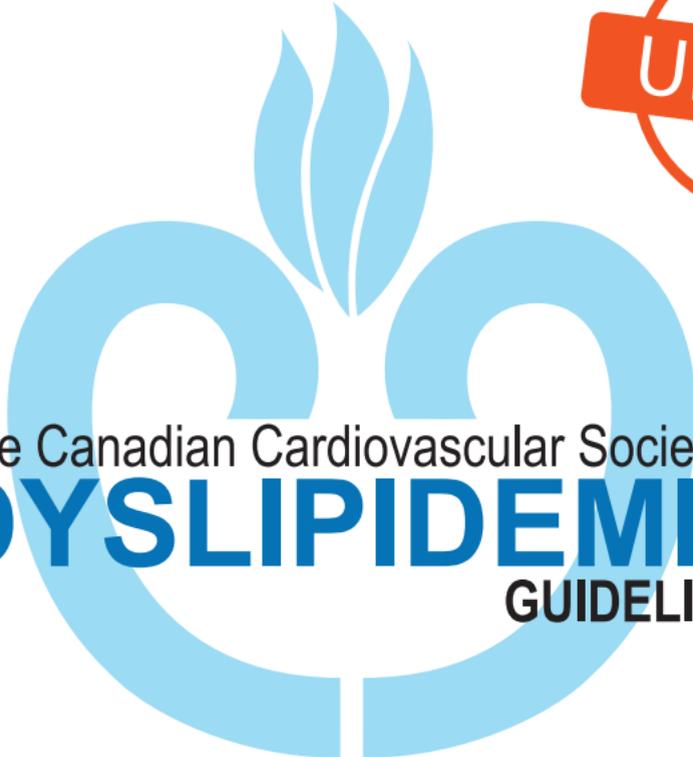


DYSLIPIDEMIA

DYSLIPIDEMIA



The Canadian Cardiovascular Society's  
**DYSLIPIDEMIA**  
GUIDELINES



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## About this Pocket Guide

This pocket guide is a quick-reference tool that features diagnostic and treatment recommendations based on the 2021 CCS Dyslipidemia Guidelines (as well as, recommendations from the previous dyslipidemia guidelines that remain unchanged [2006, 2009, 2012, and 2016]).

These recommendations are intended to provide a reasonable and practical approach to care for physicians, pharmacists, nurses and other healthcare providers. They are subject to change as scientific knowledge/technology advance and practice patterns evolve, and are not intended to be a substitute for clinical judgement. Adherence to these these recommendations will not necessarily produce successful outcomes in every case.

For information about the GRADE approach for rating the strength of recommendations and quality of evidence, visit [www.ccs.ca](http://www.ccs.ca).

Please visit [www.ccs.ca](http://www.ccs.ca) for more information and additional resources.

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## Summary of 2021 Guideline Changes and Highlights

### What's new?

- Expanded recommendations for preventative care in women with hypertensive disorders of pregnancy
- Updated recommendations for primary prevention and the importance of lipoprotein measurement, including non-HDL-C, ApoB, and Lp(a) in assessing CV risk
- The role of CAC as a clinical decision-making tool for determining the need to initiate therapy
- The benefit of icosapent ethyl (IPE) in patients with TG  $\geq$ 1.5-5.6 mmol/L and a previous ASCVD event or diabetes and  $\geq$ 1 additional risk factor
- Lack of CV benefit from omega-3 fatty acids from dietary sources or over-the-counter formulations/supplements
- New recommendations for non-statin therapies to reduce ASCVD events
- Identification of new lipid/lipoprotein thresholds for the intensification of therapy in the management of dyslipidemia, beyond statins
- Secondary prevention patients demonstrated to derive the greatest benefit with intensification with PCSK9 inhibitors are identified
- Values for non-HDL-C and ApoB have been modified to accurately represent the same percentile equivalent as LDL-C for all recommended thresholds

## WHO TO SCREEN

**Men  $\geq 40$  years of age;  
women  $\geq 40$  years of age  
(or postmenopausal)**

Consider earlier in ethnic groups at increased risk such as South Asian or Indigenous individuals

**All patients with any of the following conditions regardless of age:**

- Clinical evidence of atherosclerosis
- Abdominal aortic aneurysm
- Diabetes mellitus
- Arterial hypertension
- Current cigarette smoking
- Stigmata of dyslipidemia (corneal arcus, xanthelasma or xanthoma)
- Family history of premature CVD\*
- Family history of dyslipidemia
- Chronic kidney disease\*\*
- Obesity (BMI  $\geq 30$  kg/m<sup>2</sup>)
- Inflammatory diseases (RA, SLE, PsA, AS, IBD)
- HIV infection
- Erectile dysfunction
- Chronic obstructive pulmonary disease
- History of hypertensive disorder of pregnancy

\*Men younger than 55 years of age and women younger than 65 years of age in first degree relatives.

\*\*Chronic Kidney Disease = eGFR  $\leq 60$  mL/min/1.73 m<sup>2</sup> or ACR  $\geq 3$  mg/mmol for at least 3 months duration.

ACR = albumin-to-creatinine ratio; AS = ankylosing spondylitis; BMI = body mass index; COPD = chronic obstructive pulmonary disease; CVD = cardiovascular disease; eGFR = estimated glomerular filtration rate; IBD= inflammatory bowel disease; PsA = psoriatic arthritis; RA = rheumatoid arthritis; SLE, systemic lupus erythematosus.



### HOW TO SCREEN

#### For all:

- History and physical examination
- Standard lipid profile: TC, LDL-C, HDL-C, non-HDL-C, TG
- Fasting plasma glucose (FPG) or glycated hemoglobin (A1c)
- eGFR
- Lipoprotein(a)—once in patient's lifetime, with initial screening

#### Optional:

- ApoB
- Urine albumin:creatinine ratio (if eGFR <60 mL/min/1.73m<sup>2</sup>, hypertension or diabetes)

### RECOMMENDATION

- We recommend non-fasting lipid and lipoprotein testing can be performed in adults in whom screening is indicated as part of a comprehensive risk assessment to reduce CVD events (*Strong Recommendation, High Quality Evidence*).
- We recommend that for any patient with triglycerides >1.5 mmol/L, non-HDL-C or ApoB be used instead of LDL-C as the preferred lipid parameter for screening (*Strong Recommendation, High-Quality Evidence*).
- We suggest that for individuals with a history of triglyceride levels >4.5 mmol/L that lipid and lipoprotein levels be measured fasting (*Conditional Recommendation, Low Quality Evidence*).

