

CCPN RCPC
CANADIAN CARDIOVASCULAR
PHARMACISTS NETWORK
RÉSEAU CANADIEN DES PHARMACIENS
IMPLIQUÉS EN SOINS CARDIOVASCULAIRES



Dyslipidemia Management Resource Kit

Prepared by the Canadian
Cardiovascular Pharmacists
Network (CCPN)

Overview

1. Patient Identification
2. Risk Assessment and Targets
3. Drug Interactions
4. Monitoring
5. Treatment Alternatives
6. Heart Healthy Resources
7. The Evidence

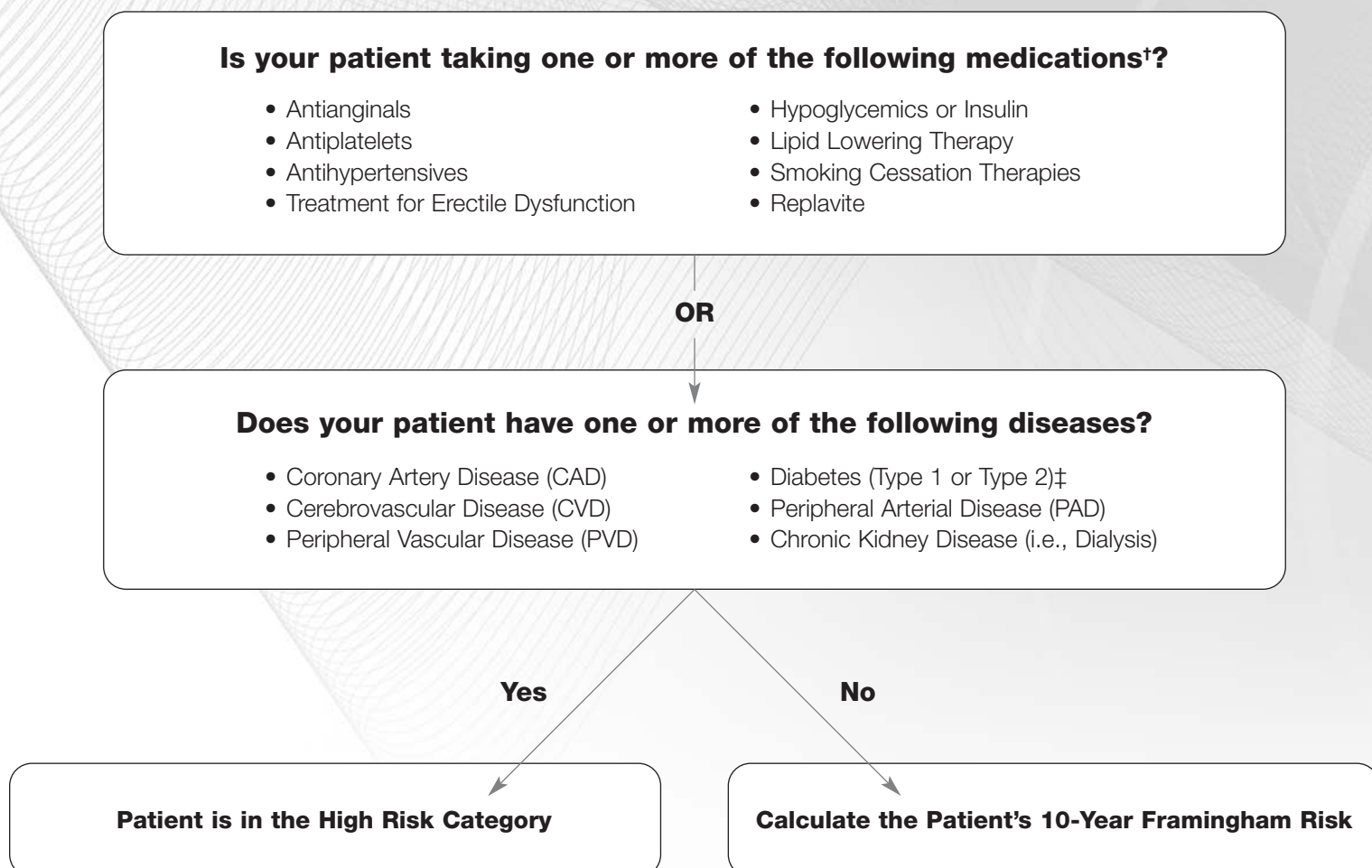
Disclaimer:

The information contained in this resource are designed to serve as a reference, only for use by pharmacists and other healthcare professionals. This information is intended only as a general reference to supplement the existing knowledge of pharmacists and other healthcare professionals and is NOT a substitute for the sound clinical judgement of the knowledgeable health professional. The authors, editors, or CCPN cannot be held responsible for any harm, direct or indirect, caused as a result of the application of the information contained in this resource.

