LIPID LOWERING THERAPY: DYSLIPIDEMIA Comparison Chart [1,2,3,4,5,6,7,8]

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	Generic/TRADE	LDL[2,7] (dose effect)	HDL[2]	TG[2]	SIDE EFFECTS /CONTRAINDICATIONS (CI) /COMMENTS/MONITOR (M)	DRUG INTERACTIONS	THERAPEUTIC BENEFITS/USES	USUAL Dose Range (Max dose/day) Studied doses in 1° or 2° prevention	$ / Month
STATINS/HMG	**Atorvastatin** **LIPITOR** ATO (10,20,40,80 elipitcal mg tablet)	↓ 35 - 60%	↑ 5 - 15%	↓ 7 - 30%	**SE≤10%**;Generally better tolerated than other agents Common: upper **GI disturbances**, muscle pains, **headache**, rash & sleep disturbances Rare: peripheral neuropathy, lupus like Sx, impotence[9] ↑ **LFT** (AST & ALT >3X Normal in < 2%)[4,7]; **dose** dependent; reversible if statin stopped **Myopathy**[10]: <1%; rhabdomyolysis <0.2%[6] (CK>10x) -if muscle pain & weakness, monitor CK ↑ creatinine kinase (CK) & darkened urine. -risk ↑ **10 fold**[11] with combinations/DI's (<1%) ↓ CNS SE: **ATO,FLU,PRA** due to↓ CNS penetration **CI**: Active Liver Dx, ↑ alcohol intake & Pregnancy **M**: Routine LFT's & CK not indicated for all pts [22,30] (LFT: 0,3,6,12 months & annually if high dose/combo or at risk) **ROS**:new; most potent statin; appears to ↑HDL even at high dose;↑levels in Asians, lacks outcome data [12,13]	**↑ effect of:** digoxin[ATO]↑20%, warfarin[FLU,LOV,ROS,SIM less effect] **FOR: LOV, SIM, ATO** **↑ toxicity with HMG &:** amiodarone, amprenavir, **clarithromycin**, cyclosporine, danazol, diltiazem, ethinyl estradiol, **erythromycin**, fenofibrate, fluoxetine, fusidic acid, **gemfibrozil**, **grapefruit juice**, ketoconazole, indinavir, **itraconazole**, nelfinavir, **niacin**, **nefazodone**, ritonavir telithromycin & **verapamil**. **↓ effect of HMG by:** cholestyramine & colestipol (space by ≥ **2hr**); carbamazepine, phenytoin, pectin, phenobarb., St. Johns Wort & rifampin. **PRA & ROS**: appears to have few interactions	↓ Cholesterol **ATO,FLU,LOV,PRA,SIM,ROS** ↓ Atherosclerosis **ATO,FLU,LOV,PRA,SIM** ↓ Coronary Heart Disease **ATO,FLU,LOV,PRA,SIM** ↓ Stroke **PRA,SIM** Pediatric FDA approval **ATO,LOV,PRA,SIM** Effective in secondary causes such as diabetes & in nephrotic syndrome	10mg po hs 1° ASCOT, CARDS, TNT 20mg po hs (80mg/d $87) AVERT,MIRACL,PROVE IT,TNT 40mg po hs	67 81 87
	Fluvastatin **LESCOL** FLU (20 & 40mg capsule)	↓ 20 - 35%						20mg po hs 40mg po hs 40mg po bid cc LIPS (80mg/d)	35 46 84
	Lovastatin LOV **MEVACOR** (20scored & 40mg tablet)	↓ 25 - 40%						20-40mg po hs 1° AFCAPS 40mg po bid cc → 40-80mg/d POST CABG (**cc**=with meals ↑ absorption) (80mg/d)	34 - 79 151
