

Supplemental Table 1: Inclusion and exclusion criteria:

<b>Disease definition</b>	Include	Chronic HBV infection: detectable HBsAg in serum for > 6 months
	Exclusion	Acute HBV infection
<b>Population</b>	Include	Children < 18 years old
	Exclusion	Adult population, co-infected with hepatitis C, D or HIV, patients receiving steroids, chemo/immunotherapy, transplant patients and hemodialysis patients
<b>Intervention</b>	Include	Antiviral therapy including: IFN $\alpha$ , lamivudine, entecavir, adefovir and tenofovir.
	Exclusion	Combination therapy and co-treatment with steroids
<b>Outcomes</b>		Cirrhosis, decompensated liver disease and hepatocellular carcinoma. ALT normalization, HBV DNA suppression, HBeAg loss/seroconversion and HBsAg loss/ seroconversion
<b>Study design</b>	Include	Randomized trials (observational studies were also included for patient-important outcomes)
	Exclusion	Studies published only as abstracts

Hepatitis B virus (HBV), Hepatitis B Surface Antigen (HBsAg), Hepatitis B e Antigen (HBeAg), Alanine Aminotransferase (ALT) , Interferon (IFN)

## Supplemental table 2: Details of search strategy:

### 2.1 Clinical outcomes:

#### Ovid

Database(s): Embase 1988 to 2014 Week 36, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to Present, EBM Reviews - Cochrane Central Register of Controlled Trials August 2014, EBM Reviews - Cochrane Database of Systematic Reviews 2005 to July 2014

Search Strategy:

#	Searches	Results
1	exp Hepatitis B/dt	26394
2	("hepatitis B" or "serum hepatitis" or "hippie hepatitis" or "injection hepatitis" or "hepatitis type B").mp.	178415
3	1 or 2	178415
4	exp Antiviral Agents/	915473
5	exp antiviral agent/ ("1-Deoxynojirimycin" or absoulone or "abt 333" or "abt 450" or Acetylcysteine or aciclovir or "acyclouridine derivative" or Acyclovir or "adenine xyloside" or "adenosine dialdehyde" or afovirsen or "al 721" or aLamivudineifovir or alisporivir or "aln rsv 01" or "alvircept sudotox" or amantadine or amenamevir or amidapsone or amitivir or "ammonium trichloro dioxyethylene o o tellurate" or amsacrine or "ana 975" or "antiviral agent" or AntiRetroviral* or "Anti-Retroviral*" or antiretrovirus or antiviral* or "anti-viral*" or Aphidicolin or arasangivamycin or arbidol or arildone or astodrimer or asunaprevir or avarol or avarone or avridine or "azd 7295" or balapiravir or bavituximab or "behenyl alcohol" or benzimidavir or besifovir or boceprevir or bonaphthone or "Brefeldin A" or brincidofovir or Bromodeoxyuridine or bropirimine or buciclovir or carbocyclic or carbodine or carrageenan or cidofovir or ciluprevir or clevidine or "cpg 10101" or crofelemer or cyclaradine or "cyclosporin A" or cytarabine or	611278
6	daclatasvir or damavaricin or danoprevir or dasabuvir or deitiphorin or deleobuvir or denotivir or deoxyaristeromycin or Deoxyglucose or deoxypenciclovir or deoxyribavirin or desciclovir or detivaciclovir or "didemnin A" or "didemnin B" or Dideoxyadenosine or Dideoxynucleoside* or disoxaril or "distamycin 5" or "distamycin A" or Ditiocarb or droxinavir or edoxudine or elbasvir or "enisamium iodide" or enviroxime or epeitrimod or eudistomin or exbivirumab or faldaprevir or famciclovir or favipiravir or felvizumab or fiacitabine or fialuridine or filibuvir or Filipin or florenal or "flucytosine arabinoside" or fomivirsen or foravirumab or fosarilate or foscarnet or fosdevirine or fucoidin or "gamma venin" or ganciclovir or "gene expression modulator" or grazoprevir or "gs 9256" or "guanine 7 oxide" or hypericin or "hypoxanthine arabinoside" or idoxuridine or "idoxuridine derivative" or "idx 184" or imexon or imiquimod or "Inosine Pranobex" or iododeoxycytidine or ipilimumab or isatoribine or "isis 13312" or "isis 14803" or laninamivir or larifan or ledipasvir or letermovir or levovirin or lexithromycin or	747307

libivirumab or litomeglovir or lomibuvir or mericitabine or merimepodib or Methisazone or methisoprinol or methylcytidine or metisazone or miravirsen or moroxydine or motavizumab or "mycophenolic acid" or "Myxovirus resistance protein" or "n bromoacetyldistamycin A" or narlaprevir or neceprevir or "neominophagen C" or nesbuvir or netivudine or netropsin or nivocasan or omaciclovir or ombitasvir or oseltamivir or palivizumab or penciclovir or "penciclovir triphosphate" or peramivir or "phosphonoacetic acid" or "Phosphonoacetic Acid" or pirazofurin or pirodavidir or pleconaril or pocapavir or "pokeweed antiviral protein" or "Poly A-U" or "Poly I-C" or pritelivir or pseudohypericin or "pyran copolymer" or "Pyran Copolymer" or radavirsen or rafivirumab or "recombinant intercellular adhesion molecule 1" or regavirumab or resiquimod or ribavirin or "ribavirin derivative" or rifabutin or rimantadine or rintatolimod or riodoxol or rociclovir or rupintrivir or samatasvir or sangivamycin or "sangivamycin derivative" or "scopadulcic acid B" or setrobuvir or sevirumab or simeprevir or sofosbuvir or sorivudine or sovaprevir or streptovaricin or Streptovaricin or streptoviridin or suramin or suvizumab or synadenol or synguanol or taribavirin or tebrofen or tecovirimat or tegobuvir or telaprevir or telbivudine or "Tenuazonic Acid" or "thiarubrine A" or "thiophene A" or "thymine arabinoside" or tilorone or Tilorone or "tilorone derivative" or tivaciclovir or tomeglovir or torcitabine or trifluridine or tromantadine or tunicamycin or tuvirumab or umifenovir or "uracil arabinoside" or valaciclovir or valganciclovir or valomaciclovir or valopicitabine or valtorcitabine or vaniprevir or varendavir or vedroprevir or vidarabine or Vidarabine or viracine or "viral inhibitor\*" or virantmycin or virostatic\* or viroxime or virucidal\* or virucide\* or "virus repressor\*" or virustatic\* or xanthogenate or "xenazoic acid" or zanamivir or Zanamivir or zinviroxime).mp.

