

Appendix A: Literature search strategies

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Search strategies used for the cirrhosis guideline are outlined below and were run in accordance with the methodology in the NICE guidelines manual 2012.^{NICE2012} All searches were run up to **24th August 2015** unless stated otherwise. Any studies added to the databases after this date (even those published prior to this date) were not included unless specifically stated in the text. We do not routinely search for electronic, ahead of print or 'online early' publications. Where possible searches were limited to retrieve material published in English.

Table 1: Database date parameters

Database	Dates searched
Medline	1946 – 24 August 2015
Embase	1980 – 24 August 2015
The Cochrane Library	Cochrane Reviews to 2015 Issue 8 of 12 CENTRAL to 2015 Issue 7 of 12 DARE, HTA and NHSEED to 2015 Issue 2 of 4

Searches for the **clinical reviews** were run in Medline (OVID) and Embase (OVID) except the risk tools question (A.4.2) which was run in Medline only. Additional searches were run in the Cochrane Library, see Table 2.

Table 2: Databases searched

Question	Question number	Databases
Diagnostic tests	A.4.3	Medline, Embase, Cochrane Library
Frequency of surveillance for HCC	A.4.5	Medline, Embase, Cochrane Library
Frequency of surveillance for varices	A.4.6	Medline, Embase, Cochrane Library
Management of acute hepatic encephalopathy	A.4.11	Medline, Embase, Cochrane Library
Primary prevention of bacterial infections	A.4.8	Medline, Embase, Cochrane Library
Prophylaxis of variceal haemorrhages	A.4.7	Medline, Embase, Cochrane Library
Risk assessment tools	A.4.2	Medline
Risk factors	A.4.1	Medline, Embase
Severity risk tools	A.4.4	Medline, Embase
TIPS vs LVP for ascites	A.4.9	Medline, Embase, Cochrane Library
Volume replacers in hepatorenal syndrome	A.4.10	Medline, Embase, Cochrane Library

Searches for **intervention and diagnostic studies** were usually constructed using a PICO format where population (P) terms were combined with Intervention (I) and sometimes Comparison (C) terms. An intervention can be a drug, a procedure or a diagnostic test. Outcomes (O) are rarely used in search strategies for interventions. Search filters were also added to the search where appropriate.

Searches for **prognostic studies** were usually constructed combining population terms with prognostic variable terms and sometimes outcomes. Search filters were added to the search where appropriate.

Searches for the **health economic reviews** were run in Medline (OVID), Embase (OVID), the NHS Economic Evaluations Database (NHS EED), the Health Technology Assessment (HTA) database and the Health Economic Evaluation Database (HEED). NHS EED and HTA databases were hosted by the Centre for Research and Dissemination (CRD). The Health Economic Evaluation Database (HEED) ceased production in 2014 with access ceasing in January 2015. For the final dates of HEED searches, please see individual economic questions.

For Medline and Embase an economic filter (instead of a study type filter) was added to the same clinical search strategy. Searches in CRD and HEED were constructed using population terms only.

A.2 Population search strategies

A.2.1 Standard cirrhosis population

The standard population was not used in questions A.4.2, A.4.5, A.4.7, A.4.9, A.4.10, A.4.11, A.5.2 and A.5.2.

Medline search terms

1.	exp liver cirrhosis/
2.	fibrosis/ and liver/
3.	((liver* or hepat*) adj5 fibro*) or cirrho*).ti,ab.
4.	or/1-3

Embase search terms

1.	exp liver cirrhosis/
2.	fibrosis/ and liver/
3.	((liver* or hepat*) adj5 fibro*) or cirrho*).ti,ab.
4.	or/1-3

Cochrane search terms

#1.	[mh "liver cirrhosis"]
#2.	(cirrho* or ((liver or hepat*) near/5 fibro*)):ti,ab
#3.	{or #1-#2}

A.3 Study filter search terms

A.3.1 Systematic review (SR) search terms

Medline search terms

1.	meta-analysis/
2.	meta-analysis as topic/
3.	(meta analy* or metanaly* or metaanaly*).ti,ab.
4.	((systematic* or evidence*) adj3 (review* or overview*).ti,ab.
5.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
6.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
7.	(search* adj4 literature).ab.
8.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
9.	cochrane.jw.
10.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
11.	or/1-10

Embase search terms

1.	systematic review/
2.	meta-analysis/
3.	(meta analy* or metanaly* or metaanaly*).ti,ab.
4.	((systematic or evidence) adj3 (review* or overview*).ti,ab.
5.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
6.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
7.	(search* adj4 literature).ab.
8.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.

9.	cochrane.jw.
10.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
11.	or/1-10

A.3.2 Randomised controlled trials (RCT) search terms

Medline search terms

1.	randomized controlled trial.pt.
2.	controlled clinical trial.pt.
3.	randomi#ed.ab.
4.	placebo.ab.
5.	randomly.ab.
6.	clinical trials as topic.sh.
7.	trial.ti.
8.	or/1-7

Embase search terms

1.	random*.ti,ab.
2.	factorial*.ti,ab.
3.	(crossover* or cross over*).ti,ab.
4.	((doubl* or singl*) adj blind*).ti,ab.
5.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
6.	crossover procedure/
7.	double blind procedure/
8.	single blind procedure/
9.	randomized controlled trial/
10.	or/1-9

A.3.3 Observational studies (OBS) search terms

Medline search terms

1.	epidemiologic studies/
2.	exp case control studies/
3.	exp cohort studies/
4.	cross-sectional studies/
5.	case control.ti,ab.
6.	(cohort adj (study or studies or analys*)).ti,ab.
7.	((follow up or observational or uncontrolled or non randomi#ed or nonrandomi#ed or epidemiologic*) adj (study or studies)).ti,ab.
8.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort*)).ti,ab.
9.	or/1-8

Embase search terms

1.	clinical study/
2.	exp case control study/
3.	family study/
4.	longitudinal study/
5.	retrospective study/

