MAKING SENSE OF THE NEW STATIN GUIDELINES

They are more than just lowering your cholesterol!
No Disclosures

Margaret (Peg) O’Donnell
DNPs, FNP, ANP B-C, FAANP
Senior Nurse Practitioner
South Nassau Communities Hospital
The History of Statin Therapy: When and Why Did They Become So Important?

- Cholesterol is essential for the functioning of all human organs.

- It is, however, a contributing cause of coronary heart disease and cerebral vascular disease. This is known after nearly a century of investigation.

- Cholesterol was first isolated from gallstones in 1784, and it has fascinated scientists ever since. How and why could a normal product of liver metabolism cause so much trouble? Answering this question has been of such concern, that thirteen Nobel Prizes have been awarded to scientists who devoted major parts of their careers to cholesterol research.

- In response to the established relationship between cholesterol and CAD/CVD, the pharmaceutical industry has been quite successfully developed a remarkably effective class of drugs—the "statins, which lower cholesterol levels in blood and reduce the frequency of CAD/CVA

3-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitor (statin)
1997: DO STATINS HELP WITH MORE THAN JUST LIPIDS?

• Studies provided strong evidence that statins could be considered as therapeutic agents in acute life-threatening disorders independently of their cholesterol lowering effects, even in the setting of normo-cholesterolemia.

• The statins can now be considered as “endogenous Nitrous Oxide Donors”.

• There is an abundant literature demonstrating that physiological levels of NO inhibits the pathophysiology of ischemia–re- perfusion, shock states and hypercholesterolemia.

• A.M. Lefer et al. / Cardiovascular Research 49 (2001) 281–287
STATINS: NON-LIPID CARDIO/CEREBRAL VASCULAR PROTECTION

• **Antioxidant:**

• Helps “Gobble-up” dangerous free radicals that are released from tissue injury

**Antithrombotic:**

- decreases levels of PAL-1, which is known to cause thrombosis  
  b) inhibits platelet aggregation  
  c) strengthens fibrous cap

• **Vascular Protective Effects:** increasing Nitrous Oxide has a vasodilatory effect  
  b) inhibits endothelial/leukocyte interactions, encourages endothelial normalization  
  c) Increases cell membrane transport of Nitrous Oxide

**Angiogenic:** encourages collateral vessel formation, which begins in response to ischemic insults

A.M. Lefer et al. / Cardiovascular Research 49 (2001) 281–287
Questions:

Knowing this information about the non-lipid reducing qualities of statins:

1. Should CVA/TIA be treated with statins whether or not there is concurring ASHD?

2. Should there be evidence of atherosclerosis?

3. Should hemorrhagic CVA/TIA be treated with statins?

- Stroke. 2004; 35: 102 doi: 10.1161/01.STR.0000122762.96972.DD
SPARCL was designed to examine whether statin treatment prevents secondary stroke among individuals with recent symptomatic cerebrovascular disease.

Prospectively, 4731 individuals with mild CVA (67% ischemic CVA, 2% hemorrhagic, and 31% TIA LDL cholesterol levels between 100 to 190 mg/dL, and no known history of coronary artery disease, were randomized between 1 to 6 months after the index event to atorvastatin 80 mg daily versus placebo. During the trial, LDL cholesterol levels dropped by 45% in the atorvastatin group (132.7 to 72.9 mg/dL) and only 4% in the placebo group (133.7 to 128.5 mg/dL).

After 5 years, the incidence of fatal or nonfatal stroke was lower in the atorvastatin arm than in the placebo arm (There was also a significant reduction in major coronary events in favor of atorvastatin (3.4% versus 5.15). 11.2% versus 13.1%, adjusted hazard ratio 0.84, 0.71 to 0.99; P=0.03, unadjusted P=0.05.

Atorvastatin had no effect on mortality (1.00, 0.82 to 1.21).

