Lipid Lowering Agents
Evidence, Questions & Comparisons

• February 2002 •

The pharmacological management of dyslipidemia has become an important topic in lowering cardiovascular risk. Several recent articles discuss current evidence, guidelines and perspectives:

CMAJ 2000;162(10):1441-7. (Canadian Dyslipidemia Guidelines [1])
Drugs 2001;61(2):197-206. (Safety Profiles for HMG-CoA's [4])
WJM 2001;175:246-250 & 396-401. (Hyperlipidemia – Best Practice [5])

OVERVIEW OF LIPID LOWERING AGENTS

STATINS (HMG-CoA Reductase Inhibitors)
Statins inhibit HMG-CoA reductase which catalyzes the rate-limiting step in cholesterol synthesis. Low density lipoprotein cholesterol (LDL) levels are lowered by inhibiting synthesis and up-regulating LDL receptors. Statins may also lower triglycerides (TGs) and raise high density lipoprotein (HDL). Studies have demonstrated their ability to prevent coronary events and reduce mortality. Those at highest risk benefit the most!

Secondary (2nd) Prevention with Statins
The benefits of statin therapy are greatest in patients who already have heart disease (2nd prevention). Reductions in coronary events, the primary endpoint for most studies, have been consistently observed. The Scandinavian Simvastatin Survival Study (4S) showed that treatment with simvastatin ZOCOR 20-40mg/day for 5.4 years reduced both all-cause mortality and major coronary events (See Figure 1). For every 30 coronary artery disease (CAD) patients treated, one death was prevented and for every 12 patients treated one major coronary event was prevented. Reductions in all-cause mortality have also been observed for pravastatin PRAVACHOL in the LIPID trial (Figure 3). The 4S was the only study where all-cause mortality was the primary endpoint.

Primary (1st) Prevention
Statins have demonstrated efficacy in reducing coronary events in two 1st prevention studies (WOSCOPS & AFCAPS/TexCAPS [7]). The WOSCOPS study evaluated the use of pravastatin in middle age men with high cholesterol. This study looked at 1st prevention in a high risk population since 44% were smokers and 16% had a prior history of vascular disease. Coronary event rates were reduced, but to a lesser extent than in 2nd prevention studies. For every 42 men treated with pravastatin 40mg/day for 4.9 years, one major coronary event was prevented. A reduction in all-cause mortality approached statistical significance (p=0.051) suggesting that for every 111 men treated, 1 death was prevented. In the AFCAPS trial, lovastatin MEVACOR 20-40mg/day for 5.2 years was effective in preventing the first cardiovascular event; however all-cause mortality was non-significantly higher in the lovastatin group due to an increase in non-cardiovascular deaths.

FIBRATES (Fibrac Acid Derivatives)
Fibrates increase HDL, decrease TGs and have modest effect on LDL (LDL may even increase if baseline TGs are highly elevated). They cause a shift in distribution of LDL to larger, less dense, less atherogenic particles. Fibrates may benefit patients who have high TGs, low HDL and low LDL. Studies show reductions in coronary event rates (See Figure 3); however no fibrate trial has reduced all-cause mortality.

RESINS (Bile Acid Sequestrants)
Resins bind bile acids in the gut and block their enterohepatic recirculation. They decrease LDL and raise HDL. They may cause TGs to increase and are contraindicated in those whose TGs are already elevated. In one 7-year, 1st prevention study cholestyramine reduced cardiovascular events in men with primary hypercholesterolemia. Reductions in all-cause mortality have not been observed.

NIACIN (Nicotinic Acid)
Niacin has the most potent effect on increasing HDL of any antihyperlipidemic. It also decreases both LDL and TGs. Plain niacin has more favorable effects on LDL and TGs than slow release preparations. (Nicotinamide is not effective!) To prevent flushing, giving 325mg regular ASA 30 minutes prior is useful when initiating therapy or increasing dosage. In a secondary prevention study (CDP), niacin 3g/day was effective in preventing coronary events. An observational follow-up showed a 6.2% absolute reduction in mortality 9 years later.

