Piedmont WellStar HealthPlans, Inc.
ADULT CHOLESTEROL MANAGEMENT CLINICAL GUIDELINE

Relevance to Population: Primary prevention of coronary heart disease offers the greatest opportunity for reducing the burden of coronary heart disease in the United States. The clinical approach to primary prevention is founded on the public health approach of therapeutic lifestyle changes. Nonetheless, some persons at higher risk because of high LDL cholesterol levels or because of multiple risk factors are candidates for LDL-lowering drugs. Piedmont WellStar HealthPlans, Inc. is committed to preventing the development and progression of cardiovascular disease and to reducing the risk for major cardiovascular events.

Population Covered by Guideline: All adult members age 18 and older

Clinical Indicators Measured by Piedmont WellStar HealthPlans, Inc.:

1. The percentage of members with a diagnosis of AMI, PTCA, CABG or ischemic vascular disease (IVD) who had an LDL-C level measured within the previous calendar year. HEDIS®
2. The percentage of members with a diagnosis of AMI, PTCA, CABG or ischemic vascular disease (IVD) who had an LDL-C level controlled (< 100mg/dl) within the previous calendar year. HEDIS®

Cholesterol Management: The current Adult Treatment Panel III (ATP III) of the National Cholesterol Education Program, National Heart, Lung, and Blood Institute 2002, American College of Cardiology Foundation, and the American Heart Association 2004 is available at http://www.nhlbi.nih.gov/guidelines/cholesterol/atp3full.pdf

Step I — First consider clinical or laboratory assessment to exclude secondary causes of elevated LDL cholesterol or other forms of hyperlipidemia. Secondary causes of hyperlipidemia include:[2]

- Type 2 diabetes
- Cholestatic liver disease
- Nephrotic Syndrome
- Hypothyroidism
- Chronic renal failure
- Cigarette smoking
- Obesity
- Drugs that increase LDL cholesterol and/or triglycerides and decrease HDL cholesterol:[2]
    - Estrogen, progesterone, birth control pills
    - Anabolic steroids
    - isotretinoin (for acne)
    - Certain anti-retroviral (HIV) drugs (especially protease inhibitors)
    - Certain immunosuppressant, anti-rejection drugs (cyclosporine, sirolimus, everolimus, mycophenylate mofetil)
    - Certain antihypertensive medications (thiazide diuretics, beta blockers)
    - Atypical antipsychotics (clozapine, olanzapine, quetiapine)

Step II — Assess the number of independent Cardiovascular Risk Factors in addition to elevated LDL cholesterol level (Table 1) [1]:

Table 1 — Independent cardiovascular risk factors besides elevated LDL cholesterol:

- Family history of premature CAD: Male 1st degree relative < 55 years old; Female 1st degree relative < 65 years old
- Age: Male > 45 years; Female > 55 years
- Hypertension: BP > 140/90 mmHg or on antihypertensive therapy
- Low HDL-C: < 40 mg/dl
- Cigarette smoking, smokeless tobacco, nicotine use

- Diabetes
- Obesity
- Metabolic Syndrome (Table 2).

Table 2 — Clinical Characteristics for Identification of Metabolic Syndrome (syndrome of excessive abdominal fat, insulin resistance, hypertension, elevated triglycerides, and low HDL-C level). [1]

Risk Factor	Defining Level	Comments
Abdominal Obesity	Waist Circumference	Abdominal obesity is more highly correlated to metabolic syndrome than is general obesity as determined by BMI.
Males	> 40 inches (> 102 cm)	
Females	> 35 inches (> 88 cm)	
Triglycerides	≥ 150 mg/dl	
HDL Cholesterol		
Males	< 40 mg/dl	
Females	< 50 mg/dl	
Blood Pressure	≥ 130/≥85 mmHg	
Fasting Glucose	≥ 110 mg/dl	

Step III — Calculate the patient's 10-year risk for developing Coronary Heart Disease (CHD) using the Framingham Risk Score Model (calculate using Appendix 1 for Males and Appendix 2 for Females. Risk factors included in the Framingham calculation are age, total cholesterol, HDL cholesterol, systolic blood pressure, treatment for hypertension, and cigarette smoking. The levels of Framingham risk used in this guideline to determine management of abnormal cholesterol levels are presented below in Table 3.

