

Hyperlipidemia in Coronary Artery Disease (CAD) Patients Guideline

These clinical guidelines are designed to assist clinicians by providing an analytical framework for the evaluation and treatment of patients. They are not intended to replace a clinician's judgment or to establish a protocol for all patients with a particular condition. A guideline will rarely establish the only approach to a problem.

GUIDELINE HISTORY and APPROVAL

ACTION	SEED GUIDELINE and/or MAIN INFORMATION & GROUP SOURCE(S)	DATE	ORGANIZATION
Guideline Reviewed and Approved	National Cholesterol Education Program. Second report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel II). NHLBI, NIH, 1993.	April 06, 2000	Geisinger Health Plan/ Clinical Guideline Committee
Guideline Reviewed and Approved		April 26, 2000	Geisinger Health Plan/ Quality Improvement Committee
Guideline Reviewed, Revised and Approved	Adult Treatment Panel for the National Cholesterol Education Program (ATP III) NHLBI. 2001.	July 06, 2001	Geisinger Health Plan/ Guideline Committee
Guideline Reviewed and Approved	Adult Treatment Panel for the National Cholesterol Education Program (ATP III) NHLBI. 2001.	July 25, 2001	Geisinger Health Plan/ Quality Improvement Committee
Guideline Reviewed, Revised and Approved	Adult Treatment Panel for the National Cholesterol Education Program (ATP III) NHLBI. 2001.	July 2, 2003	Geisinger Health Plan/Guideline Conference Hyperlipidemia Team
Guideline Reviewed, Revised and Approved	Adult Treatment Panel for the National Cholesterol Education Program (ATP III) NHLBI. 2001.	July 3, 2003	Geisinger Health Plan/ Guideline Committee
Guideline Reviewed and Approved	Adult Treatment Panel for the National Cholesterol Education Program (ATP III) NHLBI. 2001.	July 23, 2003	Geisinger Health Plan/ Quality Improvement Committee
Guideline Reviewed, Revised and Approved	<ol style="list-style-type: none"> January 2003 GHP Hyperlipidemia in CAD Patients Guideline Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (ATPIII). 2001. NCEP Report: Implications of Recent Clinical Trials for the National Cholesterol Education Program ATP III Guidelines. Circulation. 2004;110:227-239. This report was endorsed by the American College of Cardiology, National Heart, Lung, and Blood Institute, and the American Heart Association. 	March 01 - 18, 2005	Geisinger Health Plan Hyperlipidemia Guideline Team
Guideline Reviewed, Revised and Approved	Same as above	March 07 - 14, 2005	Geisinger Health Plan Pharmacy

Hyperlipidemia in Coronary Artery Disease (CAD) Patients Clinical Guideline

Guideline Reviewed, Revised and Approved	Same as above	March 19 - 22, 2005	Geisinger Health Plan Guideline Committee
Guideline Reviewed, Revised and Approved	Same as above	March 23 - 28, 2005	Geisinger Health Plan Medical Management Committee
Guideline Reviewed, Revised and Approved	Same as above	March 29 - April 02, 2005	Geisinger Health Plan Medical Directors and GHP QIC physicians
Guideline Reviewed, Revised and Approved	Same as above	April 27, 2005	Geisinger Health Plan/Quality Improvement Committee
Guideline Reviewed	Same as above	Nov. 1, 2006; Jan. 15, 2007	Geisinger Health Plan Guideline Committee
Guideline Reviewed	Same as above	Dec. 15-18, 2006	Geisinger Health Plan Pharmacy
Guideline Reviewed	Same as above	Jan. 15-22, 2007	Geisinger Health Plan Medical Directors
Guideline Reviewed	Same as above	Apr. 16, 2007	Geisinger Health Plan Medical Management Committee
Guideline Reviewed	Same as above	Apr. 25, 2007	Geisinger Health Plan/Quality Improvement Committee (QIC)
Guideline Reviewed	Same as above	Aug. 18 - , 2008	Geisinger Health Plan Guideline Committee
Guideline Reviewed	Same as above	Aug 21-22, 2008	Geisinger Health Plan Pharmacy
Guideline Reviewed	Same as above	Mar. 9-13, 2009	Geisinger Health Plan Medical Directors
Guideline Reviewed	Same as above	Mar. 16, 2009	Geisinger Health Plan Medical Management Committee
Guideline Reviewed	Same as above	Apr. 22, 2009	Geisinger Health Plan/QIC
Guideline Reviewed	Same as above	Sept. 2010	Geisinger Health Plan Guideline Committee
Guideline Reviewed	Same as above	Mar.21,2011	Geisinger Health Plan Medical Mgt Committee
Guideline Reviewed	Same as above	April 27, 2011	Geisinger Health Plan/QIC Committee