Also in this issue
Statin/Fibrate Combinations
High Dose Statins
Herbal Options
The Very Elderly/Diabetes
Trials & All-Cause Mortality
**QUESTIONS & ANSWERS**

Which lipid lowering agents have outcome evidence for reductions in rates of all-cause mortality?

Most statins have strong outcome evidence for reducing coronary event rates; however only simvastatin and pravastatin have reduced all-cause mortality (2° prevention trials). A follow-up of patients in the 4S trial showed that simvastatin continued to show survival benefit for up to 8 years. Figure 3 summarizes all-cause mortality data from major lipid trials. When evaluating this data the following should be noted:

- **only the 4S trial had all-cause mortality as a primary endpoint**; not all trials had enough patients to evaluate this endpoint.
- **benefits in cardiovascular endpoints do not always produce reductions in all-cause mortality** (e.g. BIP, AFCAPS, HHS)
- **all-cause mortality data can be found for all studies and is important in evaluating overall safety as well as efficacy.**

Which agent has the most potent LDL-lowering effect?

**Atorvastatin LIPITOR** currently has the greatest effect on LDL (but lacks evidence for long-term clinical outcome benefit).

Which statin is least likely to cause drug interactions?

**Pravastatin** has the least potential for CYP450 mediated drug interactions; but has some other drug interactions (Table 3).

What does the recent Heart Protection Study (HPS) add?

Preliminary data from the yet unpublished HPS confirms the benefits of **simvastatin 40mg od** in 2° prevention and 1° prevention in high risk patients. The trial included a broad group of high risk patients (e.g. diabetes, age ≤80, hypertension, previous stroke) whose average LDL was only 3.3 mmol/L. All-cause mortality data suggests that for every 59 patients treated for 5 years, 1 death could be prevented. The study also found that vitamins E, C, and beta-carotene did not provide any benefit.

Further analysis awaits full publication of the data.

When should statins and fibrates be co-administered?

Combinations of lipid lowering agents may be considered in severe dyslipidemia when a single drug fail to achieve targets. These combinations have not been well studied. Potential benefits must be weighed against increased risks! For statins and fibrates, the risk of myopathy is of particular concern. Twelve of 31 deaths in the atorvastatin BAYCOL occurred in patients taking gemfibrozil. Patients should be advised to report any unusual symptoms such as unexplained muscle pain, tenderness or weakness. (Table 1.)

<table>
<thead>
<tr>
<th>Table 1. COMBINATION THERAPY</th>
</tr>
</thead>
<tbody>
<tr>
<td>statin + fibrate</td>
</tr>
<tr>
<td>low-mid dose</td>
</tr>
<tr>
<td>↓ LDL, ↑ TGs, ↑ HDL, ↑↑ risk of myopathy*</td>
</tr>
<tr>
<td>if used, pravastatin least likely to cause DI's</td>
</tr>
<tr>
<td>statin + niacin</td>
</tr>
<tr>
<td>↓ LDL, ↓ TGs, ↓ HDL; lovastatin ↑↑↑↑↑ risk myopathy*</td>
</tr>
<tr>
<td>(lovastatin+ SR niacin ADVISOR - recent FDA approval) simvastatin &amp; pravastatin also studied &amp; appear safe</td>
</tr>
<tr>
<td>statin + resin</td>
</tr>
<tr>
<td>↓ LDL, ↑ HDL; safe; may ↑ CHD risk by ≥50%</td>
</tr>
<tr>
<td>niacin + resin</td>
</tr>
<tr>
<td>option in statin intolerance (ie. hepatic/muscle)</td>
</tr>
<tr>
<td>niacin + fibrate</td>
</tr>
<tr>
<td>↓ TGs, ↑ HDL</td>
</tr>
<tr>
<td>niacin + fish oil</td>
</tr>
<tr>
<td>↓ TGs; questionable efficacy</td>
</tr>
</tbody>
</table>

**MYOPATHY RISK** is dose-dependant; ↑ risk in small-framed, older & impaired renal function patients; furosemide & probenecid may ↑ risk in nephrotic syndrome patients on fibrates. DI= drug interaction

Does statin therapy work as well in smokers?