6.	prospective study/
7.	cross-sectional study/
8.	cohort analysis/
9.	follow-up/
10.	cohort*.ti,ab.
11.	9 and 10
12.	case control.ti,ab.
13.	(cohort adj (study or studies or analys*)).ti,ab.
14.	((follow up or observational or uncontrolled or non randomi#ed or nonrandomi#ed or epidemiologic*) adj (study or studies)).ti,ab.
15.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort*)).ti,ab.
16.	or/1-8,11-15

A.3.4 Prognostic studies (PROG) search terms

Medline search terms

1.	predict.ti.
2.	(validat* or rule*).ti,ab.
3.	(predict* and (outcome* or risk* or model*)).ti,ab.
4.	((history or variable* or criteria or scor* or characteristic* or finding* or factor*) and (predict* or model* or decision* or identif* or prognos*)).ti,ab.
5.	decision*.ti,ab. and logistic models/
6.	(decision* and (model* or clinical*)).ti,ab.
7.	(prognostic and (history or variable* or criteria or scor* or characteristic* or finding* or factor* or model*)).ti,ab.
8.	(stratification or discrimination or discriminate or c statistic or "area under the curve" or auc or calibration or indices or algorithm or multivariable).ti,ab.
9.	roc curve/
10.	or/1-9

Embase search terms

1.	predict.ti.
2.	(validat* or rule*).ti,ab.
3.	(predict* and (outcome* or risk* or model*)).ti,ab.
4.	((history or variable* or criteria or scor* or characteristic* or finding* or factor*) and (predict* or model* or decision* or identif* or prognos*)).ti,ab.
5.	decision*.ti,ab. and statistical model/
6.	(decision* and (model* or clinical*)).ti,ab.
7.	(prognostic and (history or variable* or criteria or scor* or characteristic* or finding* or factor* or model*)).ti,ab.
8.	(stratification or discrimination or discriminate or c statistic or "area under the curve" or auc or calibration or indices or algorithm or multivariable).ti,ab.
9.	receiver operating characteristic/
10.	or/1-9

A.3.5 Diagnostic accuracy studies (DIAG) search terms

medline search terms

1.	exp "sensitivity and specificity"/
2.	(sensitivity or specificity).ti,ab.
3.	((pre test or pretest or post test) adj probability).ti,ab.
4.	(predictive value* or ppv or npv).ti,ab.
5.	likelihood ratio*.ti,ab.
6.	likelihood function/
7.	(roc curve* or auc).ti,ab.
8.	(diagnos* adj3 (performance* or accurac* or utilit* or value* or efficien* or effectiveness)).ti,ab.
9.	gold standard.ab.
10.	or/1-9

Embase search terms

1.	exp "sensitivity and specificity"/
2.	(sensitivity or specificity).ti,ab.
3.	((pre test or pretest or post test) adj probability).ti,ab.
4.	(predictive value* or ppv or npv).ti,ab.
5.	likelihood ratio*.ti,ab.
6.	(roc curve* or auc).ti,ab.
7.	(diagnos* adj3 (performance* or accurac* or utilit* or value* or efficien* or effectiveness)).ti,ab.
8.	diagnostic accuracy/
9.	diagnostic test accuracy study/
10.	gold standard.ab.
11.	or/1-10

A.3.6 Health economics (HE) search terms

Medline search terms

1.	economics/
2.	value of life/
3.	exp "costs and cost analysis"/
4.	exp economics, hospital/
5.	exp economics, medical/
6.	economics, nursing/
7.	economics, pharmaceutical/
8.	exp "fees and charges"/
9.	exp budgets/
10.	budget*.ti,ab.
11.	cost*.ti.
12.	(economic* or pharmaco?economic*).ti.
13.	(price* or pricing*).ti,ab.
14.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
15.	(financ* or fee or fees).ti,ab.
16.	(value adj2 (money or monetary)).ti,ab.
17.	or/1-16

Embase search terms

1.	health economics/
2.	exp economic evaluation/
3.	exp health care cost/
4.	exp fee/
5.	budget/
6.	funding/
7.	budget*.ti,ab.
8.	cost*.ti.
9.	(economic* or pharmaco?economic*).ti.
10.	(price* or pricing*).ti,ab.
11.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
12.	(financ* or fee or fees).ti,ab.
13.	(value adj2 (money or monetary)).ti,ab.
14.	or/1-13

A.3.7 Quality of life (QOL) search terms

Medline search terms

1.	quality-adjusted life years/
2.	sickness impact profile/
3.	(quality adj2 (wellbeing or well-being)).ti,ab.
4.	sickness impact profile.ti,ab.
5.	disability adjusted life.ti,ab.
6.	(qal* or qtime* or qwb* or daly*).ti,ab.
7.	(euroqol* or eq5d* or eq 5d*).ti,ab.
8.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
9.	(health utility* or utility score* or disutilit*).ti,ab.
10.	(hui or hui1 or hui2 or hui3).ti,ab.
11.	health* year* equivalent*.ti,ab.
12.	(hye or hyes).ti,ab.
13.	rosser.ti,ab.
14.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
15.	(sf36 or sf 36 or short form 36 or shortform 36 or shortform36).ti,ab.
16.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
17.	(sf12 or sf 12 or short form 12 or shortform 12 or shortform12).ti,ab.
18.	(sf8 or sf 8 or short form 8 or shortform 8 or shortform8).ti,ab.
19.	(sf6 or sf 6 or short form 6 or shortform 6 or shortform6).ti,ab.
20.	or/1-19

Embase search terms

1.	quality adjusted life year/
2.	"quality of life index"/
3.	short form 12/ or short form 20/ or short form 36/ or short form 8/
4.	sickness impact profile/
5.	(quality adj2 (wellbeing or well-being)).ti,ab.