	Pravastatin PRA **PRAVACHOL** (10,20 & 40mg tablet)	↓ 20 - 35%	ROS & SIM	ATO , ROS & SIM				20mg po hs (80mg/d) 40mg po hs 1° WOSCOPS; 2° → CARE,LIPID,PROSPER {Adjust for severe renal impairment [7]}	38 44
	Rosuvastatin ROS **CRESTOR** (10,20,40mg tablet)	↓ 40 - 65%	may ↑ HDLs most [8,12]	may ↓ TGs most [3,12,14]				10mg po od 20mg po od 40mg po od (40mg/d)	56 68 78
	Simvastatin SIM **ZOCOR** (5,10,20,40, 80 rectangle mg tab)	↓ 35 - 50%						20-40mg po hs 2° 4S 40mg po hs 2° MRC/BHP: HPS 80mg po hs A to Z (80mg/d)	46 46 46
	Pravastatin & Rosuvastatin few DIs-some transplant meds like cyclosporin & GEM. Fluvastatin less DIs→ still with glyburide, phenytoin,rifampin & warfarin. **Atorvastatin similar** DIs but less dramatic. {**Primary Mechanisms**[3,11] **of DI**: **PRA⇨sulfation**; **ATO/LOV/SIM⇨CYP-3A4**; **FLU⇨CYP-2C9**}								
FIBRATES	**Bezafibrate** **BEZALIP** BEZ ☎▼ (200mg tab;400mg SR tab)	LDL shifts to larger more buoyant forms[3]	↑ 10-20%	↓ 20-50%	Common: GI upset, rash & **abdominal pain** Less common: headache, pruritis, ↓ libido, dizzy, drowsy, arthralgia, ↑glucose, sleep/vision changes Rare: ↓ renal fx, anemia, ↑ LFT's, **myopathy,** reversible impotence & **gallstones** ↑ by 1-2%[3] **CI**: severe hepatic & renal Dx & ?**smoking** (↑ in cardiac events in smokers + gemfibrozil[VA-HIT]) **M**: CBC,Scr (↓ dose if ↑ Scr),Glucose, **LFT's** (?CK's) ☎ **Criteria**: if gemfibrozil/fenofibrate intolerance or ineffective ➔ bezafibrate	**↑ toxicity/levels with**: cyclosporin, furosemide, MAOI's, probenecid, & **statins**. **↓ effect by** : cholestyramine & colestipol (space by ≥ **2hrs**); rifampin **↑ effect of**: chlorpropamide, furosemide, **repaglinide**, **rosiglitazone**, **sulfonylureas** & **warfarin**.	✓↓Cholesterol & ↓TG; ↑HDL ✓Combo with HMG/Niacin (to ↑ HDL & ↓ TG) ↓ Atherosclerosis ✓**Type III** dyslipidemia May be useful if : ♦**TG >2.3**mmol/l BIP, HHS -virtually **all** clinical benefits in patients with **diabetes & ↑ insulinemia**[7] - lack all-cause mortality ↓	200mg po bid cc 200mg po tid cc (600mg/d) 400mg SR po od 2° BIP	70 ☎▼ 102 64
	Fenofibrate **LIPIDIL MICRO** 67✗▼& 200mg cap **LIPIDIL SUPRA** (✗▼→ 100 & 160mg tab)	↓ 5-20% (LDL may ↑ if **TG very high** initially)						200mg MICRO po od cc DAIS (200mg/d) 160mg SUPRA po od cc (160mg/d)	46 ✗▼ 52
	Gemfibrozil **LOPID** GEM (300mg cap, 600mg tablet)	-fenofibrate may ↓ LDL & ↓TG more than **GEM** [3,7] -current outcome evidence best with gemfibrozil -clofibrate was associated with ↑ mortality [WHO]						300mg po bid ac (**ac**=before meals) 600mg po bid ac 1° HHS, 2° VA-HIT (1500mg/d)	21 42
