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). 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. 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 Unpublished results suggest that simvastatin may have a similar effect.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-CPT) 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. Results of studies of the fibrac 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). Subsequent analysis suggests that patients with a high LDL-C/HDL-C ratio (> 5) plus hypertriglyceridemia (≥ 205 mg/dL) benefited the most. Clofibrate is no longer used because of an unexplained increase in deaths in the WHO Cooperative Trial. To date, outcomes in fenofibrate trials have only focused on surrogate markers and not long-term clinical outcomes.

RECOMMENDATIONS FROM OTHERS The recommendations of the Third Report of the National Cholesterol Education Program (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.

REFERENCES