Cardiovascular Disease – Primary Prevention

DRAFT: For External Review

Effective Date: TBD

Online questionnaire available at: https://survey.health.gov.bc.ca/CVD

Scope

This guideline provides recommendations on the primary prevention of atherosclerotic cardiovascular disease (ASCVD/CVD) in adults aged ≥ 19 years without clinical CVD. It does not apply to patients with a known history of CVD or who currently have signs or symptoms of CVD, as this would require treatment and secondary prevention. The recommendations include how to assess a patient’s risk of CVD and how to manage their CVD risk factors.

Familial hypercholesterolemia (FH) and other genetic dyslipidaemias are out of scope of this guideline. Practitioners are recommended to access Canadian Cardiovascular Society guidelines that address this condition.¹

Key Recommendations

1. Assess CVD risk in all asymptomatic adults 40 years of age [Strong Recommendation, Strong Evidence].²⁻⁴

2. Health behaviour change (e.g., smoking cessation, healthy diet) is recommended as the first-line intervention for all risk groups in CVD primary prevention. Pharmacological management is recommended for high risk groups [Strong Recommendation, Strong Evidence].³⁻⁴

3. Initiate statin therapy only after objectively evaluating the person’s individual risks, benefits and preferences, and by having an individualized discussion with the patient. Initiate pharmaceutical management after considering the patients overall risk. [Strong Recommendation, Strong Evidence].

4. Treatment with a statin is expected to result in a significant reduction (50 - 30%) in the elevated baseline lipid levels. [Strong Recommendation, Strong Evidence].⁴⁻⁷

5. Use aspirin infrequently and know that it may benefit only certain individuals [Strong Recommendation, Strong Evidence].⁴⁻⁸⁻⁹

Assessment of Risk

➢ Who to Assess

Consider assessing CVD risk in:

- all asymptomatic men and women ≥ 40 to establish a baseline;
- all patients with pre-existing risk-related conditions (e.g., HTN, DM, CKD); and
- all patients with a known family history of premature CVD (defined as men aged < 55 years and women aged < 65 years in first degree relatives).∗

A patient may be reassessed in 1 to 5 years depending on their initial risk assessment or if their risk

* First degree relatives have a blood relationship to the patient: parents, brothers, sisters and children.
factors change significantly. For further details, refer to Appendix A: Primary Prevention of Cardiovascular Disease Algorithm.

- **Risk Assessment**
  
a. **Risk assessment tool:** The Framingham Risk Score (FRS) is recommended.†

The FRS, or any CVD risk assessment tool, is a risk estimation only of a patient’s CVD risk. Since these scores are plus or minus several percentage points, it is important to consider modifying the risk estimation based on other known risk factors (e.g., family history, ethnicity) and a practitioner’s clinical judgement. For example, the Canadian Cardiovascular Society (CCS) suggests that among individuals 30 - 59 years of age without diabetes, the presence of a positive history of premature CVD in first degree relatives increases a patient’s FRS by approximately 2-fold. ³

For risk assessment tools, refer to Associated Document: Resource Guide for Physicians - Tools for Primary Prevention of Cardiovascular Disease. Paper-based‡ scores use groups of measurements for the risk factors to assign points; and online calculators use the exact measurements for the risk factors. A risk score from an online calculator allows for a more individualized estimate of risk.

b. **Medical history:** Ask about risk factors. The major risk factors for CVD are age, gender, smoking, elevated blood pressure and elevated lipids.

  o Non-modifiable risk factors include³-⁵:
    - age - chronological and biological age,
    - gender (men)
    - family history of CVD or familial hyperlipidemia
    - ethnicity (First Nations, ⁶ South Asians (defined as Indian, Pakistani, Bangladeshi or Sri Lankan origin)¹¹
    - chronic kidney disease, chronic inflammatory diseases (e.g., rheumatoid arthritis, psoriatic arthritis, systemic lupus erythematosus, vasculitis (polyarteritis nodosa)), HIV infection, hypertensive diseases of pregnancy, Polycystic Ovarian Syndrome, gestational diabetes.

  o The modifiable risk factors are listed in Table 1.

† Though the FRS is recommended, there are other risk assessment tools. Refer to Associated Document: Resource Guide for Physicians – Tools for Primary Prevention of Cardiovascular Disease.
‡ For paper-based FRS, refer to Appendix B: Framingham 10-year Risk Estimation.
Table 1. Modifiable risk factors for CVD

<table>
<thead>
<tr>
<th>Modifiable Risk Factors</th>
<th>Mitigation Strategy</th>
<th>Resources</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking</td>
<td>Smoking cessation is probably the most important health behaviour intervention for the prevention of CVD. A linear relation exists between number of cigarettes smoked per day and CVD risk.</td>
<td>QuitNow BC Smoking Cessation Program HealthLinkBC: Quit Smoking HealthyFamiliesBC: Services to Help You Quit Smoking</td>
</tr>
<tr>
<td>Unhealthy diet</td>
<td>Diet rich in vegetables, fruits, legumes, nuts, whole grains, and lean protein (preferably fish) with inherent soluble and insoluble vegetable fiber has been consistently shown to be associated with lower all cause mortality.</td>
<td>HealthLink BC: Heart Healthy Eating DASH diet HealthyFamiliesBC: Food and Nutrition</td>
</tr>
<tr>
<td>Low physical activity/sedentary lifestyle</td>
<td>Engaging in at least 150 minutes per week of accumulated moderate to vigorous-intensity aerobic physical activity is associated with reduced ASCVD.</td>
<td>HealthLinkBC: Physical Activity HealthyFamiliesBC: Physical Activity HealthLinkBC: Referral form Canadian Physical Activity Guidelines</td>
</tr>
<tr>
<td>Excessive body weight / body mass index (BMI) / waist circumference</td>
<td>Adults diagnosed as obese (BMI ≥30 kg/m²) or overweight (BMI=25 to 29.9 kg/m²) are at increased risk of ASCVD, heart failure, and atrial fibrillation, compared with those of a normal weight.</td>
<td>HealthLink BC: Healthy Eating HealthLinkBC: Dietitian Services</td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td>Moderation in alcohol intake has been shown to reduce blood pressure. Limit alcohol consumption to ≤ 3 drinks per day for men and ≤ 2 drink per day for women.</td>
<td>HealthlinkBC: Low-risk drinking guidelines HealthyFamiliesBC: Alcohol Sense Canada’s Low-Risk Alcohol Drinking Guidelines BCGuidelines: Problem Drinking</td>
</tr>
<tr>
<td>Hypertension</td>
<td>High blood pressure has been shown to increase cardiovascular risk. Adapt health behaviours to reduce blood pressure levels. Pharmacological management may be needed for some patients along with lifestyle changes.</td>
<td>BCGuidelines: Hypertension - Diagnosis and Management HealthlinkBC: Lifestyle Steps to Lower Your High Blood Pressure Hypertension Canada: Hypertension and You</td>
</tr>
</tbody>
</table>
Diabetes Mellitus

Diabetes Mellitus is associated with 2-4 fold increase in CVD.\textsuperscript{30,31} Despite this strong link, the evidence is limited.\textsuperscript{30,32,33} Adherence to a healthier lifestyle in those with type 2 diabetes is associated with lower CVD risk.

