



## Cardiovascular Disease – Primary Prevention

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### Scope

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This guideline provides recommendations on the primary prevention of cardiovascular disease (CVD) in adults aged  $\geq 19$  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.

### Key Recommendations

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- Assess asymptomatic men (aged  $\geq 40$ ) and asymptomatic women (aged  $\geq 50$ ) for cardiovascular (CVD) risk.
- Consider lifestyle management (e.g., smoking cessation, healthy diet) as the first-line intervention for all risk groups in CVD primary prevention.
- Manage other clinical conditions (e.g., diabetes (DM), hypertension (HTN), chronic kidney disease (CKD)) in all risk groups. DM is a major risk factor for CVD, but do not automatically consider a patient with DM high risk for CVD.<sup>1</sup>
- Initiate statin therapy as a second-line intervention only after evaluating the risks and benefits objectively, by having an individualized discussion with the patient.
- Treatment with a statin is expected to result in a significant reduction ( $> 30\%$ ) in the elevated baseline lipid levels. Treating to a specific lipid target is not recommended.<sup>2</sup>

### Assessment of Risk

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#### ► Who To Assess

Consider assessing CVD risk in:

- all asymptomatic men at age  $\geq 40$  and asymptomatic women at age  $\geq 50$  to establish a baseline;
- all patients with pre-existing risk-related conditions (e.g., hypertension (HTN), diabetes (DM), chronic kidney disease (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<sup>1</sup>).

All symptomatic patients should be assessed for CVD risk, but treatment of symptoms is out of the scope of this guideline.

A patient may be reassessed in 1 to 5 years depending on their initial risk assessment or if their risk factors change significantly. For further details, refer to *Appendix A: Primary Prevention of Cardiovascular Disease Algorithm*.

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<sup>1</sup> First degree relatives have a blood relationship to the patient: parents, brothers, sisters and children.

## ► Risk Assessment Investigations:

- a. Risk assessment tool - The Framingham Risk Score (FRS) is recommended.<sup>1</sup>

**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 DM, the presence of a positive history of premature CVD in first degree relatives increases a patient's FRS by approximately 2-fold.<sup>3</sup>

For risk assessment tools, refer to *Associated Document: Cardiovascular Disease - Primary Prevention: Resource Guide for Physicians*. Paper-based<sup>2</sup> 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 (modifiable and non-modifiable) in Table 1. The major risk factors for CVD are age, gender, smoking, elevated blood pressure and elevated lipids.

**Table 1. Modifiable and non-modifiable risk factors for CVD**

Modifiable Risk Factors	Non-modifiable Risk Factors
<ul style="list-style-type: none"> <li>• <i>smoking</i><sup>4-6</sup></li> <li>• <i>low physical activity levels / sedentary lifestyle</i><sup>4,7,8</sup></li> <li>• <i>poor diet</i><sup>4,9</sup></li> <li>• <i>excessive body weight / body mass index (BMI) / waist circumference</i><sup>4,10,11</sup></li> <li>• <i>elevated blood pressure/hypertension</i><sup>4</sup></li> <li>• <i>diabetes</i><sup>4,12,13</sup></li> <li>• <i>elevated lipid levels</i><sup>4</sup></li> <li>• <i>socioeconomic factors</i><sup>14</sup> (e.g., income, level of education, employment)</li> <li>• <i>psychosocial factors</i><sup>4,15,16</sup> (e.g., stress levels, depression, anxiety)</li> </ul>	<ul style="list-style-type: none"> <li>• <i>age</i> - chronological and biological age (frailty)<sup>17</sup></li> <li>• <i>gender</i> - men</li> <li>• <i>family history of CVD</i><sup>18</sup> or <i>familial hyperlipidemia</i></li> <li>• <i>ethnicity</i><sup>19-21</sup> - First Nations, South Asians (defined as Indian, Pakistani, Bangladeshi or Sri Lankan origin)</li> <li>• <i>chronic kidney disease</i><sup>22</sup></li> <li>• <i>certain autoimmune inflammatory diseases</i><sup>23</sup> (e.g., rheumatoid arthritis, psoriatic arthritis, systemic lupus erythematosus, vasculitis (polyarteritis nodosa))</li> </ul>

- c. Physical examination - conduct a focused cardiovascular physical examination, including assessing for any physical signs of dyslipidemias.
- d. Test for lipids - order full fasting lipid profile including: total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), non-high-density lipoprotein cholesterol<sup>3</sup> (non-HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglycerides (TG).
- e. Test for type 2 diabetes - order fasting plasma glucose (FPG) **OR** hemoglobin A1c level.

No other investigations are usually indicated in the risk assessment for asymptomatic patients unless stratification of intermediate risk patients is warranted (as outlined below). Though it may have a role in intermediate risk patients, routinely testing most patient's high-sensitivity C-reactive protein (hsCRP) is not indicated.