**Practical Tip** - Compared to fasting lipid values, there will be minimal change with non-HDL-C, a slight decrease in LDL-C and small increase in triglyceride concentrations when most individuals do not fast.

## Coronary Artery Calcium (CAC) Measurement - Recommendations

- We suggest that CAC screening using computed tomography imaging may be considered for asymptomatic adults  $\geq 40$  years and at intermediate risk (FRS 10%-20%) for whom treatment decisions are uncertain (*Strong Recommendation, Moderate-Quality Evidence*).
- We recommend that CAC screening using computed tomography imaging not be undertaken for a) high risk individuals b) patients receiving statin treatment: or c) most asymptomatic, low-risk adults (*Strong Recommendation, Moderate Quality Evidence*).
- We suggest that CAC screening might be considered for a subset of low-risk middle-aged individuals  $\geq 40$  years with a family history of premature ASCVD (men  $\leq 55$  years; women  $\leq 65$  years) in addition to identifying known genetic causes of ASCVD such as elevated Lp(a) or FH (*Weak Recommendation, Low-Quality Evidence*).

**Values and preferences** - Patients with modifiable ASCVD risk factors should be counselled with respect to the potential merit of preventing atherosclerosis itself, the substrate for clinical ASCVD events in the long term, through comprehensive ASCVD risk factor management. As outlined elsewhere, RCTs show the ASCVD risk reduction value of statin therapy in patients with intermediate risk and additional ASCVD risk factors (eg, HOPE 3 and justification for the Use of Statins in Prevention: An Intervention Trial Evaluating Rosuvastatin [JUPITER] in the absence of CAC testing or any testing to identify preclinical atherosclerosis. Accordingly, the patient-physician decision often does not require CAC scoring but might be strongly influenced by these other factors, including family history of premature ASCVD, other features suggesting genetic causes of dyslipidemia, or side effects of statin therapy. In some low- to intermediate-risk subjects, it might be reasonable to withhold statin therapy for CAC = 0 AU because of a favourable intermediate-term outcome. Exceptions would include cigarette smokers, patients with diabetes, those with poorly controlled hypertension, genetic dyslipidemias such as FH or elevated Lp(a) level, and patients with strong family history of premature ASCVD events. If available, a CAC  $>100$  AU is an indication for statin therapy regardless of FRS. For those with a CAC of 1-99 AU, individual decision-making is required because risk will not be reclassified and would remain intermediate. If a decision is made to withhold statin or lipid-modifying therapy on the basis of CAC = 0, this decision should be reevaluated during follow-up or if clinical circumstances change. CAC scoring should rarely be performed sooner than within 5 years to aid in this reevaluation. Finally, this section is restricted to application in patients who are at least 40 years of age for whom the traditional FRS assessment applies. Prevalence of calcification is a sequential aspect of the atherosclerotic process and might be absent in the early phases. Although CAC has been studied extensively for ASCVD risk prediction, the prevalence of CAC is lower in young patients compared with middle-aged and older patients and also in women vs men younger than 50 years of age.



## Secondary Testing

### Lipoprotein (a) Measurement - Recommendation

- We recommend measuring Lp(a) level once in a person's lifetime as a part of the initial lipid screening. (*Strong Recommendation; High Quality Evidence*).
- For all patients in the setting of primary prevention with a Lp(a)  $\geq 50$  mg/dL (or  $\geq 100$  nmol/L), we recommend earlier and more intensive health behaviour modification counselling and management of other ASCVD risk factors (*Strong Recommendation, Expert consensus*).

**Values and preferences** - There is a large body of evidence supporting the potential causal association between Lp(a) and future ASCVD. The high prevalence of elevated Lp(a), the strength of association with incident and recurrent ASCVD events and the potential to improve CV risk stratification, strongly justify universal screening to identify individuals with very high levels. Identification of high levels of Lp(a) is a useful consideration for shared decision-making in subjects across all ASCVD risk categories, but especially in younger patients, particularly those who have a very strong family history of premature ASCVD. While further evidence that directly lowering Lp(a) reduces ASCVD risk is pending, the finding of high Lp(a) should alert primary care practitioners to more actively pursue an overall ASCVD event risk assessment, including careful discussion of current health behaviours, consideration of age-appropriate vascular imaging studies for detecting early evidence of subclinical atherosclerosis in select individuals (e.g. coronary artery calcium [CAC] score) and earlier introduction of statin or other lipidlowering therapy, especially in intermediate-risk individuals and/or low-risk individuals with moderate elevations of LDL-C between 3.5-5 mmol/L. In the setting of secondary prevention, the presence of high Lp(a) is strongly predictive of recurrent events, and suggests the need for intensification of LDL-lowering therapy, including use of PCSK9 inhibitors. Furthermore, preliminary evidence suggests that treatment with PCSK9 inhibitors post- ACS in patients with high Lp(a) reduces MACE independent of LDL-C lowering. When clinicians are uncertain of the implications of elevated Lp(a), consultation with a lipid specialist may be considered.



## RISK ASSESSMENT, STRATIFICATION & TREATMENT CONSIDERATION

Calculate risk (unless statin-indicated condition) using the Framingham Risk Score (FRS)<sup>†</sup> or Cardiovascular Life Expectancy Model (CLEM)<sup>†</sup>

Repeat screening every 5 years for FRS <5% or every year for FRS ≥5%

## RECOMMENDATIONS

- We recommend that a cardiovascular risk assessment be completed every 5 years for men and women age 40 to 75 using the modified FRS or CLEM to guide therapy to reduce major CV events. A risk assessment may also be completed whenever a patient's expected risk status changes (*Strong Recommendation, High Quality Evidence*).
- We recommend sharing the results of the risk assessment with the patient to support shared decision making and improve the likelihood that patients will reach lipid targets (*Strong Recommendation, High Quality Evidence*).

**Practical Tip** - While there is good evidence to support the use of statins in secondary prevention in patients over the age of 75 years for some outcomes, a mortality benefit has not been demonstrated. In addition, the evidence for statin use in primary prevention is lacking in this population, mainly because they have not been extensively studied. For robust elderly patients believed to be at higher risk, a discussion about the importance of statin therapy in overall management should be undertaken as these patients are often at high risk because a CVD event has important consequences for morbidity.

