Supplementary Online Content


**eMethods.** Literature Search Strategies

**eTable.** Quality Assessment Criteria

**eFigure.** Literature Flow Diagram

This supplementary material has been provided by the authors to give readers additional information about their work.
eMethods. Literature Search Strategies

Search Strategy

Sources searched:
Cochrane Central Register of Controlled Clinical Trials, via Wiley
Medline, via Ovid
PubMed, publisher-supplied

Key:
/ = MeSH subject heading
$ = truncation
ti = word in title
ab = word in abstract
adj# = adjacent within x number of words
pt = publication type
* = truncation
ae = adverse effects
ci = chemically induced
de=drug effects
mo=mortality
nm = name of substance

Cochrane Central Register of Controlled Clinical Trials

#1 (hyperlipid*emia*:ti,ab,kw or dyslipid*emia*:ti,ab,kw or hypercholesterol*emia*:ti,ab,kw or hyperlipoprotein*emia*:ti,ab,kw or hypertriglycerid*emia*:ti,ab,kw or dysbetalipoprotein*emia*:ti,ab,kw)
#2 (familial next hypercholesterol*emi*):ti,ab,kw or (familial next hyperlipid*emi*):ti,ab,kw or (essential next hypercholesterol*emi*):ti,ab,kw or (familial near/3 apolipoprotein):ti,ab,kw
#3 "heterozygous fh":ti,ab,kw or "homozygous fh":ti,ab,kw
#4 (lipid next disorder*):ti,ab,kw or (lipid near/3 dysfunction*):ti,ab,kw
#5 (high or elevated or abnormal or aberr*):ti,ab,kw near/3 (cholesterol or lipid* or LDL*):ti,ab,kw
#6 (low or decrease* or deficien* or abnormal or aberr*):ti,ab,kw near/3 HDL*:ti,ab,kw
#7 (cholesterol or lipid* or lipoprotein* or LDL* or HDL*):ti,ab,kw near/3 (detect* or measure* or check* or assess* or analyz* or analys* or test* or panel* or profile*):ti,ab,kw
#8 (fasting or nonfasting or non-fasting):ti,ab,kw next (lipid* or lipoprotein* or cholesterol):ti,ab,kw
#9 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8
#10 (child*:ti,ab,kw or adolesc*:ti,ab,kw or teen:ti,ab,kw or teens:ti,ab,kw or teenage*:ti,ab,kw or youth:ti,ab,kw or youths:ti,ab,kw or p*ediatric*:ti,ab,kw)
#11 #9 and #10 from 2007 to 2015, in Trials

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MEDLINE

Dyslipidemia screening, screening harms

Database: Ovid MEDLINE(R) without Revisions <1996 to June Week 1 2015>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <June 2, 2015>, Ovid MEDLINE(R) Daily Update <June 2, 2015>

Search Strategy:

--------------------------------------------------------------------------------
1   Hyperlipidemias/
2   Dyslipidemias/
3   Hypercholesterolemia/
4   Lipid Metabolism Disorders/
5   Hyperlipoproteinemias/
6   Hypertriglyceridemia/
7   Hyperlipoproteinemia Type II/
8   Hyperlipidemia, Familial Combined/
9   Hypobetalipoproteinemias/
10  Abetalipoproteinemia/
11  hyperlipid?emia$.ti,ab.
12  dyslipid?emia$.ti,ab.
13  hypercholesterol?emia$.ti,ab.
14  hyperlipoprotein?emia$.ti,ab.
15  hypertriglycerid?emia$.ti,ab.
16  dysbetalipoprotein?emia$.ti,ab.
17  familial hypercholesterol$emi*.ti,ab.
18  familial hyperlipid$emi*.ti,ab.
19  essential hypercholesterol?emi*.ti,ab.
20  (familial adj3 apolipoprotein).ti,ab.
21  heterozygous fh.ti,ab.
22  homozygous fh.ti,ab.
23  lipid disorder$.ti,ab.
24  or/1-23
25  Cholesterol/bl
26  Triglycerides/bl
27  Lipoproteins/bl
28  Cholesterol, HDL/
29  Cholesterol, LDL/
30  Apolipoprotein B-100/
31  Apolipoprotein B 100.ti,ab.
32  apo b 100.ti,ab.
33  ((high or elevated or abnormal or aberr$) adj3 (cholesterol or lipid$ or LDL$)).ti,ab.
34  ((low or decrease$ or deficien$ or abnormal or aberr$) adj3 HDLS).ti,ab.
35  or/25-35

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Mass screening/

screen$.ti,ab.