<sup>1</sup> Though the FRS is recommended, there are other risk assessment tools. Refer to *Associated Document: Cardiovascular Disease-Primary Prevention: Resource Guide for Physicians*.

<sup>2</sup> For paper-based FRS, refer to *Appendix B: Framingham 10-year Risk Estimation*.

<sup>3</sup> 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 Outpatient Laboratory Requisition*. For more information, refer to *Appendix C: Lipid Testing in Primary Prevention of Cardiovascular Disease*.

## ► 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 should be treated accordingly, and this would be considered as secondary prevention (out of the scope of this guideline). 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 may include exercise stress test, carotid ultrasound, hsCRP, or coronary artery calcium (CAC) scoring. In BC, CAC scoring is a patient pay test for primary prevention (i.e., those patients without signs or symptoms of CVD).<sup>1</sup>

## Management of Risk

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### 1. 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.

#### ► Smoking

Promote smoking cessation and avoidance of second-hand smoke.<sup>5,6</sup> When talking to a patient about quitting: 1) ask the patient about their degree of tobacco use, 2) advise them to quit, 3) assess for willingness to quit, 4) assist in a quit attempt, 5) arrange for a follow-up.

- For assistance to quit, refer patients to QuitNow at HealthLinkBC by telephone at 8-1-1 or website: [www.quitnow.ca](http://www.quitnow.ca).
- For more information on effective pharmacological aids for smoking cessation, refer to BC Smoking Cessation program at website: [www.health.gov.bc.ca/pharmacare/stop-smoking/](http://www.health.gov.bc.ca/pharmacare/stop-smoking/). Electronic cigarettes, also known as e-cigarettes (available with or without nicotine) may play role as an aid in smoking cessation. At present time, their risk and benefits have not been clearly established<sup>24</sup> and are not included as a pharmacological aid.

#### ► Physical Activity

Encourage 30 minutes or more of moderate to vigorous intensity physical activity on most days of the week (weekly total ≥ 150 minutes).<sup>25,26</sup> Write the patient a prescription for physical activity. Prescriptions for those at high risk, with other conditions, or who are starting from a sedentary lifestyle, may need to be adapted. Consider an exercise stress test for previously sedentary people with additional risk factors for CVD who wish to undertake exercise more vigorous than brisk walking.

- For assistance, refer patients to the Physical Activity Line (PAL) by telephone at 1-877-725-1149 (Toll Free) or 604-241-2266 or website: [www.physicalactivityline.com](http://www.physicalactivityline.com).

#### ► Diet

Recommend a well-balanced diet.<sup>9</sup> This may include the Mediterranean diet<sup>27,28</sup> (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.<sup>29</sup> Consumption of fish or fish oil supplements, high in omega-3 fatty acids may reduce CVD risk.<sup>30</sup>

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

#### ► Body Composition

Recommend maintaining a healthy body weight and composition. Emphasize healthy diet and physical activity prescription in patients with a BMI ≥ 30.

- For more information, refer to [BCGuidelines.ca](http://BCGuidelines.ca) - *Overweight and Obese Adults: Diagnosis and Management*.

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<sup>1</sup> According to the Medical Services Commission (MSC) Payment Schedule (April 2013), cardiac CT/CT coronary angiography may be covered by Medical Services Plan (MSP), but not for the purpose of CAC scoring.

## Follow-up to Lifestyle Management

Men and women with elevated lipids from their initial risk assessment may be followed up with a non-HDL-C or an apolipoprotein B (apoB) in 4 - 6 months to assess the impact of lifestyle management. If elevated lipids are still a concern consider pharmaceutical management (see Table 2).

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

Risk Level	LDL-C <sup>3</sup> (mmol/L)	Non-HDL-C (mmol/L)	ApoB* (g/L)
High	> 2.0	> 2.6	> 0.8
Intermediate	> 3.5	> 4.3	> 1.05
Low	> 5.0	-	> 1.25

\*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.<sup>31-35</sup> Non-HDL-C may also be a better indicator of residual risk after statin therapy than LDL-C.<sup>36</sup> Another advantage of these tests is that fasting is not required. Non-HDL-C has the slight advantage over apoB because it is the cheaper test (\$12.20 vs \$16.10).

## 2. Pharmaceutical Management

### ► Statin Therapy

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.

Two tools to assist in individualizing this discussion include:

- Cardiovascular Risk/Benefit Calculator, website: [www.bestsciencemedicine.com/chd/calc2.html](http://www.bestsciencemedicine.com/chd/calc2.html)
- Cardiovascular Prevention Decision Aids, website: [www.shareddecisions.mayoclinic.org/](http://www.shareddecisions.mayoclinic.org/)

If statin therapy is decided upon, consider using a low dose of one of the newer statins.<sup>37</sup> For dosages and adverse effects, refer to *Appendix D: Pharmaceutical Table - Statins*. For women, currently, there is a lack of strong evidence to support the use of statins for primary prevention. It appears that high risk women or those with persistently elevated lipids may benefit. Similarly, there is a lack of strong evidence as to the efficacy of initiating statin therapy for primary prevention in older men (e.g., aged > 65 years old) who are intermediate risk because of age alone. Older men with additional risk factors might benefit from statin therapy for primary prevention.

