Moving from dyslipidemia to cardiovascular risk management

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Faculty/Presenter Disclosure

• Faculty/Presenter: G Michael Allan

• Relationships with commercial interests:
  – Grants/Research Support: Not applicable
  – Speakers Bureau/Honoraria: Not applicable
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  – Other:
    – Employed by University of Alberta, Alberta Health
    – Non-profit sources including Alberta College of Family Physicians, TOP, IHE, CADTH, etc.

• Chair a Primary Care Guideline on Lipid Management
Cholesterol: A brief history
Testing Cholesterol
Cholesterol is not considered a nutrient of concern for overconsumption.

Food and Nutrient Intakes, and Health: Current Status and Trends
Dyslipidemia

Cardiovascular Risk Reduction
“Do I need to Fast Doctor?”

• 2 large studies (33,000 Denmark, 200,000 Canada)
  – Without fasting:
    • LDL, Total Chol, HDL 0.1-0.2 lower & Trig 0.3 higher
    • Total Chol & HDL <2% change, at most ~10% LDL

• Non-fasting & fasting correlate equally with outcomes

• Biggest change in Trig (≤20%):
  – Contribute at 1/5 ratio to Total Chol.
  – 0.5mmol/L change would change Total Chol 0.1

Testing lipids: When to start & how often?

- In Canada: Start at 40 males and 50 females
  - NZ: 45 males & 55 females (10 yrs early if risk/race)

- Lipid levels: Individual variance = 7%
  - Average annual increase 0.5-1%

- <10% move from low to high risk in ~10 yrs
  - Unclear what moving to moderate risk is?

Testing lipids: When to start & how often?

• Bottom-Line: Start age 40 men and 50 women, and then every 5 years after. Fasting is generally not required. Always do risk assessment with each lipid test.
How do we decide who to treat?
The Fallacy of Risk Factors

• There are >300 risk factors
• Associations versus causations
• Consider a few:

Homocystiene
CRP
Ear lobe creases?
Biomarkers

• We identified 68 risk factors with ≥1 meta-analyses
  – 57 (84%) were positively associated in all analyses

• Get ~75% prediction with standard risk factors, & biomarkers add 0.01 - 0.40%
  – Example: best lipoprotein ≤0.18% vs WBC 0.36%

See Biomarker in Evidence review (Chapter 2).
Target Shooting
What do lipids tell us?

• Cholesterol is a risk factor for heart disease\(^1\)
  – High levels (low HDL) associated with increase risk
  – Not always consistent (\(?\)worse if LDL <3.4 mmol/L )
• It can be very helpful to figure out CVD risk
  – We’ll come back to that
• BUT,…
• It is not a disease (there are no symptoms).
• And causation is far from confirmed

Editorial

What does it take to put an ugly fact through the heart of a beautiful hypothesis?

Can we change the way we think?

The idolatry of the surrogate

Easier to measure surrogate outcomes are often used instead of patient important outcomes such as death, quality of life, or functional capacity when assessing treatments. John Yudkin, Kasia Lipska, and Victor Montori argue that our obsession with surrogates is damaging patient care
Understanding Risks
How do I decide who to treat?

• With every lipid test, Do a risk estimate.¹
  – Biggest predictor of benefit is NOT lipid levels or statin type/dose (potency): It is Risk.²

• Example of trials with risk and lower lipids.
  – ASCOT: enrolled on hypertension.³
  – Jupiter: enrolled on CRP.⁴
  – TNT: enrolled with past CVD but low lipids.⁵

How do I decide who to treat?

• We must base it on overall risk.
  – So, Use a validated risk calculator.
• Doing Risk Assessment most important,…
  – My Recommendation: If you use one, keep using it.
• Understand: What risk and over how long?
  – They vary in duration (e.g. 5 vs 10 years)
  – They vary in outcome (MI and cardiac death, CVD mortality, All cardiovascular disease, etc)
Agreement in Risk Calculators

## Variability in Calculating Risk

- 95% Confidence Intervals (CI) around 10-year predictions of CHD

<table>
<thead>
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<th>Framingham$^1$</th>
<th>Reynolds$^2$</th>
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<tbody>
<tr>
<td></td>
<td>Baseline</td>
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</tr>
<tr>
<td>CI (+/-)</td>
<td>1.5%</td>
<td>3%</td>
</tr>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Baseline</td>
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<tr>
<td>CI (+/-)</td>
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How Relative Risk Weighting of the same Risk factors varies by Calculator
(50-year-old, Female, Smoker, 160 Systolic BP, 7 Total Chol, 0.8 HDL, Non-Diabetic).
How do I decide who to treat?