Elevated lipid levels

High blood cholesterol is a risk factor for CVD. Maintaining optimal lipid levels is recommended.\textsuperscript{32,34,35}

Psychosocial factors (e.g. stress levels, depression, anxiety)

Psychosocial factors are strongly associated with adverse CVD outcome.\textsuperscript{36–38}

Socioeconomic factors (e.g. income, level of education, employment)

Socio-economic factors may confer a risk equivalent to traditional risk factors.\textsuperscript{36,39} Health education, community-based programs, behavioural counselling have all been suggested to address the impact of these factors on CVD risk.

Medications\textsuperscript{41}

Some medications, including thiazide diuretics, beta blockers, and oral estrogens can cause modest changes in serum lipid concentrations. Some of the atypical antipsychotic agents, in particular clozapine and olanzapine, have been associated with weight gain, obesity, hypertriglyceridemia, and development of diabetes mellitus.

\begin{tabular}{|l|l|l|}
\hline
\textbf{Diabetes Mellitus} & Diabetes Mellitus is associated with 2-4 fold increase in CVD.\textsuperscript{30,31} Despite this strong link, the evidence is limited.\textsuperscript{30,32,33} Adherence to a healthier lifestyle in those with type 2 diabetes is associated with lower CVD risk. & \textbf{BCGuidelines: Diabetes Care}
HealthLinkBC: Type 2 Diabetes
Diabetes Canada: Type 2 Diabetes
\hline
\textbf{Elevated lipid levels} & High blood cholesterol is a risk factor for CVD. Maintaining optimal lipid levels is recommended.\textsuperscript{32,34,35} & \textbf{HealthLinkBC: High Cholesterol}
Heart and Stroke, Canada: High Cholesterol
\hline
\textbf{Psychosocial factors (e.g. stress levels, depression, anxiety)} & Psychosocial factors are strongly associated with adverse CVD outcome.\textsuperscript{36–38} & \textbf{HealthLinkBC: Stress Management}
HealthLinkBC: Depression, Anxiety, and Physical Health Problems
Heart and Stroke, Canada: Lifestyle risk factors
\hline
\textbf{Socioeconomic factors (e.g. income, level of education, employment)} & Socio-economic factors may confer a risk equivalent to traditional risk factors.\textsuperscript{36,39} Health education, community-based programs, behavioural counselling have all been suggested to address the impact of these factors on CVD risk. & Links to some clinical practice tools that can help practitioners improve their performance in identifying and taking action on the root causes of poor health.\textsuperscript{40}
\hline
\textbf{Medications}\textsuperscript{41} & Some medications, including thiazide diuretics, beta blockers, and oral estrogens can cause modest changes in serum lipid concentrations. Some of the atypical antipsychotic agents, in particular clozapine and olanzapine, have been associated with weight gain, obesity, hypertriglyceridemia, and development of diabetes mellitus. & \\
\hline
\end{tabular}

c. **Physical examination:** conduct a focused cardiovascular physical examination, including assessing for any physical signs of dyslipidemias (premature corneal arcus, tendon xanthomas, and xanthelasmas).

d. **Test for lipids:** order full lipid profile including total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), non-high-density lipoprotein cholesterol\textsuperscript{5} (non-HDL-C), low-density cholesterol.

\textsuperscript{5} As of October 2013, a non-HDL-C measurement has been included in the full lipid profile or as a separate test on the Standard
lipoprotein cholesterol (LDL-C), and triglycerides (TG). Non-fasting lipid testing is acceptable.\textsuperscript{42}

e. **Test for type 2 diabetes:** order fasting plasma glucose (FPG) OR hemoglobin A1c level.

f. **Assess renal function:** eGFR test, urine ACR test

No other investigations are usually indicated in the risk assessment for asymptomatic patients unless stratification of intermediate risk patients is warranted (as outlined below). Although it may have a role in intermediate risk patients, for most patients, the routine testing of high-sensitivity C-reactive protein (hsCRP) is not indicated.\textsuperscript{2}

\section*{Assessment Stratification}

The patient can be classified as low, intermediate, or high risk for CVD based on the risk assessment. Any patient that is considered very high risk or is symptomatic (defined as secondary prevention - out of the scope of this guideline) should be treated accordingly. The FRS defines low risk as < 10\%, intermediate risk as 10 - 19\% and high risk as ≥ 20\%. These groupings are an arbitrary convenience, not a scientifically validated stratification.

A patient in the intermediate risk group may warrant a secondary assessment to raise or lower their risk stratification. However, further investigations may not be appropriate if the results would not influence the decision of how to manage the risk or treat the patient.

Secondary assessment should be done on patients for whom treatment decisions are uncertain. These assessments may include carotid ultrasound, hsCRP, or coronary artery calcium (CAC) scoring.

Conduct a shared-decision making conversation regarding lifestyle changes and if necessary pharmacological interventions. Consider using cardiovascular age during the discussion.

Cardiovascular (CV) age using the Cardiovascular Life Expectancy Model (CLEM) is calculated as the patient’s age minus the difference between his or her estimated remaining life expectancy (adjusted for coronary and stroke risk) and the average remaining life expectancy of Canadians of the same age and sex (https://chiprehab.com/index.html).\textsuperscript{3,43}

\section*{Management of Risk}

\subsection*{Lifestyle Management}

Lifestyle management needs to be strongly advocated as the first-line intervention for all risk groups. Adequate explanations and support should be provided to patients, so they clearly understand the nature and significance of CVD, and that they have the primary responsibility for adopting the healthy lifestyle changes required for reducing their risk.

*Use the new prevention visit code – 14066 for discussions related to management of modifiable risks. Diagnostics codes that require a prevention focused advice include smoking (786), unhealthy eating and medical obesity (783), physically inactive (785).*

a. **Smoking:** Promote smoking cessation and avoidance of second-hand smoke. Behavioral and pharmacotherapy interventions, alone or in combination, have been shown to improve rates of smoking cessation among the general adult population.\textsuperscript{44,45} Use a Screening, Brief Intervention and Referral to Treatment (SBIRT) approach.\textsuperscript{46} When talking to a patient about smoking: 1)
Screen for use 2) Conduct a Brief Intervention by providing risks of behaviour 3) Assess for willingness to quit 4) Support behaviour change by connecting to resources or treatment.

- For support to quit, refer patients to:
  - QuitNow at www.quitnow.ca/
  - HealthLinkBC Quit Smoking – Patients can call 8-1-1 or visit the website www.healthlinkbc.ca/health-feature/quit-smoking.
  - BC Smoking Cessation Program at www.gov.bc.ca/bcsmokingcessation
  - Smokers’ Helpline at 1-866-366-3667 or online at SmokersHelpline.ca

- For more information on effective pharmacological aids for smoking cessation, refer to BC Smoking Cessation program.