<sup>†</sup> Can calculate Cardiovascular Age with the Cardiovascular Life Expectancy Model at: [www.chiprehab.com](http://www.chiprehab.com)

For mobile device applications from the CCS, please visit: [www.ccs.ca/calculators-and-forms/](http://www.ccs.ca/calculators-and-forms/)

1. Framingham Risk Score (FRS) Calculator – Courtesy of MedSquares
2. Framingham Risk Score Worksheet – Printable



## Risk Stratification

### STATIN INDICATED CONDITIONS

#### LDL $\geq 5.0$ mmol/L

(or ApoB  $\geq 1.45$  g/L or non-HDL-C  $\geq 5.8$  mmol/L) (familial hypercholesterolemia or genetic dyslipidemia)

#### Most patients with diabetes:

- Age  $\geq 40$ y
- Age  $\geq 30$ y & DM  $\geq 15$ y duration
- Microvascular disease

#### Chronic Kidney Disease

- Age  $\geq 50$ y and eGFR  $< 60$  mL/min/1.73 m<sup>2</sup> or ACR  $> 3$  mg/mmol

#### Atherosclerotic Cardiovascular Disease (ASCVD):

- Myocardial infarction (MI), acute coronary syndromes (ACS)
- Stable angina, documented coronary artery disease using angiography
- Stroke, TIA, document carotid disease
- Peripheral arterial disease, claudication, and/or ABI  $< 0.9$
- Abdominal aortic aneurysm (AAA) -- abdominal aorta  $> 3.0$  cm or previous aneurysm surgery

### PRIMARY PREVENTION<sup>†</sup>

**Low-Risk\***  
FRS  $< 10\%$

**Intermediate Risk\***  
FRS 10-19.9% and

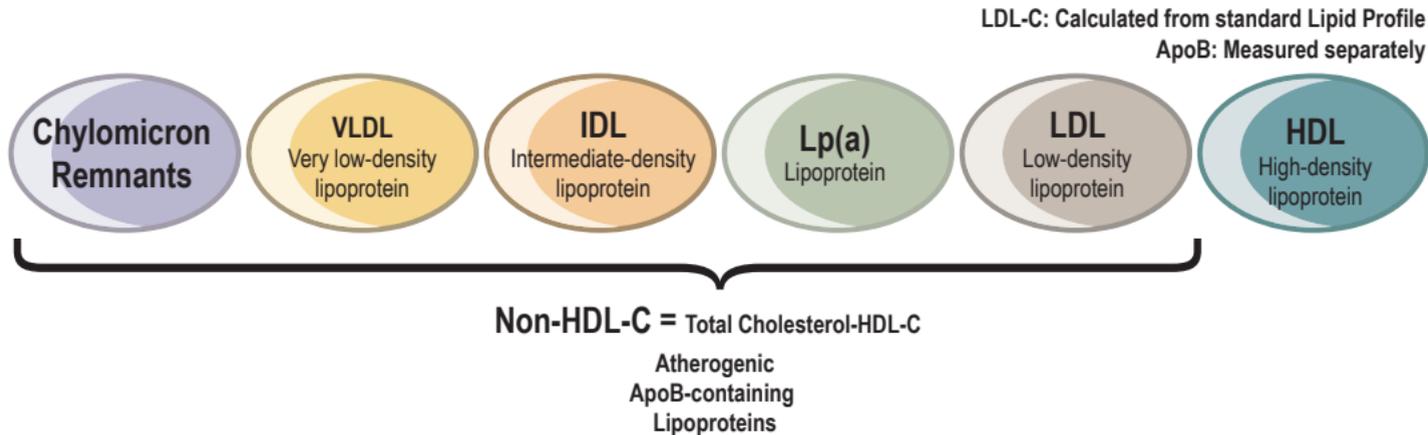
LDL-C  $\geq 3.5$  mmol/L **or**  
Non-HDL-C  $\geq 4.2$  mmol/L **or**  
ApoB  $\geq 1.05$  g/L **or**

Men  $\geq 50$  yrs and women  $\geq 60$  yrs with one additional risk factor: low HDL-C, IFG, high waist circumference, smoker, or HTN **or** with presence of other risk modifiers: hsCRP  $\geq 2.0$  mg/L, CAC  $> 0$  AU, family history of premature CAD, Lp(a)  $\geq 50$  mg/dL (100 nmol/L)

**High-Risk\***  
FRS  $\geq 20\%$

<sup>†</sup>Calculate risk using the Framingham Risk Score (FRS) --refer to [www.ccs.ca/calculators-and-forms/](http://www.ccs.ca/calculators-and-forms/)

\*Screening should be repeated every 5 years for men and women aged 40 to 75 years using the modified FRS or CLEM to guide therapy to reduce major CV events. A risk assessment might also be completed whenever a patient's expected risk status changes.



## RECOMMENDATION

•We recommend that for any patient with triglycerides >1.5 mmol/L, non-HDL-C or ApoB be used instead of LDL-C as the preferred lipid parameter for screening (*Strong Recommendation, High-Quality Evidence*).



# When to Consider Pharmacological Treatment in Risk Management

STATIN INDICATED CONDITIONS		
<b>LDL <math>\geq</math>5.0 mmol/L</b> (or ApoB $\geq$ 1.45 g/L or non-HDL-C $\geq$ 5.8 mmol/L) (familial hypercholesterolemia or genetic dyslipidemia)	<b>Most patients with diabetes:</b> <ul style="list-style-type: none"><li>• Age <math>\geq</math>40y</li><li>• Age <math>\geq</math>30y &amp; DM <math>\times</math><math>\geq</math>15y duration</li><li>• Microvascular disease</li></ul> <b>Chronic Kidney Disease</b> <ul style="list-style-type: none"><li>• Age <math>\geq</math>50y and eGFR <math>&lt;</math>60 mL/min/1.73 m<sup>2</sup> or ACR <math>&gt;</math>3 mg/mmol</li></ul>	<b>Atherosclerotic Cardiovascular Disease (ASCVD):</b> <ul style="list-style-type: none"><li>• Myocardial infarction (MI), acute coronary syndromes (ACS)</li><li>• Stable angina, documented coronary artery disease using angiography</li><li>• Stroke, TIA, document carotid disease</li><li>• Peripheral arterial disease, claudication, and/or ABI <math>&lt;</math>0.9</li><li>• Abdominal aortic aneurysm (AAA) -- abdominal aorta <math>&gt;</math>3.0 cm or previous aneurysm surgery</li></ul>

TIA - transient ischemic attack; ABI - ankle-brachial index; ACR - albumin:creatinine ratio; eGFR - estimated glomerular filtration rate

## RECOMMENDATION

### Statin-indicated conditions:

- We recommend management that includes statin therapy in high risk conditions including clinical atherosclerosis, abdominal aortic aneurysm, most diabetes mellitus, chronic kidney disease (age  $\geq$ 50 years) and those with LDL-C  $\geq$ 5.0 mmol/L to lower the risk of CVD events and mortality (*Strong Recommendation, High Quality Evidence*).