Prior to the initiation of statin therapy:

- a. Inform the patient of adverse effects and advise they be reported - adverse effects may include muscle pain/myopathy,<sup>38</sup> rhabdomyolysis,<sup>38</sup> cataracts,<sup>39</sup> elevated blood glucose and diabetes,<sup>37,40,41</sup> acute renal failure,<sup>42</sup> and liver injury.<sup>43</sup>
- 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.
- 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.<sup>44</sup>

### Follow-up to Statin Therapy

Within 4 - 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 elevated in the follow-up investigation, consider any other causes of elevated lipids (e.g., hypothyroidism).
- b. Inquire about any adverse effects. If muscle symptoms are reported, measure creatine kinase (CK).
- c. Measure liver transaminase enzyme (aspartate aminotransferase (ALT)), if recommended by product monograph. If a patient has elevated liver transaminase enzymes consider secondary causes.

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 considered not necessary for the sole purpose of treat-to-target.<sup>2</sup>

### Controversies in Care: Statin Therapy in Primary Prevention

Despite the lack of strong evidence to support the use of statins for primary prevention, both the CCS<sup>3</sup> and the American College of Cardiology and American Heart Association (ACC/AHA)<sup>2</sup> have recommended a more aggressive approach for statin use (see Table 3).

**Table 3. Comparison of statin therapy recommendations between the CCS and ACC/AHA**

Criteria	CCS Recommendations	ACC/AHA Recommendations
Risk assessment tool	FRS - low risk, intermediate risk, high risk.	Pooled Cohort Equations - elevated risk ( $\geq 7.5\%$ ), not elevated risk ( $\leq 7.5\%$ ). The 7.5% approximately equates to a FRS score of 15% +/- 3% (depending on the risk factors).
Intermediate risk	Treat with statins based on FRS (10-19%) if LDL-C $\geq 3.5$ mmol/L.	Treat with statins based on Pooled Cohort Equations $\geq 7.5\%$ .
High risk	Treat with statins based on FRS ( $\geq 20\%$ ).	Treat with statins based on Pooled Cohort Equations $\geq 7.5\%$ .
LDL-C $\geq 5$ mmol/L	Treat with statins.	Treat with statins.
DM	Treat with statins if patient aged $\geq 40$ years OR if aged $\geq 30$ years with a diagnose of DM for $> 15$ years.	Treat with statins if patient aged 40 to 75 years and LDL-C $\geq 1.8$ mmol/L.
CKD or high risk HTN	Treat with statins.	No specific recommendation.

### Controversies in Care: Treat-to-Target Approach

Both the CCS<sup>3</sup> and the ACC/AHA<sup>2</sup> acknowledge target lipid levels to be arbitrary, as they are based on extrapolation from studies that were not designed to test specific lipid targets. The ACC/AHA does not support the continued use of treat-to-target approach due to the lack of evidence,<sup>2</sup> though they do recommend a therapeutic response of 30% to 50% reduction in LDL-C. The CCS does recommend treating high risk and intermediate risk patients to a specific LDL-C target of  $\leq 2.0$  mmol/L or a  $\geq 50\%$  reduction from baseline. Alternate targets include an apoB target of  $\leq 0.8$  g/L and a non-HDL-C target of  $\leq 2.6$  mmol/L. Low risk patients are recommended to be treated to 50% of their baseline LDL-C.

This guideline is more aligned with the ACC/AHA<sup>2</sup> recommendations in that treatment with statins is expected to result in a significant reduction ( $> 30\%$ ) in the elevated baseline lipid levels.

Due to the lack of evidence, this guideline recommends no specific LDL-C, non-HDL-C and/or apoB treatment targets for primary prevention. Treat-to-target approach is not supported and may even lead to increased anxiety and adverse effects.

#### ► Acetylsalicylic Acid (ASA) Therapy:

Routine ASA therapy may have a role in primary prevention in men and women who are assessed as high CVD risk and low bleed risk.<sup>44</sup>

### Controversies in Care: ASA Therapy in Primary Prevention

Recent studies have questioned the value of routine ASA in primary prevention (see Table 4 and 5). ASA use in primary prevention may reduce the risk of myocardial infarction (MI) in men and may reduce the risk of ischemic stroke among women, with no significant effect on stroke in men and MI in women.<sup>46</sup> The risk of bleeding may outweigh the low absolute net benefit in the prevention of serious vascular events.

