Statin Initiation Protocol

Pt ≥ 21 yo, candidate for statin

Lifestyle Modifications

Clinical ASCVD (e.g. history of or current ACS, MI, SA, UA, coronary or other arterial revascularization, stroke, TIA, or PAD presumed to be of atherosclerotic origin)

Before initiating a statin, establish baseline:
- Fasting lipid panel
- ALT
- CK (if at high-risk)
- Muscle aches/pains per patient

Age ≥ 75 yo

High-intensity statin

LDL ≥ 190 mg/dL

Yes

High-intensity statin OR Moderate-intensity statin if not a candidate for high-intensity statin

No

Diabetes LDL 70-189 mg/dL

Yes

Moderate-intensity statin OR High-intensity statin if 10 yr ASCVD Risk Score ≥ 7.5%

No

Primary Prevention No Diabetes LDL 70-189 mg/dL

Yes

10 yr ASCVD Risk Score 5% to < 7.5%

No

10 yr ASCVD Risk Score ≥ 7.5%

Moderate-intensity statin

Choosing a statin:

<table>
<thead>
<tr>
<th>Statin Intensity</th>
<th>High Intensity Statin</th>
<th>Moderate Intensity Statin</th>
<th>Low Intensity Statin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Expected LDL reduction</td>
<td>(50%)</td>
<td>(30-50%)</td>
<td>&lt; (30%)</td>
</tr>
<tr>
<td>atorvastatin 40-80 mg PO daily</td>
<td>rosvastatin 20-40 mg PO daily</td>
<td>atorvastatin 10-20 mg PO daily</td>
<td>simvastatin 10 mg PO daily</td>
</tr>
<tr>
<td>rosvastatin 20-40 mg PO daily</td>
<td>rosvastatin 5-10 mg PO daily</td>
<td>rosuvastatin 80 mg PO daily</td>
<td>pravastatin 10-20 mg PO daily</td>
</tr>
<tr>
<td>simvastatin 20-40 mg PO daily</td>
<td>pravastatin 40 mg PO daily</td>
<td>pravastatin 10-20 mg PO daily</td>
<td>pravastatin 10 mg PO daily</td>
</tr>
<tr>
<td>pravastatin 40 mg PO daily</td>
<td>simvastatin 10 mg PO daily</td>
<td>pravastatin 40 mg PO daily</td>
<td>pravastatin 20 mg PO daily</td>
</tr>
</tbody>
</table>

**Excluded from UHS Formulary

PROVE-IT Trial: In stable patients who had been hospitalized with ACS in the last 10 days, atorvastatin 80 mg compared to pravastatin 40 mg resulted in a lower risk of death from any cause or major cardiac events.

Statin Dosing

<table>
<thead>
<tr>
<th>% LDL Reduction</th>
<th>Rosuvastatin</th>
<th>Atorvastatin</th>
<th>Simvastatin</th>
<th>Pravastatin</th>
</tr>
</thead>
<tbody>
<tr>
<td>25%</td>
<td>5 mg</td>
<td>10 mg</td>
<td>10 mg</td>
<td>10 mg</td>
</tr>
<tr>
<td>30%</td>
<td>10 mg</td>
<td>20 mg</td>
<td>20 mg</td>
<td>20 mg</td>
</tr>
<tr>
<td>35%</td>
<td>15 mg</td>
<td>30 mg</td>
<td>30 mg</td>
<td>30 mg</td>
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<tr>
<td>40%</td>
<td>20 mg</td>
<td>40 mg</td>
<td>40 mg</td>
<td>40 mg</td>
</tr>
<tr>
<td>45%</td>
<td>25 mg</td>
<td>50 mg</td>
<td>50 mg</td>
<td>50 mg</td>
</tr>
<tr>
<td>50%</td>
<td>30 mg</td>
<td>60 mg</td>
<td>60 mg</td>
<td>60 mg</td>
</tr>
<tr>
<td>55%</td>
<td>35 mg</td>
<td>70 mg</td>
<td>70 mg</td>
<td>70 mg</td>
</tr>
</tbody>
</table>

