

**Guideline for Lipid Testing in Adults (CLP017)**

**Revised: August, 2010**

**1. Purpose**

The OAML Guideline for Adult Lipid Testing (March, 2008) has been revised to be consistent with the Canadian Cardiovascular Society's (CCS) 2009 guideline, entitled "Guidelines for the diagnosis and treatment of dyslipidemia and prevention of cardiovascular disease in the adult."<sup>1</sup> Clinicians are encouraged to consult the reference publication for a more detailed interpretation.

Readers are reminded that OAML Guidelines will not apply to every clinical situation, nor can they serve as a substitute for sound clinical judgment.

**2. Lipid Assessment**

Assessment of dyslipidemia should include the following tests: total cholesterol (TC), high density lipoprotein cholesterol (HDL-C), triglycerides (TG), low density lipoprotein cholesterol (LDL-C) and a TC/HDL-C ratio. These tests can be ordered by checking "Lipid Assessment" on the Ontario Health Insurance Plan's (OHIP) laboratory requisition.

Blood samples for lipid assessment tests should be drawn after patients have been fasting (water only) for a minimum of 12 hours. For patients who are unable to fast for a full 12 hours (e.g. diabetic patients), an 8 hour fast (water only) can be accepted as a compromise.

**3. Other Laboratory Tests for Assessment of Cardiovascular Disease (CVD) Risk**

**(a) Apolipoprotein B (Apo B; Apo B-100)**

Apo B is the primary protein component of the atherogenic lipoproteins LDL and VLDL (very low density lipoprotein). One molecule of Apo B is associated with each LDL or VLDL molecule, making Apo B a good indicator of CVD risk. Serum Apo B concentrations > 0.80 g/L are associated with increased risk of CVD.

It has been suggested that Apo B is a more reliable indicator of CVD than LDL-C, since measurement of Apo B is a direct quantitation rather than a calculated measurement. In addition, the Apo B assay is not affected by hypertriglyceridemia, as is the case with the calculated LDL-C.

While LDL-C continues to constitute the primary target of therapy, the CCS 2009 guideline has identified Apo B as an alternate primary target of hyperlipidemia therapy. See section 5 of this Guideline.

**(b) Apolipoprotein A1 (Apo A1)**

Apo A1 is the protein component of HDL-C and its concentration is inversely related to risk of CVD. The CCS 2009 guideline includes target values for Apo B/A1 (the ratio of Apo B to Apo A1). See section 5 of this Guideline for the target values.

**(c) C-Reactive Protein (CRP)**

The CCS 2009 guideline identifies CRP as an independent modifier of CVD risk. CRP can be used as a secondary hyperlipidemia treatment target, once the primary targets have been achieved. See section 5 of this Guideline for the treatment target.

Several studies have now confirmed the correlation between an elevated baseline serum concentration of CRP and an increased risk of CVD.<sup>2-4</sup> However, CRP is an acute phase protein and as such, its serum concentration increases significantly during inflammatory and infectious disease states. *Therefore, when a CRP test is used to assess CVD risk, the blood must be collected when the patient is feeling “well”, to avoid an elevated result unrelated to CVD risk.* Clinical judgment must be exercised in the interpretation of any individual CRP result.

A specific test capable of detecting very low levels of CRP is required to accurately measure the baseline serum concentration of CRP. This test is now universally referred to as “high-sensitivity CRP” or “hs-CRP” and must be so ordered.

Quantitation of CRP is not warranted for all patients as part of their primary CVD risk assessment. Results from the JUPITER (Justification for the Use of Statins in Primary Prevention: An Intervention Trial Evaluating Rosuvastatin) study support the use of the hs-CRP test to identify two specific subgroups of patients who would otherwise not qualify for lipid-lowering drug therapy.<sup>5</sup> These subgroups are:

- Males >50 years, at moderate risk for CVD and with LDL-C levels <3.5 mmol/L and
- Females >60 years, at moderate risk for CVD and with LDL-C levels <3.5 mmol/L

Patients in these subgroups with hs-CRP test results >2.0 mg/L may benefit from statin therapy.

Apo B, Apo A1, ApoB/A1 and hs-CRP are not included in the “lipid assessment” profile, but can be ordered individually by writing the name of the required test(s) in the “**Other Tests**” section of the OHIP laboratory requisition. Currently, Apo A1, Apo B, and Apo B/A1 are not OHIP-insured tests.

#### 4. Ten Year Risk for the Development of Cardiovascular Disease

Ten year risk is defined as the probability of a subgroup of the population developing CVD within a 10 year period, if not treated. Assessment of this risk is determined by stratification of patients using clinical and laboratory data entered into the Framingham Risk Score (FRS) Tool (available at [www.oaml.com](http://www.oaml.com)). Although it is recommended that cardiovascular risk be reassessed every 3-5 years, more frequent reassessment of risk may be indicated.

The following are associated with increased risk of CVD:

- Age: Men >40 or women >50 years old
- Diabetes mellitus
- Hypertension\*
- Familial hyperlipidemia
- Family history of premature CVD (< 60 years old)
- Clinical evidence of atherosclerotic CVD

\* The Canadian Hypertension Education Program (CHEP) has set treatment targets of < 140/90 mmHg in healthy individuals and < 130/80 mmHg in people with diabetes or chronic kidney disease.

Recent studies confirm that both the Framingham and the United Kingdom Prospective Diabetes Study (UKPDS) risk engine tools underestimate CVD risk in patients with diabetes mellitus. Patients with diabetes mellitus have an extremely high long-term risk of CVD. Early intervention is therefore indicated, even when not warranted by the calculated 10 year risk for CVD.