Observations from the landmark trials show that statins reduce **↑ in smokers**; however benefit is markedly **↓**. Event rates in treated smokers were similar to those in untreated non-smokers. (Smoking also ↓ s HDL)

Can LDL be lowered too much?

The currently recommended target LDL levels vary from <2.5 mmol/L in very high risk patients to <5 mmol/L in those at low risk. Although it is generally thought that “lower is better”, the results from the CARE trial raised some question as to what the ideal LDL target should be. In this trial there was no benefit for those post-MI patients whose initial LDL was less than 3.2 mmol/L. This finding has not been confirmed in other trials. Factors yet to be fully evaluated include the safety of very high doses (see below) and the risk versus benefit in the very elderly. The HPS should provide additional information.

What evidence supports high dose statins?

Recent studies have evaluated the safety and efficacy of high dose statins in very high risk patient groups. The **Post-CABG** (coronary artery bypass graft) trial compared moderate versus aggressive lowering of LDL using various doses of lovastatin +/- cholestyramine. This study of 1,351 patients found that an aggressive LDL target of <2.6 mmol/L was beneficial, resulting in fewer new occlusions and a lower rate of revascularization. Apart from poor tolerance to cholestyramine, the regimen was safe and well tolerated over the 4.3 years of the study.

The **AVERT** trial studied 341 patients with non-acute ischemic heart disease or stable angina over 18 months. Patients were randomized to receive either atorvastatin 80mg/day or angioplasty. Ischemic events were 13% in the atorvastatin group compared to 21% in the angioplasty group (p=0.048; not statistically significant after adjustment for interim analysis). High dose atorvastatin appeared at least as effective as angioplasty in reducing the incidence of ischemic events in low-risk patients. [One reviewer noted that these patients were such low risk that they would not have been offered angioplasty in Canada and that anginal events were significantly less in the angioplasty group.]

The **MIRACL** study of 3,086 patients evaluated the role of atorvastatin 80mg/day given within 96hours post-MI. Over 16 weeks, the atorvastatin group had less recurrent symptomatic ischemia requiring rehospitalization. The results of the study have been called into question due to eleven patients lost to follow-up. The rate of liver enzyme elevation was 2.5% in the atorvastatin 80mg group and there were three cases of hepatitis. Rates of liver enzyme elevation for lower doses have commonly been in the 0.2-0.6% range.

The results of these three trials show that high dose statin therapy is effective in reducing coronary events in select high risk groups. Caution is warranted due to increased toxicity and limited data on long term use. Ongoing studies (SEARCH, TNT, SPARCL and PROVE IT) will provide more information on the relative efficacy and safety of high versus low dose therapy.

**Related question on next page (Dose-response to Statins).**
How does doubling the dose affect response to a statin?

A doubling of the dose above the minimal effective dose does not achieve a doubling of the LDL lowering effect.\(^3,29\)

Beneficial increases in HDL appear to peak at lower doses and decline slightly thereafter (Figure 2). Whether high doses provide better morbidity/mortality outcomes is not yet studied.

![Figure 2: Dose-response for Statins \(3,29\)](image)

Increasing Statin Doses ➔

Lab results: At what point should treatment be stopped?

- **aminotransferase (AST/ALT):** Discontinue drug if greater than 3X normal or if less than 3X normal and symptomatic.
- **CK:** Routine monitoring is unnecessary; check in symptomatic patients (muscle pain or weakness). If no improvement on discontinuing suspect drug(s), evaluate for other causes eg. toxic, endocrine, neurologic etc.

