

Appendix B

Key clinical questions and searches

Key clinical questions

Clinical Question	Population	Intervention(s)	Comparator(s)	Outcome(s)
<p>1. In adults and children, what is the effectiveness of the following tests to diagnose FH</p> <ul style="list-style-type: none"> • biochemical assays? • clinical signs and symptoms? • DNA testing? • combinations and/or sequences of above? 	<ul style="list-style-type: none"> • Adults with suspected FH • Children with suspected FH. 	<ul style="list-style-type: none"> • Biochemical assays i.e. measurement of cholesterol and LDL levels • Clinical signs e.g. tendon xanthoma • Tendon ultrasound as an 'add on' to scoring criteria • Scoring criteria including, Simon Broome; Danish study; MedPed • DNA testing • Combination and/or sequence testing • Family history 	<ul style="list-style-type: none"> • Biochemical assays i.e. measurement of cholesterol and LDL levels • Clinical signs e.g. tendon xanthoma • Tendon ultrasound as an 'add on' to scoring criteria • Scoring criteria including, Simon Broome; Danish study; MedPed • DNA testing • Combination and/or sequence testing • Family history) 	<ol style="list-style-type: none"> 1. Number of individuals (adults and children) identified in proportion to those assessed (diagnostic yield) 2. Measures of diagnostic performance (sensitivity, specificity, PPV, NPV) 3. Cost/QALY
<p>2. What is the cardiovascular risk of people with suspected FH: (i) who have a confirmed DNA mutation or (ii) who do not have a confirmed DNA mutation?</p>	<p>Longitudinal studies of individuals with suspected FH who undergo DNA testing</p>	<p>NA (not RCT)</p>	<p>NA (not RCT)</p>	<p>CV mortality, MI, reinfarction, angina, revasc, TIA, stroke</p>
<p>3. What is effectiveness (defined as case identification and cost-effectiveness secondarily) of the following strategies for identifying</p>	<p>Adhoc populations within these groups</p>	<p>Case identification methods</p> <ol style="list-style-type: none"> a. Cascade screening b. GP note searching using electronic data- 	<p>Usual care</p>	<ol style="list-style-type: none"> 1. Number of individuals identified in proportion to those assessed (diagnostic yield) and 2. Cost/QALY

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Clinical Question	Population	Intervention(s)	Comparator(s)	Outcome(s)
<p>people with FH: GP note searching using electronic data bases identifying patients with (i) history of early MI (<60 years) and Tcholesterol (TC) >7.5mmol/L (ii) family history of ischemic heart disease and hypercholesterolemia or; Secondary care registers (i) within coronary care units through identifying patients with history of early MI (<60 years) and Tcholesterol (TC) >7.5mmol/L or (ii) identification of patients through pathology registers with age <60 years and TC>9 mmol/L and LDL>5.5mmol/L or; Cascade screening</p>		<p>base searches c. Identification of patients through secondary care registers d. . Identification of patients through pathology registers e. Family history of CHD or hypercholesterolemia and raised LDL cholesterol</p> <p>Cholesterol levels and age ranges should be left open in search strategy</p>		
<p>4. Combined with question 1</p>	See question 1	See question 1	See question 1	See question 1
<p>5. What is effectiveness of DNA testing for FH mutations among relatives of people with identified mutations for FH?</p>	Relatives of FH probands	DNA testing in relatives of probands	FH diagnosed by clinical criteria (stigmata) and lipid levels	<ol style="list-style-type: none"> 1. Number of individuals identified in proportion to those assessed (diagnostic yield) 2. Measures of diagnostic performance (i.e sensitivity, specificity, PPV, NPV) 3. Cost/QALY
<p>6. What information and support is required for: a-adults b-children and young people being considered for diagnosis of FH?</p>	Individuals with FH (adults and children)	<ul style="list-style-type: none"> • Genetic transmission • Implications for being considered for diagnosis of FH • Information and support • Genetic counselling (if nothing specific for FH then broaden to general genetic 		<ul style="list-style-type: none"> • Better understanding of the condition (patient satisfaction) • Response rate • Adherence • Comprehension/understanding • Anxiety • Recall • Insurance • Sociological effects • Socioeconomic

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		counselling) • Patient education • Material; leaflet, • Patient support groups • Family contacts		
7. What is the effectiveness of aggressive (maximal) cholesterol lowering in people with FH using pharmacological therapy?	Individuals* with i-FH and CVD or ii-FH plus no-CVD *(adults and children either homo or hetero FH) No-stratification re: ethnic groups	Aggressive therapy Active comparator trials any combinations	<ul style="list-style-type: none"> • Conservative therapy • Active comparator trials • Any combinations 	<ul style="list-style-type: none"> • As per ground rules • Mortality and morbidity (likely to be lacking for many drugs) Total mortality, CV mortality, MI, reinfarction, angina, revascularisation, TIA, stroke • Total cholesterol or LDL lowering efficacy (mmol/L or mg/dL) - primary outcome of therapy • Supported by other surrogate endpoints where possible: • QCA (quantitative coronary angiography) • Carotid IMT • Other biochemical markers – Lp(a), ApoB • With extrapolation from Post MI research – Total mortality & cardiovascular events to inform overall safety where either outcome is absent in studies of people with FH • With extrapolation from IVUS (intra-vascular ultrasound)
8. What is the effectiveness in improving outcome in individuals with FH of the following	Individuals* with i-FH and CVD or ii-FH plus no-CVD	<ul style="list-style-type: none"> • Monotherapy: • Statins • Resins • Niacin 	Placebo	As per ground rules (detailed in outcome section in question 7)

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monotherapy i.e.: <ul style="list-style-type: none"> • Statins versus placebo • Resins versus placebo • Niacin versus placebo • Fibrates versus placebo • Fish oils (omega 3 fatty oils) versus placebo • Ezetimibe versus placebo in improving outcome in individuals with FH?	*(adults and children either homo or hetero FH) No-stratification re: ethnic groups	<ul style="list-style-type: none"> • Fibrates • Fish oils (omega 3 fatty oils) • Ezetimibe 		
9. What is the effectiveness of the following adjunctive pharmacotherapy with statins in individuals with FH: <ul style="list-style-type: none"> • Statins and resins • Statins and niacin • Statins and fibrates • Statins and fish oils • Statins and resins with nicotinic acid • Statins and ezetimibe? 	Individuals* with i-FH and CVD or ii-FH plus no-CVD *(adults and children either homo or hetero FH) No-stratification re: ethnic groups	<ul style="list-style-type: none"> • Statins and resins • Statins and niacin • Statins and fibrates • Statins and fish oils • Statins and resins with nicotinic acid 	Statins alone	As per ground rules (detailed in outcome section in question 7)
10. What is the clinical and cost effectiveness of the following interventions to reduce LDL cholesterol and improve outcome in people with either heterozygous FH or homozygous FH: <ul style="list-style-type: none"> • Apheresis alone versus no intervention/usual care • Apheresis and drug therapy versus drug therapy alone • Plasmapheresis & drug therapy versus drug therapy alone • Ileal bypass versus no intervention (heterozygote) 	Individuals with FH	1. Apheresis and drug therapy 2. Apheresis versus plasmapheresis 3. Plasmapheresis & drug therapy 4. Ileal bypass versus (homozygotes only)	1. No intervention/usual care 2. Drug therapy alone 3. Drug therapy alone 4. No intervention (homo-zygote, hetero-zygote) 5. No intervention (homo-zygotes only)	Total mortality, CV mortality, MI, reinfarction, angina, revasc, TIA, stroke, TC/LDL

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Clinical Question	Population	Intervention(s)	Comparator(s)	Outcome(s)
<ul style="list-style-type: none"> Apheresis versus plasmapheresis 				
<p>11. What are the appropriate indications for i-combined heart and liver transplantation or ii- liver transplantation alone in homozygous FH?</p>	Individuals with homozygous FH	Timing of liver and heart transplantations Early transplantation (defining what early is)	Delayed transplantation	Total mortality, CV mortality, MI, reinfarction, angina, revasc, TIA, stroke TC/LDL,
<p>12. What is the effectiveness of investigations to assess the degree of atherosclerosis to improve outcome in people with heterozygous FH? Interventions to include i) exercise ECG ii) Carotid IMT iii) Coronary calcium iv) cardiac catheterisation v) echocardiography vi) MRI vii) electron beam CT viii) coronary angiography ix) MR angiography x) carotid Doppler xii) Doppler ultrasound xiii) IVUS (intra-vascular ultrasound) xiii) thallium scan xiiii) stress echocardiography</p>	Individuals with FH	Methods of assessment	Care/no intervention	Total mortality, CV mortality, MI, reinfarction, angina, revasc, TIA, stroke, ST elevation, stable and unstable angina
<p>13. What is the effectiveness of dietary interventions to improve outcome in: a-adults b-children and young people with FH*? *heterozygous or homozygous FH</p>	Children and adolescents with FH	Dietary Advice, leaflets, dietician care, Stanols/Sterols, Soy, portfolio diet	No diet	Total mortality, CV mortality, MI, reinfarction, angina, revasc, TIA, stroke, TC/LDL, % weight loss (in childhood)
<p>14. What information/counselling should be provided to girls/women of child bearing potential with FH with respect to hormonal and other contraceptive methods?</p>	Women of childbearing age, with FH; or on statins; or women who are at high CVD	Hormonal contraceptive choice and other contraceptive choices	N/A	DVT, MI, thrombosis,

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Clinical Question	Population	Intervention(s)	Comparator(s)	Outcome(s)
	risk			
15. What information or care should be provided to: a- pregnant women or women considering pregnancy with FH with respect to: i) lipid modifying treatment use or ii) FH related complications around pregnancy/labour/delivery? b-lactating women with FH with respect to: i) lipid modifying treatment use?	Pregnant /lactating women	(1) Statin, nicotinic acid, fibrates and resins use	NA	For a (i) Teratogenesis (ii) Foetal anomalies, (iii) Total mortality, CV mortality, MI, reinfarction, angina, revasc, TIA, stroke or TC/LDL For b (i) Lipid levels in pregnancy and lactation
16. What are the key components of assessment and review for: a-adults b-children and young people with homozygous or heterozygous FH including the information and support required for individuals (adults and children) with FH regarding (i) diet, (ii) exercise and/or regular physical activity (iii) smoking cessation?	Individuals (adults and children) with homozygous or heterozygous FH	a) Components of ongoing assessment and review b) Information and support regarding diet, exercise and/or physical activity, smoking c) Information content and support for individuals (adults and children) and carers to be identified in literature search.		Total mortality, CV mortality, MI, reinfarction, angina, revasc, TIA, stroke, TC/LDL
17. What is the effectiveness of dietary interventions to improve outcome in the general population?	Adults and children	Diet (see above)	No diet	LDL/TC or other CV outcomes (as above)

Search strategies used in this guideline

The strategies were developed for use on the Ovid web interface and adapted for conducting the update searches on the Dialog Datastar interface. The following databases were searched: Cochrane Database of Systematic Reviews (CDSR), Database of Abstracts of Reviews of Effects (DARE) Health Technology Assessment Database (HTA), Medline & Medline in Process, Embase, CENTRAL, Cinahl, Science Citation Index. Where appropriate to the question PsychINFO was also searched.

The Economic literature was searched using an economic and quality of life filter developed by SchARR for Medline and Embase and then adapted for use on the ISI citation indexes via the Web of Knowledge interface. The following was searched: NHS Economic Evaluations Database (NHSEED), Medline, Embase, Science Citation Index and Social Science Citation Index.

The strategies shown are those for Medline and Embase using the Ovid interface unless otherwise stated. Copies of all the search strategies are available on request from the National Collaborating Centre for Primary Care.

It should be noted that during the development period of this guideline the MeSH heading on Medline changed from hypercholesterolemia,familial/ to Hyperlipoproteinemia Type II/

Initial searches

Questions 1,& 5 Diagnostic tests

Embase 1980-2007 week 1
Searched 09/01/07
Update search 09/01/07-04/12/07

1. Familial Hyperlipemia/
2. Familial Hypercholesterolemia/
3. familial hyperlipid?emia.ti,ab.
4. familial hypercholesterol?emia.ti,ab.
5. essential hypercholesterol?emia.ti,ab.