Other demographic and/or clinical states that confer increased risk of CVD include:

- Smoking
- Obesity
- Erectile dysfunction
- HIV infection treated with highly active antiretroviral therapy (HAART)

- Physical evidence of hyperlipidemia, such as xanthelasma, xanthoma, or arcus corneae
- Evidence of chronic kidney disease or inflammatory/autoimmune disease, such as systemic lupus erythematosus, psoriasis, rheumatoid arthritis or hypothyroidism.

## 5. Risk Categories and Target Lipid Levels

The CCS 2009 guideline recommends treatment through change in health behaviour, and/or medications and includes lipid levels that trigger treatment initiation as well as treatment target values for individual patient risk groups.

### Summary of the CCS 2009 guideline's treatment initiation levels and lipid treatment target values

10 Year Risk of CVD Calculated using FRS Tool (see Section 4)	When to consider Initiation of Therapy	Primary Lipid Treatment Target Values For LDL-C and Apo B
<b>High Risk (<math>\geq 20\%</math>)</b> Includes patients with diabetes, atherosclerotic disease and/or peripheral vascular disease	Consider in all patients	LDL-C $< 2.00$ mmol/L <i>or</i> $\geq 50\%$ decrease Apo B $< 0.80$ g/L
<b>Moderate Risk (10%-19%)</b>	LDL-C $> 3.50$ mmol/L <i>or</i> TC/HDL-C ratio $> 5.0$ <i>or</i> hs-CRP $> 2.0$ mg/L**	LDL-C $< 2.00$ mmol/L <i>or</i> $\geq 50\%$ decrease Apo B $< 0.80$ g/L
<b>Low Risk (<math>&lt; 10\%</math>)</b>	LDL-C $\geq 5.00$ mmol/L	LDL-C $\geq 50\%$ decrease

\*\* Consider treatment when LDL-C levels are  $< 3.5$  mmol/L and hs-CRP is  $> 2.0$  mg/L, in men  $> 50$  years or in women  $> 60$  years of age.

#### Primary Therapeutic Goals:

When treatment is indicated, the primary objective for lowering lipid concentration for patients in each risk category (high, moderate or low) is described in the table above.

#### Secondary Therapeutic Goals:

Once the primary LDL-C target has been achieved, a secondary treatment target for all risk categories is TC/HDL-C ratio  $< 4.0$ , when clinically possible. The CCS 2009 guideline has also included the following target values as optional secondary goals:

TC/HDL-C	$< 4.0$
Apo B/A1	$< 0.80$
hs-CRP	$< 2.0$ mg/L
Triglyceride	$< 1.70$ mmol/L

#### Triglycerides:

Reduction of serum triglyceride levels independent of any reduction in serum cholesterol levels has not been definitively shown to reduce the risk of CVD. In most patients, hypertriglyceridemia is accompanied by elevated serum LDL-C and/or low serum HDL-C levels and accordingly it is best to just treat the cholesterol problems and let the triglyceride levels decline concomitantly.

The first line of therapy for modest to moderate hypertriglyceridemias remains diet, exercise, weight loss, reduced intake of refined carbohydrates and alcohol, and increased intake of omega-3 fatty acids. Please note that extremely high serum levels of triglycerides (>10 mmol/L) carry a significant risk for pancreatitis.

## 6. Monitoring Treatment

Recommended testing protocols prior to initiation of therapy and suggestions for the frequency of testing to monitor treatment(s) for dyslipidemia are provided below:

### a) For Patients on Diet Therapy

Lipid Assessment as described in section 2 should be repeated every 6-12 months.

### b) For Patients on Diet and Drug Therapy

Lipid Assessment as described in section 2 should be repeated every 6-12 months.

Either LDL-C and/or Apo B may be used to monitor adequacy of treatment.

In addition, it is recommended that the potential toxic effects of drug therapies are monitored using the tests listed in the table below. Testing is recommended prior to starting the medication(s), and after taking the medication(s) for 3 months.

Medication	Tests to Assess Toxicity
Statins	ALT, bilirubin direct & indirect, INR, CK
Fibrates	Creatinine
Niacin	ALT, glucose, HbA1c, Uric Acid

For patients on statin drugs, additional testing for hepatotoxicity is not supported by the available evidence and need not be performed. True statin-related hepatic damage is in fact exceedingly rare. While ALT elevations are seen in 1-3% of patients on statin therapy (depending on dose), 70% of these resolve spontaneously.

Evidence shows that ongoing CK monitoring for myotoxicity is also not recommended, although a baseline CK determination in patients at high-risk for muscle toxicity should be considered. Elevated CK levels in asymptomatic patients receiving a constant dose of medication are commonly due to physical exertion or muscle injury rather than being drug-induced.<sup>6</sup>

If signs/symptoms of myotoxicity or hepatotoxicity do develop in statin-treated patients, further testing should be performed to determine the cause(s).

Unlike the situation with the statin drugs, patients on fibrates and/or niacin do require monitoring for toxicity every 6 months, or earlier if symptoms develop, using the tests indicated in the table above.

If a dose change of any of the above drugs is implemented, additional toxicity testing at dose change and 3 months post-change is recommended.

If elevations of any of these analytes persist and a decision is made to continue with drug therapy, albeit at reduced dosages, more frequent monitoring is warranted.

## 7. Cited References

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### Acknowledgements

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**Warning & Disclaimer**

This Guideline was prepared to assist clinicians who order tests from community laboratories. Users must ensure that their own practices comply with all specific government policies and specific legislative and accreditation requirements that apply to their organizations. The Guideline is not meant to be construed as legal advice or be all inclusive on this topic. Given the complexity of legal requirements, users are reminded that whenever there is uncertainty regarding whether some aspect of a Guideline is appropriate for their practice or organization, further direction should be obtained from the Laboratory Director, their own professional association, college and/or legal counsel or appropriate government ministry.