- We recommend use of high-intensity statin therapy in addition to appropriate health behaviour modifications for all secondary prevention CVD patients. For patients who do not tolerate a high-intensity statins, we recommend the maximally tolerated statin dose (*Strong Recommendation, High-Quality Evidence*).

## RECOMMENDATIONS

- We recommend treatment with a statin or statin/ezetimibe combination to reduce CVD events in adults  $\geq 50$  years with chronic kidney disease not treated with dialysis or a kidney transplant (*Strong Recommendation, High Quality Evidence*).

**Values and preferences** - If the preference is to engage in early prevention and long-term risk reduction, in subjects  $< 50$  years the absolute risk of events is lower but studies suggest that statins will result in a relative risk reduction similar to those  $\geq 50$  years. The statin/ezetimibe combination recommendation is based on the SHARP study which utilized 20 mg of simvastatin and 10 mg of ezetimibe.

- We suggest that lipid-lowering therapy not be initiated in adults with dialysis-dependent CKD (*Conditional Recommendation, Moderate Quality Evidence*).

**Values and preferences** - In younger individuals who may become eligible for kidney transplantation or with a longer life expectancy, statin or statin/ezetimibe combination therapy may be desirable although high-quality studies have not been done in this population.

- We suggest that lipid-lowering therapy be continued in adults already receiving it at the time of dialysis initiation (*Conditional Recommendation, Low Quality Evidence*).

**Values and preferences** - This recommendation reflects that fact that a substantial number of patients in SHARP transitioned to dialysis during the study and there was no heterogeneity of results for the population as a whole. The evidence is of low quality overall and there is substantial debate about best practice in this situation.

- We suggest the use of statin therapy in adults with kidney transplantation (*Conditional Recommendation, Moderate Quality Evidence*).



## Pharmacological Treatment Indications

Category	Consider Initiating pharmacotherapy if:	Recommendation
Primary Prevention <sup>†</sup>	<b>High*</b> FRS $\geq 20\%$	We recommend use of high-intensity statin therapy in addition to appropriate health behaviour modifications as initial therapy for all eligible patients to prevent CVD. For patients who do not tolerate a high-intensity statin, we recommend the maximally tolerated statin dose.
	<b>Intermediate Risk*</b> FRS 10-19.9% and LDL-C $\geq 3.5$ mmol/L or Non-HDL-C $\geq 4.2$ mmol/L or ApoB $\geq 1.05$ g/L or Men $\geq 50$ yrs and women $\geq 60$ yrs with one additional risk factor: low HDL-C, IFG, high waist circumference, smoker, or HTN or with presence of other risk modifiers: hsCRP $\geq 2.0$ mg/L, CAC $> 0$ AU, family, history of premature CAD, Lp(a), $\geq 50$ mg/dL ( $\geq 100$ nmol/L)	
	<b>Low-Risk*††</b> FRS $< 10\%$	
Statin Indicated Conditions	Atherosclerotic Cardiovascular Disease (ASCVD):	
	• Myocardial infarction (MI), acute coronary syndromes (ACS)	
	• Stable angina, documented coronary artery disease using angiography	
	• Stroke, TIA, document carotid disease	
• Peripheral arterial disease, claudication, and/or ABI $< 0.9$		
• Abdominal aortic aneurysm (AAA) -- abdominal aorta $> 3.0$ cm or previous aneurysm surgery		
Most patients with diabetes:		
• Age $\geq 40$ y		
• Age $\geq 30$ y & diabetes x $\geq 15$ y duration		
• Microvascular disease		
Chronic Kidney Disease		
• Age $\geq 50$ y and eGFR $< 60$ mL/min/1.73 m <sup>2</sup> or ACR $> 3$ mg/mmol		
LDL-C $\geq 5.0$ mmol/L (or ApoB $\geq 1.45$ g/L or non-HDL-C $\geq 5.8$ mmol/L) (familial hypercholesterolemia or genetic dyslipidemia)		

\*Screening should be repeated every 5 years for men and women aged 40 to 75 years using the modified FRS (Framingham Risk Score) or CLEM to guide therapy to reduce major CV events.

A risk assessment might also be completed whenever a patient's expected risk status changes.

†Calculate risk using the FRS

††Refer to page 19 for low-risk individuals who may benefit from statin therapy.

## RECOMMENDATIONS

- We recommend that despite concerns about a variety of possible adverse effects, all purported statin-associated symptoms should be evaluated systematically, incorporating observation during cessation, re-initiation (same or different statin, same or lower potency, same or decreased frequency of dosing) to identify a tolerated, statin-based therapy for chronic use (*Strong Recommendation, Low Quality Evidence*).
- We recommend that vitamins, minerals, or supplements for symptoms of myalgia perceived to be statin-associated not be used (*Strong Recommendation, Low Quality Evidence*).

**Values and preferences** - Always confirm that there is an indication for statin use which, if present, would suggest that benefits, clearly communicated to the patient, far outweigh the potential occurrence of any of the many side effects purported to be associated with statin use. Assess patient features that might limit dosage or preclude use of statins (e.g. potential drug-drug interactions) and always emphasize dietary, weight and exercise interventions to facilitate achievement of lipid goals and other benefits of comprehensive, CV prevention.

## Non-Statin Therapy

- We recommend intensification of lipid-lowering therapy with a PCSK9 inhibitor (evolocumab or alirocumab)—with or without the additional use of ezetimibe—for secondary CV prevention patients shown to derive the largest benefit from PCSK9 inhibitor therapy in whom LDL-C remains  $\geq 1.8$  mmol/L (or non-HDL-C  $\geq 2.4$  mmol/L or ApoB  $\geq 0.7$  g/L) while receiving the maximally tolerated statin dose (*Strong Recommendation, Moderate-Quality Evidence*).
- We recommend intensification of lipid-lowering therapy with ezetimibe and/or PCSK9 inhibitor therapy for all secondary prevention CVD patients in whom LDL-C remains  $\geq 1.8$  mmol/L (or non-HDL-C  $\geq 2.4$  mmol/L or ApoB  $\geq 0.7$  g/L) while receiving the maximally tolerated statin dose. (*Strong Recommendation; High-Quality Evidence*). If ezetimibe is used initially and LDL-C remains  $\geq 1.8$  mmol/L (or nonHDL-C  $\geq 2.4$  mmol/L or ApoB  $\geq 0.7$  g/L) PCSK9 inhibitor therapy is recommended (*Strong Recommendation, High-Quality Evidence*).