7	4 or 5 or 6	1208899
8	exp Interferons/	453504
9	exp interferon/	453504
10	("cl 884" or cl884 or ifn or interferon* or interferone* or interferonogen* or interferron* or "interleukin 28A" or "interleukin 29" or "interleukin 6" or leif or peginterferon* or peginterferone* or peginterferonogen* or peginterferron*).mp.	628658
11	8 or 9 or 10	628758
12	exp Carcinoma, Hepatocellular/	142673
13	exp liver cell carcinoma/	142673
14	exp Fibrosis/	185663
15	exp liver cirrhosis/	157165
16	exp Morbidity/	611980
17	exp Mortality/	891087
18	exp Death/	530502
19	exp Survival/	615309
20	mo.fs.	448163
21	((liver or hepatic) adj2 carcinoma*) or cirrloses or cirrhosis or death or fatal* or	4776258

fibroses or fibrosis or HCC or hepatocarcinoma\* or "hepatocellular carcinoma\*" or hepatoma\* or morbidity or mortality or myxofibroses or myxofibrosis or surviv\*).mp.

22	or/12-21	5317148
23	3 and (7 or 11) and 22	17279
24	exp evidence based medicine/	721205
25	exp meta analysis/	134011
26	exp Meta-Analysis as Topic/	29510
27	exp "systematic review"/	79207
28	exp Guideline/ or exp Practice Guideline/	344377
29	exp controlled study/	4512490
30	exp Randomized Controlled Trial/	723249
31	exp triple blind procedure/	68
32	exp Double-Blind Method/	342895
33	exp Single-Blind Method/	51259
34	exp latin square design/	276
35	exp Placebos/	267995
36	exp Placebo Effect/	7231
37	exp comparative study/	2459742
38	exp Cross-Sectional Studies/	307288
39	exp Cross-Over Studies/	101407
40	exp Cohort Studies/	1680397
41	exp longitudinal study/	1065024
42	exp retrospective study/	864314
43	exp prospective study/	701082
44	exp population research/	68087
45	exp observational study/	65081
46	exp clinical trial/	1728711
47	clinical study/	53598
48	exp Evaluation Studies/	208013
49	exp Evaluation Studies as Topic/	1130031
50	exp Twin Study/	31182
51	exp quantitative study/	5818
52	exp validation studies/	113515
53	exp experimental study/	14612
54	exp quasi experimental study/	2028
55	exp field study/	1531
56	in vivo study/	189705

57	exp panel study/	373
58	exp Pilot Projects/	171018
59	exp pilot study/	171018
60	exp prevention study/	2120
61	exp replication study/	949
62	exp theoretical study/	1368248
63	exp Feasibility Studies/	99507
64	exp Models, Theoretical/	1387826
65	exp trend study/	11365
66	exp correlational study/	11312
67	exp case-control studies/	784804
68	exp confidence interval/	122062
69	exp regression analysis/	570654
70	exp proportional hazards model/	94889
71	exp multivariate analysis/	343014
72	"limit follow up studies to medline only. embase maps to follow up".ti.	0
73	exp follow up studies/	1343640
74	exp case study/	1738225
75	"limit case study above to embase only. medline maps to case report".ti.	0
76	odds ratio/	383358
77	"limit odds ratio above to embase. medline maps to risk".ti.	0
	((evidence adj based) or (meta adj analys*) or (systematic* adj3 review*) or guideline* or (doubl* adj blind*) or (doubl* adj mask*) or (singl* adj blind*) or (singl* adj mask*) or (tripl* adj blind*) or (tripl* adj mask*) or (trebl* adj blind*) or (trebl* adj mask*) or "latin square" or placebo or random* or control* or multivariate or "comparative study" or "comparative survey" or "comparative analysis" or compar* or (intervention* adj2 study) or (intervention* adj2 trial) or "cross-sectional study" or "cross-sectional analys*" or "cross-sectional survey*" or "cross-sectional design*" or "prevalence study" or "prevalence analys*" or "prevalence survey*" or "disease frequency study" or "disease frequency analys*" or "disease frequency survey*" or crossover or "cross-over" or cohort* or	
78	"longitudinal study" or "longitudinal survey" or "longitudinal analysis" or longitudinal* or "retrospective study" or "retrospective survey" or "retrospective analysis" or retrospectiv* or "prospective study" or "prospective survey" or "prospective analysis" or prospectiv* or "population study" or "population survey" or "population analysis" or "concurrent study" or "concurrent survey" or "concurrent analysis" or "incidence study" or "incidence survey" or "incidence analysis" or "follow-up study" or "follow-up survey" or "follow-up analysis" or "observational study" or "observational survey" or "observational analysis" or "case study" or "case series" or "clinical series" or "case studies" or "clinical study" or "clinical trial" or "evaluation study" or "evaluation survey" or "evaluation analysis" or "twin study" or "twin survey" or "twin analysis" or	22128887

"quantitative study" or "quantitative analys\*" or "validation study" or "validation survey" or "validation analysis" or "experimental study" or "experimental analysis" or "quasi experimental study" or "quasi experimental analysis" or "quasiexperimental study" or "quasiexperimental analysis" or "field study" or "field survey" or "field analysis" or "in vivo study" or "in vivo analysis" or "panel study" or "panel survey" or "panel analysis" or "prevention study" or "prevention survey" or "prevention analysis" or "replication study" or "replication analysis" or "theoretical study" or "theoretical analysis" or "feasibility study" or "feasibility analysis" or "trend study" or "trend survey" or "trend analysis" or (correlation\* adj2 study) or (correlation\* adj2 analys\*) or "case control study" or "case base study" or "case referent study" or "case referent study" or "case compeer study" or "case comparison study" or study or trial or pilot or "odds ratio" or "confidence interval" or "regression analysis" or "hazards model" or "change analysis").mp.