6.	sickness impact profile.ti,ab.
7.	disability adjusted life.ti,ab.
8.	(qal* or qtime* or qwb* or daly*).ti,ab.
9.	(euroqol* or eq5d* or eq 5d*).ti,ab.
10.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
11.	(health utility* or utility score* or disutilit*).ti,ab.
12.	(hui or hui1 or hui2 or hui3).ti,ab.
13.	health* year* equivalent*.ti,ab.
14.	(hye or hyes).ti,ab.
15.	rosser.ti,ab.
16.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
17.	(sf36 or sf 36 or short form 36 or shortform 36 or shortform36).ti,ab.
18.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
19.	(sf12 or sf 12 or short form 12 or shortform 12 or shortform12).ti,ab.
20.	(sf8 or sf 8 or short form 8 or shortform 8 or shortform8).ti,ab.
21.	(sf6 or sf 6 or short form 6 or shortform 6 or shortform6).ti,ab.
22.	or/1-21

A.3.8 Economic modelling (MOD) search terms

Medline search terms

1.	exp models, economic/
2.	*models, theoretical/
3.	*models, organizational/
4.	markov chains/
5.	monte carlo method/
6.	exp decision theory/
7.	(markov* or monte carlo).ti,ab.
8.	econom* model*.ti,ab.
9.	(decision* adj2 (tree* or analy* or model*)).ti,ab.
10.	or/1-9

Embase search terms

1.	statistical model/
2.	exp economic aspect/
3.	1 and 2
4.	*theoretical model/
5.	*nonbiological model/
6.	stochastic model/
7.	decision theory/
8.	decision tree/
9.	monte carlo method/
10.	(markov* or monte carlo).ti,ab.
11.	econom* model*.ti,ab.
12.	(decision* adj2 (tree* or analy* or model*)).ti,ab.
13.	or/3-12

A.3.9 Excluded study designs and publication types

The following study designs and publication types were removed from retrieved results using the NOT operator.

Medline search terms

1.	letter/
2.	editorial/
3.	news/
4.	exp historical article/
5.	anecdotes as topic/
6.	comment/
7.	case report/
8.	(letter or comment*).ti.
9.	or/1-8
10.	randomized controlled trial/ or random*.ti,ab.
11.	9 not 10
12.	animals/ not humans/
13.	exp animals, laboratory/
14.	exp animal experimentation/
15.	exp models, animal/
16.	exp rodentia/
17.	(rat or rats or mouse or mice).ti.
18.	or/11-17

Embase search terms

1.	letter.pt. or letter/
2.	note.pt.
3.	editorial.pt.
4.	case report/ or case study/
5.	(letter or comment*).ti.
6.	or/1-5
7.	randomized controlled trial/ or random*.ti,ab.
8.	6 not 7
9.	animal/ not human/
10.	nonhuman/
11.	exp animal experiment/
12.	exp experimental animal/
13.	animal model/
14.	exp rodent/
15.	(rat or rats or mouse or mice).ti.
16.	or/8-15

A.4 Searches for specific questions

A.4.1 Risk factors

- What are the risk factors that indicate the populations at specific risk for cirrhosis?

Medline search terms

1.	Standard population (A.2)
2.	Excluded study designs and publication types (A.3.9)
3.	1 not 2
4.	exp *diabetes mellitus, type 2/
5.	(diabet* adj2 (type 2 or type2 or type ii or type two)).ti.
6.	(dm2 or t2d*).ti.
7.	(diabet* adj2 (noninsulin or non insulin or slow-onset or slow onset or adult-onset or adult onset)).ti.
8.	exp *obesity/
9.	exp *overweight/
10.	(obesity or obese).ti.
11.	(overweight or over-weight or over weight or overeating or over eating or over-eating).ti.
12.	*body mass index/
13.	(body mass index or bmi).ti.
14.	*hepatitis b/ or *hepatitis c/
15.	(hepatitis adj (b or c)).ti.
16.	(drinker* or (drink* adj2 use*) or ((alcohol* or drink*) adj5 (abstinen* or abstain* or abus* or addict* or attenuat* or binge* or crav* or dependen* or detox* or disease* or disorder* or excessiv* or harm* or hazard* or heavy or high risk or intoxicat* or misus* or overdos* or (over adj dos*) or problem* or rehab* or reliance or reliant or relaps* or withdraw*))).ti.
17.	exp *alcohol-related disorders/
18.	alcoholi*.ti.
19.	or/4-18
20.	exp risk/
21.	prevalence/
22.	incidence/
23.	(risk* or prevalence* or incidence* or predict* or associat*).ti.
24.	or/20-23
25.	Study filters SR (A.3.1) or OBS (A.3.3) or PROG (A.3.4)
26.	3 and 19 and (24 or 25)
27.	limit 26 to English language
	See Table 1 for date parameters

Embase search terms

1.	Standard population (A.2)
2.	Excluded study designs and publication types (A.3.9)
3.	1 not 2
4.	exp *non insulin dependent diabetes mellitus/
5.	(diabet* adj2 (type 2 or type2 or type ii or type two)).ti.
6.	(dm2 or t2d*).ti.
7.	(diabet* adj2 (noninsulin or non insulin or slow-onset or slow onset or adult-onset or adult onset)).ti.
8.	exp *obesity/
9.	(obesity or obese).ti.
10.	(overweight or over-weight or over weight or overeating or over eating or over-

	eating).ti.
11.	*body mass/
12.	(body mass index or bmi).ti.
13.	*hepatitis b/ or *hepatitis c/
14.	(hepatitis adj (b or c)).ti.
15.	(drinker* or (drink* adj2 use*) or ((alcohol* or drink*) adj5 (abstinen* or abstain* or abus* or addict* or attenuat* or binge* or crav* or dependen* or detox* or disease* or disorder* or excessiv* or harm* or hazard* or heavy or high risk or intoxicat* or misus* or overdos* or (over adj dos*) or problem* or rehab* or reliance or reliant or relaps* or withdraw*))).ti.
16.	*alcoholism/
17.	alcoholi*.ti.
18.	or/4-17
19.	exp *risk/
20.	*prevalence/
21.	*incidence/
22.	(risk* or prevalence* or incidence* or predict* or associat*).ti,ab.
23.	or/19-22
24.	Study filters SR (A.3.1) or OBS (A.3.3) or PROG (A.3.4)
25.	3 and 18 and (23 or 24)
26.	limit 25 to English language
	See Table 1 for date parameters

A.4.2 Risk assessment tools

- Are there any validated risk tools that indicate the populations at specific risk for cirrhosis?