### SECONDARY PREVENTION PATIENTS SHOWN TO DERIVE THE LARGEST BENEFIT FROM INTENSIFICATION OF STATIN THERAPY WITH THE ADDITIONAL USE OF A PCSK9 INHIBITOR

#### Recent acute coronary event (ACS)

- Hospitalized index ACS to 52 weeks post index ACS

#### Clinically evident ASCVD and any of the following

- Diabetes mellitus or metabolic syndrome
- Polyvascular disease (vascular disease in  $\geq 2$  arterial beds)
  - Symptomatic PAD
    - Recurrent MI
    - MI in the past 2 years
    - Previous CABG surgery
- LDL-C  $\geq 2.6$  mmol/L or heterozygous FH
- Lipoprotein(a)  $\geq 60$  mg/dL (120 nmol/L)

ACS, acute coronary syndrome; ASCVD, atherosclerotic cardiovascular disease; CABG, coronary artery bypass graft; FH, familial hypercholesterolemia; LDL-C, low density lipoprotein cholesterol; MI, myocardial infarction; PAD, peripheral arterial disease; PCSK9, proprotein convertase subtilisin/ kexin type 9.



## RECOMMENDATIONS

- We recommend the use of a PCSK9 inhibitor (alirocumab or evolocumab) to lower LDL-C level in patients with heterozygous FH without clinical ASCVD whose LDL-C remains above the target (ie, LDL-C  $\geq 2.5$  mmol/L or  $< 50\%$  reduction from baseline; or ApoB  $\geq 0.85$  mg/dL or non-HDL-C  $\geq 3.2$  mmol/L) despite maximally tolerated statin therapy with or without ezetimibe therapy (*Strong Recommendation, High-Quality Evidence*).
- We recommend the use of a PCSK9 inhibitor (alirocumab or evolocumab) for patients with heterozygous FH and ASCVD whose LDL-C remains above the threshold  $\geq 1.8$  mmol/L (or ApoB  $\geq 0.7$  mg/dL or non-HDL-C  $\geq 2.4$  mmol/L) despite maximally tolerated statin therapy, with or without ezetimibe (*Strong Recommendation, High-Quality Evidence*).
- We recommend the use of icosapent ethyl (IPE) to decrease the risk of CV events in patients with ASCVD, or with diabetes and  $\geq 1$  CVD risk factors, who have an elevated fasting triglyceride level of 1.5-5.6 mmol/L despite treatment with maximally tolerated statin therapy (*Strong Recommendation, High-Quality Evidence*).
- We suggest that bile acid sequestrants be considered for LDL-C lowering in high risk patients whose levels remain above target despite statin treatment +/- ezetimibe therapy (*Conditional Recommendation, Low Quality Evidence*).
- We recommend that niacin not be combined with statin therapy for CVD prevention in patients who have achieved LDL-C targets (*Strong Recommendation, High Quality Evidence*).
- We recommend that fibrates not be combined with statin therapy for CVD event prevention in patients who have achieved LDL-C targets (*Strong Recommendation, High Quality Evidence*).



# Lipid Lowering Medications and Approved Dosing Recommendations

Generic Name	Brand Name	Recommended Dose Range
<b>Statins</b>		
Atovastatin*	Lipitor™	10-80 mg daily
Fluvastatin	Lescol™	20-80 mg daily
Lovastatin	Mevacor™	20-80 mg daily
Pravastatin	Pravachol™	10-40 mg daily
Rosuvastatin*	Crestor™	5-40 mg daily
Simvastatin	Zocor™	10-40 mg daily
<b>Cholesterol Absorption Inhibitors</b>		
Ezetimibe	Ezetrol™	10 mg daily
<b>Proprotein Convertase Subtilisin/Kexin type 9 (PCSK9) Inhibitors</b>		
Alirocumab	Praluent™	75-150 mg SQ every 2 weeks or 300 mg SQ every 4 weeks
Evolocumab	Repatha™	140 mg SQ every 2 weeks or 420 mg SQ every 4 weeks
<b>Ethyl Eicosapentaenoic Acid (EPA)</b>		
Icosapent Ethyl	Vascepa™	2 g BID with meals
<b>Bile Acid Sequestrants (BAS)</b>		
Cholestyramine	Questran™	2-24 g daily
Colesevelam	Lodalis™	2.5-3.75 g in 1-2 divided doses daily
Colestipol	Colestipol™	5-30 g daily
<b>Fibrates</b>		
Bezafibrate	Bezalip™	400 mg daily
Fenofibrate†	Lipidil Micro/Supra/EZ™	48-200 mg daily
Gemfibrozil†‡	Lopid™	600-1200 mg daily
<b>Nicain</b>		
Nicotinic Acid	Generic Crystalline Niacin	1-3 g daily
	Niaspan™	500 mg – 2 g QHS

\*High potency statins.

†Reduce dose or avoid in renal impairment.

†‡Should not be used in combination with a statin because of the potential increased risk for rhabdomyolysis.

## Healthy Eating

- We recommend that all individuals are offered advice about healthy eating and activity and adopt the Mediterranean dietary pattern to decrease their CVD risk (*Strong Recommendation, High Quality Evidence*).

**Values and preferences** - Adherence is one of the most important determinants for attaining the benefits of any diet. Individuals should choose the dietary pattern that best fits with their values and preferences, allowing them to achieve the greatest adherence over the long term.

- We do not recommend the use of over-the-counter omega-3 polyunsaturated fatty acids supplements (marketed as natural health products in Canada) to reduce CVD risk (*Strong Recommendation; High-Quality Evidence*).

**Values and preferences** - Although there is no apparent overall CVD event risk benefit, patients may choose to use these supplements for other indications including the management of high triglycerides, for which very high doses are required (4 g/day), and for which fibrates are generally more effective. Individuals should be aware that, in addition to marine sources, there are different preparations of long chain omega-3 PUFAs high in DHA and EPA acid from algal and yeast sources, both of which are suitable for vegans. There is also alpha-linolenic acid (ALA) from plant sources that do not contain DHA or EPA including flax seeds, chia seeds, and some oils such as canola and soybean oil, which have little or no effect on triglycerides.

- We continue to recommend a Mediterranean dietary pattern, which has evidence of CV outcome benefit in systematic reviews and meta-analyses. Additionally, other dietary patterns that share important features such as the Portfolio dietary pattern, Dietary Approaches to Stop Hypertension (DASH) dietary pattern, low-glycemic index/glycemic load dietary pattern, and plant-based dietary pattern, as well as dietary patterns high in nuts, legumes, olive oil, fruits and vegetables, total fibre, and whole grains. Dietary therapy using these means can be considered to augment drug therapy with statins; however, their benefits have been shown in terms of surrogate CV measures such as blood pressure and lipoproteins.

