

# Appendix D: Literature search strategies

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## Introduction

Search strategies used for the **Hepatitis B guideline** were run in accordance with the NICE Guidelines Manual 2009. All searches were run up to 10<sup>th</sup> October 2012 unless otherwise stated. Any studies added to the databases after this date were not included unless specifically stated in the text.

## Clinical Searches

Searches for **clinical reviews** were run in Medline (OVID), Embase (OVID), and the Cochrane Library (Wiley). Typically, searches were constructed in the following way:

- A PICO format was used for intervention searches. **Population** (P) terms were combined with **Intervention** (I) and sometimes **Comparison** (C) terms (as indicated in the tables under each individual question in Section D.3). An intervention can be a drug, a procedure or a diagnostic test. **Outcomes** (O) are rarely used in search strategies for interventions. Study type filters were added where appropriate (see D.1).

## Economic searches

Searches for **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 were searched via the Cochrane (Wiley)

interface. For Medline and Embase an economic filter was added to the standard population (see D.1.4). All other searches were conducted using only population terms.

### D.1.1 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*) adj2 (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.	or/1-9

#### Embase search terms

1.	Systematic review/
2.	Meta-analysis/
3.	(meta analy* or metanaly* or metaanaly*).ti,ab.
4.	((systematic or evidence) adj2 (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.	((pool* or combined) adj2 (data or trials or studies or results)).ab.
10.	cochrane.jw.
11.	or/1-10

### D.1.2 Randomised controlled studies (RCTs) 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.

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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.	Single blind procedure/
8.	Randomized controlled trial/
9.	Rouble blind procedure/
10.	or/1-9

### D.1.3 Observational studies 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

### D.1.4 Health economic search terms

#### Medline search terms

1.	exp Economics/
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2.	exp "Costs and cost analysis"/
3.	(economic* or pharmacoeconomic*).ti,ab.
4.	(cost or costs or costed or costly or costing* or price or prices or pricing).ti.
5.	(expenditure or budget*).ti,ab.
6.	cost-effective*.ti,ab.
7.	(cost adj2 (effective* or reduce* or saving*)).ti,ab.
8.	(value adj2 money).ti,ab.
9.	Quality-adjusted life years/
10.	QALY*.ti,ab.
11.	or/1-10
12.	((metabolic or energy or oxygen) adj2 (expenditure or cost*)).ti,ab.
13.	11 not 12

#### Embase search terms

1.	exp Economic aspect/
2.	(economic* or pharmacoeconomic*).ti,ab.
3.	(cost or costs or costed or costly or costing* or price or prices or pricing).ti.
4.	(expenditure or budget*).ti,ab.
5.	(value adj1 money).tw.
6.	cost-effective*.ti,ab.
7.	(cost adj2 (effective* or reduce* or saving*)).ti,ab.
8.	(value adj2 money).ti,ab.
9.	exp Quality Adjusted Life Years/
10.	QALY*.ti,ab.
11.	or/1-10
12.	((metabolic or energy or oxygen) adj2 (expenditure or cost*)).ti,ab.
13.	11 not 12

### D.1.5 Quality of life 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/1-20

#### 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

## D.2 Standard population search strategy

#### Medline search terms

1.	exp Hepatitis B/
2.	Hepatitis B virus/
3.	Hepatitis B antibodies/
4.	exp Hepatitis B antigens/
5.	exp Hepatitis D/
6.	Hepatitis delta antigens/
7.	Hepatitis delta virus/
8.	(hepatitis adj2 (B or D or delta)).ti,ab.
9.	((HBV or CHB or HDV or hep B or hepB) not heart block).ti,ab.
10.	(anti HB* or antiHB* or HBeAg* or HBe Ag* or HbsA* or HBCA*).ti,ab.
11.	or/1-10
12.	limit 11 to english language
13.	Letter/

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14.	Editorial/
15.	News/
16.	exp Historical article/
17.	Anecdotes as Topic/
18.	Comment/
19.	Case report/
20.	(letter or comment*).ti.
21.	or/13-20
22.	21 not (randomized controlled trial/ or random*.ti,ab.)
23.	animals/ not humans/
24.	exp Animals, Laboratory/
25.	exp Animal experimentation/
26.	exp Models, Animal/
27.	exp Rodentia/
28.	(rat or rats or mouse or mice).ti.
29.	or/22-28
30.	12 not 29

#### Embase search terms

1.	Hepatitis B/
2.	Hepatitis B virus/
3.	Hepatitis B virus X protein/
4.	exp Hepatitis B antibody/
5.	exp Hepatitis B antigen/
6.	Delta agent hepatitis/
7.	Hepatitis delta virus/
8.	Hepatitis delta antigen/
9.	(hepatitis adj2 (B or D or delta)).ti,ab.
10.	((HBV or CHB or HDV or hep B or hepB) not heart block).ti,ab.
11.	(anti HB* or antiHB* or HBeAg* or HBe Ag* or HbsA* or HBCA*).ti,ab.
12.	or/1-11
13.	limit 12 to english language
14.	Letter.pt. or Letter/
15.	Note.pt.
16.	Editorial.pt.
17.	Case report/ or Case study/
18.	(letter or comment*).ti.
19.	or/14-18
20.	19 not (randomized controlled trial/ or random*.ti,ab.)
21.	Animal/ not Human/
22.	Nonhuman/
23.	exp Animal experiment/
24.	exp Experimental animal/
25.	Animal model/
26.	exp Rodent/

27.	(rat or rats or mouse or mice).ti.
28.	or/20-27
29.	13 not 28

### Cochrane search terms

#1	MeSH descriptor Hepatitis B explode all trees
#2	MeSH descriptor Hepatitis B virus, this term only
#3	MeSH descriptor Hepatitis B Antibodies, this term only
#4	MeSH descriptor Hepatitis B Antigens explode all trees
#5	(hepatitis NEAR/2 (B OR D OR delta)):ti,ab
#6	("anti HB*" or antiHB* or HBeAg* or "HBe Ag*" or HbsA* or HBcA*):ti,ab
#7	((HBV or CHB or hep B or hepB or HDV) NOT (heart NEXT block)):ti,ab
#8	MeSH descriptor Hepatitis D explode all trees
#9	MeSH descriptor Hepatitis delta Antigens, this term only
#10	MeSH descriptor Hepatitis Delta Virus, this term only
#11	(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10)

## D.3 Searches by specific questions

### D.3.1 Patient information

#### Q. What are the information needs of patients with CHB and their carers?

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention /Exposure	Study filter used	Date parameters
Hepatitis B	Patient information	None	All years - 10/10/2012

### Medline search terms

1.	((client* or patient* or user* or carer* or consumer* or customer* or health) adj5 (information* or educat* or knowledge)).ti,ab,hw.
2.	(information* adj3 (need* or requirement* or support* or seek* or access* or disseminat*)).ti,ab,hw.
3.	((patient* or user* or carer* or consumer* or customer* or health) adj3 (literature or leaflet* or booklet* or pamphlet* or questionnaire* or survey* or handout* or internet or website* or consult* or interview*)).ti,ab.
4.	Telemedicine/
5.	Interview/
6.	Telephone/
7.	Publications/
8.	Pamphlets/
9.	Internet/
10.	or/1-9