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6. essential hyperlipid?emia.ti,ab.
7. (heterozygous fh or homozygous fh).ti,ab.
8. monogenic hyperlipid?emia.ti,ab.
9. familial apolipoprotein c-II deficiency.ti,ab.
10. familial defective apolipoprotein b.ti,ab.
11. LDLR.ti,ab.
12. Idl receptor.ti,ab.
13. low density lipoprotein receptor.ti,ab.
14. Low Density Lipoprotein Receptor/
15. or/1-14
16. "sensitivity and specificity"/
17. (sensitivity or specificity or accuracy).ti,ab.
18. (predictive adj3 value\$).ti,ab.
19. (roc adj curve\$).ti,ab.
20. roc curve/
21. (false adj (positive\$ or negativ\$)).ti,ab.
22. Observer Variation/
23. (observer adj variation\$).ti,ab.
24. (likelihood adj3 ratio\$).ti,ab.
25. Differential Diagnosis/
26. diagnostic test/
27. diagnostic accuracy/
28. Diagnostic Error/
29. diagnos\$.ti.
30. (biochemical adj (marker\$ or screen\$ or test\$ or assay\$)).ti,ab.
31. (cholesterol adj2 (test\$ or screen\$ or measur\$ or assess\$ or analys\$ or analyz\$)).ti,ab.
32. (LDL-Cholesterol adj2 (test\$ or screen\$ or measur\$ or assess\$ or analys\$ or analyz\$)).ti,ab.
33. (total-C adj2 (test\$ or screen\$ or measur\$ or assess\$ or analys\$ or analyz\$)).ti,ab.
34. (LDL-C adj2 (test\$ or screen\$ or measur\$ or assess\$ or analys\$ or analyz\$)).ti,ab.
35. (VLDL-C adj2 (test\$ or screen\$ or measur\$ or assess\$ or analys\$ or analyz\$)).ti,ab.
36. (lipoprotein adj2 (test\$ or screen\$ or measur\$ or assess\$ or analys\$ or analyz\$)).ti,ab.
37. (serum adj2 (test\$ or screen\$ or measur\$ or assess\$ or analys\$ or analyz\$)).ti,ab.
38. (plasma adj2 (test\$ or screen\$ or measur\$ or assess\$ or analys\$ or analyz\$)).ti,ab.
39. (lipid\$ adj2 (test\$ or screen\$ or measur\$ or assess\$ or analys\$ or analyz\$)).ti,ab.
40. ((apolipoprotein B or apoprotein B) adj2 (test\$ or screen\$ or measur\$ or assess\$ or analys\$ or analyz\$)).ti,ab.
41. ((apoB or apo B) adj2 (test\$ or screen\$ or measur\$ or assess\$ or analys\$ or analyz\$)).ti,ab.
42. Xanthomatosis/
43. (xanthomatosis or xanthomatous or xanthelasmas or xanthelasmata).ti,ab.
44. (tendon xanthoma\$ or achilles tendon thickness).ti,ab.
45. physical examination/

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46. (physical adj (examin\$ or sign\$ or presentation or manifestation\$)).ti,ab.
47. (clinical adj (examin\$ or sign\$ or presentation or manifestation\$ or diagnos\$)).ti,ab.
48. (achilles tendon adj (utrasonograph\$ or sonograph\$ or ultrasound)).ti,ab.
49. (AT adj (utrasonograph\$ or sonograph\$ or ultrasound)).ti,ab.
50. (Medped or med ped).ti,ab.
51. make early diagnosis prevent early death.ti,ab.
52. dutch lipid clinic network.ti,ab.
53. simon broome.ti,ab.
54. (diagnos\$ adj (criteria or tool\$ or score or scoring or protocol\$)).ti,ab.
55. nucleotide sequence/
56. (DNA adj2 (analys\$ or analyz\$)).ti,ab.
57. (DNA sequencing or sequence variation).ti,ab.
58. Genetic Screening/
59. ((genetic or gene) adj screen\$).ti,ab.
60. ((genetic or gene or DNA) adj test\$).ti,ab.
61. ((genetic or gene) adj (analys\$ or analyz\$)).ti,ab.
62. ((dna or genetic) adj diagnos\$).ti,ab.
63. Diagnostic Procedure/
64. (molecular adj (test\$ or diagnos\$ or screen\$)).ti,ab.
65. Anamnesis/
66. ((famil\$ or parent\$ or grandparent\$ or clinical) adj2 histor\$).ti,ab.
67. (family backound\$ or parent\$ cases or anamnesis).ti,ab.
68. or/16-67
69. 15 and 68
70. animals/
71. Nonhuman/
72. 70 or 71
73. humans/
74. 72 not (72 and 73)
75. 69 not 74
76. (conference paper or editorial or erratum or letter or note or proceeding).pt.
77. 75 not 76

Medline 1950-2006 Dec week 4

Searched 09/01/07

Update search 09/01/07-04/12/07

1. familial hyperlipid?emia.ti,ab.
2. Hypercholesterolemia, Familial/
3. familial hypercholesterol?emia.ti,ab.
4. essential hypercholesterol?emia.ti,ab.
5. heterozygous fh.ti,ab.
6. homozygous fh.ti,ab.
7. monogenic hyperlipid?emia.ti,ab.
8. familial apolipoprotein c-II defici\$.ti,ab.

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9. familial defective apolipoprotein B.ti,ab.
10. LDLR.ti,ab.
11. LDL receptor.ti,ab.
12. low density lipoprotein receptor.ti,ab.
13. or/1-12
14. exp "Sensitivity and Specificity"/
15. (sensitivity or specificity or accuracy).ti,ab.
16. (predictive adj3 value\$).ti,ab.
17. (roc adj curve\$).ti,ab.
18. (false adj (positiv\$ or negativ\$)).ti,ab.
19. (observer adj variation\$).ti,ab.
20. (likelihood adj3 ratio\$).ti,ab.
21. Likelihood Functions/
22. Diagnosis, Differential/
23. exp Diagnostic Errors/
24. Biological Markers/bl [Blood]
25. diagnos\$.ti.
26. (biochemical adj (marker\$ or screen\$ or test\$ or assay\$)).ti,ab.
27. (cholesterol adj2 (test\$ or screen\$ or measur\$ or assess\$ or analys\$ or analyz\$)).ti,ab.
28. (total-C adj2 (test\$ or screen\$ or measur\$ or assess\$ or analys\$ or analyz\$)).ti,ab.
29. (LDL-cholesterol adj2 (test\$ or screen\$ or measur\$ or assess\$ or analys\$ or analyz\$)).ti,ab.
30. (LDL-C adj2 (test\$ or screen\$ or measur\$ or assess\$ or analys\$ or analyz\$)).ti,ab.
31. (VLDL-C adj2 (test\$ or screen\$ or measur\$ or assess\$ or analys\$ or analyz\$)).ti,ab.
32. (lipoprotein adj2 (test\$ or screen\$ or measur\$ or assess\$ or analys\$ or analyz\$)).ti,ab.
33. (serum adj2 (test\$ or screen\$ or measur\$ or assess\$ or analys\$ or analyz\$)).ti,ab.
34. (plasma adj2 (test\$ or screen\$ or measur\$ or assess\$ or analys\$ or analyz\$)).ti,ab.
35. (lipid\$ adj2 (test\$ or screen\$ or measur\$ or assess\$ or analys\$ or analyz\$)).ti,ab.
36. ((apoB or apo B) adj2 (test\$ or screen\$ or measur\$ or assess\$ or analys\$ or analyz\$)).ti,ab.
37. ((apolipoprotein B or apoprotein B) adj2 (test\$ or screen\$ or measur\$ or assess\$ or analys\$ or analyz\$)).ti,ab.
38. Xanthomatosis/
39. (xanthomatosis or xanthomatous or xanthelasmas or xanthelasmata).ti,ab.
40. (tendon xanthoma\$ or achilles tendon thickness).ti,ab.
41. Physical Examination/
42. (physical adj (examin\$ or sign\$ or presentation or manifestation\$)).ti,ab.
43. (clinical adj (examin\$ or sign\$ or presentation or manifestation\$ or diagnos\$)).ti,ab.
44. Achilles Tendon/us [Ultrasonography]
45. (achilles tendon adj (ultrasonograph\$ or sonograph\$ or ultrasound)).ti,ab.
46. (AT adj (ultrasonograph\$ or sonograph\$ or ultrasound)).ti,ab.
47. medped.ti,ab.
48. med ped.ti,ab.

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49. make early diagnosis prevent early death.ti,ab.
50. dutch lipid clinic network.ti,ab.
51. simon broome.ti,ab.
52. (diagnos\$ adj (criteria or tool\$ or score or scoring or protocol\$)).ti,ab.
53. DNA Mutational Analysis/
54. (DNA adj2 (analys\$ or analyz\$)).ti,ab.
55. (DNA sequencing or sequence variation).ti,ab.
56. Genetic Screening/
57. ((genetic or gene) adj screen\$).ti,ab.
58. ((genetic or gene or dna) adj test\$).ti,ab.
59. ((genetic or gene) adj (analys\$ or analyz\$)).ti,ab.
60. ((dna or genetic) adj diagnos\$).ti,ab.
61. Molecular Diagnostic Techniques/
62. (molecular adj (test\$ or diagnos\$ or screen\$)).ti,ab.
63. Medical History Taking/
64. ((famil\$ or parent\$ or grandparent\$ or clinical) adj2 histor\$).ti,ab.
65. (family background\$ or parent\$ cases or anamnesis).ti,ab.
66. or/14-65
67. 13 and 66
68. (editorial or comment or letter).pt.
69. 67 not 68
70. animals/
71. humans/
72. 70 not (70 and 71)
73. 69 not 72

Question 2 Cardiovascular risk of people suspected with FH

Embase 1980-2007 week 5
Searched 08/02/07
Update search 08/02/07-04/12/07

1. Familial Hyperlipemia/
2. Familial Hypercholesterolemia/
3. familial hyperlipid?emia.ti,ab.
4. familial hypercholesterol?emia.ti,ab.
5. essential hypercholesterol?emia.ti,ab.
6. essential hyperlipid?emia.ti,ab.
7. (heterozygous fh or homozygous fh).ti,ab.
8. monogenic hyperlipid?emia.ti,ab.
9. familial apolipoprotein c-II defici\$.ti,ab.
10. familial defective apolipoprotein b.ti,ab.
11. LDLR.ti,ab.
12. ldl receptor.ti,ab.
13. low density lipoprotein receptor.ti,ab.

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14. Low Density Lipoprotein Receptor/
15. or/1-14
16. risk factor/
17. RISK ASSESSMENT/
18. cardiovascular risk/
19. CORONARY RISK/
20. Statistical Model/
21. exp regression analysis/
22. "analysis of variance"/
23. exp multivariate analysis/
24. (risk\$ adj2 (factor\$ or assess\$ or status or profile\$ or analys\$ or variable or marker\$)).ti,ab.
25. ((increase\$ or high\$ or mortality or overall or relative or absolute) adj2 risk\$).ti,ab.
26. confounding.ti,ab.
27. (regression adj2 (analys\$ or model\$)).ti,ab.
28. ((multivariable or multivariate or multi varia\$) adj2 analys\$).ti,ab.
29. (risk adj2 stratification adj2 criteria).ti,ab.
30. or/16-29
31. 15 and 30
32. exp Cardiovascular Disease/
33. (cvd or coronary or heart or cardiovasc\$ or vascular\$ or chd or cad).ti,ab.
34. 32 or 33
35. 31 and 34
36. ((cvd or coronary or heart or cardiovasc\$ or vascular\$ or chd or cad) adj2 risk\$).ti,ab.
37. 36 and 15
38. 35 or 37
39. animal/
40. Nonhuman/
41. 39 or 40
42. Human/
43. 41 not (41 and 42)
44. 38 not 43
45. (conference paper or editorial or letter or note or proceeding).pt.
46. 44 not 45

Medline 1950-2007 Jan week 5

Searched 08/02/07

Update search 08/02/07-04/12/07

1. familial hyperlipid?emia.ti,ab.
2. Hypercholesterolemia, Familial/
3. familial hypercholesterol?emia.ti,ab.
4. essential hypercholesterol?emia.ti,ab.
5. heterozygous fh.ti,ab.

