RECOMMENDATIONS FOR THE DIAGNOSIS AND TREATMENT OF DYSLIPIDEMIA AND PREVENTION OF CARDIOVASCULAR DISEASE: SUMMARY

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SCREENING

Recommendations - full fasting lipid profile

Men	All men ≥ 40 years every 1 - 3 years
Women	All women postmenopausal and/or ≥ 50 years every 1 – 3 years
Children	Family history of severe hypercholesterolemia or chylomicronemia
Adults (≥ 18 years)	All adults at any age **with the following additional risk factors** or at the discretion of physician – Exertional chest discomfort, dyspnea, or erectile dysfunction – Cigarette smoking - current or within past year – Abdominal obesity - waist: men > 102 cm or women > 88 cm (lower cut-offs are appropriate in South & East Asians) – Family history of premature coronary artery disease (CAD) – Manifestations of hyperlipidemia e.g. xanthelasma, xanthoma, corneal arcus – Diabetes mellitus (DM) – Hypertension (HTN) – Chronic kidney disease GFR < 30 mL/min/1.73m^2 – Systemic lupus erythematosus – Evidence of atherosclerosis

ASSESSING RISK

- **Framingham Risk Score (FRS)** - estimates 10-year risk of hard cardiac endpoints (cardiac death & nonfatal MI). Recommended for initial assessment of most patients in the primary prevention category. (FRS provided in 2006 guidelines)
- **Family history of premature CAD** - in first-degree relatives: men < 55 years or women < 65 years. If present, then multiply by a factor of 2.0 the calculated 10-year CAD risk (%).
- **High-risk** - any patient with CAD, peripheral artery disease (PAD), cerebrovascular disease (CVD) or chronic kidney disease (CKD). Most patients with established type 1or 2 DM. These patients automatically in high-risk category - **FRS not required.**
- **Diabetes** - individuals < 40 years with recent-onset DM, a normal lipid profile and no other risk factors for vascular disease are at lower short-term risk for CAD and may not require immediate lipid-lowering therapy.
- **Metabolic syndrome** - individuals are often at higher risk than estimated by FRS. Additional investigations to further define short-term CAD risk may be appropriate.

Risk Categories and Treatment Recommendations

RISK LEVEL	10-yr CAD risk	RECOMMENDATIONS
High (includes CAD, PAD, CVD, CKD & most with DM)	≥ 20%	Treatment targets: Primary: LDL-C < 2.0 mmol/L Secondary: TC/HDL-C < 4.0
Moderate	10% - 19%	Treat when: LDL-C ≥ 3.5 mmol/L **or** TC/HDL-C ≥ 5.0
Low	<10%	Treat when: LDL-C ≥ 5.0 mmol/L **or** TC/HDL-C ≥ 6.0

Metabolic Syndrome - NCEP ATP III Criteria

(3 or more criteria define metabolic syndrome)

RISK FACTOR	DEFINING LEVEL
Abdominal Obesity	Waist Circumference
Men	> 102 cm (40 in)
Women	> 88 cm (35 in)
Triglyceride	≥ 1.7 mmol/L
HDL-C	
Men	< 1.0 mmol/L
Women	< 1.3 mmol/L
Blood Pressure	> 130/85 mmHg
Fasting Glucose	5.7-7.0 mmol/L

Additional Investigations of Potential Use in CAD Risk Assessment

[individuals with moderate-risk (FRS 10%-19%) may be moved to a higher or lower risk category based on additional investigations]

Apolipoprotein B	– **uses:** further defines risk in hypertriglyceridemia or metabolic syndrome – **optimal levels:** < 0.85 g/L in high-risk patients , < 1.05 g/L in moderate-risk, < 1.2 g/L in low-risk
Lipoprotein (a)	– **uses:** further defines risk if family history of premature CAD or FRS 10% - 19% – level >0.3 g/L & TC/HDL-C>5.0 or major risk factors indicates need for earlier, more intense LDL-C lowering
High-sensitivity Cardiac C-reactive protein	– **uses:** further defines risk in patients with abdominal obesity or FRS 10% - 19% – **levels:** < 1.0 mg/L indicates low risk for CV disease; 1.0 mg/L – 3.0 mg/L moderate risk; > 3.0 mg/L high risk
Indexes of glycemia	– measure fasting plasma glucose (FPG) every 1-3 years in adults > 40 years and in younger adults with abdominal obesity and/or a family history of type 2 DM. Consider measuring HbA1c if FPG > 6.0 mmol/L. – **uses:** moderate elevations in HbA1c may indicate increased CAD risk
Homocysteine	– although a marker of CAD risk, treatment with vitamins to lower homocysteine not currently recommended – measurement is expensive and not generally recommended