### Embase search terms

1.	((client* or patient* or user* or carer* or consumer* or customer* or health) adj5 (information* or educat* or knowledge)).ti,ab,hw.
2.	(information* adj3 (need* or requirement* or support* or seek* or access* or disseminat*)).ti,ab,hw.
3.	((patient* or user* or carer* or consumer* or customer* or health) adj3 (literature or leaflet*

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	or booklet* or pamphlet* or questionnaire* or survey* or handout* or internet or website* or consult* or interview*)):ti,ab.
4.	exp Telehealth/
5.	exp Interview/
6.	Telephone/
7.	Publication/
8.	Internet/
9.	or/1-8

### Cochrane search terms

#1.	((client* or patient* or user* or carer* or consumer* or customer* or health) NEAR/5 (information* or educat* or knowledge)):ti,ab
#2.	(information* NEAR/3 (need* or requirement* or support* or seek* or access* or disseminat*)):ti,ab
#3.	((patient* or user* or carer* or consumer* or customer* or health) NEAR/3 (literature or leaflet* or booklet* or pamphlet* or questionnaire* or survey* or handout* or internet or website* or consult* or interview*)):ti,ab
#4.	MeSH descriptor Patient Acceptance of Health Care, this term only
#5.	MeSH descriptor Patient Education as Topic, this term only
#6.	MeSH descriptor Patient Preference, this term only
#7.	MeSH descriptor Patient Satisfaction, this term only
#8.	MeSH descriptor Consumer Health Information explode all trees
#9.	MeSH descriptor Health Knowledge, Attitudes, Practice, this term only
#10.	MeSH descriptor Telemedicine, this term only
#11.	MeSH descriptor Access to Information, this term only
#12.	MeSH descriptor Information Dissemination, this term only
#13.	MeSH descriptor Information Seeking Behavior, this term only
#14.	MeSH descriptor Pamphlets, this term only
#15.	MeSH descriptor Internet, this term only
#16.	MeSH descriptor Interviews as Topic explode all trees
#17.	MeSH descriptor Telephone, this term only
#18.	MeSH descriptor Telemedicine, this term only
#19.	(#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)

## D.3.2 Assessment and referral

### D.3.2.1 Threshold for referral

**Q. What are the thresholds (e.g. HBV DNA and ALT levels) for referral to specialist services after initial diagnosis and pre-therapeutic tests of CHB?**

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention /Exposure	Study filter used	Date parameters
Hepatitis B	Clinical thresholds for referral	RCTs, SRs and Observational studies [Medline and Embase only]	All years - 10/10/2012



### Medline search terms

1.	Alanine transaminase/
2.	DNA, viral/
3.	Biological markers/
4.	Carrier state/
5.	Viral load/
6.	((ALT or alanine or DNA or HBsAg) adj4 (level* or baseline* or raise* or increas* or elevat* or normal)).ti,ab.
7.	((inactive or asymptomatic or healthy) adj3 carrier*).ti,ab.
8.	or/1-7
9.	Predictive value of tests/
10.	Disease progression/
11.	Likelihood function/
12.	exp "Sensitivity and specificity"/
13.	prognos*.ti,ab,hw.
14.	(progress* adj3 (disease or predict*)).ti,ab.
15.	(candidate* adj2 (therapy or treatment or antiviral*)).ti,ab.
16.	(cut off or cutoff or threshold* or staging).ti,ab.
17.	(select* adj2 (patient* or treatment or therapy)).ti,ab.
18.	((indicat* or start* or initiat*) adj3 (treatment or therapy)).ti,ab.
19.	predict*.ti,ab.
20.	natural history.ti,ab.
21.	(sensitivity or specificity).ti,ab.
22.	((pre test or pretest or post test) adj probability).ti,ab.
23.	(predictive value* or PPV or NPV).ti,ab.
24.	likelihood ratio*.ti,ab.
25.	(ROC curve* or AUC).ti,ab.
26.	((treatment or management) adj3 (algorithm* or plan* or strateg*)).ti,ab.
27.	or/9-26
28.	8 and 27

### Embase search terms

1.	Alanine aminotransferase/
2.	Virus DNA/
3.	Biological marker/
4.	Virus load/
5.	((ALT or alanine or DNA or HBsAg) adj4 (level* or baseline* or raise* or increas* or elevat* or normal)).ti,ab.
6.	((inactive or asymptomatic or healthy) adj3 carrier*).ti,ab.
7.	or/1-6
8.	Predictive value/
9.	Disease course/
10.	"Sensitivity and specificity"/
11.	prognos*.ti,ab,hw.
12.	(progress* adj3 (disease or predict*)).ti,ab.
13.	(candidate* adj2 (therapy or treatment or antiviral*)).ti,ab.

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14.	(cut off or cutoff or threshold* or staging).ti,ab.
15.	(select* adj2 (patient* or treatment or therapy)).ti,ab.
16.	predict*.ti,ab.
17.	natural history.ti,ab.
18.	(sensitivity or specificity).ti,ab.
19.	((pre test or pretest or post test) adj probability).ti,ab.
20.	(predictive value* or PPV or NPV).ti,ab.
21.	likelihood ratio*.ti,ab.
22.	(ROC curve* or AUC).ti,ab.
23.	((treatment or management) adj3 (algorithm* or plan* or strateg*)).ti,ab.
24.	or/8-23
25.	7 and 24

### Cochrane search terms

#1.	MeSH descriptor Alanine Transaminase, this term only
#2.	MeSH descriptor DNA, Viral, this term only
#3.	MeSH descriptor Biological Markers, this term only
#4.	MeSH descriptor Carrier State, this term only
#5.	MeSH descriptor Viral Load, this term only
#6.	((ALT or alanine or DNA or HBsAg) NEAR/4 (level* or baseline* or raise* or increas* or elevat* or normal)):ti,ab
#7.	((inactive or asymptomatic or healthy) NEAR/3 carrier*):ti,ab
#8.	(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7)
#9.	MeSH descriptor Sensitivity and Specificity explode all trees
#10.	MeSH descriptor Disease Progression, this term only
#11.	MeSH descriptor Likelihood Functions, this term only
#12.	MeSH descriptor Prognosis, this term only
#13.	(prognos*):ti,ab
#14.	(progress* NEAR/3 (disease or predict*)):ti,ab
#15.	(candidate* NEAR/2 (therapy or treatment or antiviral*)):ti,ab
#16.	("cut off" or cutoff or threshold* or staging):ti,ab
#17.	(select* NEAR/2 (patient* or treatment or therapy)):ti,ab
#18.	((indicat* or start* or initiat*) NEAR/3 (treatment or therapy)):ti,ab
#19.	predict*:ti,ab
#20.	"natural history":ti,ab
#21.	(sensitivity or specificity):ti,ab
#22.	((("pre test" or pretest or "post test") NEXT probability):ti,ab
#23.	((predictive NEXT value*) or PPV or NPV):ti,ab
#24.	"likelihood ratio":ti,ab
#25.	("ROC curve" or AUC):ti,ab
#26.	((treatment or management) NEAR/3 (algorithm* or plan* or strateg*)):ti,ab
#27.	(#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 OR #23 OR #24 OR #25 OR #26)
#28.	(#8 AND #27)