**Table 4. Absolute risk reduction (ARR) and numbers needed to treat (NNT) in ASA primary prevention trials<sup>45,47</sup>**

Event	ARR for one year	NNT for one year
Any serious vascular event *	0.07%	1,428
Major coronary event (primarily driven by a reduction in non-fatal MI) ^	0.06%	1,667
Ischemic stroke	0.02%	5,000
Mortality	No benefit	

\*defined as MI, stroke, or death from a vascular cause; ^ defined as MI, coronary death, or sudden death.

**Table 5. Absolute risk increase (ARI) and numbers needed to harm (NNH) in ASA primary prevention trials<sup>45,47</sup>**

Event	ARI for one year	NNH for one year
Major extracranial bleed	0.03%	3,333
Hemorrhagic stroke	0.01%	10,000

### 3. Management of Other Clinical Conditions<sup>1</sup>

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

#### ► Blood Pressure Control

Instigate 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](http://BCGuidelines.ca) - *Hypertension: Diagnosis and Management*.

#### ► Diabetes Care

Instigate 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.1 CCS3 defines a patient with DM high risk for CVD if they are aged ≥ 40 OR they are aged ≥ 30 with a diagnose of DM for > 15 years. 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/](http://www.dtu.ox.ac.uk/riskengine/).

- For more information, refer to [BCGuidelines.ca](http://BCGuidelines.ca) - *Diabetes Care*.

#### ► CKD Management

In patients with CKD, the combination of simvastatin plus ezetimibe has shown some benefit in reducing major atherosclerotic events when compared to placebo; however, no benefit on all-cause mortality has been demonstrated.<sup>48</sup>

- For more information, refer to [BCGuidelines.ca](http://BCGuidelines.ca) - *Chronic Kidney Disease - Identification, Evaluation and Management of Adult Patients*.

## Resources

### ► References

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<sup>1</sup> 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).

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## ► Resources

For Physicians, refer to *Associated Document: Cardiovascular Disease - Primary Prevention: Resource Guide for Physicians*.

## ► Appendices and Associated Documents

- 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

The following document accompanies this guideline:

- Cardiovascular Disease - Primary Prevention: Resource Guide for Physicians

This guideline is based on scientific evidence current as of the Effective Date.

This guideline was developed by the Guidelines and Protocols Advisory Committee, approved by the British Columbia Medical Association, and adopted by the Medical Services Commission.

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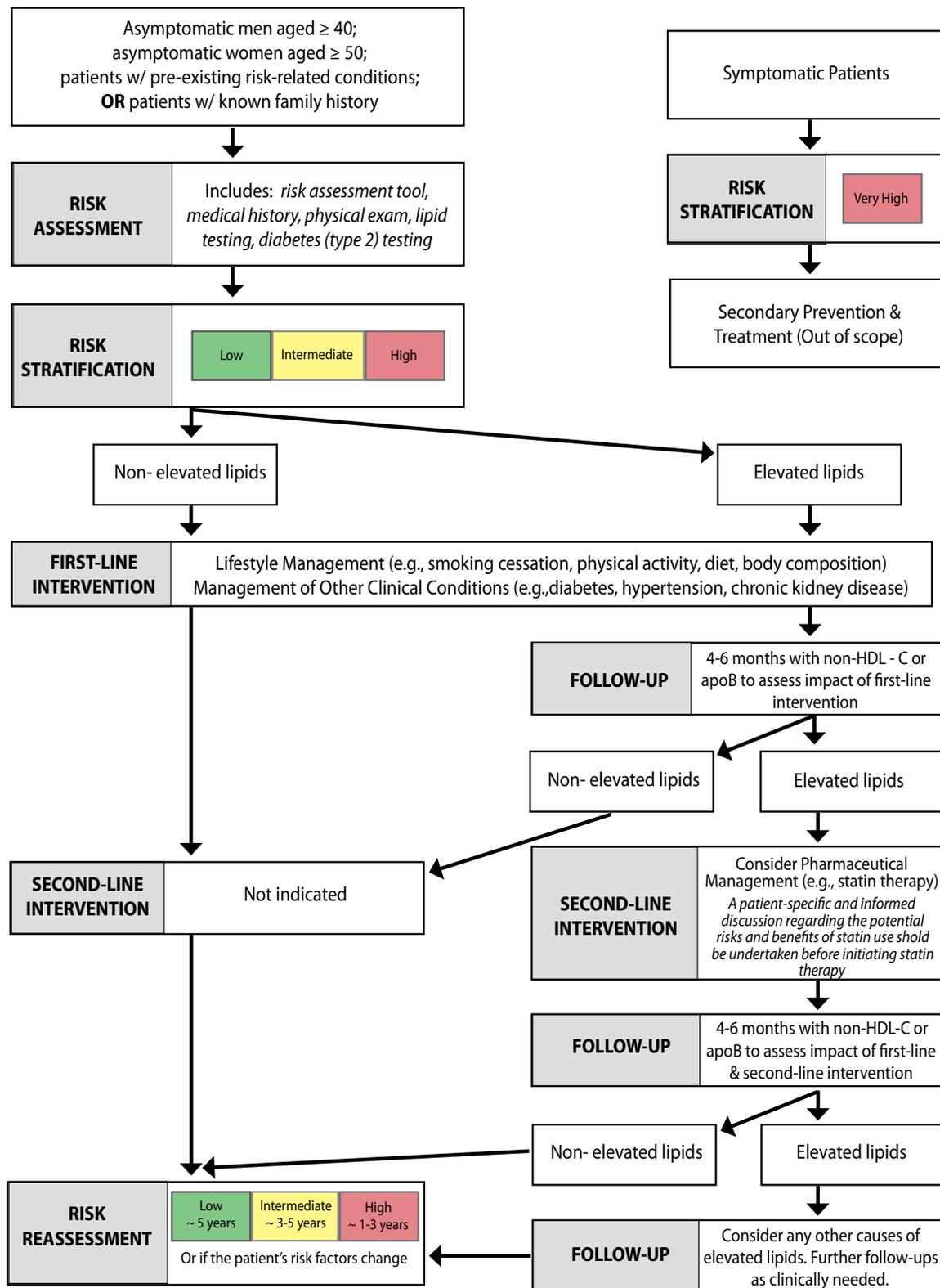
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The Clinical Practice Guidelines (the "Guidelines") have been developed by the Guidelines and Protocols Advisory Committee on behalf of the Medical Services Commission. The Guidelines are intended to give an understanding of a clinical problem, and 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





