Appendix to *Antiretroviral therapy for pregnant women living with HIV or hepatitis B: a systematic review*
Appendix 1a

Complete search strategy #1: direct evidence from comparative studies of NRTI therapy in pregnant women living with HIV

Database: Ovid MEDLINE(R) <1996 to January 12, 2017 with daily update>

Search Strategy:

1  exp HIV/ (86974)
2  (hiv-infect* or hiv-uninfected or hiv-noninfected or hiv-exposed).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (190210)
3  human immunodeficiency virus.mp. (75380)
4  hiv.mp. (277365)
5  human immune*.mp. or Acquired Immunodeficiency Syndrome/ (38306)
6  human immunodeficiency virus-exposed.mp. (33)
7  HIV Infections/ or HIV prevention.mp. (171100)
8  HIV-exposed uninfected.mp. (261)
9  AIDS.mp. (122315)
10  acquired immun*.mp. (50320)
11  human immun*.mp. (83831)
12  deficiency virus.mp. (404)
13  HIV-infected mothers.mp. (793)
14  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 (341888)
15  exp pregnancy/ (441409)
16  (Pregnan* or non-pregnant or infant* or newborn* or neonate).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1088445)
17  (breastf* or breast fe*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (30930)
Fetal Growth Retardation/ or maternal.mp. (184127)
(prenatal* or prenatal exposure or perinatal*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (147078)
lactat*.mp. (102104)
In utero exposure.mp. (1992)
(gestation* or congenital).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (292851)
(MTCT or Mother-to-child transmission or Mother to child transmission or Mother-to-infant transmission or Infectious disease transmission, vertical or Vertical transmission or disease transmission, vertical or Adult to child transmission or mother-to-infant).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (21275)
15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 (1321676)
14 and 24 (34559)
exp tenofovir/ (3395)
exp antiretroviral therapy/ (21906)
TDF.mp. (1626)
exp emtricitabine/ (1201)
FTC.mp. (1936)
Combination TDF FTC.mp. (4)
Tenofovir emtricitabine efavirenz.mp. (31)
Antiretroviral Therapy, Highly Active/ or Drug Resistance, Viral/ or Zidovudine/ or NRTI.mp. or Anti-HIV Agents/ or HIV Reverse Transcriptase/ (71025)
NRTIs.mp. (1548)
nucleotide reverse transcriptase inhibitor.mp. (142)
(preexposure prophylaxis or Pre-Exposure Prophylaxis or PrEP).mp. [mp=title, abstract,
Database: Embase <1996 to 2017 January 13>
Search Strategy:

1. exp HIV/ (210953)
2. (hiv-infect* or hiv-uninfected or hiv-noninfected or hiv-exposed or human immunodeficiency virus or human immune*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading] (337799)
3. (HIV-exposed uninfected or AIDS or acquired immun*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading] (147854)
4. exp pregnancy/ (404194)
5. (Pregnan* or non-pregnant or infant* or newborn* or neonate).mp. [mp=title, abstract, heading word, drug trade
name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading) (1100463)
6  breastf*.mp. (23599)
7  (prenatal exposure or perinatal*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading] (110164)
8  (In utero exposure or gestation*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading] (205557)
9  (MTCT or Mother-to-child transmission or Mother to child transmission or Mother-to-infant transmission or Infectious disease transmission, vertical or Vertical transmission or disease transmission, vertical or Adult to child transmission or mother-to-infant).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading] (21091)
10  1 or 2 or 3 (396132)
11  4 or 5 or 6 or 7 or 8 or 9 (1156675)
12  10 and 11 (35782)
13  exp tenofovir/ (15120)
14  exp antiretroviral therapy/ (36372)
15  tenofovir disoproxil/ or TDF.mp. (6694)
16  exp emtricitabine/ (7239)
17  (FTC or Combination TDF FTC or Tenofovir emtricitabine efavirenz).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading] (3498)
18  (AZT or 3TC).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading] (5159)
19  efavirenz.mp. or efavirenz plus emtricitabine plus tenofovir disoproxil/ or efavirenz plus lamivudine plus zidovudine/ or efavirenz plus lamivudine plus tenofovir disoproxil/ (17412)
20  (nucleoside reverse transcriptase inhibitor or nucleotide reverse transcriptase inhibitor or reverse transcriptase inhibitors).mp. [mp=title, abstract, heading word, drug trade name, original title,
device manufacturer,
drug manufacturer, device trade name, keyword, floating subheading] (7580)
21 (preexposure prophylaxis or Pre-Exposure Prophylaxis or PrEP or Combination ART or
Combination antiretroviral
therapy).mp. [mp=title, abstract, heading word, drug trade name, original title, device
manufacturer, drug manufacturer,
device trade name, keyword, floating subheading] (9760)
22 (Anti-HIV Agents or triple ART or triple antiretroviral therapy or maternal triple
antiretrovirals or mART
NRTI).mp. [mp=title, abstract, heading word, drug trade name, original title, device
manufacturer, drug manufacturer,
device trade name, keyword, floating subheading] (1156)
23 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 (75195)
24 12 and 23 (6143)
25 limit 24 to (human and yr="1996 -Current") (5867)
26 limit 25 to (clinical trial or randomized controlled trial or controlled clinical trial) (1032)
Appendix 1b

Complete search strategy #2: indirect evidence about viral load suppression and adverse effects from randomised controlled trials in non-pregnant adults living with HIV. The search was adapted from Kanters S et al. Lancet HIV. 2016;3(11):e510-e520.