RESINS	**Cholestyramine** **QUESTRAN** CME (4gram regular,4gram **light**)	Option:mix with metamucil & orangejuice/lemonade the night before; refrigerate & give next day, ½ before breakfast & ½ before supper (shake well)		NO Change or Possible INCREASE	Common(<30%): **constipation**, nausea & bloating Rare:hyperchloremic acidosis[CME] in peds/↓renal fx [3] **CI**: biliary obstruction, dysbetalipoproteinemia, **TG >4.6** mmol/l (Caution TG >2.3 mmol/l); phenylketonurics ("light" & "orange granules") ↑ fluid & bulk in diet→ **metamucil** may be required **Mix →juice**/milk/water/applesauce **M**:LFT's,TGs	**Space other meds** (by ≥ **2hrs**) with **resins since ↓ absorption** of: amiodarone, cyclosporin, digoxin, diuretics, fat soluble vitamins (A,D,E,K), **folate**, **HMG's**, l-thyroxine, methotrexate, NSAIDS, propranolol, steroids, sulfonylureas, valproate, **warfarin**, mycophenolate	✓↓ Cholesterol & ↓ LDL (Questran:pregnancy & age >2yr) ✓Combo with HMG (to ↓ LDL) ✓Pruritus esp. with certain biliary/liver dx ✓Bile acid induced diarrhea	4g po bid ac → +/- 8g/day POST CABG 8g po bid ac (16-24g/d) **Start** 4g od-bid to ↑ tolerability	53 99
	Colestipol **COLESTID** (5g granules; 7.5g **orange** granules; 1gm tab)	↓ 15-30%	↑ 3-5%					2g po bid ac 4g po bid ac (20-30g/d) **Start** 2-5g od-bid to ↑ tolerability	42 77
OTHER	**Ezetimibe** [15] **EZETROL** 10mg tablet ⊗	↓ 17%	↑ 1.3%	↓ 6%	↓'s intestinal cholesterol absorption; synergistic ↓ in LDL **when added to statin** **CI**: hepatic **M**:LFT's	•levels ↑'d by cyclosporine, fibrates •resins interfere with absorbtion	✓↓ Cholesterol (+/- Statin) -lacks outcome data	10mg od (with or without meals) {when added to statin, may allow ↓ statin dose}	⊗ 64
	Nicotinic acid [16,17] **NIACIN** (50,100,500mg tab); SR / *No-flush* niacin: non-Rx in Canada,less effective?; better tolerated?; ↑ hepatic SE?	↓5-25% -shifts to larger buoyant forms[3]	↑ 15-35%	↓ 20-50%	**Flushing** (↓ by ASA/Advil **1/2hr pre**),dry eyes, pruritus, headache,GI upset,↑ LFT's,↑uric acid & **↑ glucose** **CI**: severe peptic ulcer Dx, chronic liver Dx, overt diabetes & severe gout **M**: LFT's, glucose, uric acid	•Low dose or 325mg/d **ASA**: useful on initiating/↑ niacin dose to ↓ flushing; some pretreat X3d. ASA may also ↑ niacin levels. **HMG's**: ? ↑ myopathy if with lovastatin[18]	✓↓Cholesterol & ↓TG; ↑HDL ✓Combo with HMG/Fibrate (to ↑ HDL & ↓ TG) ✓Niacin deficiency (Pellagra)	**Start 50-100mg bid-tid (↑ tolerability) (increase weekly by ~100mg/week)** 500mg po tid **with meals** 1500mg po bid 1° ADMIT 1g po tid cc 2° CDP (3-6g/d)	 12 16 16
	~2g niacin/day helps **HDL & TG**, but **only** higher doses affect **LDL**[3,7] **NICOTINAMIDE-NOT EFFECTIVE !!**								

