Cholesterol Management 2017

Roy Gandolfi, MD
Goals

- Interpreting cholesterol guidelines
- Cholesterol treatment in diabetics
- Statin use and side effects therapy
- Reporting:
  - Comparison data among physicians
  - Compliance of cholesterol treatment
Atherosclerotic cardiovascular disease (ASCVD) is defined as:

• an acute coronary syndrome
• history of myocardial infarction
• stable or unstable angina
• coronary or other arterial revascularization
• stroke, transient ischemic attack
• Or peripheral arterial disease (PAD)
Interpreting cholesterol guidelines
Guidelines for Cholesterol Treatment

ACC/AHA
ACCE
US Preventive Task Force
European
Canadian
British/NICE
Secondary Prevention ACC/AHH

All patients with ASCVD
All patients 40-75 with diabetes
LDL greater or equal to 190 LDL
Known cardiovascular disease and similar risk

<table>
<thead>
<tr>
<th>Treatment of patients with a history of any of the following is considered &quot;secondary prevention&quot; in UpToDate:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary heart disease</td>
</tr>
<tr>
<td>Myocardial infarction</td>
</tr>
<tr>
<td>Angina</td>
</tr>
<tr>
<td>Coronary revascularization</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
</tr>
<tr>
<td>Stroke</td>
</tr>
<tr>
<td>Transient ischemic attack</td>
</tr>
<tr>
<td>Peripheral arterial disease</td>
</tr>
<tr>
<td>Multiple risk factors that confer a 10-year risk of CVD &gt;20%</td>
</tr>
<tr>
<td>Chronic kidney disease with estimated GFR &lt;45 mL/min per 1.73 m²*</td>
</tr>
</tbody>
</table>

CVD: cardiovascular disease; GFR: glomerular filtration rate.

* Statin doses may require adjustment in patients with chronic kidney disease.
2013 ACC/AHA guideline

Key Points for Practice
The guideline emphasizes that lifestyle modification remains a critical component of ASCVD reduction.

Four groups most likely to benefit from statin therapy are identified:
1. Patients with any form of clinical ASCVD
2. Patients with primary LDL-C levels of 190 mg per dL or greater
3. Patients with diabetes mellitus, 40 to 75 years of age, with LDL-C levels of 70 to 189 mg per dL
4. Patients without diabetes, 40 to 75 years of age, with an estimated 10-year ASCVD risk ≥ 7.5%

Risk assessment for 10-year and lifetime risk is recommended using an updated ASCVD risk calculator: http://my.americanheart.org/cvriskcalculator
Principles of ACC/AHA Guidelines

1. Lack of evidence to support use of specific LDL-C or non–high-density lipoprotein cholesterol (HDL-C) target levels

2. Use of the maximum tolerated statin intensity in persons who will benefit reduces ASCVD events

3. Lack of RCT which demonstrated titration of dose improves ASCVD outcomes.

4. Use of LDL-C targets could lead to undertreating with evidence–based statin therapy or over-treating with non-statin drugs that have not been shown to reduce ASCVD events in RCTs
2016 Addendum to ACC/AHA guideline

Consider adding other agents such as ezetimibe who have less than 50% LDL-C reduction for secondary prevention or PCSK9 inhibitors.
RISK ASSESSMENT

Heart-healthy lifestyle

Screen adults age ≥20 every 5 years

Clinical ASCVD?

yes → Age ≤75?

yes → High-intensity statin

no → LDL-C ≥ 190 mg/dL?

yes → High-intensity statin

no → Moderate-intensity statin

Diabetes and age 40–75 and LDL 70–189

yes → Estimated 10-year ASCVD risk ≥7.5%?

yes → High-Intensity statin

no → Moderate-intensity statin

Age 40–75?

yes → Consider additional factors

no → Consider moderate-intensity statin

Estimated 10-year ASCVD risk every 5 years using Pooled Cohort Equations:

tools.cardiosource.org/ASCVD-Risk-Estimator

10-year risk:

