

## Dyslipidemia Management - Summary

### How do I assess Dyslipidemia?

Screening of plasma lipids is recommended in adult men  $\geq 40$  and women that are  $\geq 50$  years of age or who are postmenopausal.

Adults at any age with the following risk factors should be screened for lipids at any age:

- modifiable factors: smoking, diabetes, hypertension, obesity
- others: rheumatoid arthritis, systemic lupus erythematosus, psoriatic arthritis, ankylosing spondylitis, inflammatory bowel disease, chronic obstructive pulmonary disease, chronic HIV infection, CKD, abdominal aortic aneurysm, erectile dysfunction
- individuals of First Nation or South Asian ancestry are at increased risk and consideration should be given for screening at an earlier age
- those with a family history of premature atherosclerosis in a first degree relative

Recommendations by the 2012 Update to the CCS Guidelines suggests initial risk assessment be completed using the Framingham Risk Score to estimate the 10 year risk of developing "total" cardiovascular events.

#### Initial assessment stratified by risk:

Low risk – FRS  $< 10\%$

Intermediate risk – FRS 10-19% and no high risk features

High risk FRS  $> 20\%$ , clinical valvular disease, AAA, Diabetes and age  $\geq 40$  of 15 yrs duration and age  $\geq 30$  or macrovascular disease, CKD, High risk hypertension

### How do I treat Dyslipidemias?

Low Risk- treat if LDL-C  $\geq 5.0$ mmol/L or if genetic dyslipidemia for  $\geq 50\%$  reduction in LDL-C

Intermediate Risk-treat if LDL-C  $\geq 3.5$ mmol/L

- In patients with LDL-C  $< 3.5$ mmol/L identify patients who might benefit from pharmacotherapy
- For LDL target of  $\geq 2.0$  mmol/L or  $\geq 50\%$  reduction in LDL-C from baseline for IR in whom treatment is initiated

High Risk-treat all included in risk above

- To target LDL-C  $\leq 2.0$  mmol/L or  $\geq 50\%$  reduction of LDL-C from baseline

Table 1 Summary of treatment thresholds and targets based on Framingham Risk Score (FRS)

Risk level	Health Behaviour Modification	Initiate Drug therapy if:	Primary target: LDL-C
<b>High</b> (FRS ≥ 20%)	For all	Consider treatment in all	≤ 2 mmol/L or ≥ 50% ↓ LDL-C
<b>Moderate</b> (FRS 10 to 19%)	Consider as first line treatment, If no improvement initiate drug therapy	LDL-C ≥ 3.5 mmol/L For LDL-C < 3.5	≤ 2 mmol/L or ≥ 50% ↓ LDL-C
<b>Low</b> (FRS < 10%)	For all	LDL-C ≥ 5 mmol/L Familial hypercholesterolemia	≥ 50% ↓ LDL-C

Health Behaviours – universally applied for chronic disease prevention

- Smoking cessation including pharmacological if required
- Diet low in sodium & simple sugars, and substitution of unsaturated fats for saturated and trans fats
- Caloric restrictions to achieve and maintain ideal body weight
- Moderate vigorous exercise for at least 150 min per week
- Psychological stress management
- Alcohol consumption in moderation

### Pharmacotherapy

Initiated in all high risk patients used along with lifestyle changes

In intermediate risk patients lifestyle changes should be implemented first, followed by medications if targets are not reached

In high risk patients treatment should be started immediately, the majority of patients will be able to achieve target LDL-C levels on **statin monotherapy**. However, a significant minority may require combination therapy with an agent that inhibits cholesterol absorption (ezetimibe), or bile acid reabsorption (cholestyramine, colestipol), or concomitant use of niacin.

Triglyceride therapies- in patients with extreme hypertriglyceridemia (>10mmol/L), fibrates may prevent pancreatitis.

Combinations are safe and generally reduce LDL-C by an additional 10-15%.

See table below for summary of recommendations on available pharmacotherapy choices and recommended dosage ranges.