Major RISK Factors[1,2,22]: **Diabetes,** Smoking,Hypertension(≥140/90/BP meds),Low HDL≤ 1,Family history [~1.5x Risk] premature (Age: ♂<55, ♀<65) CHD, Age(♂ ≥45, ♀ ≥55); **MODIFIABLE** ↑BP,↑Cholesterol/**LDL**,Obesity: BMI >25, Waist(♂>102cm,40"; ♀>88cm,35"), Smoking, Diet, Alcohol & sedentary lifestyle. **Screen:** pts with CAD/PVD/carotid atherosclerosis, diabetes, xanthomata or other stigmata of dyslipidemia; family history of dyslipidemia/CAD; adults with 2 or more risk factors; other pts (♂ ≥40, ♀ ≥50).

DRUG INDUCED HYPERLIPIDEMIA[19,20]: amiodarone, beta-blockers non ISA, carbamazepine, clozapine, cyclosporin, danazol, contraceptives esp. levonorgestrel, phenytoin, phenobarbital, protease inhibitors, progestins, retinoids, steroids & thiazides≥50mg/d.

CHOICE OF AGENT: **↑↑ LDL** ⇨HMG +/- resin; **↑↑ LDL & ↑TG** ⇨HMG; **↑↑ LDL & ↓HDL** ⇨HMG +/- fibrate/niacin; **Normal LDL & ↑↑TG** ⇨fibrate/niacin/?fish oils [21] or combo; **Normal LDL & ↓HDL** ⇨fibrate/niacin or combo

TARGETS 2003 [22]: for patients at:

HIGH RISK	(10yr CAD risk **≥20%**	**LDL <2.5**	& **Total Chol/HDL <4**	+Apo B <0.9)
MODERATE RISK	(10yr CAD risk **11-19%**	**LDL <3.5**	& **Total Chol/HDL <5**	+Apo B <1.05)
LOW RISK	(10yr CAD risk **6-10%**	**LDL <4.5**	& **Total Chol/HDL <6**	+Apo B <1.2)
VERY LOW RISK	(10yr CAD risk **<5%**	**LDL <5**	--	--

{**High risk**→ **ALL pts with CAD / DIABETES** adult **–incl. chronic renal dx / any atherosclerotic dx (eg. CVD,PAD)**}

High risk pts: treat medication & lifestyle changes concomitantly.
Lower risk pts: treat with meds after 3-6 months of lifestyle changes if targets not met.

♦ ***Lifestyle*** **changes for DIET, EXERCISE, moderate alcohol use & stop SMOKING!**
Consider **ASA** ~81mg/d. ***Highest*** risk benefit most!

☎ EDS Sask. ✗ Non-formulary SK ⊗not covered by NIHB ▼covered NIHB ✓Indication/Use **DI**=Drug Interaction **Dx**=disease **dysfx**=dysfunction **GI**=gastrointestinal **HDL**=high density lipoprotein **HMG** CoA reductase inhib→**STATINS** **LDL**=low density lipoprotein **SE**=side effect **TG**=triglycerides

It is unclear whether benefit derived is **solely** from achievement of targets eg. ↓ LDL alone. = ↓ dose for renal dysfx **+Apo B**: a **useful** marker, particularly if metabolic syndrome or on statin therapy. **Optimal TG** <1.7 mmol/l If >10mmol/l → risk of pancreatitis

New 2003 Canadian & USA - NCEP Working Group[2] -10yr risk of CAD in patients without diabetes or clinically evident heart disease.

RISK*	MEN									
AGE	20-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79
Age points	-9	-4	0	3	6	8	10	11	12	13
TOTAL CHOL										
<4.14 mmol/l	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		6		4		2		1	
≥ 7.21	11		8		5		3		1	
HDL mmol/l	<1.04		1.04-1.29		1.3-1.54		≥1.55			
	+2		+1		0		-1			
			Not Treated				Treated			
SYSTOLIC BP mmHg	<120		0				0			
	120-129		0				1			
	130-139		1				2			
	140-159		1				2			
	≥160		2				3			
SMOKER										
No	0		0		0		0		0	
Yes	8		5		3		1		1	
TOTAL POINTS										

POINTS	MEN: actual 10yr CAD risk %											
<0-4	5-6	7	8	9	10	11	12	13	14	15	16	≥17
1% (10yr % Risk→)	2	3	4	5	6	8	10	12	16	20	25	≥30

WOMEN										
20-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79
-7	-3	0	3	6	8	10	12	14	16
0		0		0		0		0	
4		3		2		1		1	
8		6		4		2		1	
11		8		5		3		2	
13		10		7		4		2	
<1.04		1.04-1.29		1.3-1.54		≥1.55			
+2		+1		0		-1			
		Not Treated				Treated			
<120		0				0			
120-129		1				3			
130-139		2				4			
140-159		3				5			
≥160		4				6			
0		0		0		0		0	
9		7		4		2		1	