79 from 73 keep 793339-1301733 508395

80 from 74 keep 1-25622 25622

81 from 76 keep 1-318765 318765

82 or/24-71 12606394

83 or/78-82 23255184

84 23 and 83 12634

85 from 23 keep 11770-16846 5077

limit 85 to (clinical trial, all or clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or clinical trial or comparative study or controlled clinical trial or evaluation studies or guideline or meta analysis

86 or multicenter study or observational study or practice guideline or pragmatic clinical trial or randomized controlled trial or systematic reviews or twin study or validation studies) [Limit not valid in Embase,CCTR,CDSR; records were retained] 1032

87 84 or 86 12640

limit 87 to (book or book series or editorial or erratum or letter or note or addresses or autobiography or bibliography or biography or comment or dictionary or directory or interactive tutorial or interview or lectures or legal cases

88 or legislation or news or newspaper article or overall or patient education handout or periodical index or portraits or published erratum or video-audio media or webcasts) [Limit not valid in Embase,Ovid MEDLINE(R),Ovid MEDLINE(R) In-Process,CCTR,CDSR; records were retained] 521

89 87 not 88 12119

limit 89 to ("all IFNant (birth to 23 months)" or "all child (0 to 18 years)" or

90 "newborn IFNant (birth to 1 month)" or "IFNant (1 to 23 months)" or "preschool child (2 to 5 years)" or "child (6 to 12 years)" or "adolescent (13 to 18 years)") [Limit not valid in Embase,CCTR,CDSR; records were retained] 9176

limit 90 to (embryo or IFNant or child or preschool child <1 to 6 years> or school

91 child <7 to 12 years> or adolescent <13 to 17 years>) [Limit not valid in Ovid MEDLINE(R),Ovid MEDLINE(R) In-Process,CCTR,CDSR; records were 1251

	retained]	
92	limit 89 to ("all adult (19 plus years)" or "young adult (19 to 24 years)" or "adult (19 to 44 years)" or "young adult and adult (19-24 and 19-44)" or "middle age (45 to 64 years)" or "middle aged (45 plus years)" or "all aged (65 and over)" or "aged (80 and over)") [Limit not valid in Embase,CCTR,CDSR; records were retained]	10637
93	limit 92 to (adult <18 to 64 years> or aged <65+ years>) [Limit not valid in Ovid MEDLINE(R),Ovid MEDLINE(R) In-Process,CCTR,CDSR; records were retained]	5232
94	93 not 91	4337
95	89 not 94	7782
96	(newborn* or neonat* or IFNant* or child* or adolescent* or paediatric* or pediatric*).mp.	5972815
97	95 and 96	1442
98	91 or 97	1699
99	from 23 keep 17185-17279	95
100	96 and 99	64
101	98 or 100	1763
102	remove duplicates from 101	1492

### Scopus

- 1 TITLE-ABS-KEY("hepatitis B" or "serum hepatitis" or "hippie hepatitis" or "injection hepatitis" or "hepatitis type B")
- 2 TITLE-ABS-KEY("1-Deoxynojirimycin" OR absouline OR "abt 333" OR "abt 450" OR Acetylcysteine OR aciclovir OR "acyclouridine derivative" OR Acyclovir OR "adenine xyloside" OR "adenosine dialdehyde" OR afovirsen OR "al 721" OR aLamivudineifovir OR alisporivir OR "aln rsv 01" OR "alvircept sudotox" OR amantadine OR amenamevir OR amidapsone OR amitivir OR "ammonium trichloro dioxylethylene o o tellurate" OR amsacrine OR "ana 975" OR "anti viral agent" OR AntiRetroviral\* OR "Anti-Retroviral\*" OR antiretrovirus OR antiviral\* OR "anti-viral\*" OR Aphidicolin OR arasangivamycin OR arbidol OR arildone OR astodimer OR asunaprevir OR avarol OR avarone OR avidine OR "azd 7295" OR balapiravir OR bavituximab OR "behenyl alcohol" OR benzimidavir OR besifovir OR boceprevir OR bonaphthone OR "Brefeldin A" OR brincidofovir OR Bromodeoxyuridine OR broprimine OR buciclovir OR carbocyclic OR carbodine OR carrageenan OR cidofovir OR ciluprevir OR clevidine OR "cpg 10101" OR crofelemer OR cyclaradine OR "cyclosporin A" OR cytarabine OR daclatasvir OR damavaricin OR danoprevir OR dasabuvir OR deitiphorin OR deleobuvir OR denotivir OR deoxyaristeromycin OR Deoxyglucose OR deoxypenciclovir OR deoxyribavirin OR desciclovir OR detiviciclovir OR "didemn A" OR "didemn B" OR Dideoxyadenosine OR Dideoxynucleoside\* OR disoxaril OR "distamycin 5" OR "distamycin A" OR Ditiocarb OR droxinavir OR edoxudine OR elbasvir OR "enisamium iodide" OR enviroxime OR epetirimod OR eudistomin OR exbivirumab OR faldaprevir OR famciclovir OR favipiravir

- OR felvizumab OR fiacitabine OR fialuridine OR filibuvir OR Filipin OR florenal OR "flucytosine arabinoside" OR fomivirsen OR foravirumab OR fosarilate OR foscarnet OR fosdevirine OR fucoidin OR "gamma venin" OR ganciclovir OR "gene expression modulator" OR grazoprevir OR "gs 9256" OR "guanine 7 oxide" OR hypericin OR "hypoxanthine arabinoside" OR idoxuridine OR "idoxuridine derivative" OR "idx 184" OR imexon OR imiquimod OR "Inosine Pranobex" OR iododeoxycytidine OR ipilimumab OR isatoribine OR "isis 13312" OR "isis 14803" OR laninamivir OR larifan OR ledipasvir OR letermovir OR levovirin OR lexithromycin OR libivirumab OR litomeglovir OR lomibuvir OR mericitabine OR merimepodib OR Methisazone OR methisoprinol OR methylcytidine OR metisazone OR miravirsen OR moroxydine OR motavizumab OR "mycophenolic acid" OR "Myxovirus resistance protein" OR "n bromoacetyl distamycin A" OR narlaprevir OR neceprevir OR "neominophagen C" OR nesbuvir OR netivudine OR netropsin OR nivocasan OR omaciclovir OR ombitasvir OR oseltamivir OR palvizumab OR penciclovir OR "penciclovir triphosphate" OR peramivir OR "phosphonoacetic acid" OR "Phosphonoacetic Acid" OR pirazofurin OR pirodavir OR pleconaril OR pocapavir OR "pokeweed antiviral protein" OR "Poly A-U" OR "Poly I-C" OR pritelivir OR pseudohypericin OR "pyran copolymer" OR "Pyran Copolymer" OR radavirsen OR rafivirumab OR "recombinant intercellular adhesion molecule 1" OR regavirumab OR resiquimod OR ribavirin OR "ribavirin derivative" OR rifabutin OR rimantadine OR rintatolimod OR riodoxol OR rociclovir OR rupintrivir OR samatasvir OR sangivamycin OR "sangivamycin derivative" OR "scopadulcic acid B" OR setrobuvir OR sevirumab OR simeprevir OR sofosbuvir OR sorivudine OR sovaprevir OR streptovarin OR Streptovarin OR streptoviridin OR suramin OR suvzumab OR synadenol OR synguanol OR taribavirin OR tebrofen OR tecovirimat OR tegobuvir OR telaprevir OR telbivudine OR "Tenuazonic Acid" OR "thiarubrine A" OR "thiophene A" OR "thymine arabinoside" OR tilorone OR Tilorone OR "tilorone derivative" OR tivaciclovir OR tomeglovir OR torcitabine OR trifluridine OR tromantadine OR tunicamycin OR tuvirumab OR umifenovir OR "uracil arabinoside" OR valaciclovir OR valganciclovir OR valomaciclovir OR valopicitabine OR valtorcitabine OR vaniprevir OR vapedavir OR vedroprevir OR vidarabine OR Vidarabine OR viracine OR "viral inhibitor\*" OR virantmycin OR virostatic\* OR viroxime OR virucidal\* OR virucide\* OR "virus repressor\*" OR virustatic\* OR xanthogenate OR "xenazoic acid" OR zanamivir OR Zanamivir OR zinviroxime)
- 3 TITLE-ABS-KEY("cl 884" OR cl884 OR ifn OR interferon\* OR interferone\* OR interferonogen\* OR interferron\* OR "interleukin 28A" OR "interleukin 29" OR "interleukin 6" OR leif OR peginterferon\* OR peginterferone\* OR peginterferonogen\* OR peginterferron\*)
- 4 TITLE-ABS-KEY(((liver or hepatic) W/2 carcinoma\*) OR cirrheses OR cirrhosis OR death OR fatal\* OR fibroses OR fibrosis OR HCC OR hepatocarcinoma\* OR "hepatocellular carcinoma\*" OR hepatoma\* OR morbidity OR mortality OR myxofibroses OR myxofibrosis OR surviv\*)
- 5 TITLE-ABS-KEY(chronic\*)
- 6 TITLE-ABS-KEY((evidence W/1 based) OR (meta W/1 analys\*) OR (systematic\* W/3 review\*) OR (guideline\*) OR (doubl\* W/1 blind\*) OR (doubl\* W/1 mask\*) OR (singl\* W/1 blind\*) OR (singl\* W/1 mask\*) OR (tripl\* W/1 blind\*) OR (tripl\* W/1 mask\*) OR (trebl\* W/1 blind\*) OR