Medline search terms

1.	(cirrho* adj5 (risk* adj3 (score* or stratif* or assess* or calculat* or engine* or equation* or algorithm* or chart* or table* or predict* or function*))).ti,ab.
2.	(cirrho* adj5 ((decision or predict* or assess* or screen* or score* or scoring or stratif* or prognos* or logistic*) adj3 (tool* or rule* or instrument*1 or index* or test* or technique* or analys* or model*))).ti,ab.
3.	1 or 2
4.	animals/ not humans/
5.	animals, laboratory/
6.	exp animal experiment/
7.	exp animal model/
8.	exp rodentia/
9.	(rat or rats or mouse or mice).ti.
10.	or/4-9
11.	3 not 10
12.	limit 11 to English language
	See Table 1 for date parameters

A.4.3 Diagnostic tests

Searches for the following four questions were run as one search:

- In people with suspected (or under investigation for) cirrhosis:

- a) What is the most accurate blood fibrosis test to identify whether cirrhosis is present?
- b) What is the most accurate non-invasive imaging test to identify whether cirrhosis is present?
- c) Is the most accurate blood fibrosis test more accurate compared to an individual blood test to identify whether cirrhosis is present?
- d) Is a combination of 2 non-invasive tests (a blood fibrosis test and an imaging test) more accurate compared to a blood fibrosis test alone or an imaging test alone to identify whether cirrhosis is present?

Medline search terms

1.	Standard population (A.2.1)
2.	Excluded study designs and publication types (A.3.9)
3.	1 not 2
4.	exp diagnostic tests, routine/
5.	((blood or liver) adj2 test*).ti,ab.
6.	'enhanced liver fibrosis'.ti,ab.
7.	(fibrotest* or fibrosis test*).ti,ab.
8.	elasticity imaging techniques/ or exp ultrasonography, doppler/
9.	((transient or magnetic or mr) adj3 elastogra*).ti,ab.
10.	fibroscan.ti,ab.
11.	(acoustic radiation force impulse or arfi).ti,ab.
12.	(ultrasound* or ultrason* or sonograph* or echograph*).ti,ab.
13.	ultrasonography/
14.	((shear or wave) adj4 (elastogr* or imag*)).ti,ab.
15.	or/4-14
16.	Study filters SR (A.3.1) or RCT (A.3.2) or DIAG (A.3.5)
17.	3 and 15 and 16
18.	limit 17 to English language
	See Table 1 for date parameters

Embase search terms

1.	Standard population (A.2)
2.	Excluded study designs and publication types (A.3.9)
3.	1 not 2
4.	diagnostic test/
5.	((blood or liver) adj2 test*).ti,ab.
6.	'enhanced liver fibrosis'.ti,ab.
7.	(fibrotest* or fibrosis test*).ti,ab.
8.	*echography/ or *doppler echography/ or *elastography/
9.	((transient or magnetic or mr) adj3 elastogra*).ti,ab.
10.	fibroscan.ti,ab.
11.	(acoustic radiation force impulse or arfi).ti,ab.
12.	((shear or wave) adj4 (elastogr* or imag*)).ti,ab.
13.	or/4-12
14.	Study filters SR (A.3.1) or RCT (A.3.2) or DIAG (A.3.5)
15.	3 and 13 and 14
16.	limit 15 to English language

	See Table 1 for date parameters
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Cochrane search terms

#1.	Standard population (A.2)
#2.	MeSH descriptor: [diagnostic tests, routine] explode all trees
#3.	((blood or liver) near/2 test*):ti,ab
#4.	enhanced liver fibrosis:ti,ab
#5.	(fibrotest* or fibrosis test*):ti,ab
#6.	MeSH descriptor: [elasticity imaging techniques] explode all trees
#7.	MeSH descriptor: [ultrasonography, doppler] explode all trees
#8.	MeSH descriptor: [ultrasonography] this term only
#9.	((transient or magnetic or mr) near/3 elastogra*):ti,ab
#10.	fibroscan:ti,ab
#11.	(acoustic radiation force impulse or arfi):ti,ab
#12.	(ultrasound* or ultrason* or sonograph* or echograph*):ti,ab
#13.	((shear or wave) near/4 (elastogr* or imag*)):ti,ab
#14.	{or #2-#13}
#15.	#1 and #14
	See Table 1 for date parameters

A.4.4 Severity risk tools

Searches for the following two questions were run as one search:

- Which risk assessment tool is the most accurate and cost-effective for predicting the risk of morbidity and mortality in [adults-people](#) with compensated cirrhosis?
- When (at what severity score on the risk assessment tool) should people with cirrhosis be referred to specialist care?

Medline search terms

1.	Standard population (A.2)
2.	Excluded study designs and publication types (A.3.9)
3.	1 not 2
4.	(child pugh or childpugh or child na or childna or meld or ukeld).ti,ab.
5.	(child turcotte or childturcotte).ti,ab.
6.	model for end stage liver disease.ti,ab.
7.	model for endstage liver disease.ti,ab.
8.	or/4-7
9.	elasticity imaging techniques/
10.	((transient or magnetic or mr) adj3 elastogra*):ti,ab.
11.	fibroscan.ti,ab.
12.	or/9-11
13.	8 or 12
14.	Study filters OBS (A.3.3) or PROG (A.3.4)
15.	3 and 13 and 14
16.	limit 15 to English language
	See Table 1 for date parameters

Embase search terms

1.	Standard population (A.2)
2.	Excluded study designs and publication types (A.3.9)
3.	1 not 2
4.	*child pugh score/
5.	(child pugh or childpugh or child na or childna or meld or ukeld).ti,ab.
6.	(child turcotte or childturcotte).ti,ab.
7.	*model for end stage liver disease score/
8.	model for end stage liver disease.ti,ab.
9.	model for endstage liver disease.ti,ab.
10.	or/4-9
11.	*elastography/
12.	((transient or magnetic or mr) adj3 elastogra*).ti,ab.
13.	fibroscan.ti,ab.
14.	or/11-13
15.	10 or 14
16.	Study filters OBS (A.3.3) or PROG (A.3.4)
17.	3 and 15 and 16
18.	limit 17 to English language
	See Table 1 for date parameters

A.4.5 Frequency of surveillance for HCC

- When and how frequently should surveillance testing be offered for the early detection of hepatocellular carcinoma in people with cirrhosis?