POINTS	WOMEN actual 10yr CAD risk %													
<9	9-12	13-14	15	16	17	18	19	20	21	22	23	24	≥25
<1% (10yr % Risk→)	1	2	3	4	5	6	8	11	14	17	22	27	≥30

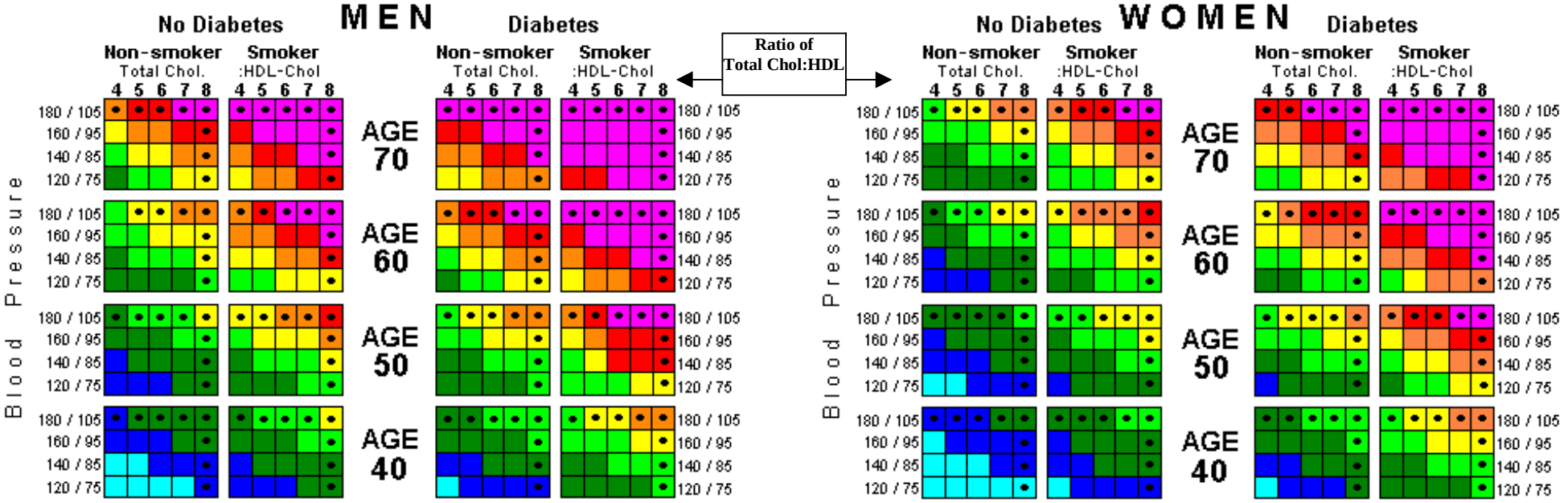
*Risk assessments based on Framingham data; other risk factors such as family history of CAD, physical inactivity, obesity & left ventricular hypertrophy should also be considered.

Patients with **CAD / DIABETES [adult] –incl. chronic renal dx / any atherosclerotic dx (eg. CVD,PAD)** are **"high risk"** regardless of risk score.

Cardiac Risk Tools: 1) www.statcoder.com 2) www.nhlbi.nih.gov/guidelines **For suggested lipid targets, see bottom of page 10.**

Comparative 10yr CAD % risks by AGE		30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74yr
Males	Low risk % →	2%	3	4	4	6	7	9	11	14
	Average risk % →	3%	5	7	11	14	16	21	25	30
Females	Low risk % →	<1%	<1	2	3	5	7	8	8	8
	Average risk % →	<1%	<1	2	5	8	12	12	13	14

Alternate CVD 5yr Risk Assessment Tables (Adapted From New Zealand Guideline Group with permission - http://www.nzgg.org.nz/library/gl_complete/bloodpressure/table1.cfm 23; also BMJ 24 & CMAJ 25)



Key to Risk Tables

RISK	Prognosis: 5 year CVD risk (non-fatal & fatal)	Benefit 1: CVD events prevented per 100 treated for 5 years *	Benefit 2: NNT for 5 years *
Very High	> 30%	> 10 per 100	< 10
	25-30%	9 per 100	11
	20-25%	7.5 per 100	13
High	15-20%	6 per 100	16
Moderate	10-15%	4 per 100	25
	5-10%	2.5 per 100	40
Mild	2.5-5%	1.25 per 100	80
	< 2.5%	< 0.8 per 100	> 120

Suggested starting point for discussion with patient about drug treatment.

