assessment, in addition to myocardial infarction (MI)
- Separate equations for nonwhite populations

Statin therapy recommended in 4 groups

The new guidelines focus appropriately on statin therapy rather than alternative unproven therapeutic agents, and recognize that more intensive treatment is superior to less intensive treatment for many patients. Furthermore, the new ACC/AHA guidelines show that for individuals in whom statin therapy is clearly indicated fall in four major primary- and secondary-prevention patient groups on the basis of randomized, controlled clinical trials showing that the benefit of treatment outweighed the risk of adverse events. The four treatment group's include[3]:

- Adults with clinical atherosclerotic cardiovascular disease
- Adults with LDL-cholesterol levels >190 mg/dL
- Adults with diabetes aged 40 to 75 years old with LDL-cholesterol levels between 70 and 189 mg/dL and without evidence of atherosclerotic cardiovascular disease
- Adults without evidence of CVD or diabetes, but who have LDL-cholesterol levels between 70 and 189 mg/dL and a 10-year risk of atherosclerotic cardiovascular disease >7.5%

The Expert Panel found extensive and consistent evidence supporting the use of statins for the prevention of ASCVD in many higher risk primary and all secondary prevention individuals without the New York Heart Association (NYHA) class II-IV heart failure and who were not receiving hemodialysis. In the RCTs reviewed, the critical factor in reducing ASCVD events were achieved through initiation of:

- Moderate intensity therapy such as 10 mg, pravastatin 40 mg, or simvastatin 20 mg to 40 mg lowers LDL–C by approximately 30% to <50%
- High-intensity statin therapy such as rosuvastatin 20 to 40 mg or atorvastatin 80 mg lowers LDL–C by approximately ≥51%[1]

Received: NA; Revised: NA; Accepted: NA
Disclosures: This article has not received any funding and has no vested commercial interest
Acknowledgements: None

Statin therapy reduces ASCVD events across the spectrum of baseline LDL-C levels >70 mg/dL. In addition, the relative reduction in ASCVD risk is consistent for primary and secondary prevention and for various patient subgroups. Therefore, statin therapy is recommended for individuals at increased ASCVD risk who are most likely to experience a net benefit in terms of the potential for ASCVD risk reduction and the potential for adverse effects.[1]

Use of pooled cohort equations for estimating the 10-year risk of cardiovascular disease events

The guideline offers a new approach to risk assessment. According to the Expert Panel, their recommendations represent a step forward in the prevention of ASCVD. This guideline recommends using the new Pooled Cohort Risk Assessment Equations developed by the Risk Assessment Work Group to estimate the 10-year ASCVD risk (defined as first occurrence non-fatal and fatal MI, and non-fatal and fatal stroke) for the identification of candidates for statin therapy. The calculator included in the guidelines aims to gauge an individual's chances of developing atherosclerotic cardiovascular disease (ASCVD) over the next 10 years. The calculator uses nine pieces of information—sex, age, race, total cholesterol, HDL cholesterol, systolic blood pressure, current treatment for high blood pressure, diagnosis of diabetes, smoking habit—to do this. Guideline recommends:

- Initiation of moderate or intensive statin therapy for patients who are eligible for primary CVD prevention and have a predicted 10-year "hard" ASCVD risk of ≥ 75%
- Initiation of moderate-intensity statin therapy be considered for patients with predicted 10-year "hard" ASCVD risk of 5.0% to <7.5%[1]

Central role of statin therapy in primary prevention

The ACC/AHA guidelines recommend initiation of statin therapy in primary prevention patients with a predicted 10-year risk of greater than or equal to 7.5%, and consideration of statin therapy in patients with 10-year risks of between 5% and 7.5%. This was on the basis of six major primary prevention trials, which included more than 55000 men and women. These trials showed statins to be effective in primary prevention for the reduction of myocardial infarction and stroke among those with raised LDL cholesterol (WOSCOPS, MEGA), reduced HDL cholesterol (AFCAPS/TexCAPS), raised concentrations of C-reactive protein (JUPITER), diabetes (CARDS), or hypertension (ASCOT-LLA).[3]

Statin treatment: Recommendations

Lowering LDL-C and non-HDL-C are important target for pharmacotherapy and statins are the first-choice agents for both. Statins are also effective in halting the progression and even reversing coronary atherosclerosis, either alone or in combination. The panel makes no recommendations for or against specific LDL-C or non-HDL-C targets for the primary or secondary prevention of ASCVD.

Primary prevention in individual's ≥21 years of age with LDL-C ≥190 mg/dL:

- Use high-intensity statin therapy unless contraindicated.
- For individuals unable to tolerate high-intensity statin therapy, use the maximum tolerated statin intensity.
- After the maximum intensity of statin therapy has been achieved, addition of a non-statin drug may be considered to further lower LDL-C. Evaluate the potential for ASCVD risk reduction benefits, adverse effects, drug-drug interactions, and consider patient preferences.

Prevention in individuals with diabetes mellitus and LDL-C 70–189 mg/dL:

- Moderate-intensity statin therapy should be initiated or continued for adults 40 to 75 years of age with diabetes mellitus.
- High-intensity statin therapy is reasonable for adults 40 to 75 years of age with diabetes mellitus with a ≥7.5% estimated 10-year ASCVD risk unless contraindicated.

Prevention in individuals without diabetes mellitus and with LDL-C 70–189 mg/dL:

- Offer treatment with a moderate intensity statin to adults 40–75 years of age, with LDL-C 70 to 189 mg/dL, without clinical ASCVD* or diabetes and an estimated 10-year ASCVD risk of 5% to <7.5%.[1]

Percentage reductions in LDL-C for a specific statin and dose were calculated for the RCTs included in individual meta-analyses conducted by the Cholesterol Treatment Trialists (CTT) in 2010 (20) in which statin therapy reduced ASCVD events as given in Table 1.

The recent ACC/AHA cholesterol guidelines take several major steps forward that will simplify and improve care for higher risk patients, including those with diabetes. However, new guidelines are not intended to provide a

Table 1: High-, Moderate- and Low-intensity statin therapy (Adapted from the ACC Guideline)[1]

High-intensity statin therapy	Moderate-intensity statin therapy	Low-intensity statin therapy
Daily dose lowers LDL-C on average, by approximately ≥50%	Daily dose lowers LDL-C on average, by approximately 30% to <50%	Daily dose lowers LDL-C on average, by <30%
Atorvastatin 40–80 mg Rosuvastatin 20–40 mg	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 Pitavastatin 2–4 mg	Simvastatin 10 mg Pravastatin 10–20 mg Lovastatin 20 mg Fluvastatin 20–40 mg Pitavastatin 1 mg

comprehensive approach to managing lipids. Let's hope that future randomized trials will examine the use of non-HDL cholesterol in decision-making, the role for treating high triglycerides, and treating markers such as apolipoprotein B or LDL particles and incorporated them in the future guidelines.

References

1. Stone NJ, Robinson J, Lichtenstein AH, Bairey Merz CN, Lloyd-Jones DM, Blum CB, et al. 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. J Am Coll Cardiol. 2013 Nov 7;pii: S0735–1097(13):06028–2.
2. Lloyd-Jones DM, Goff D, Stone NJ. Statins, risk assessment, and the new American prevention guidelines. Lancet. 2014 Feb 15;383(9917):600–2.
3. Ridker PM, Cook NR. Statins: new American guidelines for prevention of cardiovascular disease. Lancet. 2013 Nov 30;382(9907):1762–5.