- (trebl\* W/1 mask\*) OR "latin square" OR placebo OR random\* OR control\* OR multivariate OR "comparative study" OR "comparative survey" OR "comparative analysis" OR compar\* OR (intervention\* W/2 study) OR (intervention\* W/2 trial) OR "cross-sectional study" OR "cross-sectional analys\*" OR "cross-sectional survey\*" OR "cross-sectional design\*" OR "prevalence study" OR "prevalence analys\*" OR "prevalence survey\*" OR "disease frequency study" OR "disease frequency analys\*" OR "disease frequency survey\*" OR crossover OR "cross-over" OR cohort\* OR "longitudinal study" OR "longitudinal survey" OR "longitudinal analysis" OR longitudinal\* OR "retrospective study" OR "retrospective survey" OR "retrospective analysis" OR retrospectiv\* OR "prospective study" OR "prospective survey" OR "prospective analysis" OR prospectiv\* OR "population study" OR "population survey" OR "population analysis" OR "concurrent study" OR "concurrent survey" OR "concurrent analysis" OR "incidence study" OR "incidence survey" OR "incidence analysis" OR "follow-up study" OR "follow-up survey" OR "follow-up analysis" OR "observational study" OR "observational survey" OR "observational analysis" OR "case study" OR "case series" OR "clinical series" OR "case studies" OR "clinical study" OR "clinical trial" OR "evaluation study" OR "evaluation survey" OR "evaluation analysis" OR "twin study" OR "twin survey" OR "twin analysis" OR "quantitative study" OR "quantitative analys\*" OR "validation study" OR "validation survey" OR "validation analysis" OR "experimental study" OR "experimental analysis " Or "quasi experimental study" OR "quasi experimental analysis" OR "quasiexperimental study" OR "quasiexperimental analysis" OR "field study" OR "field survey" OR "field analysis" OR "in vivo study" OR "in vivo analysis" OR "panel study" OR "panel survey" OR "panel analysis" OR "prevention study" OR "prevention survey" OR "prevention analysis" OR "replication study" OR "replication analysis " OR "theoretical study" OR "theoretical analysis " OR "feasibility study" OR "feasibility analysis " OR "trend study" OR "trend survey" OR "trend analysis" OR (correlation\* W/2 study) OR (correlation\* W/2 analys\*) OR "case control study" OR "case base study" OR "case referrent study" OR "case referent study" OR "case compeer study" OR "case comparison study" OR study OR trial OR pilot OR "odds ratio" OR "confidence interval" OR "regression analysis" OR "hazards model" OR "change analysis")
- 7 TITLE-ABS-KEY(newborn\* or neonat\* or IFNant\* or child\* or adolescent\* or paediatric\* or pediatric\*)
- 8 1 and (2 or 3) and 4 and 5 and 6 and 7
- 9 DOCTYPE(le) OR DOCTYPE(ed) OR DOCTYPE(bk) OR DOCTYPE(er) OR DOCTYPE(no) OR DOCTYPE(sh)
- 10 8 and not 9
- 11 PMID(0\*) OR PMID(1\*) OR PMID(2\*) OR PMID(3\*) OR PMID(4\*) OR PMID(5\*) OR PMID(6\*) OR PMID(7\*) OR PMID(8\*) OR PMID(9\*)
- 12 10 and not 11

## 2.2 Intermediate outcomes:

### Ovid

Database(s): Embase 1988 to 2014 Week 47, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to Present, EBM Reviews - Cochrane Central Register of Controlled Trials October 2014

Search Strategy:

#	Searches	Results
1	exp Hepatitis B/dt	26515
2	("hepatitis B" or "serum hepatitis" or "hippie hepatitis" or "injection hepatitis" or "hepatitis type B").mp.	180851
3	1 or 2	180851
4	exp Antiviral Agents/	931142
5	exp antiviral agent/	618490
6	exp Lamivudineivudine/	33724
7	exp adefovir/	4377
8	exp entecavir/	4806
9	exp tenofovir/	10670
10	("1-Deoxynojirimycin" or absoulone or "abt 333" or "abt 450" or Acetylcysteine or aciclovir or "acyclouridine derivative" or Acyclovir or "adenine xyloside" or "adenosine dialdehyde" or afovirsen or "al 721" or aLamivudineifovir or alisporivir or "aln rsv 01" or "alvircept sudotox" or amantadine or amenamevir or amidapsone or amitivir or "ammonium trichloro dioxyethylene o o tellurate" or amsacrine or "ana 975" or "anti viral agent" or AntiRetroviral* or "Anti-Retroviral*" or antiretrovirus or antiviral* or "anti-viral*" or Aphidicolin or arasangivamycin or arbidol or arildone or astodrimmer or asunaprevir or avarol or avarone or avridine or "azd 7295" or balapiravir or bavituximab or "behenyl alcohol" or benzimidavir or besifovir or boceprevir or bonaphthone or "Brefeldin A" or brincidofovir or Bromodeoxyuridine or broprimine or buciclovir or carbocyclic or carbodine or carrageenan or cidofovir or ciluprevir or clevidine or "cpg 10101" or crofelemer or cyclaradine or "cyclosporin A" or cytarabine or daclatasvir or damavaricin or danoprevir or dasabuvir or deitiphorin or deleobuvir or denotivir or deoxyaristeromycin or Deoxyglucose or deoxypenciclovir or deoxyribavirin or desciclovir or detivaciclovir or "didemnin A" or "didemnin B" or Dideoxyadenosine or Dideoxynucleoside* or disoxaril or "distamycin 5" or "distamycin A" or Ditiocarb or droxinavir or edoxudine or elbasvir or "enisamium iodide" or enviroxime or epretimod or eudistomin or exbivirumab or faldaprevir or famciclovir or favipiravir or felvizumab or fiacitabine or fialuridine or filibuvir or Filipin or florenal or "flucytosine arabinoside" or fomivirsen or foravirumab or fosarilate or foscarnet or fosdevirine or fucoidin or "gamma venin" or ganciclovir or "gene expression modulator" or grazoprevir or "gs 9256" or "guanine 7 oxide" or hypericin or "hypoxanthine arabinoside" or idoxuridine or "idoxuridine derivative" or "idx 184" or imexon or imiquimod or "Inosine Pranobex" or iododeoxycytidine or ipilimumab or isatoribine or "isis 13312" or "isis 14803" or laninamivir or larifan or	775407

ledipasvir or letermovir or levovirin or lexithromycin or libivirumab or litomeglovir or lomibuvir or mericitabine or merimepodib or Methisazone or methisoprinol or methylcytidine or metisazone or miravirsen or moroxydine or motavizumab or "mycophenolic acid" or "Myxovirus resistance protein" or "n bromoacetyldistamycin A" or narlaprevir or neceprevir or "neominophagen C" or nesbuvir or netivudine or netropsin or nivocasan or omaciclovir or ombitasvir or oseltamivir or palivizumab or penciclovir or "penciclovir triphosphate" or peramivir or "phosphonoacetic acid" or "Phosphonoacetic Acid" or pirazofurin or pirodavir or pleconaril or pocapavir or "pokeweed antiviral protein" or "Poly A-U" or "Poly I-C" or pritelivir or pseudohypericin or "pyran copolymer" or "Pyran Copolymer" or radavirsen or rafivirumab or "recombinant intercellular adhesion molecule 1" or regavirumab or resiquimod or ribavirin or "ribavirin derivative" or rifabutin or rimantadine or rintatolimod or riodoxol or rociclovir or rupintrivir or samatasvir or sangivamycin or "sangivamycin derivative" or "scopadulcic acid B" or setrobuvir or sevirumab or simeprevir or sofosbuvir or sorivudine or sovaprevir or streptovaricin or Streptovaricin or streptovirudin or suramin or suvizumab or synadenol or synguanol or taribavirin or tebprofen or tecovirimat or tegobuvir or telaprevir or telbivudine or "Tenuazonic Acid" or "thiarubrine A" or "thiophene A" or "thymine arabinoside" or tilorone or Tilorone or "tilorone derivative" or tivaciclovir or tomeglovir or torcitabine or trifluridine or tromantadine or tunicamycin or tuvirumab or umifenovir or "uracil arabinoside" or valaciclovir or valganciclovir or valomaciclovir or valopicitabine or valtorcitabine or vaniprevir or varendavir or vedroprevir or vidarabine or Vidarabine or viracine or "viral inhibitor\*" or virantmycin or virostatic\* or viroxime or virucidal\* or virucide\* or "virus repressor\*" or virustatic\* or xanthogenate or "xenazoic acid" or zanamivir or Zanamivir or zinviroxime or adefovir or baraclude or "bch 189" or bch189 or "bms 200475" or bms200475 or entecavir or epivir or "epivir 3tc" or "epivir hbv" or "gr 103665" or "gr 109714x" or gr103665 or gr109714x or "gs 0393" or "gs 840" or gs0393 or gs840 or hepivir or heptodin or heptovir or inhavir or InterferonAlfa or ladiwin or Lamivudineidac or Lamivudineivir or Lamivudineivudine or "Lamivudineivudine hydrate" or "nsc 620753" or nsc620753 or PMEA or PMPA or sLamivudineivudine or "sq 34676" or sq34676 or tenofovir or zeffix or zefix).mp.

11 or/4-10	1232005
12 exp Interferons/	460592
13 exp interferon/ ("cl 884" or cl884 or ifn or interferon* or interferone* or interferonogen* or	460592
14 interferron* or "interleukin 28A" or "interleukin 29" or "interleukin 6" or leif or peginterferon* or peginterferone* or peginterferonogen* or peginterferron*).mp.	641443
15 12 or 13 or 14	641542
16 exp Carcinoma, Hepatocellular/	145477
17 exp liver cell carcinoma/	145477
18 exp Fibrosis/	190255
19 exp liver cirrhosis/	159461
20 exp Morbidity/	628934

