Non Drug Alternatives to Statins

DR JASON KAPLAN  MBBS (HONS) FRACP FCSANZ
Clinical Lead Cardiovascular Program, MUHSC
Lecturer in Medicine – Faculty of Medicine & Health Sciences, Macquarie University

Major causes of death in high income western society due to lifestyle related factors
Best approach is to use lifestyle to treat them where possible and appropriate
The absolute benefits of statins are smaller in primary prevention than in secondary prevention
Look for the presence of disease and calculate global CV risk
Dietary change is a powerful therapy in low to intermediate risk patients to lower LDL-C and a great adjunct in high risk patients to achieve target lipid levels
Overall dietary patterns matters most for chronic disease prevention, rather than focusing on single nutrients (e.g. low fat or low carbohydrate) or single foods

Important take home messages

You cannot supplement or medicate yourself out of poor lifestyle choices

Lifestyle Management

Lifestyle management remains the cornerstone for reducing cardiovascular disease risk including achieving and maintaining optimal lipid levels

Non Drug therapy of LDL

WHO IS IT FOR?
Patients at low – intermediate risk of cardiovascular events
To try and lower dose needed of statin medication in those on treatment (secondary prevention) and those experiencing side effects
4 areas to focus on:
- Lowering LDL-C
- Lowering Triglycerides
- Raising HDL-C
- Prevention of events / mortality
Primary Prevention

Global Risk Assessment

To estimate 10-year ASCVD* risk – ACC/AHA 2013
• New Pooled Cohort Risk Equations
  • More accurately identifies higher risk individuals for statin therapy
• Focuses statin therapy on those most likely to benefit
• When using a risk score calculator, know its limitations and population under consideration
  Consider MESA score - https://www.mesa-nhlbi.org/MESAHRisk/MesaRiskScore/RiskScore.aspx

*10-year ASCVD: Risk of first nonfatal myocardial infarction, coronary heart disease death, non-fatal or fatal stroke

Primary Prevention

Statin Therapy

• Thresholds for initiating statin therapy derived from 3 exclusively primary prevention RCTs (WOSCOPS, ASCOT, AFCAPS)
• Before initiating statin therapy, clinicians and patients engage in a discussion of the potential for ASCVD risk reduction benefits, potential for adverse effects, drug-drug interactions, and patient preferences
• Calculators don’t write Rx, physicians do!

Coronary Calcium Screening: Early Detection of Heart Disease

Examples of Coronary Artery Scans

Kaplan-Meier survival curves by coronary artery calcium (CAC) scores across increasing risk factor (RF) burden


Fall in LDL by 24% WOSCOPS – 20 mg pravastatin enough to reduce CVD events by 30%
Zero Calcium Score = Priceless

CAC score of 0 predicts an annual mortality rate below 1% out to at least 15 years in those at low or intermediate risk

“You’ve got a rare condition called ‘good health’. Frankly, we’re not sure how to treat it.”

Intensity statin therapy

<table>
<thead>
<tr>
<th>High-Intensity Statin Therapy</th>
<th>Moderate-Intensity Statin Therapy</th>
<th>Low-Intensity Statin Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily dose lowers LDL-Chol, on average, by approximately ≥50%</td>
<td>Daily dose lowers LDL-Chol, on average, by approximately 30% to ≤50%</td>
<td>Daily dose lowers LDL-Chol, on average, by &lt;30%</td>
</tr>
<tr>
<td>Atorvastatin 40-80 mg</td>
<td>Rosuvastatin 20-40 mg</td>
<td>Simvastatin 10-20 mg; Pravastatin 40 mg; Fluvastatin 40 mg tid</td>
</tr>
<tr>
<td>Simvastatin 10-20 mg; Pravastatin 40 mg; Fluvastatin 40 mg</td>
<td></td>
<td>Simvastatin 10 mg; Pravastatin 10-20 mg; Lovastatin 20 mg; Fluvastatin 20-40 mg; Pioglitazone 1 mg</td>
</tr>
</tbody>
</table>

Supplements with RCT / Level 1 evidence to lower LDL-C (doses)

- Dietary Fibre (5-15 g)
- Phytosterols / stanols 1-2 g (but no effect on clinical endpoints)
- Soy protein / isoflavones (50 g) - Likely on basis of reduced saturated fat
- Nuts - (50 g) – almonds, pecans, walnuts
- Red rice yeast / monocolin K / lovastatin (1-2 g)

Cumulative Incidence of Clinical Events

In the Kaplan-Meier cumulative-incidence curves for coronary heart disease (CHD) and cardiovascular disease (CVD) events, CAC = 0 and cPB = 0 were associated with low event rates. Abbreviations as in Figure 1.

