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# Title

Efficacy and safety of antiviral prophylaxis during pregnancy to prevent mother-to-child transmission of hepatitis B virus: a systematic review and meta-analysis

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#### **Abstract**

# Background

To eliminate mother-to-child transmission (MTCT) of hepatitis B virus (HBV), peripartum antiviral prophylaxis (PAP) may be required for HBV-infected pregnant women with a high risk of MTCT despite infant immunoprophylaxis. We conducted a systematic review and meta-analysis for the efficacy and safety of PAP, in order to inform the 2020 WHO guidelines.

#### Methods

We searched four English-language (PubMed/EMBASE/Scopus/CENTRAL) and two Chinese-language (CNKI/Wanfang) databases for randomized (RCT) and non-randomized controlled trials (non-RCT) of PAP versus placebo or no PAP published through March 28<sup>th</sup>, 2019. Two reviewers independently extracted data. Odds ratios (OR) were pooled for the efficacy of PAP to reduce the risk of MTCT. Subgroup analyses were performed on the timing of initiating/stopping antivirals.

# **Findings**

Of 7463 articles identified, 129 studies were included. The pooled ORs for RCTs were similar, at 0.10 (95% CI: 0.03-0.35) for 19 studies of tenofovir disoproxil fumarate (TDF), 0.16 (0.10-0.26) for 40 studies of lamivudine, and 0.14 (0.09-0.21) for 83 studies of telbivudine. The results were similar for non-RCTs. Subgroup analysis identified that initiation in the second trimester may be more beneficial than the third trimester (OR 0.23, 95% CI: 0.09-0.59). We found no increased risk of any infant or maternal safety measures following PAP, except for studies of lamivudine and telbivudine that detected drug-resistant mutations in some treated mothers.

#### Interpretation

PAP is highly effective at reducing the risk of HBV MTCT. Our findings support the 2020 WHO recommendation of administering antivirals during pregnancy, specifically TDF, for the prevention of HBV MTCT.

Funding

WHO

#### **Research in context**

Evidence before this study.

Major international guidelines for the management of chronic hepatitis B virus (HBV) infection recommend the administration of peripartum antiviral prophylaxis (PAP) to pregnant women with high HBV viral load to prevent mother-to-child transmission (MTCT). The 2015 WHO guidelines utilized a systematic review and meta-analysis on the efficacy, safety, and cost-effectiveness of PAP for the prevention of HBV MTCT. The systematic review only identified limited and low-quality evidence at that time; consequently, the WHO could not make a formal recommendation for use of PAP. Furthermore, only English-language databases were searched, although the majority of studies investigating the efficacy of PAP have been conducted in China and reported in Chinese journals that are not indexed in the English-language databases. Also, since that time, the results of several high-quality clinical trials have been published, especially for tenofovir disoproxil fumarate (TDF), a key first-line anti-HBV therapy.

# Added value of this study.

Through a comprehensive search that widely covered both the English- and Chinese-language databases, this is the largest and most up-to-date systematic review and meta-analysis on this topic, including more than twice the number of studies compared to previously published systematic reviews. Furthermore, we thoroughly excluded studies with potentially overlapping patient populations. We found high efficacy of three antiviral therapy regimens, including TDF 300 mg (19 studies), lamivudine 100-150 mg (40 studies), and telbivudine 600 mg (83 studies), with protective ORs between 0.10 and 0.16 for RCTs and between 0.09 and 0.17 for non-RCTs. The large number of studies included enabled subgroup analysis on possible sources of

heterogeneity. Although efficacy did not vary by the timing of PAP discontinuation, we found that starting earlier in the second trimester might be more efficacious than in the third trimester. There was no evidence that the use of PAP is associated with an increased risk of fetal death, neonatal death, preterm birth, congenital abnormalities, postpartum hemorrhage, or postpartum hepatitis flare. Almost all studies sysmatically provided both hepatitis B birth dose vaccine (HepB-BD) and immune globulin (HBIG) to neonates, and no study evaluated an HBIG-free strategy.

Implications of all the available evidence.

In light of the findings of this meta-analysis, the WHO has made a recommendation for administration of TDF 300 mg starting from the 28<sup>th</sup> week of pregnancy until at least birth, in addition to the recommendation for at least three doses of hepatitis B vaccination including HepB-BD. Most studies were conducted in Asia, potentially limiting the applicability of findings to other regions with high HBV prevalence such as Africa. Research on the efficacy of PAP without HBIG is urgently needed, given the limited access to HBIG in many low- and middle-income countries.

#### Introduction

Chronic infection with hepatitis B virus (CHB) represents a serious global health problem, affecting 257 million persons worldwide and causing 900,000 deaths annually due to chronic liver diseases such as cirrhosis and liver cancer. In 2016, the World Health Organization (WHO) developed a global strategy to eliminate hepatitis B as a public health threat by 2030, with a goal to reduce its incidence by 90%, and its mortality by 65%. To meet these objectives, it is crucial to eliminate mother-to-child transmission (MTCT) of HBV, because chronic infection is more likely to develop when infection occurs early in life, particularly at birth through MTCT. Moreover, the risk of developing chronic liver diseases may be higher in those who acquired HBV infection through MTCT compared to those who acquire it through horizontal transmission later in life. The serious serious serious global health problem, affecting the chronic liver diseases.

To prevent MTCT, the WHO recommends that all infants receive at least three doses of hepatitis B vaccine, with the first dose administered within 24 hours of life.<sup>6</sup> However, the birth dose of hepatitis B vaccine (HepB-BD), even if given to neonates along with combined passive immunoprophylaxis using hepatitis B immune globulin (HBIG), does not prevent all MTCT,<sup>7</sup> particularly in those born to mothers with high viremia, as reported in a companion systematic review (*Boucheron P et al.*).<sup>8-10</sup> Consequently, MTCT remains a significant contributor to HBV incidence globally, and supplementary interventions to further decrease MTCT are needed.<sup>11</sup>

In 2014, the WHO commissioned a systematic review to examine the efficacy and safety of antiviral therapy administered during pregnancy for the prevention of MTCT. This review was restricted to English-language articles and identified only one observational study assessing the efficacy of tenofovir disoproxil fumarate (TDF), a key first-line anti-HBV therapy. Moreover,

there was limited evaluation of potential harms associated with the use of antivirals during pregnancy. Consequently, the WHO did not make a formal recommendation at that time. Since then, several clinical trials using TDF have been published, and further evidence has become available regarding the risk of postpartum hepatitis flare in mothers after cessation of antivirals as well as for changes in bone mineral density in the infant. We thus conducted an updated systematic review, searching both English- and Chinese-language databases, and meta-analysis on the efficacy and safety of peripartum antiviral prophylaxis (PAP) for prevention of MTCT, in order to inform the new WHO guidelines.

#### Methods

Search strategy and selection criteria

We followed a protocol pre-registered in PROSPERO (CRD42019134614), and reported according to PRISMA guidelines. Because many studies on HBV MTCT have been published in Chinese-language articles not indexed in Engligh-language databases, we searched four English-language (PubMed/EMBASE/Scopus/CENTRAL) and two Chinese-language (CNKI/Wanfang) databases from inception until March 28<sup>th</sup>, 2019. The search strategies used terms covering HBV AND antiviral therapy AND pregnancy (Appendix A). We also manually searched the references of included studies. There were no language restrictions. Conference abstracts were not considered.

We considered randomized controlled trials (RCT) or non-randomized controlled trials (non-RCT) that enrolled pregnant women with CHB, who received antiviral prophylaxis anytime during pregnancy, and reported the following outcomes: (i) MTCT, indicated by infant HBsAg positivity and/or HBV DNA positivity at 6-12 months of age; and (ii) any infant/maternal adverse events. The following antivirals were considered: adefovir (ADV), emtricitabine (FTC), entecavir (ETV), lamivudine (LAM), telbivudine (LdT), tenofovir alafenamide fumarate (TAF), and TDF. Control groups received no intervention or placebo. Non-RCTs were eligible if they were described as prospective or retrospective cohort studies, with control populations composed of pregnant women with CHB followed during the same time period but who did not receive antiviral prophylaxis (e.g. unwilling). Non-RCTs with a high risk of bias on the Newcastle Ottawa scale (i.e. score  $\leq$ 5) were excluded. Throughout the paper, we used the term "peripartum antiviral prophylaxis (PAP)" rather than "peripartum antiviral therapy" in order to distinguish between antivirals that are given only for a few months surrounding pregnancy and delivery to prevent MTCT (the former) and antivirals given to women/mothers over a longer period, most often lifelong, for their own health benefit (the latter).

Two investigators independently: screened titles and abstracts for all publications identified through the English-language (AF and KY) and Chinese-language databases (YL and TZ); reviewed identified full-text papers; extracted data using a pre-piloted form (Appendix B); and assessed risk of bias using the Cochrane Collaboration tool for RCTs and the Newcastle-Ottawa Scale for non-RCTs (Appendix C). A third reviewer resolved any discrepancies (YS). The following data were extracted: study characteristics, primary endpoint (HBsAg detected in infants at 6-12 months of age), secondary endpoint (HBV DNA in infants at 6-12 months), and maternal and infant safety outcomes including fetal/neonatal death, preterm birth, congenital

abnormalities, postpartum hemorrhage, postpartum hepatitis flare, antiviral resistance, and infant bone mineral density. Articles from the same study sites that had overlapping recruitment periods, enrolment criteria, and treatment types were considered to evaluate the same study population unless specifically indicated otherwise by corresponding authors, who we attempted to contact in all cases. Where multiple articles of the same study population were published, only the most recent article was included unless the risk of bias was lower in a different article.

# Data analysis

The efficacy of PAP was assessed by pooling odds ratios (OR) for RCTs and non-RCTs separately. The primary and secondary endpoints were MTCT based on infant HBsAg positivity and HBV DNA positivity, respectively. The safety of PAP was assessed by pooling risk differences (RDs), rather than ORs, in order to include studies without events. Per-protocol analysis, with the denominator being the number of children with complete follow-up, was performed. If  $\geq 3$  studies were eligible for the analysis/sub-analysis, then estimates were pooled using the DerSimonian-Laird random-effects model. Statistical heterogeneity was assessed using the I<sup>2</sup> statistic. Subgroup analyses were performed for the primary endpoint on the following potential sources of heterogeneity: study design (RCT vs non-RCT), WHO region, timing of treatment start/discontinuation, maternal characteristics (mean viral load at inclusion, HBeAg, HIV/HCV/HDV co-infections, HBV genotypes), infant immunoprophylaxis regimen (HBIG, HepB-BD), language used to report the work, quality of the study for non-RCTs, sample size (smaller studies with N≤30 in either treated or control group versus larger studies with N>30 in both treated and control group), and maternal viral load criteria (pre-specified viral load threshold of ≥5.3 log10 IU/mL and mean HBV DNA level reported for participating women

versus other than that). The presence of subgroup effects was evaluated using the fixed-effects inverse-variance method. In addition to *a priori* defined subgroup analysis looking at differences by the time of treatment initiation, and in order to further explore optimal timing of PAP, *post hoc* meta-analyses were performed including only studies with multiple treatment arms. These analyses directly compared the efficacy, viral load prior to treatment initiation, and viral load prior to delivery, for participants with earlier ( $2^{nd}$  trimester) versus later ( $3^{rd}$  trimester) start. The latter two analyses involved pooling mean differences in viral load at the various timepoints in order to generate the standardized mean difference (SMD). Also *post hoc*, where possible we examined differences in safety outcomes as per timing of treatment initiation. Where there were  $\geq 10$  studies,  $^{21}$  small sample effects, a potential marker for publication bias, were evaluated using funnel plots and Egger's test. Analyses were done using STATA 13 (StataCorp LP, CollegeStation, TX). The evidence quality for primary efficacy analyses and safety analyses were evaluated using the GRADE framework,  $^{22}$  based on risk of bias, inconsistency, imprecision, indirectness, and reporting bias.

# Role of the funding source

This project was funded by the WHO. The funder formulated the review questions, but had no role in study design, data collection, analysis, interpretation, or report writing. The corresponding author had full access to all data in the study and was ultimately responsible for the decision to submit for publication.

#### **Results**

# Study selection

Of 7463 articles identified, 595 were assessed in full text, and 129 original studies (reported in 158 articles) ultimately met eligibility criteria: 33 RCTs and 96 non-RCTs (Figure 1). These studies initially enrolled a total of 18,112 HBV-infected mothers (9573 treated, 8539 untreated) and 17,582 of the infants that born to these mothers had complete follow-up (9411 from treated mothers, 8171 from non-treated mothers). The following antivirals were evaluated using meta-analysis: TDF 300 mg (19 studies, 1092 mothers/1072 infants), <sup>13-15,23-44</sup> LAM 100-150 mg (40 studies, 2080 mothers/2007 infants), <sup>32-35,39,45-88</sup> LdT 600 mg (83 studies, 6036 mothers/5971 infants). <sup>30,38,42,43,46,50,56,60,62,64,76,79,80,85,89-173</sup> No meta-analysis was done for the two eligible studies on LdT 100 mg (65 mothers/65 infants)<sup>51,174</sup> or for the one study each on ADV 10 mg (42 mothers/42 infants)<sup>175</sup> and ADV 500 mg (258 mothers/254 infants); <sup>176</sup> these results are summarized in Appendix D.

# Study characteristics (Appendix E)

Most studies (121/129, 93.8%) took place in China. One study was conducted in both China and the Philippines, and one study each was conducted in Japan, Taiwan, Thailand, Australia, Egypt, Turkey, and Ireland. Only eight studies reported HBV genotypes for all enrolled mothers: genotypes B/C in seven Asian studies; <sup>24,29,39,76,128,139,160</sup> and genotypes B/C/D/E in one Irish study. In 79/129 studies (61.2%), the inclusion criteria specified a high (>5.0 log10 IU/mL) maternal viral load threshold at baseline for all participants. Most studies exclusively included HBeAg-positive women (83/129, 64.3%), 9 studies included a mix of HBeAg-positive and HBeAg-negative women, and one study exclusively included HBeAg-negative women; the remaining 36 studies (27.9%) did not report on HBeAg positivity. All of the included studies

either excluded women co-infected with HIV, HCV, or HDV, or did not report on their prevalence. In most studies (102/129, 79.1%), timely HepB-BD and HBIG were provided to neonates; 27 studies did not clearly indicate timely administration of HepB-BD and HBIG.

#### Risk of bias within studies

Of the five RCTs evaluating TDF, two had low risk of bias for the majority of the main criteria; <sup>13,14</sup> the remaining three had a high/unclear risk of bias for the majority of criteria. <sup>24,26,27</sup> None of the RCTs investigating LAM (n=8) or LdT (n=21) achieved a 'low risk of bias' rating on the majority of the main criteria; most were either high/unclear risk for performance bias (blinding of study personnel), detection bias (blinding of outcome assessment), and attrition bias (high loss to follow-up or no reporting of loss to follow-up) (Appendix F). Of the 96 non-RCTs, 29 had a high risk of bias with a score of 6 while 67 had low risk of bias with a score ranging 7-9. There were no differences in the distributions of risk of bias scores across non-RCTs examining the three main treatment regimens (Appendix G).

# Overall efficacy

PAP was associated with a significant reduction in HBsAg positivity in infants aged 6-12 months in both RCTs and non-RCTs. The pooled ORs in RCTs were: 0.10 (95% CI: 0.03-0.35) for TDF, 0.16 (0.10-0.26) for LAM, and 0.14 (0.09-0.21) for LdT (Figure 2). Statistical heterogeneity was not present (I<sup>2</sup>=0.0%) in any of the analyses, and the three antiviral regimens were similar in efficacy without any statistically significant difference (p=0.78). The pooled ORs in non-RCTs were: 0.17 (95% CI: 0.10-0.29) for TDF, 0.17 (0.12-0.24) for LAM, and 0.09 (0.06-0.12) for LdT. Between RCTs and non-RCTs, no significant differences in treatment efficacy were

observed for each type of antiviral; therefore, these were merged for subsequent subgroup analysis. Similar efficacies were observed when using infant HBV DNA positivity as an endpoint. There was no statistical heterogeneity (I<sup>2</sup>=0.0%) seen in any of the meta-analyses that used HBV DNA positivity as an endpoint, besides that of RCTs using LAM (I<sup>2</sup>=39.8%) where only five studies were included and one outlier (OR=1.28, 95%CI: 0.20-8.32)<sup>45</sup> contributed all observed heterogeneity (Appendix H). The individual characteristics (where available) of infants with MTCT despite maternal TDF 300 mg prophylaxis can be found in Appendix I.

# Efficacy by subgroups

Efficacy did not vary according to mean maternal viral load at baseline (6.0-6.9, 7.0-7.9, 8.0-8.9 log10 IU/ml), the timing of PAP discontinuation (at delivery, 4-8, 12, 24 weeks postpartum), infant immunoprophylaxis regimen, language used to report the study (English, Chinese), risk of bias score for non-RCTs (high, 6; intermediate, 7; low, 8-9), study sample size (≤30 participants versus >30 participants in each group), or maternal viral load criteria (Appendices J-R). Although LAM 100-150 mg was associated with greater efficacy with earlier initiation, compared with later initiation, the interaction was not statistically significant (p=0.06) (Table 1). *Post hoc meta-analyses* of studies that directly compared different treatment starting times (2<sup>nd</sup> vs 3<sup>rd</sup> trimester) suggested that starting in the 2<sup>nd</sup> trimester might be more effective at reducing MTCT risk (OR 0.23, 95% CI: 0.09-0.59) (Figure 3). In the same set of analyses, while baseline viral load did not differ between women in these two timing groups prior to treatment (SMD=0.01, 95%CI: -0.16-0.19), women starting treatment earlier (in the second trimester) had significantly reduced viral load prior to delivery (SMD=-0.62, 95%CI: -0.77- -0.46) (Appendix S).

# Maternal safety

There was no evidence that PAP was associated with an increased risk of fetal death or postpartum hemorrhage, however, the number of events was small and the estimates were imprecise (Table 2, Appendices T-V). There was also no association between cessation of TDF (four studies), LAM (six studies), or LdT (three studies) and increased risk of postpartum flare, based on evaluation for flare at a fixed time in the intervention group and a matched period in the control group. The definition of flare varied across studies; however, most cases were mild and spontaneously recovered, and none progressed to hepatic decompensation (Appendix V). One TDF study investigated antiviral resistance for all women and found no HBV mutations related to antiviral therapy.<sup>24</sup> In contrast, 2/4 studies of LAM and 3/7 studies of LdT detected drugresistant mutations in some treated mothers; meta-analysis was not possible because of considerable variation in timing of testing and population tested.<sup>32,61,67,76,85,110,119,121,133,139,148</sup> There were no differences in risk of any maternal safety outcomes by timing of treatment initiation (Appendix W).

# Infant safety

There was no evidence that PAP was associated with an increased risk of neonatal death, preterm birth, and congenital abnormalities, however, given the small number of events these estimates were imprecise (Table 2, Appendices X-Z). Only one TDF study investigated bone mineral density changes in children in both groups, with no statistically significant difference detected. There were no differences in risk of any infant safety outcomes by timing of treatment initiation (Appendix W). There was heterogeneity (I<sup>2</sup>=43.0%) in the meta-analysis of the risk of preterm birth following LAM 100-150 mg which could be largely contributed to two

outlying studies, both of which were non-RCTs that started treatment very early (pre-pregnancy or in the first trimester) (Appendix Y). <sup>64,72</sup>

#### Risk of bias across studies

Funnel plots and the Egger's test did not indicate small sample effects in RCTs. In non-RCTs, however, there was evidence of potential small sample effects for the efficacy of each of the treatment types (Appendix AA).

#### GRADE assessment

The GRADE evidence quality for the primary endpoint, based on RCTs, was high for TDF and moderate for LAM and LdT (due to high/unclear risk of bias in most studies). Although GRADE was lower for non-RCTs, these studies' results were consistent with RCTs. For some safety outcomes evaluated by RCTs, including fetal death, neonatal death, and congenital abnormalities, GRADE was ranked as moderate for TDF and low for LAM and LdT. In contrast, GRADE for postpartum hemorrhage and postpartum flare were low or very low for all types of antivirals (Appendix AB). It was not possible to do GRADE evidence quality analysis for antiviral resistance.

#### **Discussion**

This systematic review and meta-analysis found evidence to support the efficacy and safety of PAP using three different types of nucleos(t)ide analogues; namely, TDF, LAM, and LdT. Meta-analysis of RCTs showed that these antivirals were associated with large and similar reductions

in the likelihood of MTCT. For safety outcomes, there was no evidence for an increased risk associated with any of the antivirals examined, though some findings were based on small number of events. However, this systematic review confirmed the low barrier to resistance of early generation nucleos(t)ide analogues (LAM and LdT). Consequently, WHO recommends TDF for HBV-infected women with high viral load to prevent MTCT.

An important strength of this systematic review is its comprehensive search, which covered both English- and Chinese-language databases, leading to the inclusion of more than twice the number of studies compared to previous systematic reviews on this topic. The large number of studies included enabled us to perform subgroup analyses for efficacy, and safety evaluations of rarer outcomes. In addition, efforts were employed to exclude articles evaluating the same patient group, in order to avoid doublecounting and overweighting of the same study samples; the inclusion of overlapping patient populations in other systematic reviews has been criticized. We also excluded poorly conducted non-RCTs with a high risk of bias. Subsequently, there was no evidence of heterogeneity in efficacy estimates between English-versus Chinese-language studies, nor between studies with smaller versus larger sample sizes.

The optimal timing to start and stop PAP has not been well established. Different guidelines recommend varying schedules, ranging from starting at 24-28 to 28-32 weeks of gestation, and from stopping at childbirth to 12 weeks postpartum. Our *post hoc* analyses suggest that starting in the second trimester might be more efficacious than in the third trimester, and that this may be linked to increased viral load reduction in women treated earlier. However, this finding should be cautiously interpreted as it is based on a small number of studies (4), 37,87,94,139 and events (23 total). Moreover, only two of the included studies in this *post hoc* analysis

administered TDF. More research is needed on this topic prior to making any conclusions. WHO recommends starting PAP from the 28<sup>th</sup> week of pregnancy, pending additional evidence to support earlier administration.

No difference was observed in the efficacy of PAP when cessation was at the time of childbirth versus at 4-8 weeks postpartum, suggesting that PAP could be stopped immediately after delivery. Another concern, however, is postpartum hepatitis flare. In HBV-infected pregnant women without concurrent antiviral therapy, rapid changes in maternal immunity being suppressed during pregnancy followed by its reconstitution after childbirth could trigger postpartum flare. Early studies have reported that initiating antivirals during pregnancy and its withdrawal at delivery might further increase the risk of postpartum flare. 188 Our meta-analysis did not observe any difference in the risk of postpartum flare between the treated group following discontinuation of PAP and controls; however, none of these comparative studies stopped PAP at the time of child delivery. In four included studies where all women were HBeAg-positive, and which reported on flare only in the treated group, the range of flare risk for women stopping treatment at childbirth was 3.5-19.2% (Appendix V). 67,84,109,145 This range overlaps with that previously reported for non-treated HBeAg-positive women (14.2-40.0%). 189,190 Few studies were included in the safety meta-analysis for postpartum flare and the GRADE evidence quality was low or very low for all treatment types for this outcome. There was also important heterogeneity in all meta-analyses for all treatments that evaluated flare, this is likely explained by the minimal number of eligible studies, as well as important differences in both the safety outcome definitions used and the treatment regimen timing across these studies. The vast majority of all flares described in the studies were mild and self-limiting; only a few required antiviral therapy, and none developed hepatic decompensation.

Our review had potential limitations. Only 6% (2/33) of the RCTs were assessed as having an overall low risk of bias (Appendix F). Very few (18%, 6/33) of the included RCTs presented adequate details of loss-to-follow-up, <sup>13,14,26,89,103,106</sup> which limited our ability to perform intention-to-treat meta-analysis. Furthermore, although non-RCTs with a very high risk of bias were excluded from analysis, 31% of the remaining non-RCTs had a score of 6 (high) on the Newcastle-Ottawa scale, indicating multiple methodological limitations (Appendix G). Many of the included studies had small sample sizes (≤30 infants) in either the treated or control group, although sensitivity analysis showed no difference in efficacy estimates between smaller and larger studies for any treatment type (Appendix Q). Some subgroup meta-analyses had few (i.e. <5) eligible studies, such as those examining differences in efficacy by mean maternal viral load at baseline (Appendix L), and therefore, these results should be interpreted cautiously. This is a meta-analysis of aggregate data, and some topics were limited in examining, such as differences in efficacy by maternal viral load, may be better evaluated using a meta-analysis of individual participant data. Importantly, the vast majority of included studies were conducted in Asia, particularly in China. Of the seven studies conducted outside of China, only one from each of Thailand and Taiwan had >30 participants in both treated and control groups. Therefore, there is very limited representation of diverse populations in this meta-analysis and the applicability of our study findings to other regions is uncertain. For example, in sub-Saharan Africa, another area with a high HBV prevalence, the major HBV genotypes, the natural history of CHB, and the current standard of care, all differ from Asia. 191,192 Many African countries have limited coverage of HepB-BD, and are without access to either HBIG or HBV DNA testing. No studies evaluated the efficacy of PAP without HBIG (i.e. with HepB-BD alone), indicating an important research

gap. A field evaluation is ongoing to assess the efficacy of HepB-BD plus PAP versus HepB-BD alone. 193

Based on the evidence provided by this study as well as a companion systematic review that addressed HBV DNA thresholds for identifying pregnant women at risk of MTCT (*Boucheron P et al.*), the WHO recommends administering TDF to HBV-infected pregnant women with high viral load (≥5.3 log10 IU/mL (≥200,000 IU/mL)) from the 28<sup>th</sup> week of pregnancy until at least childbirth to prevent MTCT, in addition to three doses of hepatitis B vaccination including HepB-BD. In order to accelerate global HBV elimination by 2030, it is essential to promote the uptake of PAP into routine healthcare, particularly in LMICs that bear the highest HBV disease burden.

# **Contributors**

AF, JVH, RC, MB, and YS formulated the research questions. AF and YS developed the study protocol, analysed the data, and wrote the manuscript. AF and YL developed the search strategy. AF, YL, KY, TZ, and PB performed the systematic review. All authors reviewed the manuscript and approved the final version.

#### **Declaration of interests**

RC received personal fees from the WHO. The rest of the authors declare no competing interests.

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Table 1. Efficacy of peripartum antiviral prophylaxis (PAP) in the prevention of MTCT\*, by subgroups

		7	TDF 300 mg (n=19)		LAN	M 100-150 mg (n=40	))	L	dT 600 mg (n=83)	
Subgroup		No. of studies	OR (95% CI)	P	No. of studies	OR (95% CI)	P	No. of studies	OR (95% CI)	P
Study design	RCTs	5	0.10 (0.03-0.35)	0.47	8	0.16 (0.10-0.26)	0.80	21	0.14 (0.09-0.21)	0.08
Study design	Non-RCTs	14	0.17 (0.10-0.29)	0.47	32	0.17 (0.12-0.24)	0.80	62	0.09 (0.06-0.12)	0.08
Timing of PAP	<28 weeks	10	0.10 (0.04-0.25)		7	0.10 (0.04-0.26)		24	0.08 (0.05-0.13)	
initiation	28 weeks	7	0.25 (0.13-0.48)	0.15	20	0.16 (0.11-0.22)	0.06	44	0.13 (0.10-0.18)	0.20
(median gestational age)	>28 weeks	5	0.10 (0.03-0.29)	0.120	11	0.31 (0.16-0.57)	†	13	0.09 (0.04-0.20)	0.1_0
T' CDAD	At delivery	5	0.11 (0.04-0.28)		13	0.15 (0.10-0.23)		16	0.10 (0.06-0.16)	0.49
Timing of PAP discontinuation	4-8 weeks	7	0.12 (0.04-0.34)	0.96	21	0.23 (0.15-0.34)	0.19	33	0.13 (0.09-0.19)	
(postpartum)	12 weeks	2	N/A	0.90	2	N/A		8	0.06 (0.02-0.16)	
(postpartam)	24 weeks	0	N/A		0	N/A		6	0.11 (0.04-0.29)	
Mean maternal	5.0-5.9	0	N/A		0	N/A	N/A	1	N/A	0.14
viral load at	6.0-6.9	0	N/A	0.96	4	0.15 (0.06-0.37)		10	0.13 (0.07-0.23)	
baseline (log	7.0-7.9	3	0.10 (0.03-0.41)	0.90	1	N/A	IN/A	13	0.06 (0.03-0.13)	0.14
IU/mL)	8.0-8.9	3	0.11 (0.02-0.51)		2	N/A		1	N/A	
Maternal	Positive	11	0.09 (0.04-0.21)		30	0.16 (0.12-0.23)		52 0.11 (0.08-0.14		
HBeAg at	Negative	0	N/A	N/A	0	N/A	0.45	1	N/A	0.65
baseline	Mixed	1	N/A		4	0.26 (0.08-0.82)		6	0.09 (0.04-0.21)	
Infant immuno-	Timely HepB- BD & HBIG	14	0.15 (0.09-0.27)	0.89	31	0.18 (0.13-0.24)		64	0.10 (0.08-0.14)	
prophylaxis regimen	No or unclear timely HepB- BD/HBIG	5	0.16 (0.06-0.43)		9	0.13 (0.06-0.25)	0.38	18	0.10 (0.06-0.16)	0.83

<sup>\*</sup> MTCT is defined as HBsAg positivity in infants aged 6-12 months.

<sup>†</sup> Non-important heterogeneity ( $I^2 = 7.7\%$ ) in the subgroup of >28 weeks may or may not render the p-value non-valid.

Table 2. Safety of peripartum antiviral prophylaxis

		<b>TDF 300</b>	mg (N=19)	)	L	AM 100-1	50 mg (N=	40)	LdT 600 mg (N=83)			
Safety	No of	Eve	ents/	RD	No of	Eve	nts/	RD	No of	Ever	nts/	RD
measure	No. of studies	Partic	ipants	(95%	No. of studies	Partic	ipants	(95%	No. of studies	Partici	pants	(95%
	studies	Treated	Control	CI)	studies	Treated	Control	CI)	studies	Treated	Control	CI)
					Mat	ernal safet	y					
				0.003				0.000				-0.001
Fetal death	19	3/1097	1/881	(-0.006-	39	1/2003	9/2087	(-0.006-	81	3/5645	20/5823	(-0.003-
				0.012)				0.005)				0.002)
Postpartum				-0.001				0.008			116/	-0.001
hemorrhage	6	9/365	7/256	(-0.024-	8	98/611	61/752	(-0.012-	19	125/1729	2020	(-0.010-
nemorrnage				0.022)				0.028)			2020	0.008)
Postpartum				-0.020				-0.020				0.022
hepatitis flare	4	28/356	20/327	(-0.082-	6	59/447	34/568	(-0.071-	3	27/431	26/565	(-0.064-
nepatitis mare				0.041)*				0.030)*				0.109)†
					Inf	ant safety						
Neonatal				0.000				0.000				0.000
death	19	2/1079	1/858	(-0.009-	39	1/2010	1/2093	(-0.006-	82	2/5752	0/5863	(-0.002-
ucani				0.009)				0.006)				0.003)
				-0.003				0.000			120/	-0.001
Preterm birth	9	19/622	22/479	(-0.024-	10	14/609	11/399	(-0.025-	24	105/2427	2191	(-0.010-
				0.019)				0.025)*			2171	0.008)
Congenital				-0.002				0.003				0.000
abnormalities	14	4/802	5/687	(-0.013-	16	8/845	5/953	(-0.007-	40	11/3585	9/2983	(-0.004-
abilormanties	1	C . 11		0.009)	1: 6:			0.014)	1 1			0.004)

Abbreviations: n, number of studies that reported on this safety outcome in a way that could be combined in the meta-analysis; RD, weighted risk difference.

<sup>\*</sup> Moderate to substantial heterogeneity in estimate ( $I^2 \ge 30\% \& < 75\%$ )

<sup>†</sup> Considerable heterogeneity ( $I^2 \ge 75\%$ )

Figure 1: Flowchart of study selection

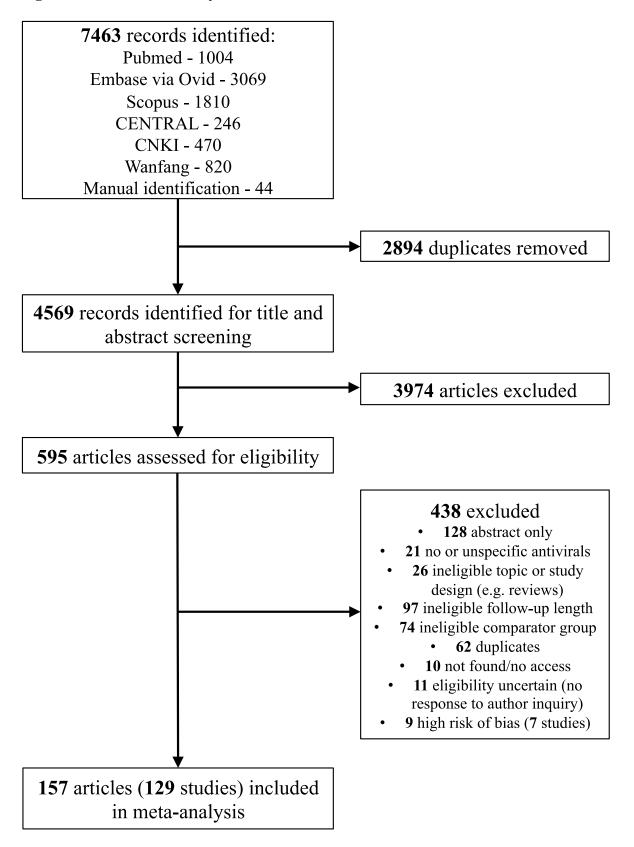


Figure 2. Efficacy of peripartum antiviral prophylaxis in the prevention of MTCT\*

Figure 2A. Efficacy of tenofovir disoproxil fumarate (TDF) 300 mg, by study design

Author	Year	Country	Tx start in weeks gestation	Tx end in weeks postpartum	Events, Treatment	Events, Control	OR (95% CI)
Randomised	controlle	d trials					
Jourdain G	2018	Thailand	26-29	8	0/149	3/147	0.14 (0.01, 2.7
Lin Y	2018	China	24	4	0/58	4/52	0.09 (0.00, 1.7
Liu MH	2017	China	28-30	0	1/20	6/20	0.12 (0.01, 1.1
Pan CQ	2016	China	30-32	4	0/92	6/88	0.07 (0.00, 1.2
Yu CY	2018	China	24	4	0/30	4/30	0.10 (0.00, 1.8
Subtotal (I-so	quared =	0.0%, p = 0	).997)			<	0.10 (0.03, 0.3
Non-randomis	sed cont	rolled trials					
Celen MK	2013	Turkey	18-27	4	0/21	2/23	0.20 (0.01, 4.4
Chen HL	2015	Taiwan	30-32	4	1/65	6/56	0.13 (0.02, 1.1
Chen WJ	2017	China	28	0	1/30	16/44	0.06 (0.01, 0.4
Gong Q	2017	China	1-6	NR	1/44	7/44	0.12 (0.01, 1.0
Greenup AJ	2014	Australia	32	12	1/69	2/10	0.06 (0.00, 0.7
He LL	2018	China	28	NR	13/50	17/35	0.37 (0.15, 0.9
Hu MF	2018	China	<0-28	NR	1/89	3/30	0.10 (0.01, 1.0
Huang Q	2017	China	24-28	12	0/20	3/20	0.12 (0.01, 2.5
Wakano Y	2018	Japan	22-28	4-8	0/2	2/3	0.12 (0.00, 4.6
Wan JY	2017	China	28	0	3/74	7/42	0.21 (0.05, 0.8
Wang HB	2018	China	20-36	NR	0/100	2/20	0.04 (0.00, 0.8
Xiao XH	2017	China	28	0 or 4	0/60	1/61	0.33 (0.01, 8.3
Zhang BF	2018	China	24-28	0	0/39	15/75	0.05 (0.00, 0.8
Zhou Y	2018	China	24-28	0	0/60	5/36	0.05 (0.00, 0.8
Subtotal (I-so	quared =	0.0%, p = 0	0.860)				0.17 (0.10, 0.2
Overall (I-squ	uared = (	0.0%, p = 0.	972)				0.16 (0.09, 0.2
						I I	I I I 10

<sup>\*</sup> MTCT is defined as HBsAg positivity in infants aged 6-12 months.

Figure 2B. Efficacy of lamivudine (LAM) 100-150 mg, by study design

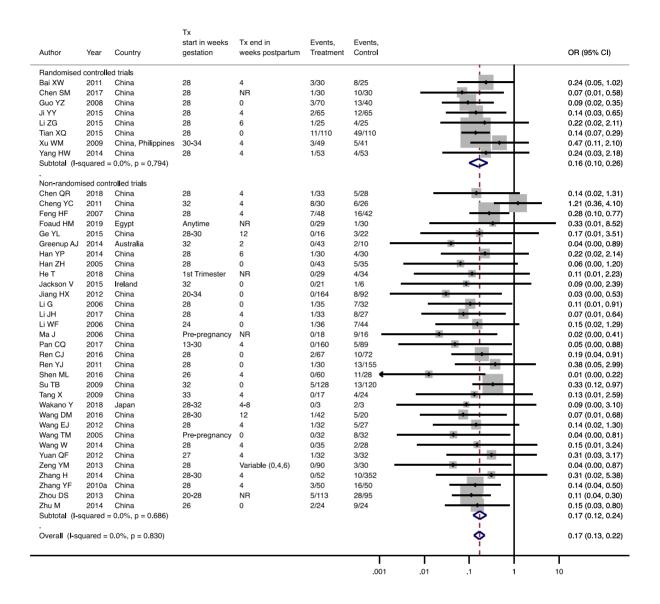
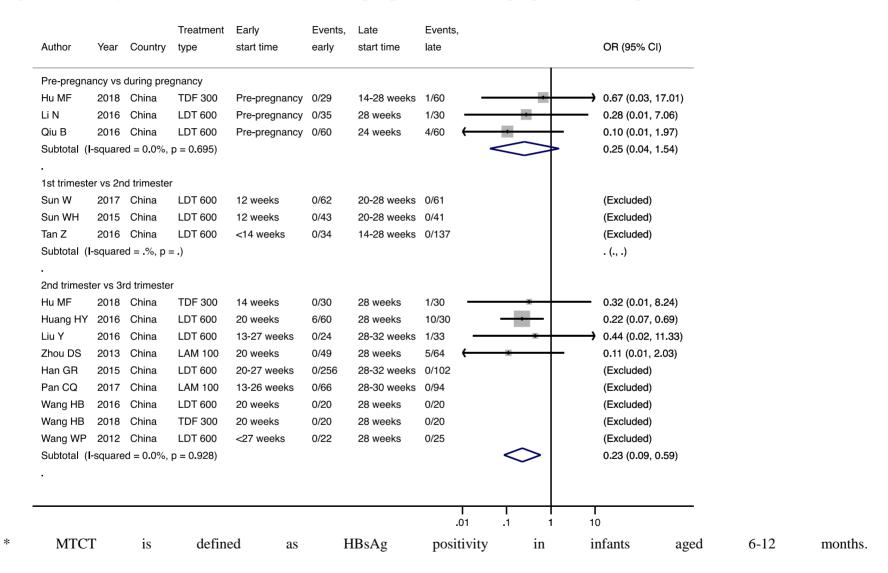