Medline search terms

1.	carcinoma, hepatocellular/
2.	liver neoplasms/
3.	((hepatocellular or liver or hepatic or hepato) adj2 (cancer or carcinoma* or neoplasm*)).ti,ab.
4.	(hepatoma* or hepatocarcinoma* or hcc).ti,ab.
5.	or/1-4
6.	exp early diagnosis/
7.	surveillance.ti,ab,hw.
8.	screen*.ti,ab.
9.	(early and (detect* or diagnos* or stage*)).ti,ab.
10.	or/6-9
11.	5 and 10
12.	Excluded study designs and publication types (A.3.9)
13.	11 not 12
14.	Study filters SR (A.3.1) or RCT (A.3.2) or OBS (A.3.3)
15.	13 and 14
16.	limit 15 to English language
	See Table 1 for date parameters

Embase search terms

1.	liver cell carcinoma/
2.	liver carcinoma/

3.	liver cancer/
4.	(hepatoma* or hepatocarcinoma* or hcc).ti,ab.
5.	((hepatocellular or liver or hepatic or hepato) adj2 (cancer or carcinoma* or neoplasm*)).ti,ab.
6.	or/1-5
7.	early diagnosis/
8.	surveillance.ti,ab,hw.
9.	screen*.ti,ab.
10.	(early and (detect* or diagnos* or stage*)).ti,ab.
11.	or/7-10
12.	6 and 11
13.	Excluded study designs and publication types (A.3.9)
14.	12 not 13
15.	Study filters SR (A.3.1) or RCT (A.3.2) or OBS (A.3.3)
16.	14 and 15
17.	limit 16 to English language
	See Table 1 for date parameters

Cochrane search terms

#1.	MeSH descriptor: [carcinoma, hepatocellular] explode all trees
#2.	MeSH descriptor: [liver neoplasms] explode all trees
#3.	(hepatoma* or hepatocarcinoma* or hcc):ti,ab
#4.	((hepatocellular or liver or hepatic or hepato) near/2 (cancer or carcinoma* or neoplasm*)).ti,ab
#5.	{or #1-#4}
#6.	MeSH descriptor: [early diagnosis] explode all trees
#7.	(surveillance or screen*):ti,ab
#8.	(early and (detect* or diagnos* or stage*)).ti,ab
#9.	{or #6-#8}
#10.	#5 and #9
	See Table 1 for date parameters

A.4.6 Frequency of surveillance for varices

- How frequently should surveillance testing using endoscopy be offered for the detection of oesophageal varices and isolated gastric varices in people with cirrhosis?

Medline search terms

1.	Standard population (A.2)
2.	Excluded study designs and publication types (A.3.9)
3.	1 not 2
4.	endoscopy, gastrointestinal/ or capsule endoscopy/ or double-balloon enteroscopy/ or duodenoscopy/ or esophagoscopy/ or gastroscopy/
5.	((gi or stomach* or gastric or gastrointest* or gastro-intest* or varic* or varix or ulcer* or duod* or oesoph* or esophag*) adj3 endoscop*).ti,ab.
6.	(ogd or egd or ugie or duodenoscop* or gastroscop* or esophagogastroduodenoscop* or oesophagogastroduodenoscop*).ti,ab.
7.	or/4-6
8.	"esophageal and gastric varices"/

9.	((gi or stomach* or gastric or gastrointest* or gastro-intest* or duod* or oesoph* or esophag*) adj3 (varic* or varix*)).ti,ab.
10.	(detect* or diag* or surveillance* or test* or imag* or assess*).ti,ab.
11.	8 or 9
12.	10 and 11
13.	7 or 12
14.	Study filters SR (A.3.1) or RCT (A.3.2) or OBS (A.3.3)
15.	3 and 13 and 14
16.	limit 15 to English language
	See Table 1 for date parameters

Embase search terms

1.	Standard population (A.2)
2.	Excluded study designs and publication types (A.3.9)
3.	1 not 2
4.	*gastrointestinal endoscopy/ or *esophagoscopy/ or *duodenoscopy/ or *gastroscopy/ or *capsule endoscopy/ or *double-balloon enteroscopy/
5.	((gi or stomach* or gastric or gastrointest* or gastro-intest* or varic* or varix or ulcer* or duod* or oesoph* or esophag*) adj3 endoscop*).ti,ab.
6.	(ogd or egd or ugie or duodenoscop* or gastroscop* or esophagogastroduodenoscop* or oesophagogastroduodenoscop*).ti,ab.
7.	or/4-6
8.	*stomach varices/
9.	*esophagus varices/
10.	((gi or stomach* or gastric or gastrointest* or gastro-intest* or duod* or oesoph* or esophag*) adj3 (varic* or varix*)).ti,ab.
11.	or/8-10
12.	(detect* or diag* or surveillance* or test* or imag* or assess*).ti,ab.
13.	11 and 12
14.	7 or 13
15.	Study filters SR (A.3.1) or RCT (A.3.2) or OBS (A.3.3)
16.	3 and 14 and 15
17.	limit 16 to English language
	See Table 1 for date parameters