There was a higher incidence of hemorrhagic strokes in the atorvastatin treatment arm compared with the placebo group (2.3% versus 1.4%, hazard ratio 1.66, 1.08 to 2.55). The high-dose statin therapy was well tolerated, with a mildly increased rate of elevated liver enzymes (2.2% versus 0.5%, P<0.001), no cases of liver failure, and no excess cases of myopathy.

• ClinicalTrials.gov number, NCT00147602.)

SPARCL conclusion:

• In patients with recent stroke or TIA and without known coronary heart disease, 80 mg of atorvastatin per day reduced the overall incidence of strokes and of cardiovascular events, despite a small increase in the incidence of hemorrhagic stroke.

• In patients with a recent stroke or TIA, treatment with 80 mg of atorvastatin per day decreased the risk of stroke, major coronary events, and revascularization procedures. These results support the initiation of atorvastatin treatment soon after a stroke or TIA.

• ClinicalTrials.gov number, NCT00147602.

After this groundbreaking 2006 SPARCL report, 2008, the NHLBI (National Heart, Lung, and Blood Institute, a division of National Institutes of Health), initiated these guidelines by sponsoring rigorous systematic review.

By 2011 the NHLBI Advisory Council recommended that the NHLBI focus specifically on reviewing the highest-quality evidence and partner with other organizations to develop recommendations.

June 2013 the NHLBI joined forces ACC (American College of Cardiology and AHA (American Heart Association), to work with other organizations to complete and publish the 4 guidelines noted above and make them available to the widest possible constituency.

Recognizing that the Expert Panels/Work Groups did not consider evidence beyond 2011 the ACC, AHA, and collaborating societies plan to begin updating these guidelines starting in 2014.

2013: THE FOUR STATIN BENEFIT GROUPS

- Individuals with clinical ASCVD
- Individuals with primary elevations of LDL-C ≥190 mg/dL
- Individuals 40 to 75 years of age with diabetes and LDL-C 70 to 189 mg/dL without clinical ASCVD
- Individuals without clinical ASCVD or diabetes who are 40 to 75 years of age and have LDL-C 70 to 189 mg/dL and an estimated 10-year ASCVD risk of ≥7.5%. This requires a clinician-patient discussion.

2013 ACC/AHA GUIDELINE ON THE TREATMENT OF GUIDELINES

PRIMARY PREVENTION

Heart-healthy lifestyle habits are the foundation of ASCVD prevention
(See 2013 AHA/ACC Lifestyle Management Guideline)

Clinical ASCVD

Age ≥21 y and a candidate for statin therapy

Yes

No

LDL-C ≥190
mg/dL

Yes

No

Diabetes

LDL-C 70-189 mg/dL
Age 40-75 y

Yes

No

Yes

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

Age >75 y OR if not candidate for high-intensity statin
Moderate-intensity statin

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

Estimated 10-y ASCVD risk ≥7.5%†
Moderate-intensity statin

High-intensity statin

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%

Regularly monitor adherence to lifestyle and drug therapy with lipid and safety assessments (See Fig 5)

Primary prevention
(No diabetes, LDL-C 70 to 189 mg/dL, and not receiving statin therapy)

Estimate 10-y ASCVD risk every 4-6 y using Pooled Cohort Equations†

<5%
10-y ASCVD risk‡

Age <40 or >75 y and LDL-C <190 mg/dL‡

≥7.5%
10-y ASCVD risk (Moderate- or high-intensity statin)

5% to <7.5%
10-y ASCVD risk (Moderate-intensity statin)

In selected individuals, additional factors may be considered to inform treatment decision making§

Clinician-Patient Discussion
Prior to initiating statin therapy, discuss:
1. Potential for ASCVD risk-reduction benefits ||
2. Potential for adverse effects and drug–drug interactions††
3. Heart-healthy lifestyle
4. Management of other risk factors
5. Patient preferences
6. If decision is unclear, consider primary LDL-C ≥160 mg/dL, family history of premature ASCVD, lifetime ASCVD risk, abnormal CAC score or ABI, or hs-CRP ≥2 mg/L§