- Electronic cigarettes, also known as e-cigarettes, vaping (available with or without nicotine), may play a role as an aid in smoking cessation. At present time, their risk and benefits have not been clearly established and are not included as a pharmacological aid.

b. Physical activity: Support patient working towards 30 minutes or more of moderate to vigorous intensity physical activity on most days of the week (weekly total ≥ 150 minutes). 22,50

Behavioural interventions for healthful diet and physical activity have been shown to generally improve participants’ dietary intake and physical activity levels at 6 to 12 months of followup. 51 Techniques such as motivational interviewing techniques and brief action planning, that promote collaborative engagement with the patient, are more effective than exercise prescription alone for patients to achieve their physical activity goals.

- Exercise stress test may be warranted for previously sedentary people with additional risk factors for CVD who wish to undertake exercise more vigorous than brisk walking. 3

- For patients who are sedentary, consider a graduated exercise program using Brief Action Planning (BAP).

- Engage the patients in completing a Physical Activity Readiness Questionnaire for Everyone (PAR-Q+) and electronic Physical Activity Readiness Medical Examination (ePARmed-X+) to help them determine their readiness. Refer them to an accessible exercise program (such as healthy heart programs used by rural communities).

- For assistance with personalized physical activity advice, refer patient to a physical activity expert at HealthLinkBC by telephone 8-1-1 or website: www.healthlinkbc.ca.

c. Diet: Encourage a well-balanced diet. There are many dietary pathways to achieve CV risk reduction such as the Mediterranean diet (which emphasizes fruits, vegetables, legumes, whole grains and olive oil, with moderate consumption of fish, dairy products, poultry and minimizing meats and sweets) or the Dietary Approaches to Stop Hypertension (DASH) diet. 3

- For assistance with personalized diet advice, refer patient to a dietitian at HealthLinkBC by telephone 8-1-1 or website: www.healthlinkbc.ca.

d. Alcohol consumption: Screen for alcohol abuse. Use a Screening, Brief Intervention, and Referral for Treatment (SBIRT) approach.

Follow-up to Lifestyle Management
- Assess success of lifestyle intervention change at first follow-up.
- Assess cardiovascular risk using lipid profile (non-fasting)
For those with elevated lipids from their initial risk assessment, they may be followed up with a lipid profile in 3 – 6 months. If elevated lipids are still a concern, consider pharmaceutical management.

Table 2. Lipids levels that may be considered elevated relative to a patient’s risk level

<table>
<thead>
<tr>
<th>Risk Level</th>
<th>LDL-C (mmol/L)</th>
<th>Non-HDL-C (mmol/L)</th>
<th>ApoB* (g/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>≥ 2.0</td>
<td>≥ 2.6</td>
<td>≥ 0.8</td>
</tr>
<tr>
<td>Intermediate</td>
<td>≥ 3.5</td>
<td>≥ 4.3</td>
<td>≥ 1.2</td>
</tr>
<tr>
<td>Low</td>
<td>≥ 5.0</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Footnote: *An apoB test is not part of the initial risk assessment, but may be used as follow-up test.

Both non-HDL-C and apoB appear to be stronger predictors than LDL-C for major future cardiovascular events. Non-HDL-C may also be a better indicator of residual risk after statin therapy than LDL-C. Non-HDL-C has the slight advantage over apoB because it is the cheaper test ($14.72 vs $16.10).

Pharmaceutical Management

Acetylsalicylic Acid (ASA) Therapy

ASA therapy in Primary Prevention: Evidence would not support the use of aspirin in low and intermediate risk patients. The evidence for use of aspirin in high risk patients is currently uncertain.

Statin Therapy

For those patients with DM, CKD, or Familial Hyperdyslipidemia, statin therapy is indicated along with lifestyle interventions. Table 3 below is adapted from CCS guidelines, 2016.

Table 3. Statin-indicated Conditions

<table>
<thead>
<tr>
<th>Clinical Atherosclerosis</th>
<th>Abdominal Aortic Aneurysm</th>
<th>Diabetes Mellitus</th>
<th>Chronic Kidney Disease</th>
<th>LDL-C ≥5.0 mmol/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Myocardial infarction</td>
<td>- Abdominal aorta &gt;3.0 cm</td>
<td>- &gt;40 years of age</td>
<td>- &gt;3 months duration and ACR &gt;3.0 mg/mmol or eGFR &lt;60 ml/min/1.73m²</td>
<td></td>
</tr>
<tr>
<td>- Acute coronary syndromes</td>
<td>or Previous aneurysm surgery</td>
<td>or &gt;15 years duration and age ≥30 years of age</td>
<td>or Microvascular complications</td>
<td></td>
</tr>
<tr>
<td>- Stable angina</td>
<td></td>
<td></td>
<td></td>
<td>≥ 50 years of age</td>
</tr>
<tr>
<td>- Documented coronary disease by angiography</td>
<td></td>
<td></td>
<td></td>
<td>or Document familial hypercholesterolemia and excluded secondary causes</td>
</tr>
<tr>
<td>- Stroke</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- TIA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Documented carotid disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Peripheral artery disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Claudication and/or ABI &lt;0.9</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

BC Guidelines: Cardiovascular Disease – Primary Prevention
Draft for External Review
Updated June 29, 2020
The decision for initiating statin therapy should not be based on lipid levels alone and should be based on cardiovascular risk assessment.\textsuperscript{55}

A patient-specific discussion regarding the potential risks and benefits of statin use should be undertaken.

Two tools to assist in individualizing this discussion include:

1. Absolute CVD Risk/Benefit Calculator, website: bestsciencemedicine.com/chd/calc2.html
2. Cardiovascular Prevention Decision Aids, website: shareddecisions.mayoclinic.org

If statin therapy is decided upon, consider using a high potency statin (such as Atorvastatin or Rosuvastatin) considering efficacy and cost considerations. For dosages and adverse effects, refer to Appendix D: Pharmaceutical Table

Prior to the initiation of statin therapy:

a. inform the patient of adverse effects\textsuperscript{56-58} - effects may include muscle pain/myopathy/weakness, rhabdomyolysis, cataracts, elevated blood glucose and diabetes, acute renal failure, and liver injury;

b. educate the patient about any possible drug interactions with other prescribed medication, over-the-counter remedies and non-pharmaceuticals - consult a pharmacist or product monograph for a complete list; and

c. emphasize the importance of long-term compliance - it is estimated that 75\% of primary prevention patients aged > 65 years old started on statins stop their therapy within 2 years.\textsuperscript{59}

**Follow-up to Statin Therapy**

Within 3 - 6 months of the initiation of statin therapy, follow-up with the patient. This may include:

a. Measure lipids with a non-HDL-C or an apoB to assess patient adherence to statin therapy and any response to statin therapy (see Controversies in Care). A full lipid profile is not indicated. If both lifestyle management and a statin intervention have not been successful and lipids are still above target in the follow-up investigation, consider any other causes of elevated lipids (e.g., hypothyroidism, non-adherence).

b. Inquire about any adverse effects. The risk of statin-induced serious muscle injury, including rhabdomyolysis, is <0.1\%, and the risk of serious hepatotoxicity is \approx0.001\%.\textsuperscript{58} If muscle pain or weakness is reported in patients, measure CK. In asymptomatic patients, CK is not necessary. CK elevation is of concern only when it is significantly elevated (i.e., > 5X)\textsuperscript{56}

c. Measure liver transaminase enzyme (aspartate aminotransferase (ALT)) only once within the first 3 months of starting statin. If a patient has elevated liver transaminase enzymes, (greater than 3X the normal) consider secondary causes.\textsuperscript{58}

Further follow-ups as clinically needed. After the initial follow-up, routine monitoring of CK and ALT is not indicated for asymptomatic patients. More frequent routine monitoring with a full lipid profile, non-HDL-C or an apoB is not considered necessary for the sole purpose of treat-to-target.