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6. homozygous fh.ti,ab.
7. monogenic hyperlipid?emia.ti,ab.
8. familial apolipoprotein c-II defici\$.ti,ab.
9. familial defective apolipoprotein B.ti,ab.
10. LDLR.ti,ab.
11. LDL receptor.ti,ab.
12. low density lipoprotein receptor.ti,ab.
13. or/1-12
14. risk factors/
15. Risk Assessment/
16. logistic models/
17. confounding factors/
18. survival analysis/
19. exp regression analysis/
20. exp "analysis of variance"/
21. exp multivariate analysis/
22. (risk\$ adj2 (factor\$ or assess\$ or status or profile\$ or analys\$ or variable or marker\$)).ti,ab.
23. ((increas\$ or high\$ or mortality or overall or relative or absolute) adj2 risk\$).ti,ab.
24. confounding.ti,ab.
25. (regression adj2 (analys\$ or model\$)).ti,ab.
26. ((multivariable or multivariate or multi varia\$) adj2 analys\$).ti,ab.
27. (risk adj2 stratification adj2 criteria).ti,ab.
28. or/14-27
29. 13 and 28
30. exp Cardiovascular Diseases/
31. (cvd or coronary or heart or cardiovasc\$ or vascular\$ or chd or cad).ti,ab.
32. 30 or 31
33. 29 and 32
34. ((cvd or coronary or heart or cardiovasc\$ or vascular\$ or chd or cad) adj2 risk\$).ti,ab.
35. 13 and 34
36. 33 or 35
37. animal/
38. human/
39. 37 not (37 and 38)
40. 36 not 39
41. (letter or comment or editorial).pt.
42. 40 not 41

Question 3 Case identification of people with FH

Embase 1980-2007 week 15

Searched 18/04/07

Updated search 18/04/07-04/12/07

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1. Familial Hyperlipemia/
2. Familial Hypercholesterolemia/
3. familial hyperlipid?emia.ti,ab.
4. familial hypercholesterol?emia.ti,ab.
5. essential hypercholesterol?emia.ti,ab.
6. essential hyperlipid?emia.ti,ab.
7. (heterozygous fh or homozygous fh).ti,ab.
8. monogenic hyperlipid?emia.ti,ab.
9. familial apolipoprotein c-II defici\$.ti,ab.
10. familial defective apolipoprotein b.ti,ab.
11. LDLR.ti,ab.
12. ldl receptor.ti,ab.
13. low density lipoprotein receptor.ti,ab.
14. Low Density Lipoprotein Receptor/
15. or/1-14
16. (cascade adj (screen\$ or test\$)).ti,ab.
17. ((famil\$ or selectiv\$ or proband\$ or risk factor\$) adj2 screen\$).ti,ab.
18. Case Finding/
19. (case\$1 adj (identif\$ or finding)).ti,ab.
20. ((identif\$ or finding) adj patient\$1).ti,ab.
21. ((gp or general practitioner\$ or doctor\$ or physician\$ or primary care or secondary care or clinic\$1) adj2 (note\$1 or record\$1)).ti,ab.
22. medical documentation/ or medical record/
23. ((patient\$ or medical or computer\$) adj2 (note\$1 or record\$1)).ti,ab.
24. data base/
25. (database\$ or GPRD).ti,ab.
26. register/
27. (registries or registers).ti,ab.
28. medical audit/
29. audit.ti,ab.
30. outreach.ti,ab.
31. family history/
32. ((famil\$ or parent\$ or grandparent\$ or relative\$ or relations) adj (histor\$ or case\$ or tracing or trace\$)).ti,ab.
33. (identif\$ adj (relations or relative\$)).ti,ab.
34. or/16-33
35. 15 and 34
36. animals/
37. Nonhuman/
38. 36 or 37
39. humans/
40. 38 not (38 and 39)
41. 35 not 40
42. (conference paper or editorial or erratum or letter or note or proceeding).pt.

Familial hypercholesterolaemia: FINAL August 2008

Appendix B: Key clinical questions and searches

Familial hypercholesterolaemia: Final August 2008

43. 41 not 42

Medline 1950-2007 April week 1

Searched 18/04/07

Update search 18/04/07-04/12/07

1. familial hyperlipid?emia.ti,ab.
2. Hypercholesterolemia, Familial/
3. familial hypercholesterol?emia.ti,ab.
4. essential hypercholesterol?emia.ti,ab.
5. heterozygous fh.ti,ab.
6. homozygous fh.ti,ab.
7. monogenic hyperlipid?emia.ti,ab.
8. familial apolipoprotein c-II defici\$.ti,ab.
9. familial defective apolipoprotein B.ti,ab.
10. LDLR.ti,ab.
11. LDL receptor.ti,ab.
12. low density lipoprotein receptor.ti,ab.
13. or/1-12
14. (cascade adj (screen\$ or test\$)).ti,ab.
15. ((famil\$ or selectiv\$ or proband\$ or risk factor\$) adj2 screen\$).ti,ab.
16. (case\$1 adj (identif\$ or finding)).ti,ab.
17. ((identif\$ or finding) adj patient\$1).ti,ab.
18. ((gp or general practitioner\$ or doctor\$ or physician\$ or primary care or secondary care or clinic\$1) adj2 (note\$1 or record\$1)).ti,ab.
19. ((patient\$ or medical or computer\$) adj2 (note\$1 or record\$1)).ti,ab.
20. databases/
21. (database\$ or GPRD).ti,ab.
22. exp Medical Records/
23. exp Registries/
24. (registries or registers).ti,ab.
25. exp Medical Audit/
26. audit.ti,ab.
27. outreach.ti,ab.
28. ((famil\$ or parent\$ or grandparent\$ or relative\$ or relations) adj (histor\$ or case\$ or tracing or trace\$)).ti,ab.
29. (identif\$ adj (relations or relative\$)).ti,ab.
30. Medical History Taking/
31. or/14-30
32. 13 and 31
33. Animals/
34. humans/
35. 33 not (33 and 34)
36. 32 not 35
37. (letter comment or editorial).pt.

Familial hypercholesterolaemia: FINAL August 2008

Appendix B: Key clinical questions and searches

38. 36 not 37

39. limit 38 to english language

Question 6,13,16 Information and support, dietary interventions, genetic counselling

Embase 1974-August 2007 via Dialog Datastar

Searched 08/08/07

Update search 08/08/07-04/12/07

1. Familial-Hyperlipemia.DE.
2. Familial-Hypercholesterolemia.DE.
3. (familial ADJ hyperlipidemia OR familial ADJ hyperlipidaemia).TI,AB.
4. (familial ADJ (hypercholesterolemia OR hypercholesterolaemia)).TI,AB.
5. (essential ADJ (hypercholesterolemia OR hypercholesterolaemia)).TI,AB.
6. (essential ADJ (hyperlipidemia OR hyperlipidaemia)).TI,AB.
7. (heterozygous ADJ fh OR homozygous ADJ fh).TI,AB.
8. (monogenic ADJ (hyperlipidemia OR hyperlipidaemia)).TI,AB.
9. (familial ADJ apolipoprotein ADJ c ADJ II ADJ defici\$4).TI,AB.
- 10 (familial ADJ defective ADJ apolipoprotein ADJ b).TI,AB.
11. LDLR.TI,AB.
12. (LDL ADJ receptor).TI,AB.
13. (low ADJ density ADJ lipoprotein ADJ receptor).TI,AB.
14. Low-Density-Lipoprotein-Receptor.DE.
15. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14
16. Family-Counseling.DE. OR Genetic-Counseling.DE. OR Nutritional-Counseling.DE. OR Patient-Counseling.DE. OR Patient-Guidance.DE. OR Peer-Counseling.DE.
17. counselling OR counseling.TI,AB.
18. Diet-Therapy.DE.
19. Dietetics.W..DE.
20. Nutrition-Education.DE. OR Nutrition-Service.DE. OR Nutritional-Counseling.DE. OR Nutritional-Support.DE.
21. (diet\$3 NEAR (advice OR advise OR information OR guidance OR education OR therap\$3 OR intervention\$1 OR treatment\$1)).TI,AB.
22. (NUTRITION\$2 NEAR (ADVICE OR ADVISE OR INFORMATION OR GUIDANCE OR EDUCATION OR THERAP\$3 OR INTERVENTION\$1 OR TREATMENT\$1)).TI,AB.
23. dietician.TI,AB.
24. Phytosterol.W..DE.
25. (phytosterols OR plant ADJ sterols OR stanol ADJ esters).TI,AB.
26. Rapeseed-Oil.DE.
27. Low-Fat-Diet.DE. OR Diet-Therapy.DE.
28. (rapeseed ADJ oil\$1 OR soy ADJ protein\$1 OR portfolio ADJ diet\$1).TI,AB.
29. Health-Education.DE.
30. Health-Behavior.DE.
31. Health-Promotion.DE.

Familial hypercholesterolaemia: FINAL August 2008

Appendix B: Key clinical questions and searches

Familial hypercholesterolaemia: Final August 2008

32. Patient-Education.DE.
33. Caregiver-Support.DE. OR Social-Support.DE.
34. Self-Help.DE.
35. Attitude-To-Health.DE.
36. Support-Group.DE.
37. ((PATIENT\$1 OR FAMIL\$3 OR SPOUSE OR PARTNER OR CARER\$1 OR GROUP\$1 OR PEER\$1) NEAR SUPPORT\$3).TI,AB.
38. (health ADJ (education OR information OR guidance OR advice OR promotion)).TI,AB.
39. (social ADJ support OR social ADJ network\$1 OR self ADJ help OR support ADJ network\$1).TI,AB.
40. ((lifestyle OR life ADJ style) ADJ (information OR advice)).TI,AB.
41. ((information OR education\$2) NEAR (need\$1 OR provision OR provide OR providing OR require\$5)).TI,AB.
42. (patient ADJ (education OR information)).TI,AB.
43. ((teaching OR education\$2) ADJ (material OR program\$3 OR intervention\$1 OR session\$1 OR group\$1)).TI,AB.
44. ((ongoing OR continu\$5 OR regular\$2) ADJ (assess\$4 OR reassess\$5 OR re ADJ assess\$5 OR review)).TI,AB.
45. 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 OR 39 OR 40 OR 41 OR 42 OR 43 OR 44
46. 15 AND 45
47. ANIMAL=YES
48. Nonhuman.W..DE.
49. HUMAN=YES
50. 47 OR 48
51. 50 NOT (50 AND 49)
52. 46 NOT 51
53. AT=EDITORIAL OR AT=LETTER OR AT=NOTE
54. 52 NOT 53

Medline 1950-August 2007 via Dialog Datastar

Searched 08/08/07

Update search 08/08/07-04/12/07

1. (FAMILIAL ADJ (HYPERLIPIDEMIA OR HYPERLIPIDAEMIA)).TI,AB.
2. HYPERLIPOPROTEINEMIA-TYPE-II.DE.
3. (FAMILIAL ADJ (HYPERCHOLESTEROLEMIA OR HYPERCHOLESTEROLAEMIA)).TI,AB.
4. (ESSENTIAL ADJ (HYPERCHOLESTEROLEMIA OR HYPERCHOLESTEROLAEMIA)).TI,AB.
5. (HETEROZYGOUS ADJ FH).TI,AB.
6. (HOMOZYGOUS ADJ FH).TI,AB.
7. (MONOGENIC ADJ (HYPERLIPIDEMIA OR HYPERLIPIDAEMIA)).TI,AB.