((cholesterol or lipid$ or lipoprotein$ or LDL$ or HDL$) adj3 (detect$ or measur$ or
check$ or assess$ or analyz$ or analys$ or test$ or panel$ or profile$)).ti,ab.

(fasting adj (lipid$ or lipoprotein$ or cholesterol)).ti,ab.

(non-fasting adj (lipid$ or lipoprotein$ or cholesterol)).ti,ab.

37 or 38 or 39 or 40 or 41

(24 or 36) and 42

adolescent/ or child/ or young adult/

43 and 44

(child$ or teen or teens or teenage$ or adolescen$ or youth or youths or young people
or pediatric$ or paediatric$).ti,ab.

47 43 and 46

limit 47 to ("in data review" or in process or "pubmed not medline")

49 45 or 48

limit 49 to english language

51 limit 50 to yr="2007 -Current"

52 remove duplicates from 51

Dx yield/accuracy

Database: Ovid MEDLINE(R) without Revisions <1996 to June Week 1 2015>, Ovid
MEDLINE(R) In-Process & Other Non-Indexed Citations <June 2, 2015>, Ovid
MEDLINE(R) Daily Update <June 2, 2015>

Search Strategy:

Hyperlipidemias/

Dyslipidemias/

Hypercholesterolemia/

Lipid Metabolism Disorders/

Hyperlipoproteinemias/

Hypertriglyceridemia/

Hyperlipoproteinemia Type II/

Hyperlipidemia, Familial Combined/

Hypobetalipoproteinemias/

Abetalipoproteinemia/

hyperlipid?emia$.ti,ab.

dyslipid?emia$.ti,ab.

hypercholesterol?emia$.ti,ab.

hyperlipoprotein?emia$.ti,ab.

hypertriglycerid?emia$.ti,ab.

dysbetalipoprotein?emia$.ti,ab.

familial hypercholesterol$emi*.ti,ab.

familial hyperlipid?emi*.ti,ab.

essential hypercholesterol?emi*.ti,ab.
(familial adj3 apolipoprotein).ti,ab.
homozygous fh.ti,ab.
heterozygous fh.ti,ab.
lipid disorder$.ti,ab.
or/1-23
Cholesterol/bl
Triglycerides/bl
Lipoproteins/bl
Cholesterol, HDL/
Cholesterol, LDL/
Apolipoprotein B-100/
Apolipoprotein B 100.ti,ab.
apob 100.ti,ab.
((high or elevated or abnormal or aberr$) adj3 (cholesterol or lipid$ or LDL$)).ti,ab.
((low or decrease$ or deficien$ or abnormal or aberr$) adj3 HDL$).ti,ab.
((cholesterol or lipid$ or lipoprotein$ or LDL$ or HDL$) adj3 (detect$ or measur$ or check$ or assess$ or analyz$ or analy$ or test$ or panel$ or profile$)).ti,ab.
(fasting adj (lipid$ or lipoprotein$ or cholesterol)).ti,ab.
(non-fasting adj (lipid$ or lipoprotein$ or cholesterol)).ti,ab.
or/25-38
"Sensitivity and Specificity"/
"Predictive Value of Tests"/
ROC Curve/
False Negative Reactions/
False Positive Reactions/
Diagnostic Errors/
"Reproducibility of Results"/
Reference Values/
Reference Standards/
Observer Variation/
Receiver operator$.ti,ab.
ROC curve$.ti,ab.
sensitivity$.ti,ab.
specificity$.ti,ab.
predictive value.ti,ab.
accuracy.ti,ab.
false positive$.ti,ab.
false negative$.ti,ab.
miss rate$.ti,ab.
error rate$.ti,ab.
40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59.
(24 or 39) and 60
adolescent/ or child/ or young adult/
61 and 62

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(child$ or teen or teens or teenage$ or adolescen$ or youth or youths or young people or pediatric$ or paediatric$).ti,ab.