Nutritional guidelines that focus on dietary patterns (Mediterranean, DASH, or Portfolio diet) were included in the 2016 CCS Dyslipidemia Guidelines and remain unchanged.

A detailed review of the effect of nutritional components on lipids and CV events was reviewed in the 2016 CCS Dyslipidemia Guidelines (Supplemental Appendix S4) and can be found in the supplementary material of the guidelines publication. To access the supplementary material, visit the online version of the Canadian Journal of Cardiology at [www.onlinecjc.ca](http://www.onlinecjc.ca) and at <https://doi.org/10.1016/j.cjca.2021.03.016>.

## Treatment: Health Behaviour Modifications

### Activity

- We recommend that adults should accumulate at least 150 minutes of moderate-to-vigorous intensity aerobic physical activity per week, in bouts of 10 minutes or more to reduce CVD risk (*Strong Recommendation, High Quality Evidence*).

### Smoking Cessation

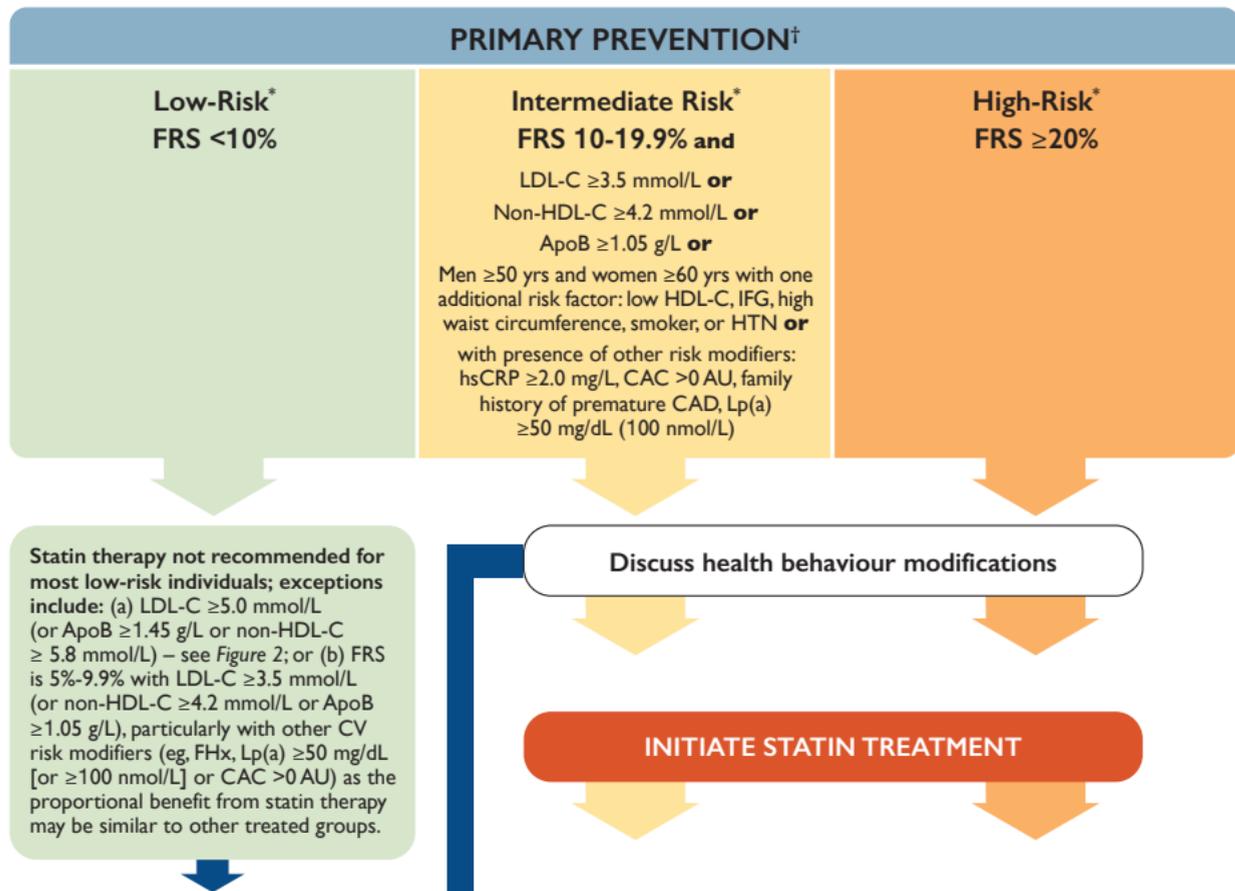
- We recommend that adults who smoke should receive clinician advice to stop smoking to reduce CVD risk (*Strong Recommendation, High Quality Evidence*).

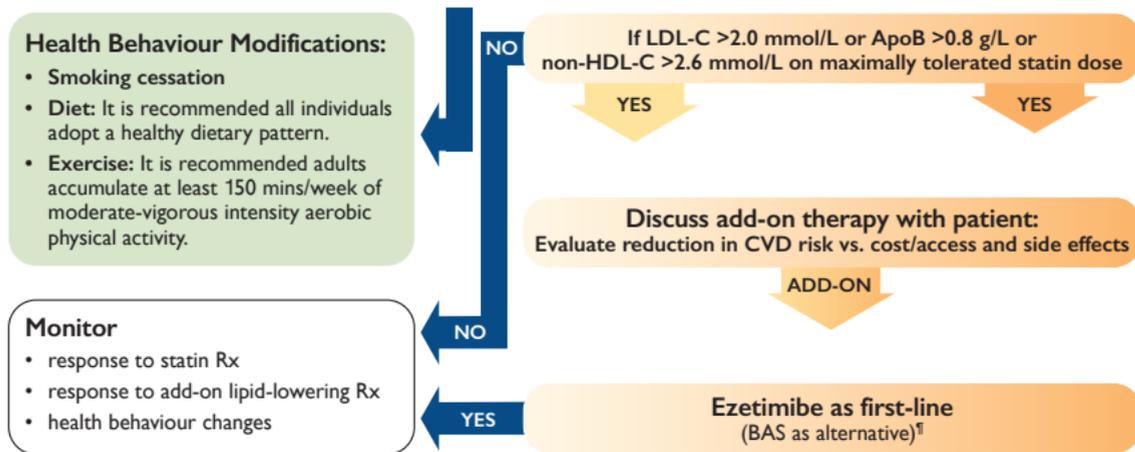
### Facilitators for Change

- We recommend combining low-risk lifestyle behaviors that include achieving and maintaining a healthy body weight, healthy diet, regular physical activity, moderate alcohol consumption, and moderate sleep duration to achieve maximal CVD risk reduction (*Strong Recommendation, High Quality Evidence*).