<5% →Consider moderate-intensity statin

5%−7.5% → Consider high- or moderate-intensity statin

≥7.5% → Consider high-intensity statin

Shared decision on statin use

no to statin

→ Emphasize lifestyle and monitor

→ Manage other risk factors

yes to statin

→ Emphasize lifestyle

→ Initiate statin

→ Monitor adherence

→ Manage other risk factors

For recommendations based on lifetime risk, including for patients who do not meet the above criteria, refer to the CPM.
Benefits and Concerns of AHA guideline

1. Pooled risk calculator appears to falsely elevate the 10 year risk
2. Lack of data in over 75 years old
3. Influenced significantly on age
4. Absolute risk reduction in ASCVD events associated with statin therapy can be estimated by multiplying the 10 year ASCVD risk by the anticipated relative risk reduction based on the intensity of the statin (30% for moderate intensity and 45% for high intensity)
## ACCE guideline for lipid therapy

**Table 6**

**Coronary Artery Disease Risk Categories and Low-Density Lipoprotein Treatment Goals**

(20 [EL 4], 22 [EL 4], 23 [EL 4])

<table>
<thead>
<tr>
<th>Risk category</th>
<th>Risk factors (^{a}/10)-year risk (^{b})</th>
<th>LDL-C treatment goal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very high risk</td>
<td>Established or recent hospitalization for coronary, carotid, and peripheral vascular disease or diabetes plus 1 or more additional risk factor(s)</td>
<td>&lt;70 mg/dL</td>
</tr>
<tr>
<td>High risk</td>
<td>(\geq 2) risk factors and 10-year risk &gt;20% or CHD risk equivalents (^{c}), including diabetes with no other risk factors</td>
<td>&lt;100 mg/dL</td>
</tr>
<tr>
<td>Moderately high risk</td>
<td>(\geq 2) risk factors and 10-year risk 10%-20%</td>
<td>&lt;130 mg/dL</td>
</tr>
<tr>
<td>Moderate risk</td>
<td>(\geq 2) risk factors and 10-year risk &lt;10%</td>
<td>&lt;130 mg/dL</td>
</tr>
<tr>
<td>Low risk</td>
<td>(\leq 1) risk factor</td>
<td>&lt;160 mg/dL</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Risk group</th>
<th>Framingham Global Risk (10-year absolute CAD risk)</th>
<th>Clinical examples</th>
</tr>
</thead>
</table>
| High       | >20%                                               | ▪ Established coronary artery disease  
▪ Cerebrovascular disease  
▪ Peripheral arterial disease  
▪ Abdominal aortic aneurysm  
▪ Diabetes mellitus  
▪ Chronic kidney disease  
▪ Subclinical coronary artery disease  
▪ Metabolic syndrome  
▪ Multiple risk factors<sup>a</sup>  
▪ Markedly elevated levels of a single risk factor<sup>b</sup>  
▪ First-degree relative(s) with early-onset coronary artery disease |
| Intermediate| 10%-20%                                           | ▪ May include women with multiple risk factors, metabolic syndrome, or 1 or no risk factors |
| Lower      | <10%                                               | ▪ Optimal levels of risk factors and heart-healthy lifestyle |
| Optimal    | <10%                                               | |

<sup>a</sup> Patients with multiple risk factors can fall into any of the 3 categories by Framingham scoring.

<sup>b</sup> Most women with a single, severe risk factor will have a 10-year risk <10%.
US Preventive Services task Force (USPSTF) Guidelines: Primary Prevention in Cardiovascular disease (CVD)

Low-moderate dose statin treatment for adults 40-75 without CVD who have 1 or more CVD risk factors and calculated 10 CVD risk 10% or greater.

