Dyslipidemia:
Present and Future...

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When a patient presents to your office…

1. Determine if they require a fasting lipid profile for screening (Table 1). If yes, perform one.
2. Risk stratify (*e.g.*, using the Framingham risk tables [Table 2]) and determine the risk category (low, moderate or high).
3. Rule out the metabolic syndrome in appropriate patients (Table 3).
4. Rule out a secondary cause of dyslipidemia (*e.g.*, thyroid-stimulating hormone for hypothyroidism, etc.).
5. Determine appropriate goals for low-density lipoprotein (LDL) cholesterol total: high-density lipoprotein cholesterol ratio and treat if indicated (Table 4).
6. In patients with metabolic syndrome, one should consider testing and adjusting treatment according to the apolipoprotein B level in addition to LDL-cholesterol.

Point #1

Screening, investigation and treatment of dyslipidemia is part of the overall strategy of global cardiovascular risk reduction (Table 1).

Table 1

Screening with lipid profile

- Men over 40 years of age and women over 50 years of age/post-menopausal
- Known atherosclerosis (MI, stroke, peripheral vascular disease)
- Diabetes mellitus
- Presence of risk factors, such as hypertension, smoking, abdominal obesity, or a strong family history of premature cardiovascular disease (CVD)
- Manifestations of hyperlipidemia (*i.e.* presence of xanthelasma, xanthoma or arcus cornea) or suspected asymptomatic atherosclerosis

Point #2

Various cardiovascular risk stratification engines can be used, but in Canada the most commonly used is one using the Framingham risk tables (Figure 1).

Patients with the metabolic syndrome (Table 2) may have their risks underestimated using the Framingham risk tables. Some suggest their estimated risk be increased by one category from that calculated.

Table 2

Diagnosis of metabolic syndrome

Look for three or more of the following in a patient:

Findings	Diagnostic
Waist circumference	Men: > 102 cm (40") Women: > 88 cm (35")
Blood pressure	≥ 130/85 mmHg
Triglycerides	≥ 1.7 mmol/L
HDL-C	Men: < 1 mmol/L Women: < 1.3 mmol/L
Fasting glucose	≥ 6.1 mmol/L

HDL-C: High-density lipoprotein-cholesterol

Dyslipidemia

In Point Form

Point #3

Current targets for treatment reflect the emphasis on reduction of LDL-cholesterol and achievement of higher HDL-cholesterol levels (as reflected in a lower Total: HDL-cholesterol ratio) (Table 3).

Table 3

Canadian working group on dyslipidemia recommendations for treatment

Risk	LDL-C target level	TC:HDL-C ratio target level
High (10-year history of CAD ≥ 20% or history of diabetes mellitus or any atherosclerotic disease)	< 2.5 mmol/L *and*	< 4.0
Moderate (10-year risk, 11% to 19%)	< 3.5 mmol/L *and*	< 5.0
Low (10-year risk ≤ 10%)	< 4.5 mmol/L *and*	≤ 6.0

Point #4

There have been recent publications of numerous clinical trials involving statins, using both surrogate (*e.g.* plaque regression measured by angiograms or intravascular ultrasound) and clinical end points (*e.g.*, need for treatment procedure, such as angioplasty, bypass or mortality). Suggestions for how these clinical trial results may affect our practice are summarized here.

Patient with stable angina
The Heart Protection Study (HPS),[2] Reversal of Atherosclerosis with Aggressive

Lipid Lowering (REVERSAL)[3] and Treating New Targets (TNT)[4]

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suggest that lowering LDL cholesterol beyond the current guideline goal of 2.5 mmol may result in further benefit. The American National Cholesterol Education Program (NCEP) guidelines have been revised to suggest reducing LDL-cholesterol in high-risk patients to below 2.8 mmol/L[5] with additional two or more risk factors . This may be achieved without significant risk of liver dysfunction or rhabdomyolysis from higher doses of statin use. However, clinical judgement regarding the costs and the "law of diminishing returns" is needed in individual cases. For example, in the TNT study the number needed to treat to prevent one event (between the choice of 10 mg or 80 mg doses of atorvastatin), ranged from 30 (composite) to 44 (defined end point) over five years.

Patient shortly after an acute MI
Myocardial Ischemia Reduction with Aggressive Cholesterol Lowering (MIRACL)[6], Pravastatin or Atorvastatin Evaluation and Infection Therapy-Thrombolysis in Myocardial Infarction 22 (PROVE-IT-TIMI-22[7]) suggest that with unstable angina (up to 10 days) or acute MI (up to four days after presentation), intensive statin treatment to lower LDL-cholesterol to 1.5-1.8 mmol/L may reduce angina, recurrent MI, need for revascularization and probably stroke. However, the total duration this treatment needs to be maintained, has not been determined.

