University Health System Hyperlipidemia Guidelines (Based on NCEP ATP III Guidelines with Update)

January 2009

1. **Determine fasting lipid levels (9 to 12 hour fast).**

2. **Does the patient have coronary heart disease (CHD) or CHD risk equivalents?**
   1 CHD (myocardial infarction, unstable angina, stable angina, angioplasty, bypass surgery, evidence of clinically significant myocardial ischemia)
   2 Risk equivalents
      - Noncoronary atherosclerotic disease (peripheral arterial disease, abdominal aortic aneurysm, carotid artery disease)
      - Diabetes mellitus
      - 2+ risk factors (RFs) with a 10 year risk for CHD > 20 % via Framingham risk score

3. **How many major risk factors for CHD does the patient have?**
   1 Cigarette smoking
   2 Hypertension (BP > 140/90 or taking antihypertensive medication)
   3 HDL < 40 mg/dL
   4 Family history of premature CHD (male 1st degree relative < 55 yrs, female 1st degree relative < 65 yrs)
   5 Age (men ≥ 45 yrs, women ≥ 55 yrs)
   6 Note: HDL > 60 mg/dL counts as a "negative" risk factor (-1 RF from the total count).

4. **If the patient has 2+ RFs without CHD or risk equivalents, assess the patient's 10 year risk of developing CHD (see Framingham tables or electronic version at http://www.nhlbi.nih.gov/guidelines/cholesterol).**

5. **Determine risk category and LDL goal.**

Risk Category	LDL Goal (mg/dL)	Initiate TLC (mg/dL)	Consider Drug Therapy (mg/dL)
High Risk CHD or CHD risk equivalents*	< 100 (optional: < 70)†	≥ 100 (optional: ≥ 70)†	≥ 100 (optional: ≥ 70)†
Moderately High Risk 2 + RFs with 10 year risk of 10 to 20 %	< 130 (optional: < 100)**	≥ 130 (optional: ≥ 100)**	≥ 130 (optional: ≥ 100)**
Moderate Risk 2 + RFs with 10 year risk of < 10 %	< 130	≥ 130	≥ 160
Lower Risk 0 or 1 RF	< 160	≥ 160	≥ 190 (optional: 160-189)

* CHD risk equivalents include other forms of atherosclerotic heart disease (peripheral artery disease, abdominal aortic aneurysm, and symptomatic carotid artery disease), diabetes, or multiple risk factors giving a 10-year risk for CHD > 20%.

† Very high risk favors the optional LDL goal of < 70 mg/dL, and in patients with high triglycerides, non-HDL cholesterol goal of < 100 mg/dL. Proposed use in patients with CHD combined with diabetes, recent MI, uncontrolled multiple risk factors (see above), or metabolic syndrome.

** For moderately high-risk patients, when LDL is 100 to 129 mg/dL, at baseline or on lifestyle therapy, initiation of an LDL lowering drug to achieve an LDL < 100 mg/dL is a therapeutic option based on results of clinical trials.

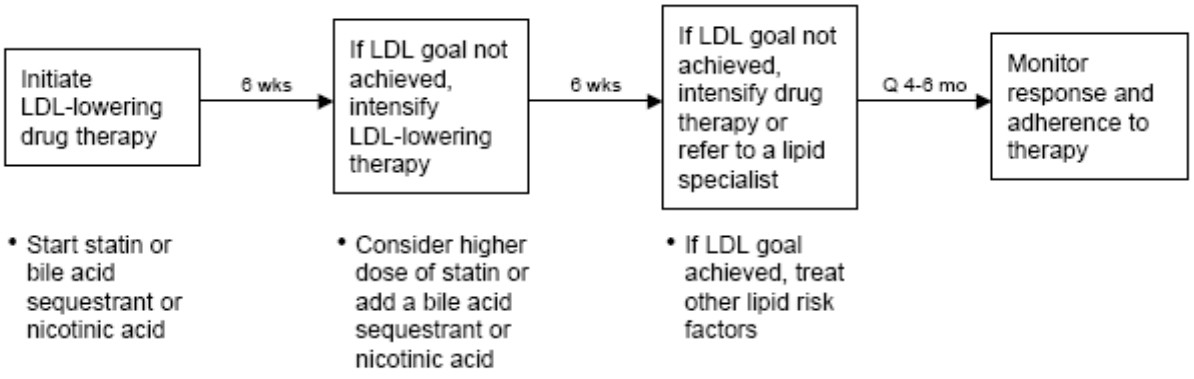
6. Initiate therapeutic lifestyle changes (TLC) if LDL is above goal.