Database: Ovid MEDLINE(R) <July 7 2015 to February Week 1 2017>
Search Strategy:

1  exp HIV/ or exp HIV Infection/ (284680)
2  (HIV Infections or HIV?1* or HIV?2* or HIV infect* or human immune?deficiency virus or human immune?deficiency virus).ti,ab. (87275)
3  (human immun* and deficiency virus).ti,ab. (481)
4  (acquired immuno?deficiency syndrome or AIDS or acquired immunodeficiency syndrome or acquired immune deficiency).ti,ab. (131687)
5  (acquired immun* and deficiency syndrome).ti,ab. (5207)
6  Salvage therapy.ti,ab. (3872)
7  exp Treatment Failure/ (30593)
8  (Treatment-experienced or Antiretroviral experienced or ART-experienced or Experienced patients).ti,ab. (2412)
9  treatment switch*.ti,ab. (280)
10 (or/1-5) not (or/6-9) (324871)
11  exp Antiretroviral Therapy, Highly Active/ (19002)
12  exp Integrase Inhibitors/ (2110)
13  exp HIV Reverse Transcriptase/ (5271)
14  exp Reverse Transcriptase Inhibitors/ (30089)
15  exp Anti-HIV Agents/ (59829)
16  exp HIV Protease Inhibitors/ (12154)
17  (atazanavir or Reyataz or a603019 or BMS-232632 or atv*).ti,ab. (1994)
18  (cobicistat or GS-9350 or Tybost).ti,ab. (142)
19  (dolutegravir or Tivicay or a613043 or S?GSK1349572 or GSK1349572).ti,ab. (284)
20  (darunavir or Prezista or TMC114 or a607042 or drv*).ti,ab. (1401)
21  (Elvitegravir or GS-9137 or Vitekta).ti,ab. (334)
22  (emtricitabine or Emtriva or Coviracil or a604004).ti,ab. (1446)
23  (lopinavir or ABT-378 or a602015 or lpr*).ti,ab. (2382)
24  (nevirapine or Viramune or a600035).ti,ab. (3484)
25  (ritonavir or Norvir or a696029).ti,ab. (4885)
26  (raltegravir or Isentress or MK-0518 or a608004).ti,ab. (1279)
27  (efavirenz or Efavir or Sustiva or Stocrin or Ef cure or Eff ven or Estiva or Evirenz or Viranz or a699004).ti,ab. (3221)
28  (Trizivir or Aluvia or Kaletra or Stribild or triumeq).ti,ab. (201)
29  or/11-28 (81501)
30  Tenofovir.ti,ab. (3901)
31  Viread.ti,ab. (50)
32  or/30-31 (3914)
33  29 and 32 (3529)
34  (Randomized Controlled Trial or Controlled Clinical Trial).pt. (534746)
35  (Clinical Trial or Clinical Trial, Phase II or Clinical Trial, Phase III or Clinical Trial, Phase IV).pt. (536698)
36  Multicenter Study.pt. (218538)
37  Randomized Controlled Trial/ or Randomized Controlled Trials as Topic/ or "Randomized Controlled Trial (topic)"/ (551676)
38  Controlled Clinical Trial/ or Controlled Clinical Trials as Topic/ or "Controlled Clinical Trial (topic)"/ (97156)
39  Clinical Trial/ or Phase 2 Clinical Trial/ or Phase 3 Clinical Trial/ or Phase 4 Clinical Trial/ (508028)
40  Clinical Trials as Topic/ or Clinical Trials, Phase II as Topic/ or Clinical Trials, Phase III as Topic/ or Clinical Trials, Phase IV as Topic/ (193281)
41  "Clinical Trial (topic)"/ or "Phase 2 Clinical Trial (topic)"/ or "Phase 3 Clinical Trial (topic)"/ or "Phase 4 Clinical Trial (topic)"/ (0)
42  or/34-41 (1108160)
43  10 and 33 and 42 (865)
44  (healthy adj3 volunteer*).ti,ab. (79538)
45  (healthy adj3 subject*).ti,ab. (112666)
46  (cohort or observational study or case-control*).ti,ab. (422308)
47  43 not (44 or 45 or 46) (751)
48  47 not (cost minimi* or cost-utilit* or health utility* or economic evaluation* or economic review* or cost outcome or cost analys?s or economic analys?s or budget* impact analys?s).ti,ab. (751)
49  48 not (review or letter or meta-analysis or case report or case series or posters or News or Newspaper article or meeting abstracts or lectures or interview or historical article or handbooks or guidelines or guidebooks or essays or editorial or comment or clinical conference or catalogs or case reports).pt. (633)
50  limit 49 to ed=20150705-20170217 (157)
Database: EMBASE <July 7 2015 to 2017 February 16>
Search Strategy:

1. exp HIV/ or exp HIV Infection/ (439172)
2. (HIV Infections or HIV?1* or HIV?2* or HIV infect* or human immune?deficiency virus or human immune?deficiency virus).ti,ab. (116054)
3. (human immun* and deficiency virus).ti,ab. (688)
4. (acquired immuno?deficiency syndrome or AIDS or acquired immunodeficiency syndrome or acquired immune deficiency).ti,ab. (159421)
5. (acquired immun* and deficiency syndrome).ti,ab. (5910)
6. Salvage therapy.ti,ab. (7322)
7. exp Treatment Failure/ (115102)
8. (Treatment-experienced or Antiretroviral experienced or ART-experienced or Experienced patients).ti,ab. (4914)
9. treatment switch*.ti,ab. (738)
10. (or/1-5) not (or/6-9) (475830)
11. exp Antiretroviral Therapy, Highly Active/ (36524)
12. exp Integrase Inhibitors/ (7636)
13. exp HIV Reverse Transcriptase/ (18528)
14. exp Reverse Transcriptase Inhibitors/ (96826)
15. exp Anti-HIV Agents/ (139471)
16. exp HIV Protease Inhibitors/ (35217)
17. (atazanavir or Reyataz or a603019 or BMS-232632 or atv*).ti,ab. (3765)
18. (cobicistat or GS-9350 or Tybost).ti,ab. (419)
19. (dolutegravir or Tivicay or a613043 or S?GSK1349572 or GSK1349572).ti,ab. (639)
20. (darunavir or Prezista or TMC114 or a607042 or drv*).ti,ab. (2946)
21. (Elvitegravir or GS-9137 or Vitekta).ti,ab. (681)
22. (emtricitabine or Emtriva or Coviracil or a604004).ti,ab. (2937)
23. (lopinavir or ABT-378 or a602015 or lpv*).ti,ab. (3848)
24. (nevirapine or Viramune or a600035).ti,ab. (4721)
25. (ritonavir or Norvir or a696029).ti,ab. (7394)
26. (raltegravir or Isentress or MK-0518 or a608004).ti,ab. (2452)
27. (efavirenz or Efavir or Sustiva or Stocrin or Efcure or Efferven or Estiva or Evirenz or Viranz or a699004).ti,ab. (5163)
28. (Trizivir or Aluvia or Kaletra or Stribild or triumeq).ti,ab. (379)
or/11-28 (183039)
Tenofovir.ti,ab. (8260)
Viread.ti,ab. (75)
or/30-31 (8276)
29 and 32 (8220)
(Randomized Controlled Trial or Controlled Clinical Trial).pt. (0)
(Clinical Trial or Clinical Trial, Phase II or Clinical Trial, Phase III or Clinical Trial, Phase IV).pt. (0)
Multicenter Study.pt. (0)
Randomized Controlled Trial/ or Randomized Controlled Trials as Topic/ or “Randomized Controlled Trial (topic)”/ (593351)
Controlled Clinical Trial/ or Controlled Clinical Trials as Topic/ or “Controlled Clinical Trial (topic)”/ (486075)
Clinical Trial/ or Phase 2 Clinical Trial/ or Phase 3 Clinical Trial/ or Phase 4 Clinical Trial/ (1091163)
Clinical Trials as Topic/ or Clinical Trials, Phase II as Topic/ or Clinical Trials, Phase III as Topic/ or Clinical Trials, Phase IV as Topic/ (121968)
“Clinical Trial (topic)”/ or “Phase 2 Clinical Trial (topic)”/ or “Phase 3 Clinical Trial (topic)”/ or “Phase 4 Clinical Trial (topic)”/ (161831)
or/34-41 (1486152)
10 and 33 and 42 (1516)
(healthy adj3 volunteer*).ti,ab. (117167)
(healthy adj3 subject*).ti,ab. (164272)
(cohort or observational study or case-control*).ti,ab. (769550)
43 not (44 or 45 or 46) (1295)
47 not (cost minimi* or cost-utilit* or health utility* or economic evaluation* or economic review* or cost outcome or cost analys?s or economic analys?s or budget* impact analys?s).ti,ab. (1288)
48 not (review or letter or meta-analysis or case report or case series or posters or News or Newspaper article or meeting abstracts or lectures or interview or historical article or handbooks or guidelines or guidebooks or essays or editorial or comment or clinical conference or catalogs or case reports).pt. (1066)
(201507* or 201508* or 201509* or 201510* or 201511* or 201512* or 201512* or 201601* or 201602* or 201603* or 201604* or 201605* or 201606* or 201607* or 201608* or 201609* or 201610* or 201611* or 201612* or 201701* or 201702*).dd. (1789047)
49 and 50 (245)
Appendix 1c

Complete search strategy #3: Search for comparative studies of lamivudine, tenofovir, emtricitabine for hepatitis B infection in pregnant women

Search to from January 1, 2014 to January 14, 2017

OVID & MEDLINE

1. exp Hepatitis B/
2. (HBV or "hepatitis B" or "serum hepatitis" or "hippie hepatitis" or "injection hepatitis" or "hepatitis type B").mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, fs, nm, kf, px, rx, ui]  3. 1 or 2
3. exp Antiviral Agents/
4. exp antivirus agent/
5. (tenofovir or "tenofovir disoproxil" or TDF or "tenofovir alafenamide" or lamivudine or 3TC or emtricitabine or "Emtricitabine/tenofovir" or Viread or Genvoya or truvada or Emtriva or Coviracil or epivir).mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, fs, nm, kf, px, rx, ui]  6. 4 or 5 or 6
7. exp Pregnancy/
8. (pregnan* or gestation* or "child bearing" or childbearing or infant* or newborn* or neonate or breast* or "breast fe*" or maternal or prenatal* or "prenatal exposure" or perinatal* or lactat* or "in utero" or "In utero exposure" or gestation* or congenital MTCT or "Mother-to-child transmission" or "Mother to child transmission" or "Mother-to-infant transmission" or "Infectious disease transmission" or "Vertical transmission disease transmission, vertical" or "vertical Adult to child transmission" or mother-to-infant).mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, fs, nm, kf, px, rx, ui]  9. 7 or 8 or 9
10. exp Vertical Transmission/
11. 8 or 9 or 10
12. exp evidence based medicine/
13. exp meta analysis/
14. exp Meta-Analysis as Topic/
15. exp "systematic review"/
16. exp "systematic review"/
17. exp Practice Guideline/
18. exp Randomized Controlled Trial/
19. exp triple blind procedure/
20. exp Double-Blind Method/
21. exp Single-Blind Method/
22. exp latin square design/
23. exp Placebos/
24. exp comparative study/
25. exp Cross-Sectional Studies/
26. exp Cross-Over Studies/
27. exp Cohort Studies/
28. exp longitudinal study/
29. exp retrospective study/
30. exp retrospective study/
31. exp population research/
32. exp observational study/
33. exp clinical trial/
34. clinical study.mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, fs, nm, kf, px, rx, ui]
35. exp Evaluation Studies/
36. exp quantitative study/
37. exp validation studies/
38. exp experimental study/
39. exp quasi experimental study/
40. exp field study/
41. in vivo study.mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, fs, nm, kf, px, rx, ui]
42. exp panel study/
43. exp Pilot Projects/
44. exp pilot study/
45. exp prevention study/
46. exp replication study/
47. exp Feasibility Studies/
48. exp Models, Theoretical/
49. exp trend study/
50. exp correlational study/
51. exp confidence interval/
52. exp regression analysis/
53. exp proportional hazards model/
54. exp multivariate analysis/
55. exp follow up studies/
56. odds ratio.mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, fs, nm, kf, px, rx, ui]
57. ((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 survey" 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 analys*" 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 analys*" 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 analys*" or "observational study" or "observational survey" or "observational analys*" 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 analys*" or "evaluation survey*" or "twin study" or "twin survey" or "twin analys*" or "quantitative study" or "quantitative analys*" or "validation study" or "validation survey" or "validation analys*" or "validation survey*" or "experimental study" or "experimental analys*" or "experimental survey" or "quasi experimental study" or "quasi experimental analys*" or "field study" or "field survey" or "field analys*" or "in vivo study" or "in vivo analys*" or "panel study" or "panel analys*" or "panel survey" or "panel survey*" or "prevention study" or "prevention survey" or "prevention analys*" or "replication study" or "replication analys*" or "theoretical study" or "theoretical analys*" or "feasibility study" or "feasibility analyse" or "trend study" or "trend survey" or "trend analys*" 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 comparison study" or "case comparison survey" or study or trial or pilot or "odds ratio" or "confidence interval" or "regression analys*" or "hazards model" or "change analys*").mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, fs, nm, kf, px, rx, ui]

