<table>
<thead>
<tr>
<th>Drug/Class</th>
<th>Generic? Y/N</th>
<th>Lipid Effects (monotherapy)</th>
<th>Lipid Effects (w/ statin)</th>
<th>Outcomes Data</th>
<th>Cost (30-day)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholestyramine (Questran)</td>
<td>Y</td>
<td>LDL ↓: 9% (4 g to 8 g/day); 21% (16 g to 20 g/day); 23% to 28% (&gt;20 g/day)</td>
<td>Further LDL ↓: about 10% (8 g) to about 20% (24 g) Further HDL ↑: 0% to 10%</td>
<td>Primary prevention, men: reduces need for bypass, and combined endpoint of coronary heart disease, death, and nonfatal MI (NNT = 59 for 7 years) Secondary prevention, men: with diet, reduces cardiac events vs usual care (not placebo-controlled; events not a primary outcome). Slows progression and increases regression of atherosclerosis.</td>
<td>$404, generic packets (16 g/day)</td>
<td>Can be difficult to tolerate due to gastrointestinal side effects such as constipation and gas Can bind to other drugs and reduce absorption (e.g. levothyroxine, OCs, vitamins, digoxin, warfarin, BBs, thiazides, fat-soluble vitamins, mycophenolate, NSAIDs/APAP) Poor compliance (4 packets/day) Avoid use if: bowel obstruction, TGs &gt; 500</td>
</tr>
<tr>
<td>Bile acid sequestrant</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colesevelam (WelChol)</td>
<td>N</td>
<td>With 3.75 g/day: LDL ↓: 15% to 19.1% HDL ↑: 3% to 8.1% TG ↑: 10% (~20% when used with insulin or SUs)</td>
<td>With 3.75 g/day: Further LDL ↓: 10% to 16% Further HDL ↑: 3% to 7%</td>
<td>None</td>
<td>$678 (3.75 g/day)</td>
<td>Studied in combo w/ atorvastatin, lovastatin, pravastatin, and simvastatin Lower risk of GI side effects compared to cholestyramine and colestipol Can bind to other drugs and reduce absorption (see above) Poor compliance (6 tabs/day) GI side effects (constipation, diarrhea, flatulence, nausea)</td>
</tr>
</tbody>
</table>
# Non-Statin Lipid-Lowering Agents

## Colestipol (Colestid)

- **Type:** Bile acid sequestrant
- **Availability:** Available as granules, packs, tablets

<table>
<thead>
<tr>
<th>Y</th>
<th>LDL ↓: 5% (2 g/day) to 26% (16 g/day)</th>
<th>Further LDL ↓: 10% (5 g/day) 12% (10 g/day)</th>
<th>Reduces progression of atherosclerosis and events when combined with niacin or lovastatin (not a primary outcome).</th>
<th>$236, generic packs (10 g/day)</th>
</tr>
</thead>
</table>

**Note:** Can be difficult to tolerate due to GI side effects such as constipation and gas. Can bind to other drugs and reduce absorption (see above). GI side effects (constipation, diarrhea, flatulence, nausea). Avoid use if: bowel obstruction, TGs > 500.

## Exetimibe (Zetia)

- **Type:** Cholesterol absorption inhibitor
- **Availability:** Available as granules, packs, tablets

<table>
<thead>
<tr>
<th>N (going generic Dec 2016)</th>
<th>LDL ↓: 15-25%</th>
<th>Further LDL ↓: 25%</th>
<th>With simvastatin 20 mg, reduces first major atherosclerotic event in chronic renal disease — SHARP trial (2011)</th>
<th>$343 (10 mg/day)</th>
</tr>
</thead>
</table>

**Note:** Consider exetimibe as a statin add-on for high-risk patients who:
- can’t tolerate a high-intensity statin
- don’t get the expected 50% LDL reduction with a high-intensity statin.

## Fenofibrate (Tricor)

- **Type:** Fibrate

| Y | LDL ↓: 10-20% | Further LDL ↓: 0% to 6% | Prevention of CV events in T2DM:  
|---|---|---|---|

- did not reduce primary composite outcome (non-fatal MI or CV death)  
- improved non-fatal MI (24%↓), coronary revascularization (21%↓), progression to

<table>
<thead>
<tr>
<th>$172 generic tablets (145 mg/day)</th>
<th>$59, generic capsules (135 mg/day)</th>
</tr>
</thead>
</table>

**Note:** First-line for TG >1000 mg/dL. Option for TG >500 mg/dL or low HDL. Preferred over gemfibrozil for use with statins (fewer AEs). Requires renal dose adjustment.
## Non-Statin Lipid-Lowering Agents