Patients not included in the treatment algorithm above may still benefit from a statin. Patient-Clinician discussion should include the following key points:
- Potential for ASCVD risk-reduction benefits
- Potential for adverse effects and drug-drug interactions
- Heart-healthy lifestyle
- Management of other risk factors
- Patient preferences
- 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
- Low-intensity statin therapy may be considered for patients not in the treatment algorithm or who cannot tolerate high- or moderate-intensity statin therapy

Abbreviations:
- ACS: acute coronary syndrome
- MI: myocardial infarction
- SA: stable angina
- UA: unstable angina
- PAD: peripheral artery disease

Circulation 2014;129[suppl 2]:S1-S45

Created by: Katherine Perry, PharmD Candidate 2017
Reviewed by: Bethany Balf, PharmD, BCPS-AQ Cardiology
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### Statin Safety

#### Contraindications
- Hypersensitivity to any component

#### Drug-Drug Interactions
- Increase statin effect (increased risk of toxicity)
  - amiodarone
  - azole antifungals
  - colchicine
  - danazol
  - diltiazem
  - glyburide

- Decrease statin effect (decreased efficacy)
  - amiodipine
  - cilostazol
  - clopidogrel
  - danazol
  - diltiazem
  - glyburide
  - imatinib
  - quinine
  - vasopressin receptor antagonists
  - macrolides, ketolides
  - niacin
  - ranolazine
  - daptomycin
  - dronedarone
  - nefazodone

- Other effects
  - antacids
  - bosentan
  - carbamazepine
  - bile acid sequestrants
  - St. John's Wort

#### Adverse Drug Effects
- Diarrhea (7-14%)
- Arthralgia (9-12%)
- Nasopharyngitis (13%)
- Nausea
- Dyspepsia
- Flatulence
- Headache
- UTI
- Muscle spasm
- Diabetes mellitus
- Limb pain
- Myalgia
- Muscle pain
- Insomnia

#### Risk Factors for Adverse Effects of Statin
- Age >75 years
- History of hemorrhagic stroke
- History of previous statin intolerance or muscle disorders
- Unexplained ALT elevations ≥3 times ULN
- Patient characteristics or concomitant use of drugs affecting statin metabolism
- Multiple or serious comorbidities, including impaired renal or hepatic function
- Asian ancestry

#### Statin Monitoring/Follow-Up Protocol

**Anticipated therapeutic response achieved?**
- High intensity statin - LDL reduced by ≥50% or moderate intensity statin - LDL reduced by 30-50% or low intensity statin - LDL reduced by <30%.

**Yes**
- Reinforce lifestyle and medication adherence
- Fasting lipid panel every 3-12 months thereafter

**No**
- Assess statin tolerance
- Exclude secondary causes of hyperlipidemia
- Fasting lipid panel in 4-12 weeks

**Anticipated therapeutic response achieved?**
- High intensity statin - LDL reduced by ≥50% or moderate intensity statin - LDL reduced by 30-50% or low intensity statin - LDL reduced by <30%.

**Yes**
- Reinforce lifestyle and medication adherence
- Fasting lipid panel every 3-12 months thereafter

**No**
- Reinforce lifestyle and medication adherence
- Increase statin intensity OR
- Add non-statin therapy
- Fasting lipid panel in 4-12 weeks

If fasting lipid panel shows LDL<40mg/dL on 2 consecutive tests: decrease statin dose

If not tolerating current statin: Decrease statin dose to highest dose tolerable
- Add non-statin therapy

Statin Monitoring:
- Fasting lipid panel in 4-12 weeks
- CK (only if muscle symptoms, including pain, tenderness, stiffness, cramping, weakness, or generalized fatigue)
- ALT (only if sx of hepatotoxicity arise (unusual fatigue or weakness, loss of appetite, abdominal pain, dark-colored urine, or yellowing of the skin or sclera)
- Evaluate for new onset diabetes according to current diabetes screening guidelines
- Confused state, memory impairment

Circulation 2014;129[suppl 2]:S1-S45.