Which herbs may effectively lower cholesterol?

Several herbs have been suggested to lower cholesterol and a few may be effective. None have evidence for lowering mortality. There are some concerns regarding long-term safety, drug interactions and purity of some products. See Table 2.

**Table 2. HERBAL OPTIONS for DYSLIPIDEMIA \(3,30\)**

- **Likely safe & effective:** Avocado, Flaxseed\(^a\), Guar gum, Niacin, Oat bran, Pectin, Psyllium, Red Yeast\(^b\), Sitostanol, Soy
- **Possibly safe/effective:** Guggul/Guggulipids\(^c\), Garlic?

\(^a\) Flaxseed: Usual dose 1 teaspoon of whole seed with 150ml liquid 2-3X/day; lack of adequate liquid causes intestinal blockage; can impair drug absorption

\(^b\) Red Yeast: 2400mg/day actually contains 7.2mg of the active sterolLovastatin

\(^c\) Guggulipids: (Commiphora mukula); a gum resin (India) may lower serum cholesterol & triglycerides. It has thyroid stimulating activity & may interfere with thyroid disorders. Side effects: GI – nausea, burping, hiccups; headache. Drug interactions (potential for bioavailability). Usual dose 100-500mg/day.

Dietary measures are encouraged recognizing that they are modestly effective in lowering total cholesterol and LDL levels.

- **Recommend in diet:** whole grain bread, cereal, rice & pasta fruits and vegetables legumes (beans, peas, lentils) & nuts some fish, skinless chicken, lean meats olive & canola oils; peanut oil skim milk/low fat dairy products
- **Avoid/minimize in diet:** fried foods high-fat meats high-fat dairy products stick/hydrogenated margarine commercial baked goods

Very aggressive dietary measures may lower LDL at the expense of lower HDL levels. The American Heart Association Step II diet (AHA-II)\(^7\) recommends the following:

- **Saturated fat:** <7% of Total Calories (TCal);
- **Polyunsaturated fat:** <10% TCal; Monounsaturated fat <20% TCal;
- **Total fat:** 25-35% TCal; Carbohydrate 50-60% TCal; Fiber 20-30g/d;
- **Protein:** ~15% TCal; Cholesterol <200mg/d.

(Consider: plant stanols/stereols – e.g. Beets Pro-activ\(^6\) SS)

**DYSLIPIDEMIA: SPECIAL CONSIDERATIONS**

**The Very Elderly**

This is an area of some controversy. The following should be considered in assessing risk versus benefit:

- **Published studies only include age ≤ 75:** HPS will include ≤ 80
- **Subanalysis of 4S & LIPID suggests benefit for 2nd prevention was greater for older patients (≥ age 65).**\(^37\)
- **The risk vs benefit of lowering cholesterol in the very old is not well established.** One study in men aged 71-93 found that mortality rates may actually increase with lower cholesterol levels.\(^72\) Another study of those aged 85 and older found that those with a higher total cholesterol level had a lower rate of all-cause mortality.\(^35\) LDL may be a better predictor.
- **Risk of myopathy increases with age & ↓ renal function.**
- **Aggressive lipid lowering for 1st prevention in age ≥ 75 years is not supported in the literature. Encourage lifestyle change!**
- **Consideration should be given to concomitant illness, general health status and social issues** of the patient’s values.

