Treating Hyperlipidemia in Severe and Very Severe Frailty
Intended for those with severe or very severe frailty according to the Clinical Frailty Scale [Rockwood]

Developed by Dalhousie University Academic Detailing Service
[http://cme.medicine.dal.ca/ADS.htm] and the Palliative and Therapeutic Harmonization (PATH) Program

Recommendations
These recommendations consider the significant impact and decreased life expectancy of severe frailty and very severe.

1. Primary Prevention
There is no reason to prescribe or continue statins for primary prevention.
   - It is unlikely that statins provide benefit in applicable outcomes.

2. Secondary Prevention
Statin treatment in severe frailty is probably not necessary, although there may be extenuating individualized circumstances that shift the risk/benefit ratio.

   With severe frailty there is:
   a. uncertainty about whether statin trial outcomes are clinically meaningful, as follows:
      - For the frail elderly, an important outcome is non-fatal stroke leading to disability. However, the outcome of non-fatal stroke in some studies sometimes includes mild strokes and TIAAs and the number of strokes leading to disability is not reported separately. Therefore, the outcome of non-fatal stroke might not be applicable to the frail.
      - In some statin studies, the primary composite outcome and the outcome of CHD events include those with asymptomatic heart disease such as silent MIs.
   b. uncertainty about the magnitude of any benefit conferred partly because of the decreased life expectancy in severe frailty.
   c. increased potential for adverse events.

3. Heart failure: There is evidence that statins are ineffective in improving clinical outcomes in the elderly and there is no reason to start or continue them for this indication.

4. Ezetimibe: There is currently no evidence that ezetimibe reduces cardiovascular events or mortality either alone or with statins in any population. There is no reason to start or continue ezetimibe for primary or secondary prevention.

5. Combination therapy with statins: There is no evidence of added benefit in clinical outcomes for combination therapies for either primary or secondary prevention in any population. There is no reason to start or continue other lipid lowering drugs in conjunction with statins.

6. Statin dosing: We suggest doses no higher than the following, and possibly lower, remembering that 2/3 of the lipid-lowering effect of a statin is realized at the starting dose. Thereafter, doubling the dose will lower LDL only by a further 4% to 7%.

<table>
<thead>
<tr>
<th>Statin</th>
<th>Dose</th>
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<tbody>
<tr>
<td>Atorvastatin 10 mg</td>
<td>Rosuvastatin 10mg</td>
</tr>
<tr>
<td>Simvastatin 20 mg</td>
<td>Pravastatin 40mg</td>
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<td></td>
<td>Fluvastatin 80mg</td>
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</tbody>
</table>
7. **Adverse events:** Advancing age is a risk factor for adverse effects from statins. Consider a trial of statin discontinuation if there is concern about myalgias, drug interactions, or other adverse effects.

**Rationale**

**Relevant outcomes with frailty**

We found no studies that report the effect of lipid lowering in severely frail older adults in primary or secondary prevention; therefore studies of the non-frail elderly that reported outcomes meaningful to the frail elderly were examined and assessed for applicability.

b. **Mortality:** There are competing causes for mortality in the frail elderly; therefore we cannot assume that a mortality benefit shown in non-frail populations applies to frail populations. In addition, the goals of therapy may not be to prolong life in the frail.

c. **CHD events:** For the frail elderly, the important outcome is symptomatic non-fatal MI (e.g., leading to morbidity such as angina or heart failure). In some statin studies, the primary composite outcome and the outcome of CHD events include those with asymptomatic heart disease such as silent MIs. Preventing asymptomatic heart disease might not prevent morbidity for the frail. Therefore, the outcome of CHD events, as reported in studies of the non-frail, might not be applicable for the frail.

d. **Stroke:** For the frail elderly, the important outcome is non-fatal stroke leading to disability. However, sometimes the outcome of non-fatal stroke includes mild strokes and TIAs and the number of strokes leading to disability is not reported separately. Therefore, the outcome of non-fatal stroke as reported in studies of the non-frail might not be applicable to the frail.

We consider the following outcomes as most meaningful for the frail elderly: *symptomatic* non-fatal myocardial infarction (MI) (e.g., leading to morbidity such as angina or heart failure) and non fatal stroke leading to *disability*. The effect of treatment on mortality is difficult to evaluate with frailty.

**Adverse events to statins**

- Advancing age is a risk factor for adverse effects of statins.
- Myopathy, including myalgia (muscle pain, weakness, stiffness, and cramps) may be a common adverse effect of statins. Female sex, a small body frame, frailty and multisystem diseases are some of the risk factors for myopathy.
- A meta-analysis [Richardson] did not suggest an association between statin use and cognition, however the strength of the evidence is limited, especially for high dose statins. Case reports, retrospective cohort studies, FDA post marketing surveillance data bases and minor changes in neuropsychological testing after statin initiation suggest a possible association between statin use and cognitive decline. While these data are not definitive, a trial of discontinuation may be appropriate to determine whether cognitive impairment is statin-related.
- Avoid adding medications to treat muscular pain, cognitive impairment or diabetes until statin-related adverse events are considered.
This poster describes the statin treatment recommendations

**Treating Hyperlipidemia in Severe and Very Severe Frailty**

These recommendations consider the significant impact and decreased life expectancy of severe and very severe frailty according to the Clinical Frailty Scale.

<table>
<thead>
<tr>
<th>CLINICAL SCENARIO</th>
<th>RECOMMENDATION</th>
<th>THE DETAILS</th>
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<tbody>
<tr>
<td>PRIMARY PREVENTION: no history of stroke or ischemic heart disease</td>
<td>Do not start or continue statins</td>
<td>It is unlikely that statins provide benefit in applicable outcomes.</td>
</tr>
<tr>
<td>SECONDARY PREVENTION: prior history of stroke or ischemic heart disease</td>
<td>Probably not necessary to start or continue statins</td>
<td>With severe frailty there is:</td>
</tr>
</tbody>
</table>
| | There may be extenuating circumstances that shift the risk/benefit ratio. | • uncertainty about whether statin trial outcomes are clinically meaningful; 
• uncertainty about the magnitude of benefit conferred, partly because of the decreased life expectancy in severe frailty; 
• increased potential for adverse events. |
| Patients with Congestive Heart Failure (CHF) only | Do not start or continue statins | There is evidence that statins are ineffective in improving clinical outcomes for older adults with CHF. |
| Patients on Ezetimibe | Stop Ezetimibe | There is no evidence that ezetimibe reduces cardiovascular events or mortality either alone or with statins. |
| Patients on combination lipid lowering therapy | Use statin only | There is no evidence of added benefit in clinical outcomes for combination therapies for either primary or secondary prevention. |

We suggest doses no higher than at right and possibly lower; 1/3 of the lipid-lowering effect is realized at the starting dose. Consider a trial of statin discontinuation if there is concern about myalgias or other adverse effects.

References

- Diabetes Care Program of Nova Scotia DHW SEAscape Database, June 2011
- Lee DH, Buth KJ, Martin BJ, Yin AM, Hirsch GM. Frail patients are at increased risk for mortality and prolonged institutional care after cardiac surgery. Circulation. 2010;121:973-978
- Lipid Lowering in Primary Prevention: a calculated risk, Dalhousie CME Academic Detailing Service, February 2013, [http://cme.medicine.dal.ca/ad_resources.htm](http://cme.medicine.dal.ca/ad_resources.htm)