Canadian Dyslipidemia Recommendations

The FAQ below presents information about the treatment of hyperlipidemia. Use shared decision making to individualize screening, assessment, and treatment. Information is from reference 1 unless otherwise denoted.

Question	Answer/Pertinent Information[1,14]

Who should be screened?	• Everyone ≥40 years of age.
	• Patients with a history of hypertensive disease in pregnancy, or who are postmenopausal.
	• Family history of hyperlipidemia or early CVD (i.e., in first-degree **male relative <55 years** of age or first-degree **female relative <65 years** of age).
	• Adults of **any age** who have one or more of the following risk factors:
	  • physical signs of hyperlipidemia (e.g., xanthoma)
	  • diabetes
	  • current smoker
	  • COPD
	  • hypertension
	  • HIV
	  • obesity (i.e., BMI ≥30 kg/m^2)
	  • CKD (ACR ≥3 mg/mmol or eGFR <60 mL/min/1.73m^2)
	  • inflammatory disease (e.g., lupus, psoriatic arthritis, rheumatoid arthritis, ankylosing spondylitis, inflammatory bowel disease)
	  • abdominal aneurysm
	  • evidence of ASCVD
	  • erectile dysfunction
	• Consider screening all adults of First Nations or South Asian ancestry.

What are the components of screening?	• History and physical. • Lipid profile, including apoB and non-HDL. Check Lp(a) once (e.g., at baseline only). • Non-fasting lipid profile is recommended for most patients (a fasting profile is still suggested for patients with known triglycerides >4.5 mmol/L). • Fasting glucose or A1c. • eGFR. Also consider ACR in patients with CKD, diabetes, or hypertension.

Question	Answer/Pertinent Information[1,14]
How is risk assessed and defined?	**Assessment** • Unless the patient has a statin-indicated condition (see below), calculate risk using modified FRS or Cardiovascular Life Expectancy Model. (The calculators are available at https://ccs.ca/calculators-and-forms/ or on the iCCS app from Google Play or App Store.) • Recheck every five years in patients 40 to 75 years of age or when patient health status changes such that a change in risk level is expected. **Risk levels for primary prevention** (primary prevention means patients without a statin-indicated condition, below): • **high risk**: FRS 10-year risk ≥20% • **intermediate risk**: FRS 10-year risk between 10% and 19.9% • **low risk**: FRS 10-year risk <10% **Statin-indicated conditions**: • ASCVD: history of MI, ACS, coronary angiography showing CAD, arterial revascularization, angina, peripheral artery disease, stroke, TIA, carotid disease; CAC >100 Agatston units; abdominal aortic aneurysm >3 cm in diameter or prior repair. • diabetes and age ≥40 years, or diabetes ≥15 years' duration and age ≥30 years, or diabetes with microvascular disease. • CKD (eGFR <60 mL/min/1.73m^2 or ACR ≥3 mg/mmol) ≥3 months' duration. • LDL ≥5 mmol/L or apo B ≥1.45 g/L or non-HDL ≥5.8 mmol/L (e.g., familial hypercholesterolemia). **Note**: non-HDL or apoB are the preferred indicators, especially if triglycerides are ≥1.5 mmol/L.

When should we treat with pharmacotherapy (i.e., a statin)?	• All **high-risk patients** (FRS 10-year risk ≥20%), and patients with a **statin-indicated condition** (above) with the following caveat regarding CKD: treat those age ≥50 years and **not** on dialysis.
	• **Intermediate** risk level **and**:
	  • LDL ≥3.5 mmol/L or apoB ≥1.05 g/L or non-HDL ≥4.2 mmol/L, or
	  • male ≥50 years of age or female ≥60 years of age with one additional risk factor (low HDL, impaired glucose tolerance, high waist circumference, smoker, hypertension), or presence of a risk modifier (e.g., CAC >0 Agatston unit, hs-CRP ≥2 mmol/L, Lp(a) ≥50 g/L, family history of premature CAD).
	• **Low** risk level **and**:
	  • **FRS 5% to 9.9%** with LDL ≥3.5 mmol/L or apoB ≥1.05 g/L or HDL ≥4.2 mmol/L, especially with risk modifiers (e.g., CAC >0 Agatston unit, Lp(a) ≥50 g/L, family history of premature CAD). These patients are essentially intermediate-risk patients.
	Note: non-HDL or apoB are the preferred indicators, especially if triglycerides are >1.5 mmol/L.