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Reviewed by: Bethany Kalich, PharmD, BCPS-QA Cardiology
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### Non-Statin Drug Options

<table>
<thead>
<tr>
<th>Non-Statin Options</th>
<th>Dose</th>
<th>Advantage</th>
<th>Disadvantage</th>
<th>Indication</th>
<th>ADE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ezetimibe</td>
<td>10mg PO daily</td>
<td>Synergistic effect with statins</td>
<td>Mild LDL lowering effect (15-20%)</td>
<td>2nd line (after statin) for all statin benefit groups</td>
<td>Fatigue, diarrhea, elevated serum transaminases, myalgia</td>
</tr>
<tr>
<td>PCSK9 Inhibitors**</td>
<td>Alirocumab: 75-150mg subQ every 2 wks</td>
<td>Patient adherence: biweekly or monthly dosing</td>
<td>Cost</td>
<td>2nd line when LDL≥190mg/dL</td>
<td>Injection site reactions, diarrhea, influenza, myalgia</td>
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<tr>
<td></td>
<td>Evolocumab: 140 subQ every 2 wks or 420 mg subQ monthly</td>
<td></td>
<td>Injection</td>
<td>3rd line for clinical ASCVD with comorbidities</td>
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<td></td>
<td>Fenofibrate 67-200 mg</td>
<td>Lowers triglycerides</td>
<td>May adversely affect T2DM</td>
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<td></td>
<td>Gemfibrozil 600 mg BID</td>
<td></td>
<td>High incidence ADE</td>
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<tr>
<td>Fibric acid derivatives</td>
<td>Niacin 1.5-6 g</td>
<td>Inexpensive</td>
<td>Poor choice for most lipid abnormalities</td>
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<td></td>
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<td>Greatest increase in HDL</td>
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<tr>
<td>Bile Acid Sequestrants</td>
<td>Colestipol: 2-16g PO daily</td>
<td>Low potential for side effects</td>
<td>3rd line in diabetes, ASCVD risk score ≥7.5%</td>
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<tr>
<td></td>
<td>Cholestyramine: 4-24g PO daily</td>
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<td>Constipation, dyspepsia, indigestion, headache</td>
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<tr>
<td></td>
<td>Colesevelam: 3.75g PO daily</td>
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</table>


**IMPROVE-IT Trial:** In patients who had been hospitalized with ACS in the last 10 days, simvastatin 40mg plus ezetimibe 10mg compared to simvastatin 40mg plus placebo resulted in a 1.8% lower risk of death from cardiovascular causes, MI or stroke.

### What if a patient develops muscle symptoms (pain, tenderness, stiffness, cramping, weakness, or fatigue)?

1. Obtain history of baseline and current muscle symptoms
2. Mild-moderate symptoms develop during statin therapy
   - Discontinue statin until symptoms resolve
   - Look for other causes of muscle symptoms
3. Symptoms resolve
   - Restart statin at same or lower dose
   - Determine causal relationship
4. Symptoms don't resolve
   - Symptoms don't resolve after 2 months
   - Consider other causes of symptoms
   - If cause is not statin related, restart at original dose
5. Causal
   - Discontinue original statin
   - Start different statin at low dose
   - (If tolerated, can increase dose gradually)
6. Not causal
   - Restart statin at original dose

### Patient Counseling in Statins (the 5 M's)

**JACC 2015;65(13):1361-1368.**

- **Muscle symptoms:** take a baseline self-inventory of current muscle symptoms before starting statin therapy (A DE may include: pain, tenderness, stiffness, cramping, weakness, or fatigue)
- **Medications:** statins may interact with several drug-interactions, both prescription or OTC; patients should let providers know if they start or stop medication
- **Metabolism:** statin metabolites in the liver; patients should self-monitor for signs/sx of hepatotoxicity (unusual fatigue or weakness, loss of appetite, abdominal pain, dark-colored urine, or yellowing of the skin or sclera)
- **Memory:** statins can unmask diabetes in a patient who is already at risk for diabetes impairment
- **Myocardial Changes:** statins can unmask diabetes in a patient who is already at risk for diabetes impairment

### References

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