### D.3.2.2 Healthcare setting

**Q. What is the most appropriate healthcare setting to initiate pre-therapeutic tests (HBeAg, quantitative HBsAg, quantitative HBV DNA, anti HCV, anti HDV, anti HIV) in people who are HBsAg positive?**

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention /Exposure	Study filter used	Date parameters
Hepatitis B	Setting for diagnostic tests	None	All years - 10/10/2012

#### Medline search terms

1.	Algorithm/
2.	Practice guideline/
3.	Health planning guidelines/
4.	Patient care planning/
5.	Patient care management/
6.	Case management/
7.	Comprehensive health care/
8.	Critical pathways/
9.	(guideline* or guidance or protocol or recommendation* or consensus or algorithm).ti.
10.	or/1-9
11.	(immuni#ation* or vaccin*).ti.
12.	10 not 11
13.	limit 12 to yr="2005 -Current"
14.	"Referral and consultation"/
15.	Patient selection/
16.	Physician's practice patterns/
17.	Clinical competence/
18.	Health knowledge, attitudes, practice/
19.	Medical audit/
20.	Guideline adherence/
21.	(candidate* adj3 (therapy or treatment)).ti,ab.
22.	(cut off or cutoff or threshold* or test* or assess* or referr*).ti,ab.
23.	(select* adj3 (patient* or treatment or therapy)).ti,ab.
24.	((indicat* or start* or initiat*) adj3 (treatment or therapy)).ti,ab.
25.	((treatment or management or care or clinical) adj3 (algorithm* or plan* or strateg* or pathway* or plan* or case)).ti,ab.
26.	(competen* or audit* or knowledge or educat*).ti,ab.
27.	or/14-26
28.	Primary health care/
29.	exp General practice/
30.	(GP* or hepatologist* or gastroenterologist* or gastro enterologist*).ti,ab.
31.	((primary or general or specialist or family or secondary or tertiary or consultant or hepatology or gastroenterology or gastro enterology) adj5 (care or service* or practice or practitioner* or physician* or doctor* or consultant* or nurse* or treatment or center* or centre* or setting or clinic*).ti,ab.
32.	or/28-31
33.	13 or (27 and 32)

### Embase search terms

1.	exp Practice guideline/
2.	Health care planning/
3.	Integrated health care system/
4.	Algorithm/
5.	(guideline* or guidance or protocol or recommendation* or consensus or algorithm).ti.
6.	or/1-5
7.	limit 6 to yr="2005 -Current"
8.	(immuni#ation* or vaccin*).ti.
9.	7 not 8
10.	exp Primary health care/
11.	General practice/
12.	General practitioner/
13.	Medical specialist/
14.	(GP* or hepatologist* or gastroenterologist* or gastro enterologist*).ti,ab.
15.	((primary or general or specialist or family or secondary or tertiary or consultant or hepatology or gastroenterology or gastro enterology) adj5 (care or service* or practice or practitioner* or physician* or doctor* or consultant* or nurse* or treatment or center* or centre* or setting or clinic*).ti,ab.
16.	or/10-15
17.	Patient referral/
18.	Patient selection/
19.	Clinical competence/
20.	Clinical practice/
21.	Medical audit/
22.	Professional knowledge/
23.	(candidate* adj3 (therapy or treatment)).ti,ab.
24.	(cut off or cutoff or threshold* or test* or assess* or referr*).ti,ab.
25.	(select* adj3 (patient* or treatment or therapy)).ti,ab.
26.	((indicat* or start* or initiat*) adj3 (treatment or therapy)).ti,ab.
27.	((treatment or management or care or clinical) adj3 (algorithm* or plan* or strateg* or pathway* or plan* or case)).ti,ab.
28.	(competen* or audit* or knowledge or educat*).ti,ab.
29.	or/17-28
30.	9 or (16 and 29)

### Cochrane search terms

#1.	MeSH descriptor Referral and Consultation, this term only
#2.	MeSH descriptor Algorithms, this term only
#3.	MeSH descriptor Patient Care Planning explode all trees
#4.	MeSH descriptor Comprehensive Health Care, this term only
#5.	MeSH descriptor Patient Selection, this term only
#6.	MeSH descriptor Physician's Practice Patterns, this term only
#7.	MeSH descriptor Clinical Competence, this term only
#8.	MeSH descriptor Health Knowledge, Attitudes, Practice, this term only
#9.	MeSH descriptor Medical Audit, this term only
#10.	MeSH descriptor Guideline Adherence, this term only

#11.	(candidate* near/3 (therapy or treatment)):ti,ab
#12.	(cut off or cutoff or threshold* or test* or assess* or referr*):ti,ab
#13.	(select* near/3 (patient* or treatment or therapy)):ti,ab
#14.	((indicat* or start* or initiat*) near/3 (treatment or therapy)):ti,ab
#15.	((treatment or management or care or clinical) near/3 (algorithm* or plan* or strateg* or pathway* or plan* or case)):ti,ab
#16.	(competen* or audit* or knowledge or educat*):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.	MeSH descriptor Primary Health Care, this term only
#19.	MeSH descriptor General Practice explode all trees
#20.	MeSH descriptor General Practitioners, this term only
#21.	(GP* or hepatologist* or gastroenterologist* or "gastro enterologist" or "gastro enterologists"):ti,ab
#22.	((primary or general or specialist or family or secondary or tertiary or consultant or hepatology or gastroenterology or gastro enterology) near/5 (care or service* or practice or practitioner* or physician* or doctor* or consultant* or nurse* or treatment or center* or centre* or setting or clinic*)):ti,ab
#23.	(#18 OR #19 OR #20 OR #21 OR #22)
#24.	(#17 AND #23)

### D.3.3 Assessment of liver disease in secondary specialist care

**Q. What is the diagnostic accuracy of non-invasive methods (e.g. transient elastography, serum fibrosis markers, aspartate aminotransferase / platelet ration index, magnetic resonance spectroscopy) to assess severity of necro-inflammatory activity and liver fibrosis?**

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention /Exposure	Comparison	Study filter used	Date parameters
Hepatitis B and (cirrhosis or fibrosis)*	Diagnostic accuracy		RCTs, SRs and Observational studies [Medline and Embase only]	All years - 10/10/2012

\*Standard population restricted to fibrosis/cirrhosis/necro-inflammation.