Figure Legend:
Cumulative incidence of clinical events

LDL targets

- “normal”: cholesterol values at which level there is no subclinical atherosclerosis
- “abnormal”: cholesterol values at which level there is subclinical atherosclerosis, with the severity of “abnormal” depending on the degree of subclinical atherosclerosis.
- Primary prevention: - For patients that need a goal – LDL C < 2.57 mmol/L
- In intravascular ultrasound studies – plaque regression was seen with LDL-C less than 1.8 (SATURN trial)
- “At any level of LDL-C – it depends on your risk”
Carbohydrate derived from unprocessed whole foods
- Reduces absorption of cholesterol, lowers glycemic index
- Ideally 10g/day for benefit

Good sources
- Oat bran / Barley / B Glucan
- Ground flaxseed

Supplements
- Psyllium husks
- Flax Seed/Meal (water-soluble, non-digestible fiber made from corn that is called: AlphaCyclodextrin (Nuvexa TM))

Effect on lipid levels in healthy overweight
- Study: Comerford KB et al.
- Study Design: Double-blind, controlled crossover study
- Treatment: 2 FBCx tablets with each fat containing meal (total of 6 tablets per day)
- Participant Profile: N = 28, overweight not obese (BMI: 25-29.9 kg/m²), 18-65 years, both males and females
- Duration: t = baseline, 30 days & 60 days
- Results:
  - Reduction in total cholesterol (-4.3%) and in LDL cholesterol (-6.7%) both p<0.05
  - Body weight lower in the active group (0.41 ± 0.2)kg when compared to placebo (p<0.05) in the absence of dietary change
  - A trend in reduction of blood insulin, ApoB, and total cholesterol/HDL-cholesterol ratio levels was observed

Red Rice Yeast
- Supplement is made by fermenting white rice with the yeast, *Monascus purpureus*.
- Fermentation process turns the yeast red and produces mevinic acids.
- Monacolin K or mevinolin is also found in the statin drug, lovastatin.
- These acids inhibit HMG CoA reductase and reduce cholesterol production from the liver.
- Red rice yeast also contains sterols, including beta-sitosterol (also in vegetables), isoflavones (also in soy), and monounsaturated fatty acids (also in olive oil).
- Practice Point: poor standardization amongst formulations

Red Rice Yeast cont’d
- Shares the same side effect profile as other statin medications and liver enzymes /CK should be monitored
- 600mg tablets = 2.5 mg Lovastatin
- 4 X 600mg tablets – for 10 mg Lovastatin equivalent = reduce LDL-C 10-20%

Randomised controlled trial
- Effect of a Dietary Portfolio of Cholesterol-Lowering Foods Given at 2 Levels of Intensity of Dietary Advice on Serum Lipids in Hyperlipidemia
- Summary: The Portfolio Diet
  - The portfolio diet is a Mediterranean style eating plan
  - It has been found to reduce LDL cholesterol by about 30% (similar to 20 mg lovastatin), when the foods were provided and more intense follow up and by 13% when only the dietary recommendations were provided.

The portfolio diet
- Daily amounts for 2000 cal (8368 KJ) / day diet
- 30 grams of almonds – about 23 almonds (30g). Walnuts, cashews, Brazil nuts and macadamia nuts are also beneficial.
- 20 grams of viscous fiber from foods such as oats, barley, psyllium, and certain fruits and vegetables.
- 50 grams of soy protein from foods such as tofu, soy meat alternatives and soy milk, 10 grams of soy can be obtained from 1 to 2 cups of soy milk, 100g of tofu, or 1/2 cup of textured soy protein
- 2 grams of plant sterols from foods such as Pro-Activ spread (one Tbsp. = 1gm). Other food sources include: avocado, soybeans, olive oil and green leafy vegetables
- Increased consumption of peas, beans, lentils, and peanuts (legumes).
Portfolio diet sample diet plan

- **Breakfast:** Hot oat bran cereal, soy beverage, strawberries, raw sugar, psyllium, oat bran bread, plant-sterol-enriched margarine, jam
- **Snack:** Almonds, fresh fruit
- **Lunch:** Black bean soup, sandwich made from soyi deli slices, oat bran bread, plant-sterol-enriched margarine, lettuce, tomato, and cucumber
- **Snack:** Almonds, psyllium, fresh fruit
- **Dinner:** Tofu (baked with eggplant, onions, and capsicum) pearled barley, vegetables (broccoli, cauliflower, etc.)
- **Snack:** Fresh fruit, psyllium, soy beverage

Diet Evidence: Effect on Lipid Parameters and CRP

46 dyslipidemia patients randomized to a low fat diet, a low fat diet and lovastatin (20 mg), or a dietary portfolio* for 4 weeks

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soluble fiber in diet (5–15 g/d) (oat bran, fruit, and vegetables)</td>
<td>↓LDL-C 1% to 10%</td>
</tr>
<tr>
<td>Soy protein (50g/d)</td>
<td>↓LDL-C 5% to 7%</td>
</tr>
<tr>
<td>Plant Sterol esters (2 g/d) (inhibit cholesterol absorption)</td>
<td>↓LDL-C 10% to 15%</td>
</tr>
<tr>
<td>Fish oils (3–9 g/d) (n-3 fatty acids)</td>
<td>↓Triglycerides 25% to 35%</td>
</tr>
</tbody>
</table>