- Use a validated risk estimation tool with every lipid test. Know what a patient's risk of CVD is.

Examples

- Know your numbers
  - [http://www.knowyournumbers.co.nz/](http://www.knowyournumbers.co.nz/)

- Edinburgh Risk Calculator

- BS Medicine Calculator
  - [http://chd.bestsciencemedicine.com/calc2.html#basic](http://chd.bestsciencemedicine.com/calc2.html#basic)
<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>HDL</th>
<th>LDL</th>
<th>Age</th>
<th>Smoke</th>
<th>BP</th>
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<td>Mr Norm</td>
<td>4.9</td>
<td>1.0</td>
<td>2.6</td>
<td>55</td>
<td>Yes</td>
<td>140</td>
<td>Not</td>
</tr>
</tbody>
</table>
Know your numbers: NZ

- **Good:** Shows you how you compare to ideal
  - Also, heart age can be informative for some people.
- **Bad:** Uses cholesterol change to estimate risk / benefit
• Good: Lots of Flexibility (time, display, equation)
• Bad: Uses cholesterol change to estimate risk / benefit
• Good: Actual benefits from research
• Bad: Less options and no life-time risk
With

**Relative Benefit:** 35%

Benefit often has nothing to do with the effect on the surrogate marker. At present, you can only select one intervention at a time.

**Harm of Intervention**
- Muscle aches and stiffness NNH 10-20 (similar to placebo in most studies)
- Increased liver function tests (3x normal) NNH 150
- Severe muscle/kidney damage NNH 10,000
- Nausea, constipation, diarrhea
- Drug Cost

**Risk Time Period**
- 10 years

**CVD Risk Status**
- 70.9% No event
- 18.9% Total with an event
- 10.2% Number who benefit from treatment

**NNT**
- 10 Number needed to treat

As with all risk calculators, calculated risk numbers are +/- 5% at best. More information.
Good Drugs?
What drug(s) should I offer?

• Reduce CVD and/or mortality.

• Lifestyle first: Samples of interventions over 2 yrs
  – Smoking: NNT for death in high risk = 11
  – Activity: NNT for any CVD in high risk = 6
  – Diet (Mediterranean): NNT for CVD in high risk = 12

# Things that change Cholesterol!!

<table>
<thead>
<tr>
<th>Drug/Intervention</th>
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<th>LDL</th>
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<tr>
<td>Torcetrapib</td>
<td>2</td>
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<td>+++</td>
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<td>+50%</td>
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<tr>
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<td>&gt;20</td>
<td>+</td>
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<tr>
<td>Omega 3</td>
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<tr>
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* To a statin
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* To a statin
What drug(s) should I offer?

• Bottom-Line: Regarding medications, only statins have a large body of consistent evidence showing meaningful reduction in CVD and small reductions in mortality.
Primary Prevention
no previous cardiovascular disease

Men aged ≥ 40
Women aged ≥ 50

OR

Compelling risk factor

Secondary Prevention
previous cardiovascular disease

Test non-fasting lipid

Estimate 10-year cardiovascular disease risk
(See calculator options*)

Risk < 10%
- Encourage lifestyle interventions
- Re-test 5 years with risk estimation

Risk 10-19%
- Encourage lifestyle interventions
- Suggest discussing moderate potency statin with patient

Risk ≥ 20%
- Encourage lifestyle interventions
- Strongly encourage discussing high potency statin with patient
- Consider ASA, balance risk/benefit

Statin Initiated?

No

Yes

• CK & ALT at baseline or for monitoring not required, perform as clinically indicated
• Encourage adherence
• Lipid monitoring not required
<table>
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<th>Intensity</th>
<th>Statin Options</th>
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<tbody>
<tr>
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<td>Pravastatin 10-20mg; Lovastatin 10-20 mg; Simvastatin 5-10mg; Atorvastatin 5mg; Rosuvastatin 2.5mg</td>
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<tr>
<td>High Intensity</td>
<td>Atorvastatin 40-80mg; Rosuvastatin 20-40mg</td>
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<table>
<thead>
<tr>
<th>Therapy</th>
<th>Estimating benefit (relative risk reduction)</th>
<th>Example if baseline risk estimated at 20% over 10 years</th>
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<td>Absolute Risk Reduction</td>
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<td>Smoking Cessation</td>
<td>Recalculate without smoking.</td>
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<td>Moderate 30%</td>
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<td></td>
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<tr>
<td>ASA</td>
<td>12%</td>
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* Example used a 53 year old male smoker with total cholesterol 5, HDL 1.2 and systolic BP 128, estimated risk
If dietary cholesterol doesn’t matter,...