<table>
<tr><th>Question</th><th>Answer/Pertinent Information[1,14]</th></tr>
<tr><td>What are the recommended treatment goals?</td><td>

Secondary prevention (ASCVD): LDL <1.8 mmol/L or non-HDL <2.4 mmol/L or apoB <0.7 g/L.
Primary prevention: LDL ≤2 mmol/L or apoB ≤0.8 g/L or non-HDL ≤2.6 mmol/L.

Very high cholesterol (e.g., familial hypercholesterolemia) without ASCVD: LDL <2.5 mmol/L (or 50% reduction), or apoB <0.85 g/L, or non-HDL <3.2 mmol/L).

Note: non-HDL or apoB are the preferred targets, especially if triglycerides are ≥1.5 mmol/L.
For patients whose LDL are below thresholds and therapy is being tolerated, it is not generally required to reduce a patient's statin dose.[1]

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<tr><td>What lifestyle changes can be recommended?</td><td>

Lifestyle changes (cornerstone; recommended for all patients):

Quit tobacco.
Consume a healthy diet: Mediterranean, Portfolio, DASH, low glycemic load, or plant-based dietary patterns, including nuts, beans, olive oil, fruits, vegetables, fibre, and whole grains.
Maintain a healthy body weight.
Exercise for 150 minutes weekly, at moderate-to-vigorous intensity, and perhaps weight-training twice weekly.
Get adequate sleep.
Drink alcohol in moderation.
Manage stress.

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<tr><td>How are statins used to treat dyslipidemia?

Continued…</td><td>

Statins are first line for all patients who require pharmacotherapy.
High-intensity statins (or max tolerated dose) are used for secondary prevention (ASCVD).
The following table shows daily adult statin doses expected to provide similar LDL reduction:[4]

<table>
<tr><th>Statin</th><th>Low-intensity statin (expected LDL reduction <30%)</th><th>Moderate-intensity statin (expected LDL reduction 30 to <50%)</th><th>High-intensity statin (expected LDL reduction ≥50%)</th></tr>
<tr><td>Atorvastatin</td><td>NA</td><td>10 to 20 mg</td><td>40 to 80 mg</td></tr>
<tr><td>Fluvastatin</td><td>20 to 40 mg</td><td>80 mg</td><td>NA</td></tr>
<tr><td>Lovastatin</td><td>20 mg</td><td>40 to 80 mg</td><td>NA</td></tr>
<tr><td>Pravastatin</td><td>10 to 20 mg</td><td>40 to 80 mg</td><td>NA</td></tr>
<tr><td>Rosuvastatin</td><td>NA</td><td>5 to 10 mg</td><td>20 to 40 mg</td></tr>
<tr><td>Simvastatin</td><td>10 mg</td><td>20 to 40 mg</td><td>NA</td></tr>
</table>

In kidney impairment:

Atorvastatin dose is 10 mg max, with caution, if CrCl <30 mL/min.[7]
Fluvastatin is NOT recommended if CrCl <30 mL/min.[8]
Lovastatin doses >20 mg should be used with caution if CrCl <30 mL/min.[9]
Pravastatin starting dose is 10 mg in patients with significant kidney impairment.[10]

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Question	Answer/Pertinent Information[1,14]
How are statins used to treat dyslipidemia, continued	• Rosuvastatin starting dose is 5 mg (max 10 mg) if CrCl <30 mL/min/1.73m^2.[11] • Simvastatin starting dose is 5 mg, and doses >10 mg should be with caution if CrCl<30 ml/min.[12] • In patients with **liver impairment**: • Pravastatin starting dose is 10 mg in significant liver impairment.[10] • Rosuvastatin max dose is 20 mg in severe liver impairment.[11] • In patients of **Asian** ancestry, the **rosuvastatin** starting dose is 5 mg (max 20 mg).[11]
What non-statin treatment options are available?	• **Ezetimibe**: statin add-on for: • primary prevention: intermediate risk, high risk, CKD, or diabetes not meeting goal despite maximally tolerated statin dose (first-line add-on; bile acid sequestrant is an alternative but has less evidence). • primary prevention: very high cholesterol (e.g., familial hypercholesterolemia) not meeting goal with statin (alternative to PCSK9 inhibitor). • secondary prevention (ASCVD): patients with LDL 1.8 to 2.2 mmol/L or apoB 0.7 to 0.8 g/L or non-HDL 2.4 to 2.9 mmol/L despite maximally tolerated statin dose (+/- PCSK9 inhibitor). • **PCSK9 inhibitor**: statin add-on for: • secondary prevention (ASCVD): patients with LDL >2.2 mmol/L or apoB >0.8 g/L or non-HDL >2.9 mmol/L despite maximally tolerated statin dose (+/- ezetimibe). See **footnote b**. • primary prevention: very high cholesterol (e.g., familial hypercholesterolemia) not meeting goal despite maximally tolerated statin (alternative to ezetimibe). • **Icosapent ethyl**: consider as a statin add-on for: • patients with ASCVD with triglycerides 1.5 to 5.6 mmol/L despite maximally tolerated statin dose. • certain high-risk diabetes patients (see **footnote a**) without ASCVD, but with triglycerides 1.5 to 5.6 mmol/L despite maximally tolerated statin dose. • **Bile-acid sequestrant**: statin add-on for: • Primary prevention in CKD or diabetes not meeting goal despite maximally tolerated statin dose (ezetimibe is first-line add-on; bile acid sequestrant has less evidence). • **Role of niacin or fibrates**:[2] • Do NOT add to statin in patients who have achieved LDL goal on a statin. • Niacin's benefit is unclear in patients who do not achieve their LDL goal on a statin, or who have low HDL or high triglycerides. • Subgroup analysis suggests fibrate might benefit high-risk patients with low HDL and high triglycerides despite statin. • For details about individual agents, see our chart, *Non-Statin Lipid-Lowering Agents*.