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PATIENT IDENTIFICATION

How to Identify Patients At Risk



[†] This list is not comprehensive. A high-risk patient with established disease may be taking other medications not on this list.

[‡] Includes most patients with diabetes. Exceptions would include younger adults with Type 1 diabetes with shorter duration of disease and without complications of diabetes (including established CVD) and without other CVD risk factors, for whom vascular risk should be calculated (UKPDS risk engine appropriate www.dtu.ox.ac.uk/riskengine).

RISK ASSESSMENT AND TARGETS

Calculate the patient's 10-year risk estimate for Coronary Artery Disease (CAD)-death or non-fatal myocardial infarction according to the Framingham Risk Score.[‡]

Assessing CHD risk in women

Step 1: Age

Years	10-yr Risk
20 - 34	-7
35 - 39	-3
40 - 44	0
45 - 49	3
50 - 59	6
60 - 64	10
65 - 69	12
70 - 74	14
75 - 79	16

Step 3: HDL-Cholesterol

HDL-C (mmol/L)	Points
≥1.55	-1
1.30 - 1.54	0
1.04 - 1.29	1
<1.04	2

Step 2: Total Cholesterol

TC mmol/L	Points at age				
	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
5.2 - 6.19	8	6	4	2	1
6.2 - 7.2	11	8	5	3	2
>7.21	13	10	7	4	2

Step 5: Smoking Status

	Points at age				
	20-39	40-49	50-59	60-69	70-79
Nonsmoker	0	0	0	0	0
Smoker	9	7	4	2	1

Step 4: Systolic Blood Pressure

Systolic BP (mmHg)	Points if untreated	Points if treated
	<120	0
120 - 129	1	3
130 - 139	2	4
140 - 159	3	5
≥160	4	6

Step 6: Adding up the points

Age	—
Total Cholesterol	—
HDL-Cholesterol	—
Systolic blood pressure	—
Smoking status	—
Point Total	—

Step 7: CHD Risk

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

‡ Patients with established CAD, CVD, PVD, PAD, CKD or Diabetes are automatically considered high risk. For patients with a family history of CAD in a first-degree relative before the age of 55 years in a male or 65 years in a female, the calculated 10-year CAD risk should be multiplied by a factor of 2.0.

Assessing CHD risk in men

Step 1: Age

Years	10-yr Risk
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

Step 3: HDL-Cholesterol

HDL-C (mmol/L)	Points
≥1.55	-1
1.30 - 1.54	0
1.04 - 1.29	1
<1.04	2

Step 2: Total Cholesterol

TC mmol/L	Points at age				
	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
5.2 - 6.19	7	5	3	1	0
6.2 - 7.2	9	7	4	2	1
>7.21	11	8	5	3	1

Step 5: Smoking Status

	Points at age				
	20-39	40-49	50-59	60-69	70-79
Nonsmoker	0	0	0	0	0
Smoker	8	5	3	1	1

Step 4: Systolic Blood Pressure

Systolic BP (mmHg)	Points if untreated	Points if treated
	<120	0
120 - 129	0	1
130 - 139	1	2
140 - 159	1	2
≥160	2	3

Step 6: Adding up the points

Age	—
Total Cholesterol	—
HDL-Cholesterol	—
Systolic blood pressure	—
Smoking status	—
Point Total	—

Step 7: CHD Risk

Point Total	10-yr Risk
<0	<1%
0	1%
1	1%
2	1%
3	1%
4	1%
5	2%
6	2%
7	3%
8	4%
9	5%
10	6%
11	8%
12	10%
13	12%
14	16%
15	20%
16	25%
≥17	≥30%

‡ Patients with established CAD, CVD, PVD, PAD, CKD or Diabetes are automatically considered high risk. For patients with a family history of CAD in a first-degree relative before the age of 55 years in a male or 65 years in a female, the calculated 10-year CAD risk should be multiplied by a factor of 2.0.

TARGET LIPID LEVELS ^{1,2}

Level of Risk (definition)	Recommendations	
High[†] (10-year risk \geq 20%)	Primary Target: LDL < 2.0	Secondary Target: TC/HDL < 4.0
Moderate[‡] (10-year risk 10-19%)	Treat when LDL \geq 3.5	Treat when TC/HDL \geq 5.0
Low[‡] (10-year risk < 10%)	Treat when LDL \geq 5.0	Treat when TC/HDL \geq 6.0

[†] High risk includes patients with established CAD, CVD, PVD, PAD, CKD or Diabetes. For those in the high-risk category it is recommended to lower LDL by at least 50%. A statin is recommended for most patients for achievement of target LDL levels.