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OVERVIEW

Elevated blood cholesterol is one of the major modifiable risk factors for coronary heart disease (CHD)¹. The leading cause of death in the U.S., CHD accounts for approximately 490,000 deaths each year,² and angina and nonfatal myocardial infarction (MI) are a source of substantial morbidity. CHD is projected to cost over \$60 billion in 1995 in the U.S. in medical expenses and lost productivity³. The incidence of CHD is low in men under age 35 and in premenopausal women (1-2/1,000 annually),⁴ but climbs exponentially during middle age for both men and women. The onset of CHD is delayed approximately 10 years in women compared with men, probably due to effects of estrogen,⁵ but women account for 49% of all CHD deaths in the U.S.² Clinical events are the result of a multifactorial process that begins years before the onset of symptoms. Autopsy studies detected early lesions of atherosclerosis in many adolescents and young adults^{6,7,8,9,10}. The onset of atherosclerosis and symptomatic CHD is earlier among persons with inherited lipid disorders such as familial hypercholesterolemia (FH)¹¹ and familial combined hyperlipidemia (FCH)¹².

Serum Cholesterol and Risk of Coronary Heart Disease

Epidemiologic, pathologic, animal, genetic, and clinical studies support a causal relationship between blood lipids (usually measured as serum levels) and coronary atherosclerosis^{1,13,14,15}. Extended follow-up of large cohorts (predominantly middle-aged men)^{16,17,18} provides evidence that CHD risk increases in a continuous and graded fashion, beginning with cholesterol levels as low as 150-180 mg/dL;(a) this association extends to cholesterol levels measured as early as age 20 in men^{14,19}. During middle age, for each 1% increase in total cholesterol, CHD risk increases by an estimated 3%²⁰. High cholesterol (greater than or equal to 240 mg/dL) is also a risk factor in middle-aged women, but most coronary events in women occur well after menopause^{5,17,21,22,23,24}. Some studies report that cholesterol alone is a weak predictor of CHD mortality in the elderly,^{24a,50} but an overview of 24 cohort studies indicates that high cholesterol remains a risk factor for CHD after age 65²³ with the strongest associations among healthier elderly populations followed over longer periods^{25,26,27}. The association is weaker in older women than in men²³ and is not consistent for cholesterol levels measured after age 75^{28,29,30,31}.

Expert panels have defined high and “borderline high” (200-239 mg/dL) cholesterol to simplify clinical decisions(1). Because CHD is a multifactorial process, however, there is no definition of high cholesterol that discriminates well between individuals who will or will not develop CHD.^{32,33} Due to nonlipid risk factors, persons with cholesterol below 240 mg/dL account for the majority of all CHD events^{34,35}. Among middle-aged men, 9-12% of those with cholesterol 240 mg/dL or greater will develop symptomatic CHD over the next 7-9 years,^{34,36} but most of them have multiple other risk factors for CHD³⁵. The excess (i.e., absolute) risk due to high cholesterol (and the probable benefit of lowering cholesterol) increases with the underlying risk of CHD. In a 12-year study of over 316,000 men aged 35-57, the excess CHD mortality attributable to high cholesterol was greatest in men over age 45, and in those who smoked or had

hypertension¹⁶. The increase in CHD mortality associated with a given increment in serum cholesterol was steepest at very high values (>300 mg/dL)¹⁶. Excess risk from high cholesterol is smaller in women, who have less than half the CHD risk as do men at any given cholesterol level^{17,23,37}. Although the relative risk associated with high serum cholesterol declines with age,^{17,23,28} the excess risk generally does not, due to the much higher incidence of CHD in older persons^{31,38,39}.

Other Lipid Constituents and Risk of Coronary Disease

The risk associated with high total cholesterol is primarily due to high levels of low-density lipoprotein cholesterol (LDL-C),¹ but there is a strong, independent, and inverse association between high-density lipoprotein cholesterol (HDL-C) levels and CHD risk^{40,41,42}. Low HDL-C increases risk even when cholesterol is below 200 mg/dL, (41) a pattern present in up to 20% of men with confirmed CHD⁴³.

In many studies, measures of HDL-C or the ratio of total cholesterol to HDL-C are better predictors of CHD risk than is serum cholesterol alone^{5,22,23,24a,41,44}. High total cholesterol in association with high HDL-C (greater than or equal to 60 mg/dL) is common in older women (especially those taking estrogen) but is not associated with an increased risk for CHD^{1,41}. The importance of triglycerides as an independent risk factor for CHD remains uncertain^{40,45}. Three large studies reported strong associations between triglyceride levels over 200-300 mg/dL (2.26-3.39 mmol/L) and cardiovascular mortality in women,^{21,22,24} but other analyses found no association after controlling for obesity, fasting glucose, or low HDL-C⁴⁶. The combination of high triglycerides and low HDL-C often occurs in association with other CHD risk factors such as hypertension and diabetes and is associated with a high risk of CHD^{46a}.