## 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.

Risk Factor	Risk Points			
	Men	Women		
<b>Age</b>				
30-34	+0	+0		
35-39	+2	+2		
40-44	+5	+4		
45-49	+6	+5		
50-54	+8	+7		
55-59	+10	+8		
60-64	+11	+9		
65-69	+12	+10		
70-74	+14	+11		
75+	+15	+12		
<b>HDL-C (mmol/L)</b>				
>1.6	-2	-2		
1.3-1.6	-1	-1		
1.5-1.3	+0	+0		
0.9-1.2	+1	+1		
<0.9	+2	+2		
<b>TC (mmol/L)</b>				
<4.1	+0	+0		
4.1-5.2	+1	+1		
5.2-6.2	+2	+3		
6.2-7.2	+3	+4		
>7.2	+4	+5		
<b>SBP (mmHG)</b>	<b>Not Treated</b>	<b>Treated</b>	<b>Not Treated</b>	<b>Treated</b>
<120	-2	+0	-3	-1
120-129	+0	+2	+0	+2
130-139	+1	+3	+1	+3
140-149	+2	+4	+2	+5
150-159	+2	+4	+4	+6
160+	+3	+5	+5	+7
<b>Diabetic</b>				
YES	+3		+4	
NO	+0		+0	
<b>Smoker</b>				
YES	+4		+3	
NO	+0		+0	

Total Risk Points	10-YR CVD FRS Risk	
	Men	Women
≤3	<1.0%	<1.0%
-2	1.1%	<1.0%
-1	1.4%	1.0%
0	1.6%	1.2%
1	1.9%	1.5%
2	2.3%	1.7%
3	2.8%	2.0%
4	3.3%	2.4%
5	3.9%	2.8%
6	4.7%	3.3%
7	5.6%	3.9%
8	6.7%	4.5%
9	7.9%	5.3%
10	9.4%	6.3%
11	11.2%	7.3%
12	13.3%	8.6%
13	15.6%	10.0%
14	18.4%	11.7%
15	21.6%	13.7%
16	25.3%	15.9%
17	29.3%	18.5%
18	>30.0%	21.5%
19	>30.0%	24.8%
20	>30.0%	27.5%
≥21	>30.0%	>30.0%

Risk Level	10-YR CVD FRS Risk
Low	<10%
Intermediate	10-19%
High	≥20%

**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:**

1. Anderson TJ, Grégoire J, Hegele RA, et al. 2012 update of the Canadian Cardiovascular Society guidelines for the diagnosis and treatment of dyslipidemia for the prevention of cardiovascular disease in the adult. *Can J Cardiol.* 2013;29(2):151-67.
2. D'Agostino RB, Vasan RS, Pencina MJ, et al. General cardiovascular risk profile for use in primary care: The Framingham heart study. *Circulation.* 2008;117:743-53.