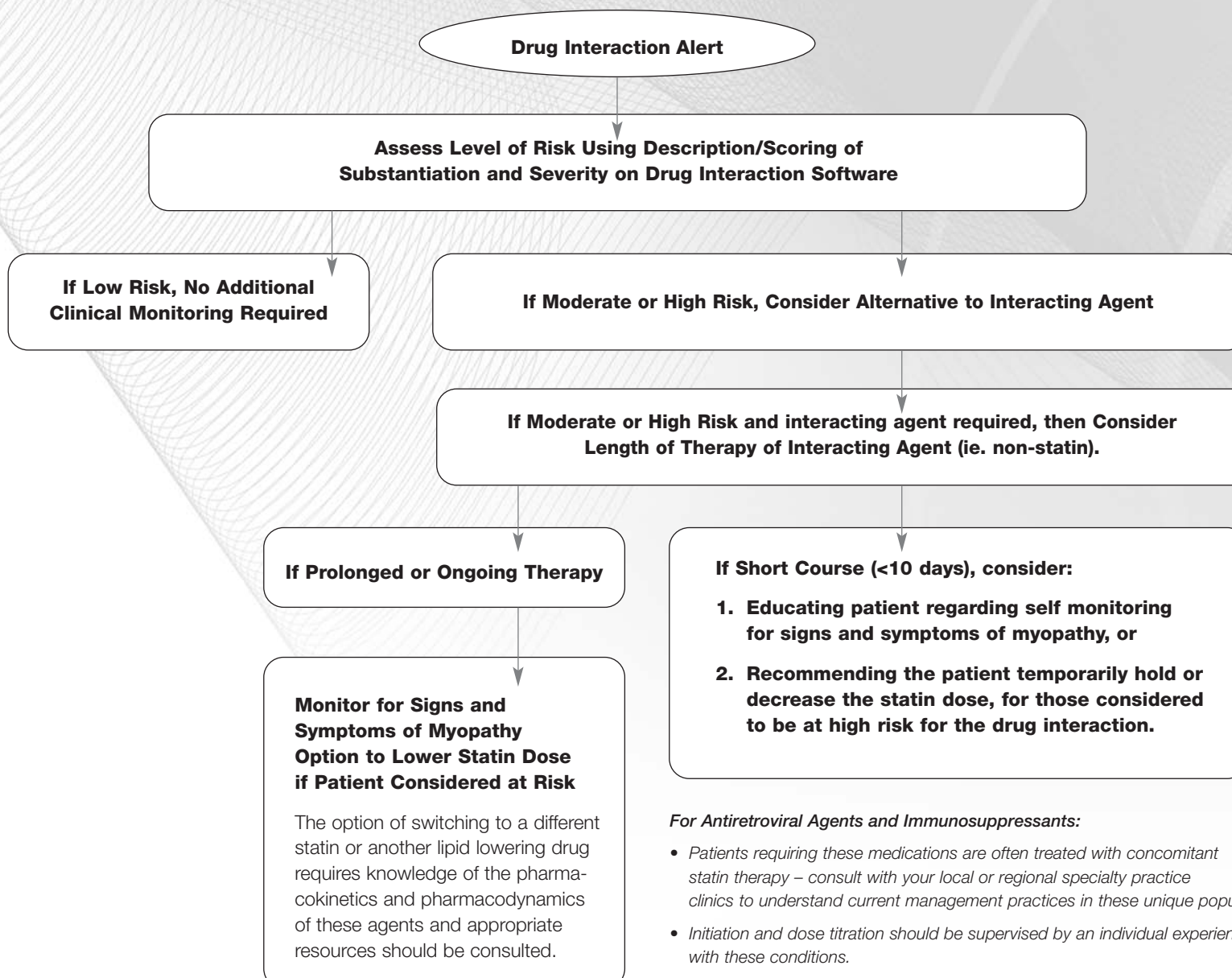
[‡] Among moderate and low-risk patients who are candidates for treatment, it is recommended to lower LDL by at least 40%.

1. McPherson R, Frohlich J, Fodor G, Genest J. Canadian Cardiovascular Society position statement - recommendations for the diagnosis and treatment of dyslipidemia and prevention of cardiovascular disease. *Can J Cardiol* 2006;22(11):913-27.

2. Pearson GJ, Thompson AE, Semchuk W. 2007 Guidelines for the management of dyslipidemia and prevention of cardiovascular disease by pharmacists. *CPJ* 2007;140(6):383-8.