**M Holler - Last updated: 10/2016**

<table>
<thead>
<tr>
<th><strong>Fibrate</strong></th>
<th><strong>LDL ↓:</strong></th>
<th><strong>HDL ↑:</strong></th>
<th><strong>TG ↓:</strong></th>
<th><strong>Further LDL ↓:</strong></th>
<th><strong>Further HDL ↑:</strong></th>
<th><strong>Cost</strong></th>
<th><strong>Overview</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gemfibrozil (Lopid)</strong></td>
<td>10-15%</td>
<td>6%</td>
<td>33% to 50%</td>
<td>8% (Niaspan 1 g/day)</td>
<td>9%</td>
<td>$146, generic (1200 mg/day)</td>
<td>First-line for TG &gt; 1000 mg/dL</td>
</tr>
<tr>
<td><strong>Niacin (Niacor – IR) (Niaspan – ER/SR)</strong></td>
<td>14% to 17%</td>
<td>12% (niacin immediate-release 1.5 g/day and Niaspan 1.5 g/day)</td>
<td>8% (Niaspan 1 g/day)</td>
<td>31% (Niaspan 2 g/day)</td>
<td>Secondary MI prevention: one less MI for every 30 patients treated for five years (Coronary Drug Project)</td>
<td>$5 (Niacor 1 g/day)</td>
<td>Option for TG &gt; 500 mg/dL</td>
</tr>
</tbody>
</table>

**Triglycerides**

- 145 mg/day (Canadian dosing)

- 1200 mg/day

**Albuminuria, and reduced laser treatments for retinopathy**

- Non-significant increase in CV death

As statin add-on, did NOT lower risk of non-fatal MI, non-fatal stroke, or CV death more than statin alone

Based on AIM-HIGH, ACCORD, HPS2-THRIVE studies...FDA removed labeling approving concomitant use of fibrates (and niacin) with statins — no clear benefit

Associated with reversible increase in Scr

Unclear risk of cholelithiasis (avoid in pts with history)

**LDL ↓:**

- 14% to 17% (Niaspan 2 g/day)

- 12% (niacin immediate-release 1.5 g/day and Niaspan 1.5 g/day)

**HDL ↑:**

- 6% (Niaspan 2 g/day)

- 15% (Niaspan 2 g/day)

**TG ↓:**

- 33% to 50%

- (greatest drop in patients with highest triglycerides)

Further TG ↓:

- 9% (Niaspan 2 g/day)

Secondary prevention of non-fatal MI plus cardiac death in men with low HDL

NNT = 23 over 5 years

No mortality benefit

Secondary MI prevention: one less MI for every 30 patients treated for five years (Coronary Drug Project)

As statin add-on, reduces carotid intima-media thickness (surrogate marker)

Available as Niaspan/lovastatin (Advicor) and Niaspan/simvastatin (Simcor)
## Non-Statin Lipid-Lowering Agents

**M Holler - Last updated: 10/2016**

<table>
<thead>
<tr>
<th>Drug</th>
<th>LDL</th>
<th>HDL</th>
<th>TG</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Icosapent ethyl (Vascepa)</strong></td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Dose-dependent risk of hyperglycemia (especially in patients with T2DM) and liver toxicity. May increase risk of statin myopathy. Most common side effects: flushing, itching, rash, HA. ER formulation better tolerated, but more hepatotoxic (though risk is relatively low for doses of 1-2g/day or less).</td>
</tr>
<tr>
<td><strong>EPA; ~1g omega-3 per capsule (ultra-pure, no DHA)</strong></td>
<td>LDL: No effect</td>
<td>HDL: No effect</td>
<td>TG: 27%</td>
<td>None available. Currently being studied in combo w/ statin; pts w/ high CV risk and high TGs – REDUCE-IT trial.</td>
</tr>
<tr>
<td><strong>Omega-3 ethyl esters (Lovaza)</strong></td>
<td>Y</td>
<td>LDL ↑: 44.5% (when TG are elevated)</td>
<td>LDL ↑: 0.7%</td>
<td>Secondary prevention: reduces cardiovascular death, sudden death, and combined endpoint of death, non-fatal MI, and non-fatal stroke. Secondary prevention in patients with, or at risk for, T2DM: did NOT reduce CV events (note: ~50% of patients were taking a statin). Study in progress – in combo.</td>
</tr>
<tr>
<td><strong>EPA/DHA; ~1g omega-3 per capsule</strong></td>
<td>LDL ↑: 9.1%</td>
<td>HDL ↑: 9.1%</td>
<td>TG ↓: 45%</td>
<td></td>
</tr>
</tbody>
</table>