Table 3 — Levels of 10-Year Risk (%) for Developing CHD (used in the ATP III Cholesterol Management Guideline — Table 4) [1]

Risk Levels	Comments
< 10%	Most patients with 0–1 CHD risk factors have a CHD risk < 10% and a Framingham Risk assessment is not considered necessary.
10 – 20%	Typically people with 2+ risk factors places them at short- and long-term risk for CHD.
> 20%	This category represents patients with known CHD or CHD equivalent conditions.
• Patients with CHD o CHD includes history of MI, unstable angina, stable angina, coronary artery revascularization (angioplasty or bypass surgery), or evidence of clinically significant myocardial ischemia.	
• Patients with CHD equivalent o CHD equivalent includes patients with non-coronary forms of atherosclerosis, including peripheral vascular disease, abdominal aortic aneurysm, carotid artery disease, diabetes, and ≥2 cardiovascular risk factors with 10-year risk for CHD >20%.	

Step IV — Select treatment options based on the Adult Treatment Panel III Guidelines (Table 4).[1]

Table 4 — Adult Treatment Panel III (ATP III) Guidelines for LDL Cholesterol Management

Number of CHD Risk Factors	Percent 10-year CHD Risk	LDL Goal	LDL at which to start TLC*	LDL at which to start Drug Therapy	Comments
0–1	< 10%	< 160	≥ 160	– > 190 (after 3 mo. lifestyle therapies)	• Therapeutic Goal: reduce long-term risk • Most with 0–1 risk factors have a < 10% 10-yr risk • LDL-lowering drug optional with LDL 160-189 • Factors favoring drug therapy: ➢ Severe single risk factor ➢ Multiple life-habit risk factors
2+ (Multiple)	< 10%	< 130	≥ 130 –	≥ 160 (after 3 mo. lifestyle therapies)	• Therapeutic Goal: reduce long-term risk
	10-20%	< 130	> 130 (Initiate immediately)	≥ 130 (after 3 mo. lifestyle therapies)	• Therapeutic Goal: reduce short- and long-term risk
CHD and Risk Equivalents	> 20%	< 100 (optional: < 70)	≥ 100 (optional: > 70)	≥ 130 (optional: 70 – 129)	• Therapeutic Goal: reduce short- and long-term risk Therapeutic Goal of LDL-lowering drug therapy (if used): achieve at least a 30 to 40% reduction in LDL cholesterol level

* Therapeutic Lifestyle Changes (Table 5)

Table 4 — Adult Treatment Panel III (ATP III) Guidelines for LDL Cholesterol Management (cont.)

CHD or Equivalent AND	Baseline (or on treatment): LDL < 100 (optional: 70)	• Further LDL-lowering is not required • TLC recommended • Consider treatment of high triglycerides/low HDL
CHD or Equivalent AND	Baseline (or on treatment): LDL 100 – 129	• Initiate or intensify TLC therapies • Initiate or intensify LDL-lowering drugs • Assess for and treat metabolic syndrome ➢ Stress weight reduction and increased exercise • Drug therapy for high triglycerides and/or low HDL ➢ Fibrates or nicotinic acid
CHD or Equivalent AND	Baseline (or on treatment): LDL ≥ 130	• Intensive lifestyle therapies • Maximal control of other risk factors • Consider starting LDL-lowering drugs simultaneously with lifestyle therapies

Table 5 — Therapeutic Lifestyle Changes (TLC):[1]