21 exp Mortality/	909898
22 exp Death/	542252
23 exp Survival/	625927
24 mo.fs.	460974
25 (((liver or hepatic) adj2 carcinoma*) or cirrhoses or cirrhosis or death or fatal* or fibroses or fibrosis or HCC or hepatocarcinoma* or "hepatocellular carcinoma*" or hepatoma* or morbidity or mortality or myxofibroses or myxofibrosis or surviv*).mp.	4882558
26 "alanine aminotransferase"/	84213
27 26 and normal*.mp.	18319
28 exp DNA, Viral/	126965
29 28 and suppres*.mp.	5283
30 exp "hepatitis B(e) antigen"/	15432
31 30 and (loss or seroconver* or "sero-conver*").mp.	4784
32 (((("Alanine aminotransferase" or ALT) adj3 normal*) or ("hbe antigen*" or HBeAg or "hepatitis b e antigen*" or "hepatitis be antigen*") adj3 (loss or seroconver* or "sero-conver*")) or (DNA adj3 suppres*)).mp.	18971
33 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 27 or 29 or 31 or 32	5463734
34 3 and (11 or 15) and 33	22702
35 exp controlled study/	4551116
36 exp Randomized Controlled Trial/	739260
37 exp triple blind procedure/	78
38 exp Double-Blind Method/	346888
39 exp Single-Blind Method/	52203
40 exp latin square design/	277
41 exp Placebos/	270310
42 exp Placebo Effect/	7409
43 exp comparative study/	2494773
44 exp clinical trial/	1759114
45 clinical study/	55566
46 (((control* adj3 study) or (control* adj3 trial) or (randomized adj3 study) or (randomized adj3 trial) or (randomised adj3 study) or (randomised adj3 trial) or "pragmatic clinical trial" or (doubl* adj blind*) or (doubl* adj mask*) or (singl* adj blind*) or (singl* adj mask*) or (tripl* adj blind*) or (tripl* adj mask*) or (trebl* adj blind*) or (trebl* adj mask*) or "latin square" or placebo* or nocebo* or "comparative study" or "comparative survey" or "comparative analysis" or "clinical study" or "clinical trial").mp,pt.	9441615
47 or/35-46	9602900
48 34 and 47	9274
49 from 34 keep 14818-21782	6965

50	limit 49 to (clinical trial, all or clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or clinical trial or controlled clinical trial or multicenter study or observational study or randomized controlled trial or pragmatic clinical trial or comparative study or controlled clinical trial or multicenter study or randomized controlled trial or pragmatic clinical trial) [Limit not valid in Embase,CCTR; records were retained]	1551
51	48 or 50	9274
52	limit 51 to (book or book series or editorial or erratum or letter or note or addresses or autobiography or bibliography or biography or comment or dictionary or directory or interactive tutorial or interview or lectures or legal cases or legislation or news or newspaper article or overall or patient education handout or periodical index or portraits or published erratum or video-audio media or webcasts) [Limit not valid in Embase,Ovid MEDLINE(R),Ovid MEDLINE(R) In-Process,CCTR; records were retained]	282
53	51 not 52	8992
54	limit 53 to ("all IFNant (birth to 23 months)" or "all child (0 to 18 years)" or "newborn IFNant (birth to 1 month)" or "IFNant (1 to 23 months)" or "preschool child (2 to 5 years)" or "child (6 to 12 years)" or "adolescent (13 to 18 years)") [Limit not valid in Embase,CCTR; records were retained]	7665
55	limit 54 to (embryo or IFNant or child or preschool child <1 to 6 years> or school child <7 to 12 years> or adolescent <13 to 17 years>) [Limit not valid in Ovid MEDLINE(R),Ovid MEDLINE(R) In-Process,CCTR; records were retained]	1632
56	limit 53 to ("all adult (19 plus years)" or "young adult (19 to 24 years)" or "adult (19 to 44 years)" or "young adult and adult (19-24 and 19-44)" or "middle age (45 to 64 years)" or "middle aged (45 plus years)" or "all aged (65 and over)" or "aged (80 and over)") [Limit not valid in Embase,CCTR; records were retained]	8574
57	limit 56 to (adult <18 to 64 years> or aged <65+ years>) [Limit not valid in Ovid MEDLINE(R),Ovid MEDLINE(R) In-Process,CCTR; records were retained]	5376
58	57 not 55	4040
59	53 not 58	4952
60	(newborn* or neonat* or IFNant* or child* or adolescent* or paediatric* or pediatric*).mp.	6076596
61	59 and 60	1307
62	55 or 61	1852
63	from 34 keep 21783-22702	920
64	60 and 63	248
65	62 or 64	1878
66	remove duplicates from 65	1600

#### Scopus

- 1 TITLE-ABS-KEY("hepatitis B" or "serum hepatitis" or "hippie hepatitis" or "injection hepatitis" or "hepatitis type B")

2 TITLE-ABS-KEY("1-Deoxynojirimycin" OR absouline OR "abt 333" OR "abt 450" OR Acetylcysteine OR aciclovir OR "acyclouridine derivative" OR Acyclovir OR "adenine xyloside" OR "adenosine dialdehyde" OR afovirsen OR "al 721" OR aLamivudineifovir OR alisporivir OR "aln rsv 01" OR "alvircept sudotox" OR amantadine OR amenamevir OR amidapsone OR amitivir OR "ammonium trichloro dioxethylene o o tellurate" OR amsacrine OR "ana 975" OR "anti viral agent" OR AntiRetroviral\* OR "Anti-Retroviral\*" OR antiretrovirus OR antiviral\* OR "anti-viral\*" OR Aphidicolin OR arasangivamycin OR arbidol OR arildone OR astodimer OR asunaprevir OR avarol OR avarone OR avridine OR "azd 7295" OR balapiravir OR bavituximab OR "behenyl alcohol" OR benzimidavir OR besifovir OR boceprevir OR bonaphthone OR "Brefeldin A" OR brincidofovir OR Bromodeoxyuridine OR bropirimine OR buciclovir OR carbocyclic OR carbodine OR carrageenan OR cidofovir OR ciluprevir OR clevidine OR "cpg 10101" OR crofelemer OR cycclaradine OR "cyclosporin A" OR cytarabine OR daclatasvir OR damavaricin OR danoprevir OR dasabuvir OR deitiphorin OR deleobuvir OR denotivir OR deoxyaristeromycin OR Deoxyglucose OR deoxypenciclovir OR deoxyribavirin OR desciclovir OR detiviciclovir OR "didemnin A" OR "didemnin B" OR Dideoxyadenosine OR Dideoxynucleoside\* OR disoxaril OR "distamycin 5" OR "distamycin A" OR Ditiocarb OR droxinavir OR edoxudine OR elbasvir OR "enisamium iodide" OR enviroxime OR epetirimod OR eudistomin OR exbivirumab OR faldaprevir OR famciclovir OR favipiravir OR felvizumab OR fiacitabine OR fialuridine OR filibuvir OR Filipin OR florenal OR "flucytosine arabinoside" OR fomivirsen OR foravirumab OR fosarilate OR foscarnet OR fosdevirine OR fucoidin OR "gamma venin" OR ganciclovir OR "gene expression modulator" OR grazoprevir OR "gs 9256" OR "guanine 7 oxide" OR hypericin OR "hypoxanthine arabinoside" OR idoxuridine OR "idoxuridine derivative" OR "idx 184" OR imexon OR imiquimod OR "Inosine Pranobex" OR iododeoxycytidine OR ipilimumab OR isatoribine OR "isis 13312" OR "isis 14803" OR laninamivir OR larifan OR ledipasvir OR letermovir OR levovirin OR lexithromycin OR libivirumab OR litomeglovir OR lomibuvir OR mericitabine OR merimepodib OR Methisazone OR methisoprinol OR methylcytidine OR metisazone OR miravirsen OR moroxydine OR motavizumab OR "mycophenolic acid" OR "Myxovirus resistance protein" OR "n bromoacetyldistamycin A" OR narlaprevir OR neceprevir OR "neominophagen C" OR nesbuvir OR netivudine OR netropsin OR nivocasan OR omaciclovir OR ombitasvir OR oseltamivir OR palivizumab OR penciclovir OR "penciclovir triphosphate" OR peramivir OR "phosphonoacetic acid" OR "Phosphonoacetic Acid" OR pirazofurin OR pirodavar OR pleconaril OR pocapavir OR "pokeweed antiviral protein" OR "Poly A-U" OR "Poly I-C" OR pritelivir OR pseudohypericin OR "pyran copolymer" OR "Pyran Copolymer" OR radavirsen OR rafivirumab OR "recombinant intercellular adhesion molecule 1" OR regavirumab OR resiquimod OR ribavirin OR "ribavirin derivative" OR rifabutin OR rimantadine OR rintatolimod OR riodoxol OR rociclovir OR rupintrivir OR samatasvir OR sangivamycin OR "sangivamycin derivative" OR "scopadulcic acid B" OR setrobuvir OR sevirumab OR simeprevir OR sofosbuvir OR sorivudine OR sovaprevir OR streptovarin OR Streptovarin OR streptovirudin OR suramin OR suvizumab OR synadenol OR synguanol OR taribavirin OR tebafen OR tecovirimat OR tegobuvir OR telaprevir OR telbivudine OR "Tenuazonic Acid" OR "thiarubrine A" OR "thiophene A" OR "thymine arabinoside" OR