61 and 64

limit 65 to ("in data review" or in process or "pubmed not medline")

67 63 or 66

limit 67 to (english language and yr="2007 -Current")

69 remove duplicates from 68

Drug Tx Harms

Database: Ovid MEDLINE(R) without Revisions <1996 to June Week 1 2015>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <June 2, 2015>, Ovid MEDLINE(R) Daily Update <June 2, 2015>

Search Strategy:

Hyperlipidemias/

Dyslipidemias/

Lipid Metabolism Disorders/

Hyperlipoproteinemias/

Hypertriglyceridemia/

Hyperlipoproteinemia Type II/

Hyperlipidemia, Familial Combined/

Hypobetalipoproteinemias/

Abetalipoproteinemia/

hyperlipidemia$.ti,ab.

dyslipidemia$.ti,ab.

hypercholesterolemia/

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hypercholesterol?emia$.ti,ab.

dyslipid?emia$.ti,ab.

hypercholesterol?emia$.ti,ab.

hyperlipoprotein?emia$.ti,ab.

hypertriglyceridemia$.ti,ab.

dysbetalipoproteinemia$.ti,ab.

familial hypercholesterol?emia$.ti,ab.

familial hyperlipid?emia*.ti,ab.

essential hypercholesterol?emia*.ti,ab.

heterozygous fh.ti,ab.

homozygous fh.ti,ab.

lipid disorder$.ti,ab.

((high or elevated or abnormal or aberr$) adj3 (cholesterol or lipid$ or LDL$)).ti,ab.

((low or decrease$ or deficien$ or abnormal or aberr$) adj3 HDLS).ti,ab.

or/1-25

hypolipidemic agents/ or bezafibrate/ or butoxamine/ or clofenapate/ or clofibrate/ or clofibric acid/ or colestipol/ or fenofibrate/ or gemfibrozil/ or halofenate/ or meglutol/ or nafenopin/ or niacin/ or niceritrol/ or pyridinolcarbamate/ or simvastatin/ or triparanol/
anticholesteremic agents/ or azacosterol/ or chitosan/ or cholestyramine resin/ or
clofibrate/ or clofibric acid/ or lovastatin/ or meglutol/ or pravastatin/ or probucol/ or
simvastatin/ or "trans-1,4-bis(2-chlorobenzaminomethyl)cyclohexane dihydrochloride"/
hydroxymethylglutaryl-coa reductase inhibitors/ or lovastatin/
3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor$.ti,ab.
hydroxymethylglutaryl coa reductase inhibitor$.ti,ab.
hydroxymethylglutaryl coa inhibitor$.ti,ab.
hydroxymethylglutaryl coenzyme a reductase.ti,ab.
hydroxymethylglutaryl coenzyme a inhibitor$.ti,ab.
hmg coa reductase inhibitor$.ti,ab.
hmg coa inhibitor$.ti,ab.
atorvastatin.ti,ab.
fluvastatin.ti,ab.
lovastatin.ti,ab.
pitavastatin.ti,ab.
pravastatin.ti,ab.
rosuvastatin.ti,ab.
simvastatin.ti,ab.
hypolipidemic$.ti,ab.
anticholesteremic$.ti,ab.
antilipidemic.ti,ab.
statin$.ti,ab.
lipid lower$.ti,ab.
(treat$ or therap$ or medicat$).ti.
or/27-49
"Drug-Related Side Effects and Adverse Reactions"/
Mortality/
Morbidity/
Death/
mo.fs.
(harm or harms or harmful or harmed).ti,ab.
(adverse adj (effect$ or event$ or outcome$)).ti,ab.
safety.ti,ab.
over$treat$.ti,ab.
drug-induced liver injury/
drug-induced liver injury, chronic/
Liver Neoplasms/ci
Liver/de
Liver failure/ci
Liver failure, acute/ci
(liver adj3 (injur$ or dysfunction$ or failure$)).ti,ab.
(Hepatic adj3 (injur$ or dysfunction$ or failure$)).ti,ab.
(transaminase adj3 (elevat$ or abnormal$ or dysfunction$)).ti,ab.
Liver enzyme$.ti,ab.
Drug and lifestyle treatment efficacy