1. Dietary Recommendations (nutrient composition of the TLC diet):

Saturated fat	Less than 7% of total daily calories
Trans-fatty acids	Reduce to a very low level
Polyunsaturated fats	Up to 10% of total daily calories
Monounsaturated fats	Up to 20% of total daily calories
Cholesterol	Less than 200 mg per day
Total fat	25%–35% of total daily calories
Carbohydrates*	50%–60% of total daily calories
Protein	15% of total daily calories
Fiber	20–30 grams per day
Viscous (soluble) fiber	Therapeutic Option: increase LDL-lowering soluble fiber (10–25 grams per
Plant stanols/sterols	Therapeutic Option: increase LDL-lowering plant stanols/sterols
Omega-3 fatty acids	Encourage consumption of omega-3 fatty acids in the form of fish or in capsule form (1g/day) for risk reduction. For treatment of elevated TG, higher doses are usually necessary for risk reduction.
Total calories (energy)**	Balance energy intake and expenditure to maintain desirable body weight/prevent weight gain

*Primarily from foods rich in complex carbohydrates, including whole grains, fruits, and vegetables

**Daily energy expenditure should include at least moderate physical activity (contributing approximately 200 Kcal per day)

2. Weight control/reduction
3. Gradually increase and maintain regular exercise (30 to 45 minutes, 3 to 6 times per week)

Table 6 — Drugs Affecting Lipoprotein Metabolism [1]

Drug Class	Agents and Daily	Lipid Effects	Major Side Effects	Contraindications	Clinical Trial Results
HMG CoA reductase inhibitors (statins)	Atorvastatin (10- 80mg) Fluvastatin (20–80 mg) Lovastatin (20–80 mg) Pitavastatin (1-4mg) Pravastatin (10-80 mg) Rosuvastatin (10–40 mg) Simvastatin (5–40 mg)	LDL – ↓ 18%–55% HDL – ↑ 5%–15% TG – ↓ 7%–30%	Myopathy; Increased liver enzymes	Absolute: active or chronic liver disease Relative: concomitant use of certain drugs*	Reduced major coronary events, CHD deaths, need for coronary procedures, stroke, and total mortality
Cholesterol absorption inhibitor	Ezetimibe (10 mg) may be used alone or with a statin **	Ezetimibe alone: LDL – ↓ 17% HDL – no **Δ** TG – no **Δ** Ezetimibe + statin: LDL – percentage of decrease from statin baseline varies with different studies.	Severe muscle pain (rarely); back pain; liver dysfunction (esp. combined w/statin; dizziness; headache; sexual dysfunction	Absolute: active liver disease when combined with a statin; avoid use with fibrate drugs Relative: caution use with certain drugs, e.g., warfarin and cyclosporine	Results of effects on cardiovascular morbidity and mortality are not yet established
Bile acid sequestrants	cholestyramine (4-16 g) colestipol (5-20 g) colesevelam (2.6-3.8 g)	LDL – ↓ 15%–30% HDL – ↑ 3%–5% TG – no **Δ** or ↑	GI distress; Constipation; Decreased absorption of other drugs	Absolute: dysbeta-lipoproteinemia; TG > 400 mg/dl Relative: TG > 200 mg/dl	Reduced major coronary events and CHD deaths
Nicotinic acid	rapid release (1.5-3 g) extended release (1-2 g) sustained release (1-2 g)	LDL – ↓ 5%–25% HDL – ↑ 15%–35% TG – ↓ 20%–50%	Flushing; Hyperglycemia; Hypereuricemia /gout; UGI distress; Hepatotoxicity	Absolute: chronic liver disease; severe gout Relative: diabetes; hyperuricemia; PUD	Reduced major coronary events and possibly total mortality
Fibric acids	gemfibrozil (600mg BID) fenofibrate (200 mg QD) clofibrate (1000 mg BID)	LDL – ↓ 5–20%*** HDL – ↑ 10–35% TG – ↓ 20–50%	Dyspepsia; Gallstones; Myopathy; Unexplained non-CHD deaths in WHO study	Absolute: severe renal disease; severe hepatic disease	Reduced major coronary events