Familial hypercholesterolaemia: FINAL August 2008

Appendix B: Key clinical questions and searches

8. (FAMILIAL ADJ APOLIPOPROTEIN ADJ C ADJ II ADJ DEFICI\$).TI,AB.
9. (FAMILIAL ADJ DEFECTIVE ADJ APOLIPOPROTEIN ADJ B).TI,AB.
- 10 LDLR.TI,AB.
11. (LDL ADJ RECEPTOR).TI,AB.
12. (LOW ADJ DENSITY ADJ LIPOPROTEIN ADJ RECEPTOR).TI,AB.
13. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12
14. COUNSELING#.W..DE.
15. GENETIC-COUNSELING.DE.
16. COUNSELLING OR COUNSELING.TI,AB.
17. DIETARY-SERVICES.DE.
18. DIETETICS.W..DE.
19. NUTRITION-THERAPY#.DE.
20. (DIET\$3 NEAR (ADVICE OR ADVISE OR INFORMATION OR GUIDANCE OR EDUCATION OR THERAP\$3 OR INTERVENTION\$1 OR TREATMENT\$1)).TI,AB.
21. (NUTRITION\$2 NEAR (ADVICE OR ADVISE OR INFORMATION OR GUIDANCE OR EDUCATION OR THERAP\$3 OR INTERVENTION\$1 OR TREATMENT\$1)).TI,AB.
22. DIETICIAN.TI,AB.
23. PHYTOSTEROLS.W..DE.
24. (PHYTOSTEROLS OR PLANT ADJ STEROLS OR STANOL ADJ ESTERS).TI,AB.
25. DIET-FAT-RESTRICTED.DE.
26. ((LOW OR LOWER\$1 OR DECREAS\$3 OR REDUC\$5 OR RESTRICT\$3) ADJ FAT\$1).TI,AB.
27. (RAPESEED ADJ OIL\$1 OR SOY ADJ PROTEIN\$1 OR PORTFOLIO ADJ DIET\$1).TI,AB.
28. HEALTH-EDUCATION.DE.
29. HEALTH-BEHAVIOR#.DE.
30. HEALTH-PROMOTION.DE.
31. PATIENT-EDUCATION.DE.
32. SOCIAL-SUPPORT.DE.
33. SELF-HELP-GROUPS.DE.
34. HEALTH-KNOWLEDGE-ATTITUDES-PRACTICE.DE.
35. ((PATIENT\$1 OR FAMIL\$3 OR SPOUSE OR PARTNER OR CARER\$1 OR GROUP\$1 OR PEER\$1) NEAR SUPPORT\$3).TI,AB.
36. (HEALTH ADJ (EDUCATION OR INFORMATION OR GUIDANCE OR ADVICE OR PROMOTION)).TI,AB.
37. (SOCIAL ADJ SUPPORT OR SOCIAL ADJ NETWORK\$1 OR SELF ADJ HELP OR SUPPORT ADJ NETWORK\$1).TI,AB.
38. ((LIFESTYLE OR LIFE ADJ STYLE) ADJ (INFORMATION OR ADVICE)).TI,AB.
39. ((INFORMATION OR EDUCATION\$2) NEAR (NEED\$1 OR PROVISION OR PROVIDE OR PROVIDING OR REQUIRE\$5)).TI,AB.
40. (PATIENT ADJ (EDUCATION OR INFORMATION)).TI,AB.
41. ((TEACHING OR EDUCATION\$2) ADJ (MATERIAL OR PROGRAM\$3 OR INTERVENTION\$1 OR SESSION\$1 OR GROUP\$1)).TI,AB.
42. ((ONGOING OR CONTINU\$5 OR REGULAR\$2) ADJ (ASSESS\$4 OR REASSESS\$4 OR RE ADJ ASSESS\$4 OR REVIEW)).TI,AB.

Familial hypercholesterolaemia: FINAL August 2008

Appendix B: Key clinical questions and searches

- 43. 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 OR 39 OR 40 OR 41 OR 42
- 44. 13 AND 43
- 45. ANIMAL=YES
- 46. HUMAN=YES
- 47. 45 NOT (45 AND 46)
- 48. 44 NOT 47
- 49. PT=COMMENT OR PT=EDITORIAL OR PT=LETTER
- 50. 48 NOT 49

Question 8b-f Resins or niacin or fibrates or omega 3 or ezetimibe versus placebo

Embase 1980-2006 week 42
Searched 25/10/06
Update search 25/10/06-04/12/07

- 1. Familial Hyperlipemia/
- 2. Familial Hypercholesterolemia/
- 3. familial hyperlipid?emia.ti,ab.
- 4. familial hypercholesterol?emia.ti,ab.
- 5. essential hypercholesterol?emia.ti,ab.
- 6. essential hyperlipid?emia.ti,ab.
- 7. (heterozygous fh or homozygous fh).ti,ab.
- 8. monogenic hyperlipid?emia.ti,ab.
- 9. familial apolipoprotein c-II defici\$.ti,ab.
- 10. familial defective apolipoprotein b.ti,ab.
- 11. LDLR.ti,ab.
- 12. ldl receptor.ti,ab.
- 13. low density lipoprotein receptor.ti,ab.
- 14. Low Density Lipoprotein Receptor/
- 15. or/1-14
- 16. Anion Exchange Resin/
- 17. Colestyramine/
- 18. Colestipol/
- 19. (anion exchange resin\$ or cholestyramine or colestyramin\$ or colestipol).ti,ab.
- 20. Nicotinic Acid/
- 21. Acipimox/
- 22. (nicotinic acid\$ or niacin or acipimox).ti,ab.
- 23. Clofibric Acid/
- 24. Bezafibrate/
- 25. Ciprofibrate/
- 26. Fenofibrate/
- 27. Gemfibrozil/
- 28. (fibrate\$ or bezafibrate or ciprofibrate or fenofibrate or gemfibrozil).ti,ab.

Familial hypercholesterolaemia: FINAL August 2008

Appendix B: Key clinical questions and searches

29. Omega 3 Fatty Acid/
30. (omega-3 or n-3 fatty acid\$ or n-3 polyunsaturated fatty acid\$ or n-3 polyunsaturated fa or n-3 pufa or fish oil\$ or omacor or maxepa).ti,ab.
31. Ezetimibe/
32. ezetimibe.ti,ab.
33. or/16-32
34. 15 and 33
35. exp meta analysis/
36. meta-analys\$.ti,ab.
37. metaanalys\$.ti,ab.
38. review\$.ti.
39. overview\$.ti.
40. (synthes\$ adj3 (literature\$ or research\$ or studies or data)).ti,ab.
41. pooled analys\$.ti,ab.
42. ((data adj2 pool\$) and studies).mp.
43. (medline or medlars or embase or cinahl or scisearch or psychinfo or psycinfo or psychlit or psyclit).ti,ab.
44. ((hand or manual or database\$ or computer\$) adj2 search\$).ti,ab.
45. ((electronic or bibliographic\$) adj2 (database\$ or data base\$)).ti,ab.
46. ((review\$ or overview\$) adj (systematic\$ or methodologic\$ or quantitativ\$ or research\$ or literature\$ or studies or trial\$ or effectiv\$)).ab.
47. or/35-46
48. editorial.pt.
49. letter.pt.
50. 48 or 49
51. 47 not 50
52. 34 and 51
53. randomized controlled trial/
54. randomization/
55. double blind procedure/
56. single blind procedure/
57. exp clinical trial/
58. controlled study/
59. clin\$ trial\$.ti,ab.
60. ((singl\$ or doubl\$ or trebl\$ or tripl\$) adj3 (blind\$ or mask\$)).ti,ab.
61. placebo\$.ti,ab.
62. placebo/
63. random.ti,ab.
64. evaluation/
65. followup/
66. exp methodology/
67. prospective study/
68. (control\$ or prospectiv\$ or volunteer\$).ti,ab.
69. or/53-68
70. 34 and 69

Familial hypercholesterolaemia: Final August 2008

71. 70 or 52
72. animals/
73. nonhuman/
74. 72 or 73
75. humans/
76. 74 not (74 and 75)
77. 71 not 76
78. (conference paper or editorial or erratum or letter or note or proceeding).pt.
79. 77 not 78

Medline 1966-2006 Oct week 2
Searched 24/10/06
Update search 24/10/06-04/12/07

1. familial hyperlipid?emia.ti,ab.
2. Hypercholesterolemia, Familial/
3. familial hypercholesterol?emia.ti,ab.
4. essential hypercholesterol?emia.ti,ab.
5. heterozygous fh.ti,ab.
6. homozygous fh.ti,ab.
7. monogenic hyperlipid?emia.ti,ab.
8. familial apolipoprotein c-II defici\$.ti,ab.
9. familial defective apolipoprotein B.ti,ab.
10. LDLR.ti,ab.
11. LDL receptor.ti,ab.
12. low density lipoprotein receptor.ti,ab.
13. or/1-12
14. Anion Exchange Resins/
15. Cholestyramine/
16. Colestipol/
17. (anion exchange resin\$ or cholestyramine or colestyramin\$ or colestipol).ti,ab.
18. Niacin/
19. (niacin or nicotinic acid\$ or acipimox).ti,ab.
20. Clofibric Acid/
21. Bezafibrate/
22. Gemfibrozil/
23. (clofibric acid\$ or fibrate\$ or bezafibrate or ciprofibrate or fenofibrate or gemfibrozil).ti,ab.
24. Fatty Acids, Omega-3/
25. (omega-3 or n-3 fatty acid\$ or n-3 polyunsaturated fatty acid\$ or n-3 polyunsaturated fa or n-3 pufa or fish oil\$ or omacor or maxepa).ti,ab.
26. ezetimibe.ti,ab.
27. or/14-26
28. 13 and 27
29. animals/

Familial hypercholesterolaemia: FINAL August 2008

Appendix B: Key clinical questions and searches

30. humans/
31. 29 not (29 and 30)
32. 28 not 31
33. (systematic\$ adj review\$).ab.
34. review.pt.
35. meta-analysis.ab.
36. meta-analysis.pt.
37. meta-analysis.ti.
38. or/33-37
39. 32 and 38
40. randomized controlled trial.pt.
41. controlled clinical trial.pt.
42. randomized controlled trials.sh.
43. random allocation.sh.
44. double blind method.sh.
45. single blind method.sh.
46. or/40-45
47. clinical trial.pt.
48. exp clinical trials/
49. (clin\$ adj5 trial\$).ti,ab.
50. ((singl\$ or doubl\$ or trebl\$ or tripl\$) adj5 (blind\$ or mask\$)).ti,ab.
51. placebos.sh.
52. placebo\$.ti,ab.
53. random\$.ti,ab.
54. or/47-53
55. 46 or 54
56. 55 and 32
57. (letter or editorial or comment).pt.
58. 56 or 39
59. 58 not 57

Question 8a Statins versus placebo and Q9 Statins in combination with other pharmaceutical agents

Embase 1980-2006 week 37
Searched 18/09/06
Update search 18/09/06-06/12/07

1. Familial Hyperlipemia/
2. Familial Hypercholesterolemia/
3. familial hyperlipid?emia.ti,ab.
4. familial hypercholesterol?emia.ti,ab.
5. essential hypercholesterol?emia.ti,ab.
6. essential hyperlipid?emia.ti,ab.
7. (heterozygous fh or homozygous fh).ti,ab.

Familial hypercholesterolaemia: FINAL August 2008

Appendix B: Key clinical questions and searches

8. monogenic hyperlipidemia.ti,ab.
9. familial apolipoprotein c-II deficiency.ti,ab.
10. familial defective apolipoprotein b.ti,ab.
11. LDLR.ti,ab.
12. Idl receptor.ti,ab.
13. low density lipoprotein receptor.ti,ab.
14. Low Density Lipoprotein Receptor/
15. or/1-14
16. animals/
17. Nonhuman/
18. 16 or 17
19. humans/
20. 18 not (18 and 19)
21. 15 not 20
22. hydroxymethylglutaryl coenzyme a reductase inhibitor/ or atorvastatin/ or pravastatin/ or rosuvastatin/ or simvastatin/
23. (simvastatin or pravastatin or rosuvastatin or fluvastatin or atorvastatin or statin\$.tw.
24. hmg-coa.tw.
25. or/22-24
26. 21 and 25
27. exp meta analysis/
28. ((meta adj analy\$) or metaanalys\$.tw.
29. (systematic adj (review\$1 or overview\$1)).tw.
30. or/27-29
31. (cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index).ab.
32. reference lists.ab.
33. bibliograph\$.ab.
34. hand-search\$.ab.
35. manual search.ab.
36. relevant journals.ab.
37. or/32-36
38. (data adj extraction).ab.
39. selection criteria.ab.
40. 38 or 39
41. review.pt.
42. 40 and 41
43. 30 or 37 or 42
44. 26 and 43
45. Clinical Trial/
46. randomized controlled trial/
47. randomization/
48. single blind procedure/
49. double blind procedure/
50. crossover procedure/

Familial hypercholesterolaemia: Final August 2008

51. placebo/
52. randomi?ed controlled trial\$.tw.
53. rct.tw.
54. random allocation.tw.
55. randomly allocated.tw.
56. allocated randomly.tw.
57. (allocated adj2 random).tw.
58. single blind\$.tw.
59. double blind\$.tw.
60. ((treble or triple) adj blind\$.tw.
61. placebo.tw.
62. prospective study/
63. or/45-62
64. abstract report/ or letter/
65. case study/
66. case report.tw.
67. or/64-66
68. 63 not 67
69. 26 and 68
70. 44 or 69
71. (letter or editorial or conference paper or note).pt.
72. 70 not 71

Medline 1966-2006 Sept week1

Searched 18/09/06

Update search 18/09/06-06/12/07

1. familial hyperlipid?emia.ti,ab.
2. Hypercholesterolemia, Familial/
3. familial hypercholesterol?emia.ti,ab.
4. essential hypercholesterol?emia.ti,ab.
5. heterozygous fh.ti,ab.
6. homozygous fh.ti,ab.
7. monogenic hyperlipid?emia.ti,ab.
8. familial apolipoprotein c-II defici\$.ti,ab.
9. familial defective apolipoprotein B.ti,ab.
10. LDLR.ti,ab.
11. LDL receptor.ti,ab.
12. low density lipoprotein receptor.ti,ab.
13. or/1-12
14. Hydroxymethylglutaryl-CoA Reductase Inhibitors/
15. Simvastatin/
16. Pravastatin/
17. (simvastatin or pravastatin or rosuvastatin or fluvastatin or atorvastatin or statin\$.tw.
18. hmg-coa.tw.