Figure 2C. Efficacy of telbivudine (LdT) 600 mg, by study design

New York   1979	uthor	Year	Country	Tx start in weeks gestation	Tx end in weeks postpartum	Events, Treatment	Events, Control		OR (95% CI)
The State   1907   China   28								i	
THE PAY OF STATE OF S	Bai HL							<del></del>	0.11 (0.01, 2.09)
Decomposition   Composition									
20.0 + 15									
Lang   Prop   2016									
No.									
Second   S									
Langer   Company   Compa									
Program   1994   China   28									
Second   2017	PengML	2014	China	28	NR	1/30			0.09 (0.01, 0.82)
Car   Fry   2018   China   201		2017	China	24	0	3/100	12/100	<del></del> -	0.23 (0.06, 0.83)
Mag   Y					24				0.07 (0.00, 1.21)
									0.24 (0.03, 2.19)
Tamp L 2009 China 2004 China 2004 A 2000 A 2									
Description   Pre-pregnancy   NR								-	
								* *	
The Prince of Control									
Day J 2017 Onna 28 0 160 0854									
The LP									
Abelease   Company   Abelease									
Part Cy   2015   China   1st Tremester   NR				20	*	0/30	3/30	<b>&gt;</b>	0.14 (0.09, 0.21)
Prime   Prime   2016				1st Trimester	NR	1/42	7/40		0.11 (0.01, 0.98)
Description   2018   China   28								-	
Chen My   2917									
Dien ZX 2917 China 15-32 NN 141 1589 0.12 (0.02 0.97 China 15-32 NN 15-32 N									0.09 (0.03, 0.30)
Dai ZL.  Dai ZL.  Dai ZL.  Dai China  Dai ZL.  Dai China  Dai ZL.  Dai China									0.12 (0.02, 0.97)
Deng Y 2015 China 24-36 4 082 4/75 0.10 (0.11, 128 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1								<del></del>	0.05 (0.01, 0.42)
miny M 2013 China 28 24 0.58 0.690					4	0/82	4/75		0.10 (0.01, 1.82)
Fings MM 2017 China 28 4 1.68 7.68 0.12 (20.11, 12.57) alor VL 2015 China 28-30 12 0.00 322 0.14 (0.01, 20.75) alor VL 2015 China 28-30 12 0.00 322 0.14 (0.01, 20.75) alor VL 2015 China 28-30 12 0.00 322 0.14 (0.01, 20.25) alor VL 2015 China 28 6 0.00 0.450 0.10 (0.00, 20.25) alor VL 2015 China 28 6 0.00 0.450 0.10 (0.00, 20.25) alor VL 2015 China 28 22 24 0.04 0.05 0.05 0.05 0.05 0.05 0.05 0.0								_*	0.10 (0.01, 1.92)
3ao P									0.07 (0.00, 1.30)
38 YL 2015 China 28-90 12 0020 3022								-	0.12 (0.01, 1.02)
tan GR   2015   China   20-32   NR   0.058   8.86									
tan YP 2014 China 28 6 0.000 4.30								10	
te T 2018 China 1st Trimester NR 002 4/34								<u> </u>	
tu WH								7.	
MY 2018 China 28-32 9-4 0105 21122									
Namp   Q   2017   China   24-28   12   0.20   3/20   0.12 (0.01, 2.58   1.00   0.04 (0.01, 0.58   1.00   0.04 (0.01, 0.58   1.00   0.04 (0.01, 0.58   1.00   0.05 (0.01, 0.58   1.00   0.05 (0.01, 0.58   1.00   0.05 (0.01, 0.58   1.00   0.05 (0.01, 0.58   1.00   0.05 (0.01, 0.58   1.00   0.05 (0.01, 0.58   1.00   0.05 (0.01, 0.58   1.00   0.05 (0.01, 0.58   1.00   0.05 (0.01, 0.58   1.00   0.05 (0.01, 0.58   1.00   0.05 (0.01, 0.58   1.00   0.05 (0.01, 0.05   1.00   0.05 (0.01, 0.05   1.00   0.05 (0.01, 0.05   1.00   0.05 (0.01, 0.05   1.00   0.05 (0.01, 0.05   1.00   0.05 (0.01, 0.05   1.00   0.05 (0.01, 0.05   1.00   0.05 (0.01, 0.05   1.00   0.05 (0.01, 0.05   1.00   0.05 (0.01, 0.05   1.00   0.05 (0.01, 0.05   1.00   0.05 (0.01, 0.05   1.00   0.05 (0.01, 0.05   1.00   0.05 (0.01, 0.05   1.00   0.05 (0.01, 0.05   1.00   0.05 (0.01, 0.05   1.00   0.05 (0.01, 0.05   1.00   0.05 (0.01, 0.05   0.05   0.05 (0.01, 0.05   0.05   0.05   0.05 (0.01, 0.05   0.05   0.05   0.05 (0.01, 0.05   0.05   0.05   0.05   0.05 (0.01, 0.05   0.05									
Isang S									
laing M. 2013 China		2017		28		1/44	15/44		
LI M 2017 China 28 4 1/50 830 0.09 (0.01, 0.02 1/1 1/1 1/1 1/1 1/1 1/1 1/1 1/1 1/1 1/			China			1/65			0.08 (0.01, 0.70)
N								<del></del>	0.09 (0.01, 0.82)
12	.i N		China			0/64	9/25	<u> </u>	0.01 (0.00, 0.24)
Ju CV         2014         China         28         4         1/34         8/34         0.10 (0.91, 0.84           Ju J         2017         China         28-36         4         0/20         5/20         0.00, 0.01, 34           JLY         2016         China         28-36         4         0/20         5/20         0.00, 0.00, 0.12           20. JJ         2015         China         28         4         0/125         3/58         0.06 (0.00, 1.24           20. JJ         2017         China         28         4         0/125         3/58         0.06 (0.00, 1.24           20. B         2017         China         28         0         1/40         10/40         0.06 (0.01, 1.24           20. B         2016         China         28         0         1/40         10/40         0.08 (0.01, 0.83           20. B         2016         China         28         24         246         11/40         10/40         0.06 (0.01, 0.06           20. B         2016         China         28         24         246         11/40         10/40         0.06 (0.01, 0.06           20. B         2018         China         28         24         246         11/								-	0.19 (0.02, 1.70)
Liu J         2017         China         30         NR         0.97         228           Liu XB         2016         China         28-96         4         0.20         550           Ju Y         2016         China         4-32         4         1/82         1978           Ju J         2015         China         28         4         0/125         3/58           Ju J         2016         China         28         4         0/125         3/58           Ju D         2016         China         28         0         0.81         21/370           Ju D         2016         China         28         0         1/40         10/40           Ju D         1016         China         40-24         0         41/20         12/60           Ju D         1016         China         28         24         2/46         11/40         10/40         10/40         0.08 (0.01, 0.38           Ju D         1106         2016         China         28         24         2/46         11/428         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.02 <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td><u>'</u></td> <td>0.38 (0.11, 1.37)</td>								<u>'</u>	0.38 (0.11, 1.37)
Liu XB         2016         China         28-36         4         0.20         5/20           Liu Y         2016         China         4-32         4         1/82         19/78         0.04 (0.00, 0.29           Jou JJ         2015         China         2.8         4         0/125         3/58         0.08 (0.00, 1.24           Pang DA         2012         China         2.8         0         1/40         10/40         0.10 (0.01, 1.36           Barg DA         1.140         10/40         1.040         0.06 (0.01, 0.33           Bib B         2016         China         2.8         2.4         2/46         11/40         1.040         0.06 (0.01, 0.36           Bib MD         2015         China         2.8         2.4         2/46         11/46         0.14 (0.03, 0.76         0.14 (0.03, 0.76           Bibra Q         2018         China         2.6         4         0/61         11/28         0.14 (0.04, 0.46         0.06         0.14 (0.04, 0.06         0.06         5/46         0.07 (0.00, 1.34         0.07 (0.00, 1.36         0.07 (0.00, 1.34         0.07 (0.00, 1.34         0.07 (0.00, 1.34         0.07 (0.00, 1.34         0.07 (0.00, 1.34         0.07 (0.00, 1.37         0.07 (0.00, 1.30         0.07 (0.00,									0.10 (0.01, 0.84)
Liu Y 2016 China 4-32 4 1/82 19/78 0.04 (0.00, 0.24 2015 China 28 4 0/125 3/58 0.06 (0.00, 1.24 2017 China 28 0 0 1/40 10/40 0.05 (0.01, 0.24 2018 China 40-24 0 0 1/40 10/40 0.05 (0.01, 0.24 2016 China 28 24 2/46 11/46 11/48 10/40 0.05 (0.01, 0.25 2016 China 28 24 2/46 11/46 11/48								-	
2015									
Pan YC 2017 China 32 0 0 0/81 21/370 0.10 (0.01) 1.86 26ng BA 2012 China 28 0 1/40 10/40 10/40 0.08 (0.01) 6.83 20/10 B 2016 China 40-24 0 4/120 12/60 0.14 (0.03) 6.75 20/10 1.86 20/10 China 28 24 24/46 11/46 0.14 (0.03) 6.75 20/10 20/16 China 28 24 24/46 11/46 0.14 (0.03) 6.75 20/16 China 28 24 24/46 11/46 0.14 (0.03) 6.75 20/16 China 28 24-28 0 0/78 22/1 0.05 (0.00) 1.68 20/16 China 24-28 0 0/78 22/1 0.05 (0.00) 1.68 20/16 China 24-28 0 0/78 22/1 0.05 (0.00) 1.68 20/16 China 24-28 0 0/78 22/1 0.05 (0.00) 1.68 20/16 China 24-28 12 0/123 12/65 0.05 (0.00) 1.68 20/16 China 12-28 12 0/123 12/65 0.05 (0.00) 1.68 20/16 China 12-28 12 0/123 12/65 0.05 (0.00) 1.68 20/16 China 12-28 12 0/123 12/65 0.05 (0.00) 1.68 20/16 China 12-28 12 0/14 16/99 0.05 (0.00) 1.69 20/16 China 28 12-28 0 0/17 11/37 15/320 0.05 (0.00) 1.69 20/16 China 28 4 3/318 17/374 0.05 (0.00) 0.39 20/16 China 28 4 3/318 17/374 0.05 (0.00) 0.39 20/16 China 28 4 0/110 18/187 0.05 (0.00) 0.39 20/16 China 28 4 0/110 18/187 0.05 (0.00) 0.39 20/16 China 28 4 0/110 18/187 0.05 (0.00) 0.39 20/16 China 28 4 0/110 18/187 0.05 (0.00) 0.39 20/16 China 28 4 0/110 18/187 0.05 (0.00) 0.39 20/17 China 28 4 0/110 18/187 0.05 (0.00) 0.39 20/17 China 28 4 0/110 18/187 0.05 (0.00) 0.39 20/17 China 28 4 0/110 18/187 0.05 (0.00) 0.39 20/17 China 28 4 0/18 5/20 0.09 (0.1) 0.00 (0.0) 1.39 20/17 China 28 4 0/18 5/20 0.09 (0.1) 0.00 (0.0) 1.39 20/17 China 28 4 0/18 5/20 0.09 (0.1) 0.00 (0.00) 1.39 20/17 China 28 4 0/18 5/20 0.09 (0.1) 0.00 (0.00) 1.39 20/17 China 28 4 0/18 20/18 China 28 4 0/18 20/1									
Pang BA 2012 China 28 0 1.4/40 10/40									
Diu B         2016         China         <0-24         0         4/120         12/80           Ren N         2015         China         28         24         2/48         11/46         0.14 (0.04, 0.45         0.04 (0.00, 0.26)           Shen ML         2016         China         28         4         0/61         11/28         0.01 (0.00, 0.26)           Sheng Q         2018b         China         24-32         0         0/79         2/21         1         0.05 (0.00, 1.06)           Shun W         2017         China         12-28         12         0/123         12/65         1         0.02 (0.00, 0.30)           Shun W         2015         China         12-28         12         0/123         12/65         1         0.02 (0.00, 0.30)           Shun W         2015         China         12-28         12         0/14         6/69         1         0.02 (0.00, 0.30)           Sian Z         2016         China         28         0         0/41         6/69         1         0.10 (0.11, 1.31)           Sian Z         China         29         4         0/135         77/203         1         0.10 (0.01, 1.21)           Sian Z         China									
See No.   2015   China   28   24   2.446   11.46									
Shen ML 2016 China 24-32 0 0 0/79 2/21 0.05 (0.00, 0.28 cheng Q 2018b China 24-28 0 0 0/66 5/46 0.06 (0.00, 1.08 cheng Q 2018b China 12-28 12 0/123 12/65 0.05 (0.00, 0.30 cheng Q 2018b China 12-28 12 0/123 12/65 0.05 (0.00, 0.30 cheng Q 2018b China 12-28 12 0/123 12/65 0.05 (0.00, 0.30 cheng Q 2018b China 12-28 12 0/123 12/65 0.05 (0.00, 0.30 cheng Q 2018b China 12-28 12 0/124 12/65 0.05 (0.00, 0.30 cheng Q 2018b China 12-28 12 0/124 12/65 0.05 (0.00, 0.30 cheng Q 2018b China 12-28 12 0/124 12/65 0.05 (0.00, 0.30 cheng Q 2018b China 12-28 0 0 0/41 6/59 0.05 (0.00, 0.30 cheng Q 2018b China 12-28 0 0 0/41 6/59 0.05 (0.00, 0.30 cheng Q 2018b China 12-28 0 0 0/15 12/65 0.05 (0.00, 0.30 cheng Q 2018b China 12-28 0 0/15 China 12-28									
Sheng Q 2018b China 24-32 0 0.079 221 Shong Q 2018b China 24-28 0 0.066 548 Shan W 2017 China 12-28 12 0/123 12/65 Shan W 2017 China 12-28 12 0/123 12/65 Shan W 2019 China 28 12 0/124 8/46 Shan W 2018 China 28 18 NR 0/171 15/320 Shan W 2018 China Anytime NR 0/171 15/320 Shan W 2018 China 28 4 3/318 17/374 Shang B 2016 China 28 4 0/110 16/187 Shang B 2016 China 28 3 4 0/110 16/187 Shang B 2016 China 28 0/110 16/187 Shang B 2016 China 28 0/110 16/187 Shang B									
Sheng Q 2018									0.05 (0.00, 1.06)
Sun W   2017   China   12-28   12   0.123   12/65     0.02 (0.00, 0.35   0.00, 0.45   0.00								-	0.06 (0.00, 1.05)
Sum WH   2015	Sun W			12-28		0/123	12/65	-	0.02 (0.00, 0.30)
an Z 2016 China								•	0.03 (0.00, 0.48)
Tian JH         2018         China         Anylime         NR         0/135         7/203           Tian RH         2016         China         28         4         3/318         17/374         1         0,20 (0.06, 0.69           Wang DM         2016         China         28         4         0/110         16/187         1         0,09 (0.01, 0.80           Wang EJ         2012         China         28         4         0/18         5/20         0.09 (0.01, 0.80           Wang EJ         2012         China         28         4         0/28         5/20         0.09 (0.01, 0.80           Wang DD         2016         China         28         4         0/28         5/27         0.04 (0.00, 0.80           Wang JD         2017         China         28         4         0/53         8/52         0.04 (0.00, 0.80           Wang TD         2015         China         28         4         0/53         8/52         0.05 (0.00, 0.81           Wang TD         2015         China         22-28         0         0/47         20/198         0.09 (0.01, 1.54           Wu C         2015         China         22-32         0 or 4         0/62         1/61								_	0.10 (0.01, 1.81)
Tian RH         2016         China         28         4         3/318         17/374         0.20 (0.06, 0.69           Wang DM         2016         China         28         4         0/110         16/187         0.20 (0.06, 0.69           Wang DM         2016         China         28-30         12         1/36         5/20         0.07 (0.00, 1.37           Wang LB         2012         China         28-30         12         1/36         5/20         0.07 (0.00, 1.37           Wang HB         2016         China         28-36         NR         0/100         2/20         0.07 (0.00, 1.37           Wang JD         2017         China         24-28         NR         1/329         9/65         0.02 (0.00, 0.15           Wang WP         2015         China         24-28         0         0.047         20/198         0.02 (0.01, 1.54           Wu O         2015         China         24-32         0         0.047         20/198         0.09 (0.01, 1.54           Giao XH         2017         China         28-32         0         0.07 (0.01, 2.37         1.01         0.09 (0.01, 1.54           dao ZC         Cull         China         28-32         4         0/62								* <u> </u>	
Vang B         2016         China         28         4         0/110         16/187         0.05 (0.00, 0.78           Vang DM         2016         China         28-30         12         1/36         5/20         0.09 (0.01, 0.80           Vang EJ         2012         China         28         4         0/28         5/27         0.07 (0.00, 1.37           Vang HB         2016         China         28-36         NR         0/100         2/20         0.04 (0.00, 0.87           Vang DD         2017         China         22-28         NR         1/329         9/65         0.02 (0.00, 0.87           Vang TD         2015         China         28         4         0/53         8/62         0.05 (0.00, 0.87           Vang WP         2012         China         28-32         0         0.047         20/198         0.01 (0.00, 0.32           Van Q         2015         China         28-32         0         0.04         1/61         0.02 (0.01, 8.08           Vao ZC         2014         China         28-32         6         0/30         2/30         0         0.19 (0.01, 2.01           Caba CF         2014         China         28-32         4         0/28								_*	
Vang DM         2016         China         28-30         12         1/36         5/20           Vang EL         2012         China         28         4         0/28         5/27         0.07 (0.00, 1.37           Vang HB         2016         China         20-36         NR         0/100         2/20         0.04 (0.00, 0.80           Vang TD         2015         China         24-28         NR         1/329         9/65         0.02 (0.00, 0.15           Vang TD         2015         China         24-28         0         0/47         20/198         0.09 (0.01, 1.54           Vu O         2015         China         24-32         0 or 4         0/62         1/61         0.09 (0.01, 1.54           Vu O         2015         China         28-32         6         0/30         2/30         1         0.02 (0.01, 8.08           Vao LF         2014         China         28-32         6         0/30         2/30         1         0.10 (0.01, 2.01           Abard LF         2014         China         28-32         6         0/30         2/30         1         0.10 (0.01, 2.01           Abard LF         2014         China         28-8         4         0/28									
Vang ELJ         2012         China         28         4         0/28         5/27           Vang HB         2016         China         20-36         NR         0/10         2/20           Vang JD         2017         China         22-28         NR         0/10         2/20           Vang TD         2015         China         22-28         NR         1/329         9/65           Vang WP         2012         China         22-728         0         0/47         20/198         0.05 (0.00, 0.87           Vu Q         2015         China         22-32         0 or 4         0/204         1/495         0.01 (0.00, 0.32           Vu Q         2015         China         22-32         0 or 4         0/62         1/61         1         0.12 (0.00, 0.32           Giao XH         2017         China         28-32         6         0/30         2/30         1         0.19 (0.01, 4.06           Yao ZC         2011         China         28-32         6         0/30         2/30         1         0.19 (0.01, 4.06           Yao ZC         2018         China         28-32         4         0/28         4/30         0.10 (0.01, 2.01           Lin									
Vang HB         2016         China         20-36         NR         0/100         2/20           Vang J         2017         China         24-28         NR         1/329         9/65           Vang TD         2015         China         28         4         0/53         8/52         1         0.05 (0.00, 0.87           Vang WP         2012         China         28         4         0/53         8/52         1         0.05 (0.00, 0.87           Van Q         2015         China         22-32         0 or 4         0/62         1/61         0.07 (0.00, 0.32         0.01 (0.00, 0.32           Jaco LF         2017         China         28         0 or 4         0/62         1/61         1/61         0.32 (0.01, 8.08           Jaco LF         2014         China         28-32         6         0/30         2/30         1         0.19 (0.01, 0.36           Jaco ZC         2011         China         28-32         6         0/30         2/30         1         0.19 (0.01, 0.36           Jaco ZD         China         28-32         4         0/28         4/30         1         0.19 (0.01, 2.01           Jaco ZD         China         24-28         0									
Vang J         2017         China         24-28         NR         1/329         9/65           Vang TD         2015         China         28         4         0/53         8/52         1         0.02 (0.00, 0.15           Vang WP         2012         China         28/7-28         0         0/47         20/198         1         0.09 (0.01, 1.56           Vu Q         2015         China         24-32         0 or 4         0/204         1/4/95         1         0.01 (0.00, 0.23           Giao XH         2017         China         28-32         6         0/30         2/30         1         0.19 (0.01, 4.06           ao LF         2014         China         28-32         6         0/30         2/30         1         0.19 (0.01, 4.06           Hang BF         2018         China         28-32         4         0/28         4/30         1         0.10 (0.01, 2.01           Chang BF         2018         China         28-32         4         0/28         4/30         1         0.10 (0.01, 2.01           Chang BF         2018         China         28         4         0/40         3/40         1         0.10 (0.01, 2.01           Chang BF									
Vang TD         2015         China         28         4         0.53         8/62           Vang WP         2012         China         24-32         0         0/47         20/198         7         0.99 (0.01, 1.54           Viu Q         2015         China         24-32         0 or 4         0/62         1/61         1         0.32 (0.01, 8.08           Jaco LF         2014         China         28-32         6         0/30         2/30         1         1.19 (0.01, 4.06           Aso ZC         2011         China         28-32         6         0/30         2/30         1         0.19 (0.01, 2.01           Hang BF         2018         China         28-32         4         0/28         4/30         1         0.10 (0.01, 2.01           Hang BF         2018         China         28-32         4         0/28         4/30         1         0.10 (0.01, 2.01           Hang BF         2018         China         28-8         4         0/40         3/40         1         0.05 (0.00, 9.22           Hang BF         2018         China         28-30         4         0/257         10/352         1         0.06 (0.00, 1.08           Hang YF									
Wang MP         2012         China         <27-28         0         0.47         20/198         0.09 (0.01, 1.54)           WLO         2015         China         24-32         0 or 4         0/62         1/61         1         0.01 (0.00, 0.32)           Clao XH         2017         China         28         0 or 4         0/62         1/61         1         0.23 (0.01, 8.08)           Gao ZC         2014         China         28-3         4         0/28         4/30         1         0.19 (0.01, 4.06)           Cab ZC         Cull         China         28         4         0/28         4/30         1         0.19 (0.01, 4.06)           Chang GH         China         24-28         0         0/36         15/75         1         0.05 (0.00, 0.92)           Chang GH         China         28         4         0/40         3/40         1         0.13 (0.01, 2.36)           Chang H         2018         China         28         4         0/40         3/40         1         0.13 (0.01, 2.36)           Chang Y         2015         China         28         4         0/25         10/352         1         0.06 (0.00, 1.09           Chang Y         China		2017	Omma	2.20		11020	0,00		
Vu O         2015         China         24-32         0 or 4         0/204         14/95           Giao XH         2017         China         28         0 or 4         0/62         1/61         1         0,32 (0,01,8,08           ao LF         2014         China         28-32         6         0/30         2/30         1         0,19 (0,01,2,01           Abang SP         2018         China         28         4         0/28         4/30         1         0,10 (0,01,2,01           Chang BF         2018         China         28         4         0/40         3/40         1         0,13 (0,01,2,65           Chang H         2014         China         28         4         0/40         3/40         1         0,13 (0,01,2,65           Chang H         2014         China         28-30         4         0/257         10/352         1         0,06 (0,00,1,09           Chang Y         2015         China         28         12         0/48         5/47         1         0,06 (0,00,1,03           Chang Y         2013         China         28         4         1/60         1/60         1         0,06 (0,01,0,36           Cheng JC         2018									0.09 (0.01, 1.54)
Jaco XH         2017         China         28         0 or 4         0/62         1/61         0.22 (0.01, 8.08           3ca LF         2014         China         28-32         6         0/30         2/30         0         19 (0.01, 4.06           3ca CF         2011         China         28-8         4         0/28         4/30         0         0.05 (0.00, 0.32           Leng GH         2018         China         24-28         0         0/36         15/75         0.05 (0.00, 0.32           Lhang GH         2018         China         28         4         0/40         3/40         1         0.13 (0.01, 2.66           Lhang Y         2015         China         28-30         4         0/257         10/352         0.06 (0.00, 1.49           Lhang YF         2015         China         28         12         0/48         5/47         1         0.06 (0.00, 1.49           Lhang YF         2010b         China         28         4         1/60         16/60         1         0.05 (0.1), 0.36           Lhang YF         2013         China         20         0         0/41         23/202         0         0.07 (0.01, 1.35           Lheng JC         2018								<del></del>	0.01 (0.00, 0.23)
ao LF 2014 China 28-32 6 0.30 220 0.19 (0.01, 4.06 a) 0.10 (0.01,								-	0.32 (0.01, 8.08)
Chang BF         2018         China         24-28         0         0,36         15/75         0,50 (0,00, 0,92           Chang GH         2018         China         28         4         0/40         3/40         1         0.13 (0.01, 2.65           Chang Y         2014         China         28         1         0.048 (0.00, 1.09         0.06 (0.00, 1.09           Chang YF         2010b         China         28         1         1/60         16/60         1         0.05 (0.00, 1.48           Chang YF         2010b         China         28         4         1/60         16/60         1         0.05 (0.01, 0.36           Cheang YF         2013         China         28         4         1/60         16/60         1         0.09 (0.01, 1.35           Cheang YF         2013         China         20         0         0/41         23/202         1         0.09 (0.01, 1.35           Cheang YF         2014         China         28         4         0/23         8/37         1         0.07 (0.00, 1.35           Cheang YF         China         1st Trimester         0         1/53         6/34         1         0.09 (0.01, 1.35           Chu Y         2014									0.19 (0.01, 4.06)
Thang GH         2018         China         28         4         0/40         3/40         15         0.13 (0.01; 2.65           Hang Y         2014         China         28-30         4         0/257         10/352         1         0.06 (0.00, 1.09           Hang Y         2015         China         28         12         0/48         5/47         1         0.06 (0.00, 1.09           Labor J         2013         China         28         4         1/60         16/60         1         0.05 (0.01, 0.36           Labor J         2013         China         20         0         0/41         23/202         1         0.09 (0.01, 1.35           Cheng JC         2018         China         28         4         0/23         8/37         1         0.07 (0.00, 1.35           Dou'N J         2014         China         1st Trimester         0         1/53         6/34         1         0.09 (0.01, 0.78           Wu X         2014         China         Anytime         NR         0/31         0.09         1         (Excluded)									0.10 (0.01, 2.01)
Phang H         2014         China         28-30         4         0.0257         10/352         0.06 (0.00, 1.09 thang)           Anang X         2015         China         28         12         0/48         5/47         1         0.06 (0.00, 1.08 thang)           Hang YF         2010b         China         28         4         1/80         18/60         1         0.05 (0.01, 0.38 thang)           Hang YF         2018         China         20         0         0/41         23/202         1         0.09 (0.01, 1.55 thang)           Heng UC         2018         China         2         4         0/23         8/37         1         0.07 (0.00, 1.38 thang)           Hou Y         2014         China         1st Trimester         0         1/53         6/34         1         0.09 (0.01, 0.78 thang)           Year Y         2014         China         Anytime         NR         0/31         0.03         1         (Excluded)								-	0.05 (0.00, 0.92)
Chang X         2015         China         28         12         0/48         5/47         0.08 (0.00, 1.48           Chang YF         2010         China         28         4         1/60         16/60         1         0.05 (0.01, 0.36           Lea J         2013         China         20         0         0/41         23/202         1         0.09 (0.01, 1.55           Cheng JC         2018         China         28         4         0/23         8/37         1         0.07 (0.00, 1.35           Chou Y J         2014         China         1st Trimester         0         1/53         6/34         1         0.09 (0.01, 0.78           Yeu X         2014         China         Anytime         NIR         0/31         0/30         1         (Excluded)								<del></del> _	0.13 (0.01, 2.65)
Phang YF         2010b         China         28         4         1/60         16/60         1         0,05 (0,01), 0.36           Phap J         2013         China         20         0         0/41         23/202         1         0,99 (0,01), 1.35           Cheng JC         2018         China         28         4         0/23         8/37         2         0,07 (0,00), 1.35           Chou Y         2014         China         1st Trimester         0         1/53         6/24         2         0,09 (0,01), 0.78           Viex X         2014         China         Anytime         NR         0/31         0/30         1         (Excluded)								* 1	0.06 (0.00, 1.09)
Chao J     2013     China     20     0     0/41     23/202     0,09 (0,01,1,55       Cheng JC     2018     China     28     4     0/23     8/37     0,07 (0,00,1,35       Chou Y J     2014     China     1st Trimester     0     1/53     6/34     0,09 (0,01,0,78       Ve X     2014     China     Anytime     NR     0/31     0/30     1     (Excluded)									
Theng JC 2018 China 28 4 0/23 8/37 - 0.07 (0.00, 1.35 Chou Y) 2014 China 1st Trimester 0 1/53 6/34 - 0.09 (0.01, 0.78 Chou Y) 2014 China Anytime NR 0/31 0/30 I (Excluded)									
Zhou YJ         2014         China         1 st Trimester         0         1/53         6/34									
/ue X 2014 China Anytime NR 0/31 0/30									
								-	
0.00 (0.00 0.10				Anydine	INT	u/31	U/JU	6	
Overall (I-squared = 0.0%, p = 0.999)								ĭ	0.10 (0.08, 0.13)

Figure 3. Efficacy of earlier versus later initiation of peripartum antiviral prophylaxis in the prevention of MTCT\*



## **Supplementary Appendix**

Efficacy and safety of antiviral prophylaxis during pregnancy to prevent mother-to-child transmission of hepatitis B virus: a systematic review and meta-analysis

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Roger Chou, Marc Bulterys, Yusuke Shimakawa

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TDF 300 mg	254
LAM 100-150 mg	
LdT 600 mg	

## **Appendix A: Search strategies**

Database: PubMed

Date searched: March 28<sup>th</sup>, 2019

Item	Search words	#
		Records
1	"hepatitis b" [MeSH] OR "hepatitis b virus" [MeSH]	63 464
2	hepatitis b[Text] OR type b hepatitis[Text] OR hepatitis type b[Text] OR hbv[Text] OR vhb[Text] OR hep b[Text] OR hbsag[Text] OR hbs antigen*[Text]	98 948
3	1 OR 2	98 948
4	"antiviral agents" [MeSH] OR "nucleosides" [MeSH] OR "nucleotides" [MeSH] OR "adefovir" [Supplementary Concept] OR "emtricitabine" [MeSH] OR "entecavir" [Supplementary Concept] OR "lamivudine" [MeSH] OR "telbivudine" [MeSH] OR "tenofovir" [MeSH]	822 520
5	antiviral*[Text] OR nucleoside*[Text] OR nucleotide*[Text] OR (nucleos*[Text] AND analog*[Text]) OR (nucleot*[Text] AND analog*[Text]) OR NA[Text] OR adefovir[Text] OR hepsera[Text] OR preveon[Text] OR bis- POM PMEA[Text] OR GS 840[Text] OR ADV[Text] OR emtricitabine[Text] OR emtriva[Text] OR FTC[Text] OR entecavir[Text] OR baraclude[Text] OR ETV[Text] OR lamivudine[Text] OR epivir[Text] OR 3TC[Text] OR telbivudine[Text] OR sebivo[Text] OR tyzeka[Text] OR LdT[Text] OR tenofovir[Text] OR viread[Text] OR TDF[Text] OR vemlidy[Text] OR TAF[Text]	755 458
6	4 OR 5	1 335 890
7	"pregnancy" [MeSH] OR "pregnant women" [MeSH] OR "maternal-fetal relations" [MeSH] OR "infectious disease transmission, vertical" [MeSH] OR "pregnancy complications, infectious" [MeSH] OR "prenatal diagnosis" [MeSH]	870 293
8	pregnan*[Text] OR trimest*[Text] OR gestation*[Text] OR antepartum[Text] OR ante-partum[Text] OR prepartum[Text] OR pre-partum[Text] OR intrapartum[Text] OR intra-partum[Text] OR peripartum[Text] OR peri-partum[Text] OR	1 793 242

	antenatal*[Text] OR ante-natal*[Text] OR prenatal*[Text]	
	OR pre-natal*[Text] OR perinatal*[Text] OR peri-	
	natal*[Text] OR intrauterine[Text] OR intra-uterine[Text]	
	OR inutero[Text] OR in utero[Text] OR	
	transplacental*[Text] OR placenta*[Text] OR	
	vertical*[Text] OR congenital*[Text] OR mother*[Text] OR	
	matern*[Text] OR fetomaternal*[Text] OR	
	foetomaternal*[Text] OR fetal*[Text] OR foetal*[Text] OR	
	fetus[Text] OR foetus[Text] OR offspring[Text] OR	
	MTCT[Text] OR TME[Text]	
9	7 OR 8	1 803
		794
10	3 AND 6 AND 9	1004

Database: Embase Classic + Embase via OvidSP (1947-2019 March 26th)

Date searched: March 28<sup>th</sup> 2019

Item	Search words	#
1	1 di PAOR II di P	Records
1	exp hepatitis B/ OR exp Hepatitis B virus/	120 132
2	(hepatitis b OR type b hepatitis OR hepatitis type b OR hbv	158 928
	OR vhb OR hep b OR hbsag OR hbs ag OR hbs	
	antigen*).mp.	1.70.020
3	1 OR 2	158 928
4	exp antiviral therapy/ OR exp antivirus agent/ OR exp	1 657
	nucleoside/ OR exp nucleotide/ OR exp adefovir/ OR exp	284
	adefovir dipivoxil/ OR exp emtricitabine/ OR exp entecavir/	
	OR exp lamivudine/ OR exp telbivudine/ OR exp tenofovir/	
	OR exp tenofovir disoproxil/ OR exp tenofovir alafenamide/	
5	(antiviral* OR nucleoside* OR nucleotide* OR (nucleos*	1 421
	AND analog*) OR (nucleot* AND analog*) OR NA OR	448
	adefovir OR hepsera OR preveon OR bis-POM PMEA OR	
	GS 840 OR ADV OR emtricitabine OR emtriva OR FTC	
	OR entecavir OR baraclude OR ETV OR lamivudine OR	
	epivir OR 3TC OR telbivudine OR sebivo OR tyzeka OR	
	LdT OR tenofovir OR viread OR TDF OR vemlidy OR	
	TAF).mp.	
6	4 OR 5	2 708
		549
7	exp pregnancy/ OR exp pregnant women/ OR exp mother	807 598
	fetus relationship/ OR exp vertical transmission/ OR exp	
	pregnancy complication/ OR exp prenatal diagnosis/	
8	(pregnan* OR trimest* OR gestation* OR antepartum OR	2 268
	ante-partum OR prepartum OR pre-partum OR intrapartum	793
	OR intra-partum OR peripartum OR peri-partum OR	
	antenatal* OR ante-natal* OR prenatal* OR pre-natal* OR	
	perinatal* OR peri-natal* OR intrauterine OR intra-uterine	
	OR inutero OR in utero OR transplacental* OR placenta*	
	OR vertical* OR congenital* OR mother* OR matern* OR	
	fetomaternal* OR foetomaternal* OR fetal* OR foetal* OR	
	fetus OR foetus OR offspring OR MTCT OR TME).mp.	
9	7 OR 8	2 274
		006
10	3 AND 6 AND 9	3 069

Database: Scopus

Date searched: March 28<sup>th</sup> 2019

Item	Search words	#
		Records
1	TITLE-ABS-KEY ("hepatitis b" OR "type b hepatitis" OR	138 899
	"hepatitis type b" OR "hbv" OR "vhb" OR "hep b" OR	
	"hbsag" OR "hbs ag" OR "hbs antigen*")	
2	TITLE-ABS-KEY ("antiviral*" OR "nucleoside*" OR	1 781
	"nucleotide*" OR ("nucleos*" AND "analog*") OR	759
	("nucleot*" AND "analog*") OR "NA" OR "adefovir" OR	
	"hepsera" OR "preveon" OR "bis-POM PMEA" OR "GS	
	840" OR "ADV" OR "emtricitabine" OR "emtriva" OR	
	"FTC" OR "entecavir" OR "baraclude" OR "ETV" OR	
	"lamivudine" OR "epivir" OR "3TC" OR "telbivudine" OR	
	"sebivo" OR "tyzeka" OR "LdT" OR "tenofovir" OR	
	"viread" OR "TDF" OR "vemlidy" OR "TAF")	
3	TITLE-ABS-KEY ("pregnan*" OR "trimest*" OR	2 892
	"gestation*" OR "antepartum" OR "ante-partum" OR	112
	"prepartum" OR "pre-partum" OR "intrapartum" OR "intra-	
	partum" OR "peripartum" OR "peri-partum" OR	
	"antenatal*" OR "ante-natal*" OR "prenatal*" OR "pre-	
	natal*" OR "perinatal*" OR "peri-natal*" OR "intrauterine"	
	OR "intra-uterine" OR "inutero" OR "in utero" OR	
	"transplacental*" OR "placenta*" OR "vertical*" OR	
	"congenital*" OR "mother*" OR "matern*" OR	
	"fetomaternal*" OR "foetomaternal*" OR "fetal*" OR	
	"foetal*" OR "fetus" OR "foetus" OR "offspring" OR	
	"MTCT" OR "TME")	
4	#1 AND #2 AND #3	1 810

Database: CENTRAL Database (The Cochrane Library)

Date searched: March 28<sup>th</sup> 2019

Item	Search words	# Trials and
		Reviews
1	hepatitis b [MeSH, exp] OR hepatitis b virus [MeSH, exp]	2 462
2	"hepatitis b" OR "type b hepatitis" OR "hepatitis type b" OR hbv OR vhb OR "hep b" OR hbsag OR "hbs ag" OR "hbs antigen" OR "hbs antigens"	7 692
3	1 OR 2	7 692
4	antiviral agents [MeSH, exp] OR nucleosides [MeSH, exp] OR nucleotides [MeSH, exp] OR emtricitabine [MeSH, exp] OR lamivudine [MeSH, exp] OR telbivudine [MeSH, exp] OR tenofovir [MeSH, exp]	17 552
5	antiviral* OR nucleoside* OR nucleotide* OR (nucleos* AND analog*) OR (nucleot* AND analog*) OR NA OR adefovir OR hepsera OR preveon OR "bis-POM PMEA" OR "GS 840" OR ADV OR emtricitabine OR emtriva OR FTC OR entecavir OR baraclude OR ETV OR lamivudine OR epivir OR 3TC OR telbivudine OR sebivo OR tyzeka OR LdT OR tenofovir OR viread OR TDF OR vemlidy OR TAF	34 424
6	4 OR 5	44 913
7	pregnancy [MeSH, exp] OR pregnant women [MeSH, exp] OR maternal-fetal relations [MeSH, exp] OR infectious disease transmission, vertical [MeSH, exp] OR pregnancy complications, infectious [MeSH, exp] OR prenatal diagnosis [MeSH, exp]	8 802
8	pregnan* OR trimest* OR gestation* OR antepartum OR ante-partum OR prepartum OR pre-partum OR intrapartum OR intra-partum OR peripartum OR peri-partum OR antenatal* OR ante-natal* OR prenatal* OR pre-natal* OR perinatal* OR peri-natal* OR intrauterine OR intra-uterine OR inutero OR "in utero" OR transplacental* OR placenta* OR vertical* OR congenital* OR mother* OR matern* OR fetomaternal* OR foetomaternal* OR fetal* OR	74 080

	foetal* OR fetus OR foetus OR offspring* OR MTCT OR TME	
9	7 OR 8	74 912
10	3 AND 6 AND 9	246

Database: CNKI

Date searched: March 28<sup>th</sup>, 2019

Search Strategy:

SU='乙型肝炎'+'乙肝'+'乙型肝炎病毒'+'乙肝病毒'+'HBV'+'乙型肝炎表面抗原'+'乙 肝表面抗原' AND SU='抗病毒'+'抗病毒药物'+'核苷'+'核苷酸'+'核苷类**似物**'+'核苷酸 类似物'+'NAs'+'阿德福韦酯'+'hepsera'+'preveon'+'bis-POM PMEA'+'GS 840'+'ADV'+' 恩曲他滨'+'emtriva'+'FTC'+' 恩替卡韦'+'baraclude'+'ETV'+' 拉米夫定 '+'epivir'+'3TC'+'LAM'+' 替 比 夫 定 '+'sebivo'+'tyzeka'+'LdT'+' 替 诺 福 韦 酯 '+'viread'+'TDF'+'替诺福韦艾拉酚胺'+'vemlidy'+'TAF' AND SU='妊娠'+'怀孕'+'孕妇'+' 孕期'+'母胎'+'母亲'+'胎儿'+'子代'+'子女'+'垂直传播'+'产**前**'+'产时'+'产间'+'围产'+'出 生前'+'围生'+'宫内'+'跨胎盘'+'胎盘'+'母婴传播'+'预防母婴传播'+'阻断母婴传播'+'妊

娠并发**症**'+'产**前**诊**断**'+'先天'

Database: Wanfang

**症**"+"产**前**诊**断**"+"先天")

Date searched: March 28<sup>th</sup>, 2019

Search Strategy:

主题: ("乙型肝炎"+"乙肝"+"乙型肝炎病毒"+"乙肝病毒"+"HBV"+"乙型肝炎表面抗 原"+"乙肝表面抗原") and 主题: ("抗病毒"+"抗病毒药物"+"核苷"+"核苷酸"+"核苷类 似物 "+" 核 苷 酸 类 似物 "+"NAs"+" 阿 德 福 韦 酯 "+"hepsera"+"preveon"+"bis-POM PMEA"+"GS 840"+"ADV"+" 恩 曲 他 滨 "+"emtriva"+"FTC"+" 恩 替 卡 韦 "+"baraclude"+"ETV"+" 拉 米 夫 定 "+"epivir"+"3TC"+"LAM"+" 替 比 夫 定 "+"sebivo"+"tyzeka"+"LdT"+" 替诺福韦酯"+"viread"+"TDF"+" 替诺福韦艾拉酚胺 "+"vemlidy"+"TAF") and 主题: ("妊娠"+"怀孕"+"孕妇"+"孕期"+"母胎"+"母亲"+"胎 儿"+"子代"+"子女"+"垂直传播"+"产前"+"产时"+"产间"+"围产"+"出生前"+"围**生**"+" 宫内"+"跨胎盘"+"胎盘"+"母婴传播"+"预防母婴传播"+"阻断母婴传播"+"妊娠并发

#### Appendix B: List of variables present on data extraction tool

#### 1. Publication details

- First author
- Year
- Journal
- Language

#### 2. Methods

- Country
- Study design
- Purpose of study
- Recruitment period
- Recruitment setting (regional details, number of sites)
- Inclusion criteria
- Exclusion criteria
- Intervention arm treatment including birth dose vaccination and/or HBIg administration if relevant
- Intervention Treatment schedule (including birth dose vaccination and/or HBIg administration if relevant) and timing (including hours since birth for birth dose/HBIg)
- Control arm treatment
- Control arm treatment schedule and timing
- Infant treatment 1. Birth dose vaccination (dose, manufacturer)
- Infant treatment 1. Birth dose vaccination (detail the number of hours since birth)
- Infant treatment 2. HBIg (dose, manufacturer)
- Infant treatment 2. HBIg (detail the number of hours since birth)
- Infant treatment 3. Non-birth dose vaccination (dose, manufacturer)
- Infant treatment 3. Non-birth dose vaccination (schedule)
- Infant treatment 4. Any other treatment (e.g., antiviral therapy in infants)
- Follow-up schedule (mothers)
- Follow-up schedule (infants)

#### 3. Number (No.) of participants at enrolment

- No. of women assessed for eligibility
- No. of women who underwent randomization (or included if non-randomized)

#### 4. Women's characteristics in Treatment arm

- Treatment arm: No. of women assigned to treatment (or included if non-randomized)
- Treatment arm: No. of women with baseline characteristics reported
- Treatment arm: Mean treatment duration
- Treatment arm: Mean or median age
- Treatment arm: No. by ethnicity
- Treatment arm: No. positive for HBeAg
- Treatment arm: HBV DNA threshold used (IU/ml or copies/ml)
- Treatment arm: Mean or median HBV DNA

- Treatment arm: No. HDV positive
- Treatment arm: No. HCV positive
- Treatment arm: No. HIV positive
- Treatment arm: No. loss to F/U or regimen change

#### 5. Women's characteristics in control arm

- Control arm: No. of women assigned to control (or included if non-randomized)
- Control arm: No. of women with baseline characteristics reported
- Control arm: Mean treatment duration
- Control arm: Mean or median age
- Control arm: No. by ethnicity
- Control arm: No. positive for HBeAg
- Control arm: HBV DNA threshold used (IU/ml or copies/ml)
- Control arm: Mean or median HBV DNA
- Control arm: No. HDV positive
- Control arm: No. HCV positive
- Control arm: No. HIV positive
- Control arm: No. loss to F/U or regimen change

#### 6. Infant outcomes at birth in treatment arm

- No. of infants in treatment arm at birth
- Treatment arm: No. of twins
- Treatment arm: No. of triplets
- Treatment arm: mean gestational age at birth (weeks)
- Treatment arm: mean birthweight (kg)
- Treatment arm: No. male
- Treatment arm: No. by each type of delivery (vaginal or caesarean)
- Treatment arm: No. of infants eventually assessed for all MTCT/ adverse event outcomes

#### 7. Infant outcomes at birth in control arm

- No. of infants in control arm at birth
- Control arm: No. of twins
- Control arm: No. of triplets
- Control arm: mean gestational age at birth (weeks)
- Control arm: mean birthweight (kg)
- Control arm: No. of male
- Control arm: No. by each type of delivery (vaginal or caesarean)
- Control arm: No. of infants eventually assessed for all MTCT/ adverse event outcomes

#### 8. MTCT definition

- MTCT definition used
- HBsAg assay method used to define MTCT
- HBV DNA assay method used to define MTCT
- Exact timing of 6-12 months assessment to define MTCT

#### 9. MTCT (intention-to-treat) in treatment arm

• Intention-to-treat or modified intention-to-treat definition used

- Denominator for intention-to-treat analysis: mothers assigned to intervention + twin/triplet
- No. of infants completed MTCT evaluation at 6-12 month timepoint
- No. of infants with HBsAg at 6-12 months (list by maternal HBeAg, HBV DNA, HDV, HIV, where possible)
- No. of infants with HBV DNA at 6-12 months (list by maternal HBeAg, HBV DNA, HDV, HIV, where possible)
- Intention-to-treat MTCT risk (defined by HBsAg)
- Intention-to-treat MTCT risk (defined by HBV DNA)

#### 10. MTCT (per protocol) in treatment arm

- Denominator for per-protocol analysis: mother-infant pairs completed the intervention treatment & completed MTCT evaluation at 6-12 months timepoint
- No. of infants with HBsAg at 6-12 months in mother-infant pairs completed the intervention treatment & completed MTCT evaluation at 6-12 months timepoint (list by maternal HBeAg, HBV DNA, HDV, HIV, where possible)
- No. of infants with HBV DNA at 6-12 months in mother-infant pairs completed the intervention treatment & completed MTCT evaluation at 6-12 months timepoint (list by maternal HBeAg, HBV DNA, HDV, HIV, where possible)
- Per-protocol MTCT risk (defined by HBsAg)
- Per-protocol MTCT risk (defined by HBV DNA)

#### 11. MTCT (intention-to-treat) in control arm

- Denominator for intention-to-treat analysis: mothers assigned to control + twin/triplet
- No. of infants completed MTCT evaluation at 6-12 month timepoint
- No. of infants with HBsAg at 6-12 months (list by maternal HBeAg, HBV DNA, HDV, HIV, where possible)
- No. of infants with HBV DNA at 6-12 months (list by maternal HBeAg, HBV DNA, HDV, HIV, where possible)
- Intention-to-treat MTCT risk (defined by HBsAg)
- Intention-to-treat MTCT risk (defined by HBV DNA)

#### 12. MTCT (per protocol) in control arm

- Denominator for per-protocol analysis: mother-infant pairs completed the control treatment & completed MTCT evaluation at 6-12 months timepoint
- No. of infants with HBsAg at 6-12 months in mother-infant pairs completed the control treatment & completed MTCT evaluation at 6-12 months timepoint (list by maternal HBeAg, HBV DNA, HDV, HIV, where possible)
- No. of infants with HBV DNA at 6-12 months in mother-infant pairs completed the control treatment & completed MTCT evaluation at 6-12 months timepoint (list by maternal HBeAg, HBV DNA, HDV, HIV, where possible)
- Per-protocol MTCT risk (defined by HBsAg)
- Per-protocol MTCT risk (defined by HBV DNA)

# 13. No. of infant adverse events in treatment arm (list by maternal HBeAg, HBV DNA, HDV, HIV, where possible)

- Treatment arm: Foetal death
- Treatment arm: Neonatal death (within 28 days)

- Treatment arm: Prematurity (give definition used)
- Treatment arm: Congenital abnormalities #
- Treatment arm: Congenital abnormalities: describe
- Treatment arm: Appar score at 1 minute is <10
- Treatment arm: Sub-optimal bone density (give definition and the age at evaluation)
- Treatment arm: Any other event

## 14. No. of infant adverse events in control arm (list by maternal HBeAg, HBV DNA, HDV, HIV, where possible)

- Control arm: Foetal death
- Control arm: Neonatal death (within 28 days)
- Control arm: Prematurity (give definition used)
- Control arm: Congenital abnormalities #
- Control arm: Congenital abnormalities: describe
- Control arm: Apgar score at 1 minute is <10
- Control arm: Sub-optimal bone density (give definition and the age at evaluation)
- Control arm: Any other event

#### 15. Hepatitis flare

• Definition of hepatitis flare used

# 16. No. of maternal adverse events in treatment arm (list by maternal HBeAg, HBV DNA, HDV, HIV, status where possible)

- Treatment arm: No. of women considered for adverse events
- Treatment arm: Foetal death or stillbirth
- Treatment arm: Hepatitis flare after treatment discontinuation
- Treatment arm: Postpartum hemorrhage
- Treatment arm: Antiviral resistance
- Treatment arm: Any other event

# 17. No. of maternal adverse events in control arm (list by maternal HBeAg, HBV DNA, HDV, HIV, status where possible)

- Control arm: No. of women considered for adverse events
- Control arm: Foetal death or stillbirth
- Control arm: Hepatitis flare after during a matched period
- Control arm: Postpartum hemorrhage
- Control arm: Antiviral resistance
- Control arm: Any other event

#### 18. Other

- Summary of study conclusions
- Funding by industry

## **Appendix C: Risk of bias assessment tools**

### Guidance - Cochrane Collaboration's risk of bias assessment tool

### (Table taken directly Higgins JPT et al., 2011)

	Source of bias	Description	Review author's judgment
Bias Domain		•	Assess as low, unclear or high risk of bias
	Sequence	Describe the method used to generate	Selection bias (biased allocation
Selection bias	generation.	the allocation sequence in sufficient	to interventions) due to
	· ·	detail to allow an assessment of	inadequate generation of a
		whether it should produce comparable	randomized sequence
		groups	
	Allocation	Describe the method used to conceal	Selection bias (biased allocation
	concealment.	the allocation sequence in sufficient detail to determine whether	to interventions) due to
		detail to determine whether intervention allocations could have	inadequate concealment of allocations before assignment
		been foreseen before or during	anocations before assignment
		enrolment	
	Blinding of	Describe all measures used, if any, to	Performance bias due to
Performance	participants,	blind trial participants and researchers	knowledge of the allocated
bias	personnel and	from knowledge of which intervention	interventions by participants and
	outcome assessors.	a participant received. Provide any	personnel during the study
	Assessments should be made for each	information relating to whether the intended blinding was effective	
	main outcome (or	intended biniding was effective	
	class of outcomes).		
		Describe all measures used, if any, to	Detection bias due to knowledge
Detection bias	Blinding of outcome	blind outcome assessment from	of the allocated interventions by
	assessment.	knowledge of which intervention a	outcome assessment
	Assessments should	participant received. Provide any	
	be made for each main outcome (or	information relating to whether the	
	class of outcomes).	intended blinding was effective	
	Incomplete outcome	Describe the completeness of outcome	Attrition bias due to amount,
Attrition bias	data. Assessments	data for each main outcome, including	nature, or handling of incomplete
	should be made for	attrition and exclusions from the	outcome data
	each main outcome	analysis. State whether attrition and	
	(or class of	exclusions were reported, the numbers	
	outcomes).	in each intervention group (compared with total randomized participants),	
		reasons for attrition or exclusions	
		where reported, and any reinclusions	
		in analyses for the review	
	Selective outcome	State how the possibility of selective	Reporting bias due to selective
Reporting bias	reporting.	outcome reporting was examined by	outcome reporting
DIAS		the review authors, and what was found.	
	Other sources of	State any important concerns about	Bias due to problems not covered
Other bias	bias.	bias not addressed in the other	elsewhere
		domains in the tool. If particular	
		questions/entries were pre-specified in	
		the review's protocol, responses	
		should be provided for each	
		question/entry.	

