What levels of cholesterol should be treated for primary prevention?

EVIDENCE-BASED ANSWER The levels of cholesterol that should be treated for primary prevention are based on low-density lipoprotein cholesterol (LDL-C) levels of > 100 mg/dL to > 190 mg/dL and vary according to whether the patient's risk is high, moderate, or low. See the table to estimate risk. Grade of recommendation for medication indications: A (on the basis of high-quality randomized controlled trials). Grade of recommendation for lifestyle indications: B (on the basis of extrapolations from randomized controlled trials).

EVIDENCE SUMMARY Statins are the most effective at reducing LDL-C and the associated cardiovascular risk. The 5-year West of Scotland study (WOSCOPS) showed that a 26% reduction in LDL-C (from a mean of 192 to 142 mg/dL) using pravastatin 40 mg per day reduced the risk of either nonfatal myocardial infarction (MI) or coronary heart disease (CHD) death (number needed to treat [NNT] = 42; relative risk [RR] = 31; 95% confidence interval [CI],17 - 43).[1] This trial enrolled middle-aged men with an LDL-C level > 155 mg/dL without a history of prior MI, although subjects with stable angina (5% of the participants) were still eligible. Similar reductions were seen in cardiovascular death and in all-cause death (RR = 22; 95% CI = 0 - 40). Lovastatin reduced the risk of a first major acute coronary event (NNT = 24) in the 5-year AFCAPS/TexCAPS trial that enrolled 5608 men and 997 women with below-average high-density lipoprotein cholesterol (HDL-C) (men, 36 mg/dL; women, 40 mg/dL) without signs or symptoms of CHD.[2] LDL-C was lowered 25% (from a mean of 156 to 115 mg/dL). Unpublished results suggest that simvastatin may have a similar effect. Primary prevention data are still lacking for atorvastatin and fluvastatin.

The 7-year Lipid Research Clinics Coronary Prevention Trial (LRC-CPPT) documented a reduction in CHD death and/or nonfatal MI (NNT = 59) with a 12.6% reduction in LDL-C with the use of cholestyramine, a bile acid resin, 24 g per day.[3]

Results of studies of the fibric acid derivatives are mixed. Subjects taking gemfibrozil 1200 mg per day in the 5-year Helsinki Heart Study had fewer coronary events compared with those taking a placebo (NNT = 71).[4] Subsequent analysis suggests that patients with a high LDL-C/HDL-C ratio (> 5) plus hypertriglyceridemia (≥ 205 mg/dL) benefited the most.[5] Clofibrate is no longer used because of an unexplained increase in deaths in the WHO Cooperative Trial.[6] To date, outcomes in fenofibrate trials have only focused on surrogate markers and not long-term clinical outcomes.

TABLE

Adult treatment recommendations from NCEP, Adult Treatment Panel III

Risk category	LDL-C level	LDL-C goal* at which to consider medication
Coronary heart disease risk equivalents	< 100 mg/dL	≥ 130 mg/dL; ≥ 100-129 mg/dL optional
2 or more major risk factors†	< 130 mg/dL	10-year risk‡ 10-20%: ≥ 130 mg/dL; 10-year risk‡ < 10%: ≥ 160 mg/dL
0 or 1 major risk factor†	< 160 mg/dL	≥ 190 mg/dL; 160-190 mg/dL optional

NOTE: CHD risk equivalents include symptomatic carotid artery disease, peripheral arterial disease, abdominal aortic aneurysm, diabetes, and a 10-year risk of > 20% (see ‡ below). The cut-off points for therapy for patients with clinical CHD are the same as for CHD risk equivalents.
* Initiate therapeutic lifestyle changes above these levels.
†Major risk factors include cigarette smoking, hypertension, HDL < 40 mg/dL, family history of premature CHD (CHD in first-degree male relative < 55 y; CHD in first-degree female relative < 65 y), age (men ≥ 45 y, women ≥ 55 y).
‡To calculate 10-year risk, use the Framingham Tables, available at http://www.nhlbi.nih.gov/guidelines/cholesterol/risk_tbl.htm.

RECOMMENDATIONS FROM OTHERS The recommendations of the Third Report of the National Cholesterol Education Program[7] (NCEP, Adult Treatment Panel III) are in the table. This report is an excellent source of additional information (http://www.nhlbi.nih.gov/guidelines/cholesterol/atp3xsum.pdf).

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Read a clinical commentary by David Switzer, MD, at www.fpin.org.

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