Familial hypercholesterolaemia: FINAL August 2008

Appendix B: Key clinical questions and searches

19. or/14-18
20. 13 and 19
21. animals/
22. humans/
23. 21 not (21 and 22)
24. 20 not 23
25. (systematic\$ adj review\$).ab.
26. review.pt.
27. meta-analysis.ab.
28. meta-analysis.pt.
29. meta-analysis.ti.
30. or/25-29
31. 24 and 30
32. randomized controlled trial.pt.
33. controlled clinical trial.pt.
34. randomized controlled trials.sh.
35. random allocation.sh.
36. double blind method.sh.
37. single blind method.sh.
38. or/32-37
39. clinical trial.pt.
40. exp clinical trials/
41. (clin\$ adj5 trial\$).ti,ab.
42. ((singl\$ or doubl\$ or trebl\$ or tripl\$) adj5 (blind\$ or mask\$)).ti,ab.
43. placebos.sh.
44. placebo\$.ti,ab.
45. random\$.ti,ab.
46. or/39-45
47. 38 or 46
48. 24 and 47
49. 31 or 48
50. (letter or editorial or comment).pt.
51. 49 not 50

Question 10 Apheresis/plasmapheresis

Embase 1980-2007 week 9

Searched 09/03/07

Update search 09/03/07-04/12/07

1. Familial Hyperlipemia/
2. Familial Hypercholesterolemia/
3. familial hyperlipid?emia.ti,ab.
4. familial hypercholesterol?emia.ti,ab.
5. essential hypercholesterol?emia.ti,ab.

Familial hypercholesterolaemia: FINAL August 2008

Appendix B: Key clinical questions and searches

Familial hypercholesterolaemia: Final August 2008

6. essential hyperlipid?emia.ti,ab.
7. (heterozygous fh or homozygous fh).ti,ab.
8. monogenic hyperlipid?emia.ti,ab.
9. familial apolipoprotein c-II deficiency.ti,ab.
10. familial defective apolipoprotein b.ti,ab.
11. LDLR.ti,ab.
12. Idl receptor.ti,ab.
13. low density lipoprotein receptor.ti,ab.
14. Low Density Lipoprotein Receptor/
15. or/1-14
16. apheresis/
17. plasmapheresis/
18. (apheresis or pheresis).ti,ab.
19. (plasmapheresis or plasmaphoresis).ti,ab.
20. membrane filter/
21. (membrane adj2 filtration).ti,ab.
22. (plasma\$ adj2 (exchange or filtration)).ti,ab.
23. (lipidfiltration or thermofiltration).ti,ab.
24. hemapheresis/
25. (haemapheresis or hemapheresis).ti,ab.
26. (cascade adj2 filtration).ti,ab.
27. (heparin induced extracorporeal LDL precipitation or heparin mediated extracorporeal LDL precipitation).ti,ab.
28. (direct adsorption lipoprotein or DALI).ti,ab.
29. dextran sulphate cellulose adsorption.ti,ab.
30. immunoabsorption.ti,ab.
31. immunoabsorption/
32. or/16-31
33. 15 and 32
34. animals/
35. Nonhuman/
36. 34 or 35
37. humans/
38. 36 not (36 and 37)
39. 33 not 38
40. (editorial or erratum or letter or note).pt.
41. 39 not 40

Medline 1950-2007 Feb week 4

Searched 09/03/07

Update search 09/03/07-04/12/07

1. familial hyperlipid?emia.ti,ab.
2. Hypercholesterolemia, Familial/
3. familial hypercholesterol?emia.ti,ab.

Familial hypercholesterolaemia: FINAL August 2008

Appendix B: Key clinical questions and searches

4. essential hypercholesterol?emia.ti,ab.
5. heterozygous fh.ti,ab.
6. homozygous fh.ti,ab.
7. monogenic hyperlipid?emia.ti,ab.
8. familial apolipoprotein c-II deficiency.ti,ab.
9. familial defective apolipoprotein B.ti,ab.
10. LDLR.ti,ab.
11. LDL receptor.ti,ab.
12. low density lipoprotein receptor.ti,ab.
13. or/1-12
14. Blood Component Removal/
15. Plasmapheresis/
16. (apheresis or pheresis).ti,ab.
17. (plasmapheresis or plasmaphoresis).ti,ab.
18. (membrane adj2 filtration).ti,ab.
19. (plasma\$ adj2 (exchange or filtration)).ti,ab.
20. (lipidfiltration or thermofiltration).ti,ab.
21. (haemapheresis or hemapheresis).ti,ab.
22. (cascade adj2 filtration).ti,ab.
23. (heparin induced extracorporeal LDL precipitation or heparin mediated extracorporeal LDL precipitation).ti,ab.
24. (direct adsorption lipoprotein or DALI).ti,ab.
25. dextran sulphate cellulose adsorption.ti,ab.
26. immunoabsorption.ti,ab.
27. or/14-26
28. 13 and 27
29. animal/
30. Humans/
31. 29 not (29 and 30)
32. 28 not 31
33. (letter or comment or editorial).pt.
34. 32 not 33

Question 11 Heart/liver transplantation

Embase 1980-2007 week 9

Searched 12/03/07

Update search 12/03/07- 06/12/07

1. Familial Hyperlipemia/
2. Familial Hypercholesterolemia/
3. familial hyperlipid?emia.ti,ab.
4. familial hypercholesterol?emia.ti,ab.
5. essential hypercholesterol?emia.ti,ab.
6. essential hyperlipid?emia.ti,ab.

Familial hypercholesterolaemia: FINAL August 2008

Appendix B: Key clinical questions and searches

Familial hypercholesterolaemia: Final August 2008

7. (heterozygous fh or homozygous fh).ti,ab.
8. monogenic hyperlipid?emia.ti,ab.
9. familial apolipoprotein c-II defici\$.ti,ab.
10. familial defective apolipoprotein b.ti,ab.
11. LDLR.ti,ab.
12. ldl receptor.ti,ab.
13. low density lipoprotein receptor.ti,ab.
14. Low Density Lipoprotein Receptor/
15. or/1-14
16. Liver Transplantation/
17. (liver adj2 transplant\$.ti,ab.
18. (liver adj2 graft\$.ti,ab.
19. (hepatic adj2 transplant\$.ti,ab.
20. (hepatic adj2 graft\$.ti,ab.
21. Liver Graft/
22. (heart adj2 liver transplant\$.ti,ab.
23. (heart adj2 liver graft\$.ti,ab.
24. or/16-23
25. 15 and 24
26. animals/
27. Nonhuman/
28. 26 or 27
29. humans/
30. 28 not (28 and 29)
31. 25 not 30
32. (editorial or letter or note).pt.
33. 31 not 32

Medline 1950-2007 Feb week 4
Searched 12/03/07
Update search 12/03/07-06/12/07

1. familial hyperlipid?emia.ti,ab.
2. Hypercholesterolemia, Familial/
3. familial hypercholesterol?emia.ti,ab.
4. essential hypercholesterol?emia.ti,ab.
5. heterozygous fh.ti,ab.
6. homozygous fh.ti,ab.
7. monogenic hyperlipid?emia.ti,ab.
8. familial apolipoprotein c-II defici\$.ti,ab.
9. familial defective apolipoprotein B.ti,ab.
10. LDLR.ti,ab.
11. LDL receptor.ti,ab.
12. low density lipoprotein receptor.ti,ab.
13. or/1-12

Familial hypercholesterolaemia: FINAL August 2008

Appendix B: Key clinical questions and searches

14. Liver Transplantation/
15. (liver adj2 transplant\$.ti,ab.
16. (liver adj2 graft\$.ti,ab.
17. (hepatic adj2 transplant\$.ti,ab.
18. (hepatic adj2 graft\$.ti,ab.
19. (heart adj2 liver transplant\$.ti,ab.
20. (heart adj2 liver graft\$.ti,ab.
21. or/14-20
22. 13 and 21
23. Animals/
24. humans/
25. 23 not (23 and 24)
26. 22 not 25
27. (letter or comment or editorial).pt.
28. 26 not 27

Question 12 Investigations to assess atherosclerosis

Embase 1980-2007 week 19
Searched 15/05/07
Update search 15/05/07-06/12/07

1. Familial Hyperlipemia/
2. Familial Hypercholesterolemia/
3. familial hyperlipid?emia.ti,ab.
4. familial hypercholesterol?emia.ti,ab.
5. essential hypercholesterol?emia.ti,ab.
6. essential hyperlipid?emia.ti,ab.
7. (heterozygous fh or homozygous fh).ti,ab.
8. monogenic hyperlipid?emia.ti,ab.
9. familial apolipoprotein c-II defici\$.ti,ab.
10. familial defective apolipoprotein b.ti,ab.
11. LDLR.ti,ab.
12. ldl receptor.ti,ab.
13. low density lipoprotein receptor.ti,ab.
14. Low Density Lipoprotein Receptor/
15. or/1-14
16. exercise electrocardiography/
17. ((exercise or stress) adj (electrocardiograph\$ or electrocardiogram\$ or cardioscope\$)).ti,ab.
18. ((exercise or stress) adj (ecg or ekg)).ti,ab.
19. execg.ti,ab.
20. exp echocardiography/
21. (echocardiograph\$ or echo cardiograph\$ or echocardiogram\$ or echo cardiogram\$ or echosound\$ or echo sound\$ or echograph\$ or echo graph\$).ti,ab.

Familial hypercholesterolaemia: FINAL August 2008

Appendix B: Key clinical questions and searches

Familial hypercholesterolaemia: Final August 2008

22. ((cardiac or heart or cardio\$ or coronary) adj scan\$).ti,ab.
23. exp angiocardiology/
24. angiograph\$.ti,ab.
25. exp heart catheterization/
26. (catheterisation or catheterization).ti,ab.
27. exp nuclear magnetic resonance imaging/
28. (magnetic resonance imag\$ or mri or nmr or fmri or mr tomograph\$ or cinemri or cine magnetic resonance or chemical shift imag\$ or mr imag\$ or proton spin tomograph\$).ti,ab.
29. (carotid int or carotid intima media thickness).ti,ab.
30. Calcinosis/
31. (calcinosis or calcification or coronary calcium or coronary arter\$ calcium).ti,ab.
32. exp computer assisted tomography/
33. (comput\$ tomograph\$ or electron beam tomograph\$ or electron beam ct or ct x ray or ct xray or cine ct or cinect or cat scan\$ or ct scan\$).ti,ab.
34. magnetic resonance angiography/
35. ((magnetic resonance or mri or mr or nmr) adj angiograph\$).ti,ab.
36. (perfusion adj2 (magnetic resonance or mri or nmr or mr)).ti,ab.
37. doppler echography/
38. (doppler adj2 (ultrasonograph\$ or sonograph\$ or ultrasound or echocardiograph\$ or echograph\$)).ti,ab.
39. (high resolution adj (ultrasonograph\$ or ultrasound)).ti,ab.
40. ((interventional or intravascular or intra-vascular) adj (ultrasonograph\$ or ultrasound)).ti,ab.
41. intravascular ultrasound/
42. ivus.ti,ab.
43. (thallium adj2 (scan\$ or test\$ or imag\$)).ti,ab.
44. or/16-43
45. 15 and 44
46. animals/
47. Nonhuman/
48. humans/
49. 46 or 47
50. 49 not (49 and 48)
51. 45 not 50
52. (conference paper or editorial or erratum or letter or note or proceeding).pt.
53. 51 not 52

Medline 1950-2007 May week 1

Searched 15/05/07

Update search 15/05/07-06/12/07

1. familial hyperlipid?emia.ti,ab.
2. Hypercholesterolemia, Familial/
3. familial hypercholesterol?emia.ti,ab.