Database: Ovid MEDLINE(R) without Revisions <1996 to June Week 1 2015>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <June 2, 2015>, Ovid MEDLINE(R) Daily Update <June 2, 2015>
Search Strategy:

1 Hyperlipidemias/
2 Dyslipidemias/
3 Hypercholesterolemia/
4 Lipid Metabolism Disorders/
5 Hyperlipoproteinemias/
6 Hypertriglyceridemia/

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7  Hyperlipoproteinemia Type II/
8  Hyperlipidemia, Familial Combined/
9  Hypobetalipoproteinemias/
10  Abetalipoproteinemia/
11  hyperlipidemia$.ti,ab.
12  dyslipidemia$.ti,ab.
13  hypercholesterolemia$.ti,ab.
14  hyperlipoproteinemia$.ti,ab.
15  hypertriglyceridemia$.ti,ab.
16  dysbetalipoproteinemia$.ti,ab.
17  familial hypercholesterolemia*.ti,ab.
18  familial hyperlipidemia*.ti,ab.
19  essential hypercholesterolemia*.ti,ab.
20  (familial adj3 apolipoprotein).ti,ab.
21  heterozygous fh.ti,ab.
22  homozygous fh.ti,ab.
23  lipid disorder$.ti,ab.
24  ((high or elevated or abnormal or aberr$) adj3 (cholesterol or lipid$ or LDL$)).ti,ab.
25  ((low or decrease$ or deficient$ or abnormal or aberr$) adj3 HDL$).ti,ab.
26  or/1-25
27  hypolipidemic agents/ or bezafibrate/ or butoxamine/ or clofenate/ or clofibrate/ or clofibrate acid/ or colesterol/ or fenofibrate/ or gemfibrozil/ or halofenate/ or meglutol/ or nafenopin/ or niacin/ or nisertol/ or pyridinolcarbamate/ or simvastatin/ or triparanol/
28  anticholesteremic agents/ or azacosterol/ or chitosan/ or cholestyramine resin/ or clofibrate/ or clofibrate acid/ or lovastatin/ or meglutol/ or pravastatin/ or probucol/ or simvastatin/ or "trans-1,4-bis(2-chlorobenzenaminomethyl)cyclohexane dihydrochloride"/
29  hydroxymethylglutaryl-coa reductase inhibitors/ or lovastatin/
30  3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor$.ti,ab.
31  hydroxymethylglutaryl coa reductase inhibitor$.ti,ab.
32  hydroxymethylglutaryl coa inhibitor$.ti,ab.
33  hydroxymethylglutaryl coenzyme a reductase,ti,ab.
34  hydroxymethylglutaryl coenzyme a inhibitor$.ti,ab.
35  hmg coa reductase inhibitor$.ti,ab.
36  hmg coa inhibitor$.ti,ab.
37  atorvastatin.ti,ab.
38  fluvastatin.ti,ab.
39  lovastatin.ti,ab.
40  pitavastatin.ti,ab.
41  pravastatin.ti,ab.
42  rosuvastatin.ti,ab.
43  simvastatin.ti,ab.
44  hypolipidemic$.ti,ab.
45  anticholesteremic$.ti,ab.
46  antilipidemic.ti,ab.
47  statin$.ti,ab.
48  lipid lower$.ti,ab.
(treat$ or therap$ or medicat$).ti.
or/27-49
diet/
diet, carbohydrate-restricted/
diet, fat-restricted/
diet, mediterranean/
diet, protein-restricted/
diet, reducing/
diet, vegetarian/
caloric restriction/
portion size/
Food habits/
Diet Therapy/
Soybean Proteins/
Fatty Acids, Omega-3/
Phytosterols/
Dietary Fiber/
Dietary Protein/
Dietary Carbohydrates/
Dietary Fats/
diet$.ti,ab.
((reduce$ or reduction$ or manipulat$ or restrict$) adj3 (fat$ or carbohydrate$ or cholesterol)).ti,ab.
low fat.ti,ab.
lowfat.ti,ab.
fiber.ti,ab.
omega 3 fatty acid$.ti,ab.
n 3 polyunsaturated fatty acid$.ti,ab.
n 3 fatty acid$.ti,ab.
n 3 pufa.ti,ab.
soy$ protein$.ti,ab.
plant stanol$.ti,ab.
esters.ti,ab.
51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65
or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80
Exercise/
Exercise therapy/
Motor activity/
Physical fitness/
Plyometric Exercise/
Physical Conditioning, Human/
Running/
Jogging/
Swimming/
Walking/
Resistance training/