#### Medline search terms

1.	exp Hepatitis B/
2.	Hepatitis B virus/
3.	Hepatitis B antibodies/
4.	exp Hepatitis B antigens/
5.	exp Hepatitis D/
6.	Hepatitis delta antigens/
7.	Hepatitis delta virus/
8.	(hepatitis adj2 (B or D or delta)).ti,ab.
9.	((HBV or CHB or HDV or hep B or hepB) not heart block).ti,ab.
10.	(anti HB* or antiHB* or HBeAg* or HBe Ag* or HbsA* or HBCA*).ti,ab.
11.	or/1-10
12.	limit 11 to english language

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Literature search strategies

13.	Letter/
14.	Editorial/
15.	News/
16.	exp Historical article/
17.	Anecdotes as Topic/
18.	Comment/
19.	Case report/
20.	(letter or comment*).ti.
21.	or/13-20
22.	21 not (randomized controlled trial/ or random*.ti,ab.)
23.	Animals/ not Humans/
24.	exp Animals, Laboratory/
25.	exp Animal experimentation/
26.	exp Models, Animal/
27.	exp Rodentia/
28.	(rat or rats or mouse or mice).ti.
29.	or/22-28
30.	12 not 29
31.	Liver cirrhosis/
32.	(cirrh* or fibro* or necro*).ti,ab.
33.	30 and (31 or 32)
34.	exp "Sensitivity and specificity"/
35.	(sensitivity or specificity).ti,ab.
36.	((pre test or pretest or post test) adj probability).ti,ab.
37.	(predictive value* or PPV or NPV).ti,ab.
38.	likelihood ratio*.ti,ab.
39.	Likelihood function/
40.	(ROC curve* or AUC).ti,ab.
41.	(diagnos* adj2 (performance* or accurac* or utilit* or value* or efficien* or effectiveness)).ti,ab.
42.	gold standard.ab.
43.	Disease progression/
44.	(degree* or stage* or staging or grade* or grading or assess* or score or scoring).ti,ab.
45.	((clinical or disease) adj3 (progress* or severity)).ti,ab.
46.	or/34-45
47.	33 and 46

#### Embase search terms

1.	Hepatitis B/
2.	Hepatitis B virus/
3.	Hepatitis B virus X protein/
4.	exp Hepatitis B antibody/
5.	exp Hepatitis B antigen/
6.	Delta agent hepatitis/
7.	Hepatitis delta virus/
8.	Hepatitis delta antigen/

9.	(hepatitis adj2 (B or D or delta)).ti,ab.
10.	((HBV or CHB or HDV or hep B or hepB) not heart block).ti,ab.
11.	(anti HB* or antiHB* or HBeAg* or HBe Ag* or HbsA* or HBcA*).ti,ab.
12.	or/1-11
13.	limit 12 to english language
14.	Letter.pt. or Letter/
15.	Note.pt.
16.	Editorial.pt.
17.	Case report/ or Case study/
18.	(letter or comment*).ti.
19.	or/14-18
20.	19 not (randomized controlled trial/ or random*.ti,ab.)
21.	Animal/ not Human/
22.	Nonhuman/
23.	exp Animal experiment/
24.	exp Experimental animal/
25.	Animal model/
26.	exp Rodent/
27.	(rat or rats or mouse or mice).ti.
28.	or/20-27
29.	13 not 28
30.	Liver fibrosis/
31.	Liver cirrhosis/
32.	(cirrho* or fibro* or necro*).ti,ab.
33.	Decompensated liver cirrhosis/
34.	or/30-33
35.	exp "Sensitivity and specificity"/
36.	(sensitivity or specificity).ti,ab.
37.	((pre test or pretest or post test) adj probability).ti,ab.
38.	(predictive value* or PPV or NPV).ti,ab.
39.	likelihood ratio*.ti,ab.
40.	(ROC curve* or AUC).ti,ab.
41.	(diagnos* adj2 (performance* or accurac* or utilit* or value* or efficien* or effectiveness)).ti,ab.
42.	Diagnostic accuracy/
43.	Diagnostic test accuracy study/
44.	gold standard.ab.
45.	Disease course/
46.	((clinical or disease) adj3 (progress* or severity)).ti,ab.
47.	(degree* or stage* or staging or grade* or grading or assess* or score* or scoring).ti,ab.
48.	or/35-47
49.	29 and 34 and 48

### Cochrane search terms

#1.	MeSH descriptor Hepatitis B explode all trees
#2.	MeSH descriptor Hepatitis B virus, this term only
#3.	MeSH descriptor Hepatitis B Antibodies, this term only
#4.	MeSH descriptor Hepatitis B Antigens explode all trees
#5.	(hepatitis NEAR/2 (B OR D OR delta)):ti,ab
#6.	("anti HB*" or antiHB* or HBeAg* or "HBe Ag*" or HbsA* or HBcA*):ti,ab
#7.	((HBV or CHB or hep B or hepB or HDV) NOT (heart NEXT block)):ti,ab
#8.	MeSH descriptor Hepatitis D explode all trees
#9.	MeSH descriptor Hepatitis delta Antigens, this term only
#10.	MeSH descriptor Hepatitis Delta Virus, this term only
#11.	(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10)
#12.	MeSH descriptor Sensitivity and Specificity explode all trees
#13.	(sensitivity or specificity):ti,ab
#14.	((("pre test" or pretest or "post test") NEXT probability):ti,ab
#15.	("predictive value*" or PPV or NPV):ti,ab
#16.	likelihood NEXT ratio*:ti,ab
#17.	MeSH descriptor Likelihood Functions, this term only
#18.	("ROC curve*" or AUC):ti,ab
#19.	(diagnos* NEAR/2 (performance* or accurac* or utilit* or value* or efficien* or effectiveness)):ti,ab
#20.	gold NEXT standard:ab
#21.	MeSH descriptor Disease Progression, this term only
#22.	((clinical or disease) near/3 (progress* or severity)):ti,ab
#23.	(degree* or stage* or staging or grade* or grading or assess* or score* or scoring):ti,ab
#24.	(#12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23)
#25.	(#11 AND #24)
#26.	MeSH descriptor Liver Cirrhosis, this term only
#27.	(cirrho* or fibro* or necro*):ti,ab
#28.	(#26 OR #27)
#29.	(#25 AND #28)

### D.3.4 Genotyping

#### Q. Does genotype testing enable better decisions on which antiviral treatment to offer and is it cost effective?

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention	Comparison	Study filter used	Date parameters
Hepatitis B	Antivirals AND Genotype		RCTs and Observational Studies [Medline and Embase only]	All years - 10/10/2012

### Medline search terms

1.	Antiviral agents/
2.	(antiviral* or anti viral*).ti,ab.
3.	exp Interferon type I/



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Literature search strategies

4.	Lamivudine/
5.	(interferon* or peginterferon*).ti,ab.
6.	(lamivudine or telbivudine or entecavir or emtricitabine or tenofovir or adefovir).ti,ab.
7.	(ETV or TDF or FTC or ADV or 3TC or IFN* or pegIFN*).ti,ab.
8.	(viread or truvada or hepsera or sebivo or tyzeka or baraclude or zeffix or pegasys).ti,ab.
9.	or/1-8
10.	Genotype/
11.	(genotyp* or subgenotyp*).ti,ab.
12.	9 and (10 or 11)