**When to refer patients to a specialist**

Consider referral to a specialist when:

- Difficulty reaching treatment targets despite maximum-tolerated lipid-lowering therapy.
• Intolerance to or adverse effects of statin treatment. Statin intolerance needs to be well documented prior to referral.56

Controversies in Care

▶ Statin Therapy in Primary Prevention

Both the Canadian Cardiovascular Society (CCS)3 and the American Heart Association (ACC/AHA)4 acknowledge that there is high interindividual variability in LDL-C levels attained with statin therapy. They agree that recent studies have demonstrated lower CVD event rates with moderate-intensity and high-intensity statin therapy that outweighed the observable risks.3,4,60 The 2016 USPSTF systematic review of statin therapy in primary prevention showed a reduced risk of all-cause and cardiovascular mortality and ASCVD events and noted greater absolute benefits in those at greater baseline risk.61 both the CCS and ACC/AHA have recommended a more aggressive approach for statin use (see Table 4).

Table 4. Comparison of statin therapy recommendations between the CCS and ACC/AHA

<table>
<thead>
<tr>
<th>Criteria</th>
<th>CCS Recommendations</th>
<th>ACC/AHA Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk assessment tool</td>
<td>FRS - low risk, intermediate risk, high risk.</td>
<td>Pooled Cohort Equations - elevated risk (≥ 7.5%), not elevated risk (≤ 7.5%).</td>
</tr>
<tr>
<td>Intermediate risk</td>
<td>Treat with statins based on FRS (10-19%) if LDL-C ≥ 3.5 mmol/L.</td>
<td>Treat with statins based on Pooled Cohort Equations ASCVD risk ≥ 7.5% to &lt;20% 10-year.</td>
</tr>
<tr>
<td>High risk</td>
<td>Treat with statins based on FRS (≥ 20%).</td>
<td>Treat with statins based on Pooled Cohort Equations ≥ 7.5%.</td>
</tr>
<tr>
<td>LDL-C ≥ 5 mmol/L</td>
<td>Treat with statins.</td>
<td>Treat with statins.</td>
</tr>
<tr>
<td>DM</td>
<td>Treat with statins for those age ≥ 40 years, &gt; 15-year duration for age ≥ 30 years (type 1 diabetes mellitus [DM]), or with the presence of microvascular disease.</td>
<td>Treat with statins if patient aged 40 to 75 years.</td>
</tr>
<tr>
<td>CKD or high risk HTN</td>
<td>Treat with statins.</td>
<td>No specific recommendation.</td>
</tr>
</tbody>
</table>

▶ Statin Use for Primary Prevention in the Elderly Population

Guidance on use of statins in the elderly population (age >65 years) differs markedly between current national and international guidelines.62 The CCS and the ACC/AHA guidelines both recommend discussion of statin use with elderly patients who are believed to be at higher risk.3,4
Treat-to-Target Approach

Both the CCS and the ACC/AHA acknowledge there is controversy regarding the use of lipid treatment targets. However, they do believe that titrating statin therapy to achieve target lipid levels will have beneficial effects on CVD outcomes, particularly for high-risk patients.

- The ACC/AHA recommends a therapeutic response of 30% to 50% reduction in LDL-C.
- The CCS recommends treating high risk and intermediate risk patients to a specific LDL-C target of ≤ 2.0 mmol/L or a ≥ 50% reduction from baseline. Alternate targets include an apoB target of ≤ 0.8 g/L and a non-HDL-C target of ≤ 2.6 mmol/L. Low risk patients are recommended to be treated to 50% of their baseline LDL-C.
- This guideline is aligned with the current CCS (2016) recommendations in that treatment with statins is expected to result in a significant reduction (> 30%) in the elevated baseline lipid levels.

The CCS guidelines are currently under revision and may include changes to their lipid target recommendations.

Management of Other Clinical Conditions**

A number of clinical conditions contribute significantly to the risk of developing CVD.

- **Blood Pressure Control**
  Support lifestyle management, followed by the use of antihypertensive medications when appropriate, with consideration for the presence of other CVD risk factors.
  
  For more information, refer to BCGuidelines.ca - Hypertension: Diagnosis and Management.

- **Diabetes Care**
  Support lifestyle management followed by the use of medications when appropriate to control blood glucose. DM is a major risk factor for CVD, but a patient with DM does not need to be automatically considered high risk for CVD. CCS defines a patient with DM high risk for CVD with age ≥ 40 years, > 15-year duration for age ≥ 30 years (type 1 diabetes mellitus), or with the presence of microvascular disease. While the current FRS now includes diabetic status to individualize a type 2 DM patient’s risk, use the United Kingdom Prospective Diabetes (UKPDS) risk calculator or table, website: www.dtu.ox.ac.uk/riskengine.
  
  For more information, refer to BCGuidelines.ca - Diabetes Care.

- **CKD Management**
  In patients with CKD, the combination of simvastatin plus ezetimibe has shown benefit in reducing major atherosclerotic events when compared to placebo; however, no benefit on all-cause mortality has been demonstrated.63
  
  For more information, refer to BCGuidelines.ca - Chronic Kidney Disease - Identification, Evaluation and Management of Adult Patients.

**BC Guidelines for these clinical conditions with effective dates before this one may not reflect the updates in this guideline (e.g., the addition of non-HDL-C as a measurement).
Methodology

These guideline recommendations are tailored to support practice in British Columbia and are based on guidance by the Canadian Cardiovascular Society (CCS)³, American Cardiology/American Heart Association (ACC/AHA)⁴, European Society of Cardiology⁵. The guideline development working group used the AGREE II tool to assess the 6 domains and the overall guideline assessment. The working group looked at the three guidelines mentioned above carefully to identify the Scope of Purpose, Stakeholder Involvement, Rigor of Development, Clarity of Presentation, Applicability, Editorial Independence and made an assessment of the overall guideline quality. The AGREE II scores of the guidelines from the working group members showed some variation in domain scoring by individual members but overall agreement of the variation in the quality of these guidelines. The team gained a significant appreciation of both the methodology behind the three guidelines as well as the content and were able to use information from all of them in the GPAC guideline development. The working group started with the draft of the previous version of the GPAC guideline and studied the recommendations from the other three groups to inform this updated version. Where available, key references are provided. In situations where there is a lack of rigorous evidence, we provide best clinical opinion to support decision making and high-quality patient care. The guideline development process included significant engagement and consultation with primary care providers, specialists and key stakeholders, including the Provincial Laboratory Medicine Services. For more information about GPAC guideline development processes, refer to the GPAC handbook available at BCGuidelines.ca.

Resources


RACE: Rapid Access to Consultative Expertise Program – www.raceconnect.ca
A telephone consultation line for select specialty services for physicians, nurse practitioners and medical residents.