*Cyclosporine, macrolide antibiotics, various antifungal agents, and cytochrome P-450 inhibitors

(fibrates and niacin) should be used with caution.
**In patients with familial hypercholesterolemia, combined therapy with ezetimibe and simvastatin did not result in significant differences in intima-media thickness, as compared with simvastatin alone, despite decreases in levels of LDL-C and C-reactive protein (ENHANCE Trial).[3]

***Correction of hypertriglyceridemia by fenofibrate may affect LDL cholesterol differently according to hyperlipidemia classification:

- Type III and IV hyperlipidemia – LDL significantly increases
- Type IIb – LDL significantly decreases

Key Points: Statins are the most effective and efficient class of drugs for lowering both LDL-C levels and cardiovascular events.

- They are effective for both primary and secondary prevention of coronary heart disease and cardiovascular events.
- The ability of statins to reduce cardiovascular events exceeds that predicted from LDL-C-lowering alone.
- Other protective actions may include intravascular anti-inflammatory, anti-thrombotic and plaque-stabilizing effects.

Appendix 1 — Framingham Estimate of 10-Year CHD Risk for Males (Framingham Point Scores) [1]

Age:

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: (This should be an avg. of at least 2 measurements from lipoprotein analysis.)

Total Cholesterol	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	1	8	5	3	1

Points in boxes

Smoking Status: (“Smoker” means any cigarette smoking in the past month.)

	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)

HDL	Points
≥ 60	-1
50-59	0
40-49	1
< 40	2

Systolic Blood Pressure: (BP reading taken at the time of assessment)

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

Point Total	10-Year Risk %
(continued)	
9	5
10	6
11	8
12	10
13	12
14	16
15	20
16	25
≥ 17	≥ 30

*HDL like Total Cholesterol should be an average of at least 2 measurements from lipoprotein analysis.

Appendix 2 — Framingham Estimate of 10-Year CHD Risk for Females (Framingham Point Scores) [1]

Age:

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: (This should be an avg. of at least 2 measurements from lipoprotein analysis.)

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

Points in boxes

Smoking Status: (“Smoker” means any cigarette smoking in the past month.)

	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)

HDL	Points
≥ 60	-1
50-59	0
40-49	1
< 40	2

Systolic Blood Pressure: (BP reading taken at the time of assessment)