- Cells with this marker indicate that in patients with very high levels of cholesterol (> about 8.5-9 mmol/L) or blood pressure (> about 170 / 100 mmHg), the risk equations may underestimate the true risk. **Therefore it is recommended that treatment be considered at lower absolute CVD risks than in other patients.**

* Assumes BP reduction of about 12 / 6 mmHg in patients with BP > 140-150 / 90, or cholesterol reduction of about 20% in patients with total cholesterol > 5.0-5.5 mmol/L, produces an approximate 30% reduction in CVD risk, whatever the pre-treatment absolute risk.

Also assess family history (↑ risk up to 50%), physical inactivity, obesity & LVH.
Risk Factors INTERHEART,CDN,JNC7**:↑ApoB/ApoA1 ratio,Smoking,Diabetes,↑BP,Obesity: waist/hip ratio** (♂ ≥0.95; ♀ ≥0.9),BMI >25,Waist (♂ >102cm/40inch, ♀ >88cm/35inch), **stress & depression; lack of vegetables, fruits, exercise & alcohol;** Low HDL ≤1, Family hx of premature heart dx (Age: ♂ <55, ♀ <65), Age (♂ >55, ♀ >65) & Microalbuminuria .

NZ-CVD-5yr Risk Tool: quick/easy way to estimate risk of CHD and stroke; the Framingham **10yr** risk assessment may also be used to estimate CHD risk. Antihypertensive benefit greater in those at highest risk!

Table 8: TARGETS Canadian

BLOOD PRESSURE 2004,26

Importance of accurate measurement e.g. 5 min resting

	Consider Treatment	Target
NO RISK FACTORS or target organ damage	**≥160/100**	**<140/90**
ISOLATED SYSTOLIC HTN (ISH)	**SBP >160**	**SBP <140**
MODERATE-HIGH RISK Patient	**≥140/90**	**<140/90**
◆**If HOME BP Measurement**	**≥135/85**	**<135/85**
DIABETES or RENAL Disease	**≥130/80**	**<130/80**
◆ **If PROTEINURIA >1g/d**	**≥125/75**	**<125/75**

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Risk (often based on Framingham 10yr CAD risk)	LDL	T.Chol/HDL	Apo B
HIGH * (10yr CAD ≥20%)	**<2.5**	<4	<0.9
MODERATE (10yr CAD 11-19%)	**<3.5**	<5	<1.05
LOW (10yr CAD 6-10%)	**<4.5**	<6	<1.2
VERY LOW (10yr CAD <5%)	**<5**	--	--

***High Risk** includes ALL pts with CAD / DIABETES adult incl. chronic renal dx / CVD / PAD.
HIGH Risk: Treat with medication & lifestyle changes concomitantly.
LOWER Risk: May try lifestyle changes for 3-6 months before drug therapy if targets not met.

BLOOD GLUCOSE 2003, 27

	Target for most	Normal range	→consider achieving
A1C q3-6 mon (calibrate meter qyr)	**≤ 7**	**≤ 6**	**if** can be done
FPG (mmol/L)	**4-7**	**4-6**	**safely** without
PPBG (mmol/L) 2hr post	**5-10**	**5-8**	hypoglycemia etc..

Individualized Target Treatment Goals: consider age[28], life expectancy, co-morbidity and risk of hypoglycemic side effects. **Monitor**: A_{1c} q3-6 months; calibrate meter yearly.