Cochrane search terms

#1.	Standard population (A.2)
#2.	MeSH descriptor: [esophagoscopy] this term only
#3.	MeSH descriptor: [endoscopy, gastrointestinal] this term only
#4.	MeSH descriptor: [duodenoscopy] this term only
#5.	MeSH descriptor: [gastroscopy] this term only
#6.	MeSH descriptor: [capsule endoscopy] this term only
#7.	MeSH descriptor: [double-balloon enteroscopy] this term only
#8.	((gi or stomach* or gastric or gastrointest* or gastro-intest* or varic* or varix or ulcer* or duod* or oesoph* or esophag*) near/3 endoscop*).ti,ab
#9.	(ogd or egd or ugie or duodenoscop* or gastroscop* or esophagogastroduodenoscop* or oesophagogastroduodenoscop*).ti,ab
#10.	{or #2-#9}

#11.	MeSH descriptor: [esophageal and gastric varices] this term only
#12.	((gi or stomach* or gastric or gastrointest* or gastro-intest* or duod* or oesoph* or esophag*) near/3 (varic* or varix*)):ti,ab
#13.	(detect* or diag* or surveillance* or test* or imag* or assess*):ti,ab
#14.	#11 or #12
#15.	#13 and #14
#16.	#10 or #15
#17.	#1 and #16
	See Table 1 for date parameters

A.4.7 Prophylaxis of variceal haemorrhages

Searches for the following three questions were run as one search:

- What is the clinical- and cost- effectiveness of non-selective beta-blockers for the primary prevention of bleeding in people with oesophageal varices due to cirrhosis?
- What is the clinical- and cost- effectiveness of [endoscopic](#) band ligation for the primary prevention of bleeding in people with oesophageal varices due to cirrhosis?
- What is the clinical- and cost- effectiveness of non-selective beta-blockers compared with [endoscopic](#) band ligation for the primary prevention of bleeding in people with oesophageal varices due to cirrhosis?

Medline search terms

1.	"esophageal and gastric varices"/
2.	((oesophag* or esophag*) adj3 (varic* or varix)).ti,ab.
3.	((varix or varic*) adj2 bleed* adj3 (prevent* or prophyla*)):ti,ab.
4.	or/1-3
5.	adrenergic beta-antagonists/
6.	propranolol/
7.	nadolol/
8.	(carvedilol or propranolol or bedranol or inderal or syprol or nadolol or corgard or solgol).ti,ab.
9.	((beta or b) adj3 (block* or antagonist*)):ti,ab.
10.	or/5-9
11.	ligation/
12.	(ligat* or (endoscop* adj2 therap*) or ebl or evl or band* or multiband*).ti,ab.
13.	or/11-12
14.	10 or 13
15.	4 and 14
16.	Excluded study designs and publication types (A.3.9)
17.	15 not 16
18.	Study filters SR (A.3.1) or RCT (A.3.2)
19.	17 and 18
20.	limit 19 to English language
	See Table 1 for date parameters

Embase search terms

1.	exp esophagus varices/
2.	((oesophag* or esophag*) adj3 (varic* or varix)).ti,ab.

3.	((varix or varic*) adj2 bleed* adj3 (prevent* or prophyla*)):ti,ab.
4.	or/1-3
5.	*beta adrenergic receptor blocking agent/
6.	*propranolol/
7.	*carvedilol/
8.	*nadolol/
9.	(carvedilol or propranolol or bedranol or inderal or syprol or nadolol or corgard or solgol):ti,ab.
10.	((beta or b) adj3 (block* or antagonist*)):ti,ab.
11.	or/5-10
12.	exp *ligation/
13.	*endoscopic therapy/
14.	(ligat* or (endoscop* adj2 therap*) or ebl or evl or band* or multiband*):ti,ab.
15.	or/12-14
16.	11 or 15
17.	4 and 16
18.	Excluded study designs and publication types (A.3.9)
19.	17 not 18
20.	Study filters SR (A.3.1) or RCT (A.3.2)
21.	19 and 20
22.	Limit 21 to English language
	See Table 1 for date parameters

Cochrane search terms

#1.	[mh ^"esophageal and gastric varices"]
#2.	((oesophag* or esophag*) near/3 (varic* or varix)):ti,ab
#3.	((varix or varic*) near/2 bleed* near/3 (prevent* or prophyla*)):ti,ab
#4.	#1 or #2 or #3
#5.	[mh ^"adrenergic beta-antagonists"]
#6.	[mh ^propranolol]
#7.	[mh ^nadolol]
#8.	(carvedilol or propranolol or bedranol or inderal or syprol or nadolol or corgard or solgol):ti,ab
#9.	((beta or b) near/3 (block* or antagonist*)):ti,ab
#10.	{or #5-#9}
#11.	[mh ^ligation]
#12.	(ligat* or (endoscop* near/2 therap*) or ebl or evl or band* or multiband*):ti,ab
#13.	#11 or #12
#14.	#10 or #13
#15.	#4 and #14
	See Table 1 for date parameters

A.4.8 Primary prevention of bacterial infections

Searches for the following two questions were run as one search:

- What is the most clinically and cost effective prophylactic antibiotic for the primary prevention of bacterial infections in people with cirrhosis and upper gastrointestinal bleeding?

- What is the clinical and cost effectiveness of antibiotics compared with placebo for the primary prevention of spontaneous bacterial peritonitis (SBP) in patients with cirrhosis and ascites?

Medline search terms

1.	Standard population (A.2)
2.	Excluded study designs and publication types (A.3.9)
3.	1 not 2
4.	exp antibacterial agents/
5.	antibiotic*.ti,ab.
6.	(anti-bacterial* or antibacterial*).ti,ab.
7.	(anti-microbial* or antimicrobial*).ti,ab.
8.	(anti-mycobacterial* or antimycobacterial*).ti,ab.
9.	(bacteriocid* or bactericid*).ti,ab.
10.	exp antibiotic prophylaxis/
11.	or/4-10
12.	Study filters SR (A.3.1) or RCT (A.3.2)
13.	3 and 11 and 12
14.	Limit 13 to English language
	See Table 1 for date parameters