If the relevant specialty area is available through your local RACE line, please contact them first. Contact your local RACE line for the list of available specialty areas. If your local RACE line does not cover the relevant specialty service or there is no local RACE line in your area, or to access Provincial Services, please contact the Vancouver/Providence RACE line.

- **Vancouver Coastal Health Region/Providence Health Care:** [www.raceconnect.ca](http://www.raceconnect.ca) ☏️ 604-696-2131 (Vancouver) or 1-877-696-2131 (toll free) Available Monday to Friday, 8 am to 5 pm
- **Northern RACE:** ☏️ 1-877-605-7223 (toll free)
- **Kootenay Boundary RACE:** [www.divisionsbc.ca/kb/race](http://www.divisionsbc.ca/kb/race) ☏️ 1-844-365-7223 (toll free)
- **For Fraser Valley RACE:** [www.raceapp.ca](http://www.raceapp.ca) (download at Apple and Android stores)
- **South Island RACE:** [www.raceapp.ca](http://www.raceapp.ca) (download at Apple and Android stores) or see [www.divisionsbc.ca/south-island/RACE](http://www.divisionsbc.ca/south-island/RACE)

Pathways – PathwaysBC.ca
An online resource that allows GPs and nurse practitioners and their office staff to quickly access current
and accurate referral information, including wait times and areas of expertise, for specialists and specialty clinics. In addition, Pathways makes available hundreds of patient and physician resources that are categorized and searchable.

General Practice Services Committee – www.gpscbc.ca

- **Practice Support Program**: offers focused, accredited training sessions for BC physicians to help them improve practice efficiency and support enhanced patient care.
- **Chronic Disease Management and Complex Care Incentives**: compensates GPs for the time and skill needed to work with patients with complex conditions or specific chronic diseases.

## References


BC Guidelines: Cardiovascular Disease – Primary Prevention
Draft for External Review
Updated June 29, 2020

13


**Appendices**

**Appendix A: Primary Prevention of Cardiovascular Disease Algorithm**

**Appendix B: Framingham 10-year Risk Estimation**

**Appendix C: Lipid Testing in Primary Prevention of Cardiovascular Disease**

**Appendix D: Pharmaceutical Table - Statins**

**Associated Documents**

This guideline is based on scientific evidence current as of the effective date. The guideline was developed by the Guidelines and Protocols Advisory Committee. For more information about how BC Guidelines are developed, refer to the GPAC Handbook available at BCGuidelines.ca: GPAC Handbook.

THE GUIDELINES AND PROTOCOLS ADVISORY COMMITTEE

The principles of the Guidelines and Protocols Advisory Committee are to:

- encourage appropriate responses to common medical situations
- recommend actions that are sufficient and efficient, neither excessive nor deficient
- permit exceptions when justified by clinical circumstances

Contact Information:
Guidelines and Protocols Advisory Committee
PO Box 9642 STN PROV GOVT
Victoria, BC V8W 9P1
Email: hlth.guidelines@gov.bc.ca
Website: www.BCGuidelines.ca

Disclaimer
The Clinical Practice Guidelines (the guidelines) have been developed by the guidelines and Protocols Advisory Committee on behalf of the Medical Services Commission. The guidelines are intended to give an understanding of a clinical problem, and outline one or more preferred approaches to the investigation and management of the problem. The guidelines are not intended as a substitute for the advice or professional judgment of a health care professional, nor are they intended to be the only approach to the management of clinical problem. We cannot respond to patients or patient advocates requesting advice on issues related to medical conditions. If you need medical advice, please contact a health care professional.
Appendix A: Primary Prevention of Cardiovascular Disease Algorithm

Risk Assessment
Calculate risk in all adults ≥ 40 using the Framingham risk score (FRS) or another tool of choice.
Repeat screening every 5 years for FRS < 5%
Medical history, clinical assessment

FRS < 10% – Low Risk

Primary Prevention Conditions

Intermediate Risk
FRS 10-19%
and
LDL-C ≥ 3.5 mmol/L
or
Non-HDL-C ≥ 4.3 mmol/L
or
ApoB ≥ 1.2 g/L
or
men ≥ 50 and women ≥ 60 with one additional risk factor: low HDL-C, impaired fasting glucose, high waist circumference, smoker, hypertension

High risk
FRS ≥ 20%
or
alternative method

Statin-Indicated Conditions
• Clinical atherosclerosis
• Abdominal aortic aneurysm
• Most diabetics including ≥ 40 years of age or
>15 years duration and age ≥ 30 years of age or Microvascular complications
• LDL-C ≥ 5 mmol/L (genetic dyslipidemia)

Discuss health behaviour modifications: smoking cessation, healthy diet, physical activity, healthy weight, alcohol reduction

Consider Statin Treatment
Undertake a patient-specific discussion regarding the potential risks and benefits of statin use
Confirm adherence and barriers to use
Follow-up 3-6 months: LDL-C < 2.0 mmol/L or > 50% reduction or ApoB < 0.8 g/L or non-HDL-C < 2.8 mmol/L

Monitor
Response to health behaviour change
Statin therapy

Target achieved on maximally tolerated dose

Discuss add-on therapy
Evaluate CVD risk vs. additional side effects and cost

YES

NO

YES
Appendix B: Framingham 10-year Risk Estimation

**Step 1:** Calculate the patient’s total points using Table 1.

**Step 2:** Determine the patient’s 10-year CVD risk using Table 2. Double risk percentage if there is a history of premature CVD (men<55 and women<65) in patient’s first degree relatives.