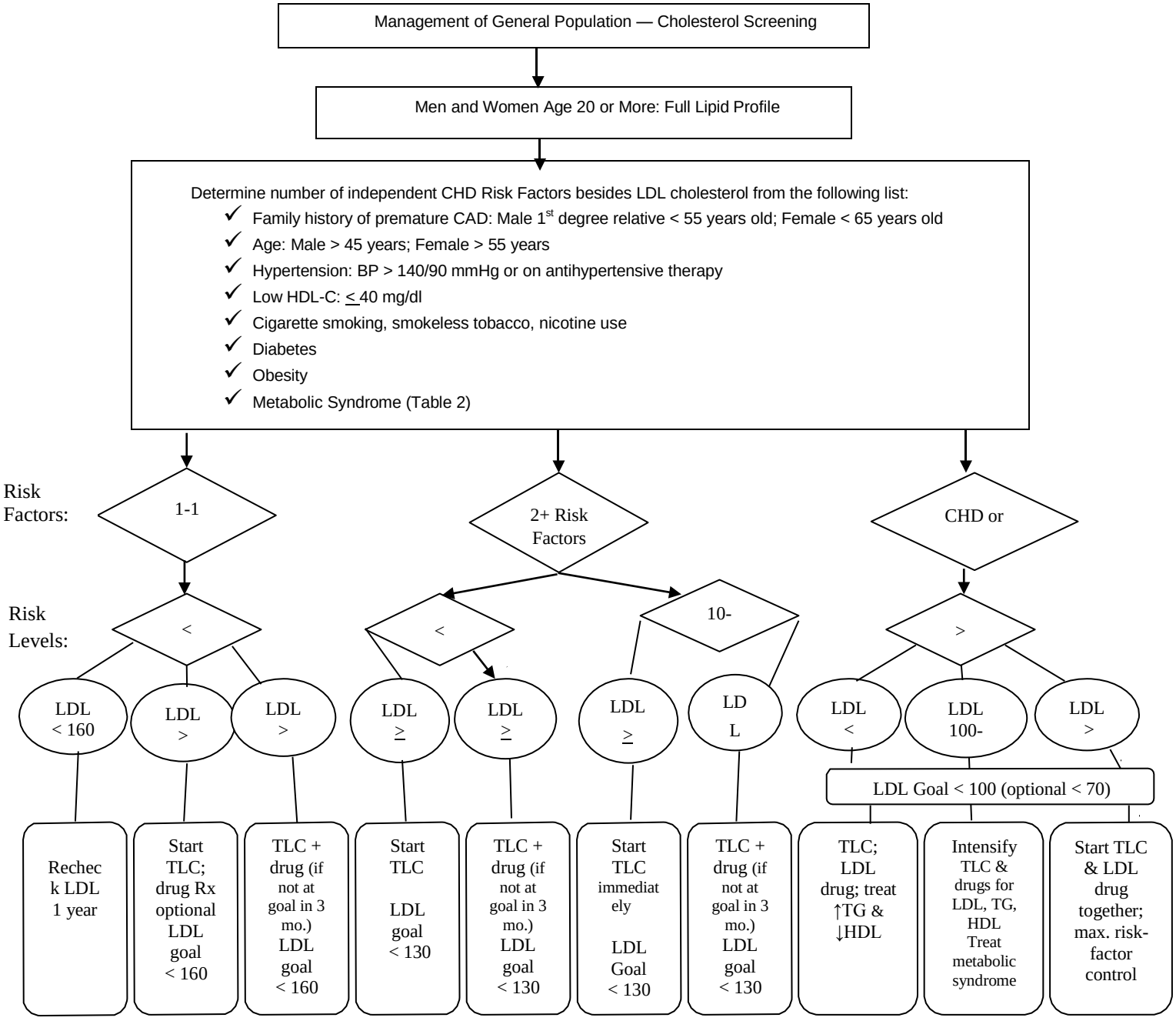
Systolic BP (mmHg)	If Untreated	If Treated
< 120	0	0
120-129	1	3
130-139	2	4
140-159	3	5
≥160	4	6