DRUG INTERACTIONS

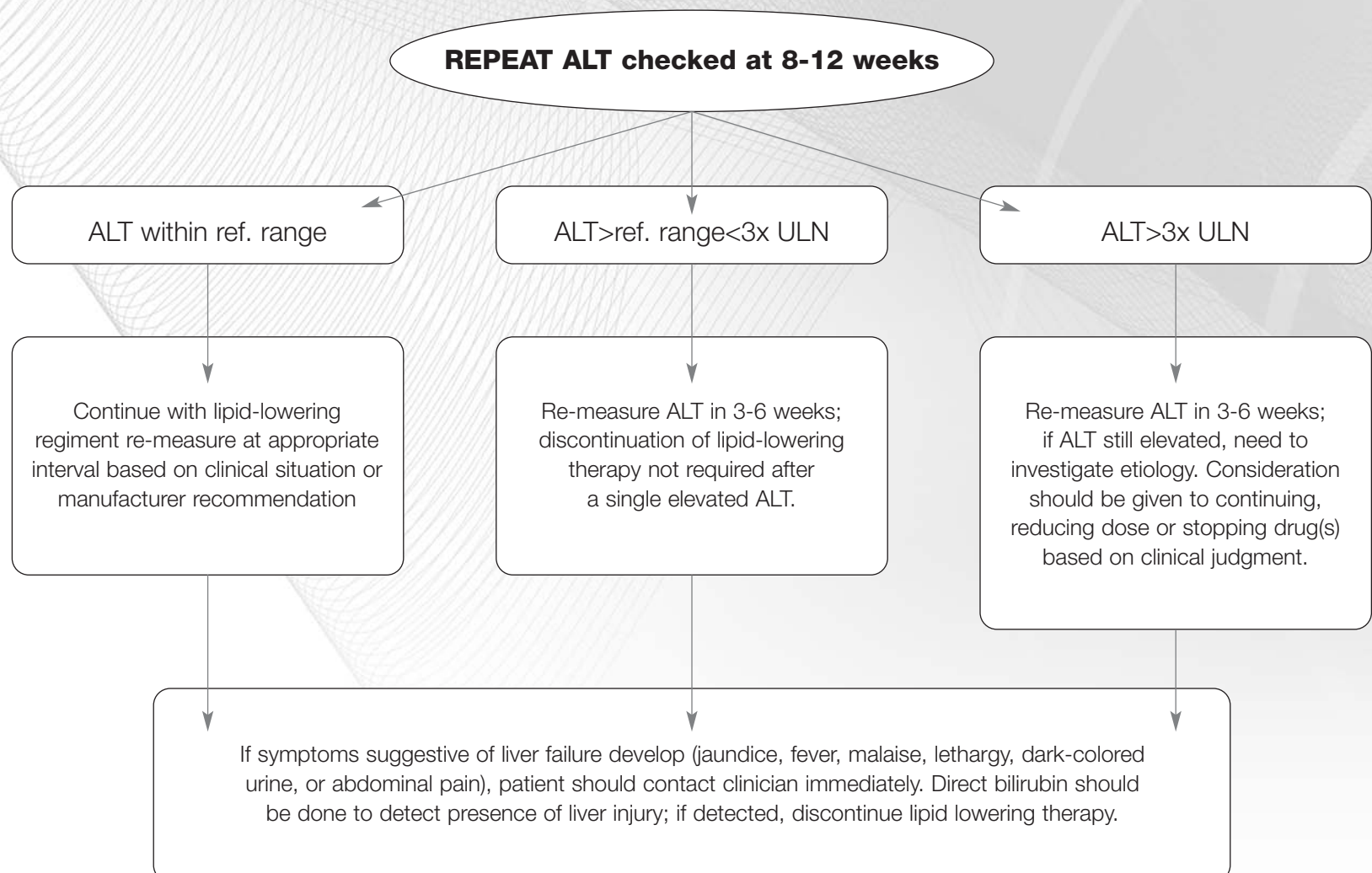
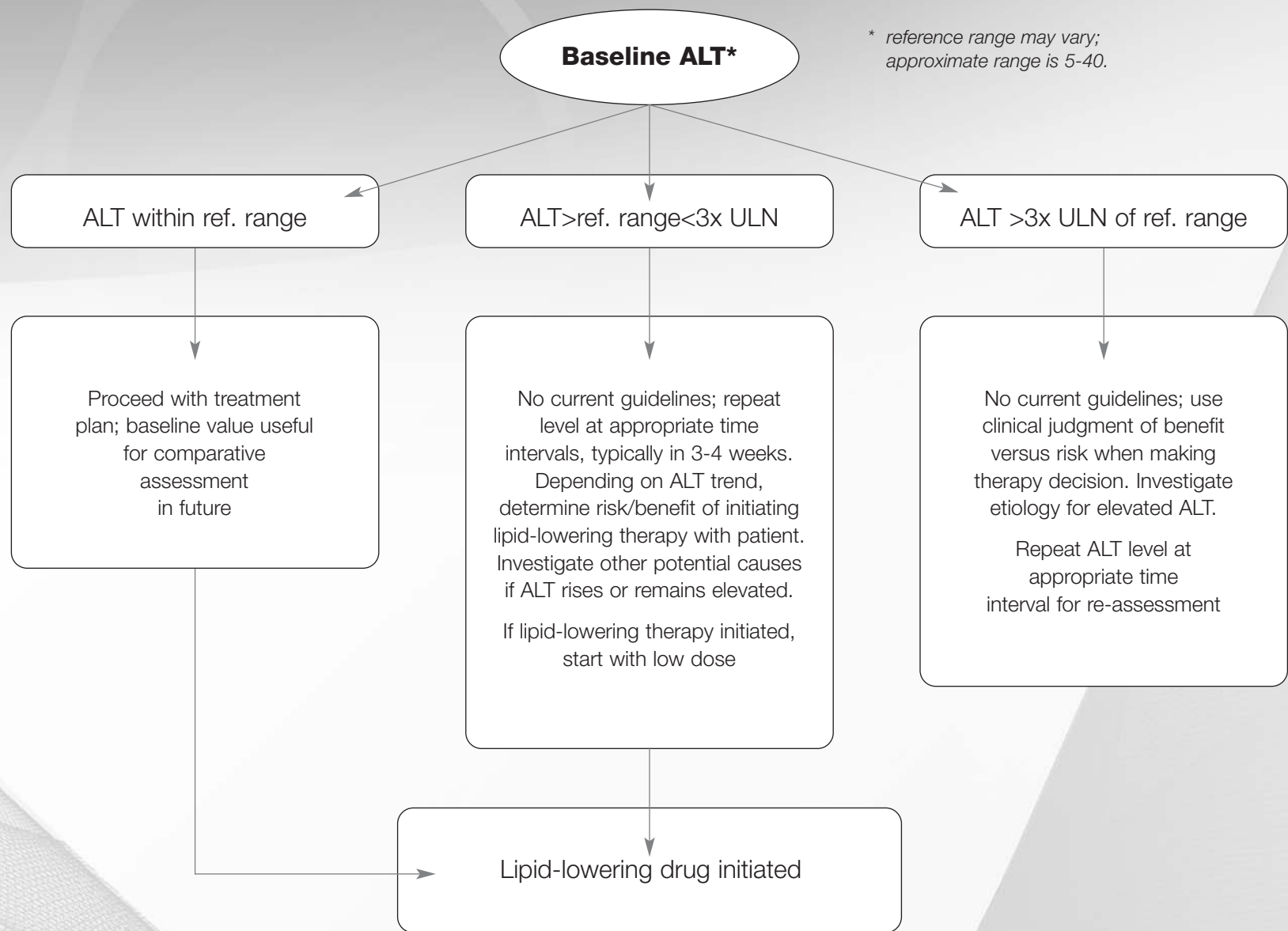
What should you do about drug interaction flags with statins?