## Appendix C: Lipid Testing in Primary Prevention of Cardiovascular Disease (CVD)

**Table 1. Lipid tests available for CVD primary prevention<sup>†</sup>**

Lipid Test	Purpose	MSP Cost*	Results Includes**	Fasting Requirements
Full lipid profile	Risk assessment	\$21.31	total cholesterol (TC); high density lipoprotein cholesterol (HDL-C); low-density lipoprotein cholesterol (LDL-C); non-HDL-C; and triglycerides (TG) May include: Total cholesterol to HDL-C ratio (TC/HDL-C)	Yes - 8 to 10 hours
Non-HDL-C <sup>†</sup>	Follow-up	\$12.20	TC; HDL-C; non-HDL-C May include: TC/HDL-C	No
Apolipoprotein B (apoB)	Follow-up	\$16.60	apoB	No

<sup>†</sup> As per outlined on the Standard Outpatient Laboratory Requisition (SOPLR). As of October 2013, non-HDL-C has been included on the SOPLR.

\* Medical Services Plan (MSP) prices as of Medical Services Commission (MSC) Payment Schedule August 2013.

\*\* Lipid reporting practices are not standardized, and what is reported may vary according to the lab.

### 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 at age  $\geq 40$  and asymptomatic women at age  $\geq 50$  to establish a baseline;
- all patients with pre-existing risk-related conditions (e.g., hypertension, diabetes mellitus, chronic kidney disease); 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**

Previous Risk Assessment Classification*	Low risk	Intermediate risk	High risk
Reassess risk in	5 years or if the patient's risk factors change significantly.	3 - 5 years or if the patient's risk factors change significantly.	1 - 3 years or if the patient's risk factors change significantly.

\*For more information on how to classify a patient's risk assessment, see BCGuidelines – Cardiovascular Disease – Primary Prevention.

### 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.

While it is not clear which test is the better predictor of major cardiovascular events, they both appear to be stronger indicators than LDL-C. Another advantage of these tests is that fasting is not required.<sup>1-5</sup> Non-HDL-C has the slight advantage over apoB because it is the cheaper test (\$12.20 vs \$16.10) and would have been calculated in the full lipid profile (a baseline measurement).

*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 4 - 6 months to assess the impact of lifestyle management.
- Follow-up within 4 - 6 months of the initiation of statin therapy to assess patient adherence and response from statin therapy.

The treat-to-target approach for lipids in primary prevention is not supported.<sup>6</sup> 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.

## References

1. Liu J, Sempos CT, Donahue RP, et al. Non-high-density lipoprotein and very-low-density lipoprotein cholesterol and their risk predictive values in coronary heart disease. *Am J Cardiol.* 2006;98:1363-8.
2. Pischon T, Girman CJ, Sacks FM, et al. Non-high-density lipoprotein cholesterol and apolipoprotein B in the prediction of coronary heart disease in men. *Circulation.* 2005;112:3375-83.
3. Ridker PM, Rifai N, Cook NR, et al. Non-HDL cholesterol, apolipoproteins A-I and B100, standard lipid measures, lipid ratios, and CRP as risk factors for cardiovascular disease in women. *JAMA.* 2005;294:326-33.
4. Emerging Risk Factors Collaboration, Di Angelantonio E, Sarwar N, et al. Major lipids, apolipoproteins, and risk of vascular disease. *JAMA.* 2009;302:1993-2000.
5. Sniderman AD, Williams K, Contois JH, et al. A meta-analysis of low-density lipoprotein cholesterol, non-high-density lipoprotein cholesterol, and apolipoprotein B as markers of cardiovascular risk. *Circ Cardiovasc Qual Outcomes.* 2011;4:337-45.
6. Stone NJ, Robinson J, Lichtenstein AH. 2013 ACC/AHA Guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: A report of the American College of Cardiology /American Heart Association task force on practice guidelines. *Circulation.* 2013.pii:S0735-1097(13)06028-2.