**Values and preferences** - Low risk lifestyle behaviours are variably defined as follows: a healthy body weight (BMI 18.5-25 to <30 kg/m<sup>2</sup> or waist circumference of <88 cm for women or <95 to <102 cm for men), healthy diet (higher fruits & vegetables to Mediterranean dietary pattern), regular physical activity (≥1 time/week to 40 min/day plus 1 hour/week of intense exercise), smoking cessation (never smoked to smoking cessation >12 months), moderate alcohol consumption (≥12-14 g/month to 46 g/day), and moderate sleep duration (6 to 8 hours/night). Individuals can achieve benefits in a dose-dependent manner.

**Health behaviour modifications remain the cornerstone of chronic disease prevention, including CVD. We recognize that health behaviour changes are not easy to achieve, but real effort should be exerted to realize the potential benefit of these nonpharmacological interventions in all CV risk patients.**





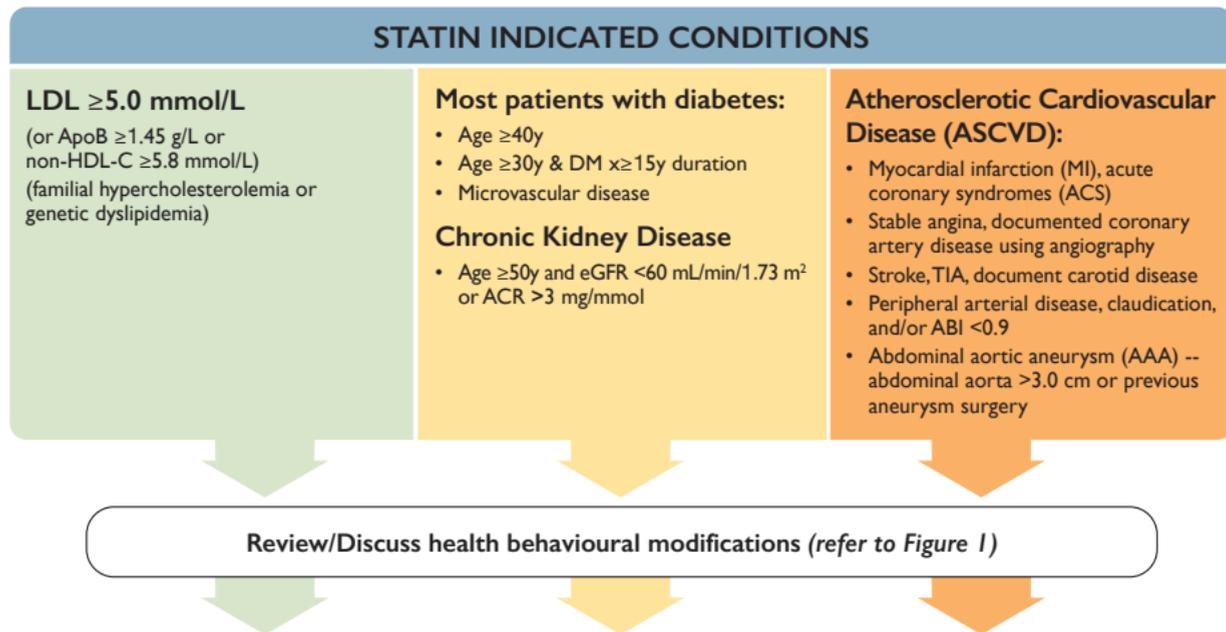
<sup>§</sup>Statin indicated conditions consists of all documented ASCVD conditions, as well as other high-risk primary prevention conditions in the absence of ACSVD, such as most patients with diabetes, those with chronic kidney disease and those with a LDL-C  $\geq 5.0$  mmol/L.

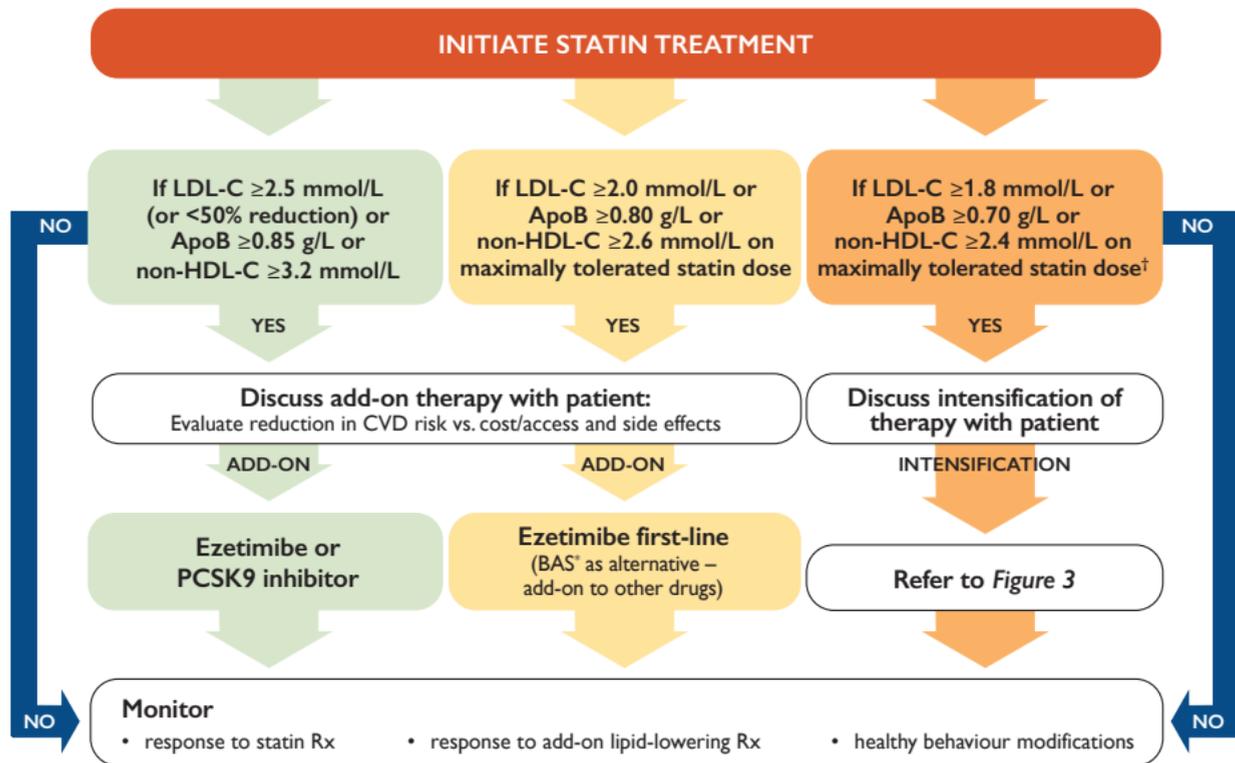
<sup>†</sup>Calculate risk using the Framingham Risk Score (FRS) – refer to the iCCS available on the App Store or on Google Play