### HDL ↑:
- 22% to 35% (2 g/day Niaspan)
- 17% (niacin immediate release 1.5 g/day)
- 20% to 22% (Niaspan 1.5 g/day)

### HDL ↓:
- 17% (niacin immediate release 1.5 g/day)
- 20% to 22% (Niaspan 1.5 g/day)

### TG ↓:
- 20% to 50%
- Further HDL ↑: 23% (Niaspan 1 g/day)
- Further TG ↓: 24% (Niaspan 1 g/day)
- Further LDL ↓: 6.2% (4 g/day)

### LDL ↓:
- 20% to 50%
- 20% to 22%
- Further LDL ↓:
  - 6.2% (4 g/day)
  - 4.5% (with 4 g/day)

### LDL ↑:
- 44.5% (when TG are elevated)
- 3.4%
- 29.5%
- (with 4 g/day)
Non-Statin Lipid-Lowering Agents
M Holler - Last updated: 10/2016

<table>
<thead>
<tr>
<th>PCSK9 inhibitors</th>
<th>LDL ↓: 38-72% (usually 50-60%)</th>
<th>Further LDL ↓: 48% (ODYSSEY, alirocumab)</th>
<th>Not available</th>
<th>$7000-$14000/year</th>
<th>Injectable biologics (monoclonal antibodies)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alirocumab (Praluent)</td>
<td>HDL ↑: 4-9%</td>
<td>50-60% (DESCARTES, evolocumab)</td>
<td>4 CV outcomes studies currently in progress – results expected 2017 (March?)</td>
<td>Preliminary data suggests ~50% decrease in CV events</td>
<td>Approved for treatment of heterozygous familial hypercholesterolemia (in combination with statin) OR in patients w/ CVD who need further lowering of LDL (on max statin, or can’t tolerate statin)</td>
</tr>
<tr>
<td>Evolocumab (Repatha)</td>
<td>TG ↓: 2-23%</td>
<td></td>
<td></td>
<td></td>
<td>Repatha also indicated for homozygous familial hypercholesterolemia</td>
</tr>
</tbody>
</table>

Lacks long-term safety data
Possible side effects: injection site reactions (7%), nasopharyngitis, URI, muscle pain, neurocognitive events (confusion/memory)

# Average effects of different classes of lipid lowering drugs on serum lipids

<table>
<thead>
<tr>
<th>Drug class</th>
<th>Serum LDL cholesterol (% change)</th>
<th>Serum HDL cholesterol (% change)</th>
<th>Serum triglycerides (% change)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bile acid sequestrants</td>
<td>† 15 to 30</td>
<td>0 to slight increase</td>
<td>No change*</td>
</tr>
<tr>
<td>Cholesterol absorption inhibitors</td>
<td>† 17</td>
<td>† 1</td>
<td>† 7 to 8</td>
</tr>
<tr>
<td>Fenofibrate (micronized form)</td>
<td>† 6 to 20</td>
<td>† 5 to 20†</td>
<td>† 41 to 53</td>
</tr>
<tr>
<td>Gemfibrozil</td>
<td>† 10 to 15</td>
<td>† 5 to 20†</td>
<td>† 35 to 50</td>
</tr>
<tr>
<td>Neomycin</td>
<td>† 20 to 25</td>
<td>No change</td>
<td>No change</td>
</tr>
<tr>
<td>Nicotinic acid (niacin)</td>
<td>† 10 to 25</td>
<td>† 15 to 35</td>
<td>† 25 to 30</td>
</tr>
<tr>
<td>Omega 3 fatty acids(\Delta)</td>
<td>† 4 to 49</td>
<td>† 5 to 9</td>
<td>† 23 to 45</td>
</tr>
<tr>
<td>PCSK9 inhibitors</td>
<td>† 38 to 72</td>
<td>† 4 to 9</td>
<td>† 2 to 23</td>
</tr>
<tr>
<td>Statins</td>
<td>† 20 to 60</td>
<td>† 5 to 10</td>
<td>† 10 to 33</td>
</tr>
</tbody>
</table>

†: increase; †: decrease; PCSK9 inhibitors: proprotein convertase subtilisin kexin type 9 inhibitors.
* Serum triglyceride levels may increase in patients with pre-existing hypertriglyceridemia.
†† Increases of 20% are seen in patients with very high triglycerides; increases of 5% are more typical with fibrate monotherapy in patients with moderate to high triglycerides.
\(\Delta\) Lovaza (US trade name) 4 g daily or 12 to 15 g of less purified form of omega-3 fatty acids.