**Patients With Diabetes**

- **Prevalence of hypercholesterolemia is similar in patients with and without diabetes; however, the CHD risk is much higher.** Patients with diabetes without MI history are at an equal 7 year risk of acute MI as patients without diabetes who have had a previous MI.\(^77\) Thus, patients with diabetes over age 30 years are classified as “very high risk” for CAD. Aggressive lifestyle measures and drug treatment is recommended.
- **Diabetic dyslipidemia:** (↑ TG; ↓ HDL; small dense LDL particles, often only borderline high) is part of the metabolic syndrome consisting of several risk factors: abdominal obesity, hypertension, insulin resistance & a procoagulant state. ATP III Guidelines consider lowering LDL to be a primary target of therapy.\(^7\) Other factors contributing to the metabolic syndrome (e.g. obesity, physical inactivity & other dyslipidemia) are 2nd targets.
- **Statins are first-line therapy when LDL is above target especially given clinical trial evidence for reducing cardiac events and overall mortality.**\(^39\) Higher doses will also lower TGs. Some literature suggests atorvastatin may be preferred when both LDL and TGs are highly elevated; however outcome data is stronger for simvastatin and pravastatin.
- **For patients with predominant hypertriglyceridemia, initial therapy should include diet, weight loss, physical activity and moderation of alcohol intake.** Improving **glucose control** is effective although high TG levels may not be adequately controlled with diet alone; treatment with fibrates may be useful. Patients with TG levels >5.65mmol/L are also at high risk of acute pancreatitis.\(^6\) Note: if TG levels are very high, fibrate treatment may ↓ LDL.
- **Caution with Niacin:** high doses may cause insulin resistance.
- **Caution with Resins:** (e.g. cholestyramine) ↑ TG levels.

**HIV Patients on Protease Inhibitors**\(^39\)

Treatment requires special considerations that are beyond the scope of this publication - reader should be aware of the need for screening; consider consultation to specialist.
Figure 3. ALL-CAUSE MORTALITY OUTCOMES from MAJOR LIPID TRIALS

**SECONDARY PREVENTION** patients with history of CHD

<table>
<thead>
<tr>
<th>Drug &amp; dose used</th>
<th>Simvastatin 20-40mg/day</th>
<th>Pravastatin 40mg/day</th>
<th>Pravastatin 40mg/day</th>
<th>Gemfibrozil 600mg BID</th>
</tr>
</thead>
<tbody>
<tr>
<td>RRR mortality</td>
<td>3.3% p&lt;0.001</td>
<td>3.1% p&lt;0.01</td>
<td>NS</td>
<td>1.7% p&lt;0.001</td>
</tr>
<tr>
<td>Tx Duration</td>
<td>5 yrs</td>
<td>6.1 yrs</td>
<td>5 yrs</td>
<td>6.2 yrs</td>
</tr>
<tr>
<td>All-cause mortality in plain English based on NNT for study</td>
<td>Treat 30 patients for 5.4 years to prevent 1 death</td>
<td>Treat 32 patients for 6.1 years to prevent 1 death</td>
<td>Treat 59 patients for 5 years to prevent 1 death</td>
<td>Treat 59 patients for 5 years to prevent 1 death</td>
</tr>
<tr>
<td>Patients studied</td>
<td>pts with angina or previous MI &amp; TC &gt;5.5 age 35-70</td>
<td>recent hx of acute MI or unstable angina; age 31-75</td>
<td>recent hx of acute MI &amp; average LDL, age 21-75</td>
<td>High risk patients: MI, CHD, PVD, PVD, DM, HTN, TC &gt;5; age 40-80</td>
</tr>
<tr>
<td>LDL (average) initial=achieved</td>
<td>4.9±3.2</td>
<td>3.9±2.9</td>
<td>3.6±2.5</td>
<td>3.3±2.3</td>
</tr>
<tr>
<td>1° Endpoint Placebo/Drug</td>
<td>↓ total mortality 11.5% / 8.2%</td>
<td>↓ death CHD 8.3% / 6.4%</td>
<td>↓ MI / death CHD 13.2% / 10.2%</td>
<td>Mortality from: all cause/CHD/other</td>
</tr>
<tr>
<td>Comments</td>
<td>impact began at ~ 1 year</td>
<td>benefit most in Δ &amp; high LDL patients</td>
<td>awaiting publication</td>
<td>benefit only in pts with TG &gt;2.3</td>
</tr>
</tbody>
</table>