1 Weight management
2 TLC Diet
- Saturated fat < 7% of calories, total fat 25-35% of total calories (keep *trans* fatty acids at a low intake), total cholesterol < 200 mg/day.
- Consider increased viscous (soluble) fiber (20-30 g/day) and plant stanols/sterols (2 g/day) to enhance LDL lowering.

3 Increased physical activity
4 Smoking cessation

7. Consider adding drug therapy if LDL exceeds threshold for drug therapy.

1 Secondary dyslipidemia should be ruled out in any patient with elevated LDL cholesterol before initiating lipid-lowering therapy. Causes of secondary dyslipidemia include: hypothyroidism, diabetes, chronic renal failure, obstructive liver disease, and drugs causing an increase in LDL or decrease in HDL (i.e. corticosteroids, progestins, anabolic steroids, etc.)



8. Identify metabolic syndrome and treat, if present, after 3 months of TLC.

1 Metabolic Syndrome (Any 3 of the following)
- Abdominal obesity (male waist > 40 inches, female waist > 35 inches)
- TG ≥ 150 mg/dL
- HDL < 40 mg/dL in men, HDL < 50 mg/dL in women
- BP ≥ 130/85 mmHg
- FBG ≥ 100 mg/dL

2 Treatment of the metabolic syndrome
- Intensify weight management
- Increase physical activity
- Treat hypertension
- Use aspirin for CHD patients to reduce prothrombotic state
- Treat elevated TG and/or low HDL (see step 9).

9. Treat elevated triglycerides and/or low HDL.

1 If TG ≥ 500 mg/dL, the first lipid-lowering priority is TG to reduce risk of acute pancreatitis.
- Very low fat diet (≤ 15 % of calories from fat)
- Weight management and physical activity
- Fibrate or nicotinic acid
- When TG < 500 mg/dL, LDL lowering becomes the top priority.

2 If TG 200 to 499 mg/dL, the first lipid-lowering priority is LDL.
- After LDL goal is reached, consider intensifying LDL lowering or adding nicotinic acid or a fibrate to further lower VLDL.

3 If HDL < 40 mg/dL, first reach LDL goal. Then:
- Intensify weight management and increase physical activity
- If TG 200 to 499 mg/dL, achieve non-HDL goal (30 mg/dL above LDL goal).
- If TG < 200 mg/dL in patients with CHD or risk equivalents, consider nicotinic acid or a fibrate.

Special considerations for the University Health System

1 ***CareLink subsidy information is available through the UHS Lexi-Comp drug formulary***.

2 Statins should be used in the following order (assuming that the agent's efficacy is appropriate for the patient and the patient has no contraindications):
   a. Generic statins: pravastatin or simvastatin are used as 1st line agents.
   b. Brand statins: atorvastatin (Lipitor®) and rosuvastatin (Crestor®) are restricted as a 2nd line agent after failure of at least one generic statin.

3 Gemfibrozil should be prescribed first-line if used as monotherapy. Fenofibrate should be the drug of choice if given in combination with other agents (such as HMG-CoA reductase inhibitors) or for patients who have a contraindication to gemfibrozil.

4 Extended release nicotinic acid (Niaspan®) is subsidized through CareLink. Standard release is available over-the-counter, and thus, not subsidized. When switching to Niaspan® from the immediate release tablet, lower the dose and titrate upwards. Flushing can be attenuated by gradually increasing the dose and taking aspirin 325 mg or a nonsteroidal anti-inflammatory drug (e.g. ibuprofen) 30-60 minutes prior to each dose.

Titration example:

Week 1-4: 500 mg at bedtime

Week 5-8: 1000 mg at bedtime

Week 9 and thereafter: adjust dose to response and tolerance; can increase dose weekly to max tolerated dose of 2000 mg/day, but only at 500 mg/day with 4-week intervals.