Risk factors: dyslipidemia, diabetes, hypertension or smoking

Use the Pooled Cohort Equations from the ACC/AHA

Possible statin use of 7.5-10% risk

Avoid use 76 and older

Risk reduction by statins in based on absolute baseline risk of future ASCVD event
Cholesterol Treatment for Patients with Diabetes
ACCE guideline for lipids in Diabetes

Additional risk factors

A. Smoking
B. Hypertension
C. HDL <40
D. Family history of coronary heart disease
E. >45 men and >55 women

• **High risk** <40 and < 1 or no major risk factors
• **Very high risk** > 2 or more or
• **Extreme** – Known ASCVD with diabetes
  *Adjust intensity of therapy based on the level of risk
## Recommendations for Statin Treatment in Diabetes (ADA)

<table>
<thead>
<tr>
<th>Age</th>
<th>Risk factors</th>
<th>Recommended statin intensity*</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40 years</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>ASCVD risk factor(s)**</td>
<td>Moderate or high</td>
</tr>
<tr>
<td></td>
<td>ASCVD</td>
<td>High</td>
</tr>
<tr>
<td>40–75 years</td>
<td>None</td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td>ASCVD risk factors</td>
<td>High</td>
</tr>
<tr>
<td></td>
<td>ASCVD</td>
<td>High</td>
</tr>
<tr>
<td></td>
<td>ACS and LDL cholesterol $&gt;$50 mg/dL (1.3 mmol/L)</td>
<td>Moderate plus ezetimibe</td>
</tr>
<tr>
<td></td>
<td>in patients who cannot tolerate high-dose statins</td>
<td></td>
</tr>
<tr>
<td>&gt;75 years</td>
<td>None</td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td>ASCVD risk factors</td>
<td>Moderate or high</td>
</tr>
<tr>
<td></td>
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<tr>
<td></td>
<td>in patients who cannot tolerate high-dose statins</td>
<td></td>
</tr>
</tbody>
</table>

*In addition to lifestyle therapy.

**ASCVD risk factors include LDL cholesterol $\geq$100 mg/dL (2.6 mmol/L), high blood pressure, smoking, overweight and obesity, and family history of premature ASCVD.

Diabetes Care, Vol 39, supplement 1, p 71
Diabetes: Secondary or Primary Prevention

ACC/AHA guideline (Care Process Model/STARS goals) include and type of diabetes as Secondary prevention and statin use is mandatory.

Concerns are risk will vary depending on age, sex other CV risk factors, duration of DM and wither type 1 or 2 DM.

Similar risk of events to those with CHD if DM present for 10 years.

Some recommend the following: If a patient-specific risk calculator cannot be accessed, we suggest considering the following patients with DM to have a similar risk those with known CVD:

- Men over age 40 with type 2 DM and any other CHD risk factor, or over age 50 with or without other CHD risk factors
- Women over age 45 with type 2 DM and any other CHD risk factor, or over age 55 with or without other CHD risk factors
- Men or women of any age who have had DM (type 1 or type 2) for more than 20 years if they have another risk factor or more than 25 years without another risk factor
Statins & Diabetes: Key Takeaways

Statin use is mandatory

Consider the following patients with DM to have a similar risk those with known CVD:

- Men over age 40 with type 2 DM and any other CHD risk factor, or over age 50 with or without other CHD risk factors
- Women over age 45 with type 2 DM and any other CHD risk factor, or over age 55 with or without other CHD risk factors
- Men or women of any age who have had DM (type 1 or type 2) for more than 20 years if they have another risk factor or more than 25 years without another risk factor
Statin use and side effects therapy
Primary Prevention Benefit with Statins

0.4% absolute risk reduction for all cause mortality and 0.43% of cardiovascular mortality

244 patients treated for 5 years to prevent one death

Absolute risk reduction will be proportional to the 20-30% relative risk reduction with statin in primary prevention

Shared decision making is key to appropriate care
Primary Prevention in Older Adults

ACC/AHA Pooled Cohort Equations will always exceed 7.5%.
No adjustment for quality adjusted life expectancy
Data limited in over 75 years of age.
PROSPER trial: pravastatin in 70-82 year old patients
• Showed no benefit on CVD outcomes.
JUPITER: Justification of Use of Statins in Prevention: An Intervention Trial Evaluating Rosuvastatin)( high CRP)
• Showed primary protection over 70 years of age.
HOPE-3: Heart Outcomes Prevention Evaluation
• Showed use pravastatin was protective.

Again - Shared decision making is key for primary prevention in the elderly as well
Compliance is key

Patients who take less than 80% of their statin dosed have a 45% relative increase in total mortality compared with more adherent patients.