<sup>\*</sup>Screening should be repeated every 5 years for men and women aged 40 to 75 years using the modified FRS or CLEM to guide therapy to reduce major CV events. A risk assessment might also be completed whenever a patient's expected risk status changes.

<sup>†</sup> studies have evaluated the efficacy of BAS for the prevention of ASCVD, but results have been inconclusive.

FRS = Framingham risk score; LDL-C = low-density lipoprotein cholesterol; HDL-C = high-density lipoprotein cholesterol; ApoB = apolipoprotein B; IFG = impaired fasting glucose; HTN = hypertension; hsCRP = high-sensitivity C-reactive protein; CAC = coronary artery calcium; AU – Agatston unit; Rx = prescription; BAS = bile acid sequestrant

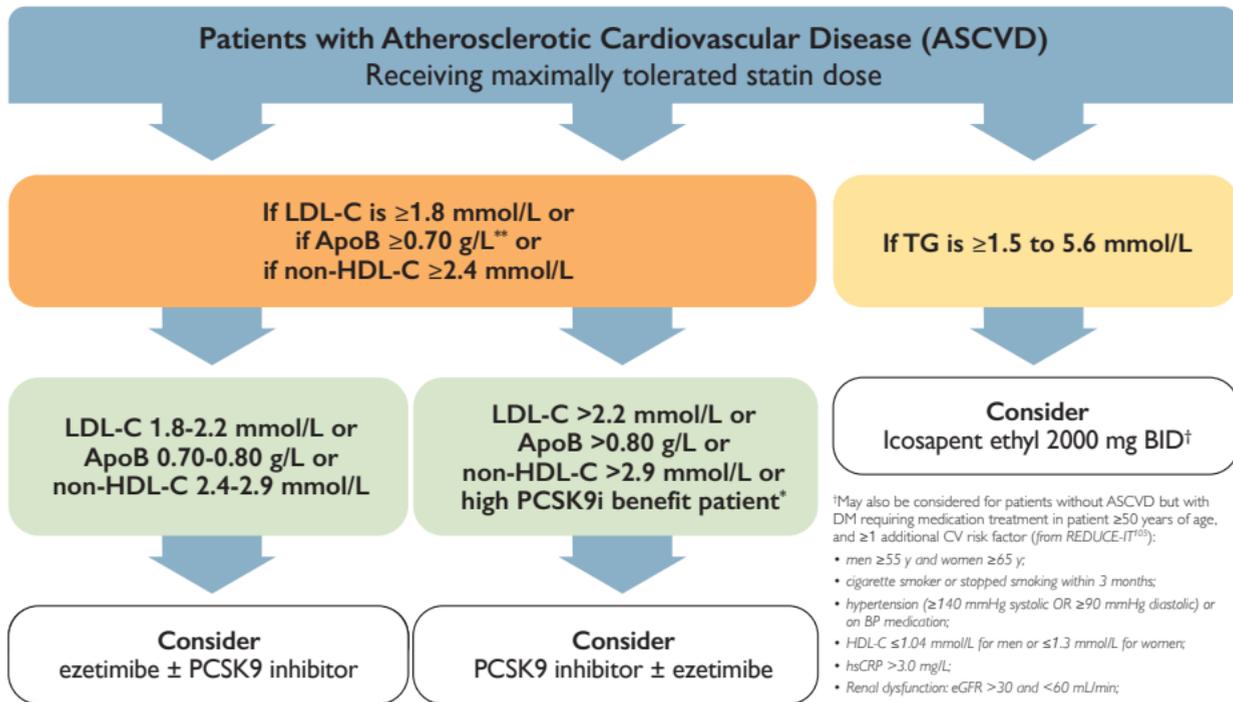




eGFR = estimated glomerular filtration rate; ACR = albumin-to-creatinine; TIA = transient ischemic attack; ABI = ankle-brachial index.

†LDL-C threshold selected on the basis of the PCSK9-inhibitor clinical trials lipid inclusion parameters (references 91 and 92) with percentile equivalents used for ApoB and non-HDL-C (see supplement).

\*studies have evaluated the efficacy of BAS for the prevention of ASCVD, but results have been inconclusive.



\*Patients shown to derive largest benefit from intensification of statin therapy with PCSK9 inhibitor therapy are identified in Table 3.

\*\*At low levels of LDL-C or non-HDL-C, measurement of apoB is more accurate than other markers.

†May also be considered for patients without ASCVD but with DM requiring medication treatment in patient  $\geq 50$  years of age, and  $\geq 1$  additional CV risk factor (from REDUCE-IT<sup>®</sup>):

- men  $\geq 55$  y and women  $\geq 65$  y;
- cigarette smoker or stopped smoking within 3 months;
- hypertension ( $\geq 140$  mmHg systolic OR  $\geq 90$  mmHg diastolic) or on BP medication;
- HDL-C  $\leq 1.04$  mmol/L for men or  $\leq 1.3$  mmol/L for women;
- hsCRP  $> 3.0$  mg/L;
- Renal dysfunction: eGFR  $> 30$  and  $< 60$  mL/min;
- Retinopathy;
- Micro- or macroalbuminuria;
- ABI  $< 0.9$  without symptoms of intermittent claudication)



## Follow-up and Referral to Specialist Clinics

### Follow-up

- Most lipid lowering medications are well-tolerated
- Serum transaminases should be checked within first 3 months
- Creatine kinase can be checked if myalgias develop
- Routine testing of ALT or CK is not required thereafter

### Referral May be Warranted in the Following Cases

- Unexplained atherosclerosis
- Severe dyslipidemias
- Genetic lipoprotein disorders
- Patients refractory to pharmacological treatment

ALT: alanine aminotransferase; CK: creatine kinase.



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