The type of statin used may be important in effecting the benefit. Most of the above studies used atorvastatin, which achieved lower LDL-cholesterol and C-reactive protein levels than pravastatin.

Point #4 Continue

Hypertensive patient

The Anglo-Scandinavian Cardiac Outcomes Trial-Lipid-Lowering Arm (ASCOT-LLA)[8] suggests that if a patient is 40 to 79 years old, has hypertension and three other risk factors, statin treatment to LDL-C >2.4 mmol/L (possibly lower) may reduce CVD events independent of BP lowering.

Another hypertension study with a lipid-lowering arm is the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT-LLT)[9] showed no benefit to lipid lowering. This may have be due to the high crossover between study and comparator arms, with only a small difference in LDL cholesterol levels between both at the end of treatment.

Type 2 diabetes patient

HPS[2] and Collaborative Atorvastatin Diabetes study[10] suggests that if you are diabetic, 40 to 50 years old, statin treatment to an LDL-cholesterol < 2.4 mmol/L may reduce new angina, recurrent MI, revascularization and stroke. If the patients is diabetic with one other risk factor, further benefit may occur with lowering LDL-cholesterol to <1.6 mmol/L if diabetes is associated with one other risk factor (about 75% of all Type 2 diabetic patients).

Patient at risk of stroke

Data from many of these trials also suggests that stroke risk may be reduced in secondary prevention with statins.

Miscellaneous

Routine screening of C-reactive protein and homocysteine is not recommended.[1]

Results of many hormone replacement studies in postmenopausal women, such as the Heart and Estrogen/Progestin Replacement Study (HERS and HERS-II) and the Womens' Health Initiative have suggested that using estrogen does not reduce cardiovascular risk in postmenopausal women and may add cardiovascular risk.

Extended-release Niacin tablets are now available in Canada.

Newer efforts to increase HDL-cholesterol using a new drug, torcetrapib (TCP), which is an inhibitor of cholesterol ester transfer protein are being reported.

It is not yet in clinical use and may eventually prove useful (*e.g.*, in combination therapy with statins to further raise HDL-cholesterol).

New lipid management guidelines incorporating the results of the clinical trials are likely to be forthcoming in Canada later this year.

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Men

Risk factor	Risk points
Age group	
20-34	-9
35-39	-4
40-44	0
45-49	3
50-54	6
55-59	8
60-64	10
65-69	11
70-74	12
75-79	13

Total cholesterol level, mmol/L	Age group				
	20-39	40-49	50-59	60-69	70-79
< 4.14	0	0	0	0	0
4.15-5.19	4	3	2	1	0
5.20-6.19	7	5	3	1	0
6.20-7.20	9	6	4	2	1
≥ 7.21	11	8	5	3	1

Smoker					
No	0	0	0	0	0
Yes	8	5	3	1	1

High-density lipoprotein cholesterol level, mmol/L	Risk points
≥ 1.55	-1
1.30-1.54	0
1.04-1.29	1
< 1.04	2

Systolic blood pressure, mmHg	Untreated	Treated
< 120	0	0
120-129	0	1
130-139	1	2
140-159	1	2
≥ 160	2	3

Total risk points	10-year risk, %
< 0	< 1
0-4	1
5-6	2
7	3
8	4
9	5
10	6
11	8
12	10
13	12
14	16
15	20
16	25
≥ 17	≥ 30

10-year risk: _____ %

Women

Risk factor	Risk points
Age group	
20-34	-7
35-39	-3
40-44	0
45-49	3
50-54	6
55-59	8
60-64	10
65-69	12
70-74	14
75-79	16

Total cholesterol level, mmol/L	Age group				
	20-39	40-49	50-59	60-69	70-79
< 4.14	0	0	0	0	0
4.15-5.19	4	3	2	1	1
5.20-6.19	8	6	4	2	1
6.20-7.20	11	8	5	3	2
≥ 7.21	13	10	7	4	2

Smoker					
No	0	0	0	0	0
Yes	9	7	4	2	1

High-density lipoprotein cholesterol level, mmol/L	Risk points
≥ 1.55	-1
1.30-1.54	0
1.04-1.29	1
< 1.04	2

Systolic blood pressure, mmHg	Untreated	Treated
< 120	0	0
120-129	1	3
130-139	2	4
140-159	3	5
≥ 160	4	6

Total risk points	10-year risk, %
< 9	< 1
9-12	1
13-14	2
15	3
16	4
17	5
18	6
19	8
20	11
21	14
22	17
23	22
24	27
≥ 25	≥ 30

10-year risk: _____ %

Figure 1. Model for estimating the 10-year risk of coronary artery disease in a patient without diabetes mellitus or clinically evident cardiovascular disease, using data from the Framingham Heart Study.