Greater mortality than that observed with poor adherence to other cardiac drugs including antihypertensive and B-adrenergic blocking agents.

Why is there such a problem with compliance?
Reported Side Effects of Statins: Myths and Data

Diabetes
Hemorrhagic stroke
Cognitive decline
Tendon rupture
Hepatic injury
Muscle related symptoms
Statins and Muscle Conditions

Most frequently reported side effect of statins

1. Myalgias: considerable debate with statins caused pain, cramps or weakness with little or no increase in CK level.
   a) Limited evidence in RCT that this occurred. Studies did not specifically ask about muscle pain and under reported this side effect
   b) Most clinicians convinced symptoms are attributed to statin use.-10% incidence
   c) STOMP (Effect of statins on Skeletal Muscle Performance). 9.4% with statins vs 4.6% placebo. P value 0.54, but 94.6 % probability statins were the cause

2. Myopathy with CPK rise, may be related to SLCO1B1 gene which regulates hepatic stain uptake, reduced uptake allows greater concentration in skeletal muscle.

3. Rhabdomyolysis

4. Necrotizing myopathy with antibodies against HMGCoA reductuase. Persistent myopathy, similar to polymyositis. Biopsy of muscle positive for antibody.
Muscle Event Terminology

- **Myalgia** – A symptom of muscle-discomfort, including muscle aches, soreness, stiffness, tenderness, or cramps with or soon after exercise, with a normal creatine kinase (CK) level. Myalgia symptoms can be described as similar to what would be experienced with a viral syndrome such as influenza.
- **Myopathy** – Muscle weakness (not due to pain), with or without an elevation in CK level.
- **Myositis** – Muscle inflammation.
- **Myonecrosis** – Elevation in muscle enzymes compared with either baseline CK levels (while not on statin therapy) or the upper limit of normal that has been adjusted for age, race, and sex:
  - Mild – Threefold to 10-fold elevation in CK.
  - Moderate – 10-fold to 50-fold elevation in CK.
  - Severe – 50-fold or greater elevation in CK.
- **Clinical rhabdomyolysis** – Defined by the Task Force as myonecrosis with myoglobinuria or acute renal failure (an increase in serum creatinine of least 0.5 mg/dL [44 micromol/L]).

2014 National Lipid Association Statin Muscle Safety Task Force
Coding Intolerance

G72.0 Drug-induced myopathy
G72.2 Myopathy due to other toxic agents
G72.9 Myopathy, unspecified
M62.82 Rhabdomyolysis
M79.1 Myalgia

*78.0 Statin Intolerant
*60.9 Statin Induced Myositis

Must be a “Problem” not an “Allergy”
Mitigating Muscle Pain with Statins

Assure the patient that most without CPK rise with pain will rarely cause severe muscle injury and resolve with discontinuation of the medication, usually within weeks.

Consider low dose statins such as rosuvastatin 5 mg or atorvastatin 10 mg. Lipophilic statins (simvastatin, lorvastatin, atorvastatin and fluvastatin) may have more muscle pain than hydrophilic rosuvastatin or pravastatin. Data may support trial of pravastatin or fluvastatin as second drug choices.

Add ezetimibe do enhance LDL reduction, IMPROVE-IT trial

Avoid niacin since combination therapy did not improve outcomes

Consider PCSK9 inhibitors, limited access thru SelectHealth and lacking clinical outcome data.

Limited data, Coenzyme Q10 (ubiquinione) does not limits muscle pain

Evaluate Vitamin D levels, low levels may be associated with stain myopathy
## ADA Table for High and Moderate Intensity Statin