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

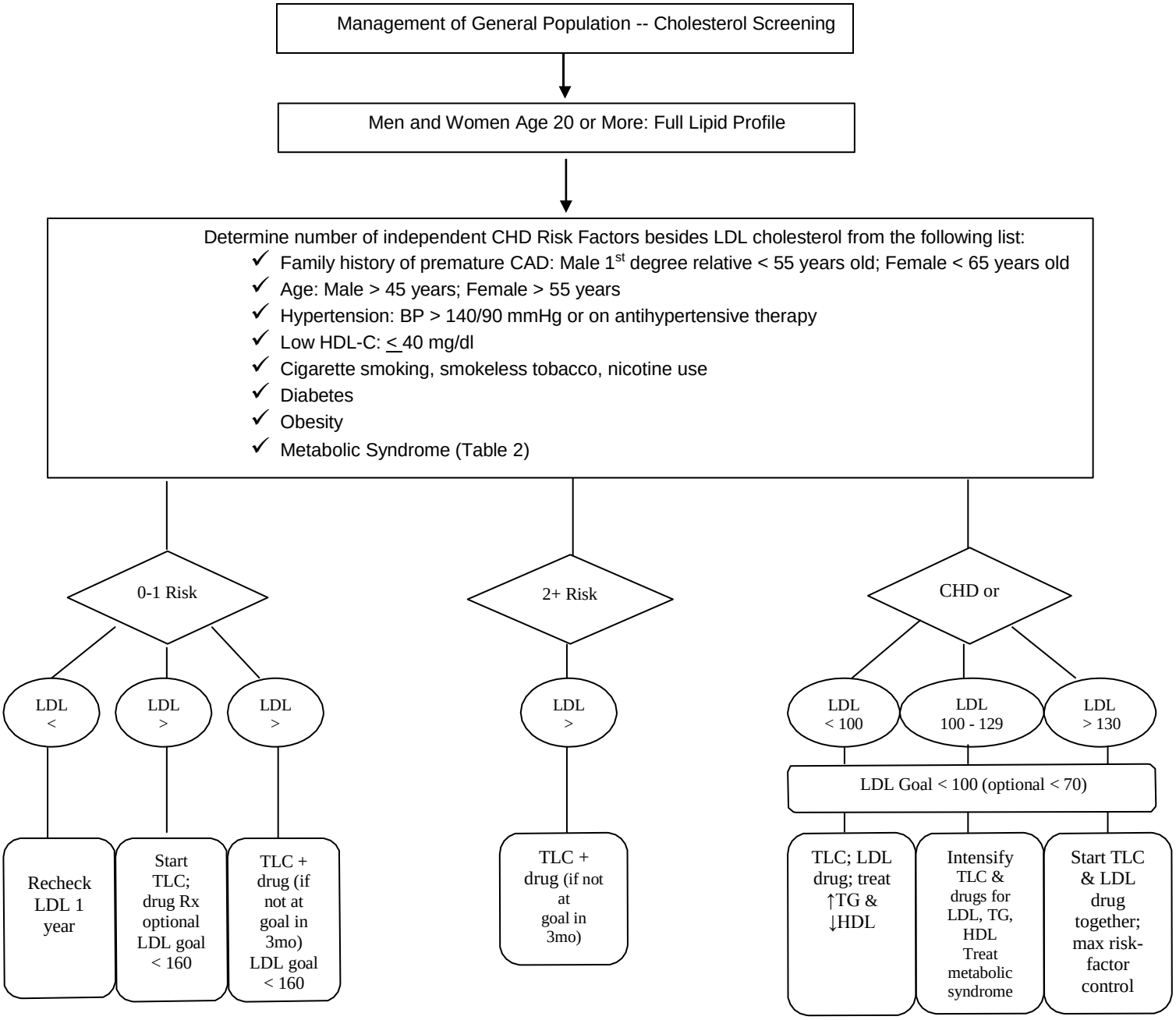
Point Total	10-Year Risk %
(continued)	
18	6
19	8
20	11
21	14
22	17
23	22
24	27
≥25	≥30

*HDL like Total Cholesterol should be an average of at least 2 measurements from lipoprotein analysis.

Cholesterol Management Algorithm Using Framingham Risk Assessment [1]



Optimal Cholesterol Management Algorithm if Framingham Risk Assessment Is Not Performed[1]



Clinical practice guidelines are designed to assist clinicians by providing a framework for the evaluation and treatment of patients. The adult cholesterol management guideline is based on the current Adult Treatment Panel III (ATP III) of the National Cholesterol Education Program, National Heart, Lung, and Blood Institute 2002, American College of Cardiology Foundation and the American Heart Association 2004. The current guideline is available at http://www.nhlbi.nih.gov/guidelines/cholesterol/index.htm.

Additional Resources for Piedmont WellStar HealthPlans, Inc. Members

- ***My*Health Advice Line** is staffed by experienced Registered Nurses and is available 24/7 to provide telephone support to members. Call 855-514-3679.

- **Online** interactive preventive health programs and resources are available in partnership with WebMD by logging in at www.pwplans.org/individuals.

Scientific Evidence Sources:

1. The Adult Treatment Panel III (ATP III) of the National Cholesterol Education Program. National Heart, Lung, and Blood Institute 2002. American College of Cardiology Foundation and the American Heart Association, 2004. Refer to http://www.nhlbi.nih.gov/guidelines/cholesterol/atp3full.pdf for complete ATP III recommendations.
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