Notes for filling out the table (adapted/made specific for this systematic review and meta-analysis from the *Cochrane Handbook 2008* and from *Higgins JPT et al.*, 2011):

- Within the table, summary descriptions should be provided in order to give an independent reader enough information to see why the specific judgment has been made. For example, if no information on sequence generation can be found in the article or correspondence with the author, you could enter "Comment: no information provided". If it states that patients were randomly allocated in the article, then you could copy out the phrase directly from the article, e.g. "Quote: "patients were randomly allocated". In any case, if you have doubts in whether or not the study actually did certain things that are mentioned in the article, please include an extra comment describing concern/contradiction in the article.
- When providing your judgment as a review author, indicate 'low risk' of bias, and 'high risk' of bias. If insufficient information is provided, then the judgment should be 'unclear' risk of bias.
  - See table 8.5c on pages 198-202 in the 2008 Cochrane Handbook for Systematic Reviews of Intervention (pages 223-227 of the PDF) for specific guidance on how to make your judgment.

#### Guidance - Newcastle - Ottawa Quality Assessment Scale for Cohort Studies

#### (Adapted to the systematic review questions)

<u>Note</u>: The below has been adapted for this specific meta-analysis from the guidance found on the Newcastle-Ottawa quality assessment group website (http://www.ohri.ca/programs/clinical\_epidemiology/oxford.asp). A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability

#### **SELECTION**

#### 1) Representativeness of the exposed cohort (0 or 1 star)

- a) Truly representative of the average HBV infected pregnant women in the community \*\*
  - Women identified to carry HBsAg at a general antenatal care clinic or general practitioner with or without subsequently referral to the specialist obstetric care centre or hepatologist or infectious disease specialist
  - Not part of a special group (e.g. all with recent treatment for hepatocellular carcinoma) then we might assume they reflect/are representative of HBV infected pregnant women in that community.
- b) Somewhat representative of the average HBV infected pregnant women in the community \*\*
  - e.g., women known to be chronically infected with HBV and have been followed by hepatologist or infectious disease specialist
  - c) Selected group of users
    - eg. Women with severe liver disease (cirrhosis or hepatocellular carcinoma) only, part of a special group (HIV-infected women, intravenous drug users (IVDU)), women working in study centres/hospitals, etc
    - Please provide a comment if you believe that the exposed group does not match well the general community
  - d) No description of the derivation of the cohort

#### 2) Selection of the non-exposed cohort (0 or 1 star)

- a) Drawn from the same community as the exposed cohort ★
  - Women presenting at the hospital, pregnant and with HBV (not, most of our studies should fall here in this review)
- b) Drawn from a different source
  - e.g. controls drawn from a historical sample
  - Please make a comment if you believe that the controls have been drawn from a different source
- c) No description of the derivation of the non exposed cohort

#### 3) Ascertainment of exposure (exposure = treatment) (0 or 1 star)

- a) Valid method was used to ascertain adherence to the antiviral therapy★
  - Ideally with some mention of methods to ascertain maternal adherence to treatment (e.g., evaluation of pill count, immunoassay to detect serum/urine

metabolite of antiviral agents, or decrease in viral load levels subsequent to the treatment)

- b) Based on a secure record about adherence ★
  - Study staff have recorded good adherence to treatment based on self-report
  - Description on the treatment duration supports the confirmation of adherence by study staff.
- c) Data collection through registry
  - Care must be taken for a study based on registry data; having started antiviral during pregnancy does not necessarily guarantee that the women adhered to the treatment throughout the intended period.
- d) No description

# 4) <u>Demonstration that outcome of interest was not present at start of study (0 or 1 star)</u>

- a) Yes \*
  - This will always be yes in our case... for this study topic as the outcome of interest is HBV status in infants and infants are born during the course of the study
- b) no

#### **COMPARABILITY**

#### 1) Comparability of cohorts on the basis of the design or analysis (0 or 1 or 2 star(s))

- a) Study controls/is comparable for both HBV DNA level (within 1 log IU/ml) and HBeAg sero-status (within 10 % points)★
  - The same threshold for HBV DNA level AND same HbeAg sero-status should be used for inclusion of treated and controls and/or the reported mean/median HBV DNA level and HbeAg sero-prevalence at baseline should be reported and should be similar.
  - If not reported threshold or not reported mean/median and/or not similar then no star. If only one is reported/similar and the other not, then no star.
- b) Study controls for child immunoprophylaxis at birth (birth dose vaccination, HBIG at birth) ★
  - All have or all don't have or similar proportions across exposed and unexposed group with a similar timeliness. If not reported at all or very different proportions then no star.

#### **OUTCOME**

#### 1) Assessment of outcome (0 or 1 star)

- a) Independent blind assessment \*
  - Examiner of infant outcome (e.g., laboratory staff) was blinded to the maternal exposure status.

- b) Medical records related to outcome were seen and verified by study personnel, or there was record linkage★
  - In the case where testing is done as part of the study, and it is indicated that the same laboratory assays were used to test all infants, then it will be assumed that there was direct verification of test results by study personnel using these medical records.
  - c) No description
    - If there is no description of laboratory methods (specifically, specifying which assay was used or indicating that all testing was done by study personnel or records were sent to study personnel) then no star will be given.

#### 2) Was follow-up long enough for outcomes to occur (0 or 1 star)

- a) Yes (at 6-12 months) \*
  - Because we have defined our inclusion criteria for the review as testing needing to be done between 6 and 12 months, all of our studies should fall here.
- b) No
  - This should not be the case for any of our studies. Please provide a detailed comment if you think it is the case.

#### 3) Adequacy of follow up of cohorts (0 or 1 star)

- a) Complete follow up all subjects accounted for and lost to follow-up reported clearly as 0  $\bigstar$
- b) Subjects lost to follow up unlikely to introduce bias small number lost > 80 % (or description provided of those lost) ★
  - c) Follow up rate < 80 % (select an adequate %) and no description of those lost
  - d) No statement about LFU
    - If not reporting any LFU, and also not mentioning clearly that 'There were no cases 'LFU' then we should assume that LFU was not well reported, and this should not be given a star.

# Appendix D: Descriptions of other antiviral therapies included (<3 studies per regimen)

Telbivudine (LdT) 100 mg

Three studies were eligible for this meta-analysis that used telbivudine (LdT) 100 mg (Ge JQ et al., 2015; Li ZG et al., 2015; Mu YSJ et al., 2018). Of these, one was an RCT and two were non-RCTs. Of the non-RCTs, the risk of bias scores, according to the Newcastle-Ottawa scale, were 5 (high) and 6 (high), respectively (Mu YSJ et al., 2018; Ge JQ et al., 2015); as per protocol, studies with high risk of bias with scores of 5 or lower were excluded from analysis. Therefore, we describe only the basic details of two studies (one RCT and one non-RCT) here.

One RCT was performed that examined use of LdT 100 mg during pregnancy for the PMTCT of HBV (*Li ZG et al., 2015*). This study took place in China from 2013 to 2014. Treatment was started at 28 weeks of pregnancy, and stopped after 6 weeks postpartum. Birth dose vaccination and HBIg were given to all infants on the first day of life, and two further vaccinations were performed at 1 and 6 months of life. Of 25 infants whose mothers were treated during pregnancy, none were positive for HBsAg at 1 year of life, compared to 4 of 25 control infants at the same timepoint (OR=0.09, 95%CI: 0.01-1.84). Infant and maternal adverse events were not well described in the article.

One non-RCT, specifically, a retrospective cohort study, was performed that examined use of LdT 100 mg during pregnancy for the PMTCT of HBV (*Ge JQ et al.*, 2015). This study took place in China from 2012 to 2013. Treatment was started between 28 and 32 weeks of pregnancy, and stopped after 6 weeks postpartum. Birth dose vaccination and HBIg were given to all infants within 12 hours of life, and two further vaccinations were performed at 1 and 6 months of life. Of 40 infants whose mothers were treated during pregnancy, one was positive for HBsAg at 12 months of life, compared to 11 of 40 control infants at the same timepoint (OR=0.07, 95%CI: 0.01-0.55). Most infant and maternal adverse events were not addressed in the article; however, authors did confirm that there were no congenital abnormalities in either the treated or control group at the time of birth.

#### Adefovir (ADV) 500 mg

One RCT was performed that examined use of ADV 500 mg during pregnancy for the PMTCT of HBV (*Feng Y et al.*, 2018). This study took place in China in 2017. Treatment was started at 28 weeks of pregnancy, and stopped at the time of delivery. HBIg was given within 24 hours of life, a vaccination was given at '0 months', and two further vaccinations were performed at 1 and 6 months of life. Of 258 mothers treated during pregnancy, 254 infants were evaluated for MTCT, 6 were positive for HBsAg at 1 year of life, compared to 24 of 251 control infants at the same timepoint (OR=0.23, 95%CI: 0.09-0.57). Infant adverse events were not well described in the article. Of maternal adverse events, the authors did report that 5.4% (95%CI: 3.0-8.9) of women in the treated arm had postpartum hemorrhage, whereas this was 10.1% (95%CI: 6.7-14.4) in the control group.

#### Adefovir (ADV) 10 mg

One non-RCT, specifically, a prospective cohort study, was performed that examined use of ADV 10 mg during pregnancy for the PMTCT of HBV (*Fang HS et al.*, 2011). This study took place in China from 2006 to 2008. Treatment with ADV was started prior to pregnancy in all women (end time not reported), and additionally, HBIg was given to women in both the treatment and control groups at 28, 32, and 36 weeks of gestation. Birth dose vaccination was done (timing unclear), and two further vaccinations were performed at 1 and 6 months of life. There was no mention of administration of HBIg to infants in the article. Of 42 infants whose mothers were treated during pregnancy, none were positive for HBsAg at 12 months of life, compared to 5 of 52 control infants at the same timepoint (OR=0.10, 95%CI: 0.01-1.89). Most infant and maternal adverse events were not addressed in the article; however, authors did confirm that there were no congenital abnormalities or cases of prematurity in either the treated or control group at the time of birth.

# Appendix E: Characteristics of the included studies by treatment type

### Aggregate study characteristics

Treatme nt	# Studi es	Study countries (% studies)	Study design (% studies)	Time perio d	# Pregnant women included (treated/no t treated)	HBeAg # studies/ total studies	Range of mean viral load at baseline (# studies reporting )	Range of treatme nt start times	Range of treatme nt disconti n-uation times	# Infants assessed (of mothers treated/ untreated)	Infants prophylax is # studies/ total studies
TDF 300 mg	19	Australia (5.3) China (73.7) Japan (5.3) Taiwan (5.3) Thailand (5.3) Turkey (5.3)	RCT= 5 (26.3) non- RCT= 14 (73.7)	2010- 2018	1974 (1092/882 )	All positive: 11/19 All negative: 0/19 Mixed: 1/19 NR: 7/19	3.6 - 8.3 log10 IU/mL (n=16)	Pre- pregnanc y to 36 weeks gestation	0 to 12 weeks post partum	1908 (1072/836 )	HBIG, Hep-B- BD, infant vaccines: 16/19
LAM 100-150 mg	40	Australia (2.5) China <sup>b</sup> (88.8) Egypt (2.5) Ireland (2.5) Japan	RCT= 8 (20.0) non- RCT= 32	2001- 2016	4200 (2080/212 0)	All positive: 30/40 All negative: 0/40 Mixed: 4/40 NR: 6/40	6.0 - 8.7 log10 IU/mL (n=26)	Pre- pregnanc y to 34 weeks gestation	0 to 12 weeks post partum <sup>e</sup>	4051 (2007/204 4)	HBIG, Hep-B- BD, infant vaccines: 34/40

		(2.5) Phillipines <sup>b</sup> (1.3)	(80.0)								
LdT 600 mg	83	China (100.0)	RCT= 21 (25.3) non- RCT= 62 (74.7)	2001- 2016	12104 (6036/606 8)	All positive: 52/83 All negative: 1/83 Mixed: 6/83 NR: 24/83	2.0- 8.3 log10 IU/mL (n=73)	Pre- pregnanc y to 36 weeks gestation	0 to 36 weeks post partum	11768 (5971/579 7)	HBIG, Hep-B- BD, infant vaccines: 78/83

**Note:** All percentages use as a denominator the total number of women/infants included/assessed studies with details reported. <sup>a</sup>In order to be considered as having 'full' prophylaxis, the study report needed to have mentioned clearly that infants were given all of HBIG at birth, HepB-BD, and subsequent HBV vaccinations in infancy. <sup>b</sup>One study took place in China and the Philippines – each have been counted as half for each country in this cell. <sup>c</sup>One study administered treatment 'anytime' which may have extended past 34 weeks gestation. <sup>d</sup>Two studies administered treatment 'anytime' which may have extended past 36 weeks gestation. <sup>e</sup>One study 'continued' treatment past 12 weeks for various and possibly indefinite periods for study participants.

### Individual study characteristics

Gener	al study de	etails and d	lesign			Treate	d pregnant v	vomen (t	x)			Untreated p	regnant	women (con	trol)	Infant in	nmunopropl infants)	nylaxis (all
Author, year	Country	Recruit- ment period	Criteria for maternal HBV DNA (log IU/mL)	#	Treatme (gestatio / Trea disconti (postp wee	n weeks) tment nuation artum	Mean/ median age (years)	HBeAg (%)	Mean/ median HBV DNA at baseline (log IU/mL)	# Infants assessed for MTCT	#	Mean/ median age (years)	HBeAg (%)	Mean/ median HBV DNA at baseline (log IU/mL)	# Infants assessed for MTCT	HBIG at birth, timing	HepB-BD,	Infant vaccine, dose 1 /dose 2 in months
									TDF	300 mg								
	T	T	1				T	Rando	mized con	trolled trials (	RCT)			T.	T	1	T	
Jourdain G, 2018 <sup>14</sup> , 15, 23	Thailand	2013- 2015	None	168	26-29	8	25.5 [18.3- 42.2]	100	7.6	149	163	26.7 [18.4- 40.9]	100	7.3	147	Yes, <3hr	Yes, <3hr	Yes, 1/2/4/6
Lin Y, 2018 <sup>24,25</sup>	China	2013- 2016	≥6.3	60	24	4	28.3 ±3.6	100	7.4	58	60	28.1 ±3.4	100	7.7	52	Yes, <24hr	Yes, 12hr	Yes, 1/6
Liu MH, 2017 <sup>26</sup>	China	2014- 2016	≥5.3	20	28-30	0	30 [22-38]	100	6.5	20	20	29 [21-38]	100	6.5	20	Yes, <24hr	Yes, <24hr	Yes, 1/6
Pan CQ, 2016 <sup>13</sup>	China	2012- 2013	≥5.3	100	30-32	4	27.4 ±3.0	100	8.2	92	100	26.8 ±3.0	100	8.0	88	Yes, <12hr	Yes, <12hr	Yes, 1/6
Yu CY, 2018 <sup>27</sup>	China	2017	≥6.0	30	24	4	26.8 ±4.2	NR	NR	30	30	27.6 ±3.6	NR	NR	30	Yes, <24hr	Yes, <24hr	NR
							No	n-rando	mized cont	rolled trials (	Non-RC	TT)						
Celen MK, 2013 <sup>28</sup>	Turkey	2010- 2012	≥6.3	21	18-27	4	28.2 ±4.1	100	8.3	21	24	26.9 ±2.9	100	8.3	23	Yes, <24hr	No	Yes, 1/2/6
Chen HL, 2015 <sup>29</sup>	China (Taiwan)	2011- 2013	≥7.5	62	30-32	4	32.4 ±3.1	100	8.3	65	56	32.5 ±3.2	100	8.2	56	Yes, <24hr	Yes, NR	Yes, 1/6
Chen WJ, 2017 <sup>30</sup>	China	2014- 2015	≥6.0	30	28	0	28.7 ±5.7	100	7.5	30	44	29.9 ±5.1	100	7.5	44	Yes, At birth	Yes, At birth	Yes, 1/6
Gong Q, 2017 <sup>31</sup>	China	2015- 2016	NR	44	1-6	NR	29.1 ±1.0	NR	NR	44	44	29.1 ±1.2	NR	NR	44	Yes, <24hr	Yes, <24hr	Yes, 1/6
Greenup AJ, 2014 <sup>32-35</sup>	Australia	2007- 2013	≥7.0±0.5	62	32	12	30 ±8.5	94.8	7.9	69	20	28±5	100	8.0	10	Yes, NR	Yes, At birth	Yes, 2/4/6

He LL, 2018 <sup>36</sup>	China	2013- 2016	NR	50	28	NR	27.7 ±3.2	NR	3.6	50	35	26.3 ±3.0	NR	3.7	35	Yes, <12hr	Yes, <12hr	Yes, 1/6
2010		2010		30	Pre- pregnancy	Various post- pregnancy	28.4 ±1.4	NR	7.4	29		±3.0				\12III	\12III	170
Hu MF, 2018 <sup>37</sup>	China	2016- 2018	≥6.0	30	14	Various post- pregnancy	23.2 ±3.3	NR	7.5	30	30	26.3 ±2.1	NR	7.5	30	Yes, At birth	Yes, At birth	Yes, 1/6
				30	28	Various post- pregnancy	24.4 ±3.1	NR	7.4	30								
Huang Q, 2017 <sup>38</sup>	China	2015	≥6.0	20	24-28	12	27.1 ±2.4	100	NR	20	20	27.0 ±2.3	100	NR	20	Yes, <6hr	Yes, <6hr	Yes, 1/6
Wakano Y, 2018 <sup>39</sup>	Japan	2011- 2015	N/A	2	22 or 28	4-8	[28-37] All groups	100	8.3	2	3	[28-37] All groups	100	8.3	3	Yes, <12 or <48hr	Yes (some), <12hr	Yes, 2/3/5 or 1/6
Wan JY, 2017 <sup>40</sup>	China	2012- 2015	≥5.3	74	28	0	28.5 ±4.2	NR	7.7	74	42	27.9 ±4.0	NR	7.6	42	NR	NR	NR
				20	20	NR	NR	NR	7.0	20								
				20	24	NR	NR	NR	7.1	20								
Wang HB, 2018 <sup>41</sup>	China	2013- 2016	NR	20	28	NR	NR	NR	7.2	20	20	NR	NR	7.2	20	Yes, <24hr	Yes, <24hr	Yes, 1/6
				20	32	NR	NR	NR	7.2	20								
				20	36	NR	NR	NR	6.7	20								
Xiao XH, 2017 <sup>42</sup>	China	2014- 2015	≥6.0	60	28	0-4	27.6 ±3.2	NR	7.6	60	60	28.5 ±3.6	NR	7.5	61	Yes, NR	Yes, NR	Yes, NR
Zhang BF, 2018 <sup>43</sup>	China	2016- 2017	≥6.0 ( <i>tx group</i> )	39	24-28	0	NR	100	4.8	39	75	NR	100	6.0	75	Yes, <6hr	Yes, At birth	Yes, 1/6
Zhou Y, 2018 <sup>44</sup>	China	2015- 2017	≥6.0	60	24-28	0	28 [21-38]	100	7.6	60	36	28 [23-39]	100	7.6	36	Yes, <6hr	Yes, <24hr	Yes, 1/6

									LAM 10	00-150 mg								
								Rando	mized con	trolled trials (	(RCT)							
Bai XW, 2011 <sup>45</sup>	China	2006- 2010	NR	30	28	4	NR	NR	NR	30	25	NR	NR	NR	25	Yes, <24hr (trt group)	Yes, <24	Yes, 1/6
Chen SM, 2017 <sup>46</sup>	China	2013- 2014	≥4.3	30	28	NR	27.9 ±3.6	100	7.5	30	30	27.5 ±3.9	100	8.0	30	Yes, NR	Yes, NR	Yes, NR
Guo YZ, 2008 <sup>47-49</sup>	China	2003- 2006	NR	70	28	0	NR	100	NR	70	40	NR	100	NR	40	Yes, <6hr	Yes, At birth	Yes, 1/6
Ji YY, 2015 <sup>50</sup>	China	2010- 2013	≥5.3	65	28	4	26.2 ±3.1	100	7.6	65	65	27.5 ±4.1	100	7.7	65	Yes, <24hr	Yes, <24hr	Yes, 1/6
Li ZG, 2015 <sup>51</sup>	2015 <sup>51</sup> China 2014 24.3 25 28 6 NR 100 NR 25 25 NR 100 NR 25 <24hr <24hr 1/6  Tian XO. Civ. 2010- 173 140 20 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0																	
Tian XQ, 2015 <sup>52</sup>	China	2010- 2014	≥5.3	110	28	0	29±3	100	7.9	110	110	28±4	100	8.1	110	Yes, <24hr	Yes, <24hr	Yes, 1/6
Xu WM, 2009 <sup>53,54</sup>	China & Philippines	NR	≥8.3	93	30-34	4	26 [19-32]	99	8.6	49	62	25 [20-36]	100	8.7	41	Yes, <24hr	Yes, <24hr	Yes, 1/6
Yang HW, 2014 <sup>55</sup>	China	2010- 2013	≥5.3	53	28	4	29±4	100	7.3	53	53	28±4	100	7.3	53	Yes, <24hr	Yes, At birth	Yes, 1/6
							No	n-rando	mized cont	rolled trials (	Non-RC	<b>(T</b> )						
Chen QR, 2018 <sup>56</sup>	China	2014- 2016	NR	33	28	4	25.0 ±3.9	100	7.6	33	28	24.1 ±4.7	100	7.7	28	Yes, <24hr	Yes, <24hr	Yes, 1/6
Cheng YC, 2011 <sup>57</sup>	China	2007- 2009	≥6.3	30	32	4	27±4	100	8.2	30	26	25±5	100	7.5	26	Yes, <24hr	Yes, <24hr	Yes, 1/6
Feng HF, 2007 <sup>58</sup>	China	2004- 2006	≥5.3	48	28	4	NR	100	7.6	48	42	NR	100	7.5	42	Yes, <24hr	Yes, <24hr	Yes, 1/6
Foaud HM, 2019 <sup>59</sup>	Egypt	2012- 2015	NR	34	Anytime	NR	27.0 ±2.9 (tx in last trimester) 27.7 ±4.0 (tx	44	NR	29	39	27.4 ±4.6 (low HBV DNA group) 25.7 ±4.3 (diagnosed	13	NR	30	Yes, At birth	Yes, At birth	Yes, 2/4/6

							throughout pregnancy)					too late for tx)						
Ge YL, 2015 <sup>60</sup>	China	NR	≥5.3	16	28-30	12	27.9 ±3.6	100	7.2	16	22	26.5 ±4.2	100	6.9	22	Yes, <24hr	Yes, At birth	Yes, 1/6
Greenup AJ, 2014 <sup>32-35,61</sup>	Australia	2007- 2013	≥7.0	48	32	2	28±5	96	7.7	43	20	28±5	100	8.0	10	Yes, NR	Yes, At birth	Yes, 2/4/6
Han YP, 2014 <sup>62</sup>	China	2010- 2012	≥4.3	30	28	6	26±4	100	7.6	30	30	26±4	100	7.7	30	Yes, <24hr	Yes, <24hr	Yes, 1/6
Han ZH, 2005 <sup>63</sup>	China	2001- 2003	≥4.9	43	28	0	NR	100	6.4	43	35	NR	100	NR	35	Yes, <4hr	No	Yes, 2/3/6
He T, 2018 <sup>64-66</sup>	China	2008- 2016	NR	27	1 <sup>st</sup> trimester	Contin- ued	29.2 ±2.9	74	6.3	29	35	29.0 ±3.6	80	6.3	34	Yes, <6hr	Yes, <12hr	Yes, 1/6
Jackson V, 2015 <sup>67</sup>	Ireland	2007- 2012	≥7.2	36	32	0	26 [16-40]	100	8.1	21	9	NR	100	NR	6	Yes, <3hr	Yes, <3hr	Yes, 2/4/6
Jiang HX, 2012 <sup>68</sup>	China	2007- 2010	≥5.3	164	20-34	0	27.3 ±4.4	100	7.1	164	92	26.4 ±3.2	100	7.2	92	Yes, <24hr	Yes, At birth	Yes, 1/6
Li G, 2006 <sup>69</sup>	China	2005- 2006	NR	40	28	0	24±3	100	NR	35	37	24±5	100	NR	32	Yes, <24hr	No	Yes, 1/2/7
Li JH, 2017 <sup>70</sup>	China	2012- 2016	NR	33	28	4	28.2 ±6.3	NR	8.0	33	27	29.4 ±5.7	NR	7.7	27	Yes, <6hr	Yes, At birth	Yes, 1/6
Li WF, 2006 <sup>71</sup>	China	2001- 2003	≥4.3	36	34	0	NR	100	6.1	36	44	NR	100	NR	44	Yes, <6hr	No	Yes, 2/3/7
Ma J, 2006 <sup>72</sup>	China	NR	NR	18	Pre- pregnancy	NR	NR	100	NR	18	22	NR	100	NR	16	Yes, At birth	Yes, At birth	NR
Pan CQ,	China	2008-	≥5.3	66	13-26	4	27.7 ±4.1	100	6.5	66	89	27.1	100	6.6	89	Yes,	Yes,	Yes,
2017 <sup>73</sup>	Cilina	2015	≥ა.ა	94	28-30	4	27.4 ±3.5	100	6.5	94	07	±4.2	100	0.0	69	<6hr	<12hr	1/6
Ren CJ, 2016 <sup>74</sup>	China	2010- 2012	≥5.3	67	28	0	25.8 ±4.7	100	6.1	67	72	25.4 ±5.1	100	6.1	72	Yes, <6hr	Yes, At birth	Yes, 1/6

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Ren YJ, 2011 <sup>75</sup>	China	2008- 2009	NR	30	28	0	NR	100	NR	30	155	NR	100	NR	155	Yes, <24hr	Yes, At birth	Yes, 1/6
Shen ML, 2016 <sup>76</sup>	China	2010- 2014	≥4.3	60	26	4	NR	NR	6.1	60	28	NR	NR	6.0	28	Yes, <24hr	Yes, NR	Yes, NR
Su TB, 2009 <sup>77</sup>	China	2004- 2007	NR	128	32	0	NR	NR	NR	128	120	NR	NR	NR	120	Yes, <2hr	Yes, 3 days	Yes, 1/6
Tang X, 2009 <sup>78</sup>	China	2007- 2008	≥5.3	17	33	4	NR	100	6.6	17	24	NR	100	6.7	24	Yes, <24hr	Yes, <24hr	Yes, 1/6
Wakano Y, 2018 <sup>39</sup>	Japan	2011- 2015	NR	3	28-32	4-8	[28-37] All groups	100	8.3	3	3	[28-37] All groups	100	8.3	3	Yes, <12 or <48hr	Yes (some), <12hr	Yes, Varied
Wang DM, 2016 <sup>79</sup>	China	2011- 2014	≥5.3	42	28-30	12	31.4 ±7.3	100	7.1	42	20	31.7 ±7.0	100	7.1	20	NR	Yes, <24hr	Yes, 1/6
Wang EJ, 2012 <sup>80</sup>	China	2008- 2010	≥6.3	32	28	4	25.0 ±3.8	100	7.6	32	27	24.0 ±4.7	100	7.7	27	Yes, <24hr	Yes, <24hr	Yes, 1/6
Wang TM, 2005 <sup>81</sup>	China	2001- 2003	≥5.7	32	Pre- pregnancy	0	NR	100	NR	32	32	NR	100	NR	32	NR	Yes, <12hr	Yes, 1/6
Wang W, 2014 <sup>82</sup>	China	2011- 2012	NR	35	28	4	28. 4±3.8	NR	7.4	35	28	27.2 ±4.2	NR	7.2	28	Yes, <24hr	Yes, At birth	Yes, 1/6
Yuan QF, 2012 <sup>83</sup>	China	2010- 2011	NR	30	27	4	26.5 ±4.5 All groups	100	NR	32	30	26.5 ±4.5 All groups	100	NR	32	Yes, <24hr	Yes, <24hr	Yes, 6/12
				30	28	0	NR	100	6.6	30								
Zeng YM, 2013 <sup>84</sup>	China	2008- 2010	≥4.3	30	28	4	NR	100	6.6	30	30	NR	100	6.5	30	Yes, At birth	Yes, At birth	Yes, 1/6
				30	28	6	NR	100	6.5	30								
Zhang H, 2014 <sup>85</sup>	China	2009- 2011	≥6.3	55	28-30	4	28.4 ±7.1	100	6.9	52	374	29.0 ±4.6	100	6.8	352	Yes, <6hr	Yes, <6hr	Yes, 1/6
Zhang YF, 2010a <sup>86</sup>	China	2006- 2007	≥5.3	50	28	4	NR	100	6.1	50	50	NR	100	6.1	50	Yes, <24hr	Yes, <24hr	Yes, 1/6

Zhou DS, 2013 <sup>87</sup>	China	2009- 2012	≥5.3	49	20	NR	27.4 ±6.7	NR	6.8	49	95	29.2 ±6.1	NR	6.9	95	Yes, <12hr	Yes, At birth	Yes, 1/6
				64	28	NR	±5.3	NR	6.7	64								
Zhu M, 2014 <sup>88</sup>	China	2012- 2013	NR	24	26	0	NR	100	NR	24	25	NR	100	NR	24	Yes, <8hr	Yes, <8hr	Yes, 1/6
									LDT	600 mg								
				I	T	1		Rando	mized con	trolled trials	(RCT)		П	Т	Т	1		
Bai HL, 2013 <sup>89</sup>	China	2009- 2011	≥6.3	30	28-32	4	NR	NR	6.5	27	30	NR	NR	6.6	30	Yes, <6hr	Yes, At birth	Yes, 1/6
Chen SM, 2017 <sup>46</sup>	China	2013- 2014	≥4.3	30	28	NR	27.4 ±3.5	100	7.8	30	30	27.5 ±3.9	100	8.0	30	Yes, NR	Yes, NR	Yes, NR
Fu PX, 2016 <sup>90</sup>	China	2014- 2015	NR	100	24-28	4	31.5 ±1.5	NR	NR	100	100	31.7 ±1.6	NR	NR	100	Yes, At birth	Yes, At birth	Yes, NR
Guan ZF, 2017 <sup>91,92</sup>	China	2005- 2015	≥6.3	12	24	12	26.5 ±9.5	100	7.1	123	120	27.2 ±9.4	100	7.1	122	Yes, <6hr	Yes, At birth	Yes, 1/6
Guo HJ, 2011 <sup>93</sup>	China	2008- 2010	≥6.3	25	28	4	28 ±3	100	7.0	28	25	27±4	100	7.2	26	Yes, <6hr	Yes, At birth	Yes, 1/6
				30	20	0	28.2 ±3.5	100	7.3	30								
Huang HY, 2016 <sup>94</sup>	China	2012- 2013	≥5.3	30	24	0	28.6 ±3.4	100	7.3	30	30	28.9 ±3.5	100	7.2	30	NR	NR	NR
				30	28	0	28.4± 3.2	100	7.3	30							_	
Ji YY, 2015 <sup>50</sup>	China	2010- 2013	≥5.3	65	28	4	27.2 ±3.6	100	7.7	65	65	27.5 ±4.1	100	7.7	65	Yes, <24hr	Yes, <24hr	Yes, 1/6
Li SF, 2015 <sup>95</sup>	China	2012- 2014	≥6.3	60	28	24	NR	NR	6.9	60	60	NR	NR	6.7	60	Yes, At birth	No	Yes, 1/6

				l			l		l	l	l	l						
Lu QY, 2016 <sup>96</sup>	China	2013- 2014	NR	152	28	0	[29-36]	47	NR	152	132	[29-36]	41	NR	132	Yes, <12hr	Yes, <12hr	Yes, 1/6
Peng ML, 2014 <sup>97</sup>	China	2011- 2012	NR	30	28	NR	25.9 ±4.2	100	6.1	30	30	26.4 ±4.4	100	6.1	30	Yes, <24hr	Yes, <24hr	Yes, 1/6
Shi QW, 2017 <sup>98</sup>	China	NR	≥5.3	100	24	0	[23-40]	NR	7.1	100	100	[23-40]	NR	6.9	100	Yes, <2hr	Yes, At birth	Yes, 1/6
Wang HY, 2018 <sup>99</sup>	China	2015- 2017	≥5.3	40	12-14	24	NR	100	6.8	40	40	NR	100	6.9	40	Yes, <6hr	Yes, <6hr	Yes, 1/6
Xie PY, 2016 <sup>100</sup>	China	2015- 2015	NR	60	28	4	26.6 ±12.5	NR	NR	60	60	26.1 ±11.6	NR	NR	60	Yes, NR	Yes, NR	Yes, NR
Xing Y, 2018 <sup>101</sup>	China	2013- 2015	NR	30	28	4	29.0 ±6.0	NR	6.5	30	30	29.5 ±5.3	NR	6.5	30	Yes, <6hr	Yes, <6hr	Yes,
Yang HW, 2015 <sup>102</sup>	China	2012- 2014	≥5.3	50	28	4	NR	100	6.1	50	50	NR	100	6.1	50	Yes, <24hr	Yes, <24hr	Yes, 1/6
Zhang LJ, 2009 <sup>103</sup>	China	2007- 2008	≥6.3	31	28-32	4	NR	NR	6.6	30	30	NR	NR	6.7	30	Yes, <6hr	Yes, At birth	Yes, 1/6
Zhang Y, 2018 <sup>104</sup>	China	2015- 2017	≥6.3	34	Pre- pregnancy	NR	28.4 ±3.1	NR	6.6	34	34	28.0 ±3.1	NR	6.9	34	Yes, NR	Yes, NR	Yes, NR
Zhao DB, 2010 <sup>105</sup>	China	2006- 2008	NR	30	28	4	NR	100	NR	30	30	NR	100	NR	30	Yes, <6hr	Yes, At birth	Yes, 1/6
Zhao Y, 2017 <sup>106</sup>	China	2013- 2016	≥6.3	40	12	12	28.1 ±4.1	100	7.3	40	40	27.9 ±3.9	100	7.2	40	Yes, At birth	Yes, At birth	Yes, 1/6
Zhu J, 2017 <sup>107</sup>	China	2012- 2015	NR	60	28	0	NR	NR	7.4	60	60	NR	NR	6.9	54	Yes, <24hr	Yes, At birth	Yes, 1/6
Zhu LP, 2014 <sup>108</sup>	China	2011- 2012	NR	30	28	4	NR	NR	6.7	30	30	NR	NR	6.6	30	Yes, <6hr	Yes, At birth	Yes, 1/6
							No	on-rando	mized cont	rolled trials (	Non-RC	<b>T</b> )						
Chen CY, 2015 <sup>109</sup>	China	2008- 2011	≥6.3	43	1 <sup>st</sup> trimester	NR	29.7 ±8.9	100	7.1	42	41	27.5 ±6.6	100	7.0	40	Yes, NR	Yes, NR	Yes, NR

CI E		2000					26.5					26.0				W	37	37
Chen F, 2016 <sup>110</sup>	China	2008- 2014	≥6.3	31	Pre- pregnancy	NR	26.5 ±4.0	100	6.9	31	33	26.0 ±4.4	100	6.7	32	Yes, NR	Yes, NR	Yes, NR
Chen QR, 2018 <sup>56</sup>	China	2014- 2016	NR	29	28	4	26.9 ±4.3	100	7.8	29	28	24.1 ±4.7	100	7.7	28	Yes, <24hr	Yes, <24hr	Yes, 1/6
Chen WJ, 2017 <sup>30</sup>	China	2014- 2015	≥6.0	79	28	0	31.1 ±6.3	100	8.3	79	44	29.9 ±5.1	100	7.5	44	Yes, <24hr	Yes, At birth	Yes, 1/6
Chen ZX, 2017 <sup>111-113</sup>	China	2001- 2015	≥5.3	43	13-32	NR	28.1 ±6.7	70	6.5	41	89	26.2 ±4.5	83	6.5	89	Yes, <6hr	Yes, <6hr	Yes, 1/6
Cui ZL, 2015 <sup>114</sup>	China	2013- 2014	≥5.3	50	28	4	28.0 ±1.8	100	7.1	50	50	27.6 ±2.1	100	6.9	46	Yes, <24hr	Yes, <24hr	Yes, 1/6
Deng Y, 2015 <sup>115</sup>	China	2011- 2014	≥6.0	82	24-36	4	25.4 ±3.7	NR	7.0	82	75	25.7 ±3.6	NR	7.0	75	Yes, At birth	Yes, At birth	Yes, 1/6
Ding XP, 2018 <sup>116</sup>	China	2013- 2017	≥6.3	38	28	4	NR	100	7.3	38	38	NR	100	7.2	38	Yes, <24hr	Yes, <24hr	Yes, 1/6
Fan LY, 2013 <sup>117</sup>	China	2010- 2011	≥5.3	58	28	24	27.8 ±3.0	100	6.9	58	60	29.0 ±2.9	100	6.7	60	Yes, <24hr	Yes, <24hr	Yes, 1/6
Feng XM, 2017 <sup>118</sup>	China	2014- 2016	≥6.3	36	28	4	29.6 ±6.3	100	6.9	36	36	28.4 ±5.1	100	6.7	36	Yes, <6hr	Yes, At birth	Yes, 1/6
Gao P, 2016 <sup>119</sup>	China	2012- 2014	NR	51	1 <sup>st</sup> trimester	0	28.4 ±3.8	NR	7.1	51	51	27.2 ±3.6	NR	7.0	51	Yes, NR	Yes, NR	Yes, NR
Ge YL, 2015 <sup>60</sup>	China	NR	≥5.3	20	28-30	12	28.6 ±3.5	100	7.1	20	22	26.5 ±4.2	100	6.9	22	Yes, <24hr	Yes, At birth	Yes, 1/6
Han GR,	China	2008-	\5 2	257	20-27	Variable	27 [20-35]	100	7.9	256	92	26	100	7.9	86	Yes,	Yes,	Yes,
2015120-125	Cililia	2010	≥5.3	105	28-32	Variable	28 [20-38]	100	7.8	102	94	[20-35]	100	7.9	00	<3hr	<12hr	1/6
Han YP, 2014 <sup>62</sup>	China	2010- 2012	≥4.3	30	28	6	26±4	100	7.7	30	30	26±4	100	7.7	30	Yes, <24hr	Yes, <24hr	Yes, 1/6
He T, 2018 <sup>64,126</sup>	China	2008- 2016	NR	32	1 <sup>st</sup> trimester	Contin- ued	29.2 ±2.9	84	6.6	32	35	29.0 ±3.6	80	6.2	34	Yes, <6hr	Yes, <12hr	Yes, 1/6