## Appendix D: Pharmaceutical Table – Statins

Statins*	Dosages for Primary Prevention <sup>†</sup>	Serious Adverse Events
<b>Atorvastatin</b> (Lipitor <sup>®</sup> , 1997, G) Tabs: 10, 20, 40, 80 mg	10 mg PO daily <sup>1</sup>	<p><b>Elevated liver enzymes:</b> statins are associated with a dose-dependent risk of elevated liver transaminases.</p> <ul style="list-style-type: none"> <li>In the absence of elevated bilirubin levels, isolated elevations of transaminases have not been linked with liver injury or dysfunction.<sup>2</sup> Refer to latest product monograph for specific recommendations on liver function testing. Although available evidence does not support routine monitoring of liver enzymes in asymptomatic patients solely for the purpose of detecting adverse drug reactions, patients on a statin who have elevated transaminases should be investigated to exclude other etiologies.<sup>2</sup></li> </ul> <p><b>Myopathy (myalgias, myositis, rhabdomyolysis):</b> A systematic review reported an incidence of myopathy of 11 per 100,000 person-years and of rhabdomyolysis of 3.4-4.2 per 100,000 person-years.<sup>3</sup> Accuracy of estimates is limited by the lack of consensus for case definitions.<sup>4,5</sup></p> <ul style="list-style-type: none"> <li>Some risk factors include: advanced age, female sex, low body mass, frailty, high statin dose, and drug interactions.<sup>5,6</sup> Combination of a statin with a fibrate or niacin can increase risk of myopathy and rhabdomyolysis.</li> <li>Before starting statin, documenting baseline muscle symptoms may be helpful.<sup>5</sup> Clinicians should monitor for muscle symptoms and advise patients to report such symptoms.<sup>6</sup></li> </ul> <p><b>Neuropathy:</b> A systematic review reported an incidence of 12 per 100,000 person-years. It is suggested that unexplained peripheral neuropathy while on statin therapy be assessed.<sup>3</sup></p> <p><b>New-onset diabetes:</b> Statins have been shown to increase risk of incident diabetes (Fasting blood glucose <math>\geq 7</math> mmol/L) by 0.4% in absolute terms (NNTH of 225 over 4 years).<sup>7</sup></p>
<b>Fluvastatin</b> (Lescol <sup>®</sup> , 1997, G) Caps: 20, 40 mg XL Tab: 80 mg		
<b>Lovastatin</b> (Mevacor <sup>®</sup> , 1997, G) Tabs: 20, 40 mg	20 - 40 mg PO daily <sup>8</sup>	
<b>Pravastatin</b> (Pravachol <sup>®</sup> , 1996, G) Tabs: 10, 20, 40 mg	20 - 40 mg PO daily <sup>9</sup>	
<b>Rosuvastatin</b> (Crestor <sup>®</sup> , 2003, G) Tabs: 5, 10, 20, 40 mg	10 - 20 mg PO daily <sup>10</sup>	
<b>Simvastatin</b> (Zocor <sup>®</sup> , 1999, G) Tabs: 5, 10, 20, 40, 80 mg	20 - 40 mg PO daily <sup>11</sup>	

**Abbreviations:** Caps capsules; G generic brand(s) available; L liter; mg milligrams; mmol millimoles; NNTH number needed to harm; Tabs tablets

For information on the current costs of statins, please visit BC PharmaCare Formulary Search ([www.health.gov.bc.ca/pharmacare/benefitslookup/](http://www.health.gov.bc.ca/pharmacare/benefitslookup/)). Drug coverage is subject to drug price limits set by PharmaCare and to the patient's PharmaCare plan rules and deductibles. See: [www.health.gov.bc.ca/pharmacare/plans/index.html](http://www.health.gov.bc.ca/pharmacare/plans/index.html) and [www.health.gov.bc.ca/pharmacare/policy.html](http://www.health.gov.bc.ca/pharmacare/policy.html) for further information.

\* Listed in alphabetical order. Consult product monographs for the most current prescribing information and regularly review current Health Canada advisories, warnings and recalls at [www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/index-eng.php](http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/index-eng.php).

<sup>†</sup> Dosages are selected from placebo-controlled pivotal trials where: 1) primary outcomes included coronary heart disease endpoints (not surrogates); 2) studies were of sufficient quality such that findings were considered to be valid; 3) statistically significant reduction in major coronary events as reported in an individual patient level meta-analysis.<sup>12</sup> Refer to product monograph for recommended starting doses, dose adjustments in renal failure, maximum doses in specific ethnic populations (e.g., rosuvastatin in Asian population).

## References

1. Sever PS, Dahlöf B, Poulter NR, et al. Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial--Lipid Lowering Arm (ASCOT-LLA): A multicentre randomised controlled trial. *Lancet*. 2003;361(9364):1149–58.
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8. Downs JR, Clearfield M, Weis S, et al. Primary prevention of acute coronary events with lovastatin in men and women with average cholesterol levels: Results of AFCAPS/TexCAPS. Air Force/Texas Coronary Atherosclerosis Prevention Study. *JAMA*. 1998;279(20):1615–22.
9. Shepherd J, Cobbe SM, Ford I, et al. Prevention of coronary heart disease with pravastatin in men with hypercholesterolemia. West of Scotland Coronary Prevention Study Group. *N Engl J Med*. 1995;333(20):1301–7.
10. Ridker PM, Danielson E, Fonseca FAH, et al. Rosuvastatin to prevent vascular events in men and women with elevated C-reactive protein. *N Engl J Med* 2008;359(21):2195–207.
11. Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: A randomised placebo-controlled trial. *Lancet*. 2002;360(9326):7–22.
12. Cholesterol Treatment Trialists' (CTT) Collaboration, Baigent C, Blackwell L, et al. Efficacy and safety of more intensive lowering of LDL cholesterol: A meta-analysis of data from 170,000 participants in 26 randomised trials. *Lancet*. 2010;376(9753):1670–81.



## Cardiovascular Disease - Primary Prevention: Resource Guide for Physicians

### Risk Assessment Resources

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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.

NOTE: The Framingham (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.