References

1. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive summary of the third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults. *JAMA*. 2001; 285:2486-97.
2. Grundy SM, Cleeman JI, Bairey CN, et al. National Cholesterol Education Program (NCEP) Report. Implications of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panel III Guidelines. *Circulation*. 2004; 110:227-239.
3. Lipitor package insert. New York, NY: Pfizer Pharmaceuticals; 2007, Nov.
4. Pravachol package insert. Princeton, NJ: Bristol-Myers Squibb Co.; 2007, Mar.
5. Zocor package insert. Whitehouse Station, NJ: 2008, Jun.
6. Zetia package insert. North Wales, PA: Merck/Schering-Plough Pharmaceuticals; 2008, Jun.
7. Questran Light package insert. Princeton, NJ: Bristol-Myers Squibb Co.; 2006 May.
8. Lopid package insert. Vega Baja, PR: Parke Davis Pharmaceuticals, Ltd.; 2006 Sept.
9. Tricor package insert. Chicago, IL: Abbott Laboratories; 2007, Oct.
10. Niaspan package insert. Miami, FL: Kos Pharmaceuticals, Inc.; 2008, Mar.
11. Crestor package insert. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2007, Nov.

Men

Estimate of 10-Year Risk for Men

(Framingham Point Scores)

Age	Points
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	Points				
	Age 20-39	Age 40-49	Age 50-59	Age 60-69	Age 70-79
<160	0	0	0	0	0
160-199	4	3	2	1	0
200-239	7	5	3	1	0
240-279	9	6	4	2	1
≥280	11	8	5	3	1

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

HDL (mg/dL)	Points
≥60	-1
50-59	0
40-49	1
<40	2

Systolic BP (mmHg)	If Untreated	If Treated
<120	0	0
120-129	0	1
130-139	1	2
140-159	1	2
≥160	2	3

Point Total	10-Year 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

10-Year risk _____%

Women

Estimate of 10-Year Risk for Women

(Framingham Point Scores)

Age	Points
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	Points				
	Age 20-39	Age 40-49	Age 50-59	Age 60-69	Age 70-79
<160	0	0	0	0	0
160-199	4	3	2	1	1
200-239	8	6	4	2	1
240-279	11	8	5	3	2
≥280	13	10	7	4	2

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

HDL (mg/dL)	Points
≥60	-1
50-59	0
40-49	1
<40	2

Systolic BP (mmHg)	If Untreated	If Treated
<120	0	0
120-129	1	3
130-139	2	4
140-159	3	5
≥160	4	6

Point Total	10-Year 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

10-Year risk _____%

Drug Selection Based on Required LDL-C Reduction

% LDL-C Reduction Required	Pravastatin	Fluvastatin	Lovastatin	Simvastatin	Rosuvastatin	Atorvastatin
18	10 mg	20 mg	10 mg	5 mg		10 mg
19						
20						
21	20 mg					
22						
23		40 mg	20 mg			
24				10 mg		
25						
26						
27		80 mg				
28	40 mg		40 mg			
29						
30						
31				20 mg		
32						
33			80 mg			
34						
35						
36				40 mg		20 mg
37						
38						
39						
40					5 mg	
41				80 mg		
42						
43						
44						40 mg
45						
46						
47						
48						
49						
50						
51					10 mg	
52					20 mg	
53					40 mg	80 mg
54						
55						
56						
57						
58						

Appendix E-5: Adapted from the DoD Pharmacoeconomic Center (PEC) Publication, July 1999.

LDL-C Reduction-Point Estimates - The point estimates provided were derived from the information obtained from the product package insert and published randomized studies. To establish an efficacy (versus effectiveness) estimate of LDL-C reduction for each drug and strength, studies and/or Product Package Inserts (PPI) must have met the following criteria: 1) published in a peer reviewed journal (not applicable to PPI) or provided in the FDA approved PPI, 2) subjects must have been randomized to treatment, 3) number of study subjects receiving each dosage strength clearly stated, and 4) duration of therapy and timing of LDL-C measurement provided. To estimate efficacy, LDL-C reductions must

have been obtained at baseline and again between six and twenty-four weeks of initiation of "statin" therapy. The final point estimate for each drug and strength is a weighted average based upon the number of study subjects evaluated in each study.