Embase search terms

1.	Standard population (A.2)
2.	Excluded study designs and publication types (A.3.9)
3.	1 not 2
4.	exp *antibiotic agent/
5.	*antibiotic prophylaxis/
6.	antibiotic*.ti,ab.
7.	(anti-bacterial* or antibacterial*).ti,ab.
8.	(anti-microbial* or antimicrobial*).ti,ab.
9.	(anti-mycobacterial* or antimycobacterial*).ti,ab.
10.	(bacteriocid* or bactericid*).ti,ab.
11.	or/4-10
12.	Study filters SR (A.3.1) or RCT (A.3.2)
13.	3 and 11 and 12
14.	Limit 13 to English language
	See Table 1 for date parameters

Cochrane search terms

#1.	Standard population (A.2)
#2.	MeSH descriptor: [antibiotic prophylaxis] explode all trees
#3.	MeSH descriptor: [anti-bacterial agents] explode all trees
#4.	(antibiotic* or anti-bacterial* or antibacterial* or anti-microbial* or antimicrobial* or anti-mycobacterial* or antimycobacterial* or bacteriocid* or bactericid*):ti,ab,kw
#5.	{or #2-#4}
#6.	#1 and #5
	See Table 1 for date parameters

A.4.9 TIPS vs LVP for ascites

- What is the clinical and cost effectiveness of transjugular intrahepatic portosystemic shunt (TIPS) compared with large-volume paracentesis (LVP) with albumin in the management of diuretic-resistant ascites due to cirrhosis?

Medline search terms

1.	ascites/
2.	ascit*.ti,ab.
3.	or/1-2
4.	Excluded study designs and publication types (A.3.9)
5.	3 not 4
6.	portasystemic shunt, transjugular intrahepatic/
7.	peritoneovenous shunt/
8.	((transjugular intrahepatic adj2 port?systemic adj2 (stent* or shunt*)) or tips* or port?systemic anastomosis).ti,ab.
9.	or/6-8
10.	paracentesis/
11.	(paracentes* or lvp).ti,ab.
12.	or/10-11
13.	9 and 12
14.	Study filters SR (A.3.1) or RCT (A.3.2)
15.	5 and 13 and 14
16.	Limit 15 to English language
	See Table 1 for date parameters

Embase search terms

1.	exp ascites/
2.	ascit*.ti,ab.
3.	or/1-2
4.	Excluded study designs and publication types (A.3.9)
5.	3 not 4
6.	transjugular intrahepatic portosystemic shunt/
7.	peritoneum vein shunt/
8.	((transjugular intrahepatic adj2 port?systemic adj2 (stent* or shunt*)) or tips* or port?systemic anastomosis).ti,ab.
9.	or/6-8
10.	paracentesis/
11.	(paracentes* or lvp).ti,ab.
12.	or/10-11
13.	9 and 12
14.	Study filters SR (A.3.1) or RCT (A.3.2)
15.	5 and 13 and 14
16.	Limit 15 to English language
	See Table 1 for date parameters

Cochrane search terms

#1.	[mh ^ascites]
#2.	ascit*:ti,ab

#3.	#1 or #2
#4.	[mh ^"portasystemic shunt, transjugular intrahepatic"]
#5.	[mh ^"peritoneovenous shunt"]
#6.	((transjugular intrahepatic near/2 (portosystemic or portasystemic or porto-systemic or porta-systemicemic) near/2 (stent* or shunt*) or tips* or ((portosystemic or portasystemic or porto-systemic or porta-systemic) next anastomosis)):ti,ab
#7.	#4 or #5 or #6
#8.	[mh ^paracentesis]
#9.	(paracentes* or lvp):ti,ab
#10.	#8 or #9
#11.	#7 and #10
#12.	#3 and #11
	See Table 1 for date parameters

A.4.10 Volume replacers in hepatorenal syndrome

- Which is the most clinically and cost-effective volume replacer for patients with hepatorenal syndrome due to cirrhosis who are also receiving vasoactive drugs?

Medline search terms

1.	hepatorenal syndrome/
2.	hepatorenal.ti,ab.
3.	((bile or cholemic) adj nephrosis).ti,ab.
4.	((flint or heyd or urohepatic) adj (syndrome* or disease*)).ti,ab.
5.	hepato-renal.ti,ab.
6.	(type adj2 hrs).ti,ab.
7.	or/1-6
8.	Excluded study designs and publication types (A.3.9)
9.	7 not 8
10.	Study filters SR (A.3.1) or RCT (A.3.2)
11.	9 and 10
12.	Limit 11 to English language
	See Table 1 for date parameters

Embase search terms

1.	*hepatorenal syndrome/
2.	hepatorenal.ti,ab.
3.	((bile or cholemic) adj nephrosis).ti,ab.
4.	((flint or heyd or urohepatic) adj (syndrome* or disease*)).ti,ab.
5.	hepato-renal.ti,ab.
6.	(type adj2 hrs).ti,ab.
7.	or/1-6
8.	Excluded study designs and publication types (A.3.9)
9.	7 not 8
10.	Study filters SR (A.3.1) or RCT (A.3.2)
11.	9 and 10
12.	Limit 11 to English language
	See Table 1 for date parameters

Cochrane search terms

#1.	MeSH descriptor: [hepatorenal syndrome] explode all trees
#2.	hepatorenal:ti,ab
#3.	((bile or cholemic) next nephrosis):ti,ab
#4.	((flint or heyd or urohepatic) next (syndrome* or disease*)):ti,ab
#5.	hepato-renal:ti,ab
#6.	(type near/2 hrs):ti,ab
#7.	#1 or #2 or #3 or #4 or #5 or #6
	See Table 1 for date parameters

A.4.11 Management of acute hepatic encephalopathy

- What is the most clinically and cost-effective intervention for the first-line treatment of acute hepatic encephalopathy?