Hu WH, 2016 <sup>127</sup>	China	2013- 2015	NR	46	28	28	28.9 ±3.3	NR	6.7	46	40	29.2 ±3.4	NR	6.6	40	Yes, <24hr	Yes, <24hr	Yes, 1/6
Hu Y, 2018 <sup>128,129</sup>	China	2012- 2014	NR	149	28-32	3-4	25.9 ±3.7	100	7.4	105	179	26.4 ±3.4	100	7.3	122	Yes, <24hr	Yes, <24hr	Yes, 1/6
Huang Q, 2017 <sup>38</sup>	China	2015- 2015	≥6.0	20	24-28	12	26.8 ±2.5	100	NR	20	20	27.0 ±2.3	100	NR	20	Yes, <6hr	Yes, <6hr	Yes, 1/6
Jiang S, 2017 <sup>130</sup>	China	2015- 2016	NR	44	28	NR	28.3 ±3.4	NR	6.1	44	44	NR	NR	6.1	44	Yes, At birth	Yes, At birth	Yes, 1/6
Jiang XN, 2013 <sup>131</sup>	China	2010- 2011	≥4.3	65	26-30	NR	NR	100	6.0	65	51	NR	100	5.9	51	Yes, NR	Yes, At birth	Yes, 1/6
Li CM, 2017 <sup>132</sup>	China	2013- 2015	≥2.3	30	28	4	43.2 ±1.3	NR	6.1	30	30	43.2 ±1.3	NR	6.1	30	Yes, <24hr	Yes, <24hr	Yes, 1/6
Li N,	China	2012-	≥4.3	35	Pre- pregnancy	NR	NR	NR	5.1	35	25	NR	NR	5.0	25	Yes,	Yes,	Yes,
2016 <sup>133</sup>	Cillia	2015	≥4.3	30	28	NR	NR	NR	5.1	30	23	NK	NK	3.0	23	<6hr	<6hr	1/6
Li YH, 2017 <sup>134</sup>	China	2015- 2017	≥6.3	30	28	~36	29.5 ±2.7	100	3.2	30	31	28.8 ±3.5	100	3.2	32	Yes, <24hr	Yes, NR	Yes, NR
Li ZY, 2018 <sup>135</sup>	China	2015- 2016	≥5.3	41	28	NR	26.2 ±4.4	100	6.1	41	41	26.3 ±4.2	100	6.1	41	Yes, <24hr	No	Yes, 1/6
Liu CY, 2014 <sup>136</sup>	China	2011- 2011	≥5.3	34	28	4	27.2 ±3.6	100	7.1	34	34	26.9 ±4.1	100	7.4	34	Yes, <6hr	Yes, At birth	Yes, 1/6
Liu J, 2017 <sup>137</sup>	China	2013- 2015	≥6.0	102	30	NR	27.8 ±4.1	100	8.1	97	28	26.7 ±3.9	100	8.1	28	NR	Yes, <12hr	Yes, 1/6
Liu XB, 2016 <sup>138</sup>	China	2014- 2015	≥6.0	20	28-36	4	25.4 ±3.7	100	7.0	20	20	25.4 ±3.6	100	7.0	20	Yes, At birth	Yes, At birth	Yes, 1/6
Liu Y,	China	2010-	>6.0	50	4-27	4	27.9 ±3.7	94	7.7	50	78	27.5	97	7.5	78	Yes,	Yes,	Yes,
2016 <sup>139</sup>	China	2012	≥6.0	32	28-32	4	28.3 ±3.8	97	7.5	32	/8	±3.5	91	1.3	/8	NR	At birth	1/6

Lou JJ, 2015 <sup>140</sup>	China	2012- 2013	≥4.6	127	28	4	30 ±6	100	6.8	125	58	31±6	100	6.7	58	Yes, <6hr	Yes, At birth	Yes, 1/6
Pan YC, 2017 <sup>141</sup>	China	2012- 2015	≥6.3	81	32	0	28.8 ±3.3	100	8.3	81	453	27.6 ±3.8	100	8.1	370	Yes, <2hr	Yes, <2hr	Yes, 1/6
Peng BA, 2012 <sup>142</sup>	China	2008- 2009	≥5.3	40	28	0	NR	100	6.0	40	40	NR	100	6.1	40	Yes, At birth	Yes, At birth	Yes, 1/6
Qiu B, 2016 <sup>143</sup>	China	2009-	≥5.3	60	Pre- pregnancy	0	NR	NR	6.91	60	60	NR	NR	6.8	60	Yes,	Yes,	Yes,
2016 <sup>143</sup>	Cilila	2014	≥ગ.૩	60	24	0	NR	NR	6.9	60	00	NK	INK	0.8	00	<12hr	<12hr	1/6
Ren N, 2015 <sup>144</sup>	China	2011- 2014	≥5.3	46	28	24	NR	100	7.2	46	46	NR	100	7.5	46	Yes, <24hr	Yes, <24hr	Yes, 1/6
Shen ML, 2016 <sup>76</sup>	China	2010- 2014	≥4.3	60	26	4	NR	NR	5.9	61	28	NR	NR	6.0	28	Yes, <24hr	Yes, NR	Yes, NR
Sheng Q, 2018a <sup>145,146</sup>	China	2013- 2015	≥5.0	91	24-32	$O^a$	27.8 ±4.2	100	8.1	79	21	26.8 ±3.7	100	8.0	21	Yes, <12hr	Yes, <12hr	Yes, 1/6
Sheng Q, 2018b <sup>147</sup>	China	2016- 2016	≥6.3	66	24-28	0	31.3 ±4.4	89	8.1	66	46	30.4 ±4.2	89	7.9	46	Yes, <12hr	Yes, <12hr	Yes, 1/6
Sun W,	China	2013-	>(2	62	12	12	28.9 ±11.8	100	7.1	62	65	27.5	100	7.0	65	Yes,	Yes,	Yes,
2017148	Cnina	2015	≥6.3	61	20-28	12	29.7 ±9.8	100	7.1	61	0.5	±12.9	100	7.0	03	<6hr	<12hr	1/6
Sun WH,	Chino	2009-	>6.2	42	12	12	28.9 ±11.8	100	7.1	43	45	27.5	100	7.1	46	Yes,	Yes,	Yes,
2015 <sup>149,150</sup>	China	2013	≥6.3	41	20-28	12	29.7 ±9.8	100	7.2	41	45	±12.9	100	/.1	46	<6hr	<6hr	1/6
Tan J, 2019 <sup>151</sup>	China	2013- 2015	NR	41	28	0	NR	NR	7.6	41	59	NR	NR	7.5	59	Yes, <24hr	Yes, At birth	Yes, 1/6
Tan Z, 2016 <sup>152</sup>	China	2012- 2015	≥6.0	145	14-28	NR	29 [23-39]	90	7.6	137	334	28 [20-41]	85	7.6	320	Yes, <6hr	Yes, At birth	Yes, 1/6

			NR	37	<14	NR	29 [20-38]	65	2.0	34								
Tian JH, 2018 <sup>153</sup>	China	2000- 2017	≥4.6	135	Anytime	NR	NR	100	NR	135	203	NR	100	NR	203	Yes, <6hr	Yes, <12hr	Yes, 1/6
Tian RH, 2016 <sup>154</sup>	China	2013- 2013	≥6.0	318	28	4	27.2 ±3.2	100	6.5	318	374	27.3 ±3.2	100	6.6	374	Yes, At birth	Yes, At birth	Yes, 1/6
Wang B, 2016 <sup>155</sup>	China	2011- 2012	≥6.0	110	28	4	24±5	100	7.9	110	187	24±4	100	7.9	187	Yes, At birth	Yes, At birth	Yes, 1/6
Wang DM, 2016 <sup>79</sup>	China	2011- 2014	≥5.3	36	28-30	12	31.4 ±7.3	100	7.1	36	20	31.7 ±7.0	100	7.1	20	NR	Yes, <24hr	Yes, 1/6
Wang EJ, 2012 <sup>80</sup>	China	2008- 2010	≥6.3	28	28	4	27.0 ±3.4	100	7.9	28	27	24.0 ±4.7	100	7.7	27	Yes, <24hr	Yes, <24hr	Yes, 1/6
				20	20	NR	NR	NR	6.9	20								
				20	24	NR	NR	NR	7.2	20								
Wang HB, 2016 <sup>156</sup>	China	2013- 2016	NR	20	28	NR	NR	NR	7.1	20	20	NR	NR	7.2	20	Yes, <24hr	Yes, <24hr	Yes, 1/6
				20	32	NR	NR	NR	7.2	20								
				20	36	NR	NR	NR	6.7	20								
Wang J, 2017 <sup>157</sup>	China	2010- 2015	≥6.0	329	24-28	NR	27.8 ±3.7	NR	7.8	329	65	27.6 ±3.5	NR	7.8	65	Yes, <12hr	Yes, <12hr	Yes, 1/6
Wang TD, 2015 <sup>158</sup>	China	2012- 2013	≥6.3	53	28	4	26.3 ±3.1	100	7.3	53	52	25.8 ±3.9	100	7.5	52	Yes, <24hr	Yes, <24hr	Yes, 1/6
Wang	China	2010-	≥4.3	22	<27	0	NR	100	6.8	22	198	NR	100	6.3	198	Yes,	Yes,	Yes,
WP, 2012 <sup>159</sup>	Ciliia	2011	≥4.3	25	28	0	NR	100	6.7	25	190	INK	100	0.5	190	<6hr	<6hr	1/6

Wu QX, 2015 <sup>160,161</sup>	China	2008- 2014	≥6.0	279	24-32	0 or 4	27 [17-38]	100	7.2	204	171	28 [18-40]	100	7.4	95	Yes, At birth	Yes, At birth	Yes, 1/6
Xiao XH, 2017 <sup>42</sup>	China	2014- 2015	≥6.0	60	28	0 or 4	28.6 ±3.2	NR	7.5	62	60	28.5 ±3.6	NR	7.5	61	Yes, NR	Yes NR	Yes, NR
Yao LF, 2014 <sup>162</sup>	China	2012- 2013	≥6.0	30	28-32	6	NR	100	7.3	30	30	NR	100	8.2	30	Yes, NR	Yes, NR	Yes, NR
Yao ZC, 2011 <sup>163,164</sup>	China	2008- 2010	≥5.3	28	28	4	NR	NR	6.8	28	30	NR	NR	6.8	30	Yes, <6hr	Yes, At birth	Yes, 1/6
Yue X, 2014 <sup>165</sup>	China	2007- 2012	≥5.3	31	Any- time	NR	29.7 ±5.1	0	5.5	31	31	27.6 ±2.9	0	5.6	30	Yes, <24hr	Yes, At birth	Yes, 1/6
Zhang BF, 2018 <sup>43</sup>	China	2016- 2017	≥6.0	36	24-28	0	NR	100	5.0	36	75	NR	100	NR	75	Yes, <6hr	Yes, At birth	Yes, 1/6
Zhang GH, 2018 <sup>166,167</sup>	China	2012- 2014	≥6.3	40	28	4	NR	100	NR	40	40	NR	100	NR	40	Yes, <24hr	Yes, At birth	Yes, 1/6
Zhang H, 2014 <sup>85</sup>	China	2009- 2011	≥5.3	263	28-30	4	29.8 ±6.3	100	6.9	257	374	29.0 ±4.6	100	6.8	352	Yes, <6hr	Yes, <6hr	Yes, 1/6
Zhang X, 2015 <sup>168</sup>	China	2012- 2013	≥6.3	48	28	12	NR	100	7.0	48	47	NR	100	6.8	47	Yes, <24hr	Yes, At birth	Yes, 1/6
Zhang YF, 2010b <sup>169</sup>	China	2008- 2009	≥5.3	60	28	4	NR	100	6.1	60	60	NR	100	6.1	60	Yes, <24hr	Yes, <24hr	Yes, 1/6
Zhao J, 2013 <sup>170</sup>	China	2010- 2011	≥6.3	41	20	0	NR	100	NR	41	202	NR	100	NR	202	Yes, <6hr	Yes, <6hr	Yes, 1/6
Zheng JC, 2018 <sup>171</sup>	China	2012- 2015	≥5.3	23	28	4	NR	100	NR	23	37	NR	100	NR	37	Yes, <6hr	Yes, <24hr	Yes, 1/6
Zhou YJ, 2014 <sup>172,173</sup>	China	2007- 2013	≥6.3	70	1 <sup>st</sup> trimester	0	NR	NR	NR	53	39	NR	NR	NR	34	Yes, NR	Yes, At birth	Yes, 1/6

<sup>&</sup>lt;sup>a</sup> 87/91 women stopped therapy at baseline and 4 others continued therapy

# Appendix F: Cochrane Collaboration's Risk of Bias Assessment Tool for RCTs

### TDF 300 mg

## A. English language studies

Study	Selection bias		Performance bias	Detection bias	Attrition bias			Reporting bias
(year), journal,	Random	Allocation	Blinding of	Blinding of	Incomplete outco	ome data addressed	1	
No.	sequence generation	concealment	participants, personnel	outcome assessment	MTCT	Infant Safety	Mother safety	Selective reporting
Pan CQ, (2016), N Engl J Med, 13	Low risk Quotes: "Enrollment at each center was performed with the use of blocks and randomized for sample balance. Using a randomization table, we randomly assigned 200 mothers, in a 1:1 ratio"	High risk Comment: no concealment described	High risk Quotes: "open- label"	High risk Quotes: "open-label"	Low risk Comment: Loss to follow-up detailed carefully in Figure 1. Minimal loss to follow-up (95% in treated group, 88% in control group), and <10% points different between control and treated groups.	Low risk Comment: Reports on all infant adverse events of interest for 88% and 97.8% of control and treated group, respectively. This excludes bone density measurements.	Low risk Comment: Reports on all maternal adverse events of interest for >95% of both treated and control groups, including antiviral resistance testing.	Low risk Comment: the protocol is available in a separate publication as well as online at NEJM.org. The current outcomes of interest that this metanalysis is recording were prespecified.
Jourdain	Low risk	Low/Unclear	Low Risk	Low Risk	Low Risk	Low risk	High risk	Low risk
G, (2018), N Engl J Med, 14	Quotes: "participants were randomly assigned in a 1:1 ratio" "Randomization	Risk Quotes: "The participants, the trial staff on site and at the coordination	Quotes: "The participants, the trial staff on site and at the coordination center, the investigators, and	Quotes: "The participants, the trial staff on site and at the coordination center, the investigators, and the laboratory	Comment: 88 and 90% with full follow-up in treated and control group respectively.	Comment: 95 and 98% of infants included in this analysis from treated and control,	Comment: although >90% women considered until discontinuatio	Comment: the protocol is available in a separate publication as well as online

	was performed with the use of permuted blocks and stratified according to trial site"	center, the investigators, and the laboratory personnel were unaware of the trial-group assignments"  Comment: no detail provided about sealed envelopes	the laboratory personnel were unaware of the trialgroup assignments." "matching placebo (similar to active tablets minus the active pharmaceutical ingredient)"	personnel were unaware of the trial- group assignments."	Numbers of mothers/infants withdrawn or LFU detailed in Figure 1. Similar withdrawal/LFU proportions in each group and 1 fetal/ infant death in each group.	respectively. All relevant adverse events addressed, including bone mineral density (although for this variable, many lost to follow-up, would have to say 'high risk')	n of the trial regimen, some key adverse events not addressed (e.g. antiviral resistance, postpartum hemorrhage)	at NEJM.org. The current outcomes of interest that this meta-analysis is recording were prespecified.
Lin Y, (2018), Sci Rep, 24	Low risk Quotes: "A random number table was used to group the pregnancies into each group (60 individuals per group) based on their enrollment time. Simple randomization was performed"	Low risk Quotes: "sealed envelopes were used for concealment of the random allocation."	High risk Quotes: "The control individuals did not receive anti- viral treatment." "The participants, care providers did not know whether the patients had accepted the intervention." Comment: Information is contradictory as it says that participants did not receive treatment (and no mention of placebo) but also that it is double blinded. Unclear if participants were actually blinded	Low/Unclear Risk Quotes: " persons who examined the viral DNA loads and evaluated the outcomes of the patients did not know whether the patients had accepted the intervention." Comment: It mentions blinding but if participants were not properly blinded then other staff etc can easily understand which treatment they are on.	High risk Comment: 100% follow-up in treated group but 87% in control. This indicates that blinding was probably not done well, and could also introduce bias with dissimilar proportions. No breakdown of LFU cases given.	High risk Comment: same numbers used and therefore comment as for MTCT outcome.	High risk Comment: same numbers used and therefore comment as for MTCT outcome.	Low risk  Comment: the protocol is available online where the article can be accessed on Scientific Reports website. The current outcomes of interest that this meta-analysis is recording were prespecified in that protocol.

**B.** Chinese language studies

Study	Selection bias		Performance bias	Detection bias	Attrition bias			Reporting bias
(year), journal,	Random	Allocation	Blinding of	Blinding of	Incomplete outco	ome data addressed		
No.	sequence generation	concealment	participants, personnel	outcome assessment	МТСТ	Infant Safety	Mother safety	Selective reporting
Yu CY,	Low	Unclear	High risk	Unclear	Unclear	High risk	High risk	Low risk
(2018), J	risk/Unclear Quotes:	Comment: the method of	Quotes: "The control group received liver	Comment: the study did not	Comment: No statement about	Comment: same numbers used as	Comment: same numbers	Comment: the protocol is
of Pub	"60 cases of pregnant women	concealment not described	protecting treatment" "The observation group	address this outcome	LFU (not reporting any	for MTCT outcome. Only	used as for MTCT	available in the method
Health	with		received antiviral		LFU, and also not	congenital	outcome.	section of the
and Prev	asymptomatic hepatitis B virus		treatment with tenofovir"		mentioning clearly that there	abnormality reported. Other	Women considered	article. The current
med, 27	were selected and randomly divided into liver protection group and tenofovir group, with 30 cases in each group"  Comment: the study did not describe the exact random component in the sequence generation process		Comment: the study did not address this outcome and no use of placebo		were no cases LFU)	key adverse events not addressed.	until late pregnancy. Only elevated bile acid level and amniotic fluid turbidity reported. Other key adverse events of interest in this review not addressed (e.g. hepatitis flare after treatment discontinuatio n, antiviral resistance)	outcomes of interest that this meta-analysis is recording were prespecified in that protocol.
Liu MH,	Low	Unclear	High risk	Unclear	Low risk	High risk	High risk	Low risk
(2017b),	risk/Unclear Quotes:	Comment: the method of	Quotes: "The control group received no	Comment: the study did not	Comment: 100% follow-up in both	Comment: same numbers used as	Comment: same numbers	Comment: the protocol is
Chinese	"participants were randomly	concealment not described	antiviral treatment" "The observation group	address this outcome	treated and control group	for MTCT outcome. Only	used as for MTCT	available in the method

Journal of	assigned in a 1:1	received antiviral	Apgar score,	outcome.	section of the
	ratio"	treatment with TDF"	premature labor,	Women	article. The
Woman	Comment: the	Comment: the study did	congenital	considered	current
and Child	study did not	not address this	abnormality and	until delivery.	outcomes of
and Ciniu	describe the exact	outcome and no	retarded	Only	interest that
Health	random	mention of placebo	development	postpartum	this meta-
	component in the		reported. Other	hemorrhage	analysis is
Research,	sequence		key adverse	reported.	recording
26	generation		events not	Other key	were pre-
20	process		addressed.	adverse events	specified in
				not addressed.	that protocol.

### LAM 100-150 mg

## A. English language studies

Study (year) ,	Selection bias		Performance bias	Detection bias	Attrition bias			Reporting bias
journal,	Random sequence	Allocation	Blinding of participants,	Blinding of outcome		me data addressed	l Mother	Selective
No.	generation	concealment	personnel	assessment	MTCT	Infant Safety	safety	reporting
Xu WM (2009), Journal of Viral Hepatitis, 53	High risk Comment: Mentions that women were randomly assigned but does not give any indication of method for randomization.	Low/unclear risk Quotes: "After written informed consent was obtained, participants were randomly assigned in a 1:1 ratio ~" Comment: No method for allocation concealment is mentioned except calling the trial 'blinded' and 'double-blind'. However, from the above quote it seems that randomization occurred after informed consent.	Low risk  Quotes: "To preserve study blinding, the investigators were instructed not to determine serum HBV DNA levels locally while the mother was receiving blinded treatment"; "matching placebo orally once daily"  Comment: Calls the trial blinded and mentions some extra efforts put in to preserve blinding with study personnel.	Low risk  Quotes: "To preserve study blinding, the investigators were instructed not to determine serum HBV DNA levels locally while the mother was receiving blinded treatment"  Comment: Calls the trial blinded and mentions some extra efforts put in to preserve blinding with study personnel (specifically lab personnel)	Unclear risk  Comment: All lost to follow-up, withdrawals, etc detailed carefully in text and a figure within the report.  Appropriate analysis methods used to consider loss to follow-up (e.g. mITT analysis).  However, only 78% and 66% retention in treated and control groups, respectively (these proportions also differ by >10% points)	High risk  Comment: Though all the infants were included in this analysis from three arms, respectively, some key adverse events including prematurity, Apgar and bone density were not reported.	High risk Comment: Though >90% women were included in this analysis, some key adverse events, were not addressed (e.g. antiviral resistance, postpartum hemorrhage)	Unclear risk Comment: Both reviewers were unable to find the trial protocol online.

**B.** Chinese language studies

Study	Selection bias		Performance bias	Detection bias	Attrition bias		Reporting bias
(year), journal,	Random sequence	Allocation	Blinding of participants,	Blinding of outcome		ome data addressed  Mother	Selective
No.	generation	concealment	personnel	assessment	MTCT	Infant Safety safety	reporting
Chen SM	Low	Unclear	High risk	Unclear	Unclear	Unclear Unclear	Low risk
(2017),	risk/Unclear Quotes:	Comment: the method of	Quotes: "The control group received no	Comment: the study did not	Comment: No statement about	Comment: the   Comment: the study did not study did not	protocol is
Journal of	"90 cases of pregnant women	concealment not described	antiviral treatment" "The observation	address this outcome	LFU (not reporting any	address this address this outcome	the method
China	chronically		groups received		LFU, and also not		section of the
Prescripti	infected with HBV were		antiviral treatment with lamivudine or		mentioning clearly that there		article. The current
on Drug,	selected and randomly divided		telbivudine"  Comment: the study did		were no cases LFU)		outcomes of interest that
46	into lamivudine group, telbivudine group and control group, with 30 cases in each group"  Comment: the study did not describe the exact random component in the sequence generation process		not address this outcome and no mention of placebo				this meta- analysis is recording were pre- specified in that protocol.
Ji YY (2015), Chin J Postgrad	Low risk Quotes: "Referring to random number table, the patients were divided into	Unclear Comment: the method of concealment described	High risk Quotes: "The control group received no antiviral treatment" "The observation group received antiviral	Unclear Comment: the study did not address this outcome	Unclear Comment: No statement about LFU (not reporting any LFU, and also not	Unclear Comment: the study did not address this outcome  Unclear Comment: the study did not address this outcome	protocol is

Med, 50	telbivudine group, lamivudine group and control group, with 65 cases in each group"		treatment with telbivudine or lamivudine"  Comment: the study did not address this outcome and no mention of placebo		mentioning clearly that there were no cases LFU)			article. But not all of the study's prespecified primary outcomes have been reported (e.g. maternal liver function after antiviral treatment).
Li ZG (2015), World Latest Medicine Informati on, 51	Low risk/Unclear Quotes: "The patients were randomly divided into lamivudine group, telbivudine group and control group, with 25 cases in each group" Comment: the study did not describe the exact random component in the sequence generation process	Unclear Comment: the method of concealment described	f group received no	Unclear Comment: the study did not address this outcome	Unclear Comment: No statement about LFU (not reporting any LFU, and also not mentioning clearly that there were no cases LFU)	Unclear Comment: the study did not address this outcome	Unclear Comment: the study did not address this outcome	Low risk Comment: the protocol is available in the method section of the article. The current outcomes of interest that this metanalysis is recording were prespecified in that protocol.
Tian XQ (2015), Shanxi Med J, 52	Low risk Quotes: "Referring to random number table, the patients were divided into the observation group and the	Unclear Comment: the method o concealment no described	group received HBIG"	Unclear Comment: the study did not address this outcome	Unclear Comment: No statement about LFU (not reporting any LFU, and also not mentioning clearly that there	High risk  Comment: Though all the infants were included in this analysis, some key adverse	High risk  Comment: Though all women were included in this analysis, the adverse	High risk Comment: the protocol is available in the method section of the article. But one or more

	control group, with 110 cases in each group"		not address this outcome and no mention of placebo		were no cases LFU)	events including Apgar and bone density were not reported.	events observed, were not addressed	reported primary outcomes were not pre- specified (mainly maternal and infantile adverse reactions)
Yang HW	Low	Unclear	High risk	Unclear	Unclear	High risk	High risk	High risk
(2014),	risk/Unclear	Comment: the		Comment: the	Comment: No	Comment:	Comment:	Comment: the
	Quotes: "152 cases of	method of concealment no	1 0 1	study did not address this	statement about LFU (not	Though all the	Though all	protocol is available in
Hebei	pregnant women	described	experimental I group	outcome	reporting any	infants were	women were	the method
Medical	with chronic		received lamivudine on		LFU, and also not	included in this	included in	section of the
Journal,	hepatitis B were		the basis of HBIG"		mentioning	analysis, some key adverse	this analysis, some key	article. But
· ·	randomly divided into experimental		<i>Comment</i> : the study did not address this		clearly that there	events including	adverse	one or more
55	•		not address this outcome and no		were no cases LFU)	Apgar and bone	events, were	reported primary
	I group, experimental II group and control group, 53, 53 and 46 cases in the above three groups, respectively" Comment: the study did not describe the exact random component in the sequence generation process; and importantly, there's a disparity between the number of cases in the experimental		outcome and no mention of placebo		LFU)	density were not reported.	not addressed (e.g. antiviral resistance)	primary outcomes were not pre- specified (mainly maternal and infantile adverse reactions)

	group and that of									
Bai XW	the control group  Low	Unclear		High risk	Unclear		Unclear	Unclear	Unclear	Low risk
Dai AW	risk/Unclear	Comment:	the	Quotes: "The control	Comment:	the	Comment: No	Comment: the	Comment: the	Comment: the
(2011),	Quotes: "The	method	of	group received no	study did	not	statement about	study did not	study did not	protocol is
Maternal	patients were randomly divided	concealment described	not	antiviral treatment" "The observation group	address outcome	this	LFU (not reporting any	address this outcome	address this outcome	available in the method
and Child	into observation			1 received HBIG and			LFU, and also not			section of the
Health	group 1, observation group			the observation group 2 antiviral treatment with			mentioning clearly that there			article. The current
Care of	2 and control group, with 30, 30			lamivudine"  Comment: the study did			were no cases LFU)			outcomes of interest that
China, 45	and 25 cases, respectively"  Comment: the study did not describe the exact random component in the sequence generation process.  Importantly, disparity exists between the number of cases in observation groups and control groups.			not address this outcome and no mention of placebo						this meta- analysis is recording were pre- specified in that protocol.
Guo YZ	Low risk/Unclear	Unclear Comment:	the	High risk Quotes: "The control	Unclear Comment:	the	Unclear Comment: No	Unclear Comment: the	Unclear Comment: the	Low risk Comment: the
(2008),	Quotes: "The	method	of	group received no	study did	not	statement about	study did not	study did not	protocol is
Chin J of	patients were randomly divided	concealment described	not	antiviral treatment" "The observation group	address outcome	this	LFU (not reporting any	address this outcome	address this outcome	available in the method
Clinical	into the	20011200		received antiviral	Sucomo		LFU, and also not			section of the
Rational	observation group and the control			treatment with lamivudine"			mentioning clearly that there			article. The current
Drug	group, with 70 cases in the observation group			Comment: the study did not address this outcome and no			were no cases LFU)			outcomes of interest that this meta-

Use , 47	and 40 cases in	mention of placebo			analysis is
	the control group"				recording
	Comment: the				were pre-
	study did not				specified in
	describe the exact				that protocol.
	random				
	component in the				
	sequence				
	generation				
	process;				
	importantly,				
	there's a huge				
	disparity between				
	the numbers of				
	cases in				
	observation and				
	control groups				

### LDT 600 mg

# A. English language studies

None

**B.** Chinese language studies

Study (year), journal, No.	Selection bias		Performance bias Detection bias A		Attrition bias			Reporting bias
	Random sequence generation	Allocation concealment	Blinding of participants, personnel	Blinding of outcome assessment	MTCT	ome data addressed	Mother safety	Selective reporting
Wang HY (2018), Contemp orary Medicine, 99	Low risk/Unclear Quotes: "80 cases of pregnant women with chronic hepatitis B were randomly divided into experimental group and control group, 40 cases in each group" Comment: the study did not describe the exact random component in the sequence generation process	Unclear Comment: the method of concealment described	High risk Quotes: "The experimental group received LdT" "The control individuals did not receive antiviral treatment and were given supportive treatment or observation" Comment: the study did not address this outcome and no mention of placebo	Unclear Comment: the study did not address this outcome	Unclear Comment: No statement about LFU (not reporting any LFU, and also not mentioning clearly that there were no cases LFU)	High risk Comment: same numbers used as for MTCT outcome. Some key adverse events not addressed (e.g. prematurity, neonatal death, sub-optimal bone density)	Unclear Comment: the study did not address this outcome	High risk  Comment: the protocol is available in the method section of the article. But not all of the study's prespecified primary outcomes have been reported (i.e. maternal ALT). One or more reported primary outcomes were not prespecified (body length, birth weight,

Xing Y (2018), Clinical Research, 101	Low risk  Quotes:  "Referring to random number table, the patients were divided into the observation group and the control group, with 30 cases in each group"	concealment nedescribed	f group received regular liver protecting treatment with compound glycyrrhizin" "The observation group received LdT on the basis of regular liver protecting treatment for the control group" Comment: the study did not address this outcome and no mention of placebo	Unclear Comment: the study did not address this outcome	Unclear Comment: No statement about LFU (not reporting any LFU, and also not mentioning clearly that there were no cases LFU)	High risk Comment: same numbers used as for MTCT outcome. Only Apgar score reported. Some key adverse events not addressed (e.g. neonatal death, prematurity, congenital abnormality, sub- optimal bone density)	Unclear  Comment: the study did not address this outcome	age and congenital abnormality)  Low risk  Comment: the protocol is available in the method section of the article. The current outcomes of interest that this metanalysis is recording were prespecified in that protocol.
Zhang Y (2018), Chinese Journal of Woman and Child Health Research, 104	Low risk Quotes: "Referring to random number table, the patients were divided into the observation group and the control group, with 34 cases in each group"	Unclear Comment: the method concealment described	f group received regular	Unclear Comment: the study did not address this outcome	Unclear Comment: No statement about LFU (not reporting any LFU, and also not mentioning clearly that there were no cases LFU)	High risk Comment: same numbers used as for MTCT outcome. Only congenital abnormality and Apgar score reported. Other key adverse events not addressed.	High risk Comment: same numbers used as for MTCT outcome. Only CK reported. Key adverse events not addressed.	High risk  Comment: the protocol is available in the method section of the article. But not all of the study's pre- specified primary outcomes have been reported (e.g. maternal adverse events, HBV serological markers).
Chen SM (2017),	Low risk/Unclear Quotes:	Unclear Comment: the method	High risk e Quotes: "The control f group received no	Unclear Comment: the study did not	Unclear Comment: No statement about	Unclear Comment: the study did not	Unclear Comment: the study did not	Low risk Comment: the protocol is

Journal of China Prescripti on Drug, 46	"90 cases of pregnant women chronically infected with HBV were selected and randomly divided into lamivudine group, telbivudine group and control group, with 30 cases in each group"  Comment: the study did not describe the exact random component in the sequence generation process	concealment n described	antiviral treatment"  "The observation groups received antiviral treatment with lamivudine or telbivudine"  Comment: the study did not address this outcome and no mention of placebo	address this outcome	LFU (not reporting any LFU, and also not mentioning clearly that there were no cases LFU)	address this outcome	address this outcome	available in the method section of the article. The current outcomes of interest that this metanalysis is recording were prespecified in that protocol.
Guan ZF (2017), Acta Med Univ Sci Technol Huazhong , 91	Low risk Quotes: "Referring to random number table, the patients were divided into the observation group and the control group, with 120 cases in each group"	method	High risk Quotes: "The control group received liver protecting treatment with compound glycyrrhizin" "The observation group received antiviral treatment with telbivudine" Comment: the study did not address this outcome and no use of placebo	Unclear Comment: the study did not address this outcome	Unclear Comment: No statement about LFU (not reporting any LFU, and also not mentioning clearly that there were no cases LFU)	High risk Comment: same numbers used as for MTCT outcome. Only Apgar score reported. Other key adverse events not addressed.	High risk Comment: same numbers used as for MTCT outcome. Women considered until delivery. Only postpartum hemorrhage reported. Other key adverse events not addressed.	High risk  Comment: the protocol is available in the method section of the article. But one or more reported primary outcomes were not prespecified (e.g. maternal HBV DNA and ALT)
Shi QW (2017),	Low risk/Unclear Quotes:		High risk  Quotes: "The control group received HBIG"	Unclear Comment: the study did not	Unclear Comment: No statement about	High risk  Comment:	High risk  Comment:	High risk Comment: the protocol is

Mod Diagn Treat, 98	"200 cases of pregnant women with chronic hepatitis B were randomly divided into experimental group and control group, 100 cases in each group"  Comment: the study did not describe the exact random component in the sequence generation process	concealment not described	"The observation group received telbivudine on the basis of HBIG for the control group" Comment: the study did not address this outcome and no mention of placebo	address the outcome	LFU (not reporting any LFU, and also not mentioning clearly that there were no cases LFU)	Though all the infants were included in this analysis, some key adverse events including neonatal death and bone density were not reported.	Though all women were included in this analysis, some key adverse events, were not addressed (e.g. antiviral resistance, postpartum hemorrhage)	available in the method section of the article. But one or more reported primary outcomes were not pre- specified (mainly maternal adverse reactions)
Zhao Y (2017), J Prac Hepatol, 106	Low risk Quotes: "Referring to random number table, the patients were divided into the observation group and the control group, with 40 cases in each group"	Low risk Quotes: "sealed and opaque envelopes were used for concealment of the random allocation."	High risk Quotes: "The control group received compound glycyrrhizin" "The observation group received antiviral treatment with telbivudine on the basis of compound glycyrrhizin" Comment: the study did not address this outcome and no mention of placebo	Unclear Comment: the study did not address the outcome	t follow-up in both	High risk Comment: same numbers used as for MTCT outcome. Only Apgar score reported. Other key adverse events not addressed.	High risk Comment: same numbers used as for MTCT outcome. Women considered until 12 weeks after delivery. Only fever, chill and rash reported. Other key adverse events not addressed.	Low risk Comment: the protocol is available in the method section of the article. The current outcomes of interest that this meta- analysis is recording were pre- specified in that protocol.
Zhu J (2017), Maternal and Child Health	Low risk Quotes: "Referring to random number table, the patients were divided into the observation group and the	Unclear Comment: the method of concealment described	High risk Quotes: "The control group received no antiviral treatment" "The observation group received antiviral treatment with telbivudine"	Unclear Comment: the study did not address the outcome	t statement about	High risk Comment: same numbers used as for MTCT outcome. Only Apgar score and neonatal asphyxia reported. Other	High risk Comment: same numbers used as for MTCT outcome. Women considered	Low risk Comment: the protocol is available in the method section of the article. The current

Care of China, 107	control group, with 60 cases in each group"		Comment: the study did not address this outcome and no mention of placebo		were no cases LFU); 6 cases of foetal death in control group	key adverse events not addressed.	until delivery. Only foetal death and postpartum hemorrhage reported. Other key adverse events not addressed	outcomes of interest that this meta-analysis is recording were prespecified in that protocol.
Fu PX (2016), Psycholog ist, 90	risk/Unclear Quotes: "200 cases of pregnant women chronically infected with HBV were randomly divided into treated group and control group, with 100 cases in each group" Comment: the study did not describe the exact random component in the sequence generation process	Unclear Comment: the method of concealment described	High risk  Quotes: "The control group received no antiviral treatment" "The observation group received antiviral treatment with telbivudine"  Comment: the study did not address this outcome and no mention of placebo	Unclear Comment: the study did not address this outcome	Unclear  Comment: No statement about LFU (not reporting any LFU, and also not mentioning clearly that there were no cases LFU)	Unclear Comment: the study did not address this outcome	High risk Comment: same numbers used as for MTCT outcome. Women considered until delivery. Only CK elevation reported. Other key adverse events not addressed	High risk Comment: the protocol is available in the method section of the article. But not all of the study's pre- specified primary outcomes have been reported (e.g. maternal liver function, viral variants). One or more reported primary outcomes were not pre- specified (e.g. maternal CK)
Huang	Low risk	Unclear	High risk	Unclear	Unclear	Unclear	Unclear	Low risk
HY	Quotes: "Referring to	Comment: the method of	Quotes: "The control group received no	Comment: the study did not	Comment: No statement about	Comment: the study did not	Comment: the study did not	Comment: the protocol is
(2016), Chinese	random number table, the patients were divided into	concealment not described	antiviral treatment" "The observation group 1, 2 and 3 received	address this outcome	LFU (not reporting any LFU, and also not	address this outcome	address this outcome	available in the method section of the
	the observation		antiviral treatment with		mentioning			article. The

Journal of Eugenics and Genetics, 94	group 1, 2, 3 and the control group, with 30 cases in each group"		telbivudine at 20, 24 and 28 weeks, respectively"  Comment: the study did not address this outcome and no mention of placebo		clearly that there were no cases LFU)			current outcomes of interest that this meta- analysis is recording were pre- specified in that protocol.
Xie PY (2016), Psycholog ist, 100	Low risk Quotes: "Referring to random number table, the patients were divided into the observation group and the control group, with 60 cases in each group"	Unclear Comment: the method of concealment described	High risk  Quotes: "The control group received no antiviral treatment" "The observation group received antiviral treatment with telbivudine"  Comment: the study did not address this outcome and no mention of placebo	Unclear Comment: the study did not address this outcome	Unclear Comment: No statement about LFU (not reporting any LFU, and also not mentioning clearly that there were no cases LFU)	Unclear  Comment: the study did not address outcome	Unclear Comment: the study did not address this outcome	Low risk  Comment: the protocol is available in the method section of the article. The current outcomes of interest that this metaanalysis is recording were prespecified in that protocol
Lu QY (2016), Henan J Prev Med, 96	risk/Unclear Quotes: "The patients were randomly divided into the observation group and the control group, with 152 cases in the observation group and 132 cases in the control group" Comment: the study did not describe the exact	Unclear Comment: the method of concealment described	High risk Quotes: "The control group received HBIG" "The observation group received telbivudine on the basis of HBIG for the control group" Comment: the study did not address this outcome and no mention of placebo	Unclear Comment: the study did not address outcome	Unclear Comment: No statement about LFU (not reporting any LFU, and also not mentioning clearly that there were no cases LFU)	High risk  Comment: Though all the infants were included in this analysis, some key adverse events including Apgar and bone density were not reported.	High risk  Comment: Though all women were included in this analysis, some key adverse events, were not addressed (e.g. antiviral resistance, postpartum hemorrhage)	High risk  Comment: the protocol is available in the method section of the article. But one or more reported primary outcomes were not prespecified (mainly maternal and infantile

Ji YY (2015), Chin J Postgrad Med, 50	random component in the sequence generation process; and importantly, there's a huge disparity between the number of cases in the observation group and that of the control group  Low risk Quotes: "Referring to random number table, the patients were divided into telbivudine group, lamivudine group, with 65 cases in each group"	Unclear  Comment: the method of concealment described	group received no antiviral treatment" "The observation group received antiviral treatment with telbivudine or lamivudine"  Comment: the study did not address this outcome and no mention of placebo	Unclear Comment: the study did not address this outcome	Unclear  Comment: No statement about LFU (not reporting any LFU, and also not mentioning clearly that there were no cases LFU)	Unclear  Comment: the study did not address this outcome	Unclear Comment: the study did not address this outcome	High risk Comment: the protocol is available in the method section of the article. But not all of the study's prespecified primary outcomes have been reported (e.g. maternal liver function after antiviral treatment).
Li SF. (2015), World of Mother and	risk/Unclear Quotes: "The patients were randomly divided into the observation group and the control	Unclear Comment: the method of concealment not described	High risk Quotes: "The control group received no antiviral treatment" "The observation group received antiviral treatment with telbivudine"	Unclear Comment: the study did not address this outcome	Unclear Comment: No statement about LFU (not reporting any LFU, and also not mentioning clearly that there	High risk Comment: same numbers used as for MTCT outcome. Only Apgar score reported. Other key adverse	High risk Comment: same numbers used as for MTCT outcome. Women considered	High risk Comment: the protocol is available in the method section of the article. But one or more