Familial hypercholesterolaemia: FINAL August 2008

Appendix B: Key clinical questions and searches

Familial hypercholesterolaemia: Final August 2008

4. essential hypercholesterolaemia.ti,ab.
5. heterozygous fh.ti,ab.
6. homozygous fh.ti,ab.
7. monogenic hyperlipidaemia.ti,ab.
8. familial apolipoprotein c-II deficiency.ti,ab.
9. familial defective apolipoprotein B.ti,ab.
10. LDLR.ti,ab.
11. LDL receptor.ti,ab.
12. low density lipoprotein receptor.ti,ab.
13. or/1-12
14. exp Electrocardiography/
15. ((exercise or stress) adj (ecg or ekg)).ti,ab.
16. ((exercise or stress) adj (electrocardiograph\$ or electrocardiogram\$ or cardioscope\$)).ti,ab.
17. execg.ti,ab.
18. exp Echocardiography/
19. (echocardiograph\$ or echo cardiograph\$ or echocardiogram\$ or echo cardiogram\$ or echosound\$ or echo sound\$ or echograph\$ or echo graph\$).ti,ab.
20. ((cardiac or heart or cardio\$ or coronary) adj scan\$).ti,ab.
21. Coronary Angiography/
22. angiograph\$.ti,ab.
23. exp Heart Catheterization/
24. (catheterisation or catheterization).ti,ab.
25. exp Magnetic Resonance Imaging/
26. (magnetic resonance imag\$ or mri or nmr or fmri or mr tomograph\$ or cinemri or cine magnetic resonance or chemical shift imag\$ or mr imag\$ or proton spin tomograph\$).ti,ab.
27. (carotid int or carotid intima media thickness).ti,ab.
28. Calcinosis/
29. (calcinosis or calcification or coronary calcium or coronary arter\$ calcium).ti,ab.
30. exp Tomography, X-Ray Computed/
31. (comput\$ tomograph\$ or electron beam tomograph\$ or electron beam ct or ct x ray or ct xray or cine ct or cinect or cat scan\$ or ct scan\$).ti,ab.
32. Magnetic Resonance Angiography/
33. ((magnetic resonance or mri or mr or nmr) adj angiograph\$).ti,ab.
34. (perfusion adj2 (magnetic resonance or mri or nmr or mr)).ti,ab.
35. exp Ultrasonography, Doppler/
36. (doppler adj2 (ultrasonograph\$ or sonograph\$ or ultrasound or echocardiograph\$ or echograph\$)).ti,ab.
37. Ultrasonography, Interventional/
38. (high resolution adj (ultrasonograph\$ or ultrasound)).ti,ab.
39. ((interventional or intravascular or intra-vascular) adj (ultrasonograph\$ or ultrasound)).ti,ab.
40. ivus.ti,ab.
41. (thallium adj2 (scan\$ or test\$ or imag\$)).ti,ab.

Familial hypercholesterolaemia: FINAL August 2008

Appendix B: Key clinical questions and searches

42. or/14-41
43. 13 and 42
44. Animals/
45. humans/
46. 44 not (44 and 45)
47. 43 not 46
48. (letter or comment or editorial).pt.
49. 47 not 48

Question 14 Contraceptive information for women/girls with FH or on statins or at high CVD risk

Embase 1980-2007 week 25
Searched 25/06/07
Update search 25/06/07-04/12/07

1. Familial Hyperlipemia/
2. Familial Hypercholesterolemia/
3. familial hyperlipid?emia.ti,ab.
4. familial hypercholesterol?emia.ti,ab.
5. essential hypercholesterol?emia.ti,ab.
6. essential hyperlipid?emia.ti,ab.
7. (heterozygous fh or homozygous fh).ti,ab.
8. monogenic hyperlipid?emia.ti,ab.
9. familial apolipoprotein c-II defici\$.ti,ab.
10. familial defective apolipoprotein b.ti,ab.
11. LDLR.ti,ab.
12. ldl receptor.ti,ab.
13. low density lipoprotein receptor.ti,ab.
14. Low Density Lipoprotein Receptor/
15. or/1-14
16. risk factor/
17. RISK ASSESSMENT/
18. cardiovascular risk/
19. CORONARY RISK/
20. Statistical Model/
21. exp regression analysis/
22. "analysis of variance"/
23. exp multivariate analysis/
24. (risk\$ adj2 (factor\$ or assess\$ or status or profile\$ or analys\$ or variable or marker\$)).ti,ab.
25. ((increase\$ or high\$ or mortality or overall or relative or absolute) adj2 risk\$).ti,ab.
26. confounding.ti,ab.
27. (regression adj2 (analys\$ or model\$)).ti,ab.
28. ((multivariable or multivariate or multi varia\$) adj2 analys\$).ti,ab.

Familial hypercholesterolaemia: FINAL August 2008

Appendix B: Key clinical questions and searches

Familial hypercholesterolaemia: Final August 2008

29. (risk adj2 stratification adj2 criteria).ti,ab.
30. or/16-29
31. exp Cardiovascular Disease/
32. (cvd or coronary or heart or cardiovasc\$ or vascular\$ or chd or cad).ti,ab.
33. 31 or 32
34. 30 and 33
35. ((cvd or coronary or heart or cardiovasc\$ or vascular\$ or chd or cad) adj2 risk\$).ti,ab.
36. 34 or 35
37. hydroxymethylglutaryl coenzyme a reductase inhibitor/
38. atorvastatin/
39. pravastatin/
40. rosuvastatin/
41. simvastatin/
42. (simvastatin or pravastatin or rosuvastatin or fluvastatin or atorvastatin or statin\$).tw.
43. hmg-coa.tw.
44. or/37-43
45. 15 or 44
46. exp contraception/
47. exp contraceptive device/
48. contraceptive\$.ti,ab.
49. (progestogen adj pill\$).ti,ab.
50. ((intrauterine or intra uterine) adj progestogen).ti,ab.
51. (iud or iuds or coiled spring).ti,ab.
52. (vaginal adj (ring or shield or sponge)).ti,ab.
53. ((intracervical or intra cervical) adj (device\$ or coil or pessar\$)).ti,ab.
54. ((intrauterine or intra uterine) adj (device\$ or coil or pessar\$)).ti,ab.
55. (barrier method\$ or condom\$ or diaphragm or cervical cap).ti,ab.
56. or/46-55
57. 45 and 56
58. exp meta analysis/
59. meta-analys\$.ti,ab.
60. metaanalys\$.ti,ab.
61. review\$.ti.
62. overview\$.ti.
63. (synthes\$ adj3 (literature\$ or research\$ or studies or data)).ti,ab.
64. pooled analys\$.ti,ab.
65. ((data adj2 pool\$) and studies).mp.
66. (medline or medlars or embase or cinahl or scisearch or psychinfo or psycinfo or psychlit or psyclit).ti,ab.
67. ((hand or manual or database\$ or computer\$) adj2 search\$).ti,ab.
68. ((electronic or bibliographic\$) adj2 (database\$ or data base\$)).ti,ab.
69. ((review\$ or overview\$) adj (systematic\$ or methodologic\$ or quantitativ\$ or research\$ or literature\$ or studies or trial\$ or effectiv\$)).ab.
70. or/58-69

Familial hypercholesterolaemia: FINAL August 2008

Appendix B: Key clinical questions and searches

Familial hypercholesterolaemia: Final August 2008

71. 36 and 56 and 70
72. 57 or 71
73. female/
74. women/
75. (wom?n or female\$ or girl\$).ti,ab.
76. or/73-75
77. 72 and 76
78. animal/
79. nonhuman/
80. 78 or 79
81. human/
82. 80 not (80 and 81)
83. 77 not 82
84. (conference paper or editorial or letter or note or proceeding).pt.
85. 83 not 84

Medline 1950-2007 June week 2
Searched 25/06/07
Update search 25/06/07-04/12/07

1. familial hyperlipid?emia.ti,ab.
2. Hypercholesterolemia, Familial/
3. familial hypercholesterol?emia.ti,ab.
4. essential hypercholesterol?emia.ti,ab.
5. heterozygous fh.ti,ab.
6. homozygous fh.ti,ab.
7. monogenic hyperlipid?emia.ti,ab.
8. familial apolipoprotein c-II defici\$.ti,ab.
9. familial defective apolipoprotein B.ti,ab.
10. LDLR.ti,ab.
11. LDL receptor.ti,ab.
12. low density lipoprotein receptor.ti,ab.
13. or/1-12
14. risk factors/
15. Risk Assessment/
16. logistic models/
17. confounding factors/
18. survival analysis/
19. exp regression analysis/
20. exp "analysis of variance"/
21. exp multivariate analysis/
22. (risk\$ adj2 (factor\$ or assess\$ or status or profile\$ or analys\$ or variable or marker\$)).ti,ab.
23. ((increas\$ or high\$ or mortality or overall or relative or absolute) adj2 risk\$).ti,ab.
24. confounding.ti,ab.

Familial hypercholesterolaemia: FINAL August 2008

Appendix B: Key clinical questions and searches

Familial hypercholesterolaemia: Final August 2008

25. (regression adj2 (analys\$ or model\$)).ti,ab.
26. ((multivariable or multivariate or multi varia\$) adj2 analys\$).ti,ab.
27. (risk adj2 stratification adj2 criteria).ti,ab.
28. or/14-27
29. exp Cardiovascular Diseases/
30. (cvd or coronary or heart or cardiovasc\$ or vascular\$ or chd or cad).ti,ab.
31. 29 or 30
32. 28 and 31
33. ((cvd or coronary or heart or cardiovasc\$ or vascular\$ or chd or cad) adj2 risk\$).ti,ab.
34. 32 or 33
35. Hydroxymethylglutaryl-CoA Reductase Inhibitors/
36. Simvastatin/
37. Pravastatin/
38. (simvastatin or pravastatin or rosuvastatin or fluvastatin or atorvastatin or statin\$).tw.
39. hmg-coa.tw.
40. or/35-39
41. 13 or 40
42. exp Contraceptive Agents/
43. exp Contraceptive Devices/
44. contraceptive\$.ti,ab.
45. (progestogen adj pill\$).ti,ab.
46. ((intrauterine or intra uterine) adj progestogen).ti,ab.
47. ((intrauterine or intra uterine) adj (device\$ or coil or pessar\$)).ti,ab.
48. (iud or iuds or coiled spring).ti,ab.
49. (vaginal adj (ring or shield or sponge)).ti,ab.
50. ((intracervical or intra cervical) adj (device\$ or coil or pessar\$)).ti,ab.
51. (barrier method\$ or condom\$ or diaphragm or cervical cap).ti,ab.
52. or/42-51
53. 41 and 52
54. (systematic adj review\$).tw.
55. (published adj studies).ab.
56. (data adj synthesis).tw.
57. (data adj extraction).ab.
58. meta-analysis/
59. meta-analysis.ti,ab.
60. meta-analysis.pt.
61. or/54-60
62. 34 and 52 and 61
63. 53 or 62
64. animals/
65. humans/
66. 64 not (64 and 65)
67. 63 not 66
68. letter.pt.

Familial hypercholesterolaemia: FINAL August 2008

Appendix B: Key clinical questions and searches

- 69. comment.pt.
- 70. editorial.pt.
- 71. or/68-70
- 72. 67 not 71

Question 15 Information and care for pregnant and lactating women with FH

Embase 1980-2007 week 25
Searched 25/06/07
Update search 25/06/07-06/12/07

- 1. Familial Hyperlipemia/
- 2. Familial Hypercholesterolemia/
- 3. familial hyperlipid?emia.ti,ab.
- 4. familial hypercholesterol?emia.ti,ab.
- 5. essential hypercholesterol?emia.ti,ab.
- 6. essential hyperlipid?emia.ti,ab.
- 7. (heterozygous fh or homozygous fh).ti,ab.
- 8. monogenic hyperlipid?emia.ti,ab.
- 9. familial apolipoprotein c-II deficiency.ti,ab.
- 10. familial defective apolipoprotein b.ti,ab.
- 11. LDLR.ti,ab.
- 12. ldl receptor.ti,ab.
- 13. low density lipoprotein receptor.ti,ab.
- 14. Low Density Lipoprotein Receptor/
- 15. or/1-14
- 16. exp maternal care/
- 17. exp prenatal care/
- 18. prenatal period/
- 19. perinatal care/
- 20. perinatal period/
- 21. exp postnatal care/
- 22. puerperium/
- 23. exp pregnancy/
- 24. birth/
- 25. exp childbirth/
- 26. exp LABOR/
- 27. exp delivery/
- 28. breast feeding/
- 29. LACTATION/
- 30. exp Pregnancy Complication/
- 31. exp Labor Complication/
- 32. (preconcept\$ or pre-concept\$).ti,ab.