58. 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 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58
59. 3 and 7 and 11 and 59
60. limit 60 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)
61. 60 not 61
62. 62 not (exp animals/ not exp humans/)
63. remove duplicates from 63
64. exp HIV infections/
65. exp AIDS/
66. (HIV or "hiv-infect*" or "hiv-noninfected" or "hiv-exposed" or "human immunodeficiency virus" or "human immune*" or "human immunodeficiency" or "virexposed" or "HIV prevention" or "HIV-exposed" or "uninfected AIDS" or "acquired immun* human" or "immun* deficiency virus" or "HIV-infected mothers" or "Viral load").mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, fs, nm, kf, px, rx, ui]
67. 65 or 66 or 67
68. 64 and 68
69. limit 64 to yr="2014-2017"
70. 69 or 70
Appendix 2. Methods continued

Subgroups

We planned to use published criteria for assessing the certainty of any subgroup effect (Xin Sun’s subgroup BMJ study). We prespecified the expected direction of effect for each of the subgroup analyses for each outcome. Our planned sub-group analyses were:

- Low vs. high risk of bias
- Placebo control vs. dual NRTI control
- Intervention arm that includes both tenofovir/FTC vs. tenofovir or FTC alone
- Class of third antiretroviral
  - Protease inhibitors
  - Non-nucleoside reverse transcriptase inhibitors
  - Integrase strand inhibitors
- Low and middle income settings vs. high income settings
- HIV-positive versus pre-exposure prophylaxis (PrEP)
- Mother starting CD4<350 vs CD4 >350 cells/mm³
- Alternative NRTI (abacavir/lamivudine or AZT/lamivudine)
Appendix 3a

Figure. PRISMA Flow diagram of evidence for comparative studies of nucleoside reverse transcriptase inhibitors in pregnancy

All unique citations identified following initial search of electronic databases MEDLINE (n=1577), EMBASE (n=1032), Cochrane Registry for Systematic Reviews (n=14), and Cochrane Central for Clinical Trials (n=51), PubMed (n=76)

Total unique citations (n=2,750)

Excluded (n=2711)

Full-text review n=39

Wrong intervention and/or comparison (n=10)
Wrong population (n=16)
No relevant outcomes (n=3)
Case series (n=1)
Review (n=3)

RCTs eligible (n=7)
Observational studies eligible (n=3)
Appendix 3b

Figure. PRISMA flow diagram for randomised controlled trials comparing two different NRTI regimens with the same non-NRTI antiretroviral

Update search of electronic databases MEDLINE (n=157) and EMBASE (n=245); Unique citations (n=297)

Excluded (n=292)

Full-text review n= 5

Secondary analysis (n=2) Wrong comparison (n=1)

RCTs included from previous systematic review (n=5) Studies identified from reference list (n=2)

RCTs eligible (n=8), from 9 publications
Appendix 3c

Figure. PRISMA flow diagram for randomised controlled trials comparing NRTI regimens in pregnant women with hepatitis B infection

Update search of electronic databases MEDLINE and EMBASE (n=1437); Unique citations (n=1035)

Excluded (n=958)

Full-text review n= 60

Eligible studies (n=33)
RCTs (n=11)
Non-randomised (n=22)

Records obtained from the prior meta-analysis (n=14)
Record obtained from registry search (n=1)
Record obtained from reference list (n=1)

Duplicates, citation or study population (n=19)
No outcomes of interest (n=12)
Different interventions (n=4)
No comparator arm (n=4)
Not an original study (n=3)
Not accessible (n=1)
Appendix 4a

<table>
<thead>
<tr>
<th>Study</th>
<th>Random sequence generation (selection bias)</th>
<th>Allocation concealment (selection bias)</th>
<th>Blinding of participants and personnel (performance bias)</th>
<th>Blinding of outcome assessment (detection bias)</th>
<th>Incomplete outcome data (attrition bias)</th>
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</table>

**Figure.** Risk of bias summary of randomised trials comparing different NRTI regimens in HIV-positive adults
### Appendix 4b

| Study          | Random sequence allocation (selection bias) | Allocation concealment (selection bias) | Blinding of participants and personnel (performance bias) | Blinding of outcome assessment (detection bias) | Blinding of data collectors (detection bias) | Incomplete outcome data (attrition bias) | Selective reporting (reporting bias) | Sponsorship bias |
|----------------|-------------------------------------------|-----------------------------------------|----------------------------------------------------------|-------------------------------------------------|---------------------------------------------|----------------------------------------|-------------------------------------|
| Pan, 2016      | +                                         | +                                       | -                                                        | +                                               | -                                           | +                                      | +                                   |
| Wang, 2016     | +                                         | +                                       | -                                                        | +                                               | -                                           | +                                      | +                                   |
| Chasela, 2014  | -                                         | -                                       | -                                                        | +                                               | -                                           | +                                      | +                                   |
| Guo, 2008      | +                                         | +                                       | -                                                        | +                                               | -                                           | +                                      | +                                   |
| Xu, 2009       | +                                         | +                                       | -                                                        | +                                               | -                                           | +                                      | +                                   |
| Yang, 2008     | +                                         | +                                       | -                                                        | +                                               | -                                           | +                                      | +                                   |
| Zhang, 2010    | +                                         | +                                       | -                                                        | +                                               | -                                           | +                                      | +                                   |
| Li, 2003       | +                                         | +                                       | -                                                        | +                                               | -                                           | +                                      | +                                   |
| Shi, unpublished | +                                         | +                                       | -                                                        | +                                               | -                                           | +                                      | +                                   |
| Shi, 2005      | +                                         | +                                       | -                                                        | +                                               | -                                           | +                                      | +                                   |
| Xiang, 2007    | +                                         | +                                       | -                                                        | +                                               | -                                           | +                                      | +                                   |
Figure. Risk of bias for randomised controlled trials of antiviral therapy in pregnant women with hepatitis B
### Appendix 4c

