Screening for lipid disorders in children and adolescents: systematic evidence review for the U.S. Preventive Services Task Force


CRD summary
This was a wide ranging review addressing all aspects of the effectiveness of screening for lipid disorders in children. A large number of studies were included, but evidence was limited. The authors’ conclusions – that pharmaceutical therapies are effective in improving lipid levels in monogenetic dyslipidaemia and that current screening methods for lipid disorders are inadequate – are likely to be reliable.

Authors' objectives
To assess the clinical effectiveness of screening for and treating of lipid disorders (dyslipidaemia) in children and adolescents.

Searching
MEDLINE, EMBASE, PsycInfo and the Cochrane databases were searched from inception to September 2005 for English language studies. Additional studies were sought from recent reviews, bibliographies of included studies, editorials, internet searches and contact with experts. Search strategies were reported in full in an appendix.

Study selection
Eligible studies were those assessing: effectiveness of screening for dyslipidaemia in delaying and reducing incidence of coronary heart disease (CHD)-related events; the accuracy and adverse effects of tests for dyslipidaemia in identifying children and adolescents at increased risk of CHD-related events; and effectiveness of diet, exercise and pharmaceutical therapies in treating dyslipidaemia in childhood and adolescence, reducing incidence of adult dyslipidaemia and delaying and reducing the incidence of CHD-related events. Studies of other treatments (for example, surgery) were excluded.

For treatment studies, only randomized controlled trials (RCTs) that reported serum lipid outcomes were included; information about adverse effects of treatment was obtained from other study types.

Studies of children and adolescents with conditions known to cause dyslipidaemia and with rare conditions such as familial hypercholesterolaemia (FH) were excluded, but treatment studies of children with FH were presented in the report.

Included studies were of dietary education programs and supplements, physical exercise programs, statins and bile acid binding resins.

The authors state neither how studies were selected for the review nor how many reviews were involved in the study selection process.

Assessment of study quality
Two reviewers independently assessed the quality of RCTs using the US Preventive Services Task Force criteria, which provide an overall rating combining internal and external validity. Any disagreements were resolved by consensus.

Data extraction
Data were extracted directly into evidence tables separately for studies of test performance, RCTs of treatment and adverse effects. For treatment studies, mean percentage change and standard error were extracted; where these were not reported they were calculated by the authors. The authors did not state how many reviewers performed the data extraction.

Methods of synthesis
Meta-analyses were conducted to assess the effectiveness of statins on improving lipid levels in children and adolescents with FH and the effectiveness of exercise on improving lipid levels in normal or overweight children and adolescents without FH. Studies were pooled using a random-effects model. Other studies were combined in a narrative synthesis and evidence tables, grouped by research question.

Results of the review
The review included 160 studies on screening and testing for dyslipidaemia, 68 studies of interventions or of lipid level monitoring over time, eight studies of the adverse effects of screening and 81 studies of the adverse effects of treatment.

No studies evaluated the effect of screening for dyslipidaemia in childhood and adolescence on adult lipid levels and CHD.

Normal ranges for lipids in children and adolescents were currently defined by population levels; recent studies had shown age, gender and racial variations. Current screening recommendations based on family history had limited accuracy (missing 30 per cent to 60 per cent of children with elevated lipids), low adherence by service providers and limited acceptance by parents and children. Single measures of total cholesterol (TC) are inadequate to classify children correctly.

Studies of statin treatment in children with monogenic dyslipidaemias (FH or familial combined hyperlipidaemia (FCH)) showed effectiveness in reducing TC (mean reduction 24.4 per cent (95% CI: 19.5, 29.2, n = 9 studies), and low density lipoprotein (LDL) (mean reduction 30.8 per cent, 95% CI: 24.1, 37.5, n = 8 studies). Two trials showed benefit from bile acid binding resins in this population. RCTs of dietary supplements and advice showed marginal improvements.

Six trials of exercise interventions in children without monogenic dyslipidaemias showed no effect on lipid levels percentage mean reduction in TC 0% (95% CI: -5.6, 5.6) and percentage mean reduction in LDL 3.1% (95% CI: -7.7, 1.5). One study showed that high intensity counselling was effective, but effectiveness ceased when the intervention was stopped. Studies of dietary advice and supplements showed no effect.

A variety of adverse effects of therapy were reported (full details in the report), but none were serious. Studies were generally small and of insufficient duration to determine long-term effects.

Authors’ conclusions
Screening using family history missed significant numbers of children with elevated lipids. Trials of pharmaceutical therapies showed improvement in lipid levels in children with monogenic dyslipidaemias. Evidence was lacking to assess the effectiveness of screening or treatment in childhood on adult CHD or lipid outcomes, optimal ages and intervals for screening and cost-effectiveness of screening.

CRD commentary
This was a wide-ranging review addressing all aspects of the evidence for screening for lipid disorders in childhood and adolescence. A number of research questions were clearly stated and inclusion criteria were listed, though it was sometimes unclear which criteria had been applied to which questions. Search strategies were extensive, though the limitation to English language studies may have resulted in the loss of some relevant data. A large number of studies were included in the review and these were summarized in extensive evidence tables. Reporting of the review methodology was limited and the application of processes to reduce error and bias was unclear. Meta-analyses, where applied, were appropriate. Evidence to address the majority of the authors’ stated research questions was lacking. The authors' conclusions are based upon what data were available and are likely to be reliable.

Implications of the review for practice and research
Practice: the authors made no recommendations for practice.

Research. The authors recommended: research to develop risk assessment tools in order to narrow the population of children requiring lipid testing; evaluations of the performance of non-invasive screening strategies such as arterial intima-media thickness (IMT); RCTs to establish the comparative effectiveness of screening strategies in terms of
provider and participant adherence; follow-up of existing cohorts to establish the impact of childhood screening on adult CHD; long-term follow-up of children treated with statins to assess their safety and efficacy in terms of adult outcomes; further investigation of the impact of exercise on lipid levels, particularly in children with lipid levels above the 95th centile; improved and standardised reporting of adverse events; cost-effectiveness studies of universal screening versus screening via family history.

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