A_{1c}=glycosolated hemoglobin A_{1C} **BP**=blood pressure **CAD**=coronary artery disease **CVD**= cardiovascular disease **Dx**=disease **FPG**=fasting plasma glucose **HDL**=high density lipoprotein **Hx**=history **LDL**=low density lipoprotein **PAD**=peripheral arterial disease **PPBG**=postprandial (2hr) blood glucose **TG**=triglycerides ♂=male ♀=female

[1] Fodor JG, Frohlich JJ, Jacques JG et al. **Canadian** Recommendations for the management and treatment of dyslipidemia. CMAJ **2000**;162:1441-7.
[2]NCEP Expert Panel. Executive summary-3rd national cholesterol education program on detection, evaluation and treatment of high blood cholesterol in adults (**A**dult **T**reatment **P**anel **III**). JAMA **2001**;285:2486-97. Implications of Recent Clinical Trials for the NCEP ATP Panel III Guidelines July **2004** http://www.acc.org/clinical/adoptions/ncep_report.pdf
[3] Knopp RH. Drug treatment of lipid disorders. N Eng J Med 1999;341:498-511.
[4] Davidson MH. Safety profiles for the HMG-CoA Reductase Inhibitors. Drugs 2001;61:197-206
[5] Link N, Tanner M. Hyperlipidemia: Part 1. Evaluation and dietary management. WJM 2001;175:246-250.
[6] Link N, Tanner M. Hyperlipidemia: Part 2. Pharmacologic management. WJM 2001;175:396-401.
[7] Anonymous. Choice of lipid-regulating drugs. Med Lett 2001;43:43-48.
[8] **Treatment Guidelines**: Drugs for Lipid Disorders. **The Medical Letter**: August, **2003**; (12) pp. 77-82 & March, **2005**; (3;31) pp. 15-22.
[9] Rizvi K, Hampson JP, Harvey JN. Do lipid-lowering drugs cause erectile dysfunction? A systematic review. Fam Pract 2002;19(1):95-8.
[10] Thompson PD, Clarkson P, Karas RH. Statin-associated myopathy. JAMA. 2003 Apr 2;289(13):1681-90.
[11] Herman, RJ. Drug interactions and the statins. CMAJ 1999;161:1281-6.
[12] Carswell CI, Plosker GL, Jarvis B. Rosuvastatin. Drugs. 2002;62(14):2075-85; discussion 2086-7.
[13] Rosuvastatin--a new lipid-lowering drug. Med Lett Drugs Ther. 2003 Oct 13;45(1167):81-3.
[14] Jones P, et al. Comparative dose efficacy study of atorvastatin versus simvastatin, pravastatin, lovastatin and fluvastatin in patients with hypercholesterolemia (The **CURVES** study). Am J Cardiol 1998;81:582-7.
[15] Three new drugs for hyperlipidemia. Med Lett Drugs Ther. 2003 Mar 3;45(1151):17-9.
[16] Grundy SM, Vega GL, McGovern ME, Tulloch BR, Kendall DM, Fitz-Patrick D, Ganda OP, Rosenson RS, Buse JB, Robertson DD, Sheehan JP; Diabetes Multicenter Research Group. Efficacy, safety, and tolerability of once-daily niacin for the treatment of dyslipidemia associated with type 2 diabetes: results of the assessment of diabetes control and evaluation of the efficacy of niaspan trial. Arch Intern Med. 2002 Jul 22;162(14):1568-76.
[17] Elam MB, Hunninghake DB, Davis KB, Garg R, Johnson C, Egan D, Kostis JB, Sheps DS, Brinton EA. Effect of niacin on lipid and lipoprotein levels and glycemic control in patients with diabetes and peripheral arterial disease: the ADMIT study: A randomized trial. Arterial Disease Multiple Intervention Trial. JAMA. 2000 Sep 13;284(10):1263-70.
[18] Jacobson TA. Combination Lipid-Altering Therapy. Current Atherosclerosis Reports 2001;3:373-382.
[19] Mantel-Teeuwisse AK, Kloosterman ME, Maitland-van der Zee AH, et al. Drug-induced lipid changes. Drug Safety 2001;24:443-56.
[20] Unintended serum lipid level changes induced by some commonly used drugs. Drugs & Therapy Perspectives 2001; 17(23).
[21] Din JN, Newby DE, Flapan AD. Omega 3 fatty acids and cardiovascular disease--fishing for a natural treatment. BMJ. 2004 Jan 3;328(7430):30-5.
[22] Genest J, Frohlich J, Fodor G, McPherson R; Working Group on Hypercholesterolemia and Other Dyslipidemias. Recommendations for the management of dyslipidemia and the prevention of cardiovascular disease: summary of the **Canadian 2003 update**. CMAJ. 2003 Oct 28;169(9):921-4. http://www.cmaj.ca/cgi/data/169/9/921/DC1/1 Full Report.
[23] New Zealand Guideline Group. http://www.nzgg.org.nz/library/gl_complete/bloodpressure/table1.cfm (access verified Jan 30/03).
[24] Jackson R. Updated New Zealand cardiovascular disease risk-benefit prediction guide. BMJ 2000;320:709-10.
[25] Campbell NRC, Drouin D, Feldman RD, for the Canadian Hypertension Recommendations Working Group. The **2001 Canadian** hypertension recommendations take-home messages. CMAJ 2002:167(6):661-8.
[26] Canadian Hypertension Society-**2004 Canadian** Hypertension **Recommendations** Working Group-downloadable Summary & Slides; http://www.chs.md/index2.html (access verified 20 Nov, 2003).
[27] **Canadian 2003 Diabetes Guidelines** http://www.diabetes.ca/cpg2003/download.aspx (Meltzer S, Leiter L, Daneman D, et al 1998. Clinical practice guidelines for the management of diabetes in Canada. CMAJ 1998;159 (8 Suppl).)
[28] Brown AF, Mangione CM, Saliba D, Sarkisian CA; California Healthcare Foundation/**American Geriatrics Society** Panel on Improving Care for Elders with Diabetes. Guidelines for improving the care of the older person with diabetes mellitus. J Am Geriatr Soc. **2003** May;51(5 Suppl Guidelines):S265-80.