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(exercise or exercising or exercises).ti,ab.
physical fitness.ti,ab.
physical conditioning.ti,ab.
(running or jog$ or swim$ or walk$).ti,ab.
(lifestyle$ or life style$).ti,ab.
82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or 90 or 91 or 92 or 93 or 94 or 95 or 96 or 97
26 and (50 or 81 or 98)
Hyperlipidemias/dh, dt, pc, th [Diet Therapy, Drug Therapy, Prevention & Control, Therapy]
Dyslipidemias/dh, dt, pc, th
Hypercholesterolemia/dh, dt, pc, th
Lipid Metabolism Disorders/dh, dt, pc, th
Hyperlipoproteinemias/dh, dt, pc, th
Hypertriglyceridemia/dh, dt, pc, th
Hyperlipoproteinemia Type II/dh, dt, pc, th
Hyperlipidemia, Familial Combined/dh, dt, pc, th
Hypobetalipoproteinemias/dh, dt, pc, th
Abetalipoproteinemia/dh, dt, pc, th
99 or 100 or 101 or 102 or 103 or 104 or 105 or 106 or 107 or 108 or 109
adolescent/ or child/ or young adult/
110 110 and 111
(child$ or teen or teens or teenager$ or adolescence$ or youth or youths or young people or pediatric$ or paediatric$).ti,ab.
113 110 and 113
limit 114 to ("in data review" or in process or "pubmed not medline")
116 112 or 115
clinical trials as topic/ or controlled clinical trials as topic/ or randomized controlled trials as topic/ or meta-analysis as topic/
118 (clinical trial or controlled clinical trial or meta-analysis or randomized controlled trial).pt.
119 Random$.ti,ab.
control groups/ or double-blind method/ or single-blind method/
121 clinical trial$.ti,ab.
controlled trial$.ti,ab.
meta analy$.ti,ab.
124 117 or 118 or 119 or 120 or 121 or 122 or 123
125 116 and 124
limit 125 to (english language and yr="2007 -Current")
127 remove duplicates from 126

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<table>
<thead>
<tr>
<th>Search</th>
<th>Query</th>
</tr>
</thead>
<tbody>
<tr>
<td>#11</td>
<td>Search #10 AND publisher[sb] Filters: Publication date from 2007/01/01 to 2015/06/02; English</td>
</tr>
<tr>
<td>#10</td>
<td>Search #8 AND #9</td>
</tr>
<tr>
<td>#8</td>
<td>Search #1 or #2 or #3 or #4 or #5 or #6 or #7</td>
</tr>
<tr>
<td>#7</td>
<td>Search (fasting[tiab] or non fasting[tiab] OR nonfasting[tiab]) AND (lipid*[tiab] OR lipoprotein*[tiab] OR cholesterol[tiab])</td>
</tr>
<tr>
<td>#4</td>
<td>Search lipid disorder*[tiab] OR lipid dysfunction*[tiab]</td>
</tr>
<tr>
<td>#3</td>
<td>Search familial[tiab] AND apolipoprotein[tiab]</td>
</tr>
</tbody>
</table>
**eTable. Quality Assessment Criteria**