MANAGEMENT

Lifestyle	
Smoking Cessation	Results in a 36% reduction in the relative risk of mortality from CAD.
Diet	↓ saturated and trans fats ↓ simple sugars and refined carbohydrates ↑ fruits and vegetables ↑ whole-grain cereals ↑ proportion of mono- and polyunsaturated oils, including omega-3 fatty acids
Optimal Waist Circumference	< 94 cm (37 in) for men < 80 cm (32 in) for women Differs by ethnicity with lower cut-offs appropriate for South and East Asians.
Optimal BMI	< 25 kg/m^2
Exercise	30 min. daily moderate physical activity

Treatment	
High-risk Patients	- start meds immediately along with lifestyle - primary treatment goal is LDL-C < 2.0 mmol/L - for most CAD patients, optimal LDL-C reduction is at least 50% - achieve secondary treatment target of TC/HDL-C < 4.0 by further lifestyle changes; consider adjuvant lipid-modifying therapy
Moderate-risk and Low-risk Patients	- lifestyle modifications are the first intervention - treatment to lower LDL-C by at least 40% is generally appropriate in candidates for statins - treatment may be initiated at lower or higher lipid levels if family history or other investigations indicate elevated or reduced risk

Currently Available Lipid-Lowering Medications

Generic Name	Trade Name (* generic available)	Recommended Dose Range
Statins		
Atorvastatin	Lipitor	10 mg - 80 mg
Fluvastatin	Lescol, Lescol XL	20 mg - 80 mg
Lovastatin	Mevacor *	20 mg - 80 mg
Pravastatin	Pravachol *	10 mg - 80 mg
Rosuvastatin	Crestor	5 mg - 40 mg
Simvastatin	Zocor *	10 mg - 80 mg
Bile acid and/or cholesterol absorption inhibitors		
Cholestyramine	Questran*	2 g - 24 g
Colestipol	Colestid	5 g - 30 g
Ezetimibe	Ezetrol	10 mg
Fibrates		
Bezafibrate	Bezalip *	400 mg
Fenofibrate	Lipidil	
	-Micro*	67 mg, 200 mg
	-Supra*	100 mg, 160 mg
	-EZ	48 mg, 145mg
Gemfibrozil	Lopid *	600 mg – 1200 mg
Niacins		
Nicotinic acid	Crystalline niacin*	1 g - 3 g
	Niaspan	0.5 g - 2 g

Medication Pearls

Statins
- contraindicated in women who are or may become pregnant
- use lower dose ranges in persons of South and East Asian origin
- statin monotherapy will achieve target LDL-C levels in most patients
- for patients with moderate hypertriglyceridemia, the addition of salmon oil (1 - 2 g three times daily) to statin therapy may be useful to lower triglyceride (TG) levels; helping to achieve TC/HDL-C ratio

Bile acid and/or cholesterol absorption inhibitors
- combination with a statin can decrease LDL-C levels by an additional 10% - 20%

Fibrates
- do not use gemfibrozil in combination with a statin
- increases in plasma creatinine of 15%-20% common in patients on fibrates
- if renal insufficiency (CrCl 20 - 100 mL/min) start fibrate at the lowest dose; increase only after re-evaluation of renal function and lipids
- fibrates should generally be reserved if TG levels > 10 mmol/L despite lifestyle changes (optimal TG level is < 1.5 mmol/L)

Niacins
- in patients with DM or glucose intolerance, initiate therapy at 500 to 1000 mg/day and adjust glycemic control
- slow-release niacin not recommended due to greater hepatotoxicity risk
- 'flush-free' niacin preparations are ineffective

MONITORING

- **ALT (alanine aminotransferase)**
  - baseline ALT levels; repeat between 1 and 3 months after initiating statin or niacin therapy
  - significant increases in ALT levels > 3 times ULN (upper limit of normal) occur in 0.3% - 2.0% of patients on statins and are generally dose-related
- **CK (creatine kinase)**
  - baseline CK levels
  - patients with significant symptoms of muscle discomfort or weakness should be advised to immediately stop statin and report for lab investigation
  - discontinue drug therapy promptly if muscle discomfort or weakness is accompanied by CK levels > 10 times ULN
  - increased risk of myositis if statins administered with interacting medications e.g. cyclosporine, gemfibrozil, certain antifungals & macrolide antibiotics