2009 Dyslipidemia Guidelines

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Learning Objectives

- To review the new changes to the Canadian Dyslipidemia Guidelines (2009) to:
  - Discuss changes since 2006 guidelines
  - Review guiding principles
  - Treatment thresholds and targets
  - Treatment strategies
  - Monitoring strategies

Changes Since 2006

- Process – more transparency
- Involvement of the Canadian Vascular Coalition and CIHR
- Secondary and high-risk prevention:
  - Strategy better defined
  - Clinical studies on end-stage disease (advanced heart failure and hemodialysis)
- Primary prevention
  - Cardiovascular risk evaluation tools
  - Framingham risk score includes cardiovascular diseases (CVD)
  - Moderate risk defined as FRS 10–19% 10-year risk
  - Family history part of risk stratification
  - hsCRP part of risk stratification in moderate risk subjects whose LDL-C does not already suggest treatment (men > 50 and women > 60 years)
- Targets
  - Simplified target levels
  - Apo B role defined
  - Secondary targets evaluated according to available evidence

Guiding Principles

Who to Screen?

Patients should be screened every 1-to-3 years, with a full lipid profile and other investigations as indicated:

- All men ≥ 40 years and all women who are post-menopausal and/or ≥ 50 years
- Other adults of any age with CVD risk factors
  - Diabetes (maturity-onset diabetes)
  - Arteriosclerosis (arteriosclerosis)” “atherosclerotic vascular disease”
  - Hypertension (chronic hypertension, preeclampsia)
  - Family history of premature CVD
  - Familial hypercholesterolemia
  - Familial hypertriglyceridemia
  - Familial combined hyperlipidemia
  - Familial dysbetalipoproteinemia
  - Chronic renal disease (eGFR < 60 mL/min/1.73 m²)
  - HIV/AIDS treated with HAART therapy
  - Children of patients with severe dyslipidemia

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  - AstraZeneca, Sanofi-Aventis, Bl, Bayer, Merck, Pfizer, BMS

Risk Assessment

CV risk assessment remains imperfect

- Framingham Risk Score (CVD)
  - FRS has been shown to underestimate the risk of some patients (e.g., the young and women, and possibly those with the metabolic syndrome)

- Reynolds Risk Score (CVD)
  - Is an alternative and includes family history and hsCRP
  - Web-based version www.reynoldsriskscore.org

Total cardiovascular risk (total CVD) assessment, not only CAD is now recommended.

Short-term vs. Long-term Risk

- FRS estimates 10-year risk
- Family history increases risk 1.7–2.0 fold
- Risk levels can change over time
- CVD risk needs reassessment every 3-to-5 years


High Risk: Defined

Any one of the following = HIGH RISK:

- Documented evidence of atherosclerosis, PAD or CVD
- Diabetic adults (men > 45, women > 50)
- FRS or RRS 10-year risk score ≥ 20%

Requires intensive lifestyle modification advice
Requires pharmacological lowering of LDL-C


Moderate Risk: Defined

- Major health concern among midlife Canadians
- FRS 10-19% at 10 years
  - Family history and elevated hsCRP modulate risk
  - Reynolds Risk Score potentially useful
- Requires lifestyle changes
- May require pharmacological therapy
  - LDL-C > 3.5 mmol/L (Apo B > 1.0 g/L)
  - TC/HDL-C ratio > 5.0
  - hsCRP > 2 mg/L in men > 50, women > 60
  - hsCRP should be performed selectively
  - Patient’s input required


Low Risk: Defined

Framingham Risk Score (FRS) < 10%

Suggestions:

- Pharmacological treatment indicated for severe genetic dyslipidemia
- Use clinical judgment, proper timing
- Assess family history for added risk factors