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. One study estimated that using CVD as an endpoint instead of CHD in the FRS has increased the number of patients into the high-risk group leading to a 2.3-fold increase in the need for lipid-lowering treatment.<sup>1</sup>

#### ► Risk Assessment Tools

- **Canadian Cardiovascular Society:** estimates the 10-year risk of developing CVD, with paper-base and an online calculator, using FRS.  
Website: [www.ccsguidelineprograms.ca/index.php](http://www.ccsguidelineprograms.ca/index.php) - under dyslipidemia program
- **Framingham Heart Study:** a FRS risk calculator for various CVD outcomes (e.g., CVD, CHD) and time frames (e.g., 10-year risk, 30-year risk).  
Website: [www.framinghamheartstudy.org](http://www.framinghamheartstudy.org)
- **Cardiovascular Risk/Benefit Calculator:**  
Website: [www.bestsciencemedicine.com/chd/calc2.html](http://www.bestsciencemedicine.com/chd/calc2.html)
- **The University of Edinburgh Cardiovascular Risk Calculator:** a 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.  
Website: [www.cvrisk.mvm.ed.ac.uk/index.htm](http://www.cvrisk.mvm.ed.ac.uk/index.htm)
- **The United Kingdom Prospective Diabetes Study (UKPDS):** a risk calculator that estimates the 10-year CHD and stroke risk for adults with type 2 diabetes.  
Website: [www.dtu.ox.ac.uk/riskengine/](http://www.dtu.ox.ac.uk/riskengine/)
- **QRISK2:** a risk calculator that estimates the 10-year risk of a heart attack or stroke.  
Website: [www.qrisk.org/](http://www.qrisk.org/)



## Lifestyle Management Resources

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### ► Smoking

- **QuitNow Services:** provides free help to quit smoking.  
Telephone: 8-1-1 and ask for QuitNow, Website: [www.quitnow.ca](http://www.quitnow.ca)
- **BC Smoking Cessation Program:** helps patients to stop smoking or stop using other tobacco products by helping them with the cost.  
Website: [www.health.gov.bc.ca/pharmacare/stop-smoking/](http://www.health.gov.bc.ca/pharmacare/stop-smoking/)

### ► Physical Activity

- **Canadian Physical Activity and Sedentary Behaviour Guidelines:** provides patients with guidelines and resources to help become more active from the Canadian Society for Exercise Physiology.  
Website: [www.csep.ca](http://www.csep.ca) – under Guidelines.
- **Physical Activity Line (PAL):** provides free physical activity counselling, resources and information.  
Telephone: (Toll Free) 1-877-725-1149 or (Lower Mainland) 604-241-2266, website: [www.physicalactivityline.com](http://www.physicalactivityline.com)

### ► Healthy Diet

- **Dietitian Services at HealthLinkBC (formerly Dial-A-Dietitian):** provides free nutrition information and resources.  
Telephone: 8-1-1, Website: [www.healthlinkbc.ca/healthyeating/](http://www.healthlinkbc.ca/healthyeating/)

### ► Others

- **HealthlinkBC:** provides health information and resources to help patients.  
Telephone: 8-1-1, Website: [www.healthlinkbc.ca](http://www.healthlinkbc.ca)
- **Public Health Agency of Canada:** provides resources to help patients make wise choices about healthy living, including increasing physical activity and eating well.  
Website: [www.phac-aspc.gc.ca/](http://www.phac-aspc.gc.ca/)
- **Heart & Stroke Foundation of BC & Yukon:** provides resources on heart diseases and stroke.  
Website: [www.heartandstroke.bc.ca](http://www.heartandstroke.bc.ca)
- **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. Referral form accessible on their website.  
Website: [www.heartcentre.ca](http://www.heartcentre.ca)
- **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.  
Website: [www.gpsc.bc.ca/billing-fees/complete-guide](http://www.gpsc.bc.ca/billing-fees/complete-guide)



## Statins – Resources for a Patient Discussion

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- **Cardiovascular Risk/Benefit Calculator:** from James McCormack  
Website: [www.bestsciencemedicine.com/chd/calc2.html](http://www.bestsciencemedicine.com/chd/calc2.html)
- **Cardiovascular Prevention Decision Aids (Statin & Aspirin):** from the Mayo Clinic  
Website: [www.shareddecisions.mayoclinic.org/](http://www.shareddecisions.mayoclinic.org/)
- **NNT - Statin for heart disease prevention without prior heart disease:** from the NNT  
Website: [www.thennt.com/](http://www.thennt.com/)

## Other BC Guidelines

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- **BC Guidelines**  
Website: [www.BCGuidelines.ca](http://www.BCGuidelines.ca)
  - Hypertension Diagnosis and Management
  - Diabetes Care
  - Chronic Kidney Disease - Identification, Evaluation and Management of Adult Patients
  - Stroke and Transient Ischemic Attack - Management and Prevention
  - Overweight and Obese Adults: Diagnosis and Management

## References

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