**PRIMARY PREVENTION** pts without CHD

<table>
<thead>
<tr>
<th>Drug Tx</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.2</td>
<td>4.1</td>
</tr>
<tr>
<td>2.4</td>
<td>2.3</td>
</tr>
<tr>
<td>2.2</td>
<td>2.1</td>
</tr>
<tr>
<td>Trend: 1 death prevented per 111 patients over 4.9 yrs</td>
<td></td>
</tr>
</tbody>
</table>

Drugs: **Simvastatin**, **Pravastatin**, **Gemfibrozil**, **Lovastatin**, **Clopibrate**

ARR = % absolute risk reduction
CHD = coronary heart disease
CV = cardiovascular
CVD = cardiovascular death
DM = diabetes
GI = gastrointestinal
hx = history
MI = myocardial infarction
MI NF = nonfatal MI
NNH = # needed to harm one
NTT = # needed to treat to benefit one (e.g. in 4S trial, treating 30 patients for 5.4 yr would prevent 1 death)
NS = not statistically significant
pts = patients
RRR = relative risk reduction
Tx = treatment

**Summary of All-Cause Mortality Evidence**

- **Statins**: good evidence for 2° prevention; some evidence for 1° prevention of middle-age male patients at ↑d risk of CHD; lack evidence for 1° prevention in low risk patients
- **Fibrates**: no evidence yet for reductions in 1° or 2° all-cause mortality; possible benefit in subset of patients with low HDL, TG’s >2.3 &/or patients with diabetes
- Lack of published data to evaluate risk vs benefit in age ≥75; all-cause mortality risk vs benefit of aggressive pursuit of targets (e.g. high dose/combinations) is not studied
**Table 3. DYSLIPIDEMIA – PHARMACOLOGICAL MANAGEMENT**

**Generic/ Trade**

<table>
<thead>
<tr>
<th>Generic/ TRADE</th>
<th>LDL (dose effect)</th>
<th>HDL</th>
<th>TG</th>
<th>SIDE EFFECTS/ CONTRAINDICATIONS (CI)</th>
<th>DRUG INTERACTIONS</th>
<th>THERAPEUTIC BENEFITS/USES</th>
<th>USUAL Dose Range (Max dose/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>STATINS/ HM</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>LIPI TON ATO</td>
<td>35-60%</td>
<td>↑5-15%</td>
<td>↓7-30%</td>
<td>SE≤10%; generally better tolerated than other agents.</td>
<td>Effect of: digoxin/ warfarin</td>
<td>Cholesterol: ATO, FLU, LOV, PRASIM</td>
</tr>
<tr>
<td>Fluvastatin</td>
<td>LEGO SL FLU</td>
<td>20-35%</td>
<td>↑10%</td>
<td>↓5-15%</td>
<td>Common: GI upset, rash &amp; abdominal pain. Rare: peripheral neuropathy, lupus like Sx, impotence. ↑ LFT (AST &amp; ALT &gt;3X Normal in ≤2%).</td>
<td>Effect of: toxicity with HMG &amp; clofibrate.</td>
<td>Atherosclerosis: FLU, LOV, PRASIM</td>
</tr>
<tr>
<td>Lovastatin</td>
<td>MEVACOR LOV</td>
<td>25-40%</td>
<td>↑20%</td>
<td>↓5-15%</td>
<td>Myopathy: &lt;1%; rhabdomyolysis &lt;0.2% (CK≤10x).</td>
<td>Coronary Heart Disease: FLU, LOV, PRASIM</td>
<td></td>
</tr>
<tr>
<td>Pravastatin</td>
<td>PRAVACHOL</td>
<td>20-35%</td>
<td>↑10%</td>
<td>↓5-15%</td>
<td>Effect of: toxicity with HMG &amp; clofibrate.</td>
<td>Stroke: PRASIM</td>
<td></td>
</tr>
<tr>
<td>Simvastatin</td>
<td>ZOCOR</td>
<td>25-50%</td>
<td>↑10%</td>
<td>↓5-15%</td>
<td>Effect of: toxicity with HMG &amp; clofibrate.</td>
<td>Study in effective secondary causes such as diabetes &amp; in nephrotic syndrome</td>
<td></td>
</tr>
</tbody>
</table>