Recommended Lifestyle Changes

- Smoking cessation, including the use of pharmacological therapy, as required
- A diet low in sodium and simple sugars, with substitution of unsaturated fats for saturated and trans fats and increased consumption of fruits and vegetables
- Caloric restriction to achieve and maintain ideal body weight
- Moderate to vigorous exercise for 30-60 minutes on most, and preferably all, days of the week
- Psychological stress management


Risk Assessment and Treatment Targets

<table>
<thead>
<tr>
<th>Risk Assessment</th>
<th>Initiate/consider treatment if any of the following</th>
<th>Primary Target: LDL-C</th>
<th>Class, Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIGH</td>
<td>Consider treatment in all patients</td>
<td>LDL-C &lt; 2 mmol/L or ≥ 50% ↓ LDL-C</td>
<td>Class I, Level A</td>
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<tr>
<td>MODERATE</td>
<td>LDL-C &lt; 2 mmol/L or ≥ 50% ↓ LDL-C</td>
<td>Primary alternate Target: ApoB &lt; 1.0 g/L</td>
<td>Class IIa, Level A</td>
</tr>
<tr>
<td>LOW</td>
<td>LDL-C &lt; 5.0 mmol/L or ≥ 50% ↓ LDL-C</td>
<td>Alternate treatment: ApoB &lt; 1.0 g/L</td>
<td>Class IIa, Level A</td>
</tr>
</tbody>
</table>

* Only screen for hsCRP in men > 50 and women > 60 if they are at moderate risk for CVD AND have LDL-C > 3.5 mmol/L.


Pharmacotherapy (LDL-C)

- Immediate treatment for high-risk patients
- Concomitant diet and lifestyle changes
- Statin monotherapy decreases LDL-C level - each 1.0 mmol/L reduction in LDL-C is associated with a corresponding 20–25% reduction in CVD mortality and non-fatal myocardial infarction. (Cholesterol Treatment Trials meta-analysis of 14 statin trials)
- A 50% relative reduction in LDL-C confers close to optimal benefit.
- A minority will need combination therapy
  - Ezetimibe, cholestyramine, niacin, fibrates
  - Clinical trials ongoing (combination versus monotherapy)

### Pharmacotherapy (HDL-C)
- Healthy lifestyle measures increase HDL-C
- Controversy surrounds low HDL-C treatment
- Genetic low HDL-C often poses no risk
- Current medications not effective
- Statins and fibrates have little effect
- New clinical trials ongoing


### Pharmacotherapy (Triglycerides)
- Levels for high-risk subjects not established
- Studies show gemfibrozil reduces CVD
- Gemfibrozil and statins contraindicated
- Diet/lifestyle first-line therapies for hypertriglyceridemia
- Fibrates prevent pancreatitis (with extreme hypertriglyceridemia)
- Impact of fibrates on CVD mortality unproven


### Pharmacotherapy (Combination Therapy)
- Statin + niacin helps dyslipidemia with low HDL-C
- Niacin raises HDL-C better than fibrates
- Crystalline niacin side effects
- Follow serum transaminase levels (hepatotoxicity)
- Awaiting AIM-High and HPS-THRIVE trial results
- Fibrates effectiveness/safety under study
- Omega 3 fatty acids + statins


### Safety and Laboratory Monitoring
- Measure baseline lipoproteins before pharmacological therapy
- Follow-up measurements semi-annually or with therapy changes
- Statin side effects: myalgias, myositis, rhabdomyolysis
- Niacin can elevate ALT
- Monitor parameters and adjust/withdraw doses
- Fibrates can raise plasma creatinine: avoid in renal insufficiency
- Re-evaluate renal functions and lipid parameters


### Summary
- 2009 guidelines provide direction in the evidence based management of patients with dyslipidemia
- Use of Framingham risk for Total CVD not just CAD
- Inclusion of family history in risk stratification
- Use of biomarkers such as hsCRP in moderate risk patients
- Simplified target levels
- Emerging role of ApoB
- Re-emphasis on lifestyle
- Statins as primary therapy

Use clinical judgment