Emphasize adherence to lifestyle
Manage other risk factors
Monitor adherence

No to statin

Yes to statin

Encourage adherence to lifestyle
Initiate statin at appropriate intensity
Manage other risk factors
Monitor adherence* (See Fig 5)
"I found 1837 web sites about 'alternative medicine' but none of them recommend pizza or chocolate for lowering our cholesterol."
ACUTE CARE GUIDELINES

• All CVA/TIA/symptomatic CVD patients = Lipid profile within 48 hours Lipid

• Unless drawn in the past 30 days

• Target goal LDL < 100

• Target goal with multiple risk factors < 70 (DM)

• LDL < 100 on statin therapy + increase the statin

• CVA of atherosclerotic origin with LDL > 100 = intensive statin therapy with target goal LDL < 100
• Adding a drug called ezetimibe to statin therapy significantly reduced the risk of heart attack and stroke in high-risk patients with established heart disease, according to a long-awaited, large, randomized and controlled trial presented at the American Heart Association’s Scientific Sessions 2014.

• Circulation. 2014; 129: e28-e292 doi: 10.1161/01.cir.0000441139.02102.80
From 2001 to 2011, the relative rate of stroke death fell by 35.1% and the actual number of stroke deaths declined by 21.2%!

Each year, however, ≈79,5000 people continue to experience a new or recurrent stroke (ischemic or hemorrhagic).

610,000 of these are first events 185,000 are recurrent stroke events.

In 2011, stroke caused ≈1 of every 20 deaths in the United States. On average, every 40 seconds, someone in the United States has a stroke, and someone dies of one approximately every 4 minutes.

Stroke kills over 128,000 people each year and is a leading cause of serious, long-term disability. The outcome depends in large part on how and when the patient is treated

HOW CAN WE HELP THESE NUMBERS?

Circulation.2015; 131: e29-e322 doi: 10.1161/CIR.0000000000000152
• Web based program which has demonstrated improved adherence to evidence-based care of patients hospitalized with stroke.

• **EXAMPLE:** For every eight patients treated with intravenous thrombolysis, one additional patient returns to living a normal life. And the sooner, the better, since reducing the time between emergency department arrival and IV thrombolysis improves each patient’s odds of a good outcome.

• The American Stroke Association is ready to help you make that happen through our new campaign, Target: Stroke.

• **Target:** Stroke provides health care professionals with **10 Best Practice Strategies** for achieving door-to-needle (DTN) times of 60 minutes or less for ischemic stroke patients. The strategies include protocols, clinical decision support, order sets, guidelines, data measurement tools, feedback processes and other resources for improving and reporting DTN times.

• To learn more about Target: Stroke go to [www.strokeassociation.org/targetstroke](http://www.strokeassociation.org/targetstroke).
• **STK -1**: Ischemic and hemorrhagic stroke patients who received VTE prophylaxis or have documentation why no VTE prophylaxis was given the day of or the day after hospital admission.

• **STK-2**: Ischemic stroke patients prescribed antithrombotic therapy at hospital discharge.

• **STK-3**: Ischemic stroke patients with atrial fibrillation/flutter who are prescribed anticoagulant therapy at discharge.

• **STK-4**: Acute ischemic stroke patients who arrive at this hospital within 2 hours of time last known well and for whom IV t-PA was initiated at this hospital within 3 hours of time last known well.

• **STK-5**: Ischemic stroke patients administered antithrombotic therapy by the end of hospital day 2.

• **STK-6**: Ischemic stroke patients with LDL greater than or equal to 100 mg/dL, or LDL not measured, or who were on a lipid-lowering medication prior to hospital arrival are prescribed statin medication at hospital discharge.

• **STK-8**: Ischemic or hemorrhagic stroke patients or their caregivers who were given educational materials during the hospital stay addressing all of the following: activation of emergency medical system, need for follow-up after discharge, medications prescribed at discharge.

  - www.strokeassociation.org/targetstroke. April 2014 fact sheet
QUESTIONS?
• http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3108295/

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