<table>
<thead>
<tr>
<th>Study</th>
<th>Same population</th>
<th>Exposure assessment</th>
<th>Outcome not present at start of study</th>
<th>Matched for all variables associated with outcome</th>
<th>Assessment of prognostic factors</th>
<th>Assessment of outcome</th>
<th>Adequate follow-up</th>
<th>Similar co-interventions</th>
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<td>Zhang, 2014</td>
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<tr>
<td>Zhang, 2016</td>
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</tbody>
</table>
Figure. Risk of bias for observational studies of antiviral therapy in pregnant women with hepatitis B
Appendix 5a

Figure. Forest plot of risk ratio for study medication discontinuations because of patient decision or clinical adverse events in randomised trials comparing different NRTI regimens in HIV-positive adults

TDF-ART, tenofovir disoproxil fumarate-based antiretroviral therapy; NRTI, nucleoside/nucleotide reverse transcriptase inhibitor; M-H, Mantel-Haenszel; CI, confidence interval

Appendix 5b

Figure. Forest plot of risk difference in mortality in randomised trials comparing different NRTI regimens in HIV-positive adults

TDF-ART, tenofovir disoproxil fumarate-based antiretroviral therapy; NRTI, nucleoside/nucleotide reverse transcriptase inhibitor; M-H, Mantel-Haenszel; CI, confidence interval

Appendix 5c
Figure. Forest plot of risk ratio for stillbirth and early neonatal mortality of tenofovir-based antiretroviral therapy, by study design

TDF-ART, tenofovir disoproxil fumarate-based antiretroviral therapy; NRTI, nucleoside/nucleotide reverse transcriptase inhibitor; M-H, Mantel-Haenszel; CI, confidence interval

Appendix 5d

Appendix 5e

Figure. Forest plot of risk difference in vertical transmission of HIV with tenofovir-based ART from randomised and observational studies

M-H, Mantel-Haenszel; ART, antiretroviral therapy
### Figure
Forest plot of risk difference in birth defects in fetuses exposed to tenofovir and alternative antiretroviral therapies in the first trimester, by study design

ART, antiretroviral therapy; M-H, Mantel-Haenszel; ARV, antiretroviral; TDF, tenofovir disoproxil fumarate

#### Appendix 5f

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>TDF-based ART Events</th>
<th>Total</th>
<th>Alternatives Events</th>
<th>Total</th>
<th>Weight</th>
<th>Risk Difference M-H, Random, 95% CI</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
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<tr>
<td><strong>4.4.3 Randomised trials</strong></td>
<td></td>
<td></td>
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<tr>
<td>Campbell, 2012</td>
<td>9</td>
<td>20</td>
<td>0</td>
<td>22</td>
<td>0.6%</td>
<td>0.0000 [-0.0882, 0.0882]</td>
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<tr>
<td>Mugo, 2013</td>
<td>4</td>
<td>34</td>
<td>4</td>
<td>46</td>
<td>6.6%</td>
<td>-0.0176 [-0.1217, 0.0866]</td>
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<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>13</td>
<td>60</td>
<td>4</td>
<td>66</td>
<td>1.2%</td>
<td>-0.0176 [-0.0826, 0.0468]</td>
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<tr>
<td><strong>Total events</strong></td>
<td>4</td>
<td>71</td>
<td>4</td>
<td>77</td>
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<tr>
<td><strong>Heterogeneity</strong></td>
<td>Tau² = 0.69; Chi² = 9.62; df = 1 (P = 0.0029); I² = 0%</td>
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<tr>
<td><strong>Test for overall effect</strong></td>
<td>Z = 2.58 (P = 0.0105)</td>
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</table>

**Total (95% CI)**: 3249 / 5315; 100.0% / -0.0094 [-0.0164, -0.0024]

#### Figure
Forest plot of risk ratio for spontaneous abortion with tenofovir/FTC versus alternative NRTIs in studies with first trimester antiretroviral exposure. Mugo randomised HIV-negative women to tenofovir/emtricitabine or placebo; Gibb observed risk of spontaneous abortion in fetuses exposed to tenofovir versus no tenofovir-containing ART.

M-H, Mantel-Haenszel; TDF, tenofovir disoproxil fumarate; FTC, emtricitabine; ART, antiretroviral therapy

#### Appendix 5g
Figure. Forest plot of risk ratio for premature delivery <37 weeks gestation, by study design.

M-H, Mantel-Haenszel; TDF, tenofovir disoproxil fumarate; ART, antiretroviral therapy

Appendix 5h

Figure. Forest plot of risk ratio for early or very early premature delivery <32 to <34 weeks gestation, by study design.

M-H, Mantel-Haenszel; TDF, tenofovir disoproxil fumarate; FTC, emtricitabine; ART, antiretroviral therapy
**Appendix 5i**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>TDF–ART Events</th>
<th>Total</th>
<th>Alternatives Events</th>
<th>Total</th>
<th>Risk Ratio M–H, Random, 95% CI</th>
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<tr>
<td>1.10.1 Randomised trials</td>
<td>51</td>
<td>301</td>
<td>65</td>
<td>319</td>
<td>0.83 [0.60, 1.16]</td>
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<tr>
<td>Rough, 2017</td>
<td>30</td>
<td>128</td>
<td>175</td>
<td>954</td>
<td>1.28 [0.92, 1.80]</td>
</tr>
</tbody>
</table>

**Figure.** Forest plot of risk ratio for low birth weight <2500g, by study design.

M–H, Mantel–Haenszel; TDF, tenofovir disoproxil fumarate; ART, antiretroviral therapy

**Appendix 5j**

<table>
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<tr>
<th>Study or Subgroup</th>
<th>TDF–ART Events</th>
<th>Total</th>
<th>Alternatives Events</th>
<th>Total</th>
<th>Risk Ratio M–H, Random, 95% CI</th>
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<td>1.11.1 Randomised trials</td>
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<td>335</td>
<td>2</td>
<td>346</td>
<td>3.61 [0.76, 17.28]</td>
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<tr>
<td>Rough, 2016</td>
<td>1</td>
<td>128</td>
<td>18</td>
<td>954</td>
<td>0.41 [0.06, 3.08]</td>
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**Figure.** Forest plot of risk ratio for very low birth weight <1500g, by study design.