Prevalence of High Cholesterol and Low HDL-C

Serum total cholesterol and LDL-C increase 1-2 mg/dL per year in men from ages 20-40, 2 mg/dL per year in women from ages 40-60,⁴⁷ and an average 18% during the perimenopausal period, due in part to age-related increases in weight⁴⁸. The prevalence of serum cholesterol 240 mg/dL or higher increases from 8-9% in adults under age 35 to nearly 25% for men age 55 and nearly 40% for women over 65⁴⁹. Approximately 1% of men and 3% of women over age 20 have low HDL-C (<35 mg/dL) with desirable or borderline-high total cholesterol⁴⁹.

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(Online) <http://odphp.osophs.dhhs.gov/pubs/GUIDECPS>

SEED GUIDELINE(S)

This guideline was developed based on:

1. Adult Treatment Panel for the National Cholesterol Education Program (ATP III) NHLBI. 2001.
2. NCEP Report: Implications of Recent Clinical Trials for the National Cholesterol Education Program ATP III Guidelines. *Circulation*. 2004;110:227-239.

Endorsing Organizations:

American College of Cardiology Foundation. May 2004.

National Heart, Lung, and Blood Institute. April 2004.

American Heart Association. Science Advisory and Coordinating Committee. May 2004.

GOALS

1. Primary Goal: LDL < 100 mg/dl
2. Optional Primary Goal for High Risk* Patients: LDL<70mg/dl
3. Secondary Goals: HDL > or = 40 mg/dl; TG < 200 mg/dl
4. Start AHA Therapeutic Lifestyle Changes (TLC) Diet.
<http://www.americanheart.org/presenter.jhtml?identifier=4764>
5. Obtain LP on admission. If not at goal or historical data shows elevated total cholesterol > 170 or LDL > 100, begin therapy immediately.

* High Risk Patients: CHD or CHD risk equivalents

CHD includes history of myocardial infarction, unstable angina, stable angina, coronary artery procedures (angioplasty or bypass surgery), or evidence of clinically significant myocardial ischemia.

CHD risk equivalents include clinical manifestations of noncoronary forms of atherosclerotic disease (peripheral artery disease, abdominal aortic aneurysm, and carotid artery disease), diabetes, and 2+ risk factors with 10-year risk for hard CHD>20%. This includes: diabetes, smoking, metabolic syndromes.

FAST FACTS

1. All individuals with known cardiovascular disease (CVD) should have a lipid profile done.
2. Primary Target LDL goal for individuals with CVD should be <100.
3. Optional Primary target LDL goal for high risk patients can be <70 mg/dl
4. Patients should be aggressively managed to obtain appropriate LDL goals.

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NCEP Report: Implications of Recent Clinical Trials for the National Cholesterol Education Program ATP III Guidelines. *Circulation*. 2004;110:227-239.

Endorsing organizations:

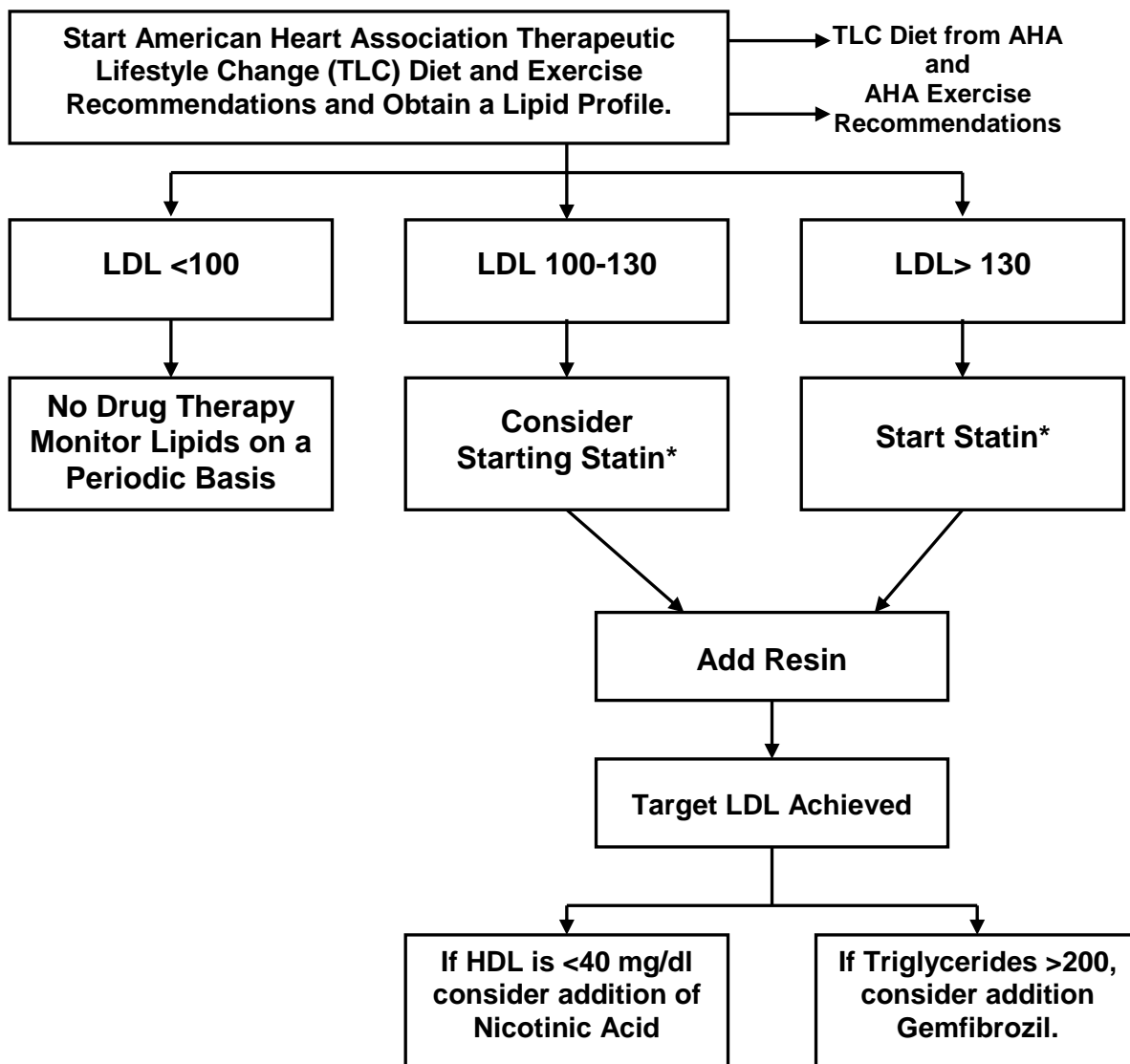
American College of Cardiology Foundation. May 2004.

National Heart, Lung, and Blood Institute. April 2004.

American Heart Association. Science Advisory and Coordinating Committee. May 2004.

ALGORITHM

Lipid Management In Patients with Known Coronary Artery Disease



*For patients intolerant of this therapy, consider Zetia (ezetimibe).

Note: Pharmaceutical coverage is dependent upon individual pharmacy benefit design and certain drugs may require prior authorization. Providers are encouraged to review the GHP formulary at <http://www.thehealthplan.com> or contact the GHP Pharmacy Department at 1-800-988-4861

PRIMARY GOAL: LDL <100 mg/dl
SECONDARY GOAL: HDL greater than or equal to 40 MG/dl
 TG <200 mg/dl

PRIMARY GOAL OPTION:
 70 mg/dl for high risk patients (CHD, diabetics, and/or CHD risk equivalents. Definitions on page 5, Goals Section.

Note: In a patient presenting with an acute myocardial infarction, start statin IMMEDIATELY if total cholesterol on admission or documented within the last year is > 200 (or LDL >130).

ANNOTATIONS

The algorithm is primarily based on:

1. The Adult Treatment Panel for the National Cholesterol Education Program (ATP III) NHLBI 2001.
2. NCEP Report: Implications of Recent Clinical Trials for the National Cholesterol Education Program ATP III Guidelines. *Circulation*. 2004;110:227-239.

Endorsing Organizations:

American College of Cardiology Foundation. May 2004.

National Heart, Lung, and Blood Institute. April 2004.

American Heart Association. Science Advisory and Coordinating Committee. May 2004.

American Heart Association (AHA)*** homepage at:<http://www.americanheart.org/>

AHA Dietary Recommendations at: <http://www.americanheart.org/presenter.jhtml?identifier=1330>

AHA Therapeutic Lifestyle Changes (TLC) diet:
<http://www.americanheart.org/presenter.jhtml?identifier=4764>

AHA exercise and fitness web address: <http://www.americanheart.org/presenter.jhtml?identifier=1200013>

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The information contained at the American Heart Association (AHA) Web site is not a substitute for medical advice or treatment, and the AHA recommends consultation with your doctor or health care professional.

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MEASURES

Percent with cardiovascular conditions with lipid profile

Percent with CAD and lipid profile and target LDL < 100

Percent with CAD and lipid profile and target LDL < 70

Percent on statin therapy