**Authors' objectives**

To examine the evidence about the benefits and harms of screening and treatment of lipid disorders in adults, adolescents and children for the U.S. Preventive Services Task Force (USPSTF). The review addressed three key questions (KQ).

**KQ1.** Will treatment with drug therapy of patients (similar to those who would be identified by screening) without known coronary heart disease (CHD) but with 'abnormal' lipid levels improve outcomes compared with no treatment?

**KQ2.** Will treatment with diet or exercise therapy of patients (similar to those who would be identified by screening) without known CHD but with 'abnormal' lipid levels improve outcomes compared with no treatment?

**KQ3.** Is there a reliable, accurate acceptable and feasible screening test (or tests) that can be used to detect lipid disorders? If so, who should be screened and how often should screening be performed.

**Searching**

The following sources were searched to identify key articles published before 1994: MEDLINE from 1994 to December 1999; the Cochrane Controlled Trials Register; the USPSTF Guide to Clinical Preventive Services (2nd edition); and systematic reviews, meta-analyses and evidence-based practice guidelines that addressed screening and treatment of lipid disorders. In addition, bibliographies were handsearched.

**Study selection**

**Study designs of evaluations included in the review**

For KQ1 and KQ2, only randomised controlled trials of at least one year in duration were eligible for the review. For KQ3, all study designs were eligible for inclusion.

**Specific interventions included in the review**

KQ1: any pharmacological agent used to lower blood lipids, but excluding oestrogen and dietary supplements, was included. The drug therapies in the included studies were cholestyramine, gemfibrozil, pravastatin and lovastatin.

KQ2: any diet or exercise therapy for lipid disorders was included. The dietary interventions were rated as low-, medium- or high-intensity interventions. The included studies looked at diet therapy in primary care, multiple risk factor interventions (including diet), informing individuals of their cholesterol level, and dietary interventions in children. KQ3: any study that investigated any screening for abnormal lipids was included in the review.

**Reference standard test against which the new test was compared**

The review did not include any diagnostic accuracy studies that compared the performance of the index test with a reference standard of diagnosis.

**Participants included in the review**

For the review of the effectiveness of drug, diet or exercise therapy (KQ1 and 2), studies that included participants with abnormal blood lipids but without known CHD were included. For the review of screening (KQ3), studies of all populations apart from those with known CHD were eligible.

**Outcomes assessed in the review**

For KQ1 and KQ2, the outcomes to be included were total mortality, CHD mortality, CHD events and CHD procedures required; total cholesterol, high-density lipoprotein (HDL)-cholesterol and low-density lipoprotein-cholesterol were also eligible for KQ2. For KQ3, the eligible outcomes were prevalence measures, precision and accuracy measures and also natural history studies of cholesterol levels.
How were decisions on the relevance of primary studies made?
Two Evidence-based Practice Centre staff independently reviewed the titles and abstracts of the articles identified by the literature searches. The Evidence-based Practice Centre team members reviewed the full articles of those retrieved, and the decision on whether to include or exclude them was made by consensus.

Assessment of study quality
The internal and external validity of each study was rated using criteria specific to study design that were developed by the USPSTF Methods Work Group; details of these were given in the review. The aggregate internal and external validity score was calculated. The authors do not state how the papers were assessed for validity, or how many of the reviewers performed the validity assessment.

Data extraction
The data were entered into an electronic database and evidence tables were constructed. The categories of data abstracted were study design, intervention, results and quality (validity) assessment.

Methods of synthesis
How were the studies combined?
KQ1 was addressed in a narrative synthesis and a meta-analysis (see Other Publications of Related Interest no.1). The pooled odds ratios (ORs) were calculated with 95% confidence intervals (CIs) for the outcomes of CHD events, CHD mortality and all-cause mortality using fixed-effect (Mantel-Haenszel) and random-effects (DerSimonian and Laird) models via RevMan software.

KQ2 study results were pooled in a narrative synthesis, which included a discussion of earlier meta-analyses of small subsets of trials within the ones included here and published by different authors.

A narrative synthesis was undertaken for KQ3.

How were differences between studies investigated?
Within the narrative syntheses the trials were grouped appropriately, e.g. by type of dietary intervention. For the authors' own meta-analysis, graphs of outcomes were examined visually and the chi-squared test for heterogeneity was performed to assess differences between the studies. The authors also performed sensitivity analyses comparing the results for statins alone with the overall results.

Results of the review
There were 4 trials included that addressed KQ1 (drug therapy), and 19 that addressed KQ2 (diet or exercise). It was unclear how many studies were included in relation to KQ3 (screening).

There was strong direct evidence that drug therapy reduced CHD events and CHD mortality in middle-aged men (35 to 70 years) with abnormal lipids and a potential risk of CHD events greater than 1% per year. Drug therapy may also reduce total mortality in patients at higher risk (greater than 1.5% per year). Less direct evidence suggested that drug therapy was also effective in other adults, including older men (aged over 70 years) and women (aged 45 years or more), with similar levels of risk.

Trials of diet therapy for primary prevention have led to long-term reductions in cholesterol of 3 to 6% but have not demonstrated a reduction in CHD events overall. Exercise programmes that maintain or reduce body weight can produce short-term reductions in total cholesterol of 3 to 6%, whereas longer-term results in unselected populations have found small reductions or no effect.

Screening middle-aged and older men and women for lipid disorders can accurately identify persons at increased CHD risk who may benefit from therapy. There was insufficient evidence regarding the benefits and harms of screening and treating persons at low absolute risk, including most men under 35 years of age, women under 45 years, children and adolescents. To identify accurately persons with abnormal lipids, at least 2 measurements of total cholesterol and HDL-
cholesterol are required. The role of measuring triglycerides and optimal screening interval was unclear from the available evidence.

Authors' conclusions
Strong evidence showed the effectiveness of therapy for lipid disorders in (European) middle-aged men; indirect evidence showed effectiveness in older men and women of sufficient risk. Screening for lipid disorders on the basis of total cholesterol and HDL-cholesterol, and performing a global assessment of CHD risk, can accurately identify those at sufficient risk who can benefit from treatment.

CRD commentary
This was a very wide-ranging review that addressed three questions relating to the screening for and treating of lipid disorders, and the relevance of these in terms of cardiovascular outcomes. The inclusion and exclusion criteria for the review were adequately defined, although there was some lack of clarity in the report. The search strategy employed was rather unsystematic, but given that the large-scale studies in this area are probably well known, this approach is unlikely to have omitted relevant studies. The quality of the studies included in the review was assessed and the levels of evidence incorporated into the results. The details of the individual studies were presented in the text and in tabular format, although some of the details in the screening part of the review were difficult to follow. The review synthesis employed meta-analysis and narrative synthesis where appropriate.

Overall, the authors' conclusions appear to be supported by the available evidence.

Implications of the review for practice and research
Practice: The authors state that 'The evidence is good that treating lipid disorders in middle-aged men of European descent reduces CHD events, CHD mortality, and perhaps total mortality in patients with sufficient CHD risk'.

Research: The authors highlighted several areas for further research. These included: the effect of lipid therapy in non-European men; the effect of specific diets in other populations; the real-world use of screening; the significance of triglycerides; and the analysis of the relative importance of treating various risk factors for CHD disease.

Bibliographic details

Original Paper URL

Other publications of related interest

Indexing Status
Subject indexing assigned by CRD

MeSH
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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.