M–H, Mantel–Haenszel; TDF, tenofovir disoproxil fumarate; ART, antiretroviral therapy
### Table 6

**Study characteristics of comparative studies of antivirals in pregnant women living with hepatitis B**

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Comparison</th>
<th>Country</th>
<th>Maternal viral inclusion criteria</th>
<th>Gestational age at start</th>
<th>Infant follow-up</th>
<th>Maternal Sample Size</th>
<th>Maternal Age*</th>
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<tbody>
<tr>
<td>Chasela, 2014</td>
<td>RCT</td>
<td>3TC vs. control</td>
<td>Malawi</td>
<td>HIV &amp; HBsAg+</td>
<td>≤30 weeks</td>
<td>48 wks.</td>
<td>72</td>
<td>25 (22-29)</td>
</tr>
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<td>Guo, 2008</td>
<td>RCT</td>
<td>3TC vs. control</td>
<td>China</td>
<td>HBsAg+</td>
<td>28 weeks</td>
<td>26-52 wks.</td>
<td>110</td>
<td>27 (4.9)</td>
</tr>
<tr>
<td>Li, 2003</td>
<td>RCT</td>
<td>3TC vs. control</td>
<td>China</td>
<td>HBsAg+</td>
<td>28 weeks</td>
<td>24h</td>
<td>151</td>
<td>NR</td>
</tr>
<tr>
<td>Pan, 2016</td>
<td>RCT</td>
<td>TDF vs. control</td>
<td>China</td>
<td>HBeAg+ &amp; &gt;200,000IU/mL</td>
<td>30-32 weeks</td>
<td>28 wks.</td>
<td>200</td>
<td>27.4 (3.0)</td>
</tr>
<tr>
<td>Shi, 2005</td>
<td>RCT</td>
<td>3TC vs. control</td>
<td>China</td>
<td>NR</td>
<td>28 weeks</td>
<td>24h</td>
<td>39</td>
<td>27.9 (2.9)</td>
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<td>Wang, 2016</td>
<td>RCT</td>
<td>TDF/3TC vs 3TC</td>
<td>China</td>
<td>HIV &amp; HBV</td>
<td>14-27 weeks</td>
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<td>35</td>
<td>29 (24 - 36)</td>
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<td>Xiang, 2007</td>
<td>RCT</td>
<td>3TC vs. control</td>
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<td>NR</td>
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<td>China and Philippines</td>
<td>&gt;1000 MEq/mL</td>
<td>30-34 weeks</td>
<td>52 wks.</td>
<td>150</td>
<td>19-36</td>
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<td>China</td>
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<td>24 weeks</td>
<td>26-52 wks.</td>
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<td>27</td>
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<td>3TC vs. control</td>
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<td>28 weeks</td>
<td>26-52 wks.</td>
<td>100</td>
<td>NR</td>
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<td>Ayres, 2011</td>
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<td>UK</td>
<td>&gt;10^6 IU/mL</td>
<td>32 weeks</td>
<td>--</td>
<td>59</td>
<td>NR</td>
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<tr>
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<td>Observational</td>
<td>3TC vs. control</td>
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<td>36 wks.</td>
<td>26</td>
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<td>30 weeks</td>
<td>52 wks.</td>
<td>401</td>
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<td>Celen, 2013</td>
<td>Observational</td>
<td>TDF vs. control</td>
<td>Turkey</td>
<td>HBeAg+ &amp; &gt;200,000 IU/mL</td>
<td>18-27 weeks</td>
<td>28 wks.</td>
<td>45</td>
<td>27.5 (3.5)</td>
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<td>TDF vs. control</td>
<td>Taiwan</td>
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<td>30-32 weeks</td>
<td>26 wks.</td>
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<td>Observational</td>
<td>3TC vs. TDF vs. control</td>
<td>China</td>
<td>&gt;10^6.5 IU/mL</td>
<td>32 weeks</td>
<td>48 wks.</td>
<td>120</td>
<td>28</td>
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<td>Han G., 2009</td>
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<td>3TC vs. control</td>
<td>China</td>
<td>NR</td>
<td>20 weeks</td>
<td>26-52 wks.</td>
<td>123</td>
<td>27 (3)</td>
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<tr>
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<td>NR</td>
<td>28 weeks</td>
<td>26-52 wks.</td>
<td>78</td>
<td>NR</td>
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<td>Observational</td>
<td>TDF vs. TDF/3TC</td>
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<td>HBeAg+</td>
<td>Anytime</td>
<td>20-48 wks.</td>
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<td>Canada</td>
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<td>28-32 weeks</td>
<td>13-26 wks.</td>
<td>161</td>
<td>30 (28 - 34)</td>
</tr>
<tr>
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<td>Observational</td>
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<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>67</td>
<td>NR</td>
</tr>
<tr>
<td>Li, 2006</td>
<td>Observational</td>
<td>3TC vs. control</td>
<td>China</td>
<td>&gt;10^7 IU/mL</td>
<td>32 weeks</td>
<td>39 wks.</td>
<td>80</td>
<td>NR</td>
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<tr>
<td>Pan C., 2013</td>
<td>Observational</td>
<td>TDF vs. control</td>
<td>NR</td>
<td>All HBV</td>
<td>33 weeks</td>
<td>28 wks.</td>
<td>34</td>
<td>NR</td>
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<td>Pan Q., 2014</td>
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<td>3TC vs. TDF vs. control</td>
<td>China and USA</td>
<td>HBeAg+ &amp; &gt;10^6 copies/mL</td>
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<td>28-58 wks.</td>
<td>220</td>
<td>27.7 (4.4)</td>
</tr>
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<td>HBeAg+ &amp; &gt;10^6 copies/mL</td>
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<td>40-52 wks.</td>
<td>249</td>
<td>27.3 (3.9)</td>
</tr>
<tr>
<td>Sellier, 2014</td>
<td>Observational</td>
<td>3TC vs. control</td>
<td>France</td>
<td>HIV &amp; HBV</td>
<td>NR</td>
<td>104 wks.</td>
<td>49</td>
<td>NR</td>
</tr>
<tr>
<td>Tan, 2012</td>
<td>Observational</td>
<td>3TC vs. control</td>
<td>Australia</td>
<td>High HBV viral load</td>
<td>32 weeks</td>
<td>&gt;13 wks.</td>
<td>64</td>
<td>NR</td>
</tr>
<tr>
<td>Virine, 2015</td>
<td>Observational</td>
<td>TDF vs. control</td>
<td>Canada</td>
<td>All HBV</td>
<td>NR</td>
<td>26-52 wks.</td>
<td>21</td>
<td>31 (21 - 37)</td>
</tr>
<tr>
<td>Study (Year)</td>
<td>Design Type</td>
<td>Treatment Group</td>
<td>Country</td>
<td>Inclusion Criteria</td>
<td>Duration</td>
<td>Follow-up</td>
<td>Mean (SD/IR)</td>
<td></td>
</tr>
<tr>
<td>-------------</td>
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<td>-----------------</td>
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<td></td>
</tr>
<tr>
<td>Yi, 2014</td>
<td>Observational</td>
<td>TDF vs. control</td>
<td>China</td>
<td>All HBV</td>
<td>1st trimester</td>
<td>28 wks.</td>
<td>85</td>
<td>30.46 (3.24)</td>
</tr>
<tr>
<td>Yu, 2014</td>
<td>Observational</td>
<td>3TC vs. HBIG</td>
<td>China</td>
<td>HBeAg+ &amp; &gt;10^6 copies/mL</td>
<td>8-32 weeks</td>
<td>4 wks.</td>
<td>487</td>
<td>26.81 (3.85)</td>
</tr>
<tr>
<td>Zhang, 2016</td>
<td>Observational</td>
<td>TDF vs. control</td>
<td>China</td>
<td>HBeAg+ &amp; &gt;10^6 copies/mL</td>
<td>28-38 weeks</td>
<td>26 wks.</td>
<td>289</td>
<td>NR</td>
</tr>
<tr>
<td>Zhang, 2014</td>
<td>Non-randomized intervention trial</td>
<td>3TC vs. control</td>
<td>China</td>
<td>HBeAg+ &amp; &gt;10^6 copies/mL</td>
<td>28-30 weeks</td>
<td>52 wks.</td>
<td>700</td>
<td>29 (4.7)</td>
</tr>
</tbody>
</table>