- tilorone OR Tilorone OR "tilorone derivative" OR tivaciclovir OR tomeglovir OR torcitabine OR trifluridine OR tromantadine OR tunicamycin OR tuvirumab OR umifenovir OR "uracil arabinoside" OR valaciclovir OR valganciclovir OR valomaciclovir OR valopicitabine OR valtorcitabine OR vaniprevir OR vapedavir OR vedroprevir OR vidarabine OR Vidarabine OR viracine OR "viral inhibitor\*" OR virantmycin OR virostatic\* OR viroxime OR virucidal\* OR virucide\* OR "virus repressor\*" OR virustatic\* OR xanthogenate OR "xenazoic acid" OR zanamivir OR Zanamivir OR zinviroxime or adefovir OR baraclude OR "bch 189" OR bch189 OR "bms 200475" OR bms200475 OR entecavir OR epivir OR "epivir 3tc" OR "epivir hbv" OR "gr 103665" OR "gr 109714x" OR gr103665 OR gr109714x OR "gs 0393" OR "gs 840" OR gs0393 OR gs840 OR hepivir OR heptodin OR heptovir OR inhavir OR InterferonAlfa OR ladiwin OR Lamivudineidac OR Lamivudineivir OR Lamivudineivudine OR "Lamivudineivudine hydrate" OR "nsc 620753" OR nsc620753 OR PMEa OR PMPA OR sLamivudineivudine OR "sq 34676" OR sq34676 OR tenofovir OR zeffix OR zefix)
- 3 TITLE-ABS-KEY("cl 884" OR cl884 OR ifn OR interferon\* OR interferone\* OR interferonogen\* OR interferron\* OR "interleukin 28A" OR "interleukin 29" OR "interleukin 6" OR leif OR peginterferon\* OR peginterferone\* OR peginterferonogen\* OR peginterferron\*)
- 4 TITLE-ABS-KEY(((liver or hepatic) W/2 carcinoma\*) OR cirrheses OR cirrhosis OR death OR fatal\* OR fibroses OR fibrosis OR HCC OR hepatocarcinoma\* OR "hepatocellular carcinoma\*" OR hepatoma\* OR morbidity OR mortality OR myxofibroses OR myxofibrosis OR surviv\* OR (("Alanine aminotransferase" or ALT) adj3 normal\*) or (("hbe antigen\*" or HBeAg or "hepatitis b e antigen\*" or "hepatitis be antigen\*") adj3 (loss or seroconver\* or "sero-conver\*")) or (DNA adj3 suppres\*))
- 5 TITLE-ABS-KEY((control\* W/3 study) OR (control\* W/3 trial) OR (randomized W/3 study) OR (randomized W/3 trial) OR (randomised W/3 study) OR (randomised W/3 trial) OR "pragmatic clinical trial" OR (doubl\* W/1 blind\*) OR (doubl\* W/1 mask\*) OR (singl\* W/1 blind\*) OR (singl\* W/1 mask\*) OR (tripl\* W/1 blind\*) OR (tripl\* W/1 mask\*) OR (trebl\* W/1 blind\*) OR (trebl\* W/1 mask\*) OR "latin square" OR placebo\* OR nocebo\* OR "comparative study" OR "comparative survey" OR "comparative analysis" OR "clinical study" OR "clinical trial")
- 6 TITLE-ABS-KEY(newborn\* or neonat\* or IFNant\* or child\* or adolescent\* or paediatric\* or pediatric\*)
- 7 1 and (2 or 3) and 4 and 5 and 6
- 8 DOCTYPE(le) OR DOCTYPE(ed) OR DOCTYPE(bk) OR DOCTYPE(er) OR DOCTYPE(no) OR DOCTYPE(sh)
- 9 7 and not 8
- 10 PMID(0\*) OR PMID(1\*) OR PMID(2\*) OR PMID(3\*) OR PMID(4\*) OR PMID(5\*) OR PMID(6\*) OR PMID(7\*) OR PMID(8\*) OR PMID(9\*)
- 11 9 and not 10

Supplemental Table 3: Evidence summary for antiviral therapy in management of chronic hepatitis B virus infection in children