MONITORING



MONITORING (CONTINUED)



* timelines are approximate and can be altered to suit clinical situation

TREATMENT ALTERNATIVES

Available by Prescription

Agent	Place in Therapy	LDL-c	HDL-c	TG	Comments
Statins	Statins have the most evidence for reduction in cardiovascular outcomes. They may also possess benefits outside of direct lowering of lipid levels such as plaque stabilization.				"Rule of Sixes": Doubling of statin dose provides approximately 6% further reduction in LDL.
Atorvastatin 10-80mg/d		↓ 34 - 60%	↑ 4 - 8%	↓ 19 - 37%	
Fluvastatin 20-60mg/d		↓ 15 - 25%	↑ 2 - 7%	↓ 7 - 10%	
Lovastatin 20-60mg/d		↓ 17 - 35%	↑ 7 - 9%	↓ 10 - 16%	
Pravastatin 10-40mg/d		↓ 22 - 40%	↑ 8 - 14%	↓ 25%	
Rosuvastatin 5-20mg/d		↓ 40 - 65%	↑ 12 - 13%	↓ 18 - 30%	
Simvastatin 10-80mg/d		↓ 25 - 46%	↑ 6 - 8%	↓ 10 - 20%	
Fibrates (gemfibrozil 300-600mg/d, fenofibrate 160-200mg/d, bezafibrate 200-600mg/d)	Fibrates are very effective in reducing triglycerides. May consider combination therapy with a statin in patients who exhibit significant hypertriglyceridemia despite statin monotherapy.	↓ 5 - 20%	↑ 10 - 20%	↓ 20 - 50%	Gemfibrozil has been associated with a higher risk of myotoxicity and should likely be avoided as the choice of fibrate to be combined with a statin
Resins (colestipol 2-15g bid, cholestyramine 4-8g bid)	Consider combination therapy with a statin in patients who have not achieved target LDL reduction with statin monotherapy. The combination can generally decrease LDL a further 10-20%.	↓ 15 - 30%	↑ 3 - 5%	~ ↑ 3 - 10%	Caution - may INCREASE triglycerides.
Ezetimibe 10mg/d	Consider combination therapy with a statin in patients who have not achieved target LDL reduction with statin monotherapy. The combination can generally decrease LDL a further 10-20%.	↓ 16 - 20%	↑ 2 - 3%	↓ 10 - 15%	Long term data regarding the effect of ezetimibe on cardiovascular outcomes is not yet available.
+ Atorvastatin		↓ 50 - 60%	↑ 5 - 9%	↓ 30 - 40%	
+ Lovastatin		↓ 33 - 45%	↑ 8 - 9%	↓ 19 - 27%	
+ Pravastatin		↓ 34 - 41%	↑ 7 - 8%	↓ 21 - 23%	
+ Simvastatin		↓ 44 - 51%	↑ 8 - 11%	↓ 20 - 28%	
Niacin (ER = 500-2000 mg/day; IR = 250-3000 mg/day) Note: Immediate Release (IR) niacin (crystalline) is available OTC	Niacin is one of the most effective agents to increase HDL. In patients with combined dyslipidemia and low HDL levels, consider the combination of a statin with niacin.	↓ 15 - 25%	↑ 20 - 25%	↓ 30 - 60%	"Flush-free" (inositol hexaniacinate) and nicotinamide do not have anti-lipemic properties & are not recommended. To avoid /minimize the risk of hepatotoxicity, preference should be given to using ER (prescription) when considering long-acting formulations.

TREATMENT ALTERNATIVES

Non- Prescription

Agent	Proposed Mechanism of Action	TC	LDL-c	HDL-c	TG	Comments
Fish Oils (Salmon Oil) 1-4g/d Seal Oil Omega-3 Compounds	Source of omega-3 fatty acids (DHA + EPA). Multiple theoretical mechanisms for proposed benefits: ↓ production of thromboxane, ↑ prostacyclin production by endothelial cells, ↓ blood viscosity, ↓ vasospastic response to catecholamines, ↑ fibrinolysis, ↓ blood pressure, ↓ triglycerides		~↑ 5 - 10% (Thought to consist of less dense, less atherogenic forms)	↑ 1 - 3%	↓ 25 - 30%	Salmon oil provides most concentrated amounts of DHA + EPA. Epidemiological evidence shows ↓CVD with high fish diets. In the JELIS trial, there was a 19% relative reduction in major coronary events (p=0.011) in the EPA treated patients; this benefit was limited to secondary prevention patients. Seal oil and other omega-3 polyunsaturated fatty acid compounds may provide similar benefits, but is not well studied. Less effective than gemfibrozil 1200mg/day in patients with severe hypertriglyceridemia
Garlic 600-900mg/d	Inhibits cholesterol synthesis in liver. S-allyl constituent (allin) is the active ingredient.	↓ 4 - 12%	↓ 11.4%		↓ 9.9%	Several studies show only modest or NO benefit. No benefit seen >6 months.
Flaxseed 30-50g/d	Source of fibre and α - linoleic acid (converted to DHA + EPA at a ratio of 10:1), providing multiple mechanisms.	↓ 4 - 7%	↓ 7 - 14%	No effect	No effect; defatted flaxseed may ↑ ~10%	Studies used dietary flaxseed. Flaxseed oil has not been studied but may provide similar benefits attributable to α - linoleic acid.
Guggulipids 50mg guggulsterones bid	Inhibit cholesterol synthesis in liver and antioxidant effects	↓ 11.7% to ↑ 5%	↓ 0 - 12.7%		↓ 12%	Scant evidence for use. Conflicting evidence in those consuming "Western" diets which show no effects or increased LDL vs studies in Indian populations which show decreased in TC, LDL and TG.
Lecithin 0.5-2g/d	May Inhibit cholesterol absorption	↓ 0 - 10%	↓ 0 - 14.3%			Scant evidence for use. Conflicting information on influence on lipoproteins
Grape Seed 50-300mg/d	Source of α - linoleic acid and antioxidant effects	↓ 2.5%	↓ 1%	No effect	No effect	Scant evidence for use. Also reported to ↓ PVD & atherosclerosis by an unknown mechanism.