Infant, 95	group, with 60 cases in each group"  Comment: the study did not describe the exact random component in the sequence generation process		Comment: the study did not address this outcome and no mention of placebo		were no cases LFU)	events not addressed.	until 6 months after delivery. Only adverse reactions, abnormal pregnancy, and CK elevation reported. Other key adverse events not addressed	reported primary outcomes were not pre- specified (e.g. abnormal pregnancy). One or more outcomes of interest in the review are reported incompletely so that they cannot be entered in a meta-analysis (e.g. Apgar score).
Yang HW	Low	Unclear	High risk	Unclear	Unclear	Unclear	High risk	High risk
(2015),	risk/Unclear Quotes: "The	method of	~	Comment: the study did not	Comment: No statement about	Comment: the study did not	Comment: same numbers	Comment: the protocol is
1 '								
Journal of	patients were randomly divided	concealment no described		address this outcome	LFU (not reporting any	address this outcome	used as for MTCT	available in the method
Journal of Hainan	randomly divided into the	concealment no described	"The observation group received antiviral	address this outcome	reporting any LFU, and also not		MTCT outcome.	the method section of the
	randomly divided into the intervention group		"The observation group received antiviral treatment with		reporting any LFU, and also not mentioning		MTCT outcome. Women	the method section of the article. But
Hainan	randomly divided into the intervention group and the control group, with 50		"The observation group received antiviral treatment with telbivudine" <i>Comment</i> : the study did		reporting any LFU, and also not mentioning clearly that there were no cases		MTCT outcome. Women considered until delivery.	the method section of the article. But one or more reported
Hainan Medical	randomly divided into the intervention group and the control group, with 50 cases in each group"		"The observation group received antiviral treatment with telbivudine"  Comment: the study did not address this outcome and no		reporting any LFU, and also not mentioning clearly that there		MTCT outcome. Women considered until delivery. Only adverse reactions	the method section of the article. But one or more reported primary outcomes
Hainan Medical Universit	randomly divided into the intervention group and the control group, with 50 cases in each group"  Comment: the study did not		"The observation group received antiviral treatment with telbivudine"  Comment: the study did not address this		reporting any LFU, and also not mentioning clearly that there were no cases		MTCT outcome. Women considered until delivery. Only adverse reactions reported. Other key	the method section of the article. But one or more reported primary outcomes were not pre- specified (e.g.
Hainan Medical Universit	randomly divided into the intervention group and the control group, with 50 cases in each group"  Comment: the study did not describe the exact		"The observation group received antiviral treatment with telbivudine"  Comment: the study did not address this outcome and no		reporting any LFU, and also not mentioning clearly that there were no cases		MTCT outcome. Women considered until delivery. Only adverse reactions reported. Other key adverse events	the method section of the article. But one or more reported primary outcomes were not pre- specified (e.g. maternal
Hainan Medical Universit	randomly divided into the intervention group and the control group, with 50 cases in each group"  Comment: the study did not		"The observation group received antiviral treatment with telbivudine"  Comment: the study did not address this outcome and no		reporting any LFU, and also not mentioning clearly that there were no cases		MTCT outcome. Women considered until delivery. Only adverse reactions reported. Other key	the method section of the article. But one or more reported primary outcomes were not pre- specified (e.g.
Hainan Medical Universit	randomly divided into the intervention group and the control group, with 50 cases in each group"  Comment: the study did not describe the exact random component in the sequence		"The observation group received antiviral treatment with telbivudine"  Comment: the study did not address this outcome and no		reporting any LFU, and also not mentioning clearly that there were no cases		MTCT outcome. Women considered until delivery. Only adverse reactions reported. Other key adverse events	the method section of the article. But one or more reported primary outcomes were not pre- specified (e.g. maternal adverse
Hainan Medical Universit	randomly divided into the intervention group and the control group, with 50 cases in each group"  Comment: the study did not describe the exact random component in the		"The observation group received antiviral treatment with telbivudine"  Comment: the study did not address this outcome and no		reporting any LFU, and also not mentioning clearly that there were no cases		MTCT outcome. Women considered until delivery. Only adverse reactions reported. Other key adverse events	the method section of the article. But one or more reported primary outcomes were not pre- specified (e.g. maternal adverse

D 3/1	т	TT1		TT' - 1	TT1		TT1	TT		TT1	T
Peng ML	Low	Unclear	.1	High risk	Unclear	.1	Unclear	Unclear	41	Unclear	Low risk
(2014),	risk/Unclear		the	Quotes: "The control	Comment:	the	Comment: No	Comment:	the	Comment: the	Comment: the
(2014),	Quotes:	method	of	group received HBIG"	study did	not	statement about	study did	not	study did not	protocol is
Chin J	"60 cases of		not	"The observation group	address	this	LFU (not	address	this	address this	available in
	pregnant women	described		received telbivudine on	outcome		reporting any	outcome		outcome	the method
Nosocomi	with chronic			the basis of HBIG for			LFU, and also not				section of the
ol, 97	hepatitis B were			the control group"			mentioning				article. The
01, 77	randomly divided			Comment: the study did			clearly that there				current
	into experimental			not address this			were no cases				outcomes of
	group and control			outcome and no			LFU)				interest that
ı	group, 30 cases in			mention of placebo							this meta-
ı	each group"										analysis is
ı	Comment: the										recording
ı	study did not										were pre-
ı	describe the exact										specified in
i l	random										that protocol.
i l	component in the										
	sequence										
	generation										
	process										
Zhu LP	Low	Unclear		High risk	Unclear		Unclear	Unclear		High risk	High risk
(2014)	risk/Unclear		the	Quotes: "The control	Comment:	the	Comment: No	Comment:	the	Comment:	Comment: the
(2014),	Quotes: "The	method	of	group received no	study did	not	statement about	study did	not	same numbers	protocol is
, ,					address	this		address	this	used as for	available in
Chin J	patients were		not	antiviral treatment"		uns	LFU (not		tills		
Chin J	randomly divided	concealment described	not	"The observation group	outcome	uns	reporting any	outcome	uns	MTCT	the method
Chin J Mod	randomly divided into the		not	"The observation group received antiviral		uns	reporting any LFU, and also not		uns	MTCT outcome.	the method section of the
Mod	randomly divided into the observation group		not	"The observation group received antiviral treatment with		uns	reporting any LFU, and also not mentioning			MTCT outcome. Women	the method section of the article. But
	randomly divided into the observation group and the control		not	"The observation group received antiviral treatment with telbivudine"		uns	reporting any LFU, and also not mentioning clearly that there			MTCT outcome. Women considered	the method section of the article. But one or more
Mod Drug	randomly divided into the observation group and the control group, with 30		not	"The observation group received antiviral treatment with telbivudine"  Comment: the study did		uns	reporting any LFU, and also not mentioning clearly that there were no cases		uns	MTCT outcome. Women considered until delivery.	the method section of the article. But one or more reported
Mod	randomly divided into the observation group and the control group, with 30 cases in each		not	"The observation group received antiviral treatment with telbivudine"  Comment: the study did not address this		uns	reporting any LFU, and also not mentioning clearly that there			MTCT outcome. Women considered until delivery. Only adverse	the method section of the article. But one or more reported primary
Mod Drug	randomly divided into the observation group and the control group, with 30 cases in each group"		not	"The observation group received antiviral treatment with telbivudine"  Comment: the study did not address this outcome and no		uns	reporting any LFU, and also not mentioning clearly that there were no cases			MTCT outcome. Women considered until delivery. Only adverse reactions,	the method section of the article. But one or more reported primary outcomes
Mod Drug	randomly divided into the observation group and the control group, with 30 cases in each group"  Comment: the		not	"The observation group received antiviral treatment with telbivudine"  Comment: the study did not address this		uns	reporting any LFU, and also not mentioning clearly that there were no cases			MTCT outcome. Women considered until delivery. Only adverse reactions, renal function	the method section of the article. But one or more reported primary outcomes were not pre-
Mod Drug	randomly divided into the observation group and the control group, with 30 cases in each group"  Comment: the study did not		not	"The observation group received antiviral treatment with telbivudine"  Comment: the study did not address this outcome and no		uns	reporting any LFU, and also not mentioning clearly that there were no cases			MTCT outcome. Women considered until delivery. Only adverse reactions, renal function despair, and	the method section of the article. But one or more reported primary outcomes were not pre- specified (e.g.
Mod Drug	randomly divided into the observation group and the control group, with 30 cases in each group"  Comment: the study did not describe the exact		not	"The observation group received antiviral treatment with telbivudine"  Comment: the study did not address this outcome and no		uns	reporting any LFU, and also not mentioning clearly that there were no cases			MTCT outcome. Women considered until delivery. Only adverse reactions, renal function despair, and CK elevation	the method section of the article. But one or more reported primary outcomes were not prespecified (e.g. maternal
Mod Drug	randomly divided into the observation group and the control group, with 30 cases in each group"  Comment: the study did not describe the exact random		not	"The observation group received antiviral treatment with telbivudine"  Comment: the study did not address this outcome and no		uns	reporting any LFU, and also not mentioning clearly that there were no cases			MTCT outcome. Women considered until delivery. Only adverse reactions, renal function despair, and CK elevation reported.	the method section of the article. But one or more reported primary outcomes were not prespecified (e.g. maternal adverse
Mod Drug	randomly divided into the observation group and the control group, with 30 cases in each group"  Comment: the study did not describe the exact random component in the		not	"The observation group received antiviral treatment with telbivudine"  Comment: the study did not address this outcome and no		uns	reporting any LFU, and also not mentioning clearly that there were no cases			MTCT outcome. Women considered until delivery. Only adverse reactions, renal function despair, and CK elevation reported. Other key	the method section of the article. But one or more reported primary outcomes were not prespecified (e.g. maternal
Mod Drug	randomly divided into the observation group and the control group, with 30 cases in each group"  Comment: the study did not describe the exact random component in the sequence		not	"The observation group received antiviral treatment with telbivudine"  Comment: the study did not address this outcome and no		uns	reporting any LFU, and also not mentioning clearly that there were no cases			MTCT outcome. Women considered until delivery. Only adverse reactions, renal function despair, and CK elevation reported. Other key adverse events	the method section of the article. But one or more reported primary outcomes were not prespecified (e.g. maternal adverse
Mod Drug	randomly divided into the observation group and the control group, with 30 cases in each group"  Comment: the study did not describe the exact random component in the		not	"The observation group received antiviral treatment with telbivudine"  Comment: the study did not address this outcome and no		uns	reporting any LFU, and also not mentioning clearly that there were no cases			MTCT outcome. Women considered until delivery. Only adverse reactions, renal function despair, and CK elevation reported. Other key	the method section of the article. But one or more reported primary outcomes were not prespecified (e.g. maternal adverse
Mod Drug	randomly divided into the observation group and the control group, with 30 cases in each group"  Comment: the study did not describe the exact random component in the sequence		not	"The observation group received antiviral treatment with telbivudine"  Comment: the study did not address this outcome and no		uns	reporting any LFU, and also not mentioning clearly that there were no cases			MTCT outcome. Women considered until delivery. Only adverse reactions, renal function despair, and CK elevation reported. Other key adverse events	the method section of the article. But one or more reported primary outcomes were not prespecified (e.g. maternal adverse

Bai HL (2013), China Medical Engineeri ng, 89	risk/Unclear Quotes: "The patients were randomly divided into the observation group and the control group, with 30 cases in each group" Comment: the study did not describe the exact random component in the sequence generation process	method	High risk Quotes: "The control group received no antiviral treatment" "The observation group received antiviral treatment with telbivudine" Comment: the study did not address this outcome and no mention of placebo		Low risk Comment: 100% follow-up in both treated and control group	High risk Comment: same numbers used as for MTCT outcome. Only CK elevation reported. Other key adverse events not addressed.	High risk Comment: same numbers used as for MTCT outcome. Women considered until delivery. Only adverse reactions, renal function despair, and CK elevation reported. Other key adverse events not addressed.	High risk  Comment: the protocol is available in the method section of the article. But one or more reported primary outcomes were not prespecified (e.g. maternal and infantile adverse effects). One or more outcomes of interest in the review are reported incompletely so that they cannot be entered in a meta-analysis (e.g. postpartum hemorrhage)
Guo HJ	Low risk/Unclear	Unclear Comment: t	Unclear ne Quotes: "The control	Unclear Comment: the	Unclear Comment: No	Unclear Comment: the	Unclear Comment: the	High risk Comment: the
(2011),	Quotes: "The patients were		of group received placebo	study did not address this	statement about LFU (not	study did not address this	study did not address this	protocol is available in
Journal of	randomly divided	described	manufacturer" "The	outcome	reporting any	outcome	outcome	the method
Changzhi	into the		observation group received antiviral		LFU, and also not			section of the article. But
Medical	observation group and the control		treatment with		mentioning clearly that there			one or more
College,	group, with 25 cases in each		telbivudine"  Comment: the study did		were no cases LFU)			reported primary

93	group"  Comment: the study did not describe the exact random component in the sequence generation process		not address this outcome, though mention of placebo					outcomes were not pre- specified (e.g. maternal liver function, total bilirubin, and HBV DNA).
Zhao DB	Low	Unclear	High risk	Unclear	Unclear	Unclear	Unclear	High risk
(2010),	risk/Unclear Quotes: "The	method	ne Quotes: "The control group received no	Comment: the study did not	Comment: No statement about	Quotes: "no adverse reactions	Quotes: "no adverse	Comment: the protocol is
Chin J	patients were randomly divided	concealment n described	antiviral treatment" "The observation group	address this outcome	LFU (not reporting any	found in two groups of mothers	reactions found in two	available in the method
Mod	into the		received antiviral		LFU, and also not	and infants"	groups of	section of the
Drug	observation group and the control		treatment with telbivudine"		mentioning clearly that there	Comment: insufficient	mothers and infants"	article. But one or more
Appl, 105	group, with 30 cases in each group"  Comment: the study did not describe the exact random component in the sequence generation process		Comment: the study did not address this outcome and no mention of placebo		were no cases LFU)	reporting	Comment: insufficient reporting	reported primary outcomes were not prespecified (e.g. maternal and infantile adverse reactions). One or more outcomes of interest in the review are reported incompletely so that they cannot be entered in a meta-analysis (e.g. maternal and infantile adverse reactions).

Zhang LJ	Low	Unclear		High risk	Unclear		Low risk	High risk	High risk	High risk
(2000)	risk/Unclear	Comment:	the	Quotes: "The control	Comment: th	ıe	Comment: 96.8%	Comment: all	Comment: All	Comment: the
(2009),	Quotes: "The	method	of	group received no	study did no	ot	and 100.0% with	infants included in	women	protocol is
Chin J	patients were		not	antiviral treatment"	address th	is	full follow-up in	this analysis from	considered	available in
	randomly divided	described		"The observation group	outcome		treated and	both treated and	until delivery.	the method
Hepatol,	into the			received antiviral			control group	control groups.	Only adverse	section of the
102	observation group			treatment with			respectively.	Only CK	reactions,	article. But
103	and the control			telbivudine"			Similar follow-up	elevation	renal function	one or more
	group, with 31			Comment: the study did			proportions in	reported. Other	despair, and	reported
	cases in the			not address this			each group.	key adverse	CK elevation	primary
	observation group			outcome and no				events not	reported.	outcomes
	and 30 cases in			mention of placebo				addressed.	Other key	were not pre-
	the control group"								adverse events	specified (e.g.
	Comment: the								not addressed.	maternal and
	study did not									infantile
	describe the exact									adverse
	random									effects). One
	component in the									or more
	sequence									outcomes of
	generation									interest in the
	process									review are
										reported
										incompletely
										so that they
										cannot be
										entered in a
										meta-analysis
										(e.g.
										postpartum
										hemorrhage).

## **Appendix G: Newcastle-Ottawa Risk of Bias Assessment Tool for non-RCTs** TDF 300 mg

A. English Language Observational Studies

3	0 0	Jusci vationa		Demonstration			Was follow-		Total
	Representa	Selection of		that outcome of	Comparability of		up long		number
Study	tive-ness of	the non-		interest was	cohorts on the basis		enough for	Adequacy of	of stars
(year),	the exposed	exposed	Ascertainment	not present at	of the design or	Assessment of	outcomes	follow up of	(risk of
journal, No.	cohort	cohort	of exposure	baseline	analysis	outcomes	occur	cohorts	bias) <sup>a</sup>
Celen MK,	☆	☆	Do not provide	☆	<b>44</b>	☆	☆	None reported	7
(2013),	,		many details on	,		,		(retrospective)	(low)
World J	At least	Drawn from the	decrease of HBV	Always the case	Comparable for HBV	Describes testing	Yes		
	somewhat	same	DNA levels, no		DNA level and	done and refers to			
Gastroenter	representative	community	other discussion		comparable HBeAg	a central			
ol, 28	of the average	(same inclusion	of maternal		positive. Same regimen	laboratory			
	HBV infected	and exclusion	adherence.		for infant	employed for this			
	pregnant	criteria also)			immunoprophylaxis.	study.			
	woman								
Greenup AJ	攻	☆	<b>☆</b>	<b>☆</b> Always the	<b>☆☆</b> Comparable for	No details given	☆	> 20% LFU in	7
(2014), J	·					on laboratory	,	control group,	(low)
	At least	Drawn from the	Reporting on	case	HBV DNA level and	methods for	Yes	although <20% LFU	` /
Hepatol, 32	somewhat	same	adherence within		comparable HBeAg	infants, and no		in two treatment	
	representative	community	the paper,		positive. Same regimen	details of which		groups	
	of the average	(same inclusion	reduction of viral		for infant	assay was used for			
	HBV infected	and exclusion	load used to		immunoprophylaxis and	testing HBsAg			
	pregnant	criteria also)	assess women's		confirmation that all				
	woman		response to		infants received it.				
			treatment.						

Chen HL,	☆	*	*	☆	**	☆	*	☆	9
(2015), Hepatology, 29	At least somewhat representative of the average HBV infected pregnant woman	Drawn from the same community (same inclusion and exclusion criteria also)	Regular testing (and pre-delivery testing) of HBV DNA levels were correlated with duration of treatment in mothers	Always the case	Comparable for HBV DNA level and comparable HBeAg positive. Same regimen for infant immunoprophylaxis.	Describes test assays used for HBsAg and HBV DNA and acknowledges a study laboratory.	Yes	LFU reported and <20% LFU in all treatment and control groups	(low)
Kochaksarei GS, (2016) <sup>1</sup>	At least somewhat representative of the average HBV infected pregnant woman	Not same population, the untreated did not have high viremia or pre-existing liver disease, whereas the treated did.	Adherence is mentioned but was ascertained in 16/23 women (<70%), and only 2/3rds had good adherence.	<b>☆</b> Always the case	Not comparable for HBV DNA level or HBeAg positive. Apparently the same regimen for infant immunoprophylaxis, however very few details stated.	Testing done centrally, and methods/assays for testing described.	<b>★</b> Yes	<80% follow-up in both treated and control groups	5 (high)
Wakano Y, (2018), J Obstet Gynaecol Res, 39	Not representative of the general population (women who've had a child infected previously)	Drawn from the same community with same inclusion and exclusion criteria.	>2 log reduction of HBV DNA levels in all treated women	<b>☆</b> Always the case	HBV DNA level and comparable HBeAg positive. Different immunoprophylaxis regimens mixed amongst the groups of treated and	Laboratory assays not well described.	<b>☆</b> Yes	☆ 100% retention	6 (high)

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<sup>&</sup>lt;sup>1</sup> Kochaksaraei GS, Castillo E, Osman M, et al. Clinical course of 161 untreated and tenofovir-treated chronic hepatitis B pregnant participants in a low hepatitis B virus endemic region. *J Viral Hepat* 2016; **23(1)**:15-22.

ſ			non-treated.		

<sup>&</sup>lt;sup>a</sup>Risk of bias assessments should be classified as being either low (≥ 7) or high (< 7) by the Newcastle-Ottawa scale

**B.** Chinese Language Observational Studies

	anguage Obse			Demonstration	Comparability of		Was follow-		
		Selection of		that outcome of	cohorts on the		up long	Adequacy	Total
	Representative	the non-		interest was not	basis of the		enough for	of follow	number of
Study (year),	-ness of the	exposed	Ascertainment	present at	design or	Assessment	outcomes	up of	stars (risk of
journal, No.	exposed cohort	cohort	of exposure	baseline	analysis	of outcomes	occur	cohorts	bias) <sup>a</sup>
He LL, (2018), Maternal and	At least somewhat	Drawn from the same	★ Valid method was used to	Always the	★ Comparable for HBV DNA	<b>☆</b> Laboratory	<b>★</b> Yes	No statement of LFU	7 (low)
Child Health	representative of	community	ascertain		levels at baseline but	methods		Of Life	
Care of China,	the average HBV	(same inclusion	adherence to the		HBeAg sero-status	described in			
36	infected pregnant	and exclusion	antiviral therapy		not described. Same	detail (which			
	woman	criteria also)	(decrease in viral		regimen for infant	assay used),			
			load levels		immunoprophylaxis	indicating use			
			subsequent to the		at birth	of a central			
			treatment)			laboaratory			
						and/or record			
						linkage.			
Hu MF,	🖈 At least	<b>☆</b> Drawn	★ Valid method	Always the	<b>★</b> Comparable	*	<b>≯</b> Yes	No	7 (low)
(2018), Chin J	somewhat	from the same	was used to	case	for HBV DNA	Laboratory		statement of LFU	
Drug Depend,	representative of	community	ascertain		levels at baseline but	methods		of Live	
37	the average HBV	(same inclusion	adherence to the		HBeAg sero-status	described in			
	infected pregnant	and exclusion	antiviral therapy		not described. Same	detail (which			
	woman	criteria also)	(decrease in viral		regimen for infant	assay used),			
			load levels		immunoprophylaxis	indicating use			
			subsequent to the		at birth	of a central			
			treatment)			laboaratory			
						and/or record			
						linkage.			

Wang HB,	<b>★</b> At least	<b>☆</b> Drawn	★ Valid method	☆	Always the	★ Same threshold	Laboratory	<b>★</b> Yes	No	7 (low)
(2018), Chin J Exp Clin	somewhat representative of	from the same community	was used to ascertain	case		for HBV DNA level but HBeAg sero-	methods described in		statement of LFU	
Infect Dis, 41	the average HBV infected pregnant woman	(same inclusion and exclusion criteria also)	adherence to the antiviral therapy (decrease in viral load levels subsequent to the treatment)			status not described.  Same regimen for infant immunoprophylaxis at birth	detail (which assay used), indicating use of a central laboaratory and/or record linkage.			
Zhang BF, (2018), Chin J Hepatol, 43	At least somewhat representative of the average HBV infected pregnant woman	Drawn from the same community (same inclusion and exclusion criteria also)	▼ Valid method  was used to ascertain  adherence to the antiviral therapy (decrease in viral load levels subsequent to the treatment)	<b>☆</b> case	Always the	sero-status but different thresholds for HBV DNA level. Same regimen for infant immunoprophylaxis at birth	No description	<b>★</b> Yes	No statement of LFU	6 (high)
Zhou Y, (2018), New Medical Science, 44	At least somewhat representative of the average HBV infected pregnant woman	Drawn from the same community (same inclusion and exclusion criteria also)	Valid method was used to ascertain adherence to the antiviral therapy (decrease in viral load levels subsequent to the treatment)	case	Always the	HBeAg sero-status and same thresholds for HBV DNA level. Same regimen for infant immunoprophylaxis at birth	Laboratory methods described in detail (which assay used), indicating use of a central laboaratory	<b>☆</b> Yes	No statement of LFU	8 (low)

Chen WJ, (2017), Shandong Medicine, 30	At least somewhat representative of the average HBV infected pregnant woman	Drawn from the same community (same inclusion and exclusion criteria also)	▼ Valid method  was used to ascertain  adherence to the antiviral therapy (decrease in viral load levels subsequent to the treatment)  ▼ Valid method	☆ case	Always the	★★ Same  HBeAg sero-status and same thresholds for HBV DNA level.  Same regimen for infant immunoprophylaxis at birth	and/or record linkage.  **Laboratory methods described in detail (which assay used), indicating use of a central laboaratory and/or record linkage.  No	<b>★</b> Yes	No statement of LFU	8 (low) 6 (high)
(2017), China Continuing Medical Education, 31	At least somewhat representative of the average HBV infected pregnant woman	from the same community (same inclusion and exclusion criteria also)	was used to ascertain adherence to the antiviral therapy (decrease in viral load levels subsequent to the treatment)	case	Always the	sero-status and threshold for HBV DNA level not described. Same regimen for infant immunoprophylaxis at birth	description	₹ Yes	statement of LFU	
Huang Q, (2017), Qinghai Medical Journal, 38	At least somewhat representative of the average HBV infected pregnant woman	Drawn from the same community (same inclusion and exclusion criteria also)	▼ Valid method  was used to ascertain  adherence to the antiviral therapy (decrease in viral load levels	<b>☆</b> case	Always the	HBeAg sero-status and same thresholds for HBV DNA level. Same regimen for infant immunoprophylaxis	No description	<b>★</b> Yes	No statement of LFU	7 (low)

Wan JY, (2017), China Tropical Medicine, 40	At least somewhat representative of the average HBV infected pregnant woman	Drawn from the same community (same inclusion and exclusion criteria also)	subsequent to the treatment)  Valid method was used to ascertain adherence to the antiviral therapy (decrease in viral load levels subsequent to the treatment)	★ Always the case	at birth  Same thresholds for HBV DNA level but HBeAg sero-status not described. Regimen for infant immunoprophylaxis at birth not described	★Laboratory methods described in detail (which assay used), indicating use of a central laboaratory and/or record	<b>≯</b> Yes	No statement of LFU	6 (high)
Xiao XH, (2017), Maternal and Child Health Care of China, 42	At least somewhat representative of the average HBV infected pregnant woman	Drawn from the same community (same inclusion and exclusion criteria also)	▼ Valid method  was used to ascertain  adherence to the antiviral therapy (decrease in viral load levels subsequent to the treatment)	<b>★</b> Always the case	Same thresholds for HBV DNA level but HBeAg sero-status not described. Regimen for infant immunoprophylaxis at birth not clearly described	Laboratory methods described in detail (which assay used), indicating use of a central laboaratory and/or record linkage.	<b>☆</b> Yes	There is a description of LFU for the exposed but not for the control group	6 (high)

<sup>&</sup>lt;sup>a</sup>Risk of bias assessments should be classified as being either low ( $\geq$  7) or high (< 7) by the Newcastle-Ottawa scale

## LAM 100-150 mg

A. English Language Observational Studies

3	0 0	Jusci vationa		Demonstration			Was follow-		Total
	Representa	Selection of		that outcome of	Comparability of		up long		number
	tive-ness of	the non-		interest was	cohorts on the basis		enough for	Adequacy of	of stars
Study	the exposed	exposed	Ascertainment	not present at	of the design or	Assessment of	outcomes	follow up of	(risk of
(year)	cohort	cohort	of exposure	baseline	analysis	outcomes	occur	cohorts	bias) <sup>a</sup>
Greenup AJ	☆	☆	*	★ Always the	Comparable for	No details given	₩ ₩	> 20% LFU in	7
(2014), J	At least	Drawn from the	Reporting on	case	HBV DNA level and	on laboratory	Yes	control group,	(low)
Hepatol, 32	somewhat	same	adherence within	case	comparable HBeAg	methods for infants, and no	165	although <20% LFU in two treatment	
_	representative	community	the paper,		positive. Same regimen	details of which		groups	
	of the average	(same inclusion	reduction of viral		for infant	assay was used for		groups	
	HBV infected	and exclusion	load used to		immunoprophylaxis and	testing HBsAg			
	pregnant	criteria also)	assess women's		confirmation that all				
	woman		response to		infants received it.				
			treatment.						
Zhang H	☆	❖	☆	<b>☆</b>	**	☆	*	☆	9
(2014),	At least	Drawn from	Monthly HBV	Always the case	Comparable for HBV	Describes testing	Yes	LFU reported and	(low)
Hepatology,	somewhat	the same	DNA level testing	7 ii ways the case	DNA level and	done and refers to	105	<20% LFU in all	
85	representative	community	was done to check		comparable HBeAg	a central		treatment and	
	of the average	(same inclusion	maternal		positive. Same regimen	laboratory		control groups	
	HBV infected	and exclusion	adherence		for infant	employed for this			
	pregnant	criteria also)			immunoprophylaxis.	study.			
	woman								
Jackson V	<b>☆</b>	<b>☆</b>	女	女	HBV DNA level and	☆	<b>☆</b>	<80% retention in	6
(2015), Eur	At least	Drawn from the	Mentions good	Always the case	HBeAg not described in control group. Mentions	Laboratory	Yes	both treated and control groups	(high)

J	Clin	somewhat	same	treatment		that all infants received	assays described,			
Microb	io1	representative	community	compliance in all		the same regimen for	with indication of			
		of the average	(same inclusion	but one patient,		infant	record linkage			
Infect	Dis,	HBV infected	and exclusion	and measures		immunoprophylaxis,	(results viewed			
67		pregnant	criteria also)	decrease in viral		however, in the control	retrospectively in			
		woman		load in 35/36		group, many women	medical records)			
				women taking		defaulted from				
				treatment just		care/moved to other				
				prior to delivery		maternities, so this does				
				and saw a		not seem well verified.				
				significant						
				decrease in most						
				patients (also						
				show these results						
				in a figure in the						
				paper).						
Liu	CP	女	Many more	Some limited data	☆	<b>☆</b>	☆	☆	No loss to follow-up	5 (high)
$(2015)^2$	!		women	presented on	,				described because it	
		At least	included in the	decrease of	Always the case	HBV DNA level and/or	Laboratory	Yes	was a retrospective	
		somewhat .	control group	maternal viral		HBeAg not described for	assays described,		cohort study (or	
		representative	(highly	load, but no		both treated and control	with indication of		listed as such) where	
		of the average	disproportionate	mention of linking		groups. Similar infant	record linkage		the infants needed to	
		HBV infected	which could	this with		prophylaxis between	(results viewed		have had test results	
		pregnant	indicate non-	compliance/adher		treated and control	retrospectively in		at the testing	
		woman	similarity with	ence/time on		groups.	medical records)		timepoint (this is	
			the treated)	treatment, and no					therefore	
				detailed results					misclassified as a	
				provided.					cohort study, and	

\_

<sup>&</sup>lt;sup>2</sup> Liu CP, Zeng YL, Zhou M, et al. Factors Associated with Mother-to-child Transmission of Hepatitis B Virus Despite Immunoprophylaxis. *Intern Med* 2015; **54(7)**: 711-716.

Pan CQ (2017), J Viral Hepat, 73	At least somewhat representative of the average HBV infected pregnant woman	Same population and criteria, however, no indication of how this group was chosen (usually says 'unwillingness', for example)	Some data presented on decrease of maternal viral load, but no mention of linking this with compliance/adher ence/time on treatment.  Additionally, because of study design (retrospective) there is low/no chance of	<b>☆</b> Always the case	Comparable for HBV DNA level and comparable HBeAg positive. Same regimen for infant immunoprophylaxis	Reference to the hospital's centralized laboratory and linkage to medical records for assessing infant outcome.	<b>☆</b> Yes	has a high risk of bias for loss to follow-up)  No loss to follow-up described because it was a retrospective cohort study (or listed as such) where the infants needed to have had test results at the testing time-point (this is therefore misclassified as a cohort study, and has a high risk of bias for loss to follow-up)	6 (high)
Не Т			adherence monitoring.					Retrospective cohort	8
(2018), Hepatol Int, 64	At least somewhat representative of the average HBV infected pregnant woman	Drawn from the same community with same inclusion and exclusion criteria.	Detailed information on reduction of viral load given, including specific data for each women (every one had a -6 to -8 log	Always the case	Comparable for HBV  DNA level and comparable HBeAg positive. Same regimen for infant immunoprophylaxis	★     Linkage to medical records	<b>☆</b> Yes	mentioned but no loss to follow-up described, no mention of how there was perfect retention.	o (low)

			reduction)						
Wakano Y	Not	☆	☆	*	*	Laboratory assays	☆	☆	6
(2018), J	representative of the general	Drawn from	>2 log reduction	Always the case	Comparable for HBV	not well described.	Yes	100% retention	(high)
Obstet	population	the same	of HBV DNA	Timays the case	DNA level and	described.	105	100 /0 1010111011	
Gynaecol	(women	community with	levels in all		comparable HBeAg				
Res, 39	who've had a	same inclusion	treated women		positive. Different				
,	child infected	and exclusion			immunoprophylaxis				
	previously)	criteria.			regimens mixed amongst				
					the groups of treated and				
					non-treated.				
Foaud HM	な	Control group	☆	☆	☆	☆	☆	<80% follow-up at	6
(2019),	<b></b>	was comprised						6-12 months in	(high)
Arab J	Truly	of women who	States that women	Always the case	HBeAg proportion not	Lab testing done	Yes	control group,	
	representative	were not a	were given		comparable, and HBV	centrally as part of		though ~86%	
Gastroenter	of the average	candidate for	lamivudine		DNA at baseline not	the study,		follow-up in treated	
ol, 59	HBV infected	lamivudine	monthly and were		given. Same regimen for	laboratory assays		group at that	
	pregnant	(likely to be	questioned		infant	for defining infant		timepoint. (Note: at	
	woman	quite different	regarding		immunoprophylaxis	outcome		later timepoint, that	
		from those who	compliance at			described.		study defined, there	
		received it)	each visit.					was >80% followup)	

<sup>&</sup>lt;sup>a</sup>Risk of bias assessments should be classified as being either low (≥ 7) or high (< 7) by the Newcastle-Ottawa scale

**B.** Chinese Language Observational Studies

	aliguage Obse			Demonstration	Comparability of		Was follow-		
		Selection of		that outcome of	cohorts on the		up long	Adequacy	Total
	Representative	the non-		interest was not	basis of the		enough for	of follow	number of
Study (year),	-ness of the	exposed	Ascertainment	present at	design or	Assessment	outcomes	up of	stars (risk of
journal, No.	exposed cohort	cohort	of exposure	baseline	analysis	of outcomes	occur	cohorts	bias) <sup>a</sup>
Chen QR	<b>☆</b> At least	<b>☆</b> Drawn	No description	<b>☆</b> Always the	<b>☆☆</b> Same	No description	<b>☆</b> Yes	No statement	6 (high)
(2018),	somewhat	from the same		case	HBeAg sero-status	description		of LFU	
Maternal and	representative of	community			and comparable			of Life	
Child Health	the average HBV	(same inclusion			HBV DNA levels at				
Care of China,	infected pregnant	and exclusion			baseline. Same				
56	woman	criteria also)			regimen for infant				
30					immunoprophylaxis				
					at birth				
Li JH (2017),	☆	*	★ Valid method	*	<b>☆</b> Comparable	☆	☆	None	7 (low)
Chinese	At least	Drawn from	was used to	Always the case	for HBV DNA	Indication of	Yes (always	reported	
General	somewhat	the same	ascertain	711ways the case	levels at baseline but	record	the case)	(retrospecti ve)	
Practice, 70	representative of	community	adherence to the		HBeAg sero-status	linkage	,	vc)	
,	the average HBV	(same inclusion	antiviral therapy		not described. Same	(results			
	infected pregnant	and exclusion	(decrease in viral		regimen for infant	viewed			
	woman	criteria also)	load levels		immunoprophylaxis.	retrospectivel			
			subsequent to the			y in medical			
			treatment)			records)			
Ren CJ (2016),	<b>★</b> At least	<b>☆</b> Drawn	★ Valid method	<b>★</b> Always the	<b>★★</b> Same HBeAg	☆	<b>☆</b> Yes	No	8 (low)
J Med Theor &				•	sero-status and same	Laboratory		statement	
3 Mica Theor &	14	£ 41							
Prac, 74	somewhat	from the same	was used to	case		1		of LFU	
	somewhat representative of the average HBV	from the same community (same inclusion	was used to ascertain adherence to the	case	thresholds for HBV  DNA level. Same	methods described in		of LFU	

	infected pregnant	and exclusion	antiviral therapy			regimen for infant	detail (which			
	woman	criteria also)	(decrease in viral			immunoprophylaxis	assay used),			
		·	load levels			at birth	indicating use			
			subsequent to the				of a central			
			treatment)				laboaratory			
							and/or record			
							linkage.			
Shen ML	<b>★</b> At least	<b>☆</b> Drawn	<b>≯</b> Valid method	☆	Always the	Same thresholds for HBV DNA level but	*	<b>☆</b> Yes	No statement	6 (high)
(2016), WCJD,	somewhat	from the same	was used to	case		HBeAg sero-status	Laboratory		of LFU	
76	representative of	community	ascertain			not described.	methods		0.1 2.1 0	
	the average HBV	(same inclusion	adherence to the			Regimen for infant	described in			
	infected pregnant	and exclusion	antiviral therapy			immunoprophylaxis	detail (which			
	woman	criteria also)	(decrease in viral			at birth not clearly	assay used),			
			load levels			described	indicating use			
			subsequent to the				of a central			
			treatment)				laboaratory			
							and/or record			
							linkage.			
Wang DM (2016),	<b>★</b> At least	<b>☆</b> Drawn	★ Valid method	*	Always the	<b>☆☆</b> Same HBeAg	☆	<b>☆</b> Yes	No statement	8 (low)
	somewhat	from the same	was used to	case		sero-status and same	Laboratory		of LFU	
Chinese	representative of	community	ascertain			thresholds for HBV	methods			
Hepatology,	the average HBV	(same inclusion	adherence to the			DNA level. Same	described in			
79	infected pregnant	and exclusion	antiviral therapy			regimen for infant	detail (which			
	woman	criteria also)	(decrease in viral			immunoprophylaxis	assay used),			
			load levels			at birth	indicating use			
			subsequent to the				of a central			
			treatment)				laboaratory			
							and/or record			
							linkage.			