<table>
<thead>
<tr>
<th>High-intensity statin therapy</th>
<th>Moderate-intensity statin therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lowers LDL cholesterol by ≥50%</td>
<td>Lowers LDL cholesterol by 30% to &lt;50%</td>
</tr>
<tr>
<td>Atorvastatin 40–80 mg</td>
<td>Atorvastatin 10–20 mg</td>
</tr>
<tr>
<td>Rosuvastatin 20–40 mg</td>
<td>Rosuvastatin 5–10 mg</td>
</tr>
<tr>
<td></td>
<td>Simvastatin 20–40 mg</td>
</tr>
<tr>
<td></td>
<td>Pravastatin 40–80 mg</td>
</tr>
<tr>
<td></td>
<td>Lovastatin 40 mg</td>
</tr>
<tr>
<td></td>
<td>Fluvastatin XL 80 mg</td>
</tr>
<tr>
<td></td>
<td>Pitavastatin 2–4 mg</td>
</tr>
</tbody>
</table>
Reporting-Comparison and Compliance
HEDIS Measures – Statin Compliance Therapy Measures

For Patients with ASCVD
2 rates
• Patients dispensed 1 *high or moderate* intensity statin during measurement year
• Patients who remained on high or moderate for at least 80% of the treatment period

For patients with Diabetes without ASCVD
2 rates- *also*
• Patients dispensed *any* intensity statin during measurement year
• Patients who remained on high or moderate for at least 80% of the treatment period
Cholesterol Medication Adherence
STARS Goals 2017

Cholesterol medication adherence Measure

# of member-years of enrolled beneficiaries 18 years and older with a proportion of days covered (PDC) at 80 percent or higher for statin cholesterol medication(s) during the measurement period

(numerator)

# of member-years of enrolled beneficiaries 18 years and older with at least two fills of either the same medication or medication in the drug class during the measurement period

(denominator)
Statin Use in Persons with Diabetes (SUPD)  
STARS Measure

% of patients between 40 and 75 years old who received at least two diabetes medication fills and also received a statin medication during the measurement period.
Patients excluded from Measure- STARS and HEDIS

<table>
<thead>
<tr>
<th>STARS</th>
<th>HEDIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>• None</td>
<td>• Myalgia</td>
</tr>
<tr>
<td></td>
<td>• Myositis</td>
</tr>
<tr>
<td></td>
<td>• Myopathy</td>
</tr>
<tr>
<td></td>
<td>• Rhabdomyolysis</td>
</tr>
<tr>
<td></td>
<td>• CKD-Stage 5 (ESRD)</td>
</tr>
<tr>
<td></td>
<td>• Cirrhosis</td>
</tr>
</tbody>
</table>
Diabetes Patient Statin Therapy Dashboard

This dashboard includes diabetic patients ages 40-75, and displays the percent who are meeting selected HEDIS measures related to statin therapy. For data definitions, such as descriptions of Cohorts and HEDIS Measures, see the Info Sheet tab.

Diabetes REGION

Diabetes CLINIC

Diabetes PROVIDER

Diabetes RUNCHART
Region: All Clinic: All Provider: All
## Diabetic Patient Statin Therapy List

<table>
<thead>
<tr>
<th>Provider Name</th>
<th>HEDIS Measure Compliance</th>
<th>Patient Name</th>
<th>EMPI</th>
<th>Age</th>
<th>Days on Statin Pct</th>
<th>Filled Rx</th>
<th>Most Recent Statin Order Date</th>
<th>Most Recent Statin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gandolfi, Roy J.</td>
<td>No</td>
<td></td>
<td></td>
<td></td>
<td>0%</td>
<td>No</td>
<td>Null</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td></td>
<td></td>
<td>95.17%</td>
<td>Yes</td>
<td>10/05/2016</td>
<td>PRAVASTATIN SODIUM TAB 20 MG</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>98.21%</td>
<td>Yes</td>
<td>9/23/2016</td>
<td>ATORVASTATIN CALCIUM TAB 40 MG</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>95.61%</td>
<td>Yes</td>
<td>11/15/2016</td>
<td>LOVASTATIN TAB 40 MG</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>83.61%</td>
<td>Yes</td>
<td>11/18/2016</td>
<td>SIMVASTATIN TAB 40 MG</td>
<td></td>
</tr>
</tbody>
</table>

## Cohort Selection
- **HEDIS Cohort**

## HEDIS Measure Selection
- Statin Rx Last 12 Mo

## Payer Group
- SELECTHEALTH MEDICARE ADVANTAGE