Clinically Significant Statin Drug Interactions

Interacting Drug	Result of Interaction	Recommendations/Comments
Amiodarone	• Increased risk for myopathy/rhabdomyolysis	• Avoid medium to high doses of atorvastatin and simvastatin • Use pravastatin or rosuvastatin
Azole Antifungals Fluconazole Itraconazole Ketoconazole Voriconazole	• Increased risk for myopathy/rhabdomyolysis	• If coadministration of ketoconazole or itraconazole unavoidable, hold atorvastatin or simvastatin during antifungal treatment. Caution with fluconazole or voriconazole • Use pravastatin or rosuvastatin for patients requiring frequent or prolonged ketoconazole or itraconazole treatment
Calcium Channel Blockers Diltiazem Verapamil	• Increased risk for myopathy/rhabdomyolysis	• Avoid medium to high doses of atorvastatin and simvastatin • Use pravastatin or rosuvastatin • Use another calcium channel blocker that does not inhibit statin metabolism
Bile Acid Sequestrants Cholestyramine Colestipol	• Decreased bioavailability of statins	• Administer statin 1 hr before or 4 hrs after cholestyramine or colestipol
Cimetidine	• Decrease TG-lowering effect of atorvastatin from 34% to 26%	• Use another H_2-antagonist if TG-lowering effect not satisfactory
Cyclosporine	• Increased risk for myopathy/rhabdomyolysis	• Avoid medium to high doses of atorvastatin, simvastatin, pravastatin, or rosuvastatin
Danazol	• Increased risk for myopathy/rhabdomyolysis	• Avoid medium to high doses of atorvastatin and simvastatin • Use pravastatin or rosuvastatin
Digoxin	• Increased digoxin steady-state concentration by 20% when coadministered with atorvastatin • Slight elevation (< 0.3 ng/mL) when coadministered with simvastatin	• Monitor serum levels at initiation of digoxin dose and after dose adjustments with atorvastatin and simvastatin • Adjust digoxin dose accordingly
Fibric Acid Derivatives Fenofibrate Gemfibrozil	• Increased risk for myopathy/rhabdomyolysis via additive effects of both drugs	• Avoid medium to high doses of atorvastatin and simvastatin in patients treated with fibric acid derivatives • Avoid rosuvastatin or use low-dose rosuvastatin if coadministration cannot be avoided • Avoid coadministration with pravastatin
Grapefruit/Grapefruit Juice	• Increased risk for myopathy/rhabdomyolysis	• Avoid administration of atorvastatin and simvastatin with grapefruit products • If unable to avoid, use pravastatin or rosuvastatin
Macrolide Antibiotics Clarithromycin Erythromycin	• Increased risk for myopathy/rhabdomyolysis	• Avoid coadministration with atorvastatin or simvastatin or hold during course of macrolide treatment • Use azithromycin if treatment with macrolide is unavoidable • Use pravastatin or rosuvastatin in patients requiring frequent/prolonged clarithro or erythro treatment
Niacin (≥ 1 gram/day)	• Increased risk for myopathy/rhabdomyolysis	• Avoid medium to high doses of statins
Nefazodone	• Increased risk for myopathy/rhabdomyolysis	• Avoid coadministration with atorvastatin or simvastatin • Use pravastatin or rosuvastatin if nefazodone treatment is unavoidable
Protease Inhibitors Amprenavir Atazanavir Fosamprenavir Indinavir Nelfinavir Ritonavir Saquinavir Tipranavir	• Increased risk for myopathy/rhabdomyolysis	• Avoid coadministration with atorvastatin or simvastatin • Use pravastatin or rosuvastatin if protease inhibitor treatment is unavoidable
Telithromycin	• Increased risk for myopathy/rhabdomyolysis	• Avoid coadministration with atorvastatin or simvastatin or hold during course of telithromycin treatment if unavoidable • Use pravastatin or rosuvastatin in patients requiring frequent/prolonged telithromycin treatment
Warfarin	• Potential increase in INR • Rosuvastatin can result in clinically significant increase in INR	• Monitor INR closely when initiating, stopping, or changing dose of simvastatin or rosuvastatin • Use atorvastatin or pravastatin cautiously

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