| **FIBRATES** |                  |     |    |                                     |                   |                          |                             |
| Bezafibrate | BEZALIP BEZ  | 5-20% | ↑10-20% | ↓20-50% | Common: Gl upset, rash & abdominal pain. | Combination with HMG/Niacin: (to ↓ LDL & TG) |
| Fenofibrate | LIPIDIL         | 67% | ↑5-10% | ↓10-20% | Fenofibrate may ↓ TG more than gemini current outcome evidence best with gemfibrozil. | Combination with HMG/Fibrate (to ↓ LDL & TG) |
| Gemfibrozil | LOPID GEM      | 50% | ↑5-10% | ↓15-20% | Combination: Constipation, nausea & bloating, drowsiness, dizzy, arthralgia. | Combination with HMG/Fibrate (to ↓ LDL & TG) |

| **RESINS** |                  |     |    |                                     |                   |                          |                             |
| Cholestyramine | QUESTRAN CME  | 15-30% | ↑3-5% | NO Change or Possible INCREASE | Space other meds (by ≥ 2 hrs) | Cholesterol & LDL: (esp. pregnancy & age >2 yrs) |
| Colestipol | COLESTID           | 5-15% | ↑5-15% | ↓20-50% | Common: Constipation, nausea & bloating. Rare: hypercholesterolemia. | Combination with HMG/Niacin (to ↓ LDL) |

| **NICOTINIC ACID** |                  |     |    |                                     |                   |                          |                             |
| Nicotinic acid | NICA  | 5-15% | ↑5-15% | ↓20-50% | Flushing (by ASA 1/2hr pre): dry eyes, pruritus, headache, GI upset, ↑ uric acid & ↑ glucose. | Combination with HMG/Fibrate (to ↓ HDL & TG) |

**MAJOR RISK FACTORS**

- **Diabetes:** Smoking, Hypertension, DM (type 1 & 2)
- **Hypertension:** Blood Pressure, Low HDL, Cholesterol
- **LDL:** Low Density Lipoprotein
- **HDL:** High Density Lipoprotein
- **TG:** Triglycerides

**DRUG INDUCED HYPERLIPIDEMIA**

- Amiodarone, Beta-blockers, Non-Statin Drugs, Barbareine, Cyclosporin, Cyclosporin, Donor, Contrast Agents
- Low dose cholesterol or HMG CoA Reductase Inhibitor
- Malignant Hyperbilirubinemia
- High dose statins

**CHOICE OF AGENT**

- **HMG & Fibrate (i.e.,盼美服RA) + Niacin**
- **HMG & Fibrate (i.e.,盼美服RA) + Niacin**
- **HMG & Fibrate (i.e.,盼美服RA) + Niacin**
- **HMG & Fibrate (i.e.,盼美服RA) + Niacin**
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- **HMG & Fibrate (i.e.,盼美服RA) + Niacin**
- **HMG & Fibrate (i.e.,盼美服RA) + Niacin**
- **HMG & Fibrate (i.e.,盼美服RA) + Niacin**
- **HMG & Fibrate (i.e.,盼美服RA) + Niacin**

**TARGETS**

- **Very High Risk** (10yr CAD risk >20%)
  - LDL <2.5
  - HDL <1.8
  - TG <1.7

- **High Risk** (10yr CAD risk 20-30%)
  - LDL <3
  - HDL <1.8
  - TG <1.7

- **Moderate Risk** (10yr CAD risk 10-20%)
  - LDL <4
  - HDL <1.8
  - TG <1.7

- **Low Risk** (10yr CAD risk <10%)
  - LDL <5
  - HDL <1.8
  - TG <1.7

**LIFESTYLE CHANGES**

- Diet, Exercise, Moderate Alcohol use & STOP SMOKING!
Table 4. CDN Working Group\(^1\) - 10yr risk of CAD in patients without diabetes or clinically evident heart disease. Framingham data.