**Step 3:** Determine the patient’s 10-year CVD risk level using Table 3.

---

**Table 1. Patient’s Total Points**

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Risk Points</th>
<th>MEN</th>
<th>WOMEN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30-34</td>
<td>+0</td>
<td>+0</td>
<td></td>
</tr>
<tr>
<td>35-39</td>
<td>+2</td>
<td>+2</td>
<td></td>
</tr>
<tr>
<td>40-44</td>
<td>+5</td>
<td>+4</td>
<td></td>
</tr>
<tr>
<td>45-49</td>
<td>+6</td>
<td>+5</td>
<td></td>
</tr>
<tr>
<td>50-54</td>
<td>+8</td>
<td>+7</td>
<td></td>
</tr>
<tr>
<td>55-59</td>
<td>+10</td>
<td>+8</td>
<td></td>
</tr>
<tr>
<td>60-64</td>
<td>+11</td>
<td>+9</td>
<td></td>
</tr>
<tr>
<td>65-69</td>
<td>+12</td>
<td>+10</td>
<td></td>
</tr>
<tr>
<td>70-74</td>
<td>+14</td>
<td>+11</td>
<td></td>
</tr>
<tr>
<td>75+</td>
<td>+15</td>
<td>+12</td>
<td></td>
</tr>
<tr>
<td>HDL-C (mmol/L)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;1.6</td>
<td>-2</td>
<td>-2</td>
<td></td>
</tr>
<tr>
<td>1.3-1.6</td>
<td>-1</td>
<td>-1</td>
<td></td>
</tr>
<tr>
<td>1.2-1.3</td>
<td>+0</td>
<td>+0</td>
<td></td>
</tr>
<tr>
<td>0.9-1.2</td>
<td>+1</td>
<td>+1</td>
<td></td>
</tr>
<tr>
<td>&lt;0.9</td>
<td>+2</td>
<td>+2</td>
<td></td>
</tr>
<tr>
<td>TC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;4.1</td>
<td>+0</td>
<td>+0</td>
<td></td>
</tr>
<tr>
<td>4.1-5.2</td>
<td>+1</td>
<td>+1</td>
<td></td>
</tr>
<tr>
<td>5.2-6.2</td>
<td>+2</td>
<td>+3</td>
<td></td>
</tr>
<tr>
<td>6.2-7.2</td>
<td>+3</td>
<td>+4</td>
<td></td>
</tr>
<tr>
<td>&gt;7.2</td>
<td>+4</td>
<td>+5</td>
<td></td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;120</td>
<td>-2</td>
<td>+0</td>
<td>-3</td>
</tr>
<tr>
<td>120-129</td>
<td>+0</td>
<td>+2</td>
<td>+0</td>
</tr>
<tr>
<td>130-139</td>
<td>+1</td>
<td>+3</td>
<td>+1</td>
</tr>
<tr>
<td>140-149</td>
<td>+2</td>
<td>+4</td>
<td>+2</td>
</tr>
<tr>
<td>150-159</td>
<td>+2</td>
<td>+4</td>
<td>+4</td>
</tr>
<tr>
<td>160+</td>
<td>+3</td>
<td>+5</td>
<td>+5</td>
</tr>
<tr>
<td>Diabetic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>YES</td>
<td>+3</td>
<td>+4</td>
<td></td>
</tr>
<tr>
<td>NO</td>
<td>+0</td>
<td>+0</td>
<td></td>
</tr>
<tr>
<td>Smoker</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>YES</td>
<td>+4</td>
<td>+3</td>
<td></td>
</tr>
<tr>
<td>NO</td>
<td>+0</td>
<td>+0</td>
<td></td>
</tr>
</tbody>
</table>

**Table 2. Patient’s 10-YR FRS Risk**

<table>
<thead>
<tr>
<th>Total Risk Points</th>
<th>10-YR CVD FRS Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>MEN</td>
<td>WOMEN</td>
</tr>
<tr>
<td>≤3</td>
<td>&lt;1.0%</td>
</tr>
<tr>
<td>&lt;6</td>
<td>1.1%</td>
</tr>
<tr>
<td>7-10</td>
<td>1.4%</td>
</tr>
<tr>
<td>11-13</td>
<td>1.6%</td>
</tr>
<tr>
<td>14-19</td>
<td>1.9%</td>
</tr>
<tr>
<td>20-29</td>
<td>2.3%</td>
</tr>
<tr>
<td>30-39</td>
<td>2.8%</td>
</tr>
<tr>
<td>40-49</td>
<td>3.3%</td>
</tr>
<tr>
<td>50-59</td>
<td>3.9%</td>
</tr>
<tr>
<td>60-69</td>
<td>4.7%</td>
</tr>
<tr>
<td>70-74</td>
<td>5.6%</td>
</tr>
<tr>
<td>80-89</td>
<td>6.7%</td>
</tr>
<tr>
<td>90-99</td>
<td>7.9%</td>
</tr>
<tr>
<td>100-119</td>
<td>9.4%</td>
</tr>
<tr>
<td>120-139</td>
<td>11.2%</td>
</tr>
<tr>
<td>140-159</td>
<td>13.3%</td>
</tr>
<tr>
<td>160-179</td>
<td>15.3%</td>
</tr>
<tr>
<td>180-199</td>
<td>18.4%</td>
</tr>
<tr>
<td>≥200</td>
<td>&gt;30.0%</td>
</tr>
<tr>
<td>≥210</td>
<td>&gt;30.0%</td>
</tr>
</tbody>
</table>

**Table 3. Patient’s Risk Level**

<table>
<thead>
<tr>
<th>Risk Level</th>
<th>10-YR FRS CVD Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>&lt;10%</td>
</tr>
<tr>
<td>Intermediate</td>
<td>10-19%</td>
</tr>
<tr>
<td>High</td>
<td>≥20%</td>
</tr>
</tbody>
</table>

The FRS, or any CVD risk assessment tool, is a risk estimation only of a patient’s CVD risk. Since these scores are plus or minus several percentage points, it is important to consider modifying the risk estimation based on other known risk factors (e.g., family history, ethnicity) and a practitioner’s clinical judgement.

**Abbreviations:** CVD cardiovascular disease; HDL-C high-density lipoprotein cholesterol; TC total cholesterol; SBP systolic blood pressure; YR year; FRS Framingham Risk Score.

**Derived from:**
Appendix C: Lipid Testing in Primary Prevention of Cardiovascular Disease (CVD)

Table 1. Lipid tests available for CVD Primary Prevention†

<table>
<thead>
<tr>
<th>Lipid Test</th>
<th>Purpose</th>
<th>MSP Cost*</th>
<th>Includes</th>
<th>Fasting Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full lipid profile</td>
<td>Risk assessment</td>
<td>$21.31</td>
<td>total cholesterol (TC); high-density lipoprotein cholesterol (HDL-C); low-density lipoprotein cholesterol (LDL-C); non-high-density lipoprotein cholesterol (non-HDL-C); and triglycerides (TG)</td>
<td>Yes - 8 to 10 hours</td>
</tr>
<tr>
<td>Non-HDL-C*</td>
<td>Follow-up</td>
<td>$14.72</td>
<td>TC; HDL-C</td>
<td>No</td>
</tr>
<tr>
<td>Apolipoprotein B (apoB)</td>
<td>Follow-up</td>
<td>$16.60</td>
<td>apoB</td>
<td>No</td>
</tr>
</tbody>
</table>

Footnotes:  † As per outlined on the Standard Outpatient Laboratory Requisition (SOPLR). As of October 2013, non-HDL-C has been included on the SOPLR. * Prices as of Laboratory Services Outpatient Payment Schedule. Revised, June 1, 2020. Available at: [http://www.bccss.org/clinical-services/bcaplm/health-professionals/laboratory-facilities](http://www.bccss.org/clinical-services/bcaplm/health-professionals/laboratory-facilities)

Full Lipid Profile Testing in CVD primary prevention

Indications for a full lipid profile include:
- CVD Risk Assessment
  Consider to assess CVD risk in:
  → all asymptomatic men and women ≥ 40 to establish a baseline;
  → all patients with pre-existing risk-related conditions (e.g., HTN, DM, CKD); and
  → all patients with a known family history of premature CVD (defined as men aged < 55 years and women aged < 65 years in first degree relatives).
- Reassessment of CVD Risk
  → A patient may be reassessed in 1 to 5 years depending on their initial risk assessment or if their risk factors change significantly.