<table>
<thead>
<tr>
<th>Study Design</th>
<th>Adapted Quality Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Randomized controlled trials, adapted from the USPSTF methods¹</td>
<td>• Valid random assignment?</td>
</tr>
<tr>
<td></td>
<td>• Was allocation concealed?</td>
</tr>
<tr>
<td></td>
<td>• Was eligibility criteria specified?</td>
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<tr>
<td></td>
<td>• Were groups similar at baseline?</td>
</tr>
<tr>
<td></td>
<td>• Were measurements equal, valid, and reliable?</td>
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<tr>
<td></td>
<td>• Was there intervention fidelity?</td>
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<tr>
<td></td>
<td>• Was there adequate adherence to the intervention?</td>
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<tr>
<td></td>
<td>• Were outcome assessors blinded?</td>
</tr>
<tr>
<td></td>
<td>• Was there acceptable followup?</td>
</tr>
<tr>
<td></td>
<td>• Were the statistical methods acceptable?</td>
</tr>
<tr>
<td></td>
<td>• Was the handling of missing data appropriate?</td>
</tr>
<tr>
<td></td>
<td>• Was there evidence of selective reporting of outcomes?</td>
</tr>
<tr>
<td></td>
<td>• Was the device calibration and/or maintenance reported?</td>
</tr>
</tbody>
</table>

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<thead>
<tr>
<th>Observational studies (e.g., prospective cohort studies), adapted from the Newcastle-Ottawa Scale (NOS)²</th>
<th>• Was the cohort systematically selected to avoid bias?</th>
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<tbody>
<tr>
<td></td>
<td>• Was eligibility criteria specified?</td>
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<td>• Were groups similar at baseline?</td>
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<td>• Was the outcome of interest not present at baseline?</td>
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<td>• Were measurements equal, valid, and reliable?</td>
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<td>• Were outcome assessors blinded?</td>
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<td>• Was there acceptable followup?</td>
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<td>• Were the statistical methods acceptable?</td>
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<td>• Was the handling of missing data appropriate?</td>
</tr>
</tbody>
</table>

Abbreviations: USPSTF = U.S. Preventive Services Task Force

Good quality studies generally meet all quality criteria. Fair quality studies do not meet all the criteria but do not have critical limitations that could invalidate study findings. Poor quality studies have a single fatal flaw or multiple important limitations that could invalidate study findings. Critical appraisal of studies using a priori quality criteria are conducted independently by at least two reviewers. Disagreements in final quality assessment are resolved by consensus, and, if needed, consultation with a third independent reviewer.

References


KQ indicates key question.
aIncludes 122 articles that were reviewed for all KQs.
bDetails about reasons for exclusion are as follows. Relevance: study aim not relevant. Design: study did not use an included design. Setting: study was not conducted in a setting or country relevant to US primary care. Population: study was not conducted in a population of children and adolescents aged 0 to 20 years. For KQs 1 to 4, studies were excluded if they involved children and adolescents with known dyslipidemia, and for KQs 5 to 8, studies were excluded if they involved children and adolescents with familial hypercholesterolemia. Outcomes: study did not have relevant outcomes or had incomplete outcomes. Intervention: study used an excluded intervention approach. Quality: study did not meet criteria for fair or good quality (ie, it was poor quality). Language: study was published in a non-English language. Screening: study used an excluded screening approach. Overlapping population: study population overlapped with 1 or more studies included for this KQ.
cNumber of articles that were not included in the prior review: KQ1, 0; KQ2, 0; KQ3, 7; KQ4, 0; KQ5, 0; KQ6, 3; KQ7, 3; KQ8, 1.