<table>
<thead>
<tr>
<th>RISK*</th>
<th>MEN</th>
<th>WOMEN</th>
<th>10yr CAD risk %</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20-34</td>
<td>-9</td>
<td>-9</td>
<td>&lt;1</td>
</tr>
<tr>
<td>35-39</td>
<td>-4</td>
<td>-4</td>
<td>&lt;1</td>
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<tr>
<td>40-44</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>45-49</td>
<td>1</td>
<td>1</td>
<td>2</td>
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<td>50-54</td>
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<td>65-69</td>
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<tr>
<td>70-74</td>
<td>7</td>
<td>6</td>
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</tr>
</tbody>
</table>

TOTAL CHOL

-4.14<\(\leq\) -3.57<\(\leq\) 4.58<\(\leq\) 5.8<\(\leq\) 6.22<\(\leq\) 6.22<\(\leq\) 7.25<\(\leq\)

HDL<0.9<\(\leq\) 0.91-1.16<\(\leq\) 1.17-1.29<\(\leq\) 1.3-1.55<\(\leq\) 1.56<\(\leq\)

SYSTOLIC BP<120<\(\leq\) 120-129<\(\leq\) 130-139<\(\leq\) 140-159<\(\leq\) 160<\(\leq\)

CAUTION: Risk Tables only a tool; some parameters variable. Identification of patient specific risk factors (see bottom Table 3) may be more valuable in some cases. Specialist opinion.

TOTAL POINTS:

- Risk assessments based on Framingham data; other risk factors such as family history of CAD should also be considered.

For suggested lipid targets, see bottom of Table 3.

Cardiac Risk Tools:
1) www.statcoder.com
2) www.nhlbi.nih.gov/guidelines

Table 5. USA-NCEP Working Group\(^2\) - 10yr risk of CAD in patients without diabetes or clinically evident heart disease.

<table>
<thead>
<tr>
<th>RISK*</th>
<th>MEN</th>
<th>WOMEN</th>
<th>10yr CAD risk %</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20-34</td>
<td>-7</td>
<td>-7</td>
<td>&lt;1</td>
</tr>
<tr>
<td>35-39</td>
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<td>&lt;1</td>
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<td>0</td>
<td>1</td>
</tr>
<tr>
<td>45-49</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
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<td>1</td>
<td>3</td>
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<td>5</td>
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</tr>
<tr>
<td>70-74</td>
<td>7</td>
<td>6</td>
<td>7</td>
</tr>
</tbody>
</table>

TOTAL CHOL

-4.13<\(\leq\) 4.14-5.15<\(\leq\) 5.16-6.19<\(\leq\) 6.2-7.24<\(\leq\) 7.25<\(\leq\)

HDL<1.03<\(\leq\) 1.04-1.28<\(\leq\) 1.29-1.54<\(\leq\) >1.55<\(\leq\)

SYSTOLIC BP<120<\(\leq\) 120-129<\(\leq\) 130-139<\(\leq\) 140-159<\(\leq\) >160<\(\leq\)

SMOKER Yes No

TOTAL POINTS:

- Risk assessments based on Framingham data; other risk factors such as family history of CAD should also be considered. Patients with clinical CAD, CVD, PVD, and DIABETES age 30+ are "very high risk" regardless of risk score. Cardiac Risk Tools: 1) www.statcoder.com 2) www.nhlbi.nih.gov/guidelines
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