Table 2. CVD Risk Reassessments

<table>
<thead>
<tr>
<th>Previous Risk Assessment Classification</th>
<th>Low risk</th>
<th>Intermediate risk</th>
<th>High risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reassess risk in</td>
<td>5 years or if the patient’s risk factors change significantly.</td>
<td>3 - 5 years or if the patient’s risk factors change significantly.</td>
<td>1 - 3 years or if the patient’s risk factors change significantly.</td>
</tr>
</tbody>
</table>

Non-HDL-C & ApoB Testing in CVD Primary Prevention

As of October 2013, non-HDL-C has been included in the full lipid profile and as separate measurement. It is calculated from subtracting HDL-C from TC; and represents all the cholesterol carried in lipoproteins other than HDL particles (e.g., intermediate density lipoproteins (IDL), very low density lipoproteins (VLDL), chylomicrons, chylomicron remnants, and lipoprotein(a)). Therefore, non-HDL-C measures the cholesterol present on all atherogenic lipoproteins.

ApoB is the primary protein for all atherogenic lipoproteins, and each atherogenic particle contains one molecule of apoB. Therefore, the concentration of apoB directly reflects the number of atherogenic particles.
Both non-HDL-C and apoB appear to be stronger predictors than LDL-C for major future cardiovascular events. Non-HDL-C may also be a better indicator of residual risk after statin therapy than LDL-C. Non-HDL-C has the slight advantage over apoB because it is the cheaper test ($14.72 vs $16.10).

*Indications for a non-HDL-C or apoB include:*
- Men and women with elevated lipids from their initial risk assessment may be followed up with a non-HDL-C or an apoB after 3 - 6 months to assess the impact of lifestyle management.
- Follow-up within 3 - 6 months of the initiation of statin therapy to assess patient adherence and response from statin therapy.

More frequent routine monitoring with a full lipid profile, non-HDL-C or an apoB is considered not necessary for the sole purpose of treat-to-target.
Appendix D: HMG-CoA reductase inhibitors (Statins)\textsuperscript{1-5, a,b}

The decision for initiating statin therapy should not be based on lipid levels alone. A patient-specific discussion regarding the potential risks and benefits of statin use should be undertaken.

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>trade name</th>
<th>dosage form and strengths</th>
<th>Low Intensity Dosage for &lt; 30% reduction in LDL\textsuperscript{c}</th>
<th>Moderate Intensity Dosage for 30-49% reduction in LDL\textsuperscript{c}</th>
<th>High Intensity Dosage for &gt;50% reduction in LDL\textsuperscript{c}</th>
<th>Annual Cost\textsuperscript{d}</th>
<th>PharmaCare Coverage</th>
<th>Therapeutic Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>atorvastatin</td>
<td>Lipitor, G</td>
<td>Tabs: 10, 20, 40, 80 mg</td>
<td>-</td>
<td>10-20 mg PO once daily</td>
<td>40-80 mg PO once daily</td>
<td>$70-90</td>
<td>Regular benefit, RDP Reference Drug</td>
<td>Max 10 mg in patients with renal impairment Metabolized by CYP3A4</td>
</tr>
<tr>
<td>rosuvastatin</td>
<td>Crestor, G</td>
<td>Tabs: 5, 10, 20, 40 mg</td>
<td>-</td>
<td>5-10 mg PO once daily</td>
<td>20-40 mg PO once daily</td>
<td>$50-80</td>
<td>Regular benefit, RDP Reference Drug</td>
<td>Start with 5 mg in patients of Asian descent Max 20 mg in patients with severe liver impairment</td>
</tr>
<tr>
<td>fluvastatin</td>
<td>Lescol XL, G</td>
<td>Caps: 20, 40 mg XL tabs: 80 mg</td>
<td>20-40 mg PO once daily</td>
<td>Caps: 40 mg PO BID XL tabs: 80 mg PO once daily</td>
<td>-</td>
<td>$175-580</td>
<td>Partial Benefit, RDP</td>
<td>Not recommended CrCl &lt; 30 ml/min Metabolized by CYP2C9 *Not indicated for primary prevention</td>
</tr>
<tr>
<td>lovastatin</td>
<td>mevacor, G</td>
<td>Tabs: 20, 40 mg</td>
<td>20 mg PO once daily</td>
<td>40 mg PO once daily</td>
<td>-</td>
<td>$190-350</td>
<td>Partial Benefit, RDP</td>
<td>Caution CrCl &lt;30 ml/min Metabolized by CYP3A4 *Not indicated for primary prevention</td>
</tr>
<tr>
<td>pravastatin</td>
<td>Pravachol, G</td>
<td>Tabs: 10, 20, 40 mg</td>
<td>10-20 mg PO once daily</td>
<td>40-80 mg PO once daily</td>
<td>-</td>
<td>$120-330</td>
<td>Partial Benefit, RDP</td>
<td>Start with 10 mg in patients with renal or liver impairment</td>
</tr>
<tr>
<td>simvastatin</td>
<td>Zocor, G</td>
<td>Tabs: 5, 10, 20, 40, 80 mg</td>
<td>10 mg PO once daily</td>
<td>20-40 mg PO daily</td>
<td>-</td>
<td>$60-100</td>
<td>Partial Benefit, RDP</td>
<td>Start with 5 mg in patients with severe renal insufficiency 80 mg is no longer recommended Metabolized by CYP3A4</td>
</tr>
</tbody>
</table>

**Adverse Effects of Statins**

The most common adverse events in patients treated with a statin include headache, GI disturbances, and myalgia.\textsuperscript{6} Meta-analyses of RCTs show no significant difference in the rate of adverse events, or in the rate of discontinuation due to adverse events between those taking a statin vs placebo.\textsuperscript{5,6} There continued to be no significant difference when looking at subgroups such as primary vs secondary prevention, the statin used or discontinuation specifically due to myalgia, muscle pain or myopathy.\textsuperscript{6,7} There is increasing awareness and concern about rare but serious adverse effects of statins.
The development of diabetes is associated with an NNH of 255 over 4 years.4,7 While the risk of myalgia is common (2-11%), the risk of more serious adverse events such as rhabdomyolysis is low (<0.1%; NNH 22,727 over 1 year)9 and is seen in patients with additional risk factors such as comorbidities (i.e. hypothyroid, renal/hepatic impairment), age (>80), genetic factors (i.e. SLCO1B1), or concurrent drug therapy (i.e. CYP3A4 inhibitors or inducers, gemfibrozil, protease inhibitors, cyclosporine).5,6 Advise patients to report muscle pain and/or weakness. CK elevation is of concern only when it is significantly elevated (i.e., >5X).4 Statins are associated with a dose-dependent risk of elevated liver enzymes (NNH of 96).4 Investigations are warranted if ALT >3 times the upper limit of normal.

Statin therapy was not associated with cognitive impairment in a meta-analysis of RCTs involving cognitively normal and cognitively impaired patients.10

Management options for the above adverse effects include statin discontinuation, switching to an alternative statin, dose decreases, and alternate day dosing.4,5 Data on efficacy of these management options is limited or missing.

Abbreviations: BID = twice daily; CrCl = creatinine clearance in milliliters per minute; G = generics available; mg = milligram; RDP = reference drug program; Tabs = tablets; XL = extended release.

Footnotes: * Not an exhaustive list; 1 Consult product monograph for detailed dosing instructions, dose adjustments for unique patient populations, and drug interactions. Product monographs available from hc-sc.gc.ca/dhp-mps/prodpharma/databasdon/index-eng.php, Health Canada advisories, warnings and recalls available from www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/index_e.html, and drug interaction software such as Lexicomp. 1 For normal renal and hepatic function. Consult product monograph for detailed dosing instructions and dose adjustments for unique patient populations. 4 Pricing is approximate as of June 2020 and does not include dispensing fees or additional markups.