Question	Answer/Pertinent Information[1,14]

Are statins appropriate for patients <40 years of age?	• Use **shared decision making** regarding statin decisions. Review risks, benefits, and alternatives. Share risk assessment results with the patient.[2]
	• Emphasize **lifestyle** changes (healthy diet, weight loss, exercise) to meet lipid and other goals as part of a **comprehensive** CVD risk reduction plan in all patients.[2]
	• Treat patients who have a **statin-indicated condition** (see "How is Risk Assessed and Defined?" section above).[2]
	• For patients **without** a statin-indicated condition**, assess CVD risk if appropriate** (see "Who should be screened" section of chart, above).
	  • 10-year risk for adults ≥30 years of age can be **estimated** using the FRS modified to include family history of premature CVD (https://medsquares.com/).[2] Use this result to help guide statin decisions.
	  • MyHealthCheckup (https://myhealthcheckup.com) can be used to calculate 10-year risk and cardiovascular age, and to show patients how various interventions might reduce their CVD risk.[2] This calculator can also be used as a teaching/discussion tool in patients <30 years of age by putting in "30" as the age.[3]
	  • In patients who have a strong family history of premature CVD, checking an **Lp(a) level** might help guide statin decisions.[2]
	• After estimating risk:
	  • Recommend a statin for **high-risk** patients (e.g., FRS ≥20%).[2]
	  • Advise only lifestyle changes for **low-risk** patients (e.g., FRS <10%).[2]
	  • Recommend a statin if 10-year risk is 10% to 19%, and LDL is ≥3.5 mmol/L. Consider a statin if LDL <3.5 mmol/L and apoB ≥1.2 g/L, or non-HDL ≥4.3 mmol/L.[2]

Can pregnant patients take statins?	• Although statins have been considered teratogenic, this is based on animal studies. Data from human pregnancies do not consistently suggest that statins cause birth defects; comorbidities confound these studies. • Miscarriage risk is unclear, and because statins inhibit cholesterol production, fetal harm remains a concern.[5] • In general, limit statin use during pregnancy to those patients who are very high-risk (e.g., homozygous familial hypercholesterolemia, secondary prevention).[1,5] The safest statin alternatives are bile acid sequestrants because they are not systemically absorbed.[6] • If the decision is made to use a statin in a patient of childbearing potential, a hydrophilic statin (pravastatin, rosuvastatin) may be preferred because they may transfer across the placenta less readily than other statins.[1] • In most cases, if a statin is used for primary prevention, advise use of effective contraception, and discontinuation of therapy before planning pregnancy or when pregnancy is discovered.[1] Most patients should stop their statin one to two months before planning a pregnancy, or as soon as they are aware of the pregnancy.[4,5] • Statins may pass into breast milk, posing a theoretical risk to the infant.[5] • When making decisions about lipid treatment in patients of childbearing potential, use of cardiovascular age is recommended over 10-year risk calculators.