Ge YL (2015), Chin J Clin Pharmacol, 60	At least somewhat representative of the average HBV infected pregnant woman	Drawn from the same community (same inclusion and exclusion criteria also)	Was used to ascertain adherence to the antiviral therapy (decrease in viral load levels subsequent to the treatment)	case	Always the	sero-status and same thresholds for HBV DNA level. Same regimen for infant immunoprophylaxis at birth	No description	<b>★</b> Yes	No statement of LFU	7 (low)
Han YP (2014), Hebei Medical Journal, 62	At least somewhat representative of the average HBV infected pregnant woman	Drawn from the same community (same inclusion and exclusion criteria also)	Was used to ascertain adherence to the antiviral therapy (decrease in viral load levels subsequent to the treatment)	case	Always the	sero-status and same thresholds for HBV DNA level. Same regimen for infant immunoprophylaxis at birth	No description	<b>★</b> Yes	No statement of LFU	7 (low)
Wang W (2014), Hebei Medical Journal, 82	At least somewhat representative of the average HBV infected pregnant woman	Drawn from the same community (same inclusion and exclusion criteria also)	▼ Valid method  was used to ascertain  adherence to the antiviral therapy (decrease in viral load levels subsequent to the treatment)	<b>☆</b> case	Always the	★ Comparable for  HBV DNA levels  but HBeAg sero- status not described.  Same regimen for infant immunoprophylaxis at birth	Laboratory methods described in detail (which assay used), indicating use of a central laboaratory and/or record	<b>★</b> Yes	No statement of LFU	7 (low)

						linkage.			
Zhu M (2014),	*	*	★ Valid method	*	Comparable for	*	*	No statement	6 (high)
Hebei	At least	Drawn from	was used to	Always the case	HBeAg sero-status	Laboratory	Yes (always	of LFU	
Medicine, 88	somewhat	the same	ascertain		but HBV DNA	assays	the case)		
	representative of	community	adherence to the		levels not described.	described			
	the average HBV		antiviral therapy		Same regimen for				
	infected pregnant		(decrease in viral		infant				
	woman		load levels		immunoprophylaxis.				
			subsequent to the						
			treatment)						
Zeng YM (2013), J Med	<b>★</b> At least	<b>☆</b> Drawn	<b>★</b> Valid method	<b>★</b> Always the	<b>★</b> Same HBeAg	☆	<b>☆</b> Yes	No statement	7 (low)
	somewhat	from the same	was used to	case	sero-status and same	Laboratory		of LFU	
Res, 84	representative of	community	ascertain		thresholds for HBV	methods			
	the average HBV	(same inclusion	adherence to the		DNA level.	described in			
	infected pregnant	and exclusion	antiviral therapy		Regimen for infant	detail (which			
	woman	criteria also)	(decrease in viral		immunoprophylaxis	assay used),			
			load levels		at birth not	indicating use			
			subsequent to the		described clearly	of a central			
			treatment)			laboaratory			
						and/or record			
						linkage.			
Zhou DS	<b>☆</b> At least	<b>☆</b> Drawn	No description	<b>☆</b> Always the	<b>★</b> Same thresholds	₩	<b>☆</b> Yes	No statement	6 (high)
(2013), Hainan	somewhat	from the same		case	for HBV DNA level	Laboratory		of LFU	
Med J, 87	representative of	community			but HBeAg sero-	methods			
	the average HBV	(same inclusion			status not described.	described in			
	infected pregnant	and exclusion			Same regimen for	detail (which			
	woman	criteria also)			infant	assay used),			
					immunoprophylaxis	indicating use			

Jiang HX (2012), Chin J	<b>☆</b> At least	<b>☆</b> Drawn	<b>☆</b> Valid method	<b>★</b> Always the	at birth  ★★ Same HBeAg	of a central laboaratory and/or record linkage.	<b>★</b> Yes	No statement	8 (low)
Hepatol, 68	somewhat representative of the average HBV infected pregnant woman	from the same community (same inclusion and exclusion criteria also)	was used to ascertain adherence to the antiviral therapy (decrease in viral load levels subsequent to the treatment)	case	sero-status and same thresholds for HBV DNA level. Same regimen for infant immunoprophylaxis at birth	Laboratory methods described in detail (which assay used), indicating use of a central laboaratory and/or record linkage.		of LFU	
Wang EJ (2012), Chinese General Practice, 80	At least somewhat representative of the average HBV infected pregnant woman	Drawn from the same community (same inclusion and exclusion criteria also)	▼ Valid method  was used to ascertain adherence to the antiviral therapy (decrease in viral load levels subsequent to the treatment)	★ Always the case	Same HBeAg sero-status and same thresholds for HBV DNA level. Same regimen for infant immunoprophylaxis at birth	Laboratory methods described in detail (which assay used), indicating use of a central laboaratory and/or record linkage.	<b>≯</b> Yes	No statement of LFU	8 (low)
Yuan QF (2012),	<b>★</b> At least	<b>☆</b> Drawn from	Adherence/compli ance not mentioned and no	<b>☆</b> Always the case	★ Comparable for HBeAg sero-status	<b>☆</b> Indication of	<b>☆</b> Yes (always	No statement of LFU	6 (high)

Chinese	somewhat	the same	data presented on		but HBV DNA level	record	the case)		
Manipulation	representative of	community	decrease in HBV		not described. Same	linkage			
•	the average HBV	(same inclusion	DNA levels		regimen for infant				
&	infected pregnant	and exclusion			immunoprophylaxis.				
Rehabilitation	woman	criteria also)							
Medicine, 83									
Cheng YC	<b>★</b> At least	<b>☆</b> Drawn	★ Valid method	<b>★</b> Always the	<b>★★</b> Same HBeAg	☆	<b>☆</b> Yes	No	8 (low)
(2011),		6 4		•		T 1		statement	
Zhejiang	somewhat	from the same	was used to	case	sero-status and same thresholds for HBV	Laboratory methods		of LFU	
Practical	representative of	community (same inclusion	ascertain adherence to the		DNA level. Same	described in			
	the average HBV infected pregnant	and exclusion	antiviral therapy		regimen for infant	described in detail (which			
Medicine, 57	woman	criteria also)	(decrease in viral		immunoprophylaxis	assay used),			
	woman	criteria aiso)	load levels		at birth	indicating use			
			subsequent to the		at ontii	of a central			
			treatment)			laboaratory			
			troutment)			and/or record			
						linkage.			
Ren YJ (2011),	☆	*	٠ بىلا	*	<b></b>	*	*	No	7 (low)
Hebei Medical	<b>~</b>	*	★ Valid method	7*	Comparable for	7	7	statement	,
	At least	Drawn from	was used to	Always the case	HBeAg sero-status	Laboratory	Yes (always	of LFU	
Journal, 75	somewhat	the same	ascertain		but not for HBV	assays	the case)		
	representative of	community	adherence to the		DNA level. Same	described			
	the average HBV		antiviral therapy		regimen for infant				
	infected pregnant		(decrease in viral		immunoprophylaxis.				
	woman		load levels						
			subsequent to the						
			treatment)						
Zhang YF	<b>★</b> At least	<b>☆</b> Drawn	★ Valid method	<b>★</b> Always the	<b>☆☆</b> Same HBeAg	No	<b>☆</b> Yes	No	7 (low)
(2010a),	somewhat	from the same	was used to	case	sero-status and same	description		statement of LFU	
								<b>23</b> C	

Journal of	representative of	community	ascertain		thresholds for HBV				
Practical	the average HBV	(same inclusion	adherence to the		DNA level. Same				
Obstetrics and	infected pregnant	and exclusion	antiviral therapy		regimen for infant				
	woman	criteria also)	(decrease in viral		immunoprophylaxis				
Gynecology,			load levels		at birth				
86			subsequent to the						
			treatment)						
Su TB (2009), Chinese	☆	☆	Do not provide any details on	*	<b>★</b> Both HBeAg	☆	☆	No statement	6 (high)
	At least	Drawn from	adherence.	Always the case	sero-status and HBV	Testing done	Yes (always	of LFU	
Journal of	somewhat	the same			DNA not described.	centrally in	the case)		
Coal Industry	representative of	community			Same regimen for	the hospital			
Medicine, 77	the average HBV	(same inclusion			infant	that study			
	infected pregnant	and exclusion			immunoprophylaxis.	staffs worked			
	woman	criteria also)				in.			
Tang X (2009), Jiangxi	<b>☆</b> At least	<b>☆</b> Drawn	★ Valid method	<b>★</b> Always the	<b>☆☆</b> Same HBeAg	☆	<b>☆</b> Yes	No statement	8 (low)
, ,,	somewhat	from the same	was used to	case	sero-status and same	Laboratory		of LFU	
Medical						•			
	representative of	community	ascertain		thresholds for HBV	methods			
Journal, 78	representative of the average HBV	community (same inclusion	ascertain adherence to the		thresholds for HBV DNA level. Same	_			
Journal, 78	•	ř				methods			
Journal, 78	the average HBV	(same inclusion	adherence to the		DNA level. Same	methods described in			
Journal, 78	the average HBV infected pregnant	(same inclusion and exclusion	adherence to the antiviral therapy		DNA level. Same regimen for infant	methods described in detail (which assay used), indicating use			
Journal, 78	the average HBV infected pregnant	(same inclusion and exclusion	adherence to the antiviral therapy (decrease in viral		DNA level. Same regimen for infant immunoprophylaxis	methods described in detail (which assay used), indicating use of a central			
Journal, 78	the average HBV infected pregnant	(same inclusion and exclusion	adherence to the antiviral therapy (decrease in viral load levels		DNA level. Same regimen for infant immunoprophylaxis	methods described in detail (which assay used), indicating use of a central laboaratory			
Journal, 78	the average HBV infected pregnant	(same inclusion and exclusion	adherence to the antiviral therapy (decrease in viral load levels subsequent to the		DNA level. Same regimen for infant immunoprophylaxis	methods described in detail (which assay used), indicating use of a central laboaratory and/or record			
,	the average HBV infected pregnant	(same inclusion and exclusion	adherence to the antiviral therapy (decrease in viral load levels subsequent to the		DNA level. Same regimen for infant immunoprophylaxis	methods described in detail (which assay used), indicating use of a central laboaratory			
Journal, 78 Feng HF	the average HBV infected pregnant	(same inclusion and exclusion	adherence to the antiviral therapy (decrease in viral load levels subsequent to the	<b>★</b> Always the	DNA level. Same regimen for infant immunoprophylaxis	methods described in detail (which assay used), indicating use of a central laboaratory and/or record	<b>★</b> Yes	No	8 (low)
,	the average HBV infected pregnant woman	(same inclusion and exclusion criteria also)	adherence to the antiviral therapy (decrease in viral load levels subsequent to the treatment)		DNA level. Same regimen for infant immunoprophylaxis at birth	methods described in detail (which assay used), indicating use of a central laboaratory and/or record linkage.	<b>☆</b> Yes	statement	8 (low)
Feng HF	the average HBV infected pregnant woman	(same inclusion and exclusion criteria also)	adherence to the antiviral therapy (decrease in viral load levels subsequent to the treatment)	<b>★</b> Always the case	DNA level. Same regimen for infant immunoprophylaxis at birth	methods described in detail (which assay used), indicating use of a central laboaratory and/or record linkage.	<b>★</b> Yes		8 (low)

58	the average HBV	(same inclusion	adherence to the		DNA level. Same	described in			
	infected pregnant	and exclusion	antiviral therapy		regimen for infant	detail (which			
	woman	criteria also)	(decrease in viral		immunoprophylaxis	assay used),			
			load levels		at birth	indicating use			
			subsequent to the			of a central			
			treatment)			laboaratory			
						and/or record			
						linkage.			
Li G (2006),	*	*	★ Valid method	*	<b>★</b> Comparable	*	*	*	8 (low)
Journal of	At least	Drawn from	was used to	Always the case	HBeAg sero-status	Laboratory	Yes (always	LFU	
Wenzhou	somewhat	the same	ascertain	711 ways the case	but HBV DNA	assays	the case)	reported	
Medical	representative of	community	adherence to the		levels not described.	described	ine case)	and <20%	
	the average HBV	(same inclusion	antiviral therapy		Same regimen for			LFU in	
College, 69	infected pregnant	and exclusion	(decrease in viral		infant			both	
	woman	criteria also)	load levels		immunoprophylaxis.			treatment	
		ŕ	subsequent to the		1 1 2			group and	
			treatment)					control	
								group	
Li WF (2006),	<b>★</b> At least	<b>☆</b> Drawn	★ Valid method	<b>★</b> Always the	<b>☆☆</b> Same HBeAg	★Laboratory	<b>≯</b> Yes	No	8 (low)
Chinese	somewhat	from the same	was used to	case	sero-status and same	methods		statement	
Hepatology,	representative of	community	ascertain	cuse	thresholds for HBV	described in		of LFU	
71	the average HBV	(same inclusion	adherence to the		DNA level. Same	detail (which			
, 1	infected pregnant	and exclusion	antiviral therapy		regimen for infant	assay used),			
	woman	criteria also)	(decrease in viral		immunoprophylaxis	indicating use			
		ĺ	load levels		at birth	of a central			
			subsequent to the			laboaratory			
			treatment)			and/or record			

Ma J (2006),	☆	☆	<b>≯</b> Valid method	*	Comparable HBeAg	☆	☆	No	6 (high)
China Practical	At least	Drawn from	was used to	Always the case	sero-status but HBV DNA levels not	Laboratory	Yes (always	statement of LFU	
Medical, 72	somewhat	the same	ascertain	Tilways the case	described. Regimen	assays	the case)	OI LFU	
	representative of	community	adherence to the		for infant	described	,		
	the average HBV	(same inclusion	antiviral therapy		immunoprophylaxis				
	infected pregnant	and exclusion	(decrease in viral		not described				
	woman	criteria also)	load levels						
			subsequent to the						
			treatment)						
Han ZH	<b>★</b> At least	<b>☆</b> Drawn	<b>≯</b> Valid method	<b>★</b> Always the	<b>★★</b> Same HBeAg	Laboratory	<b>≯</b> Yes	No statement	8 (low)
(2005), Chin J	somewhat	from the same	was used to	case	sero-status and same	methods		of LFU	
Intern Med, 63	representative of	community	ascertain		thresholds for HBV	described in			
	the average HBV	(same inclusion	adherence to the		DNA level. Same	detail (which			
	infected pregnant	and exclusion	antiviral therapy		regimen for infant	assay used),			
	woman	criteria also)	(decrease in viral		immunoprophylaxis	indicating use			
			load levels		at birth	of a central			
			subsequent to the			laboaratory			
			treatment)			and/or record			
***						linkage.		No	
Wang TM (2005),	<b>★</b> At least	<b>☆</b> Drawn	<b>★</b> Valid method	<b>★</b> Always the	<b>★</b> Same HBeAg	No description	<b>≯</b> Yes	statement	6 (high)
	somewhat	from the same	was used to	case	sero-status but HBV			of LFU	
Chinese	representative of	community	ascertain		DNA level not				
Journal of	the average HBV	(same inclusion	adherence to the		described. Same				
Eugenics and	infected pregnant	and exclusion	antiviral therapy		regimen for infant				
Genetics, 81	woman	criteria also)	(decrease in viral		immunoprophylaxis				
,			load levels		at birth				
			subsequent to the						
			treatment)						

<sup>a</sup>Risk of bias assessments should be classified as being either low ( $\geq 7$ ) or high (< 7) by the Newcastle-Ottawa scale

## LDT 600 mg

A. English Language Observational Studies

		Jusei valiona		Demonstration			Was follow-		Total
	Representa	Selection of		that outcome of	Comparability of		up long		number
Study	tive-ness of	the non-		interest was	cohorts on the basis		enough for	Adequacy of	of stars
(year),	the exposed	exposed	Ascertainment	not present at	of the design or	Assessment of	outcomes	follow up of	(risk of
journal, No.	cohort	cohort	of exposure	baseline	analysis	outcomes	occur	cohorts	bias) <sup>a</sup>
Zhang H,	☆	☆	*	☆	**	*	*	☆	9
(2014), Hepatology, 85	At least somewhat representative of the average HBV infected pregnant woman	Drawn from the same community (same inclusion and exclusion criteria also)	Monthly HBV DNA level testing was done to check maternal adherence	Always the case	Comparable for HBV DNA level and comparable HBeAg positive. Same regimen for infant immunoprophylaxis.	Describes testing done and refers to a central laboratory employed for this study.	Yes	LFU reported and <20% LFU in all treatment and control groups	(low)
Han GR, (2015), J Viral Hepat, 120	At least somewhat representative of the average HBV infected pregnant woman	Drawn from the same community (same inclusion and exclusion criteria also)	Regular testing (and pre-delivery testing) of HBV DNA levels were done in mothers and each treated mother had at least a 3-log decrease in HBV DNA level prior to delivery.	★ Always the case	Comparable for HBV DNA level and comparable HBeAg positive. Same regimen for infant immunoprophylaxis	Describes test assays used for HBsAg and HBV DNA of infants and describes that samples were taken by study personnel themselves (meaning they would have direct	<b>☆</b> Yes	LFU reported and <20% LFU in all treatment and control groups	9 (low)

							linkage to results)			
Liu C	CP,	*	Many more	Some limited data	*	₩	*	*	No loss to follow-up	5
$(2015)^3$		14	women in the	presented on	A 1 41	HDV DNA 111/	I ahawatawa	V	described because it	(high)
	At		control group	decrease of	Always the case	HBV DNA level and/or	Laboratory	Yes	was a retrospective	
		mewhat	when compared	maternal viral		HBeAg not described for	assays described,		cohort study (or	
	-	presentative	to the treated	load, but no		both treated and control	with indication of		listed as such) where	
		the average	group – this	mention of linking		groups. Similar infant	record linkage		the infants needed to	
	HE	3V infected	could indicate	this with		prophylaxis between	(results viewed		have had test results	
	pre	egnant	dissimilarity	compliance/adher		treated and control	retrospectively in		at the testing	
	wo	man	between the two	ence/time on		groups.	medical records)		timepoint (this is	
			groups	treatment, and no					therefore	
				detailed results					misclassified as a	
				provided.					cohort study, and	
									has a high risk of	
									bias for loss to	
									follow-up)	
Wu Q	Х,	*	❖	☆	☆	**	*	☆	<80% follow-up for	8
(2015),			·	,	,		,		both treated and	(low)
Clinical	At		Drawn from	Fairly detailed	Always the case	Comparable for HBV	Laboratory	Yes	control groups	, ,
		mewhat	the same	data provided on		DNA level and	assays described			
Gastroente	er rep	presentative	community	maternal viral		comparable HBeAg	in detail with			
ology a	IIu	the average	(same inclusion	load decrease.		positive. Same regimen	indication that			
Hepatolog	v. HE	3V infected	and exclusion	>80% of women		for infant	testing (and			
	pre	egnant	criteria also)	taking treatment		immunoprophylaxis.	viewing of			
160	wo	oman		had >2 log			medical records,			
				decrease in viral			was done by study			
				load compared to			personnel)			
				none of the						

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<sup>&</sup>lt;sup>3</sup> Liu CP, Zeng YL, Zhou M, et al. Factors Associated with Mother-to-child Transmission of Hepatitis B Virus Despite Immunoprophylaxis. *Intern Med* 2015; **54(7)**: 711-716.

			controls.						
Liu Y, (2016),	☆	₩	Some limited data presented on	*	*	*	☆	Loss to follow-up not mentioned and	6 (high)
	At least	Drawn from	decrease of	Always the case	HBV DNA level and	Laboratory assays	Yes	flow-chart of	(mgn)
Hepatology	somewhat	the same	maternal viral		HBeAg comparable	described in detail		patients not given.	
Research,	representative	community	load, but no		between treated and non	with indication		This may indicate	
139	of the average	(same inclusion	mention of linking		treated groups. Infant	that testing (and		omitting of loss to	
	HBV infected	and exclusion	this with		immunoprophylaxis not	viewing of		follow-up details	
	pregnant	criteria also)	compliance/adher		described clearly (no	medical records,		rather than perfect	
	woman		ence/time on		timing of HBIg).	was done by study		(100%) retention,	
			treatment, and no			personnel)		and does not allow	
			detailed results					one to assume the	
			provided.					latter.	
Tan Z,	†	None (Arm 1)	Adherence or	*	<b>☆</b> (Arm 1) <b>☆☆</b> (Arm 2)	☆	☆	*	6 (high)
(2016),		<b>☆</b> (Arm 2)	compliance to						(Arm 1)
Medicine,	Truly		treatment not	Always the case	Comparable for HBV	Lab testing done	Yes	>80% follow-up in	
,	representative	For arm 2 it is	examined, little		DNA level and	centrally as part of		across all treatment	8 (low)
152	of the average	drawn from the	data on tracking		comparable HBeAg	the study,		arms and control	(Arm 2)
	HBV infected	same	of viral load		positive for the second	laboratory assays		groups.	
	pregnant	community	decrease.		treatment arm compared	for defining infant			
	woman	(same inclusion			to the control arm. For	outcome			
		and exclusion			the first arm of the study	described.			
		criteria also).			they are not comparable.				
		However, arm 1			Same regimen for infant				
		is not			immunoprophylaxis.				
		comparable							
		with the control							
		group.							
Chen ZX,	*	*	Adherence/compli	☆	❖	*	*	Loss to follow-up	6
(2017), J	At least	Drawn from the	ance not mentioned and no	Always the case	Comparable for HBV	Lab testing done	Yes	not mentioned and flow-chart of	(high)

infect, 111	somewhat	same	data presented on		DNA level but more than	centrally as part of		patients not given.	
11115Ct, 111	representative	community	decrease in HBV		10% points different for	the study,		This may indicate	
	of the average	(same inclusion	DNA levels		HBeAg positive. Same	laboratory assays		omitting of loss to	
	HBV infected	and exclusion	DIVA levels		regimen for infant	for defining infant		_	
					=			1	
  -	pregnant	criteria also)			immunoprophylaxis	outcome		rather than perfect	
  -	woman					described.		(100%) retention,	
<u> </u>								and does not allow	
								one to assume the	
								latter.	
Sun W,	☆	☆	☆	☆	**	Laboratory assays	☆	Loss to follow-up	7
(2017),	,		·	,		used not well		not mentioned and	(low)
BMC	At least	Drawn from the	HBV DNA	Always the case	Comparable for HBV	described	Yes	flow-chart of	, ,
	somewhat	same	changes specified		DNA level and			patients not given.	
Gastroenter	representative	community with	with some detai.		comparable HBeAg			This may indicate	
ology, 148	of the average	same inclusion	~7 log decrease in		positive. Same regimen			omitting of loss to	
]	HBV infected	and exclusion	both treatment		for infant			follow-up details	
  -	pregnant	criteria.	groups compared		immunoprophylaxis			rather than perfect	
	woman	Mentions	to the control					(100%) retention,	
		allocation of	group.					and does not allow	
		women into						one to assume the	
		three groups						latter.	
He T,	*	*	☆	₩	 ☆☆	☆	<b>→</b>	Retrospective cohort	8
·	74	74	7	74	74.74	7	74	mentioned but no	(low)
(2018),	At least	Drawn from the	Detailed	Always the case	Comparable for HBV	Linkage to	Yes	loss to follow-up	(IOW)
Hepatol Int,	somewhat	same	information on		DNA level and	medical records		described, no	
64	representative	community with	reduction of viral		comparable HBeAg			mention of how	
  -	of the average	same inclusion	load given,		positive. Same regimen			there was perfect	
	HBV infected	and exclusion	including specific		for infant			retention.	
	pregnant	criteria.	data for each		immunoprophylaxis				
	woman		women (every one						
			had a -6 to -8 log						
			- 8						

			reduction)						
Hu Y,	*	*	☆	*	**	☆	*	Only ~70 % follow- up between 7 to 12	8
(2018), J Viral Hepat, 128	At least somewhat representative of the average HBV infected pregnant	Drawn from the same community with same inclusion and exclusion criteria.	Detailed info on reduction of viral load given, only ~5% of women in the treated group did not have a	Always the case	Comparable for HBV DNA level and comparable HBeAg positive. Same regimen for infant immunoprophylaxis	Lab testing done centrally as part of the study, laboratory assays for defining infant outcome	Yes	months (although some others were included and tested at 13-14 months not actually completely lost to	(low)
	woman		reduction below 2x10^7 log			described.		follow-up)	
Sheng QJ, (2018a), Int J med Sci, 145	At least somewhat representative of the average HBV infected pregnant woman	Drawn from the same community with same inclusion and exclusion criteria.	Mentions careful monitoring of HBV DNA level for checking maternal adherence/changin g treatment regimen when needed.	<b>☆</b> Always the case	Comparable for HBV DNA level and comparable HBeAg positive. Same regimen for infant immunoprophylaxis	Lab testing done centrally as part of the study, laboratory assays for defining infant outcome described.	<b>★</b> Yes	>80% follow-up in both treatment and control group	9 (low)
Sheng QJ, (2018b), Medicine, 147	At least somewhat representative of the average HBV infected pregnant woman	Drawn from the same community with same inclusion and exclusion criteria.	Mentions that all treated women received 8 weeks of therapy. Provides detailed information on decrease in HBV	☆ Always the case	Comparable for HBV DNA level. HBeAg comparability not clear as they only give the proportion overall of women who were HBeAg positive. Same	Lab testing done centrally as part of the study, laboratory assays for defining infant outcome described.	<b>☆</b> Yes	No description of any loss to follow- up or confirmation that there was no loss-to-follow-up.	7 (low)

DNA level for	regimen for infant	
treated cohort.	immunoprophylaxis	

<sup>&</sup>lt;sup>a</sup>Risk of bias assessments should be classified as being either low (≥ 7) or high (< 7) by the Newcastle-Ottawa scale

**B.** Chinese Language Observational Studies

<b>D.</b> Chinese La	anguage Obse	i vanonai Su	uuics	<b>.</b>	G 1711 A		***		
				Demonstration	Comparability of		Was follow-		
		Selection of		that outcome of	cohorts on the		up long	Adequacy	Total
	Representative	the non-		interest was not	basis of the		enough for	of follow	number of
Study (year),	-ness of the	exposed	Ascertainment	present at	design or	Assessment	outcomes	up of	stars (risk of
journal, No.	exposed cohort	cohort	of exposure	baseline	analysis	of outcomes	occur	cohorts	bias) <sup>a</sup>
Tan J, (2019),	<b>★</b> At least	<b>☆</b> Drawn	<b>☆</b> Valid	<b>★</b> Always the	Comparable for	☆	<b>☆</b> Yes	No	7 (low)
J Prac Hepatol,	somewhat	from the same	method was used	case	HBV DNA levels at	Laboratory		statement of LFU	
151	representative of	community	to ascertain	Cusc	baseline but HBeAg	methods		OI LIV	
	the average HBV	(same inclusion	adherence to the		sero-status not	described in			
	infected pregnant	and exclusion	antiviral therapy		described. Same	detail (which			
	woman	criteria also)	(decrease in viral		regimen for infant	assay used),			
			load levels		immunoprophylaxis	indicating use			
			subsequent to the		at birth	of a central			
			treatment)			laboaratory			
						and/or record			
						linkage.			
Chen QR,	<b>★</b> At least	<b>☆</b> Drawn	No description	<b>★</b> Always the	<b>☆☆</b> Same	No	<b>≯</b> Yes	No	6 (high)
(2018),		6 4		·	IID A	description		statement	
Maternal and	somewhat representative of	from the same community		case	HBeAg sero-status and comparable			of LFU	
Child Health	the average HBV	(same inclusion			HBV DNA levels at				
	infected pregnant	and exclusion			baseline. Same				
Care of China,	woman	criteria also)			regimen for infant				
56		,			immunoprophylaxis				
					at birth				
Ding XP,	<b>★</b> At least	<b>☆</b> Drawn	★ Valid method	<b>☆</b> Always the	<b>☆☆</b> Same	No	<b>★</b> Yes	No	7 (low)
(2018), Health	,			•		description	, 100	statement	
Research, 116	somewhat	from the same	was used to	case	HBeAg sero-status			of LFU	
1.05carcii, 110									

	representative of	community	ascertain			and compara	rable				
	the average HBV	(same inclusion	adherence to the			HBV DNA level					
	infected pregnant	and exclusion	antiviral therapy				Same				
	woman	criteria also)	(decrease in viral			regimen for in					
	woman	criteria aiso)	load levels			immunoprophyla					
						at birth	axis				
			subsequent to the			at birth					
			treatment)								
Li ZY, (2018), Drug	*	*	★ Valid method	☆		<b>☆☆</b> Compara	rable	*	*	None reported	8 (low)
	At least	Drawn from	was used to	Alwa	ys the case	for HBeAg se	sero-	Indication of	Yes (always	(retrospecti	
Evaluation	somewhat	the same	ascertain			status and H	HBV	record	the case)	ve)	
Research, 135	representative of	community	adherence to the			DNA level. Sa	Same	linkage			
	the average HBV	(same inclusion	antiviral therapy			regimen for in	nfant	(results			
	infected pregnant	and exclusion	(decrease in viral			immunoprophyla	axis.	viewed			
	woman	criteria also)	load levels					retrospectivel			
			subsequent to the					y in medical			
			treatment)					records)			
Tian JH,	<b>★</b> At least	<b>☆</b> Drawn	No description	*	Always the	<b>☆☆</b> Sa	Same	*	<b>☆</b> Yes	No statement	7 (low)
(2018), China	somewhat	from the same		case		threshold for H	HBV	Laboratory		of LFU	
& Foreign	representative of	community				DNA level and sa	same	methods			
Medical	the average HBV	(same inclusion				HBeAg sero-sta	tatus	described in			
Treatment, 153	infected pregnant	and exclusion				used. Same regin	imen	detail (which			
Treatment, 133	woman	criteria also)				for in	nfant	assay used),			
						immunoprophyla	axis	indicating use			
						at birth		of a central			
								laboaratory			
								and/or record			
								linkage.			
Zhang BF,								No		No	6 (high)

(2018), Chin J	somewhat	from the same	was used to	case		sero-status but			of LFU	
Hepatol, 43	representative of	community	ascertain			different thresholds				
Tiepatoi, 43	the average HBV	(same inclusion	adherence to the			for HBV DNA level.				
	infected pregnant	and exclusion	antiviral therapy			Same regimen for				
	woman	criteria also)	(decrease in viral			infant				
			load levels			immunoprophylaxis				
			subsequent to the			at birth				
			treatment)							
Zhang GH,	<b>★</b> At least	<b>☆</b> Drawn	★ Valid method	*	Always the	<b>☆☆</b> Same	No description	<b>☆</b> Yes	No statement	7 (low)
(2018), China	somewhat	from the same	was used to	case		HBeAg sero-status	T.		of LFU	
Health Care &	representative of	community	ascertain			and same thresholds				
Nutrition, 166	the average HBV	(same inclusion	adherence to the			for HBV DNA level.				
	infected pregnant	and exclusion	antiviral therapy			Same regimen for				
	woman	criteria also)	(decrease in viral			infant				
			load levels			immunoprophylaxis				
			subsequent to the			at birth				
			treatment)							
Zheng JC,	<b>★</b> At least	<b>☆</b> Drawn	No description	☆	Always the	<b>☆☆</b> Same	☆	<b>☆</b> Yes	No	7 (low)
(2018), China								,	statement	
Rural	somewhat	from the same		case		HBeAg sero-status	Laboratory		of LFU	
	representative of	community				and same thresholds	methods			
Medicine, 171	the average HBV	(same inclusion				for HBV DNA level.	described in			
	infected pregnant	and exclusion				Same regimen for	detail (which			
	woman	criteria also)				infant	assay used),			
						immunoprophylaxis	indicating use			
						at birth	of a central			
							laboaratory			
							and/or record			
							linkage.			

Chen WJ,	<b>★</b> At least	<b>☆</b> Drawn	★ Valid method	☆	Always the	<b>☆☆</b> Same	☆	<b>☆</b> Yes	No	8 (low)
(2017),	somewhat	from the same	was used to	case		HBeAg sero-status	Laboratory		statement	
Shandong	representative of	community	ascertain	case		and same thresholds	methods		of LFU	
Medicine, 30	the average HBV	(same inclusion	adherence to the			for HBV DNA level.	described in			
Wedleme, 50	infected pregnant	and exclusion	antiviral therapy			Same regimen for	detail (which			
	woman	criteria also)	(decrease in viral			infant	assay used),			
		ŕ	load levels			immunoprophylaxis	indicating use			
			subsequent to the			at birth	of a central			
			treatment)				laboaratory			
							and/or record			
							linkage.			
Feng XM,	<b>★</b> At least	<b>☆</b> Drawn	★ Valid method	☆	Always the	<b>☆☆</b> Same	☆	<b>☆</b> Yes	No	8 (low)
(2017),					riiways the			, 103	statement	
Clinical	somewhat	from the same	was used to	case		HBeAg sero-status	Laboratory		of LFU	
	representative of	community	ascertain			and same thresholds	methods			
Research and	the average HBV	(same inclusion	adherence to the			for HBV DNA level.	described in			
Practice, 118	infected pregnant	and exclusion criteria also)	antiviral therapy (decrease in viral			Same regimen for infant	detail (which			
	woman	criteria aiso)	load levels			immunoprophylaxis	assay used), indicating use			
			subsequent to the			at birth	of a central			
			treatment)			at onth	laboaratory			
			treatment)				and/or record			
							linkage.			
Huang Q,	<b>★</b> At least	<b>☆</b> Drawn	★ Valid method	☆	Always the	<b>☆☆</b> Same	No	<b>≯</b> Yes	No	7 (low)
(2017),					Aiways the		description	r ies	statement	
	somewhat	from the same	was used to	case		HBeAg sero-status			of LFU	
Qinghai	representative of	community	ascertain			and same thresholds				
Medical	the average HBV	(same inclusion	adherence to the			for HBV DNA level.				
Journal, 38	infected pregnant	and exclusion	antiviral therapy			Same regimen for				
	woman	criteria also)	(decrease in viral			infant				

			load levels		immunoprophylaxis				
			subsequent to the		at birth				
			treatment)		ut on ut				
I. C			treatment)			No		No	6 (1: 1)
Jiang S, (2017), Diet	★ At least	<b>☆</b> Drawn	★ Valid method	<b>★</b> Always the	★ Comparable for	description a	<b>☆</b> Yes	statement	6 (high)
,	somewhat	from the same	was used to	case	HBV DNA level but			of LFU	
Health, 130	representative of	community	ascertain		HBeAg sero-status				
	the average HBV	(same inclusion	adherence to the		not described. Same				
	infected pregnant	and exclusion	antiviral therapy		regimen for infant				
	woman	criteria also)	(decrease in viral		immunoprophylaxis				
			load levels		at birth				
			subsequent to the						
			treatment)						
Li CM, (2017),	☆	☆	★ Valid method	*	* Comparable	Laboratory	☆	No	6 (high)
Northern	At least	Drawn from	was used to	Always the case	for HBV DNA level	assays used not well	Yes (always	statement of LFU	
Pharmacy, 132	somewhat	the same	ascertain	Tilways the case	but HBeAg sero-	described wen	the case)	OI LFU	
	representative of	community	adherence to the		status not described.	described	ine ease)		
	the average HBV	(same inclusion	antiviral therapy		Same regimen for				
	infected pregnant	and exclusion	(decrease in viral		infant				
	woman	criteria also)	load levels		immunoprophylaxis.				
		,	subsequent to the						
			treatment)						
Li YH, (2017),	<u></u>	L	<u> </u>	L	L L	☆		No	8 (low)
Northern	<b>★</b> At least	<b>☆</b> Drawn	★ Valid method	<b>★</b> Always the	<b>☆☆</b> Same	74	<b>☆</b> Yes	statement	o (==)
	somewhat	from the same	was used to	case	HBeAg sero-status	Laboratory		of LFU	
Pharmacy, 134	representative of	community	ascertain		and same thresholds	methods			
	the average HBV	(same inclusion	adherence to the		for HBV DNA level.	described in			
	infected pregnant	and exclusion	antiviral therapy		Same regimen for	detail (which			
	woman	criteria also)	(decrease in viral		infant	assay used),			
			load levels		immunoprophylaxis	indicating use			
	l	1			1	1			

			subsequent to the			at birth	of a central			
			treatment)				laboaratory			
							and/or record			
							linkage.			
Liu J, (2017), Maternal and	★ At least	Drawn from the same	★ Valid method was used to	<b>☆</b>	Always the	₩₩ Same  HBeAg sero-status	No description	<b>≯</b> Yes	There is a description of LFU for	7 (low)
Child Health	representative of	community	ascertain			and comparable for			the exposed	
Care of China,	the average HBV	(same inclusion	adherence to the			HBV DNA levels.			but not for	
137	infected pregnant	and exclusion	antiviral therapy			Same regimen for			the control	
	woman	criteria also)	(decrease in viral			infant			group	
			load levels			immunoprophylaxis				
			subsequent to the			at birth				
			treatment)							
Luo DX, (2017) <sup>4</sup>	<b>☆</b> At least	<b>☆</b> Drawn	★ Valid method	☆	Always the	Comparable for HBV DNA levels	No description	<b>☆</b> Yes	No statement	5 (high)
(2017)	somewhat representative of	from the same community	was used to ascertain	case		but HBeAg sero-			of LFU	
	the average HBV	(same inclusion	adherence to the			status not described.				
	infected pregnant	and exclusion	antiviral therapy			Regimen for infant immunoprophylaxis				
	woman	criteria also)	(decrease in viral			at birth not clearly				
		,	load levels			described				
			subsequent to the			described				
			treatment)							
Pan YC,	<b>☆</b> At least	<b>☆</b> Drawn	No description	*	Always the	<b>☆☆</b> Same	☆	<b>☆</b> Yes	☆	8 (low)
(2017), J Clin	somewhat	from the same		case		HBeAg sero-status	Laboratory		Subjects	
Hepatol, 141	representative of	community				and same thresholds	methods		lost to	

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<sup>&</sup>lt;sup>4</sup> Luo D, He K. A study on the effect of telbivudine to interrupt mother-to-child transmission of hepatitis B virus and nursing intervention. *Chin J Woman Child Health Res* 2017; **28 (2)**: 626.

	the average HBV	(same inclusion		1		for HBV DNA level.	described in		follow up	
	infected pregnant	and exclusion				Same regimen for	detail (which		unlikely to	
	woman	criteria also)				infant	assay used),		introduce	
	woman	criteria aiso)					•			
						immunoprophylaxis	indicating use		bias, small	
						at birth	of a central		number lost	
							laboaratory			
							and/or record			
							linkage.			
Wang J,	<b>★</b> At least	<b>≯</b> Drawn	★ Valid method	☆	Always the	★ Same thresholds	No description	<b>≯</b> Yes	No statement	6 (high)
(2017),	somewhat	from the same	was used to	case		for HBV DNA level			of LFU	
Chinese	representative of	community	ascertain			but HBeAg sero-			of Li C	
Journal of	the average HBV	(same inclusion	adherence to the			status not described.				
	infected pregnant	and exclusion	antiviral therapy			Same regimen for				
Woman and	woman	criteria also)	(decrease in viral			infant				
Child Health	Woman	emena also)	load levels			immunoprophylaxis				
Research, 157			subsequent to the			at birth				
			treatment)			ut ontil				
Xiao XH,			<u> </u>			Same thresholds for		<b>.</b>	There is a	6 (high)
· ·	<b>★</b> At least	<b>★</b> Drawn	★ Valid method	☆	Always the	HBV DNA level but	₩	<b>☆</b> Yes	description	o (mgn)
(2017),	somewhat	from the same	was used to	case		HBeAg sero-status	Laboratory		of LFU for	
Maternal and	representative of	community	ascertain			not described.	methods		the exposed	
Child Health	the average HBV	(same inclusion	adherence to the			Regimen for infant	described in		but not for	
Care of China,	infected pregnant	and exclusion	antiviral therapy			immunoprophylaxis	detail (which		the control	
	woman	criteria also)	(decrease in viral			at birth not clearly	assay used),		group	
42			load levels			described	indicating use		group	
			subsequent to the			described	of a central			
			treatment)				laboaratory			
			treatment)				and/or record			
							linkage.			

Chen F,	<b>☆</b> At least	<b>☆</b> Drawn	★ Valid method	☆	Always the	<b>☆</b> Same HBeAg	☆	<b>☆</b> Yes	No	7 (low)
(2016), Journal	somewhat	from the same	was used to	case		sero-status and same	Laboratory		statement of LFU	
of Practical	representative of	community	ascertain	cuse		thresholds for HBV	methods		OI LIV	
Medicine, 110	the average HBV	(same inclusion	adherence to the			DNA level.	described in			
,	infected pregnant	and exclusion	antiviral therapy			Regimen for infant	detail (which			
	woman	criteria also)	(decrease in viral			immunoprophylaxis	assay used),			
			load levels			at birth not clearly	indicating use			
			subsequent to the			described	of a central			
			treatment)				laboaratory			
							and/or record			
							linkage.			
Gao P, (2016),	<b>★</b> At least	<b>☆</b> Drawn	<b>≯</b> Valid method	☆	Always the	Comparable for	☆	<b>☆</b> Yes	No	6 (high)
J Medical	At least	Diawii	r valid illethod		Aiways the	HBV DNA levels	•	r ies	statement	
	somewhat	from the same	was used to	case		but HBeAg sero-	Laboratory		of LFU	
Forum, 119	representative of	community	ascertain			status not described.	methods			
	the average HBV	(same inclusion	adherence to the			Regimen for infant	described in			
	infected pregnant	and exclusion	antiviral therapy			immunoprophylaxis	detail (which			
	woman	criteria also)	(decrease in viral			at birth not clearly	assay used),			
			load levels			described	indicating use			
			subsequent to the				of a central			
			treatment)				laboaratory			
							and/or record			
							linkage.			
Hu WH,	<b>★</b> At least	<b>☆</b> Drawn	<b>★</b> Valid method	☆	Always the	Comparable for	<b>☆</b>	<b>☆</b> Yes	No	7 (low)
(2016), Journal						_			statement	
of Qiqihar	somewhat	from the same	was used to	case		HBV DNA levels	Laboratory		of LFU	
	representative of	community	ascertain			but HBeAg sero-	methods			
University of	the average HBV	(same inclusion	adherence to the			status not described.	described in			
Medicine, 127	infected pregnant	and exclusion	antiviral therapy			Same regimen for	detail (which			
	woman	criteria also)	(decrease in viral			infant	assay used),			

Li N, (2016), Medical Innovation of China, 133	At least somewhat representative of the average HBV infected pregnant woman	Drawn from the same community (same inclusion and exclusion criteria also)	load levels subsequent to the treatment)  *Valid method was used to ascertain adherence to the antiviral therapy (decrease in viral	<b>☆</b> case	Always the	immunoprophylaxis at birth  Comparable for HBV DNA levels but HBeAg serostatus not described. Same regimen for infant	indicating use of a central laboaratory and/or record linkage.  No description	<b>★</b> Yes	No statement of LFU	6 (high)
			load levels subsequent to the treatment)			immunoprophylaxis at birth	N		N.	
Liu XB, (2016), Journal of Contemporary Clinical Medicine, 138	At least somewhat representative of the average HBV infected pregnant woman	Drawn from the same community (same inclusion and exclusion criteria also)	was used to ascertain adherence to the antiviral therapy (decrease in viral load levels subsequent to the treatment)	case	Always the	sero-status and same thresholds for HBV DNA level. Same regimen for infant immunoprophylaxis at birth	No description	<b>☆</b> Yes	No statement of LFU	7 (low)
Qiu B, (2016), J Prac Hepatol, 143	At least somewhat representative of the average HBV infected pregnant	Drawn from the same community (same inclusion and exclusion	▼ Valid method  was used to ascertain  adherence to the antiviral therapy	case	Always the	Same thresholds  for HBV DNA level but HBeAg sero- status not described. Same regimen for	Laboratory methods described in detail (which	<b>≯</b> Yes	No statement of LFU	7 (low)

Shen ML, (2016), WCJD, 76	★ At least somewhat representative of the average HBV infected pregnant woman	★ Drawn from the same community (same inclusion and exclusion criteria also)	(decrease in viral load levels subsequent to the treatment)  *Valid method was used to ascertain adherence to the antiviral therapy (decrease in viral load levels subsequent to the treatment)	★ Always the case	infant immunoprophylaxis at birth  Same thresholds for HBV DNA level but HBeAg sero-status not described. Regimen for infant immunoprophylaxis at birth not clearly described	assay used), indicating use of a central laboaratory and/or record linkage.  Laboratory methods described in detail (which assay used), indicating use of a central laboaratory and/or record linkage.	<b>★</b> Yes	No statement of LFU	6 (high)
Tian RH, (2016), Chinese Journal of Clinical Research, 154	At least somewhat representative of the average HBV infected pregnant woman	Drawn from the same community (same inclusion and exclusion criteria also)	No description	★ Always the case	sero-status and same thresholds for HBV DNA level. Same regimen for infant immunoprophylaxis at birth	No description	<b>★</b> Yes	No statement of LFU	6 (high)
Wang B, (2016), Chinese Remedies &	At least somewhat representative of	Drawn from the same community	★ Valid method         was used to         ascertain         adherence to the	☆ Always the case	for HBeAg sero- status and HBV DNA level. Same	★     Laboratory     assays     described	Yes (always the case)	No statement of LFU	8 (low)

Clinics, 155	the average HBV	(same inclusion	antiviral therapy			regimen for infant				
	infected pregnant	and exclusion	(decrease in viral			immunoprophylaxis.				
	woman	criteria also)	load levels							
			subsequent to the							
			treatment)							
Wang DM,	<b>★</b> At least	<b>≯</b> Drawn	<b>☆</b> Valid method	☆	Always the	<b>☆☆</b> Same HBeAg	*	<b>☆</b> Yes	No statement	8 (low)
(2016),	somewhat	from the same	was used to	case		sero-status and same	Laboratory		of LFU	
Chinese	representative of	community	ascertain			thresholds for HBV	methods		or Lr c	
Hepatology,	the average HBV	(same inclusion	adherence to the			DNA level. Same	described in			
79	infected pregnant	and exclusion	antiviral therapy			regimen for infant	detail (which			
,,	woman	criteria also)	(decrease in viral			immunoprophylaxis	assay used),			
			load levels			at birth	indicating use			
			subsequent to the				of a central			
			treatment)				laboaratory			
							and/or record			
							linkage.			
Wang HB, (2016), Journal	<b>★</b> At least	<b>☆</b> Drawn	★ Valid method	*	Always the	<b>☆</b> Comparable for	No description	<b>☆</b> Yes	No statement	6 (high)
	somewhat	from the same	was used to	case		HBV DNA level but			of LFU	
of Practical	representative of	community	ascertain			HBeAg sero-status				
Medicine, 156	the average HBV	(same inclusion	adherence to the			not described. Same				
	infected pregnant	and exclusion	antiviral therapy			regimen for infant				
	woman	criteria also)	(decrease in viral			immunoprophylaxis				
			load levels			at birth				
			subsequent to the							
			treatment)							

Zhang R,	<b>★</b> At least	<b>☆</b> Drawn	No description	☆	Always the	HBeAg sero-status	No	<b>★</b> Yes	No	4 (high)
$(2016)^5$					<b>3</b>	and threshold for	description		statement	
,	somewhat	from the same		case		HBV DNA level not			of LFU	
	representative of	community				described. Regimen				
	the average HBV	(same inclusion				for infant				
	infected pregnant	and exclusion				immunoprophylaxis				
	woman	criteria also)				at birth not clearly				
						described				
Chen CY,	<b>★</b> At least	<b>☆</b> Drawn	★ Valid method	☆	Always the	<b>★</b> Same HBeAg	☆	<b>≯</b> Yes	No statement	7 (low)
(2015), Chin J	somewhat	from the same	was used to	case		sero-status and same	Laboratory		of LFU	
Hepatol, 109	representative of	community	ascertain			thresholds for HBV	methods		01 22 0	
	the average HBV	(same inclusion	adherence to the			DNA level.	described in			
	infected pregnant	and exclusion	antiviral therapy			Regimen for infant	detail (which			
	woman	criteria also)	(decrease in viral			immunoprophylaxis	assay used),			
		,	load levels			at birth not clearly	indicating use			
			subsequent to the			described	of a central			
			treatment)				laboaratory			
			,				and/or record			
							linkage.			
Cui ZL,	<b>★</b> At least	<b>≯</b> Drawn	<b>☆</b> Valid method	☆	Always the	<b>☆☆</b> Same HBeAg	*	<b>☆</b> Yes	No statement	8 (low)
(2015),	somewhat	from the same	was used to	case		sero-status and same	Laboratory		of LFU	
IMHGN, 114	representative of	community	ascertain			thresholds for HBV	methods			
	the average HBV	(same inclusion	adherence to the			DNA level. Same	described in			
	infected pregnant	and exclusion	antiviral therapy			regimen for infant	detail (which			
	woman	criteria also)	(decrease in viral			immunoprophylaxis	assay used),			
			load levels			at birth	indicating use			

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<sup>&</sup>lt;sup>5</sup> Zhang R, Lu F, Liu M. Analysis of nursing management of antiviral intrauterine interruption of patients with HBV during pregnancy. *China Health Industry* 2016; **13 (31)**: 145-147.

			subsequent to the				of a central			
			treatment)				laboaratory			
							and/or record			
							linkage.			
Deng Y,	<b>☆</b> At least	<b>☆</b> Drawn	<b>☆</b> Valid method	*	Always the	<b>★</b> Same thresholds	No	<b>☆</b> Yes	No	6 (high)
(2015), Chin J	1 .	c a			•		description		statement	
Hepatol, 115	somewhat	from the same	was used to	case		for HBV DNA level			of LFU	
Tiepatoi, TTS	representative of	community	ascertain			but HBeAg sero-				
	the average HBV	(same inclusion	adherence to the			status not described.				
	infected pregnant	and exclusion	antiviral therapy (decrease in viral			Same regimen for infant				
	woman	criteria also)	`							
			load levels			immunoprophylaxis at birth				
			subsequent to the			at birth				
G 777			treatment)				No		No	
Ge YL,	<b>★</b> At least	<b>☆</b> Drawn	★ Valid method	*	Always the	<b>★★</b> Same HBeAg	description	<b>☆</b> Yes	statement	7 (low)
(2015), Chin J	somewhat	from the same	was used to	case		sero-status and same	description		of LFU	
Clin	representative of	community	ascertain			thresholds for HBV			of LIV	
Pharmacol, 60	the average HBV	(same inclusion	adherence to the			DNA level. Same				
, , , , , , , , , , , , , , , , , , , ,	infected pregnant	and exclusion	antiviral therapy			regimen for infant				
	woman	criteria also)	(decrease in viral			immunoprophylaxis				
			load levels			at birth				
			subsequent to the							
			treatment)							
Lou JJ, (2015),	<b>★</b> At least	<b>☆</b> Drawn	٠	₩	41 .1	ب ۱۱۲۰ و بدید	☆	<b>☆</b> Yes	No	8 (low)
Chinese	<b>☆</b> At least	<b>☆</b> Drawn	★ Valid method	74	Always the	★★ Same HBeAg	<b>^</b>	Y Yes	statement	` /
	somewhat	from the same	was used to	case		sero-status and same	Laboratory		of LFU	
Journal of	representative of	community	ascertain			thresholds for HBV	methods			
Microecology,	the average HBV	(same inclusion	adherence to the			DNA level. Same	described in			
140	infected pregnant	and exclusion	antiviral therapy			regimen for infant	detail (which			
	woman	criteria also)	(decrease in viral			immunoprophylaxis	assay used),			

			load levels subsequent to the treatment)			at birth	indicating use of a central laboaratory and/or record			
							linkage.			
Ren N, (2015), China Medicine and Pharmacy, 144	At least somewhat representative of the average HBV infected pregnant woman	from the same community (same inclusion and exclusion criteria also)	was used to ascertain adherence to the antiviral therapy (decrease in viral load levels subsequent to the	case	Always the	sero-status and same thresholds for HBV DNA level. Same regimen for infant immunoprophylaxis at birth	Laboratory methods described in detail (which assay used), indicating use of a central	<b>≯</b> Yes	No statement of LFU	8 (low)
S WII			treatment)				laboaratory and/or record linkage.		No	9 (1)
Sun WH, (2015), Chin J Hepatol, 149	At least somewhat representative of the average HBV infected pregnant woman	Drawn from the same community (same inclusion and exclusion criteria also)	was used to ascertain adherence to the antiviral therapy (decrease in viral load levels subsequent to the treatment)	case	Always the	sero-status and same thresholds for HBV DNA level. Same regimen for infant immunoprophylaxis at birth	Laboratory methods described in detail (which assay used), indicating use of a central laboaratory and/or record linkage.	<b>☆</b> Yes	No statement of LFU	8 (low)
Wang TD,	<b>★</b> At least	<b>★</b> Drawn	¥ Valid method	₩	Always the	<b>★★</b> Same HBeAg	な	<b>≯</b> Yes	No statement	8 (low)

(2015), China	somewhat	from the same	was used to	case		sero-status and same	Laboratory		of LFU	
Pharmaceutica	representative of	community	ascertain			thresholds for HBV	methods			
	the average HBV	(same inclusion	adherence to the			DNA level. Same	described in			
ls, 158	infected pregnant	and exclusion	antiviral therapy			regimen for infant	detail (which			
	woman	criteria also)	(decrease in viral			immunoprophylaxis	assay used),			
			load levels			at birth	indicating use			
			subsequent to the				of a central			
			treatment)				laboaratory			
							and/or record			
							linkage.			
Zhang X,	<b>★</b> At least	<b>☆</b> Drawn	<b>≯</b> Valid method	☆	Always the	<b>★★</b> Same HBeAg	*	<b>☆</b> Yes	No statement	8 (low)
2015), J Prac	somewhat	from the same	was used to	case		sero-status and same	Laboratory		of LFU	
Hepatol, 168	representative of	community	ascertain			thresholds for HBV	methods			
	the average HBV	(same inclusion	adherence to the			DNA level. Same	described in			
	infected pregnant	and exclusion	antiviral therapy			regimen for infant	detail (which			
	woman	criteria also)	(decrease in viral			immunoprophylaxis	assay used),			
			load levels			at birth	indicating use			
			subsequent to the				of a central			
			treatment)				laboaratory			
							and/or record			
							linkage.			
Chen YL,	No description	No description	<b>≯</b> Valid method	☆	Always the	Comparable for	No	<b>☆</b> Yes	No	4 (high)
$(2014)^6$	of the derivation	of the derivation	7- vanu memou		Aiways the	r- Comparable for	description	7. 108	statement	
(==:/	of the cohort	of the non	was used to	case		HBV DNA levels			of LFU	
		exposed cohort	ascertain			but HBeAg sero-				
			adherence to the			status not described.				
			antiviral therapy			Same regimen for				

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<sup>&</sup>lt;sup>6</sup> Chen Y, Gao X, Li J. Telbivudine combined with hepatitis B vaccine to interrupt hepatitis B virus intrauterine infection. *Acta Universitatis Medicinalis Nanjing (Natural Science)* 2014; **34 (1)**: 67-68.