Medline & Embase search terms

1.	hepatic encephalopathy/
2.	((portalsystemic or portal systemic or portosystemic or porto systemic) adj1 encephalopath*).ti,ab.
3.	hepatic encephalopath*.ti,ab.
4.	((hepatic or hepaticum) adj1 coma*).ti,ab.
5.	or/1-4
6.	Excluded study designs and publication types (A.3.9)
7.	5 not 6
8.	Study filters SR (A.3.1) or RCT (A.3.2)
9.	7 and 8
10.	Limit 9 to English language
	See Table 1 for date parameters

Cochrane search terms

#1.	MeSH descriptor: [hepatic encephalopathy] explode all trees
#2.	((portalsystemic or portal systemic or portosystemic or porto systemic) near/1 encephalopath*).ti,ab
#3.	hepatic encephalopath*:ti,ab
#4.	((hepatic or hepaticum) near/1 coma*):ti,ab
#5.	{or #1-#4}
	See Table 1 for date parameters

A.5 Health economics search

A.5.1 Health economic reviews

Economic searches were conducted in Medline, Embase, HEED and CRD for NHS EED and HTA.

Medline & Embase search terms

1.	Standard population (A.2)
2.	Excluded study designs and publication types (A.3.9)
3.	1 not 2
4.	Study filter HE (A.3.6)

5.	3 and 4
6.	Limit 5 to English language
	Date parameters: 2013 – 24 August 2015

CRD search terms

#1.	MeSH descriptor liver cirrhosis explode all trees in NHSEED,HTA
#2.	MeSH descriptor fibrosis in NHSEED,HTA
#3.	MeSH descriptor liver in NHSEED,HTA
#4.	#2 and #3
#5.	((((liver* or hepat*) adj5 fibro*) or cirrho*)) in NHSEED, HTA
#6.	#1 or #4 or #5
#7.	MeSH descriptor ascites explode all trees in NHSEED,HTA
#8.	(ascit*) in NHSEED, HTA
#9.	#6 or #7 or #8
	Date parameters: Inception to 24 August 2015

HEED search terms

1.	ax=cirrho*
2.	ax=liver* or hepat*
3.	ax=fibro*
4.	cs=2 and 3
5.	ax=ascit*
6.	cs=1 or 4 or 5
	Date parameters: Inception to 12 June 2014

A.5.2 Quality of life reviews

Quality of life searches were conducted in Medline and Embase only. The populations for cirrhosis and NAFLD were combined for this search.

Medline search terms

1.	fatty liver/
2.	non-alcoholic fatty liver disease/
3.	((fatty or fat or steato*) adj3 (liver* or hepat*)) or steatohepat* or (visceral adj2 steato*).ti,ab.
4.	(naf1* or nash).ti,ab.
5.	or/1-4
6.	Excluded study designs and publication types (Error! Reference source not found.)
7.	5 not 6
8.	Study filter QOL (A.3.7)
9.	7 and 8
10.	Limit 9 to English language & date parameters: 1946 to 27 August 2015
11.	exp liver cirrhosis/
12.	fibrosis/ and liver/
13.	((liver* or hepat*) adj5 fibro*) or cirrho*).ti,ab.
14.	or/11-13
15.	ascites/
16.	ascit*.ti,ab.

17.	or/15-16
18.	14 or 17
19.	18 not 6
20.	19 and 8
21.	Limit 20 to English language & date parameters: 1946 to 13 June 2014
22.	10 or 21

Embase search terms

1.	nonalcoholic fatty liver/
2.	((fatty or fat or steato*) adj3 (liver* or hepat*)) or steatohepat* or (visceral adj2 steato*).ti,ab.
3.	(nafl* or nash).ti,ab.
4.	or/1-3
5.	Excluded study designs and publication types (Error! Reference source not found.)
6.	4 not 5
7.	Study filter QOL (A.3.7)
8.	6 and 7
9.	Limit 8 to English language & date parameters: 1980 to 27 August 2015
10.	exp liver cirrhosis/
11.	fibrosis/ and liver/
12.	((liver* or hepat*) adj5 fibro*) or cirrho*).ti,ab.
13.	or/10-12
14.	exp *ascites/
15.	ascit*.ti,ab.
16.	or/15-15
17.	13 or 16
18.	17 not 5
19.	18 and 7
20.	Limit 20 to English language & date parameters: 1946 to 13 June 2014
21.	9 or 20

A.5.3 Economic modelling

Economic modelling searches were conducted in Medline, Embase, HEED and CRD for NHS EED and HTA

Medline search terms

1.	exp *liver diseases/
2.	(liver* or hepat* or steatohepat* or cirrho*).ti.
3.	or/1-2
4.	Excluded study designs and publication types (A.3.9)
5.	3 not 4
6.	Study filter MOD (A.3.8)
7.	5 and 6
8.	Limit 7 to English language
	Date parameters: 1946 to 27 August 2015

Embase search terms

1.	exp *liver disease/
----	---------------------

2.	(liver* or hepat* or steatohepat* or cirrho*).ti.
3.	or/1-2
4.	Excluded study designs and publication types (A.3.8)
5.	3 not 4
6.	Study filter MOD (A.3.8)
7	5 and 6
8	Limit 7 to English language
	Date parameters: 1980 to 27 August 2015

CRD search terms

#1.	MeSH descriptor liver diseases explode all trees in NHSEED,HTA
#2.	(liver* or hepat* or steatohepat* or cirrho*):ti in NHSEED, HTA
#3.	#1 or #2
#4.	MeSH descriptor models, economic explode all trees in NHSEED,HTA
#5.	MeSH descriptor models, theoretical in NHSEED,HTA
#6.	MeSH descriptor models, organizational in NHSEED,HTA
#7.	MeSH descriptor markov chains in NHSEED,HTA
#8.	MeSH descriptor monte carlo method in NHSEED,HTA
#9.	MeSH descriptor decision theory explode all trees in NHSEED,HTA
#10.	(markov* or monte carlo) OR (econom* model*) in NHSEED, HTA
#11.	((decision* adj2 (tree* or analy* or model*))) in NHSEED, HTA
#12.	#4 or #5 or #6 or #7 or #8 or #9 or #10 or #11
#13.	#3 and #12
	Date parameters: Inception to 27 August 2015

HEED search terms

1.	ti=liver* or hepat* or steatohepat* or cirrho*
2.	ax=model* or markov or monte carlo
3.	cs=1 and 2
	Date parameters: Inception to 27 August 2014

A.6 References