*Mean and (standard deviation) or Median and (interquartile range)

RCT, randomised controlled trial; TDF, tenofovir disoproxil fumarate; 3TC, lamivudine; TDF, emtricitabine; HBIG, hepatitis B immunoglobulin; HIV, human immunodeficiency virus; HBsAg, hepatitis B surface antigen; HBeAg, hepatitis B e antigen; NR, not report
### Appendix 7

**Table.** Study outcomes for comparative studies of antivirals in pregnant women living with hepatitis B

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Vertical transmission lamivudine</th>
<th>Vertical transmission tenofovir</th>
<th>Vertical transmission dual</th>
<th>Vertical transmission control</th>
<th>HBV flare lamivudine</th>
<th>HBV flare tenofovir</th>
<th>HBV flare control</th>
<th>Lamivudine resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chasela, 2014&lt;sup&gt;1&lt;/sup&gt;</td>
<td>RCT</td>
<td>2/20</td>
<td></td>
<td></td>
<td></td>
<td>3/31</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Guo, 2008&lt;sup&gt;2&lt;/sup&gt;</td>
<td>RCT</td>
<td>4/70</td>
<td></td>
<td></td>
<td></td>
<td>12/40</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Li, 2003&lt;sup&gt;3&lt;/sup&gt;</td>
<td>RCT</td>
<td>1/43</td>
<td></td>
<td></td>
<td></td>
<td>8/52</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pan, 2016&lt;sup&gt;4&lt;/sup&gt;</td>
<td>RCT</td>
<td>0/92</td>
<td></td>
<td></td>
<td>6/88</td>
<td></td>
<td>6/97</td>
<td>9/100</td>
<td></td>
</tr>
<tr>
<td>Shi, 2005&lt;sup&gt;5&lt;/sup&gt;</td>
<td>RCT</td>
<td>1/21</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1/18</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wang, 2016&lt;sup&gt;6&lt;/sup&gt;</td>
<td>RCT</td>
<td>0/15</td>
<td>0/16 (TDF/3TC)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Xiang, 2007&lt;sup&gt;7&lt;/sup&gt;</td>
<td>RCT</td>
<td>1/21</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5/18</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Xu, 2009&lt;sup&gt;8&lt;/sup&gt;</td>
<td>RCT</td>
<td>3/46</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5/36</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yang, 2008&lt;sup&gt;9&lt;/sup&gt;</td>
<td>RCT</td>
<td>2/20</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2/19</td>
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<td></td>
</tr>
<tr>
<td>Zhang, 2010&lt;sup&gt;10&lt;/sup&gt;</td>
<td>RCT</td>
<td>1/50</td>
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<td></td>
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<td>8/50</td>
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<td>Ayres, 2011&lt;sup&gt;11&lt;/sup&gt;</td>
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<td>0/18</td>
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<td></td>
<td>1/3</td>
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<td>0/18</td>
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<td></td>
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<td></td>
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<td></td>
<td>0/21</td>
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<td>2/23</td>
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<td></td>
<td>2/62</td>
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<td></td>
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<td>Greenup, 2014&lt;sup&gt;16&lt;/sup&gt;</td>
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<td>1/44</td>
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<td></td>
<td></td>
<td>2/10</td>
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<td></td>
<td>0/46</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Han Z., 2005&lt;sup&gt;18&lt;/sup&gt;</td>
<td>Observational</td>
<td></td>
<td>0/43</td>
<td></td>
<td></td>
<td></td>
<td>5/35</td>
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<td>Observational</td>
<td></td>
<td>0/21</td>
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<td>0/14 (TDF/3TC)</td>
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<td></td>
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<td></td>
<td>4/23</td>
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<tr>
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<td>Year</td>
<td>Design</td>
<td>RR</td>
<td>CI</td>
<td>N</td>
<td>RR</td>
<td>CI</td>
<td>N</td>
<td>RR</td>
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<td>Li, 2006</td>
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<td>7/44</td>
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<td></td>
<td>0/11</td>
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<td></td>
<td></td>
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</tr>
<tr>
<td>Tan, 2012</td>
<td></td>
<td>Observational</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>14/48</td>
<td></td>
<td></td>
<td>3/16</td>
</tr>
<tr>
<td>Virine, 2015</td>
<td></td>
<td>Observational</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Yi, 2014</td>
<td></td>
<td>Observational</td>
<td>0/39</td>
<td></td>
<td>3/46</td>
<td></td>
<td></td>
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<td>Yu, 2014</td>
<td></td>
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<td></td>
<td>25/171</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Zhang, 2016</td>
<td></td>
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<td>0/0/25</td>
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<td></td>
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<td></td>
<td>Non-randomized</td>
<td></td>
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<td></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>intervention trial</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