#### Embase search terms

1.	Antiviral therapy/
2.	Antivirus agent/
3.	(antiviral* or anti viral*).ti,ab.
4.	exp Recombinant interferon/
5.	Lamivudine/
6.	Telbivudine/
7.	Entecavir/
8.	Emtricitabine/
9.	tenofovir.hw,ti,ab.
10.	adefovir.hw,ti,ab.
11.	(interferon* or peginterferon*).ti,ab.
12.	(lamivudine or telbivudine or entecavir or emtricitabine).ti,ab.
13.	(ETV or TDF or FTC or ADV or 3TC or IFN* or pegIFN*).ti,ab.
14.	(viread or truvada or hepsera or sebivo or tyzeka or baraclude or zeffix or pegasys).ti,ab.
15.	or/1-14
16.	Genotype/
17.	(genotyp* or subgenotyp*).ti,ab.
18.	15 and (16 or 17)

#### Cochrane search terms

#1	MeSH descriptor Interferon Type I explode all trees
#2	MeSH descriptor Lamivudine, this term only
#3	(interferon* or peginterferon*):ti,ab
#4	(lamivudine or telbivudine or entecavir or emtricitabine or tenofovir or adefovir):ti,ab
#5	(ETV or TDF or FTC or ADV or 3TC or IFN or pegIFN):ti,ab
#6	(viread or truvada or hepsera or sebivo or tyzeka or baraclude or zeffix or pegasys):ti,ab
#7	MeSH descriptor Antiviral Agents, this term only
#8	(antiviral* or anti viral*):ti,ab
#9	(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8)
#11	MeSH descriptor Genotype, this term only
#12	(genotyp* or subgenotyp*):ti,ab
#13	(#11 OR #12)
#14	(#9 AND #13)

## D.3.5 Antivirals

### D.3.5.1 Antiviral treatment choice

Two searches (S1 and S2) covered the following three questions:

- Q1. In people with CHB, what is the clinical and cost effectiveness of pharmacological monotherapies and combinations in achieving remission of the activity of CHB?**
- Q2. In people with CHB, what is the clinical and cost-effectiveness of sequential drug therapy (add-on or switching monotherapies) in achieving remission of the activity of CHB?**
- Q3. In people with CHB and with advanced cirrhosis, including those with liver decompensation, what is the clinical and cost effectiveness of antiviral treatment to prevent recurrent reactivation and liver transplantation?**

#### S1: All antivirals with standard population

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention	Study filter used	Date parameters
Hepatitis B	Pegylated interferon OR lamivudine OR telbivudine OR entecavir monohydrate OR tenofovir disoproxil OR adefovir dipivoxil OR ribavirin	RCTs and SRs [Medline and Embase only]	All years - 10/10/2012

#### Medline search terms

1.	Antiviral agents/
2.	(antiviral* or anti viral*).ti,ab.
3.	exp Interferon type I/
4.	Lamivudine/
5.	Ribavirin/
6.	(interferon* or peginterferon*).ti,ab.
7.	(lamivudine or telbivudine or entecavir or emtricitabine or tenofovir or adefovir or ribavirin).ti,ab.
8.	(ETV or TDF or FTC or ADV or 3TC or IFN* or pegIFN*).ti,ab.
9.	(viread or truvada or hepsera or sebivo or tyzeka or baraclude or zeffix or pegasys).ti,ab.
10.	or/1-9

#### Embase search terms

1.	Antiviral therapy/
2.	Antivirus agent/
3.	(antiviral* or anti viral*).ti,ab.
4.	exp Recombinant interferon/
5.	Lamivudine/
6.	Telbivudine/
7.	Entecavir/
8.	Emtricitabine/
9.	tenofovir.hw,ti,ab.
10.	adefovir.hw,ti,ab.
11.	ribavirin.hw,ti,ab.
12.	(interferon* or peginterferon*).ti,ab.

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Literature search strategies

13.	(lamivudine or telbivudine or entecavir or emtricitabine).ti,ab.
14.	(ETV or TDF or FTC or ADV or 3TC or IFN* or pegIFN*).ti,ab.
15.	(viread or truvada or hepsera or sebivo or tyzeka or baraclude or zeffix or pegasys).ti,ab.
16.	or/1-15

### Cochrane search terms

#1	MeSH descriptor Antiviral Agents, this term only
#2	(antiviral* or anti viral*):ti,ab
#3	MeSH descriptor Interferon Type I explode all trees
#4	MeSH descriptor Lamivudine, this term only
#5	MeSH descriptor Ribavirin, this term only
#6	(interferon* or peginterferon*):ti,ab
#7	(lamivudine or telbivudine or entecavir or emtricitabine or tenofovir or adefovir or ribavirin):ti,ab
#8	(ETV or TDF or FTC or ADV or 3TC or IFN or pegIFN):ti,ab
#9	(viread or truvada or hepsera or sebivo or tyzeka or baraclude or zeffix or pegasys):ti,ab
#10	(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9)

### S2: Lamivudine with restricted population

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention	Study filter used	Date parameters
Hepatitis B and viral resistance*	Lamivudine	Observational [Medline and Embase only]	All years - 10/10/2012

\*Standard population restricted. Search was not run in Cochrane as only observational studies included.

### Medline search terms

1.	exp Hepatitis B/
2.	Hepatitis B virus/
3.	Hepatitis B antibodies/
4.	exp Hepatitis B antigens/
5.	exp Hepatitis D/
6.	Hepatitis delta antigens/
7.	Hepatitis delta virus/
8.	(hepatitis adj2 (B or D or delta)).ti,ab.
9.	((HBV or CHB or HDV or hep B or hepB) not heart block).ti,ab.
10.	(anti HB* or antiHB* or HBeAg* or HBe Ag* or HbsA* or HBcA*).ti,ab.
11.	or/1-10
12.	limit 11 to english language
13.	Letter/
14.	Editorial/
15.	News/
16.	exp Historical article/
17.	Anecdotes as topic/
18.	Comment/
19.	Case report/
20.	(letter or comment*).ti.

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Literature search strategies

21.	or/13-20
22.	21 not (Randomized controlled trial/ or random*.ti,ab.)
23.	Animals/ not Humans/
24.	exp Animals, Laboratory/
25.	exp Animal experimentation/
26.	exp Models, Animal/
27.	exp Rodentia/
28.	(rat or rats or mouse or mice).ti.
29.	or/22-28
30.	12 not 29
31.	exp Drug resistance, Viral/
32.	Drug resistance/
33.	resistan*.ti,ab.
34.	or/31-33
35.	30 and 34
36.	(lamivudine or LMV or 3TC or zeffix).ti,ab,hw.
37.	35 and 36
38.	Epidemiologic studies/
39.	exp Case control studies/
40.	exp Cohort studies/
41.	Cross-sectional studies/
42.	case control.ti,ab.
43.	(cohort adj (study or studies or analys*)).ti,ab.
44.	((follow up or observational or uncontrolled or non randomi#ed or nonrandomi#ed or epidemiologic*) adj (study or studies)).ti,ab.
45.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort*)).ti,ab.
46.	or/38-45
47.	37 and 46

#### Embase search terms

1.	Hepatitis B/
2.	Hepatitis B virus/
3.	Hepatitis B virus X protein/
4.	exp Hepatitis B antibody/
5.	exp Hepatitis B antigen/
6.	Delta agent hepatitis/
7.	Hepatitis delta virus/
8.	Hepatitis delta antigen/
9.	(hepatitis adj2 (B or D or delta)).ti,ab.
10.	((HBV or CHB or HDV or hep B or hepB) not heart block).ti,ab.
11.	(anti HB* or antiHB* or HBeAg* or HBe Ag* or HbsA* or HbCA*).ti,ab.
12.	or/1-11
13.	limit 12 to english language
14.	Letter.pt. or Letter/
15.	Note.pt.