Intervention (Follow up)	Outcome	No of participants (Study design)	Quality of the evidence (GRADE)	Relative effect (95% CI)
Antiviral therapy vs control (Post-treatment follow up < 12 months)	ALT normalization	1009 (8 RCTs)	⊕⊕○○ <sup>1,3</sup> LOW	RR 2.32 (1.69 to 3.18)
	HBeAg clearance/loss	732 (7 RCTs)	⊕⊕○○ <sup>1,3</sup> LOW	RR 2.15 (1.50 to 3.08)
	HBV DNA suppression	923 (9 RCTs)	⊕○○○ <sup>1,2,3</sup> VERY LOW	RR 3.34 (1.84 to 6.03)
	HBeAg seroconversion	637 (4 RCT)	⊕⊕○○ <sup>1,3</sup> LOW	RR 2.14 (1.41 to 3.26)
	HBsAg clearance	430 (2 RCTs)	⊕⊕○○ <sup>3,4</sup> LOW	RR 5.78 (1.06 to 31.5)
Antiviral therapy vs control (Post-treatment follow up ≥12 months)	ALT normalization	192 (2 RCTs)	⊕⊕○○ <sup>1,3</sup> LOW	RR 1.36 (1.10 to 1.69)
	HBeAg clearance/loss	242 (5 RCTs)	⊕○○○ <sup>1,3,4</sup> VERY LOW	RR 1.95 (1.18 to 3.23)
	HBV DNA suppression	455 (7 RCTs)	⊕⊕○○ <sup>1,3</sup> LOW	RR 1.39 (1.09 to 1.76)
	HBeAg seroconversion	290 (3 RCTs)	⊕⊕○○ <sup>1,3</sup> LOW	RR 2.12 (1.27 to 3.53)
	HBsAg clearance	81 (2 RCTs)	⊕○○○ <sup>1,3,4</sup> VERY LOW	RR 3.25 (0.38 to 27.79)
	HBsAg seroconversion	81 (2 RCT)	⊕○○○ <sup>1,3,4</sup> VERY LOW	RR 2.49 (0.27 to 22.71)
IFN-alpha vs control (Post-treatment follow up < 12 months)	ALT normalization	264 (4 RCTs)	⊕○○○ <sup>1,3,4</sup> VERY LOW	RR 1.41 (0.88 to 2.25)
	HBeAg clearance/loss	302 (4 RCTs)	⊕⊕○○ <sup>1,3</sup> LOW	RR 3.19 (1.79 to 5.69)
	HBV DNA suppression	371 (6 RCTs)	⊕⊕○○ <sup>1,3</sup> LOW	RR 2.16 (1.43 to 3.28)
	HBeAg seroconversion	61 (1 RCT)	⊕○○○ <sup>1,3,4</sup> VERY LOW	RR 2.76 (0.81 to 9.41)
	HBsAg clearance	144 (1 RCT)	⊕○○○ <sup>1,3,4</sup> VERY LOW	RR 7.40 (0.93 to 58.62)
IFN-alpha vs control (Post-treatment follow up ≥12 months)	ALT normalization	22 (1 RCTs)	⊕○○○ <sup>1,3,4</sup> VERY LOW	RR 1.38 (0.59 to 3.23)
	HBeAg clearance/loss	242 (5 RCTs)	⊕⊕○○ <sup>1,3</sup> LOW	RR 1.95 (1.18 to 3.23)
	HBV DNA suppression	295 (6 RCTs)	⊕⊕○○ <sup>1,3</sup> LOW	RR 1.46 (0.99 to 2.14)
	HBeAg seroconversion	120 (2 RCT)	⊕⊕○○ <sup>1,3</sup> LOW	RR 3.08 (1.17 to 8.09)
	HBsAg clearance	81 (2 RCT)	⊕○○○ <sup>1,3,4</sup> VERY LOW	RR 3.25 (0.38 to 27.79)
	HBsAg seroconversion	72 (2 RCT)	⊕○○○ <sup>1,3,4</sup> VERY LOW	RR 2.49 (0.27 to 22.71)
Lamivudine vs control	ALT normalization	286 (1 RCT)	⊕⊕⊕○ <sup>3</sup>	RR 4.50 (2.25 to 9.09)



(End of treatment duration 48 weeks)			MODERATE	
	HBeAg clearance/loss	286 (1 RCT)	⊕⊕⊕○ <sup>3</sup> MODERATE	RR 1.78 (1.04 to 3.05)
	HBV DNA suppression	286 (1 RCTs)	⊕⊕⊕○ <sup>3</sup> MODERATE	RR 3.88 (2.41 to 6.26)
	HBeAg seroconversion	286 (1 RCTs)	⊕⊕⊕○ <sup>3</sup> MODERATE	RR 1.74 (0.96 to 3.15)
	HBsAg clearance	286 (1 RCT)	⊕⊕○○ <sup>3,4</sup> LOW	RR 3.50 (0.18 to 67.07)
Adefovir vs control (End of treatment duration 48 weeks)	ALT normalization	200 (1 RCT)	⊕⊕⊕○ <sup>3</sup> MODERATE	RR 2.69 (1.58 to 4.57)
	HBeAg seroconversion	170 (1 RCT)	⊕⊕○○ <sup>3,4</sup> LOW	RR 3.03 (0.93 to 9.85)
Tenofovir vs Control (End of treatment duration 72 weeks)	ALT normalization	106 (1 RCT)	⊕⊕⊕○ <sup>3</sup> MODERATE	RR 1.98 (1.37 to 2.85)
	HBeAg clearance/loss	96 (1 RCT)	⊕⊕○○ <sup>3,4</sup> LOW	RR 1.43 (0.59 to 3.44)
	HBV DNA suppression	96 (1 RCT)	⊕⊕○○ <sup>3,4</sup> LOW	RR 92.4 (5.76 to 146.7)
Entecavir vs placebo (End of treatment duration 48 weeks)	ALT normalization	180 (1RCT)	⊕⊕⊕○ <sup>3</sup> MODERATE	RR 2.89 (1.80 to 4.65)
	HBV DNA suppression	180 (1RCT)	⊕⊕○○ <sup>3,4</sup> LOW	RR 14.75 (3.75 to 58.32)
	HBeAg seroconversion	180 (1RCT)	⊕⊕⊕○ <sup>3</sup> MODERATE	RR 2.42 (1.06 to 5.50)
Entecavir vs placebo (96 weeks)	ALT normalization	170 (1RCT)	⊕⊕○○ <sup>3,4</sup> LOW	RR 1.13 (0.94 to 1.38)
	HBV DNA suppression	170 (1RCT)	⊕⊕○○ <sup>3,4</sup> LOW	RR 1.23 (0.92 to 1.66)
	HBeAg seroconversion	170 (1RCT)	⊕⊕⊕○ <sup>3</sup> MODERATE	RR 1.1 (1.00 to 3.35)

Footnotes: <sup>1</sup>Increased risk of bias <sup>2</sup>Inconsistency <sup>3</sup>Indirectness <sup>4</sup>Imprecision