Familial hypercholesterolaemia: Final August 2008

33. (antenatal or ante-natal or prenatal or pre-natal or pregnan\$ or antepartum or antepartum or intrapartum or intra-partum or perinatal or peri-natal or postpartum or postpartum or peurperal or puerperium or postnatal or post-natal).ti,ab.
34. (birth or childbirth or postbirth or prebirth or parturition or labour or labor).ti,ab.
35. (breastfeed\$ or breast-feed\$ or breastfed or breast-fed or breastmilk or breast-milk or lactat\$).ti,ab.
36. or/16-35
37. 15 and 36
38. animals/
39. Nonhuman/
40. 38 or 39
41. humans/
42. 40 not (40 and 41)
43. 37 not 42
44. (conference paper or editorial or erratum or letter or note or proceeding).pt.
45. 43 not 44

Medline 1950-2007 June week 2

Searched 25/06/07

Update search 25/06/07-06/12/07

1. familial hyperlipid?emia.ti,ab.
2. Hypercholesterolemia, Familial/
3. familial hypercholesterol?emia.ti,ab.
4. essential hypercholesterol?emia.ti,ab.
5. heterozygous fh.ti,ab.
6. homozygous fh.ti,ab.
7. monogenic hyperlipid?emia.ti,ab.
8. familial apolipoprotein c-II defici\$.ti,ab.
9. familial defective apolipoprotein B.ti,ab.
10. LDLR.ti,ab.
11. LDL receptor.ti,ab.
12. low density lipoprotein receptor.ti,ab.
13. or/1-12
14. Preconception Care/
15. Prenatal Care/
16. Perinatal Care/
17. Postnatal Care/
18. exp Pregnancy/
19. exp Postpartum Period/
20. exp Parturition/
21. Breast Feeding/
22. Lactation/
23. exp Pregnancy Complications/
24. exp obstetric labor/

Familial hypercholesterolaemia: FINAL August 2008

Appendix B: Key clinical questions and searches

25. obstetric delivery/
26. exp Obstetric Labor Complications/
27. (preconcept\$ or pre-concept\$).ti,ab.
28. (antenatal or ante-natal or prenatal or pre-natal or pregnan\$ or antepartum or antepartum or intrapartum or intra-partum or perinatal or peri-natal or postpartum or postpartum or puerperal or puerperium or postnatal or post-natal).ti,ab.
29. (birth or childbirth or postbirth or prebirth or parturition or labour or labor).ti,ab.
30. Breast Feeding/
31. Lactation/
32. (breastfeed\$ or breast-feed\$ or breastfed or breast-fed or breastmilk or breast-milk or lactat\$).ti,ab.
33. or/14-32
34. 13 and 33
35. animals/
36. humans/
37. 35 not (35 and 36)
38. 34 not 37
39. (letter or editorial or comment).pt.
40. 38 not 39

Economics search

Embase 1980-week 39 2006
Searched 06/10/06
Update search 06/10/06-04/12/07

1. Familial Hyperlipemia/
2. Familial Hypercholesterolemia/
3. familial hyperlipid?emia.ti,ab.
4. familial hypercholesterol?emia.ti,ab.
5. essential hypercholesterol?emia.ti,ab.
6. essential hyperlipid?emia.ti,ab.
7. (heterozygous fh or homozygous fh).ti,ab.
8. monogenic hyperlipid?emia.ti,ab.
9. familial apolipoprotein c-II defici\$.ti,ab.
10. familial defective apolipoprotein b.ti,ab.
11. LDLR.ti,ab.
12. ldl receptor.ti,ab.
13. low density lipoprotein receptor.ti,ab.
14. Low Density Lipoprotein Receptor/
15. or/1-14
16. animals/
17. Nonhuman/
18. 16 or 17
19. humans/

Familial hypercholesterolaemia: FINAL August 2008

Appendix B: Key clinical questions and searches

20. 18 not (18 and 19)
21. 15 not 20
22. (conference paper or editorial or erratum or letter or note or proceeding).pt.
23. 21 not 22
24. exp 'economic aspect'/
25. cost\$.tw.
26. (cost\$ adj2 (effective\$ or utilit\$ or benefit\$ or minimi\$)).ab.
27. (economic\$ or pharmacoeconomic\$ or pharmaco-economic\$).ti.
28. (price or pricing).tw.
29. (financial or finance or finances or financed).tw.
30. (fee or fees).tw.
31. (value adj2 (money or monetary)).tw.
32. quality adjusted life.tw.
33. (qaly\$ or qald\$ or qale\$ or qtime\$).tw.
34. disability adjusted life.tw.
35. daly\$.tw.
36. (sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw.
37. (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw.
38. (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sf twelve or shortform twelve or shortform twelve or short form twelve or short form twelve).tw.
39. (sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sf sixteen or shortform sixteen or shortform sixteen or short form sixteen or short form sixteen).tw.
40. (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sf twenty or shortform twenty or shortform twenty or short form twenty or short form twenty).tw.
41. (euroqol or euro qol or eq5d or eq 5d).tw.
42. (hql or hqol or h qol or hrqol or hr qol).tw.
43. (hye or hyes).tw.
44. health\$ year equivalent\$.tw.
45. health utilit\$.tw.
46. (hui or hui1 or hui2 or hui3).tw.
47. disutilit\$.tw.
48. rosser.tw.
49. quality of wellbeing.tw.
50. quality of well being.tw.
51. qwb.tw.
52. willingness to pay.tw.
53. standard gamble\$.tw.
54. (time trade off or time tradeoff).tw.
55. tto.tw.
56. exp 'mathematical model'/
57. economic model\$.tw.
58. markov\$.tw.
59. monte carlo method/

Familial hypercholesterolaemia: Final August 2008

60. monte carlo.tw.
61. exp decision theory/
62. (decision\$ adj2 (tree\$ or analy\$ or model\$)).tw.
63. or/24-62
64. 23 and 63

Medline 1966-2006 Sept wk 4
Searched 06/10/06
Update search 06/10/06-04/12/07

1. familial hyperlipid?emia.ti,ab.
2. Hypercholesterolemia, Familial/
3. familial hypercholesterol?emia.ti,ab.
4. essential hypercholesterol?emia.ti,ab.
5. heterozygous fh.ti,ab.
6. homozygous fh.ti,ab.
7. monogenic hyperlipid?emia.ti,ab.
8. familial apolipoprotein c-II defici\$.ti,ab.
9. familial defective apolipoprotein B.ti,ab.
10. LDLR.ti,ab.
11. LDL receptor.ti,ab.
12. low density lipoprotein receptor.ti,ab.
13. or/1-12
14. Animals/
15. humans/
16. 14 not (14 and 15)
17. 13 not 16
18. exp "costs and cost analysis"/
19. economics/
20. exp economics,hospital/
21. exp economics,medical/
22. economics,nursing/
23. economics,pharmaceutical/
24. exp "fees and charges"/
25. exp budgets/
26. budget\$.tw.
27. cost\$.tw.
28. (cost\$ adj2 (effective\$ or utilit\$ or benefit\$ or minimi\$)).ab.
29. (economic\$ or pharmaco-economic\$ or pharmaco-economic\$).ti.
30. (price or pricing).tw.
31. (financial or finance or finances or financed).tw.
32. (fee or fees).tw.
33. (value adj2 (money or monetary)).tw.
34. value of life/
35. quality adjusted life year/

Familial hypercholesterolaemia: FINAL August 2008

Appendix B: Key clinical questions and searches

36. quality adjusted life.tw.
37. (qaly\$ or qald\$ or qale\$ or qtime\$).tw.
38. disability adjusted life.tw.
39. daly\$.tw.
40. health status indicators/
41. (sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw.
42. (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw.
43. (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sf twelve or shortform twelve or shortform twelve or short form twelve or short form twelve).tw.
44. (sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sf sixteen or shortform sixteen or shortform sixteen or short form sixteen or short form sixteen).tw.
45. (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sf twenty or shortform twenty or shortform twenty or short form twenty or short form twenty).tw.
46. (euroqol or euro qol or eq5d or eq 5d).tw.
47. (hql or hqol or h qol or hrqol or hr qol).tw.
48. (hye or hyes).tw.
49. health\$ year equivalent\$.tw.
50. health utilit\$.tw.
51. (hui or hui1 or hui2 or hui3).tw.
52. disutilit\$.tw.
53. rosser.tw.
54. quality of wellbeing.tw.
55. quality of well being.tw.
56. qwb.tw.
57. willingness to pay.tw.
58. standard gamble\$.tw.
59. (time trade off or time tradeoff).tw.
60. tto.tw.
61. exp models, economic/
62. *models, theoretical/
63. *models, organizational/
64. economic model\$.tw.
65. markov chains/
66. markov\$.tw.
67. monte carlo method/
68. monte carlo.tw.
69. exp decision theory/
70. (decision\$ adj2 (tree\$ or analy\$ or model\$)).tw.
71. or/18-70
72. (letter or editorial or comment).pt.
73. 71 not 72
74. 17 and 73

Supplementary searches

Safety of resins or fibrates for children

Embase 1980-2007 week 4

Update search 29/01/07-04/12/07

1. Familial Hyperlipemia/
2. Familial Hypercholesterolemia/
3. familial hyperlipid?emia.ti,ab.
4. familial hypercholesterol?emia.ti,ab.
5. essential hypercholesterol?emia.ti,ab.
6. essential hyperlipid?emia.ti,ab.
7. (heterozygous fh or homozygous fh).ti,ab.
8. monogenic hyperlipid?emia.ti,ab.
9. familial apolipoprotein c-II defici\$.ti,ab.
10. familial defective apolipoprotein b.ti,ab.
11. LDLR.ti,ab.
12. ldl receptor.ti,ab.
13. low density lipoprotein receptor.ti,ab.
14. Low Density Lipoprotein Receptor/
15. or/1-14
16. anion exchange resin/
17. colestyramine/
18. colestipol/
19. (anion exchange resin\$ or colestyramine or colestyramin\$ or colestipol).ti,ab.
20. clofibric acid/
21. bezafibrate/
22. ciprofibrate/
23. fenofibrate/
24. gemfibrozil/
25. (fibrate\$ or bezafibrate\$ or ciprofibrate\$ or fenofibrate\$ or gemfibrozil).ti,ab.
26. or/16-25
27. 15 and 26
28. exp child/
29. pediatrics/
30. JUVENILE/
31. Adolescent/
32. (child\$ or pediatric\$ or paediatric\$ or boy\$ or girl\$ or juvenil\$ or teen\$ or adolescens\$ or minor or minors or youth\$).ti,ab.
33. or/28-32
34. 27 and 33
35. safety/ or child safety/ or patient safety/
36. drug safety/

Familial hypercholesterolaemia: FINAL August 2008

Appendix B: Key clinical questions and searches

Familial hypercholesterolaemia: Final August 2008

37. exp Adverse Drug Reaction/
38. MEDICAL ERROR/ or MEDICATION ERROR/
39. exp risk/
40. ae.fs.
41. (safe\$ or unsafe or risk\$ or adverse\$).ti,ab.
42. (regulat\$ or protect\$ or safeguard\$ or caution\$ or precaution or prevent\$).ti,ab.
43. (injur\$ or damag\$ or detriment\$ or harm\$ or mistake\$ or error\$ or risk\$).ti,ab.
44. or/35-43
45. 34 and 44
46. animals/
47. Nonhuman/
48. 46 or 47
49. humans/
50. 48 not (48 and 49)
51. 45 not 50
52. (letter or comment or editorial).pt.
53. 51 not 52

Medline 1950-2007 jan week 3

Update search 29/01/07-04/12/07

1. familial hyperlipid?emia.ti,ab.
2. Hypercholesterolemia, Familial/
3. familial hypercholesterol?emia.ti,ab.
4. essential hypercholesterol?emia.ti,ab.
5. heterozygous fh.ti,ab.
6. homozygous fh.ti,ab.
7. monogenic hyperlipid?emia.ti,ab.
8. familial apolipoprotein c-II defici\$.ti,ab.
9. familial defective apolipoprotein B.ti,ab.
10. LDLR.ti,ab.
11. LDL receptor.ti,ab.
12. or/1-11
13. exp Child/
14. Pediatrics/
15. Adolescent/
16. Minors/
17. (child\$ or pediatric\$ or paediatric\$ or boy\$ or girl\$ or juvenil\$ or teen\$ or adolescen\$ or minor or minors or youth\$).ti,ab.
18. or/13-17
19. 12 and 18
20. anion exchange resins/ or cholestyramine/ or colestipol/
21. (anion exchange resin\$ or cholestyramine or colestyramin\$ or colestipol).ti,ab.
22. clofibrac acid/ or bezafibrate/ or gemfibrozil/