Table 2 Lipid-lowering medications (1)

Generic name	Trade name	Recommended dose range (daily)
<b>Statins</b>		
Atorvastatin	Lipitor	10 mg – 80 mg
Fluvastatin	Lescol	20 mg – 80 mg
Lovastatin	Mevacor	20 mg – 80 mg
Pravastatin	Pravachol	10 mg – 40 mg
Rosuvastatin	Crestor	5 mg – 40 mg
Simvastatin	Zocor	10 mg – 80 mg*
<b>Bile acid and/or cholesterol absorption inhibitors</b>		
Cholestyramine	Questran	2 g – 24 g
Colestipol	Colestid	5 g – 30 g
Ezetimibe	Ezetrol	10 mg
<b>Fibrates</b>		
Bezafibrate	Bezalip	400 mg
Fenofibrate†	Lipidil Micro/Supra/EZ	48 mg – 200 mg
Gemfibrozil‡	Lopid	600 mg – 1200 mg
<b>Niacin</b>		
Nicotinic acid	Generic crystalline niacin	1 g – 3 g
	Niaspan	0.5 g – 2 g

\*Increased myopathy on 80 mg;

†Reduce dose or avoid in renal impairment;

‡Should not be used with a statin because of an increased risk of rhabdomyolysis

### How do I monitor for safety?

Before initiation of pharmacological therapy for dyslipidemias:

- baseline lipoprotein profile should be obtained after 10-12 hr fast, preferably with patient refraining from alcohol for 24-48 hours. The profile should include Total Cholesterol, HDL-C, and triglycerides.

- baseline fasting glucose level should be obtained at baseline to identify the presence of impaired fasting blood glucose or diabetes.

- in patients with Low HDL-C baseline Thyroid stimulating hormone level helps uncover the occasional hypothyroid induced hyperlipidemia.

-baseline alanine aminotransferase (ALT), and aspartate aminotransferase (AST)), serum creatinine (SCr), creatinine kinase (CK) are useful to monitor potential side effects associated with therapy.

### **How and what do I monitor for follow-up?**

Re-checking of Lipoprotein panel based on risk assessment with FRS. If <5% then every 3-5 years, if ≥5% then yearly.

### Statins

Repeat of ALT, AST, SCr and CK is not indicated unless indicated by symptoms

Myalgias- can occur in approximately 5 % of patients

- Characterized by dull muscle aches, worsening with exercise
- Serum CK levels may remain normal
- Diagnosis made with drug discontinuation and re-challenge

Myositis – inflammation of skeletal muscles

- Diagnosis made based on muscle discomfort and elevation of CK to more than three times the upper limit of normal
- Serious condition potentially caused by strenuous exercise
- Dose reduction and close monitoring of CK levels or d/c of statin often required

Rhabdomyolysis-life threatening condition of prevalence of less than 1:100,000 statin treated patients

- Characterized by severe muscle pains, myoglobinuria, and possibly ARF and CK level greater than 10,000U/L
- discontinue statin and hospitalization for supportive treatment required

LFT elevations-ALT level of greater than three times the upper level of normal

- occurs in 0.3-2.0% of patients and generally dose related

### Niacin

- can result in elevations of ALT up to 3 times the upper limit of normal
- measure ALT at baseline and 1-3 months after initiation of therapy
- measure fasting blood glucose and glycosylated haemoglobin every 6-12 months

### Fibrates

- can cause reversible increases in GFR of 10-15%

- should be initiated at the lowest dose available, and only increased after re-evaluation of renal function and lipid parameters

### **What should I tell the patient?**

Health behaviours remain the cornerstone of management of dyslipidemias. These include:

- smoking cessation
- diet restrictions
- exercise
- stress management
- limitations on alcohol consumption

-these behaviours should be universally applied to all patients for the prevention of chronic disease and are outlined under Health Behaviours under treatments for dyslipidemias.

Patients should be advised to stop statin therapy and contact prescribing health care provider if worrisome symptoms develop. The effort spent preserving statin therapy in subjects with adverse effects should be directly related to the level of risk for each individual patient. In high risk patients all options should be exercised before changing to alternative therapy or withdrawing treatment. Lower dose combination therapy remains an option for those patients, with emphasis on more aggressive non-pharmacologic approach such as diet modification and exercise. For subjects with lower risk, re-evaluation of the need for the lipid lowering therapy should precede a change to alternative therapy because outcomes studies are not as robust.

## References

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