29. Nissen S, Tuzcu E, et al. Effect of Intensive Compared With Moderate Lipid-Lowering Therapy on Progression of Coronary Atherosclerosis A Randomized Controlled Trial (**REVERSAL**). JAMA. 2004;291:1071-1080.
30. Heart Protection Study (**HPS**) Collaborative Group. Effects of cholesterol-lowering with simvastatin on stroke and other major vascular events in 20 536 people with cerebrovascular disease or other high-risk conditions. Lancet 2004 Mar 6;363(9411): 757-67.
31. Cannon CP, Braunwald E, McCabe CH, ET AL. Comparison of Intensive and Moderate Lipid Lowering with Statins after Acute Coronary Syndromes. (**PROVE IT-TIMI 22**) N Engl J Med. 2004 Mar 8
32. Colhoun HM, Betteridge DJ, Durrington PN, Hitman GA, Neil HA, Livingstone SJ, Thomason MJ, Mackness MI, Charlton-Menys V, Fuller JH; CARDS investigators. Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin Diabetes Study (**CARDS**): multicentre randomised placebo-controlled trial. Lancet. 2004 Aug 21;364(9435):685-96.
33. Sever PS, Dahlof B, Poulter NR, Wedel H, Beevers G, Caulfield M, Collins R, Kjeldsen SE, Kristinsson A, McInnes GT, Mehlsen J, Nieminen M, O'Brien E, Ostergren J; ASCOT investigators. Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial--Lipid Lowering Arm (**ASCOT-LLA**): a multicentre randomised controlled trial. Lancet. 2003 Apr 5;361(9364):1149-58.
34. De Lemos et al. Early Intensive vs a Delayed Conservative Simvastatin Strategy in Patients with Acute Coronary Syndromes Phase Z of the **A to Z Trial** JAMA. 2004 Sept 15;292 (11):1307-16.
35. LaRosa JC. et al. Intensive Lipid Lowering with Atorvastatin in Patients with Stable Coronary Disease (**TNT**) . N Engl J Med. 2005 Mar 8;352 online.
36. Ko DT, Mamdani M, Alter DA. Lipid-lowering therapy with statins in high-risk elderly patients: the treatment-risk paradox. JAMA. 2004 Apr 21;291(15):1864-70.