16.	Editorial.pt.
17.	Case report/ or Case study/
18.	(letter or comment*).ti.
19.	or/14-18
20.	19 not (Randomized controlled trial/ or random*.ti,ab.)
21.	Animal/ not Human/
22.	Nonhuman/
23.	exp Animal experiment/
24.	exp Experimental animal/
25.	Animal model/
26.	exp Rodent/
27.	(rat or rats or mouse or mice).ti.
28.	or/20-27
29.	13 not 28
30.	Drug resistance/
31.	Antiviral resistance/
32.	resistan*.ti,ab.
33.	or/30-32
34.	29 and 33
35.	(lamivudine or 3TC or LMV or zeffix).ti,ab,hw.
36.	34 and 35
37.	Clinical study/
38.	exp Case control study/
39.	Family study/
40.	Longitudinal study/
41.	Retrospective study/
42.	Prospective study/
43.	Cross-sectional study/
44.	Cohort analysis/
45.	Follow-up/
46.	cohort*.ti,ab.
47.	45 and 46
48.	case control.ti,ab.
49.	(cohort adj (study or studies or analys*)).ti,ab.
50.	((follow up or observational or uncontrolled or non randomi#ed or nonrandomi#ed or epidemiologic*) adj (study or studies)).ti,ab.
51.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort*)).ti,ab.
52.	or/37-44,47-51
53.	36 and 52

#### D.3.5.2 Tenofovir (treatment naïve V lamivudine resistant)

**Q. Is tenofovir's efficacy different when compared in nucleoside naïve and lamivudine resistant HBV DNA strains?**

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Literature search strategies

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention /Exposure	Comparison	Study filter used	Date parameters
Hepatitis B*	Tenofovir	Lamivudine and resistance	None	All years - 10/10/2012

\*Standard population changed so that animal studies were not excluded.

#### Medline search terms

1.	exp Hepatitis B/
2.	Hepatitis B virus/
3.	Hepatitis B antibodies/
4.	exp Hepatitis B antigens/
5.	exp Hepatitis D/
6.	Hepatitis delta antigens/
7.	Hepatitis delta virus/
8.	(hepatitis adj2 (B or D or delta)).ti,ab.
9.	((HBV or CHB or HDV or hep B or hepB) not heart block).ti,ab.
10.	(anti HB* or antiHB* or HBeAg* or HBe Ag* or HbsA* or HBcA*).ti,ab.
11.	or/1-10
12.	limit 11 to english language
13.	Letter/
14.	Editorial/
15.	News/
16.	exp Historical article/
17.	Anecdotes as Topic/
18.	Comment/
19.	Case report/
20.	(letter or comment*).ti.
21.	or/13-20
22.	12 not 21
23.	(tenofovir or TDF or viread).ti,ab.
24.	22 and 23
25.	(lamivudine or 3TC or zeffix).ti,ab.
26.	Lamivudine/
27.	24 and (25 or 26)
28.	resist*.ti,ab,hw.
29.	27 and 28

#### Embase search terms

1.	Hepatitis B/
2.	Hepatitis B virus/
3.	Hepatitis B virus X protein/
4.	exp Hepatitis B antibody/
5.	exp Hepatitis B antigen/
6.	Delta agent hepatitis/
7.	Hepatitis delta virus/
8.	Hepatitis delta antigen/

9.	(hepatitis adj2 (B or D or delta)).ti,ab.
10.	((HBV or CHB or HDV or hep B or hepB) not heart block).ti,ab.
11.	(anti HB* or antiHB* or HBeAg* or HBe Ag* or HbsA* or HBcA*).ti,ab.
12.	or/1-11
13.	limit 12 to english language
14.	Letter.pt. or Letter/
15.	Note.pt.
16.	Editorial.pt.
17.	Case report/ or Case study/
18.	(letter or comment*).ti.
19.	or/14-18
20.	13 not 19
21.	Tenofovir/ or Tenofovir disoproxil/
22.	(tenofovir or TDF or viread).ti,ab.
23.	20 and (21 or 22)
24.	Lamivudine/
25.	(lamivudine or 3TC or zeffix).ti,ab.
26.	23 and (24 or 25)
27.	resist*.ti,ab,hw.
28.	26 and 27

#### Cochrane search terms

#1.	MeSH descriptor Hepatitis B explode all trees
#2.	MeSH descriptor Hepatitis B virus, this term only
#3.	MeSH descriptor Hepatitis B Antibodies, this term only
#4.	MeSH descriptor Hepatitis B Antigens explode all trees
#5.	(hepatitis NEAR/2 (B OR D OR delta)):ti,ab
#6.	("anti HB*" or antiHB* or HBeAg* or "HBe Ag*" or HbsA* or HBcA*):ti,ab
#7.	((HBV or CHB or hep B or hepB or HDV) NOT (heart NEXT block)):ti,ab
#8.	MeSH descriptor Hepatitis D explode all trees
#9.	MeSH descriptor Hepatitis delta Antigens, this term only
#10.	MeSH descriptor Hepatitis Delta Virus, this term only
#11.	(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10)
#12.	(tenofovir or TDF or viread):ti,ab
#13.	(#11 AND #12)
#14.	(lamivudine or zeffix or 3TC):ti,ab
#15.	(#13 AND #14)
#16.	resist*.ti,ab
#17.	(#15 AND #16)

#### D.3.5.3 Vertical transmission

- Q. In pregnant/lactating women with chronic hepatitis B what is the clinical and cost-effectiveness of pharmacological or anti-viral therapy in order to reduce risk of vertical transmission from mother to infant?**

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention /Exposure	Study filter used	Date parameters
Hepatitis B	Antivirals AND pregnancy	None	All years - 10/10/2012