HBV, hepatitis B virus; RCT, randomised controlled trial; TDF, tenofovir disoproxil fumarate; 3TC, lamivudine; FTC, emtricitabine; NR, not reported
Appendix 8

Figure. Network plot of randomised controlled trials for maternal antiviral therapy to prevent vertical transmission of hepatitis B. The size of the treatment nodes represents number of patients and width of the lines represents the number of randomised trials.

TDF, tenofovir disoproxil fumarate; Control, no active antiviral therapy; 3TC, lamivudine

Table. Network meta-analysis results of antiviral therapy for the prevention of vertical transmission of hepatitis B, randomised trials only.

<table>
<thead>
<tr>
<th></th>
<th>Lamivudine</th>
<th>Tenofovir</th>
<th>No antiviral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lamivudine</td>
<td>Lamivudine</td>
<td>0.26 (0.01, 4.77)</td>
<td>3.52 (2.05, 6.05)</td>
</tr>
<tr>
<td>Tenofovir</td>
<td>3.86 (0.21, 70.97)</td>
<td>Tenofovir</td>
<td>13.59 (0.77, 237.69)</td>
</tr>
<tr>
<td>No antiviral</td>
<td>0.28 (0.17, 0.49)</td>
<td>0.07 (0.00, 1.29)</td>
<td>No antiviral</td>
</tr>
</tbody>
</table>

All results presented with relative risk, 95% confidence interval.
Relative risk <1 favour the column.
Global $I^2=0\%$, $p$ for inconsistency = 0.51
Appendix 9

Figure. Network plot of RCTs and comparative observational studies of maternal antiviral therapy to prevent vertical transmission of hepatitis B. The size of the treatment nodes represents number of patients and width of the lines represents the number of studies.
TDF, tenofovir disoproxil fumarate; dual, dual antiviral therapy; Control, no active antiviral therapy; 3TC, lamivudine

Table. Network meta-analysis results of antiviral therapy for the prevention of vertical transmission of hepatitis B, including observational data.
<table>
<thead>
<tr>
<th></th>
<th>Lamivudine</th>
<th>Tenofovir</th>
<th>Dual antivirals</th>
<th>No antiviral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lamivudine</td>
<td>0.99 (0.38,2.59)</td>
<td>0.48 (0.02,9.43)</td>
<td>4.29 (2.63,6.96)</td>
<td></td>
</tr>
<tr>
<td>Tenofovir</td>
<td>1.01 (0.39,2.66)</td>
<td>0.49 (0.02,10.94)</td>
<td>4.34 (1.86,10.94)</td>
<td></td>
</tr>
<tr>
<td>Dual antivirals</td>
<td>2.08 (0.11,40.95)</td>
<td>2.06 (0.09,46.31)</td>
<td>8.93 (0.45,179.27)</td>
<td></td>
</tr>
<tr>
<td>No antiviral</td>
<td><strong>0.23 (0.14,0.38)</strong></td>
<td><strong>0.23 (0.10,0.54)</strong></td>
<td>0.11 (0.01,2.25)</td>
<td>No antiviral</td>
</tr>
</tbody>
</table>

Relative risk <1 favour the column.

Global $I^2=0\%$, $p$ for inconsistency = 0.76
**Figure.** Network plot of randomised controlled trials and comparative observational studies reporting maternal hepatitis B flares in women who took antivirals in pregnancy. The size of the treatment nodes represents number of patients and width of the lines represents the number of studies. TDF, tenofovir disoproxil fumarate; dual, dual antiviral therapy; Control, no active antiviral therapy; 3TC, lamivudine

**Table.** Network meta-analysis results of risk of hepatitis B flares with antiviral therapy during pregnancy, randomised and observational studies.

<table>
<thead>
<tr>
<th></th>
<th>Lamivudine</th>
<th>Tenofovir</th>
<th>No antiviral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lamivudine</td>
<td>Lamivudine</td>
<td>0.48 (0.06,3.70)</td>
<td>0.52 (0.10,2.71)</td>
</tr>
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<td>Tenofovir</td>
<td>2.10 (0.27,16.39)</td>
<td>Tenofovir</td>
<td>1.10 (0.32,3.73)</td>
</tr>
<tr>
<td>No antiviral</td>
<td>1.92 (0.37,9.97)</td>
<td>0.91 (0.27,3.10)</td>
<td>No antiviral</td>
</tr>
</tbody>
</table>

All results presented with relative risk, 95% confidence interval.
Relative risk <1 favour the column.
Global $I^2$=63.5%, $p$ for inconsistency = 0.042
References