Perspective Points

- The recommended dose of EPA + DHA is 1000 mg daily for prevention and up to 4000 mg daily for lowering triglycerides. (4 – 6 high strength capsules a day)
- **Dosing fish oil:** Fish oil capsules will often come in a total oil dose of 500-1000 mg.
- When dosing for therapeutic benefit, to look at the amount of EPA + DHA in each capsule.
- If 1 gm of fish oil capsule has 300 mg of EPA and 200 mg of DHA (total of 500 mg EPA + DHA), need to prescribe 2 capsules to = 1 gm of therapeutic omega-3 essential fatty acids.
- **Freezing the capsules and taking them at night can also reduce the side effect of burping and fishy taste.**
Lifestyle Modifications to Raise HDL-C Levels

- **Smoking Cessation**
  - HDL-C levels are lower in smokers (by 7%-20%), and return towards normal after smoking cessation
  - Whole Food, Plant Based, Mostly green

- **Weight Reduction**
  - For every 3 kg of weight loss, HDL-C levels increase by 2-4%, but only after stabilization at new lower weight
  - Exercise
    - Aerobic exercise (40 min, 3-4 x weekly) may increase HDL-C by 5-10%
    - Physical exercise also reduced TG and reduced statin initiation.

- **Exercise**
  - Aerobic exercise (40 min, 3-4 x weekly) may increase HDL-C by 5-10%
  - Physical exercise also reduced TG and reduced statin initiation.

- **Krill oil**
  - no outcomes data – higher doses needed

- **Policosanol**
  - wax derived from sugar cane may be promising

- **Coconut oil**
  - may be promising

- **Garlic**
  - limited effect on LDL-C in large study, Budoff has shown aged garlic may retard athersonclerosis progression.

- **Polyphenols**
  - anti-oxidant effects – resveratrol

- **Tea**
  - may reduce LDL by 0.5 mmol - more data needed.

- **Probiotics**
  - Lactobacillus plantarum may promote breakdown bile salts, absorb cholesterol from GUT – limited in Vivo studies. Small studies, industry sponsored

**What doesn't work / little evidence/ Could be promising**

- **Krill oil** – no outcomes data – higher doses needed
- **Policosanol** - wax derived from sugar cane - may be promising
- **Coconut oil** - ?? Raise HDL – limited studies
- **Garlic** – limited effect on LDL-C in large study, Budoff has shown aged garlic may retard atherosclerosis progression.
- **Polyphenols** – anti-oxidant effects – resveratrol
- **Tea** – may reduce LDL by 0.5 mmol - more data needed.
- **Probiotics** - Lactobacillus plantarum may promote breakdown bile salts, absorb cholesterol from GUT – limited in Vivo studies. Small studies, industry sponsored

**FROM NEW ENGLAND JOURNAL MEDICINE 2013**

**ORIGINAL ARTICLE**

Primary Prevention of Cardiovascular Disease with a Mediterranean Diet

Ramón Estruch, M.D., Dr P. Emilio Ros, M.D., Ph.D., Jordi Surni, M.D., M.P.H., María Isabel Casas, B.Pharm., Ph.D., Delores Colella, D.Pharm., Ph.D., Fernando Azu, M.D., Ph.D., Enric Gómez-Gracia, M.D., Ph.D., Valentín Ruíz-Gutierrez, Ph.D., Miguel Ferr, M.D., Ph.D., Josep Lluna, M.D., Ph.D., Rosa Maria Lamuela-Raventos, D.Pharm., Ph.D., Lluis Serra-Majem, M.D., Ph.D., Xavier Pinto, M.D., Ph.D., Josep Batlle, M.D., Ph.D., Miguel Angel Munoz, M.D., Ph.D., José V. Core, M.D., Ph.D., Jose Alberdi Martinez, D.Pharm., M.D., Ph.D., and Miguel Angel Martinez-Gonzalez, M.D., Ph.D., for the PREVEND Study Investigators.

Among persons at high cardiovascular risk, a Mediterranean diet supplemented with extra-virgin olive oil or nuts reduced the incidence of major cardiovascular events.

Most striking things is supplemental foods – not dietary advice- nuts(30g/day), EVOO (1 litre/week)

Reduction in cardiovascular events most evident in stroke.
Major causes of death in high income western society due to lifestyle related factors
Best approach is to use lifestyle to treat them where possible and appropriate
The absolute benefits of statins are smaller in primary prevention than in secondary prevention
Look for the presence of disease and calculate global CV risk
Dietary change is a powerful therapy in low to intermediate risk patients to lower LDL-C and a great adjunct in high risk patients to achieve target lipid levels
Overall dietary patterns matter most for chronic disease prevention, rather than focusing on single nutrients (e.g. low fat or low carbohydrate) or single foods