			(decrease in viral load levels			infant immunoprophylaxis				
			subsequent to the			at birth				
			treatment)							
Han YP,	<b>☆</b> At least	<b>☆</b> Drawn	★ Valid method	☆	Always the	<b>☆☆</b> Same HBeAg	No	<b>☆</b> Yes	No	7 (low)
(2014), Hebei	somewhat	from the same	was used to	case		sero-status and same	description		statement of LFU	
Medical	representative of	community	ascertain	cuse		thresholds for HBV			OI LFU	
Journal, 62	the average HBV	(same inclusion	adherence to the			DNA level. Same				
	infected pregnant	and exclusion	antiviral therapy			regimen for infant				
	woman	criteria also)	(decrease in viral			immunoprophylaxis				
			load levels			at birth				
			subsequent to the							
T. CV			treatment)						No	0 (1 )
Liu CY,	🖈 At least	<b>☆</b> Drawn	★ Valid method	*	Always the	<b>☆☆</b> Same HBeAg	*	<b>☆</b> Yes	statement	8 (low)
(2014), Journal	somewhat	from the same	was used to	case		sero-status and same	Laboratory		of LFU	
of Yanan	representative of	community	ascertain			thresholds for HBV	methods			
University,	the average HBV	(same inclusion	adherence to the			DNA level. Same	described in			
136	infected pregnant	and exclusion	antiviral therapy			regimen for infant	detail (which			
	woman	criteria also)	(decrease in viral			immunoprophylaxis	assay used),			
			load levels subsequent to the			at birth	indicating use of a central			
			treatment)				laboaratory			
			,				and/or record			
							linkage.			
Yao LF,	<b>★</b> At least	<b>☆</b> Drawn	<b>☆</b> Valid method	☆	Always the	<b>★</b> Same HBeAg	☆	<b>★</b> Yes	No	7 (low)
(2014), Chin J		,					·	. 100	statement	
Obstet	somewhat representative of	from the same community	was used to ascertain	case		sero-status and same thresholds for HBV	Laboratory methods		of LFU	
Gynecol	the average HBV	(same inclusion	adherence to the			DNA level.	described in			

Pediatr, 162	infected pregnant	and exclusion	antiviral therapy			Regimen for infant	detail (which			
	woman	criteria also)	(decrease in viral			immunoprophylaxis	assay used),			
			load levels			at birth not clearly	indicating use			
			subsequent to the			described	of a central			
			treatment)				laboaratory			
							and/or record			
							linkage.			
Yue X, (2014), Chin J Infect	<b>★</b> At least	<b>☆</b> Drawn	<b>★</b> Valid method	☆	Always the	<b>☆☆</b> Same HBeAg	No description	<b>☆</b> Yes	*	8 (low)
	somewhat	from the same	was used to	case		sero-status and same	-		Complete	
Dis, 165	representative of	community	ascertain			thresholds for HBV			follow-up	
	the average HBV	(same inclusion	adherence to the			DNA level. Same				
	infected pregnant	and exclusion	antiviral therapy			regimen for infant				
	woman	criteria also)	(decrease in viral			immunoprophylaxis				
			load levels			at birth				
			subsequent to the							
			treatment)							
Zhou YJ, (2014), Chin J	<b>★</b> At least	<b>☆</b> Drawn	No description	☆	Always the	<b>☆</b> Comparable	☆	<b>☆</b> Yes	No statement	6 (high)
	somewhat	from the same		case		HBeAg sero-status	Laboratory		of LFU	
Hepatol, 172	representative of	community				and same thresholds	methods			
	the average HBV	(same inclusion				for HBV DNA level.	described in			
	infected pregnant	and exclusion				Regimen for infant	detail (which			
	woman	criteria also)				immunoprophylaxis	assay used),			
						at birth not	indicating use			
						described clearly	of a central			
							laboaratory			
							and/or record			
							linkage.			
Fan LY,	<b>★</b> At least	<b>☆</b> Drawn	★ Valid method	<b>☆</b>	Always the	<b>★★</b> Same HBeAg	No description	<b>☆</b> Yes	No statement	7 (low)

(2013), J Med	somewhat	from the same	was used to	case		sero-status and same			of LFU	
,	representative of	community	ascertain			thresholds for HBV				
Res, 117	the average HBV	(same inclusion	adherence to the			DNA level. Same				
	infected pregnant	and exclusion	antiviral therapy			regimen for infant				
	woman	criteria also)	(decrease in viral			immunoprophylaxis				
			load levels			at birth				
			subsequent to the							
			treatment)							
Jiang XN,	<b>★</b> At least	<b>☆</b> Drawn	<b>☆</b> Valid method	☆	Always the	<b>★</b> Same HBeAg	No description	<b>☆</b> Yes	☆	7 (low)
(2013), J Clin	somewhat	from the same	was used to	case		sero-status and same	•		Complete	
Hepatol, 131	representative of	community	ascertain			thresholds for HBV			follow-up	
	the average HBV	(same inclusion	adherence to the			DNA level.				
	infected pregnant	and exclusion	antiviral therapy			Regimen for infant				
	woman	criteria also)	(decrease in viral			immunoprophylaxis				
			load levels			at birth not				
			subsequent to the			described clearly				
			treatment)							
Zhao J, (2013),	<b>★</b> At least	<b>☆</b> Drawn	No description	☆	Always the	<b>☆☆</b> Same HBeAg	☆	<b>☆</b> Yes	No	7 (low)
China					mways the			, 103	statement	
Clinician, 170	somewhat	from the same		case		sero-status and same	Laboratory		of LFU	
Cilincian, 170	representative of	community				thresholds for HBV	methods			
	the average HBV	(same inclusion				DNA level. Same	described in			
	infected pregnant	and exclusion				regimen for infant	detail (which			
	woman	criteria also)				immunoprophylaxis	assay used),			
						at birth	indicating use			
							of a central			
							laboaratory			
							and/or record			
							linkage.			

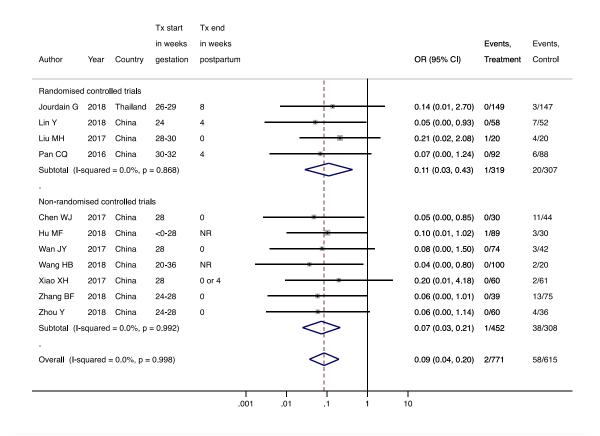
Peng BA,	<b>★</b> At least	<b>☆</b> Drawn	★ Valid method	☆	Always the	<b>☆☆</b> Same HBeAg	No	<b>☆</b> Yes	No	7 (low)
(2012), Chin Pharm J, 142	somewhat representative of	from the same	was used to	case		sero-status and same thresholds for HBV	description		statement of LFU	
	the average HBV infected pregnant	(same inclusion and exclusion	adherence to the antiviral therapy			DNA level. Same regimen for infant				
	woman	criteria also)	(decrease in viral load levels			immunoprophylaxis at birth				
			subsequent to the treatment)							
Wang EJ, (2012),	<b>★</b> At least	<b>☆</b> Drawn	★ Valid method	<b>☆</b>	Always the	<b>☆☆</b> Same HBeAg	<b>☆</b>	<b>☆</b> Yes	No statement	8 (low)
Chinese	somewhat representative of	from the same community	was used to ascertain	case		sero-status and same thresholds for HBV	Laboratory methods		of LFU	
General	the average HBV	(same inclusion	adherence to the			DNA level. Same	described in			
Practice, 80	infected pregnant	and exclusion	antiviral therapy			regimen for infant	detail (which			
	woman	criteria also)	(decrease in viral			immunoprophylaxis	assay used),			
			load levels			at birth	indicating use			
			subsequent to the				of a central			
			treatment)				laboaratory			
							and/or record			
M. MD							linkage.		No	0.4
Wang WP,	🗱 At least	<b>≯</b> Drawn	★ Valid method	¥	Always the	<b>★★</b> Same HBeAg	☆	<b>☆</b> Yes	statement	8 (low)
(2012), Prog	somewhat	from the same	was used to	case		sero-status and same	Laboratory		of LFU	
Obstet	representative of	community	ascertain			thresholds for HBV	methods			
Gynecol, 159	the average HBV	(same inclusion	adherence to the			DNA level. Same	described in			
	infected pregnant	and exclusion	antiviral therapy			regimen for infant	detail (which			
	woman	criteria also)	(decrease in viral			immunoprophylaxis	assay used),			
			load levels			at birth	indicating use			
			subsequent to the				of a central			

(2011), J Clin Hepatol, 163  Hepatol, 163  The average HBV (same inclusion and exclusion woman  The average HBV (same inclusion and exclusion infant immunoprophylaxis at birth  The average HBV (same inclusion infant immunoprophylaxis at birth  The average HBV (same inclusion infant immunoprophylaxis and birth  The average HBV (same inclusion infant immunoprophylaxis and birth  The average HBV (same inclusion infant immunoprophylaxis at birth  The average HBV (same inclusion infant immunoprophylaxis at birth  The average HBV (same inclusion infant immunoprophylaxis at birth  The average HBV (same inclusion infant immunoprophylaxis at birth  The average HBV (same inclusion infant immunoprophylaxis at birth  The average HBV (same inclusion infant immunoprophylaxis at birth  The average HBV (same inclusion infant immunoprophylaxis at birth  The average HBV (same inclusion infant immunoprophylaxis at birth  The average HBV (same inclusion infant immunoprophylaxis at birth  The average HBV (same inclusion infant immunoprophylaxis at birth  The average HBV (same inclusion infant immunoprophylaxis at birth  The average HBV (same inclusion infant immunoprophylaxis at birth  The average HBV (same inclusion infant immunoprophylaxis at birth  The average HBV (same inclusion infant immunoprophylaxis at birth  The average HBV (same inclusion infant immunoprophylaxis at birth  The average HBV (same inclusion infant immunoprophylaxis at birth  The average HBV (same inclusion infant immunoprophylaxis at birth  The average HBV (same inclusion infant immunoprophylaxis at birth				treatment)				laboaratory			
Yao ZC, (2011), J Clin somewhat somewhat representative of the average HBV infected pregnant woman  Zhang YF, (2010b), ADRJ, 169  Zhang YF, (2010b), ADRJ, 169  Zhang YF, (2010b), above the average HBV infected pregnant woman  Zhang YF, (2010b), above the average HBV infected pregnant woman  Zhang YF, (2010b), above the average HBV infected pregnant woman  Zhang YF, (2010b), above the average HBV infected pregnant woman  Zhang YF, (2010b), above the average HBV infected pregnant woman  Zhang YF, (2010b), above the average HBV infected pregnant woman  Zhang YF, (2010b), above the average HBV infected pregnant woman  Zhang YF, (2010b), above the average HBV infected pregnant woman  Zhang YF, (2010b), above the average HBV infected pregnant woman  Zhang YF, (2010b), above the average HBV infected pregnant woman  Zhang YF, (2010b), above the average HBV infected pregnant woman  Zhang YF, (2010b), above the average HBV infected pregnant woman  Zhang YF, (2010b), above the average HBV infected pregnant woman  Zhang YF, (2010b), above the average HBV infected pregnant woman  Zhang YF, (2010b), above the average HBV infected pregnant woman  Zhang YF, (2010b), above the average HBV infected pregnant woman  Zhang YF, (2010b), above the average HBV infected pregnant woman  Zhang YF, (2010b), above the average HBV infected pregnant woman  Zhang YF, (2010b), above the average HBV infected pregnant woman  Zhang YF, (2010b), above the average the ave								and/or record			
(2011), J Clin Hepatol, 163  The average HBV (same inclusion and exclusion woman  The average HBV (stame inclusion infected pregnant								linkage.			
Somewhat representative of the average HBV infected pregnant woman    Application   Ap		<b>★</b> At least	<b>☆</b> Drawn	<b>≯</b> Valid method	☆	Always the	<b>★</b> Same thresholds	*	<b>≯</b> Yes		7 (low)
representative of the average HBV infected pregnant woman criteria also)  Zhang YF, (2010b), ADRJ, 169  Tepresentative of the average HBV infected pregnant woman criteria also)  Tepresentative of the average HBV infected pregnant woman criteria also)  The proposed of the average HBV infected pregnant woman criteria also)  The proposed HBP (same inclusion and exclusion and exclu	(2011), J Clin	somewhat	from the same	was used to	case		for HBV DNA level	Laboratory			
the average HBV infected pregnant woman criteria also)  The average HBV infected pregnant woman criteria also)  The average HBV infected pregnant woman  The ave	Hepatol, 163							,		OI LIV	
infected pregnant woman and exclusion antiviral therapy woman criteria also) (decrease in viral load levels subsequent to the treatment)  Zhang YF, (2010b), ADRJ, 169  ADRJ, 169  ADRJ, 169  Infected pregnant woman and exclusion and exclusio		1	1								
woman criteria also) (decrease in viral load levels subsequent to the treatment)  Zhang YF, (2010b), ADRJ, 169  ADRJ, 169  Woman criteria also) (decrease in viral load levels subsequent to the treatment)  ADRJ, 169  Woman criteria also) (decrease in viral load levels subsequent to the treatment)  ADRJ, 169  Woman criteria also) (decrease in viral load levels subsequent to the antiviral therapy (decrease in viral load levels subsequent to the antiviral therapy (decrease in viral load levels subsequent to the subsequent to the automatory and/or record linkage.  No description  Y Yes  No statement of LFU  No description  No description  No description			· ·								
Ioad levels subsequent to the treatment   Ioad levels				1.7			_	,			
subsequent to the treatment)    Subsequent to the treatment   Subsequent treatment   Subsequent treatment   Subsequent treatment   Subsequent treatment   Su		woman	criteria aiso)	`							
Thang YF, At least somewhat representative of the average HBV infected pregnant woman criteria also)  The subsequent to the subsequent								_			
Zhang YF, (2010b), ADRJ, 169    X				•			at birth				
Zhang YF, (2010b), ADRJ, 169    At least representative of the average HBV infected pregnant woman   Criteria also)   Conduction   Cond				treatment)				_			
Zhang YF, (2010b), (2010b), somewhat representative of the average HBV infected pregnant woman (decrease in viral woman)  **No prawn the valid method was used to ascertain adherence to the infected pregnant woman (decrease in viral load levels subsequent to the average HBV)  **No description (description)  **Always the the Always the Always the case was used to ascertain adherence to the infected pregnant woman (decrease in viral load levels subsequent to the was used to ascertain adherence to the infected pregnant woman (decrease in viral load levels subsequent to the was used to ascertain adherence to the infected pregnant woman (decrease in viral load levels subsequent to the load levels subsequent levels subseque											
(2010b), ADRJ, 169  Somewhat representative of the average HBV infected pregnant woman criteria also)  (decrease in viral load levels subsequent to the subs								_			
(2010b), ADRJ, 169  somewhat from the same representative of community the average HBV (same inclusion infected pregnant woman criteria also)  (decrease in viral load levels subsequent to the subsequent to the load levels subsequent load levels load levels subsequent load levels load level	Zhang YF,	★ At least	<b>☆</b> Drawn	★ Valid method	☆	Always the	₩₩ Same HBeAg		<b>☆</b> Yes	No	7 (low)
ADRJ, 169    Somewhat   from the same representative of the average HBV (same inclusion infected pregnant woman   criteria also)   (decrease in viral load levels subsequent to the subsequent to the subsequent to the load levels subsequent load levels load levels subsequent load levels load levels subsequent load levels load lev	(2010b),							description			
the average HBV (same inclusion infected pregnant and exclusion woman criteria also) (decrease in viral load levels subsequent to the					case					of LFU	
infected pregnant woman and exclusion criteria also) antiviral therapy (decrease in viral load levels subsequent to the	ADKJ, 109	representative of	community	ascertain							
woman criteria also) (decrease in viral load levels subsequent to the immunoprophylaxis at birth		the average HBV	(same inclusion				DNA level. Same				
load levels at birth subsequent to the		infected pregnant	and exclusion	antiviral therapy			regimen for infant				
subsequent to the		woman	criteria also)	(decrease in viral			immunoprophylaxis				
				load levels			at birth				
treatment)				subsequent to the							
				treatment)							

<sup>a</sup>Risk of bias assessments should be classified as being either low (≥ 7) or high (< 7) by the Newcastle-Ottawa scale

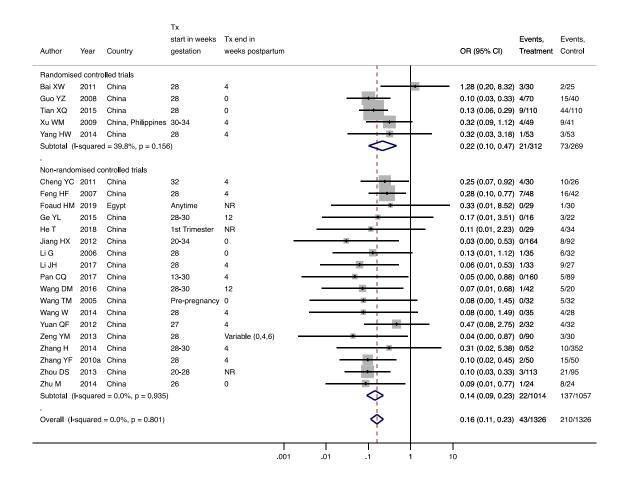
## Appendix H: Efficacy on the infants' HBV DNA positivity

- TDF 300 mg (infants' HBV DNA positivity)
  - Overall pooled OR= 0.09 (95% CI: 0.04-0.20), p<0.001,  $I^2=0$ %
- RCTs only (n=4): pooled OR=0.11 (95%CI: 0.03-0.43), p=0.001,  $I^2$ =0%
- Non-RCTs only (n=7): pooled OR=0.07 (95%CI: 0.03-0.21), p<0.001, I<sup>2</sup>=0%
- The p-value for heterogeneity between RCTs and non-RCTs was 0.64



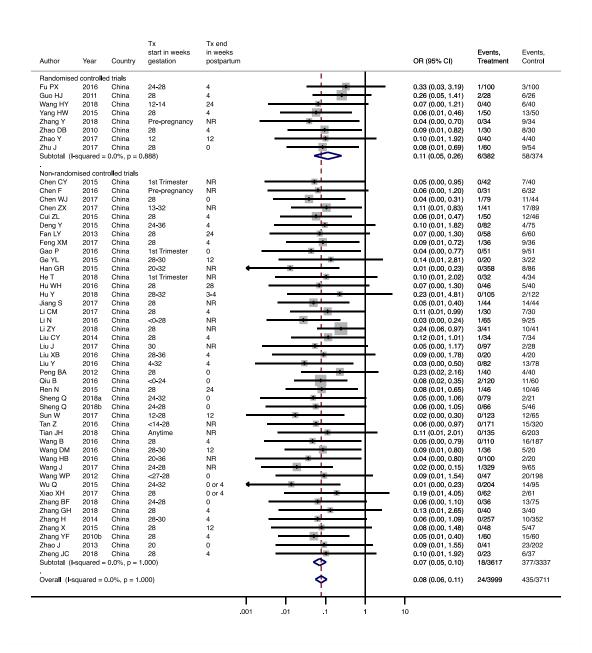
## • LAM 100-150 mg (infants' HBV DNA positivity)

- Overall pooled OR= 0.16 (95% CI: 0.11-0.23), p<0.001,  $I^2=0.0\%$
- RCTs only: pooled OR= 0.22 (95% CI: 0.10-0.47), p<0.001,  $I^2$ =39.8%
- Non-RCTs only: pooled OR=0.14 (95%CI: 0.09-0.23), p<0.001, I<sup>2</sup>=0%
- The p-value for heterogeneity between RCTs and non-RCTs was 0.47



## • LdT 600 mg (infants' HBV DNA positivity)

- Overall pooled OR= 0.08 (95% CI: 0.06-0.11), p<0.001,  $I^2$ =0.0%
- RCTs only: pooled OR= 0.11 (95%CI: 0.05-0.26), p<0.001, I<sup>2</sup>=0%
- Non-RCTs only: pooled OR=0.07 (95%CI: 0.05-0.10), p<0.001,  $I^2$ =0%
- The p-value for heterogeneity between RCTs and non-RCTs was 0.29



Appendix I: Characteristics of infants with MTCT despite maternal TDF 300 mg prophylaxis

	Author.			Charac	teristics of	mothers			um antiviral phylaxis	(	Characteristi	cs of infant	S
ID	year	Country	Age at baseline	HBV DNA at baseline (log IU/mL)	HBeAg at baseline	Other (e.g. HIV, HDV, etc)	HBV DNA at delivery (log IU/mL)	Treatment start	Treatment discontinuation	Mode of delivery	HepB-BD	HBIG	Infant vaccines (HepB3)
1	Liu MH, 2017	China	Between 20-40 years	≥5.3	Positive	No HCV/HIV	>6.0	Between weeks 28 and 30	At delivery	N/R	Yes, <24hr	Yes, <24hr	Yes, 1/6
2	Chen HL, 2015	Taiwan	N/R	8.2	Positive	No HCV/HIV	4.2	Between weeks 30 and 32	1 month postpartum	N/R	Yes, NR	Yes, <24hr	Yes, 1/6
3	Chen WJ, 2017	China	N/R	≥6.0	Positive	No HCV/HIV	N/R	28	At delivery	N/R	Yes, At birth	Yes, At birth	Yes, 1/6
4	Gong Q, 2017	China	Between 22-36 years	N/R	N/R	N/R	N/R	Between weeks 1 and 6	N/R	N/R	Yes, <24hr	Yes, <24hr	Yes, 1/6
5	Greenup AJ, 2014	Australia	N/R	N/R	Positive	N/R	4.4	32	12 weeks postpartum	Vaginal	Yes, At birth	Yes, NR	Yes, 2/4/6
6	He LL, 2018	China	Between 22-36 years	N/R	N/R	N/R	N/R	28	N/R	N/R	Yes, <12hr	Yes, <12hr	Yes, 1/6
7	He LL, 2018	China	Between 22-36 years	N/R	N/R	N/R	N/R	28	N/R	N/R	Yes, <12hr	Yes, <12hr	Yes, 1/6
8	He LL, 2018	China	Between 22-36 years	N/R	N/R	N/R	N/R	28	N/R	N/R	Yes, <12hr	Yes, <12hr	Yes, 1/6
9	He LL, 2018	China	Between 22-36 years	N/R	N/R	N/R	N/R	28	N/R	N/R	Yes, <12hr	Yes, <12hr	Yes, 1/6
10	He LL, 2018	China	Between 22-36 years	N/R	N/R	N/R	N/R	28	N/R	N/R	Yes, <12hr	Yes, <12hr	Yes, 1/6
11	He LL, 2018	China	Between 22-36 years	N/R	N/R	N/R	N/R	28	N/R	N/R	Yes, <12hr	Yes, <12hr	Yes, 1/6
12	He LL,	China	Between	N/R	N/R	N/R	N/R	28	N/R	N/R	Yes,	Yes,	Yes,

	2018		22-36 years								<12hr	<12hr	1/6
13	He LL, 2018	China	Between 22-36 years	N/R	N/R	N/R	N/R	28	N/R	N/R	Yes, <12hr	Yes, <12hr	Yes, 1/6
14	He LL, 2018	China	Between 22-36 years	N/R	N/R	N/R	N/R	28	N/R	N/R	Yes, <12hr	Yes, <12hr	Yes, 1/6
15	He LL, 2018	China	Between 22-36 years	N/R	N/R	N/R	N/R	28	N/R	N/R	Yes, <12hr	Yes, <12hr	Yes, 1/6
16	He LL, 2018	China	Between 22-36 years	N/R	N/R	N/R	N/R	28	N/R	N/R	Yes, <12hr	Yes, <12hr	Yes, 1/6
17	He LL, 2018	China	Between 22-36 years	N/R	N/R	N/R	N/R	28	N/R	N/R	Yes, <12hr	Yes, <12hr	Yes, 1/6
18	He LL, 2018	China	Between 22-36 years	N/R	N/R	N/R	N/R	28	N/R	N/R	Yes, <12hr	Yes, <12hr	Yes, 1/6
19	Wan JY, 2017	China	N/R	≥5.3	N/R	No HCV/HIV	N/R	28	At delivery	N/R	N/R	N/R	N/R
20	Wan JY, 2017	China	N/R	≥5.3	N/R	No HCV/HIV	N/R	28	At delivery	N/R	N/R	N/R	N/R
21	Wan JY, 2017	China	N/R	≥5.3	N/R	No HCV/HIV	N/R	28	At delivery	N/R	N/R	N/R	N/R
22	Hu MF, 2018	China	N/R	≥6.0	N/R	No HCV/HIV	N/R	28	N/R	N/R	Yes, At birth	Yes, At birth	Yes, 1/6

Abbreviations: N/R, not reported Sex of infant was not reported in any of the MTCT cases.

# Appendix J: Efficacy by timing of PAP initiation

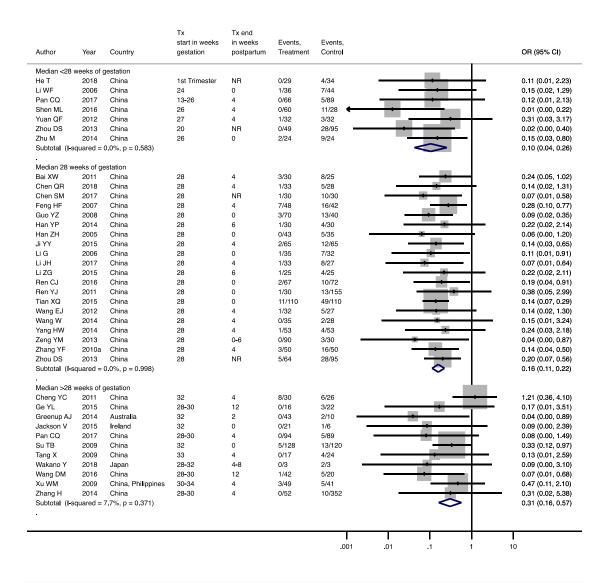
## • TDF 300 mg by timing of PAP initiation

- <28 weeks gestation (n=10): pooled OR= 0.10 (95% CI: 0.04-0.25), p<0.001,  $I^2$ =0%
- 28 weeks gestation (n=7): pooled OR=0.25 (95%CI: 0.13-0.48), p<0.001, I<sup>2</sup>=0%
- >28 weeks gestation (n=5): pooled OR=0.10 (95% CI: 0.03-0.29), p<0.001,  $I^2$ =0%
- The p-value for heterogeneity between subgroups was 0.15

Author	Year	Country	in weeks gestation	in weeks postpartum	Events, Treatment	Events, Control		OR (95% CI)
Median <28	weeks	of gestation	ı					
Celen MK	2013	Turkey	18-27	4	0/21	2/23	-	0.20 (0.01, 4.42
Gong Q	2017	China	1-6	NR	1/44	7/44	-	0.12 (0.01, 1.05
Hu MF	2018	China	14	NR	0/30	3/30		0.13 (0.01, 2.61
Huang Q	2017	China	24-28	12	0/20	3/20	-	0.12 (0.01, 2.53
Lin Y	2018	China	24	4	0/58	4/52		0.09 (0.00, 1.75
Wakano Y	2018	Japan	22-28	4-8	0/2	2/3		0.12 (0.00, 4.61
Wang HB	2018	China	20-24	NR	0/40	2/20	-	0.09 (0.00, 2.00
Yu CY	2018	China	24	4	0/30	4/30	-	0.10 (0.00, 1.88
Zhang BF	2018	China	24-28	0	0/39	15/75		0.05 (0.00, 0.85
Zhou Y	2018	China	24-28	0	0/60	5/36	-	0.05 (0.00, 0.88
Subtotal (I-s	squared	= 0.0%, p	= 1.000)					0.10 (0.04, 0.25
Median 28 w	eeks of	gestation						
Chen WJ		China	28	0	1/30	16/44		0.06 (0.01, 0.49
He LL	2018	China	28	NR	13/50	17/35		0.37 (0.15, 0.93
Hu MF	2018	China	28	NR	1/30	3/30		0.31 (0.03, 3.17
Jourdain G	2018	Thailand	26-29	8	0/149	3/147		0.14 (0.01, 2.70
Wan JY	2017	China	28	0	3/74	7/42		0.21 (0.05, 0.87
Wang HB	2018	China	28	NR	0/20	2/20		0.18 (0.01, 4.01
Xiao XH		China	28	0 or 4	0/60	1/61	-	0.33 (0.01, 8.35
Subtotal (I-s							$\Diamond$	0.25 (0.13, 0.48
Median >28	weeks (	of gestation	1					
Chen HL		Taiwan	30-32	4	1/65	6/56		0.13 (0.02, 1.12
Greenup AJ		Australia	32	12	1/69	2/10		0.06 (0.00, 0.72
Liu MH	2017	China	28-30	0	1/20	6/20		0.12 (0.01, 1.14
Pan CQ	2016	China	30-32	4	0/92	6/88		0.07 (0.00, 1.24
Wang HB	2018		32-36	NR	0/40	2/20		0.09 (0.00, 2.00
Subtotal (I-s				•	• =			0.10 (0.03, 0.29
	1	<b>, F</b>	,					
						<u> </u>	<del>- 1 - 1</del>	1

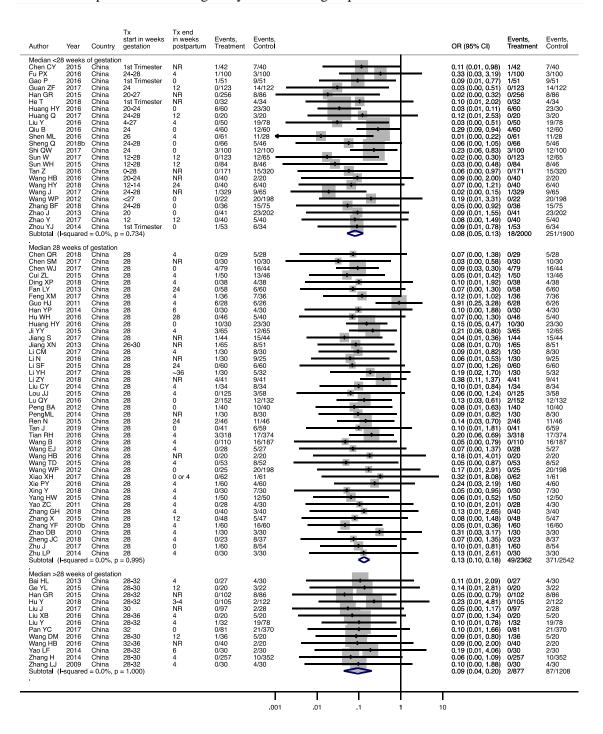
## • LAM 100-150 mg by timing of PAP initiation

- <28 weeks gestation (n=7): pooled OR= 0.10 (95%CI: 0.04-0.26), p<0.001,  $I^2$ =0%
- 28 weeks gestation (n=20): pooled OR=0.16 (95% CI: 0.11-0.22), p<0.001,  $I^2$ =0%
- >28 weeks gestation (n=11): pooled OR=0.31 (95%CI: 0.16-0.57), p<0.001, I<sup>2</sup>=0%
- The p-value for heterogeneity between subgroups was 0.06



## LdT 600 mg by timing of PAP initiation

- <28 weeks gestation (n=24): pooled OR=0.08 (95% CI: 0.05-0.13), p<0.001, I<sup>2</sup>=0%
- 28 weeks gestation (n=44): pooled OR=0.13 (95% CI: 0.10-0.18), p<0.001,  $I^2$ =0%
- >28 weeks gestation (n=13): pooled OR=0.09 (95%CI: 0.04-0.20), p<0.001,  $I^2$ =0%
- The p-value for heterogeneity between subgroups was 0.20



# **Appendix K: Efficacy by timing of PAP discontinuation**

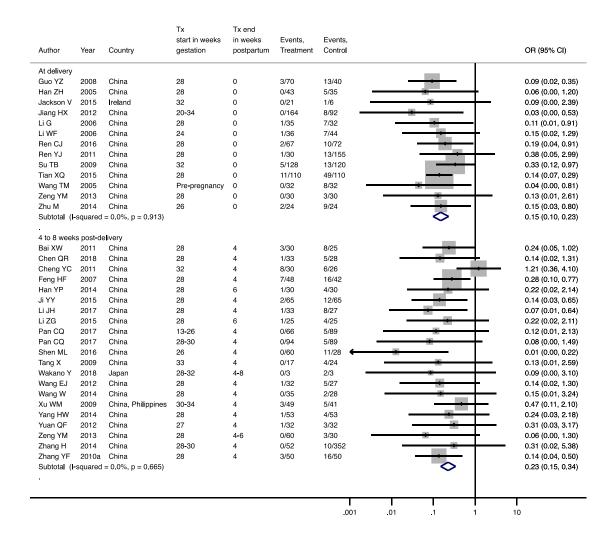
# • TDF 300 mg by timing of PAP discontinuation

- At delivery (n=5): pooled OR= 0.11 (95% CI: 0.04-0.28), p<0.001,  $I^2$ =0%
- 4-8 weeks after delivery (n=7): pooled OR=0.12 (95%CI: 0.04-0.34), p<0.001,  $I^2$ =0%
- The p-value for heterogeneity between subgroups was 0.96

			Tx start	Tx end					
			in weeks	in weeks	Events,	Events,			
Author	Year	Country	gestation	postpartum	Treatment	Control			OR (95% CI)
At delivery									
Chen WJ	2017	China	28	0	1/30	16/44	-		0.06 (0.01, 0.49)
Liu MH	2017	China	28	0	1/20	6/20			0.12 (0.01, 1.14)
Wan JY	2017	China	28	0	3/74	7/42		•	0.21 (0.05, 0.87)
Zhang BF	2018	China	24-28	0	0/39	15/75			0.05 (0.00, 0.85)
Zhou Y	2018	China	24-28	0	0/60	5/36			0.05 (0.00, 0.88)
Subtotal (I-s	quared =	= 0.0%, p = 0	0.751)				<	>	0.11 (0.04, 0.28)
•									
4 to 8 weeks	post-del	livery							
Celen MK	2013	Turkey	18-27	4	0/21	2/23		*	0.20 (0.01, 4.42)
Chen HL	2015	Taiwan	30-32	4	1/65	6/56			0.13 (0.02, 1.12)
Jourdain G	2018	Thailand	26-29	8	0/149	3/147	-		0.14 (0.01, 2.70)
Lin Y	2018	China	24	4	0/58	4/52		<del></del>	0.09 (0.00, 1.75)
Pan CQ	2016	China	30-32	4	0/92	6/88	-		0.07 (0.00, 1.24)
Wakano Y	2018	Japan	22-28	4-8	0/2	2/3			0.12 (0.00, 4.61)
Yu CY	2018	China	24	4	0/30	4/30			0.10 (0.00, 1.88)
Subtotal (I-s	quared =	= 0.0%, p = 0	0.999)				<	>	0.12 (0.04, 0.34)

## • LAM 100-150 mg by timing of PAP discontinuation

- At delivery (n=13): pooled OR= 0.15 (95% CI: 0.10-0.23), p<0.001,  $I^2=0\%$
- 4-8 weeks after delivery (n=21): pooled OR=0.23 (95%CI: 0.15-0.34), p<0.001, I<sup>2</sup>=0%
- The p-value for heterogeneity between subgroups was 0.19



## • LdT 600 mg by timing of PAP discontinuation

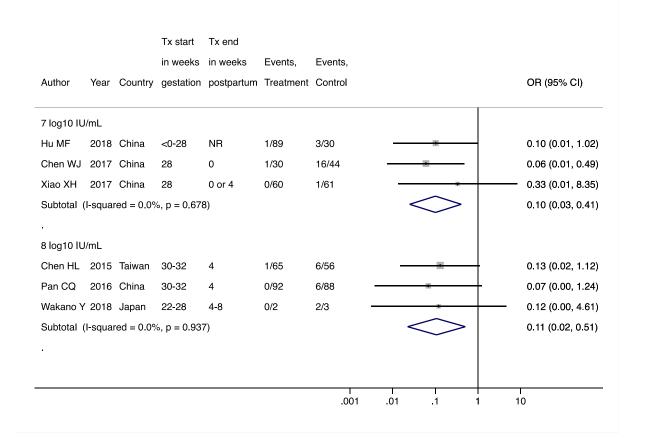
- At delivery (n=16): pooled OR=0.10 (95% CI: 0.06-0.16), p<0.001,  $I^2$ =0%
- 4-8 weeks after delivery (n=33): pooled OR=0.13 (95% CI: 0.09-0.19), p<0.001,  $I^2$ =0%
- 12 weeks after delivery (n=8): pooled OR=0.06 (95% CI: 0.02-0.16), p<0.001, I<sup>2</sup>=0%
- 24+ weeks after delivery (n=6): pooled OR=0.11 (95%CI: 0.04-0.29), p<0.001, I<sup>2</sup>=0%
- The p-value for heterogeneity between subgroups was 0.49