PharmaCare Coverage Definitions: Regular Benefit: Eligible for full reimbursement*; does not require Special Authority. Limited Coverage: Requires Special Authority to be eligible for reimbursement*. RDP: Reference Drug Program. Drugs included in the RDP are comparable agents of the same therapeutic class. RDP Reference Drug: Eligible for full reimbursement* within the therapeutic class, subject to Benefit status of the therapeutic class. Partial Benefit RDP: Eligible for limited reimbursement* under the RDP program up to the price of the Reference Drug. Non-benefit: Not eligible for coverage under any circumstances.

Note: Information on which products PharmaCare covers can be obtained using the B.C. PharmaCare Formulary Search (www.health.gov.bc.ca/pharmacare/benefitslookup/).

*Reimbursement is subject to the rules of a patient’s PharmaCare plan, including any deductibles. In all cases, coverage is subject to drug price limits set by PharmaCare. See: www.health.gov.bc.ca/pharmacare/plans/index.html and www.health.gov.bc.ca/pharmacare/policy.html for further information.

References:
5. Jobson MD. UpToDate [Internet]. Waltham, MA: UpToDate Inc.; c2019 [Accessed June 4, 2020]
6. e-CPS [Internet]. Ottawa, ON: Canadian Pharmacists Association Monograph: HMG-CoA Reductase Inhibitors (Statins); c2019 [Accessed June 4, 2020]
Risk Assessment Resources

There are a number of tools to assist in determining a patient’s risk to cardiovascular disease (CVD). Each tool varies in the risk factors, time frame and CVD outcomes. There are known limitations to each of the risk tools, and the risk categories are based on consensus rather than by scientific evidence.

Older risk tools used only hard endpoints (e.g., coronary heart disease (CHD) deaths) to calculate one’s risk. Newer risk tools have expanded their endpoints to include more CVD outcomes.

NOTE: The FRS, or any CVD risk assessment tool, is a risk estimation only of a patient’s CVD risk. Since these scores are plus or minus several percentage points, it is important to consider modifying the risk estimation based on other known risk factors (e.g., family history, ethnicity) and a practitioner’s clinical judgement. For example, the Canadian Cardiovascular Society (CCS) suggests that among individuals 30 - 59 years of age without diabetes, the presence of a positive history of premature CVD in first degree relatives increases a patient’s FRS by approximately 2-fold.

Risk Assessment Tools

- **Canadian Cardiovascular Society**: estimates the 10-year risk of developing CVD, with paper-base and an online calculator, using FRS. [https://www.ccs.ca/en/resources/calculators-forms](https://www.ccs.ca/en/resources/calculators-forms)


- **Absolute CVD Risk/Benefit Calculator**: from James McCormack (for patients age ≤80) [http://chd.bestsciencemedicine.com/calc2.html](http://chd.bestsciencemedicine.com/calc2.html)

- **The University of Edinburgh Cardiovascular Risk Calculator**: risk calculator that estimates 10-year CVD risk using the FRS, ASSIGN or the Joint British Societies / British National Formulary. Includes risk calculators that also estimate the 10-year risk for CHD, heart attack or stroke. [https://www.bloodpressureclinic.ed.ac.uk/calculating-cardiovascular-risk](https://www.bloodpressureclinic.ed.ac.uk/calculating-cardiovascular-risk)

- **The United Kingdom Prospective Diabetes Study (UKPDS)**: risk calculator that estimates the 10-year CHD and stroke risk for adults with type 2 diabetes. [www.dtu.ox.ac.uk/riskengine/](http://www.dtu.ox.ac.uk/riskengine/)

- **QRISK3**: risk calculator (for patients age ≤84) that estimates the 10-year risk of a heart attack or stroke. [https://qrisk.org/three/](https://qrisk.org/three/)

Lifestyle Management Resources

Smoking

- QuitNow at [www.quitnow.ca/](http://www.quitnow.ca/)
- HealthLinkBC Quit Smoking – Patients can call 8-1-1 or visit [www.healthlinkbc.ca/health-feature/quit-smoking](http://www.healthlinkbc.ca/health-feature/quit-smoking).
- Smokers’ Helpline at 1-866-366-3667 or visit [SmokersHelpline.ca](http://SmokersHelpline.ca)
- For more information on effective pharmacological aids for smoking cessation, refer to BC Smoking Cessation program at [www.gov.bc.ca/bcsmokingcessation](http://www.gov.bc.ca/bcsmokingcessation).
• Healthy Families BC quit smoking resources at HealthyFamiliesBC: Services to Help You Quit Smoking

Physical Activity
• For patients who are sedentary, consider a graduated exercise program using Brief Action Planning (BAP).
• Engage the patients in completing a Physical Activity Readiness Questionnaire for Everyone (PAR-Q+) and electronic Physical Activity Readiness Medical Examination (ePARmed-X+) to help them determine their readiness. Refer them to an accessible exercise program (such as healthy heart programs used by rural communities).
• For assistance with personalized physical activity advice, refer patient to a physical activity expert at HealthLinkBC or by calling 8-1-1.
• Canadian Physical Activity and Sedentary Behaviour Guidelines provide patients with guidelines and resources to help become more active.

Healthy Diet
• Dietitian Services at HealthLinkBC (formerly Dial-A-Dietitian) provides free nutrition information and resources. Call 8-1-1, or visit HealthLink BC: Heart Healthy Eating, DASH diet
• Healthy Families BC nutrition resources at HealthyFamiliesBC: Food and Nutrition
• Public Health Agency of Canada provides resources to help patients make wise choices about healthy living, including increasing physical activity and eating well. https://www.canada.ca/en/services/health/food-nutrition.html
• Heart & Stroke Foundation of BC & Yukon provides resources on heart diseases and stroke.
• St Paul’s Heart Centre provides information on the prevention of cardiovascular disease. As well, it has a Healthy Heart Program Prevention Clinic for those with a referral.
• Personal Health Risk Assessment Incentive (14066): This General Practice Services Committee (GPSC) fee is payable to the general or family practitioner who undertakes a Personal Health Risk Assessment with a patient belonging to one of the at-risk populations (smoker, unhealthy eating, physically inactive, obese), either as part of proactive care or in response to a request for preventive care from the patient. http://www.gpscbc.ca/what-we-do/incentives/fees

Statins – Resources for a Patient Discussion
• Cardiovascular Prevention Decision Aids (Statin & Aspirin): from the Mayo Clinic https://shareddecisions.mayoclinic.org/
• NNT - Statin for heart disease prevention without prior heart disease: from the NNT https://www.thennt.com/

Other BC Guidelines
• BC Guidelines at www.BCGuidelines.ca
  o Hypertension: Diagnosis and Management
  o Diabetes Care
  o Chronic Kidney Disease - Identification, Evaluation and Management of Adult Patients
  o Stroke and Transient Ischemic Attack - Management and Prevention
  o Overweight and Obese Adults: Diagnosis and Management