Familial hypercholesterolaemia: FINAL August 2008

Appendix B: Key clinical questions and searches

23. (clofibrac acid\$ or fibrate\$ or bezafibrate\$ or ciprofibrate\$ or fenofibrate\$ or gemfibrozil).ti,ab.
24. or/20-23
25. 19 and 24
26. Safety/
27. exp risk/
28. (ae or st).fs.
29. (safe\$ or unsafe or risk\$ or adverse\$).ti,ab.
30. medical errors/ or medication errors/
31. (regulat\$ or protect\$ or safeguard\$ or caution\$ or precaution or prevent\$).ti,ab.
32. (injur\$ or damag\$ or detriment\$ or harm\$ or mistake\$ or error\$ or risk\$).ti,ab.
33. or/26-32
34. 25 and 33
35. animals/
36. humans/
37. 35 not (35 and 36)
38. 34 not 37
39. (letter or comment or editorial).pt.
40. 38 not 39

Cholesterol lowering diets in the general population

Embase 1974-2007 via Dialog Datastar

Searched 30/10/07

1. Diet-Therapy.DE.
2. low-fat-diet.DE.
3. Fat-Intake.DE.
4. Cholesterol-Intake.DE.
5. (diet\$3 ADJ (lipid\$1 OR cholesterol)).TI,AB.
6. (diet\$3 ADJ (change OR advice)).TI,AB.
7. (Diet\$3 ADJ (therap\$3 OR educat\$3 OR counsel\$4 OR intervention\$1 OR treatment\$1)).TI,AB.
8. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7
9. Cholesterol.W..DE.
- 10 Low-Density-Lipoprotein.DE.
11. Low-Density-Lipoprotein-Cholesterol.DE.
12. ((low OR lower OR restrict\$3 OR reduc\$5 OR decreas\$3 OR modify) NEAR (fat OR fats OR cholesterol)).TI,AB.
13. (lipid\$1 ADJ (lower OR reduc\$5 OR restrict\$3)).TI,AB.
14. 9 OR 10 OR 11 OR 12 OR 13
15. 8 AND 14
16. Meta-Analysis.DE.
17. (meta ADJ analy\$3 OR metaanaly\$3).TI,AB.
18. (systematic ADJ review\$1).TI,AB.

Familial hypercholesterolaemia: FINAL August 2008

Appendix B: Key clinical questions and searches

Familial hypercholesterolaemia: Final August 2008

19. 16 OR 17 OR 18
20. 15 AND 19
21. Animal.W..DE.
22. Nonhuman.W..DE.
23. 21 OR 22
24. Human.W..DE.
25. 23 NOT (23 AND 24)
26. 20 NOT 25

Medline 1950-2007 Searched via Dialog Datastar
Searched 29/10/07

- 1 DIET-THERAPY.DE.
2. DIET-FAT-RESTRICTED.DE.
3. DIETARY-FATS.DE.
4. CHOLESTEROL-DIETARY.DE.
5. (DIET\$3 ADJ (LIPID\$1 OR CHOLESTEROL)).TI,AB.
6. (DIET\$3 ADJ (CHANGE OR ADVICE)).TI,AB.
7. (DIET\$3 ADJ (THERAP\$3 OR EDUCAT\$3 OR COUNSEL\$4 OR INTERVENTION\$1 OR TREATMENT\$1)).TI,AB.
8. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7
9. ((LOW OR LOWER OR RESTRICT\$3 OR REDUC\$5 OR DECREAS\$3 OR MODIFY) NEAR (FAT OR FATS OR CHOLESTEROL)).TI,AB.
- 10 (LIPID\$1 ADJ (LOWER OR REDUC\$5 OR RESTRICT\$3)).TI,AB.
11. CHOLESTEROL.W..DE.
12. LIPOPROTEINS-LDL#.DE.
- 13 9 OR 10 OR 11 OR 12
14. 8 AND 13
15. META-ANALYSIS.DE.
16. PT=META-ANALYSIS
17. (META ADJ ANALY\$3 OR METAAANALY\$3).TI,AB.
18. (SYSTEMATIC ADJ REVIEW\$1).TI,AB.
19. 15 OR 16 OR 17 OR 18
20. 14 AND 19
21. ANIMAL=YES
22. HUMAN=YES
23. 21 NOT (21 AND 22)
24. 20 NOT 23

Risk of fetal abnormalities from taking lipid lowering drugs

Embase 1974-2007 via Dialog Datastar
searched 21/09/07
update search 21/09/07-06/12/07

Familial hypercholesterolaemia: FINAL August 2008

Appendix B: Key clinical questions and searches

1. HYDROXYMETHYLGLUTARYL-COENZYME-A-REDUCTASE-INHIBITOR.DE.
2. ATORVASTATIN.W..DE.
3. PRAVASTATIN.W..DE.
4. ROSUVASTATIN.W..DE.
5. SIMVASTATIN.W..DE.
6. (SIMVASTATIN OR PRAVASTATIN OR ROSUVASTATIN OR FLUVASTATIN OR ATORVASTATIN OR STATIN\$1).TI,AB.
7. (HMG ADJ COA).TI,AB.
8. ANION-EXCHANGE-RESIN.DE.
9. COLESTYRAMINE.W..DE.
- 10 COLESTIPOL.W..DE.
11. (ANION ADJ EXCHANGE ADJ RESIN\$1 OR CHOLESTYRAMINE OR COLESTYRAMIN\$ OR COLESTIPOL).TI,AB.
12. NICOTINIC-ACID.DE.
13. ACIPIMOX.W..DE.
14. (NIACIN OR NICOTINIC ADJ ACID\$1 OR ACIPIMOX).TI,AB.
15. CLOFIBRIC-ACID.DE.
16. BEZAFIBRATE.W..DE.
17. CIPROFIBRATE.W..DE.
18. FENOFIBRATE.W..DE.
19. GEMFIBROZIL.W..DE.
20. (FIBRATE\$1 OR BEZAFIBRATE OR CIPROFIBRATE OR FENOFIBRATE OR GEMFIBROZIL).TI,AB.
21. EZETIMIBE.W..DE.
22. EZETIMIBE.TI,AB.
23. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22
24. TERATOGENIC-AGENT.DE.
25. FETUS-DEATH.DE.
26. CONGENITAL-MALFORMATION.DE.
27. FETUS-DISEASE.DE.
28. SPONTANEOUS-ABORTION.DE.
29. PREGNANCY-OUTCOME.DE.
30. PREGNANCY-COMPLICATION.DE.
31. PRENATAL-DRUG-EXPOSURE.DE.
32. (TETRAOGEN\$2 OR TERATOGEN\$2).TI,AB.
33. ((FOETAL OR FETAL) ADJ (ABNORMAL\$5 OR ANOMAL\$3 OR DEFECT\$1)).TI,AB.
34. (CONGENITAL ADJ (ABNORMAL\$5 OR ANOMAL\$3 OR DEFECT\$1)).TI,AB.
35. STILLBIRTH.W..DE.
36. (ABORTION OR MISCARRIAGE OR MISCARRY).TI,AB.
37. ((PREGNAN\$4 OR MATERNAL) NEAR (COMPLICATION\$1 OR EXPOS\$3)).TI,AB.
38. (MATERNAL ADJ EXCHANGE).TI,AB.
39. (BIRTH ADJ (DEFECT\$1 OR ABNORMAL\$5 OR ANOMAL\$3)).TI,AB.

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40. 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 OR 39
41. 23 AND 40
42. NONHUMAN.W..DE.
43. ANIMAL=YES
44. 42 OR 43
45. HUMAN=YES
46. 44 NOT (44 AND 45)
47. 41 NOT 46

Medline 1950-2007

Searched 21/09/07

Update 21/09/07-06/12/07

1. HYDROXYMETHYLGLUTARYL-COA-REDUCTASE-INHIBITORS.DE.
2. SIMVASTATIN.W..DE.
3. PRAVASTATIN.W..DE.
4. (SIMVASTATIN OR PRAVASTATIN OR ROSUVASTATIN OR FLUVASTATIN OR ATORVASTATIN OR STATIN\$1).TI,AB.
5. (HMG ADJ COA).TI,AB.
6. ANION-EXCHANGE-RESINS.DE.
7. CHOLESTYRAMINE.W..DE.
8. COLESTIPOL.W..DE.
9. (ANION ADJ EXCHANGE ADJ RESIN\$1 OR CHOLESTYRAMINE OR COLESTYRAMIN\$ OR COLESTIPOL).TI,AB.
10. NIACIN.W..DE.
11. (NIACIN OR NICOTINIC ADJ ACID\$1 OR ACIPIMOX).TI,AB.
12. CLOFIBRIC-ACID.DE.
13. BEZAFIBRATE.W..DE.
14. BEZAFIBRATE.W..DE. OR GEMFIBROZIL.W..DE.
15. (CLOFIBRIC ADJ ACID\$1 OR FIBRATE\$1 OR BEZAFIBRATE OR CIPROFIBRATE OR FENOFIBRATE OR GEMFIBROZIL).TI,AB.
16. EZETIMIBE.TI,AB.
17. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16
18. TERATOGENS#.W..DE.
19. FETAL-DEATH.DE.
20. ABNORMALITIES-DRUG-INDUCED.DE.
21. ABORTION-SPONTANEOUS.DE.
22. PREGNANCY-OUTCOME.DE.
23. PREGNANCY-COMPLICATIONS.DE.
24. MATERNAL-EXPOSURE.DE.
25. MATERNAL-FETAL-EXCHANGE.DE.
26. FETUS-AB.DE. OR FETUS-DE.DE.
27. PREGNANCY-DE.DE.

Familial hypercholesterolaemia: FINAL August 2008

Appendix B: Key clinical questions and searches

28. (TETRAOGEN\$2 OR TERATOGEN\$2).TI,AB.
29. ((FOETAL OR FETAL) ADJ (ABNORMAL\$5 OR ANOMAL\$3 OR DEFECT\$1)).TI,AB.
30. ABNORMALITIES.W..DE.
31. (CONGENITAL ADJ (ABNORMAL\$5 OR ANOMAL\$3 OR DEFECT\$1)).TI,AB.
32. (ABORTION OR MISCARRIAGE OR MISCARRY).TI,AB.
33. ((PREGNAN\$4 OR MATERNAL) NEAR (COMPLICATION\$1 OR EXPOS\$3)).TI,AB.
34. (MATERNAL ADJ EXCHANGE).TI,AB.
- 35 (BIRTH ADJ (DEFECT\$1 OR ABNORMAL\$5 OR ANOMAL\$3)).TI,AB.
36. 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35
37. 17 AND 36
38. ANIMAL=YES
39. HUMAN=YES
40. 38 NOT (38 AND 39)
41. 37 NOT 40

Ezetimibe for children or adults with homozygous FH

Embase 1980-2007 wk 1

Searched 11/01/07

Update search 11/01/07-06/12/07

1. homozygous.ti,ab.
2. exp child/
3. pediatrics/
4. JUVENILE/
5. Adolescent/
6. (child\$ or pediatric\$ or paediatric\$ or boy\$ or girl\$ or juvenil\$ or teen\$ or adolescen\$ or minor or minors or youth\$).ti,ab.
7. or/1-6
8. Ezetimibe/
9. ezetimibe.ti,ab.
10. or/8-9
11. 7 and 10
12. animals/
13. Nonhuman/
14. 12 or 13
15. humans/
16. 14 not (14 and 15)
17. 11 not 16
18. (letter or comment or editorial).pt.
19. 17 not 18

Medline 1950 2007 jan wk 1

Familial hypercholesterolaemia: FINAL August 2008

Appendix B: Key clinical questions and searches

Familial hypercholesterolaemia: Final August 2008

Searched 11/01/07

Update search 11/01/07-06/12/07

1. Homozygote/
2. homozygous.ti,ab.
3. exp Child/
4. Pediatrics/
5. Adolescent/
6. Minors/
7. (child\$ or pediatric\$ or paediatric\$ or boy\$ or girl\$ or juvenil\$ or teen\$ or adolescen\$ or minor or minors or youth\$.ti,ab.
8. or/1-7
9. ezetimibe.ti,ab.
10. 8 and 9
11. animals/
12. humans/
13. 11 not (11 and 12)
14. 10 not 13
15. (letter or comment or editorial).pt.
16. 14 not 15

Familial hypercholesterolaemia: FINAL August 2008

Appendix B: Key clinical questions and searches