### Medline search terms

1.	exp Interferon type I/
2.	Lamivudine/
3.	(interferon* or peginterferon*).ti,ab.
4.	(lamivudine or telbivudine or entecavir or emtricitabine or tenofovir or adefovir).ti,ab.
5.	(ETV or TDF or FTC or ADV or 3TC or IFN* or pegIFN*).ti,ab.
6.	(viread or truvada or hepsera or sebivo or tyzeka or baraclude or zeffix or pegasys).ti,ab.
7.	or/1-6
8.	Infectious disease transmission, Vertical/
9.	Pregnancy complications, Infectious/
10.	Pregnancy/
11.	Breast feeding/
12.	Lactation/
13.	(pregnan* or trimester* or breastfe* or breast fe* or lactat* or breast milk).ti,ab.
14.	((in utero or prenatal* or perinatal* or peripartum or intrapartum or antepartum or vertical* or intrafamilial* or familial* or congenital* or intrauterine or intra uterine or matern* or f?etomaternal* or maternof?etal* or neonat* or transplacental* or placenta* or f?etal* or f?etus) adj4 (transmi* or transfer* or infect* or pathogen* or acqui* or prevent* or interrupt* or antiviral* or anti viral*).ti,ab.
15.	((matern* or mother*) adj5 (f?eto or f?etal* or f?etus or child* or baby or infant* or newborn* or neonat* or offspring)).ti,ab.
16.	or/8-15
17.	7 and 16

### Embase search terms

1.	exp Recombinant interferon/
2.	Lamivudine/
3.	Telbivudine/
4.	Entecavir/
5.	Emtricitabine/
6.	tenofovir.hw,ti,ab.
7.	adefovir.hw,ti,ab.
8.	(interferon* or peginterferon*).ti,ab.
9.	(lamivudine or telbivudine or entecavir or emtricitabine).ti,ab.
10.	(ETV or TDF or FTC or ADV or 3TC or IFN* or pegIFN*).ti,ab.
11.	(viread or truvada or hepsera or sebivo or tyzeka or baraclude or zeffix or pegasys).ti,ab.
12.	or/1-11
13.	Vertical transmission/
14.	Intrauterine infection/
15.	Pregnancy/
16.	Pregnancy complication/
17.	Breast feeding/
18.	Lactation/



19.	(pregnan* or trimester* or breastfe* or breast fe* or lactat* or breast milk).ti,ab.
20.	((in utero or prenatal* or perinatal* or peripartum or intrapartum or antepartum or vertical* or intrafamilial* or familial* or congenital* or intrauterine or intra uterine or matern* or f?etomaternal* or maternof?etal* or neonat* or transplacental* or placenta* or f?etal* or f?etus) adj4 (transmi* or transfer* or infect* or pathogen* or acqui* or prevent* or interrupt* or antiviral* or anti viral*).ti,ab.
21.	((matern* or mother*) adj5 (f?eto or f?etal* or f?etus or child* or baby or infant* or newborn* or neonat* or offspring)).ti,ab.
22.	or/13-21
23.	12 and 22

**Cochrane search terms**

#1.	MeSH descriptor Interferon Type I explode all trees
#2.	MeSH descriptor Lamivudine, this term only
#3.	(interferon* or peginterferon*):ti,ab
#4.	(lamivudine or telbivudine or entecavir or emtricitabine or tenofovir or adefovir):ti,ab
#5.	(ETV or TDF or FTC or ADV or 3TC or IFN or pegIFN):ti,ab
#6.	(viread or truvada or hepsera or sebivo or tyzeka or baraclude or zeffix or pegasys):ti,ab
#7.	(#1 OR #2 OR #3 OR #4 OR #5 OR #6)
#8.	MeSH descriptor Infectious Disease Transmission, Vertical, this term only
#9.	MeSH descriptor Pregnancy Complications, Infectious, this term only
#10.	MeSH descriptor Pregnancy, this term only
#11.	MeSH descriptor Breast Feeding, this term only
#12.	MeSH descriptor Lactation, this term only
#13.	(pregnan* or trimester* or breastfe* or "breast feeding" or lactat* or "breast milk"):ti,ab
#14.	((utero or prenatal* or perinatal* or peripartum or intrapartum or antepartum or vertical* or intrafamilial* or familial* or congenital* or intrauterine or "intra uterine" or matern* or neonat* or transplacental* or placenta* or fetal* or foetal* or foetus or fetus or fetomaternal* or foetomaternal* or maternofetal* or maternofetal*) NEAR/4 (transmi* or transfer* or infect* or pathogen* or acqui* or prevent* or interrupt* or antiviral* or "anti viral" or "anti virals")):ti,ab
#15.	((matern* or mother*) NEAR/5 (foeto or feto or fetal* or foetal* or foetus or fetus or child* or baby or infant* or newborn* or neonat* or offspring)):ti,ab
#16.	(#8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15)
#17.	(#7 AND #16)

**D.3.5.4 Prophylactic treatment**

**Q. In people who are immunocompromised, what is the clinical and cost effectiveness of prophylactic treatment in reducing risk of hepatitis B virus reactivation and severity of flares?**

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention /Exposure	Study filter used	Date parameters
Hepatitis B	Antivirals and (reactivation or immunocompromisation)	RCTs and SRs [Medline and Embase only]	All years - 10/10/2012

**Medline search terms**

1.	Antiviral agents/
2.	(antiviral* or anti viral*).ti,ab.

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Literature search strategies

3.	Lamivudine/
4.	(lamivudine or telbivudine or entecavir or emtricitabine or tenofovir or adefovir).ti,ab.
5.	(ETV or TDF or FTC or ADV or 3TC).ti,ab.
6.	(viread or truvada or hepsera or sebivo or tyzeka or baraclude or zeffix or pegasys).ti,ab.
7.	or/1-6
8.	Virus activation/
9.	Recurrence/
10.	Chemoprevention/
11.	Immunosuppression/
12.	(reactivat* or re activat* or flare* or recur*).ti,ab.
13.	(prophyl* or preempti* or pre empti*).ti,ab.
14.	chemo*.ti,ab.
15.	(immunocomp* or immuno comp* or immunosup* or immuno sup*).ti,ab.
16.	or/8-15
17.	7 and 16

#### Embase search terms

1.	Antiviral therapy/
2.	Antivirus agent/
3.	(antiviral* or anti viral*).ti,ab.
4.	Lamivudine/
5.	Telbivudine/
6.	Entecavir/
7.	Emtricitabine/
8.	tenofovir.hw,ti,ab.
9.	adefovir.hw,ti,ab.
10.	(lamivudine or telbivudine or entecavir or emtricitabine).ti,ab.
11.	(viread or truvada or hepsera or sebivo or tyzeka or baraclude or zeffix or pegasys).ti,ab.
12.	(ETV or TDF or FTC or ADV or 3TC).ti,ab.
13.	or/1-12
14.	Virus activation/
15.	Virus reactivation/
16.	Chemoprophylaxis/
17.	Immunosuppressive treatment/
18.	Prophylaxis/
19.	Chemotherapy/
20.	(reactivat* or re activat* or flare* or recur*).ti,ab.
21.	(prophyl* or preempti* or pre empti*).ti,ab.
22.	chemo*.ti,ab.
23.	(immunocomp* or immuno comp* or immunosup* or immuno sup*).ti,ab.
24.	Recurrent disease/
25.	or/14-24
26.	13 and 25