HEART HEALTHY LIFESTYLE INFORMATION RESOURCES

Healthy Living

- Recommendations for a healthy lifestyle (diet, activity, positive lifestyle choices).
 - o www.hc-sc.gc.ca/hl-vs/index_e.html
 - o <http://www.phac-aspc.gc.ca/pau-uap/paguide/index.html>
 - o www.heartandstroke.com/site/c.ikiQLcMWJtE/b.3483949/

Food and Nutrition

- Canada's Food Guide and related topics
 - o Broad array of information pieces that included food guide basics, choosing foods, and maintaining healthy habits.
 - o www.hc-sc.gc.ca/fn-an/food-guide-aliment/index_e.html
- Reading food labels
 - o www.metro.ca/art-de-vivre/alim-bien-etre/conseils-nutrition/lire-etiquette.en.html

Heart Smart Cookbooks

- <http://www.heartandstroke.com/site/c.ikiQLcMWJtE/b.3484333/>

Finding a Dietitian

- http://www.dietitians.ca/public/content/find_a_nutrition_professional/find_a_dietitian.asp

Nutrition Facts and Calorie Counter

- http://www.nutritiondata.com/tools/calories-burned?mbid=google&npu=1&gclid=CK3V5_vly5ACFSeDYAodZx85Uw

Body Mass Index (BMI) is a measurement of weight in relation to height. It is one of the tools that is used to create guidelines for healthy living.

- <http://ww2.heartandstroke.ca/Page.asp?PageID=1187>

Smoking Cessation

- Smokers Helpline is a free confidential telephone service for smokers who want to quit, are thinking about quitting, have stopped smoking and need support, and for those who don't want to quit.
- The Lung Association provides information and resources about quitting smoking and second hand smoke.
 - o http://www.lung.ca/protect-protegez/tobacco-tabagisme_e.php

Newfoundland/Labrador	1-800-363-5864
Prince Edward Island	1-888-818-6300
Nova Scotia New Brunswick Ontario Manitoba Saskatchewan	1-877-513-5333
Quebec	1-866-527-7383
Alberta	1-866-332-2322
British Columbia	1-877-455-2233

THE EVIDENCE

Here's how to use the major statin trials in the care of your patient.

The first trial in which statins were shown to reduce mortality in patients with coronary artery disease was published in 1994. Subsequent trials demonstrated similar results which has led to statins being a mainstay therapy in the treatment of dyslipidemia. More recently, trials have demonstrated that early initiation of statins in patients suffering an acute coronary syndrome was safe and had short term benefits and that intensive statin therapy had additional benefits compared to less intense therapy. In patients at high risk of developing heart disease, statins have been shown to reduce mortality and in those who are at risk for cardiovascular disease, to reduce myocardial infarction. Other therapies such as fibrates, while effective in treating lipid abnormalities have not been shown to consistently decrease clinical events such as death and myocardial infarction. There are many trials that measure surrogate markers (e.g., percent of patients to reach target LDL levels, regression/progression of plaques) and other potential mechanisms (e.g., antiplatelet and pleiotropic effects) however these should not be considered as strong evidence of benefit as those trials that have looked at clinical outcomes (e.g., mortality, myocardial infarction)

A summary of the results are provided in the table. But the question is, how do these results apply to your patients?

This information can be used to help educate patients on the value of their medications. A large meta-analysis looked at all the major statin trials that had been conducted in a variety of patients with or at risk of cardiovascular disease. The results of the meta-analysis demonstrated that total mortality was reduced from 9.7% to 8.5% and myocardial infarctions from 6.2% to 4.4%. There are two ways to relay this information to the patient. One is to inform him that if 100 people were like him, approximately 10 people (actually 9.7) would die in the next 5 years and 6 of them would suffer a myocardial infarction. If they took their prescribed statin, mortality would be reduced to 9 people and myocardial infarctions to 5 (actually 4.4). Another way of presenting this information is using the NNT or number needed to treat which is calculated by dividing one (1) by the difference between the two groups multiplied by 100 ($1 / (9.5 - 8.7) \times 100 = 83$). This would mean that for every 83 people who took this medication for 5 years, one fewer person would die during that time and that for every 55 people who took this medication, one fewer person would have a myocardial infarction. Trials that have included higher risk patients, for example the 4S trial has a NNT of 32 – that is 32 people would have to take simvastatin 40 mg daily for 5 years for one fewer person to die during that time.

