

Abstract

JAMA. 2007 Aug 15;298(7):786-98.

High-density lipoprotein as a therapeutic target: a systematic review.

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CONTEXT: High-density lipoprotein cholesterol (HDL-C) is a cardiovascular risk factor that is gaining substantial interest as a therapeutic target.

OBJECTIVES: To review the current and emerging strategies that modify high-density lipoproteins (HDLs).

DATA SOURCES: Systematic search of English-language literature (1965-May 2007) in MEDLINE and the Cochrane database, using the key words HDL-C and apolipoprotein A-I and the subheadings reverse cholesterol transport, CVD [cardiovascular disease] prevention and control, drug therapy, and therapy; review of presentations made at major cardiovascular meetings from 2003-2007; and review of ongoing trials from ClinicalTrials.gov and current guidelines from major cardiovascular societies.

STUDY SELECTION AND DATA EXTRACTION: Study selection was prioritized to identify randomized controlled trials over meta-analyses over mechanistic studies; identified studies also included proof-of-concept studies and key phase 1 through 3 trials of novel agents. Study eligibility was assessed by 2 authors; disagreements were resolved by consensus with the third.

DATA SYNTHESIS: Of 754 studies identified, 31 randomized controlled trials met the inclusion criteria. Currently available therapeutic and lifestyle strategies, when optimized, increase HDL-C levels by 20% to 30%. While basic and small pilot studies have shown promise, proof that increasing HDL-C levels confers a reduction in major cardiovascular outcomes independent of changes in levels of low-density lipoprotein cholesterol or triglycerides has been more elusive. Some novel therapeutic agents in human studies appear to effectively increase HDL-C levels, whereas other novel strategies that target HDL metabolism or function may have minimal effect on HDL-C levels.

CONCLUSIONS: At present there is modest evidence to support aggressively increasing HDL-C levels in addition to what is achieved by lifestyle modification alone. Ongoing clinical trials that target specific pathways in HDL metabolism may help expand cardiovascular treatment options.

PMID: 17699012