#### Cochrane search terms

#1.	MeSH descriptor Lamivudine, this term only
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#2.	(lamivudine or telbivudine or entecavir or emtricitabine or tenofovir or adefovir):ti,ab
#3.	(ETV or TDF or FTC or ADV or 3TC):ti,ab
#4.	(viread or truvada or hepsera or sebivo or tyzeka or baraclude or zeffix or pegasys):ti,ab
#5.	MeSH descriptor Antiviral Agents, this term only
#6.	(antiviral* or anti viral*):ti,ab
#7.	(#1 OR #2 OR #3 OR #4 OR #5 OR #6)
#8.	MeSH descriptor Virus Activation, this term only
#9.	MeSH descriptor Recurrence, this term only
#10.	MeSH descriptor Chemoprevention, this term only
#11.	MeSH descriptor Immunosuppression, this term only
#12.	(reactivat* or "re activate" or "re activation" or flare* or recur*):ti,ab
#13.	(prophyl* or preempti* or "pre emptive"):ti,ab
#14.	(chemo* or immuno*):ti,ab
#15.	(#8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14)
#16.	(#7 AND #15)

### D.3.6 Frequency of monitoring

**Q. How frequently should monitoring tests be done to ascertain virological, serological and biochemical response and resolution of fibrosis (HBeAg and antibody, HBsAg and antibody and transient elastography) and resistance (HBV DNA) in people with chronic hepatitis B?**

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention /Exposure	Study filter used	Date parameters
Hepatitis B	Monitoring frequency	RCTs, SRs and Observational studies [Medline and Embase only]	All years - 10/10/2012

#### Medline search terms

1.	Endpoint determination/
2.	Disease progression/
3.	Time factors/
4.	prognos*.ti,ab,hw.
5.	((interval* or every) adj5 (month* or year* or week*)):ti,ab.
6.	(treatment adj3 (nonresponse* or failure* or response* or duration or outcome*)):ti,ab,hw.
7.	(predict* adj2 value*):ti,ab,hw.
8.	((review* or recall* or follow up* or regular* or periodic*) adj (interval* or visit* or inspect* or examin* or attend* or test* or measure*)):ti,ab.
9.	((virologic* or serologic* or clinical or biochemical) adj2 (status or response*)):ti,ab.
10.	(management adj (strateg* or protocol* or plan*)):ti,ab.
11.	(test* or measure* or prevent*).ti.
12.	(endpoint* or clearance or disappearance or seroconversion or breakthrough).ti,ab.
13.	natural histor*.ti,ab.
14.	or/1-13
15.	monitor*.ab,hw.
16.	14 and 15
17.	monitor*.ti.
18.	(predict* adj2 (treatment* or response* or outcome* or factor*)):ti,ab.

19.	or/16-18
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**Embase search terms**

1.	Disease course/
2.	Therapy delay/
3.	prognos*.ti,ab,hw.
4.	((interval* or every) adj5 (month* or year* or week*)).ti,ab.
5.	(treatment adj3 (nonresponse* or failure* or response* or duration or outcome* or planning)).ti,ab,hw.
6.	(predict* adj2 value*).ti,ab,hw.
7.	((review* or recall* or follow up* or regular* or periodic*) adj (interval* or visit* or inspect* or examin* or attend* or test* or measure*)).ti,ab.
8.	((virologic* or serologic* or clinical or biochemical) adj2 (status or response*)).ti,ab.
9.	(management adj (strateg* or protocol* or plan*)).ti,ab.
10.	(test* or measure* or prevent*).ti.
11.	(endpoint* or clearance or disappearance or seroconversion or breakthrough).ti,ab.
12.	natural histor*.ti,ab.
13.	or/1-12
14.	monitor*.ab,hw.
15.	13 and 14
16.	monitor*.ti.
17.	(predict* adj2 (treatment* or response* or outcome* or factor*)).ti,ab.
18.	15 or 16 or 17

**Cochrane search terms**

#1	MeSH descriptor Endpoint Determination, this term only
#2	MeSH descriptor Time Factors, this term only
#3	MeSH descriptor Disease Progression, this term only
#4	MeSH descriptor Prognosis, this term only
#5	MeSH descriptor Predictive Value of Tests, this term only
#6	MeSH descriptor Treatment Outcome explode tree 1
#7	prognos*:ti,ab
#8	((interval* or every) near/5 (month* or year* or week*)):ti,ab
#9	(treatment near/3 (nonresponse* or failure* or response* or duration or outcome*)):ti,ab
#10	(predict* near/2 value*):ti,ab
#11	((review* or recall* or "follow up" or regular* or periodic*) next (interval* or visit* or inspect* or examin* or attend* or test* or measure*)):ti,ab
#12	((virologic* or serologic* or clinical or biochemical) near/2 (status or response*)):ti,ab
#13	(management next (strateg* or protocol* or plan*)):ti,ab
#14	(test* or measure* or prevent*):ti
#15	(endpoint* or clearance or disappearance or seroconversion or breakthrough):ti,ab
#16	(natural next histor*):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	monitor*:ab
#19	monitoring:kw
#20	(#18 OR #19)

#21	(#17 AND #20)
#22	monitor*:ti
#23	(predict* near/2 (treatment* or response* or outcome* or factor*)):ti,ab
#24	(#21 OR #22 OR #23)

### D.3.7 Surveillance for hepatocellular carcinoma

#### Q. When and how frequently should surveillance testing be offered to detect early hepatocellular carcinoma in people with chronic hepatitis B?

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention /Exposure	Study filter used	Date parameters
Hepatitis B	Surveillance and hepatocellular carcinoma	RCTs, SRs and Observational studies [Medline and Embase only]	All years - 10/10/2012

#### Medline search terms

1.	Carcinoma, hepatocellular/
2.	Liver neoplasms/
3.	(hepatoma* or hepatocarcinoma* or HCC).ti,ab.
4.	((hepatocellular or liver or hepatic or hepato) adj2 (cancer or carcinoma* or neoplasm*)).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

#### 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

#### Cochrane search terms

#1.	MeSH descriptor Carcinoma, Hepatocellular, this term only
#2.	MeSH descriptor Liver Neoplasms, this term only
#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.	(#1 OR #2 OR #3 OR #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.	(#6 OR #7 OR #8)
#10.	(#5 AND #9)

## D.4 Economic searches

### D.4.1 Economic evaluations

Economic searches were run in Medline and Embase by combining the standard population with the economic filter (D.1.4) and limiting by date range (see table below). Economic searches were executed in the HEED and Cochrane (NHS EED and HTA) databases by simply running a standard population without a date limitation. Search terms for the HEED database are given below.

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Study filter used	Date parameters
Hepatitis B	Economic [Embase and Medline only]	<ul style="list-style-type: none"> <li>• 2009 - 10/10/2012 (Medline and Embase)</li> <li>• All years - 10/10/2012 (NHS EED, HTA and HEED)</li> </ul>

#### HEED search terms

1.	AB='hepatitis B' OR 'hep B' OR hepB
2.	TI='hepatitis B' OR 'hep B' OR hepB
3.	CS=1 OR 2

### D.4.2 Quality of life studies

Quality of life (QOL) searches were run in Medline and Embase by combining the standard population with the QOL filter (D.1.5) without a date limitation. Search terms for the HEED database are given above.

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Study filter used	Date parameters
Hepatitis B	QOL [Embase and Medline]	All years - 10/10/2012