THE EVIDENCE (CONTINUED)

Study/ Year published	N	Population/ cholesterol (mmol/L)	Follow-up (yrs)	Drug/dose	Outcome		
					CHD mortality	Total mortality	Others
Meta-analysis							
1995	90056	Both with and without cardiovascular disease	1.8 to 5.8 years	Various	Treatment 3.4% Control 4.4%	Treatment 8.5% Control 9.7%	Non-Fatal MI Treatment 4.4% Control 6.2%
Atorvastatin							
MIRACL ⁴ 2001	3086	Non-Q MI/USA within 96 hrs	16 weeks	Atorvastatin 80 mg vs placebo		Atorva 4.2% Placebo 4.4%	Death/MI/arrest/ recurrent ischemia Atorva 4.8% Placebo 17.4%
PROVE-IT TIMI 22 ⁶ 2004	4162	Age > 18 Acute Coronary Syndrome within 10 days T Chol < 6.21	24 months	Atorvastatin 80 mg vs pravastatin 40 mg	Atorva 1.1% Prava 1.4%	Atorva 2.2% Prava 3.2%	Death/MI/USA/revasc /stroke Atorva 22.4% Prava 26.3%
TNT ¹³ 2005	10001	Age 35 - 75 Stable CAD	4.9 years	Atorvastatin 80 mg vs atorvastatin 10 mg	Atorva 80 mg 2.5% Atorva 10 mg 2.0%	Atorva 80 mg 5.6% Atorva 10 mg 5.7%	CHD death/AMI/ CA/stroke Atorva 80 8.7% Atorva 10 10.9%
IDEAL ¹⁴ 2005	8888	Age < 80, History of CAD/MI	4.8 years	Atorvastatin 80 mg vs simvastatin 20 mg		Total mortality Simv 20 8.2% Atova 80 8.4%	MI Simva 20 7.2% Atova 80 6.0%
ASCOTT-LLA ¹⁰	10,305	HTN + 3 CV risk factors	3.3 years	Atorvastatin 10 mg vs placebo			Non-fatal MI/ fatal CHD 0.64 (0.5 - 0.83)
Lovastatin							
AFCAPS/TexCAPS ⁹	6605	Age 57 - 63	5 years	Lova 20 - 40 vs placebo			Fatal/non-fatal MI, USA/SCD 10.9% vs 6.8%

Study/ Year published	N	Population/ cholesterol (mmol/L)	Follow-up (yrs)	Drug/dose	Outcome		
					CHD mortality	Total mortality	Others
Pravastatin							
CARE ² 1996	4159	Post-MI 3 - 20 months Total c < 6.2 LDL-c 3.0 - 4.5	5.0	Pravastatin 40 mg daily vs placebo	Prava 4.6% Placebo 5.7%	Prava 8.7% Placebo 9.4%	Death/MI Prava 10.2% Placebo 13.2%
LIPID ³ 1998	9014	MI/USA within 3 - 36 months Total -c 4 - 7 TG < 5	6.1	Pravastatin 40 mg vs placebo	Prava 6.4% Placebo 8.3%	Prava 11% Placebo 14.1%	
WOSCOPS ¹¹	6595	Men 45 - 64 T Chol > 6.5 mmol/L LDL > 4.5 mmol/L	4.9 years	Pravastatin 40 mg vs placebo	2.3% vs 1.6% p=0.033	4.1% vs 3.2% p=0.051	Nonfatal MI, CHD death 7.9% vs 5.5%
ALLHAT-LTT ⁸	10, 355	Age > 55 HTN + 1 CAD risk factor	4 years	Pravastatin 40 mg vs placebo	0.99 (0.8 - 1.24)	RR 0.99(0.89-1.11)	
Simvastatin							
4S ¹ 1994	4444	Documented CAD Total-c 5.5 - 8 TG < 2.5	5.4	Simvastatin 20 - 40 mg daily vs placebo	Simva 6.1% Placebo 9.3%	Simva - 8.2% Placebo 11.5%	
HPS ⁵ 2002	20,536	Age 40 - 80 T chol > 3.5 CAD/stroke/DM/HTN	5 years	Simvastatin 40 mg vs placebo	Simva 5.7% Placebo 6.9%	Simva 12.9% Placebo 14.7%	
A to Z ⁷ 2004	4497	Age 21 - 80 ACS within 2 weeks T chol < 6.48	2 years	Placebo x 4 mos, simva 20 mg vs Simva 40 mg x 1 mos, simva 80 mg	Placebo/simva 5.4% Simva 40/80 4.1%	Placebo/simva 6.7% Simva 40/80 5.5%	CHD death/MI/ACS /stroke Placebo/simva 16.7% Simva 40/80 14.4%

**Statistically significant results are in bold

1. Scandinavian Simvastatin Survival Study Group Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S) *Lancet* 1994;244:1383-89.
2. Sacks FM, Pfeffer MA, Moye LA, et al The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels *N Engl J Med* 1996;335:1001-9.
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4. Effects of atorvastatin on Early Recurrent ischemic events in acute coronary syndromes. The effects of atorvastatin when introduced early after an acute coronary syndrome *JAMA* 2001;285:1711-1718
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13. LaRosa JC et al Intensive Lipid Lowering with Atorvastatin in patients with stable coronary disease *N Engl J Med* 2005;352
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