Question	Answer/Pertinent Information[1,14]
How should patients ≥75 years of age be managed?	• There is good evidence to support statin use for **secondary prevention** of CVD events in these patients, although a mortality benefit has not been shown.[2] • Statins have not been studied extensively for **primary prevention** in these patients.[2] Use of risk estimators (FRS) in these patents may lead to overestimation of risk, and thus inappropriate prescribing of statins.[2] • However, statins should be discussed as part of overall cardiovascular risk reduction in "robust" elderly thought to be at higher CVD risk, because cardiovascular events (e.g., stroke) can lead to significant morbidity.[2]
How should statin patients be monitored?	Consider US guidelines:[4] • Check **transaminases** at baseline. Unless the patient has chronic stable liver disease, repeat only if signs/symptoms suggestive of liver toxicity occur. • Document any pre-existing muscle symptoms before starting a statin to establish a baseline. If severe muscle symptoms or objective weakness occur, hold the statin and check **creatinine kinase**. • Check fasting **lipid panel** four to 12 weeks after statin initiation or dosage change, then every three to 12 months. Check adherence to statin and lifestyle interventions if LDL drop is less than expected. In patients with chronic inflammatory disease or HIV, check fasting lipids before and four to 12 weeks after starting a chronic anti-inflammatory drug or antiretroviral. • Statins seem to cause a small increase in the risk of diabetes (~0.2% absolute risk per year, depending on statin, dose, and underlying diabetes risk factors). Consider diabetes screening in patients at elevated risk, especially those on a high-intensity statin.[13]
How should statin side effects be managed?	**General approach to side effects**:[2] • Confirm statin benefit justifies risk. • Hold statin and assess, then rechallenge with same or different statin, at same or lower dose or frequency. • Look for drug interactions. • Emphasize lifestyle modification. • Do not treat side effects with supplements. • See our FAQ, *Statin Muscle Symptoms: Managing Statin Intolerance*, for more information.

a. Icosapent ethyl: medication-treated diabetes patients ≥50 years of age with one additional risk factor: age ≥55 (male) or ≥65 (female) years; smoker or stopped in the past three months; blood pressure ≥140/90 mm Hg or treated; HDL ≤1.04 mmol/L (male) or ≤1.3 mmol/L (female); hs-CRP >3 mg/L; eGFR >30 to <60 mL/min/1.73 m^2; albuminuria; retinopathy; ABI <0.9 without claudication symptoms.

b. PCSK9 inhibitor: patients most likely to benefit are those with a recent ACS within the past year; or MI within two years or recurrent MI; diabetes or metabolic syndrome; vascular disease in more than one arterial bed; symptomatic peripheral artery disease; history of CABG; LDL ≥2.6 mmol/L; heterozygous; familial hypercholesterolemia; Lp(a) ≥60 g/L.

Abbreviations: ABI = ankle brachial index; ACR = albumin:creatinine ratio; ACS = acute coronary syndrome; apoB = apolipoprotein B; ASCVD = atherosclerotic cardiovascular disease; BMI = body mass index; CABG = coronary artery bypass graft; CAC = coronary artery calcium score; CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease; CrCl = creatinine clearance; CVD = cardiovascular disease; eGFR = estimated

glomerular filtration rate; FRS = Framingham Risk Score; HDL = high-density lipoprotein cholesterol; HIV = human immunodeficiency virus; hs-CRP = high-sensitivity C-reactive protein; LDL = low-density lipoprotein cholesterol; Lp(a) = lipoprotein (a); MI = myocardial infarction; TIA = transient ischemic attack

Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.

Levels of Evidence

In accordance with our goal of providing Evidence-Based information, we are citing the **LEVEL OF EVIDENCE** for the clinical recommendations we publish.

Level	Definition	Study Quality
A	Good-quality patient-oriented evidence.*	1. High-quality randomized controlled trial (RCT) 2. Systematic review (SR)/Meta-analysis of RCTs with consistent findings 3. All-or-none study
B	Inconsistent or limited-quality patient-oriented evidence.*	1. Lower-quality RCT 2. SR/Meta-analysis with low-quality clinical trials or of studies with inconsistent findings 3. Cohort study 4. Case control study
C	Consensus; usual practice; expert opinion; disease-oriented evidence (e.g., physiologic or surrogate endpoints); case series for studies of diagnosis, treatment, prevention, or screening.	

***Outcomes that matter to patients** (e.g., morbidity, mortality, symptom improvement, quality of life).

[Adapted from Ebell MH, Siwek J, Weiss BD, et al. Strength of recommendation taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. Am Fam Physician. 2004 Feb 1;69(3):548-56. https://www.aafp.org/pubs/afp/issues/2004/0201/p548.html.]

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Cite this document as follows: **Clinical Resource,** ***Canadian Dyslipidemia Recommendations. Pharmacist's Letter/Pharmacy Technician's Letter/Prescriber Insights.*** **July 2023. [390714]**