Idelivery Inter NVJ 2017 Isia PP 2016 Isian PP 2017 Isian PP 2017 Isian PP 2018 Isian	China   Chin	China 18 Trimester China 20-28 China 28 China 28 China 28 China 28 China 24-28 China 24-28 China 24-28 China 25-28 China 25-28 China 25-28 China 26-28 China 27 China 28 China	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	4/79 1/51 16/90 2/152 0/81 1/40 4/120 0/79 0/66 3/100 0/41 0/47 0/36 0/41 1/53 1/60  0/27 0/29 1/50 0/82 0/38 1/36 1/100 0/105 3/66 1/30 0/105 3/66 1/30 1/34 0/20 1/82	16/44 9/51 23/30 12/132 22/13/70 10/40 12/30 12/30 12/30 12/30 12/100 6/59 15/75 23/202 6/54 8/54 4/30 5/28 13/46 4/75 4/38 3/100 6/26 4/30 2/12/2 12/65 8/34 5/20 8/34 5/20			0.09 (0.03, 0.30) 0.09 (0.01, 0.77) 0.07 (0.02, 0.18) 0.13 (0.03, 0.61) 0.10 (0.01, 1.66) 0.08 (0.01, 0.83) 0.14 (0.04, 0.45) 0.05 (0.00, 1.06) 0.06 (0.00, 1.05) 0.23 (0.06, 0.83) 0.10 (0.01, 1.63) 0.10 (0.01, 1.81) 0.09 (0.01, 1.54) 0.05 (0.00, 0.83) 0.10 (0.01, 1.55) 0.09 (0.01, 1.55) 0.09 (0.01, 1.55) 0.09 (0.01, 0.78) 0.10 (0.01, 0.78) 0.11 (0.01, 0.81) 0.10 (0.06, 0.16) 0.11 (0.01, 0.81) 0.17 (0.01, 0.81) 0.19 (0.06, 0.16) 0.11 (0.01, 1.92) 0.10 (0.01, 1.92) 0.10 (0.01, 1.92) 0.11 (0.01, 1.92) 0.12 (0.01, 1.02) 0.23 (0.03, 3.19) 0.21 (0.25, 3.28) 0.10 (0.00, 1.88) 0.23 (0.01, 4.81) 0.21 (0.06, 0.80) 0.09 (0.01, 0.85)
then WJ. 2017 asia P 2016 asia P 2016 asia P 2016 asia P 2016 an YC 2016 asia P 2012 asia P 2013 asia P 2014 asia P 2014 asia P 2015 asia P 2015 asia P 2015 asia P 2015 asia P 2016 asia P 2	China   Chin	China 1st Trimester China 20-28 China 28 China 28 China 28 China 28 China 24-28 China 24-28 China 24-28 China 24-28 China 24-28 China 25 China 28	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	1/51 16/90 2/152 0/81 1/40 4/120 0/79 0/66 3/100 0/41 0/47 0/36 0/41 1/53 1/60   0/27 0/29 1/50 0/82 0/38 1/36 1/100 6/28 0/30 0/105 3/65 1/30 1/34 0/20 1/82	9/51 23/30 12/132 21/370 10/40 12/80 12/100 5/46 12/100 6/59 20/198 15/75 23/202 6/34 8/54 4/30 5/28 13/46 4/30 5/28 13/46 4/30 6/26 4/30 6/26 4/30 6/26 6/30 8/34 8/34 8/34			0.09 (0.01, 0.77) 0.07 (0.02, 0.18) 0.13 (0.03, 0.61) 0.10 (0.01, 1.66) 0.08 (0.01, 0.83) 0.14 (0.04, 0.45) 0.05 (0.00, 1.06) 0.06 (0.00, 1.05) 0.23 (0.06, 0.83) 0.10 (0.01, 1.81) 0.09 (0.01, 1.54) 0.05 (0.00, 0.09) 0.09 (0.01, 1.55) 0.09 (0.01, 1.55) 0.09 (0.01, 0.78) 0.10 (0.01, 0.81) 0.10 (0.06, 0.81) 0.11 (0.01, 0.81) 0.10 (0.06, 0.16)  0.11 (0.01, 2.09) 0.07 (0.00, 1.38) 0.05 (0.01, 0.78) 0.10 (0.01, 1.92) 0.12 (0.01, 1.92) 0.12 (0.01, 1.08) 0.13 (0.03, 3.19) 0.15 (0.01, 1.88) 0.23 (0.01, 1.88) 0.23 (0.01, 1.88) 0.24 (0.01, 1.88) 0.24 (0.01, 1.88) 0.24 (0.01, 0.88)
aiso P 2016 aison P 2016 aison P 2016 ain YC 2017 ain Y 2016 ain YC 2017 ain YC 2017 ain J 2012 ain B 2016 ain YC 2017 ain J 2018 ain Heng Q 2018 ain Heng Q 2018 ain Heng Q 2018 ain G 20	166 China 167 China 168 China 168 China 169 China 169 China 169 China 160 China 161 China 161 China 162 China 163 China 164 China 164 China 165 China 165 China 165 China 166 China 167 China 167 China 168 China 168 China 168 China 169 China 160 China 160 China 161 Ch	China 20-28 China 28 China 28 China 29 China 29 China 24-28 China 24 China 28 China 24-28 China 24-28 China 24-28 China 24-28 China 24-28 China 28	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	16/90 2/152 0/81 1/40 4/120 0/79 0/66 3/100 0/41 0/47 0/36 0/41 1/53 1/60    0/27 0/29 1/50 0/82 0/38 1/36 1/100 6/28 0/30 0/105 3/65 1/30 1/34 0/20 1/82	23/30 12/132 12/1370 10/40 12/60 22/1 5/46 12/100 6/59 20/198 15/75 23/202 6/24 8/54 4/30 5/28 13/46 4/75 4/38 7/36 3/100 6/26 4/30 2/122 12/65 8/30 8/34			0.09 (0.01, 0.77) 0.07 (0.02, 0.18) 0.13 (0.03, 0.61) 0.10 (0.01, 1.66) 0.08 (0.01, 0.83) 0.14 (0.04, 0.45) 0.05 (0.00, 1.06) 0.06 (0.00, 1.05) 0.23 (0.06, 0.83) 0.10 (0.01, 1.81) 0.09 (0.01, 1.54) 0.05 (0.00, 0.09) 0.09 (0.01, 1.55) 0.09 (0.01, 1.55) 0.09 (0.01, 0.78) 0.10 (0.01, 0.81) 0.10 (0.06, 0.81) 0.11 (0.01, 0.81) 0.10 (0.06, 0.16)  0.11 (0.01, 2.09) 0.07 (0.00, 1.38) 0.05 (0.01, 0.78) 0.10 (0.01, 1.92) 0.12 (0.01, 1.92) 0.12 (0.01, 1.08) 0.13 (0.03, 3.19) 0.15 (0.01, 1.88) 0.23 (0.01, 1.88) 0.23 (0.01, 1.88) 0.24 (0.01, 1.88) 0.24 (0.01, 1.88) 0.24 (0.01, 0.88)
u OY 216	161 China 172 China 182 China 183 China 184 China 185 China 186 China 187 China 187 China 187 China 187 China 188 China 187 China 188 China 189 China 181 China 181 China 182 China 183 China 184 China 185 China 185 China 186 China 187 China 187 China 188 China 188 China 189 China 181 Ch	China         28           China         32           China         28           China         24-32           China         24-28           China         24-28           China         24-28           China         22-28           China         20           China         20           China         28           - 0.999         28           China         28           China <td< td=""><td>0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0</td><td>2/152 0/81 1/40 4/1/20 0/79 0/66 3/100 0/41 0/47 0/36 0/41 1/53 1/60    0/27 0/29 1/50 0/82 0/38 1/36 1/100 6/28 0/30 0/105 3/65 1/30 1/34 0/20 1/82</td><td>12/132 21/370 10/40 12/60 12/60 22/1 5/46 12/100 6/59 20/198 15/75 23/202 6/34 8/34 4/30 5/28 13/46 4/75 4/38 7/26 3/100 6/26 4/30 6/26 8/30 8/34 5/30 8/34 5/30 8/34</td><td></td><td></td><td>0.07 (0.02, 0.18) 0.13 (0.03, 0.61) 0.10 (0.01, 1.86) 0.08 (0.01, 0.83) 0.14 (0.04, 0.45) 0.05 (0.01, 0.08) 0.16 (0.01, 0.08) 0.16 (0.00, 1.05) 0.23 (0.06, 0.83) 0.10 (0.01, 1.154) 0.05 (0.00, 1.05) 0.09 (0.01, 1.54) 0.05 (0.00, 0.92) 0.09 (0.01, 0.78) 0.10 (0.01, 1.81) 0.10 (0.06, 0.16)  0.11 (0.01, 0.81) 0.10 (0.06, 0.16)  0.11 (0.01, 2.09) 0.07 (0.00, 1.38) 0.05 (0.01, 0.42) 0.10 (0.01, 1.82) 0.10 (0.01, 1.92) 0.12 (0.01, 1.92) 0.12 (0.01, 1.92) 0.12 (0.01, 1.02) 0.13 (0.00, 3.19) 0.19 (0.01, 3.88) 0.10 (0.01, 1.88) 0.10 (0.01, 1.89) 0.12 (0.01, 1.02) 0.13 (0.00, 3.19) 0.14 (0.01, 1.89) 0.15 (0.01, 0.18)</td></td<>	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	2/152 0/81 1/40 4/1/20 0/79 0/66 3/100 0/41 0/47 0/36 0/41 1/53 1/60    0/27 0/29 1/50 0/82 0/38 1/36 1/100 6/28 0/30 0/105 3/65 1/30 1/34 0/20 1/82	12/132 21/370 10/40 12/60 12/60 22/1 5/46 12/100 6/59 20/198 15/75 23/202 6/34 8/34 4/30 5/28 13/46 4/75 4/38 7/26 3/100 6/26 4/30 6/26 8/30 8/34 5/30 8/34 5/30 8/34			0.07 (0.02, 0.18) 0.13 (0.03, 0.61) 0.10 (0.01, 1.86) 0.08 (0.01, 0.83) 0.14 (0.04, 0.45) 0.05 (0.01, 0.08) 0.16 (0.01, 0.08) 0.16 (0.00, 1.05) 0.23 (0.06, 0.83) 0.10 (0.01, 1.154) 0.05 (0.00, 1.05) 0.09 (0.01, 1.54) 0.05 (0.00, 0.92) 0.09 (0.01, 0.78) 0.10 (0.01, 1.81) 0.10 (0.06, 0.16)  0.11 (0.01, 0.81) 0.10 (0.06, 0.16)  0.11 (0.01, 2.09) 0.07 (0.00, 1.38) 0.05 (0.01, 0.42) 0.10 (0.01, 1.82) 0.10 (0.01, 1.92) 0.12 (0.01, 1.92) 0.12 (0.01, 1.92) 0.12 (0.01, 1.02) 0.13 (0.00, 3.19) 0.19 (0.01, 3.88) 0.10 (0.01, 1.88) 0.10 (0.01, 1.89) 0.12 (0.01, 1.02) 0.13 (0.00, 3.19) 0.14 (0.01, 1.89) 0.15 (0.01, 0.18)
u OY 216	161 China 177 China 182 China 183 China 184 China 185 China 186 China 187 China 187 China 187 China 187 China 188 China 187 China 188 China 189 China 181 China 181 China 182 China 183 China 184 China 185 China 185 China 186 China 187 China 187 China 188 China 189 China 181 Ch	China         28           China         32           China         28           China         24-32           China         24-28           China         24-28           China         24-28           China         22-28           China         20           China         20           China         28           - 0.999         28           China         28           China <td< td=""><td>0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0</td><td>2/152 0/81 1/40 4/1/20 0/79 0/66 3/100 0/41 0/47 0/36 0/41 1/53 1/60    0/27 0/29 1/50 0/82 0/38 1/36 1/100 6/28 0/30 0/105 3/65 1/30 1/34 0/20 1/82</td><td>12/132 21/370 10/40 12/60 12/60 22/1 5/46 12/100 6/59 20/198 15/75 23/202 6/34 8/34 4/30 5/28 13/46 4/75 4/38 7/26 3/100 6/26 4/30 6/26 8/30 8/34 5/30 8/34 5/30 8/34</td><td></td><td></td><td>0.13 (0.03, 0.61) 0.10 (0.01, 1.86) 0.08 (0.01, 0.63) 0.14 (0.04, 0.45) 0.05 (0.00, 1.06) 0.06 (0.00, 1.06) 0.23 (0.06, 0.83) 0.10 (0.01, 1.81) 0.09 (0.01, 1.84) 0.05 (0.00, 0.92) 0.09 (0.01, 1.55) 0.09 (0.01, 0.75) 0.10 (0.01, 0.81) 0.10 (0.01, 0.81) 0.11 (0.01, 2.09) 0.07 (0.00, 1.38) 0.05 (0.01, 0.78) 0.10 (0.01, 1.82) 0.10 (0.01, 1.82) 0.10 (0.01, 1.82) 0.10 (0.01, 1.82) 0.12 (0.01, 1.02) 0.13 (0.03, 3.19) 0.14 (0.01, 2.83) 0.15 (0.01, 0.88) 0.23 (0.03, 3.19) 0.21 (0.01, 1.88) 0.23 (0.01, 0.88) 0.23 (0.01, 0.88)</td></td<>	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	2/152 0/81 1/40 4/1/20 0/79 0/66 3/100 0/41 0/47 0/36 0/41 1/53 1/60    0/27 0/29 1/50 0/82 0/38 1/36 1/100 6/28 0/30 0/105 3/65 1/30 1/34 0/20 1/82	12/132 21/370 10/40 12/60 12/60 22/1 5/46 12/100 6/59 20/198 15/75 23/202 6/34 8/34 4/30 5/28 13/46 4/75 4/38 7/26 3/100 6/26 4/30 6/26 8/30 8/34 5/30 8/34 5/30 8/34			0.13 (0.03, 0.61) 0.10 (0.01, 1.86) 0.08 (0.01, 0.63) 0.14 (0.04, 0.45) 0.05 (0.00, 1.06) 0.06 (0.00, 1.06) 0.23 (0.06, 0.83) 0.10 (0.01, 1.81) 0.09 (0.01, 1.84) 0.05 (0.00, 0.92) 0.09 (0.01, 1.55) 0.09 (0.01, 0.75) 0.10 (0.01, 0.81) 0.10 (0.01, 0.81) 0.11 (0.01, 2.09) 0.07 (0.00, 1.38) 0.05 (0.01, 0.78) 0.10 (0.01, 1.82) 0.10 (0.01, 1.82) 0.10 (0.01, 1.82) 0.10 (0.01, 1.82) 0.12 (0.01, 1.02) 0.13 (0.03, 3.19) 0.14 (0.01, 2.83) 0.15 (0.01, 0.88) 0.23 (0.03, 3.19) 0.21 (0.01, 1.88) 0.23 (0.01, 0.88) 0.23 (0.01, 0.88)
ran YC 2017 eng BA 2012 lu B 2016 heng Q 2018 hid QW 2017 an J 2019 heng Q 2018 heng Q 2018 heng Q 2017 heng Q 2018 heng Q 2017 lu BA 2018 heng Q 2017 heng Q 2018 heng Q 2017 heng Q 2017 heng Q 2017 heng Q 2018 heng Q 2017 heng Q 2017 heng Q 2018 heng Q 2017 heng Q 2018 heng Q 2017 heng Q 2018	177 China 161 China 162 China 163 China 164 China 165 China 167 China 167 China 168 Ch	China 32 China 28 China 42-28 China 24-28 China 24-28 China 24-28 China 24-28 China 24-28 China 28 Chi	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0/81 1/40 4/120 0/79 0/66 3/100 0/41 0/47 0/36 0/41 1/53 1/60  0/27 0/29 1/50 0/82 0/38 1/36 1/100 0/105 3/65 1/30 1/34 0/20 1/82	21/370 10/40 12/60 12/60 2/21 5/46 12/100 6/59 20/198 15/75 23/202 6/54 8/54 4/30 5/28 13/46 4/38 7/36 4/38 7/36 3/100 6/26 4/30 2/122 2/126 8/30 8/34			0.10 (0.01.1.86) 0.08 (0.01.0.83) 0.14 (0.04.0.45) 0.05 (0.00.1.05) 0.23 (0.00.1.05) 0.23 (0.00.0.83) 0.10 (0.01.1.81) 0.09 (0.01.1.84) 0.05 (0.00.0.92) 0.09 (0.01.1.55) 0.09 (0.01.0.78) 0.10 (0.01.0.81) 0.10 (0.06.0.0.82) 0.09 (0.01.0.78) 0.10 (0.01.0.81) 0.10 (0.06.0.16)  0.11 (0.01.2.09) 0.07 (0.00.1.38) 0.05 (0.01.0.42) 0.10 (0.01.1.82) 0.10 (0.01.1.82) 0.10 (0.01.1.82) 0.10 (0.01.1.82) 0.10 (0.01.1.82) 0.10 (0.01.1.82) 0.10 (0.01.1.82) 0.12 (0.01.1.82) 0.12 (0.01.1.82) 0.13 (0.03.3.19) 0.14 (0.01.1.88) 0.10 (0.01.88) 0.23 (0.01.88)
eng BA 2012   Ibin B 2016   Ib	12	China         28           China         -0-24           China         24-32           China         24-28           China         28           China         28           China         20           China         20           China         28           = 0.999)         28           China         28           China         28           China         28           China         24-36           China         28           China	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	1/40 4/120 0/79 0/66 3/100 0/41 0/47 0/36 0/41 1/53 1/60    0/27 0/29 1/50 0/82 0/38 1/36 1/100 6/28 0/30 0/105 3/65 1/30 1/34 0/20 1/82	10/40 12/80 2/21 5/46 12/100 6/59 20/198 15/75 23/202 6/34 8/34 4/30 5/28 13/46 4/75 4/38 3/100 6/26 4/30 6/26 6/36 6/36 6/36 6/36 6/36 6/36 6/36			0.98 (0.01, 0.83) 0.14 (0.04, 0.45) 0.05 (0.00, 1.06) 0.06 (0.00, 1.06) 0.23 (0.06, 0.83) 0.10 (0.01, 1.81) 0.09 (0.01, 1.81) 0.09 (0.01, 1.55) 0.09 (0.01, 1.55) 0.09 (0.01, 0.78) 0.10 (0.01, 0.81) 0.10 (0.01, 0.81) 0.11 (0.01, 2.09) 0.07 (0.00, 1.38) 0.05 (0.01, 0.78) 0.10 (0.01, 1.82) 0.10 (0.01, 1.82) 0.10 (0.01, 1.82) 0.12 (0.01, 1.82) 0.12 (0.01, 1.82) 0.13 (0.03, 3.19) 0.25 (0.01, 0.48) 0.21 (0.05, 3.88) 0.23 (0.01, 4.81) 0.21 (0.06, 0.80)
No B	165 China 188b China 188b China 187 China 187 China 187 China 187 China 187 China 188	China	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	4/120 0/79 0/66 3/100 0/41 0/47 0/36 0/41 1/53 1/60  0/27 0/29 1/50 0/82 0/38 1/36 1/100 6/28 0/30 0/105 3/66 1/30 1/34 0/20 1/82	12/80 2/21 5/46 12/100 6/59 20/198 15/76 23/202 6/54 8/54 4/30 5/28 13/46 4/37 5/28 3/100 6/26 4/30 2/122 12/66 8/30 8/34 5/20		*	0.14 (0.04, 0.45) 0.05 (0.00, 1.06) 0.06 (0.00, 1.05) 0.23 (0.06, 0.83) 0.10 (0.01, 1.81) 0.09 (0.01, 1.54) 0.05 (0.00, 0.92) 0.09 (0.01, 1.55) 0.09 (0.01, 0.78) 0.10 (0.01, 0.81) 0.10 (0.06, 0.16)  0.11 (0.01, 2.09) 0.07 (0.00, 1.38) 0.05 (0.01, 0.42) 0.10 (0.01, 1.92) 0.12 (0.01, 1.92) 0.12 (0.01, 1.92) 0.13 (0.01, 1.88) 0.14 (0.01, 1.88) 0.15 (0.01, 0.88) 0.16 (0.01, 0.88) 0.17 (0.00, 1.88) 0.18 (0.01, 0.88) 0.19 (0.01, 1.88) 0.21 (0.01, 1.88) 0.21 (0.01, 1.88)
heng Q 2018 heng Q 2018 heng Q 2018 heng Q 2018 hi I OW 2017 an J 2019 Zang BF 2018 hang BF 2018 hang BF 2018 hang BF 2018 hang J 2017 to 8 weeks post-delivery lei HL u J 2017 to 8 weeks post-delivery lei HL u J 2017 to 8 weeks post-delivery lei HL u J 2017 to 8 weeks post-delivery lei HL u J 2015 heng Q 2017 to 8 weeks post-delivery lei HL u V 2018 to 9 2016 to 9 2017 to 9 2017 to 9 2017 to 9 2018 to 9 2017 to 9 2018 to 9	188a China 177 China 177 China 181 China 181 China 181 China 184 China 185 China 185 China 186 China 187 China 188 China 187 China 187 China 188 China 187 China 187 China 188 China 189 China 187 China 181	China 24-32 China 24-28 China 28 China 24-28 China 24-28 China 24-28 China 28 China 28 China 28 China 28 China 28 China 24-36 China 24-36 China 28	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0/79 0/66 3/100 0/41 0/47 0/36 0/41 1/53 1/60  0/27 0/29 1/50 0/82 0/38 1/36 1/100 6/28 0/30 0/105 3/65 1/30 1/34 0/20 1/82	221 5/46 12/100 6/59 20/198 15/76 23/202 6/54 8/54 8/54 8/54 8/54 8/54 8/54 8/54 8			0.05 (0.00, 1.06) 0.06 (0.00, 1.05) 0.23 (0.06, 0.83) 0.10 (0.01, 1.81) 0.09 (0.01, 1.54) 0.05 (0.00, 0.92) 0.09 (0.01, 1.55) 0.09 (0.01, 0.78) 0.10 (0.01, 0.78) 0.10 (0.01, 0.81) 0.10 (0.06, 0.16)  0.11 (0.01, 2.09) 0.07 (0.00, 1.38) 0.05 (0.01, 0.78) 0.10 (0.01, 1.82) 0.10 (0.01, 1.92) 0.12 (0.01, 1.02) 0.12 (0.01, 1.82) 0.10 (0.01, 1.82) 0.10 (0.01, 1.82) 0.10 (0.01, 1.82) 0.10 (0.01, 1.82) 0.10 (0.01, 1.82) 0.10 (0.01, 1.82) 0.12 (0.01, 1.02) 0.13 (0.03, 3.19) 0.14 (0.01, 1.88) 0.23 (0.01, 4.81) 0.21 (0.06, 0.80)
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to 8 weeks post-delivery ais I+L. 2013 ais I+L. 2013 ais I+L. 2013 ais I+L. 2013 ais I+L. 2015 ais I+L. 2016 ais I	0.0%, p = 0.999)  rery  13 China 18 China 18 China 15 China 15 China 16 China 16 China 11 China	= 0.999)  China 28-32 China 28 China 28 China 28 China 28 China 25 China 25 China 25 China 26 China 27 China 28 China 28 China 28 China 28 China 28 China 28 China 26 China 26 China 27 China 28	4 4 4 4 4 4 5 5 3-4 4 4 4 4	0/27 0/29 1/50 0/82 1/36 1/36 1/100 6/28 0/30 0/105 3/65 1/30 1/34 0/20 1/82	4/30 5/28 13/46 4/75 4/38 7/36 3/100 6/26 4/30 2/1/22 12/65 8/30 8/34			0.10 (0.06, 0.16)  0.11 (0.01, 2.09) 0.07 (0.00, 1.38) 0.05 (0.01, 0.42) 0.10 (0.01, 1.82) 0.10 (0.01, 1.92) 0.12 (0.01, 1.02) 0.33 (0.03, 3.19) 0.91 (0.25, 3.28) 0.10 (0.00, 1.88) 0.23 (0.01, 4.81) 0.21 (0.06, 0.80)
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hen OR	18	China         28           China         24-36           China         23           China         28           China         28           China         28           China         28           China         28-32           China         28           China         28           China         28           China         28           China         28-36           China         4-32           China         28           China         28           China         28           China         28	4 4 4 4 4 4 6 3-4 4 4 4	0/29 1/50 0/82 0/38 1/36 1/100 6/28 0/30 0/105 3/65 1/30 1/34 0/20 1/82	5/28 13/46 4/75 4/38 7/36 3/100 6/26 4/30 2/122 12/65 8/30 8/34 5/20			0.07 (0.00, 1.38) 0.05 (0.01, 0.42) 0.10 (0.01, 1.82) 0.10 (0.01, 1.92) 0.12 (0.01, 1.02) 0.33 (0.03, 3.19) 0.31 (0.25, 3.28) 0.10 (0.00, 1.88) 0.23 (0.01, 4.81) 0.21 (0.06, 0.80)
vai ZL         2015           vai ZL         2015           eng Y         2015           eng Y         2015           eng XM         2017           ue XP         2018           ue QM         2017           ui DH         2011           ui DH         2011           ui V         2018           ui Y         2015           ICM         2017           ui V         2016           ui V         2016           ui V         2015           ic M         2017           iu V         2016           ui V         2014           ui V         2016           ui V         2016           ui V         2016           ui V         2016           uang E         2012           uang E         2012           uang E         2014           uang C         2014           uang C         2014           uang C         2018           uang C         2018           uang C         2018           uang C         2016           uang C         2017 <td>15 China 15 China 16 China 17 China 16 China 16 China 11 China 11 China 11 China 11 China 11 China 11 China 12 China 14 China 14 China 15 China 16 China 16 China 16 China</td> <td>China 28 China 24-36 China 28 China 43 China 28 China 28 China 4-32 China 4-32 China 28 China 28</td> <td>4 4 4 4 4 6 3-4 4 4 4</td> <td>1/50 0/82 0/38 1/36 1/100 6/28 0/30 0/105 3/65 1/30 1/34 0/20 1/82</td> <td>13/46 4/75 4/38 7/36 3/100 6/26 4/30 2/122 12/65 8/30 8/34 5/20</td> <td></td> <td></td> <td>0.05 (0.01, 0.42) 0.10 (0.01, 1.82) 0.10 (0.01, 1.82) 0.12 (0.01, 1.02) 0.33 (0.03, 3.19) 0.91 (0.25, 3.28) 0.10 (0.00, 1.88) 0.23 (0.01, 4.81) 0.21 (0.06, 0.80)</td>	15 China 15 China 16 China 17 China 16 China 16 China 11 China 11 China 11 China 11 China 11 China 11 China 12 China 14 China 14 China 15 China 16 China 16 China 16 China	China 28 China 24-36 China 28 China 43 China 28 China 28 China 4-32 China 4-32 China 28	4 4 4 4 4 6 3-4 4 4 4	1/50 0/82 0/38 1/36 1/100 6/28 0/30 0/105 3/65 1/30 1/34 0/20 1/82	13/46 4/75 4/38 7/36 3/100 6/26 4/30 2/122 12/65 8/30 8/34 5/20			0.05 (0.01, 0.42) 0.10 (0.01, 1.82) 0.10 (0.01, 1.82) 0.12 (0.01, 1.02) 0.33 (0.03, 3.19) 0.91 (0.25, 3.28) 0.10 (0.00, 1.88) 0.23 (0.01, 4.81) 0.21 (0.06, 0.80)
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eng XM 2017 u PX 2016 uo HJ 2011 un Y 2014 u Y 2014 u Y 2015 u Y 2015 u Y 2015 u Y 2016 u Y 2016 u X 2017 u X 2	17 China 16 China 11 China 11 China 14 China 15 China 17 China 16 China	China         28           China         4-32           China         28           China         28           China         28           China         28	4 4 6 3-4 4 4 4 4	1/36 1/100 6/28 0/30 0/105 3/65 1/30 1/34 0/20 1/82	7/36 3/100 6/26 4/30 2/122 12/65 8/30 8/34 5/20			0.12 (0.01, 1.02) 0.33 (0.03, 3.19) 0.91 (0.25, 3.28) 0.10 (0.00, 1.88) 0.23 (0.01, 4.81) 0.21 (0.06, 0.80)
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iu XB 2016 iu Y 2016 iu Y 2016 iu Y 2015 hen ML 2016 lan RH 2016 lan RH 2016 lan RH 2016 lang B 2016 lang Y 2018 lang HW 2015 lang HW 2015 lang HW 2015 lang HW 2016 lang Y 2018 lang HW 2015 lang HW 2016 lang Y 2018 lang HW 2016 lang W 2018 lang HW 2016 lang W 2018 lang HW 2016 lang W 2018 lang	16 China 16 China 15 China 16 China	China         28-36           China         4-32           China         28           China         26	4 4 4	0/20 1/82	5/20			
iu Y 2016 uu J 2015 bhem ML 2016 lan RH 20	16 China 15 China 16 China	China 4-32 China 28 China 26	4 4	1/82				0.10 (0.01, 0.84)
ou JJ 2015 henn ML 2016 han RH 2016 han RH 2016 han RH 2016 hang B 2016 hang H 2015 hang H 2014 hang L 2016 hang H 2016 hang H 2016 hang H 2016 hang H 2016 hang L 2017 hang D	15 China 16 China	China 28 China 26	4		19/78			0.07 (0.00, 1.34)
ou JJ 2015 henn ML 2016 han RH 2016 han RH 2016 han RH 2016 hang B 2016 hang H 2015 hang H 2014 hang L 2016 hang H 2016 hang H 2016 hang H 2016 hang H 2016 hang L 2017 hang D	15 China 16 China	China 28 China 26	4			-		0.04 (0.00, 0.29)
hen ML 2016 inan RH 2016 fang B 2016 fang	16 China	China 26		0/125	3/58			0.06 (0.00, 1.24)
ian RH 2016 Vang B 2016 Vang EJ 2012 Vang TD 2015 Vang TD 2016 Vang TD 2016 Vang TD 2016 Vang TD 2017 Vang TD			4	0/61	11/28			0.01 (0.00, 0.22)
Vang B 2016 Vang T 2012 Vang T D 2015 Vang T D 2015 Vang T D 2015 Vang T D 2016 Vang T D 2017 Vang T								
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ing Y 2018 ang HW 2017 ao LF 2014 ao ZC 2011 ao ZC 2011 ao ZC 2011 ang GH 2018	15 China	China 28	4	0/53	8/52			0.05 (0.00, 0.87)
ing Y 2018 ang HW 2017 ao LF 2014 ao ZC 2011 ao ZC 2011 ao ZC 2011 ang GH 2018	16 China	China 28	4	1/60	4/60			0.24 (0.03, 2.19)
ang HW 2015 ao LE 2014 ao ZC 2011 hang GH 2018 hang GH 2018 hang H 2014 hang LJ 2009 hang JF 2010 hang DB 2010 hang DB 2010 hang JC 2018 hubbotal (I-aquared = 0.0 2 weeks post-delivery ie YL 2015 huan ZF 2017 huang Q 2017 huang M 2017			4	0/30	7/30			0.05 (0.00, 0.95)
ao LF 2014 ao C 2 2014 hang GH 2018 hang H 2014 hang LJ 2016 hang YF 2010 hang YF 2010 hang YF 2010 hang YF 2010 hang YF 2016 hang JC 2018 hu LP 2015 hu LP 2015 hu LP 2017 hu LP 2	15 China	China 28	4	1/50	12/50			0.06 (0.01, 0.52)
ao ZC 2011 hang GH 2018 hang H 2014 hang LU 2009 hang YF 2010 hang JE 2010 hang JE 2010 hang JE 2010 hang JE 2011 hu LP 2014 ubibotal (Lequared = 0.0 2 weeks post-delivery is YL 2015 huan ZF 2017 huang Q 2017 huang Q 2017 huang W 2017			6	0/30	2/30			0.19 (0.01, 4.06)
hang GH 2018 hang LJ 2009 hang YF 2010 hang JG 2018 hang JC 2018 hu LP 2014 ubtotal (l-squared = 0.0  2 weeks post-delivery is YL 2015 luang Q 2017 un W 2017 un W 2017								
hang H 2014 hang LJ 2009 hang YF 2010t hao DB 2010 heng JC 2018 hu LP 2014 hubtotal (I-squared = 0.0 2 weeks post-delivery ie YL 2015 suan ZF 2017 huang Q 2017 hu W 2017			4	0/28	4/30		-	0.10 (0.01, 2.01)
hang LJ 2009 hang YF 2010k hang DB 2010 heng JC 2018 hu LP 2014 kubtotal (I-squared = 0.0 2 weeks post-delivery tei YL 2015 huang Q 2017 hung Q 2017 hun WH 2015			4	0/40	3/40			0.13 (0.01, 2.65)
hang VF 2010k hang JC 2018 hu LP 2014 hu LP 2014 hu LP 2014 cubtotal (I-squared = 0.0 2 weeks post-delivery is et YL 2015 huang Q 2017 hung Q 2017 hun W 2015 huan VH 2015	14 China		4	0/257	10/352	-	-	0.06 (0.00, 1.09)
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hao DB 2010 heng JC 2018 hu LP 2014 hubtotal (I-squared = 0.0  2 weeks post-delivery is YL 2015 duan ZF 2017 huang Q 2017 hun W 2017 hun WH 2015	10b China	China 28	4	1/60	16/60	-		0.05 (0.01, 0.36)
theng JC 2018 thu LP 2014 ubtotal (I-squared = 0.0 2 weeks post-delivery tie YL 2015 tiuan ZF 2017 tuang Q 2017 tun W 2017 tun WH 2015			4	1/30	3/30	_	-	0.31 (0.03, 3.17)
thu LP 2014 ubtotal (I-squared = 0.0 2 weeks post-delivery 6 YL 2015 30an ZF 2017 luang Q 2017 uun WH 2015	18 China	China 28	4	0/23	8/37			0.07 (0.00, 1.35)
2 weeks post-delivery ise YL 2015 Suan ZF 2017 Ituang Q 2017 Itun W 2015 Itun WH 2015			4	0/30	3/30		_	0.13 (0.01, 2.61)
2 weeks post-delivery se YL 2015 suan ZF 2017 luang Q 2017 sun W 2017 sun WH 2015			*	0/30	3/30		~	0.13 (0.09, 0.19)
ie YL 2015 Guan ZF 2017 Iluang Q 2017 Iun W 2017 Iun WH 2015	o.o.n, p = 0.832)	- 0.002)					~	0.13 (0.08, 0.18)
ie YL 2015 Guan ZF 2017 Iluang Q 2017 Iun W 2017 Iun WH 2015								
Buan ZF 2017 Iluang Q 2017 Iun W 2017 Iun WH 2015		China 28-30	12	0/20	3/22			0.14 (0.01, 2.81)
luang Q 2017 iun W 2017 iun WH 2015			12	0/123	14/122			0.03 (0.00, 0.51)
iun W 2017 iun WH 2015				0/123	3/20			
iun WH 2015		011110	12					0.12 (0.01, 2.53)
			12	0/123	12/65			0.02 (0.00, 0.30)
			12	0/84	8/46			0.03 (0.00, 0.48)
Vang DM 2016	16 China	China 28-30	12	1/36	5/20		•	0.09 (0.01, 0.80)
hang X 2015	15 China	China 28	12	0/48	5/47	_		0.08 (0.00, 1.48)
hao Y 2017	17 China	China 12	12	0/40	5/40			0.08 (0.00, 1.49)
iubtotal (I-squared = 0.0							<b>&gt;</b>	0.06 (0.02, 0.16)
,		*					_	()
4+ weeks post-delivery	ry					_		
an LY 2013		China 28	24	0/58	6/60			0.07 (0.00, 1.30)
lu WH 2016	13 China		28	0/46	5/40			0.07 (0.00, 1.30)
iSF 2015			24	0/60	6/60			0.07 (0.00, 1.36)
	16 China				5/32			
	16 China 15 China		~36	1/30				0.19 (0.02, 1.70)
len N 2015	16 China 15 China 17 China		24	2/46	11/46	_		0.14 (0.03, 0.70)
Vang HY 2018	16 China 15 China 17 China 15 China	China 12-14	24	0/40	6/40		-	0.07 (0.00, 1.21)
subtotal (I-squared = 0.0	16 China 15 China 17 China 15 China					<	$\Rightarrow$	0.11 (0.04, 0.29)
	16 China 15 China 17 China 15 China 18 China	= 0.980)						
	16 China 15 China 17 China 15 China 18 China	= 0.980)						
	16 China 15 China 17 China 15 China 18 China	= 0.980)						

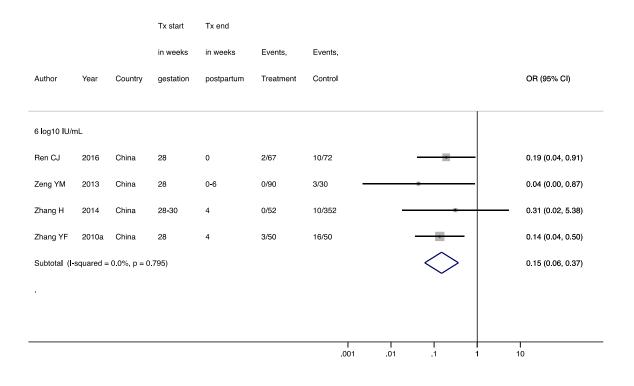
## Appendix L: Efficacy by mean maternal viral load at baseline

#### • TDF 300 mg by mean maternal viral load at baseline

- 7.0-7.9 log10 IU/mL (n=3): pooled OR= 0.10 (95%CI: 0.03-0.41), p=0.001,  $I^2$ =0%
- $8.0-8.9 \log 10 \text{ IU/mL}$  (n=3): pooled OR= 0.11 (95%CI: 0.02-0.51), p<0.001,  $I^2=0\%$
- The p-value for heterogeneity between subgroups was 0.96
- Note: Studies were only included in this analysis if the standard deviation for the mean viral load at baseline was less than or equal to 1

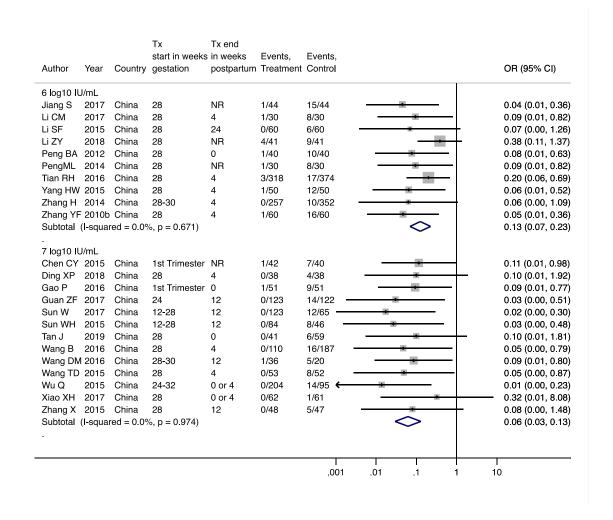


**LAM 100-150 mg by mean maternal viral load at baseline**• 6.0-6.9 log10 IU/mL (n=4): pooled OR= 0.15 (95%CI: 0.06-0.37), p=0.001, I<sup>2</sup>=0%



### • LdT 600 mg by mean maternal viral load at baseline

- 6.0-6.9 log10 IU/mL (n=10): pooled OR= 0.13 (95%CI: 0.07-0.23), p<0.001, I<sup>2</sup>=0%
- 7.0-7.9 log10 IU/mL (n=13): pooled OR= 0.06 (95% CI: 0.03-0.13), p<0.001,  $I^2$ =0%
- The p-value for heterogeneity between subgroups was 0.14



# Appendix M: Efficacy by maternal HBeAg status at baseline

TDF 300 mg by maternal HBeAg status at baseline
 HBeAg positive only (n=11): pooled OR= 0.09 (95%CI: 0.04-0.21), p<0.001, I²=0%</li>

			Tx start in weeks	Tx end in weeks	Events,	Events,			
Author	Year	Country	gestation	postpartum	Treatment	Control			OR (95% CI)
All HBeAg po	sitive								
Celen MK	2013	Turkey	18-27	4	0/21	2/23		-	0.20 (0.01, 4.42)
Chen HL	2015	Taiwan	30-32	4	1/65	6/56	_	-	0.13 (0.02, 1.12)
Chen WJ	2017	China	28	0	1/30	16/44			0.06 (0.01, 0.49)
Huang Q	2017	China	24-28	12	0/20	3/20		-	0.12 (0.01, 2.53)
Jourdain G	2018	Thailand	26-29	8	0/149	3/147	-		0.14 (0.01, 2.70)
Lin Y	2018	China	24	4	0/58	4/52			0.09 (0.00, 1.75)
Liu MH	2017	China	28-30	0	1/20	6/20	_	-	0.12 (0.01, 1.14)
Pan CQ	2016	China	30-32	4	0/92	6/88			0.07 (0.00, 1.24)
Wakano Y	2018	Japan	22-28	4-8	0/2	2/3			0.12 (0.00, 4.61)
Zhang BF	2018	China	24-28	0	0/39	15/75			0.05 (0.00, 0.85)
Zhou Y	2018	China	24-28	0	0/60	5/36		-	0.05 (0.00, 0.88)
Subtotal (I-so	quared =	0.0%, p = 1.	000)					$\Diamond$	0.09 (0.04, 0.21)
								-	
						.001	.01	.1	 

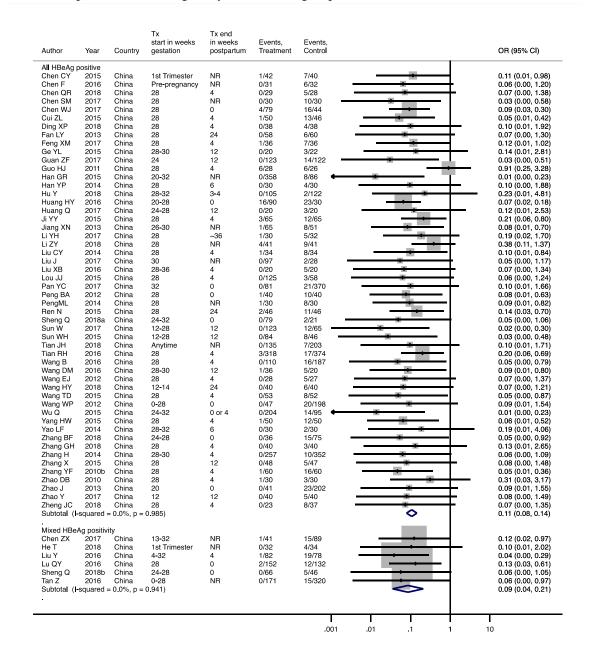
# • LAM 100-150 mg by maternal HBeAg status at baseline

- HBeAg positive only (n=30): pooled OR= 0.16 (95% CI: 0.12-0.23), p<0.001,  $I^2=0$ %
- Mixed HBeAg positivity (n=4): pooled OR=0.26 (95%CI: 0.08-0.82), p=0.022, I<sup>2</sup>=0%
- The p-value for heterogeneity between subgroups was 0.45

Author	Year	Country	start in weeks gestation	in weeks postpartum	Events, Treatment	Events, Control	OR (95% CI)
All HBeAg po	ositive						
Chen QR	2018	China	28	4	1/33	5/28	0.14 (0.02, 1.31)
Chen SM	2017	China	28	NR	1/30	10/30	0.07 (0.01, 0.58)
Cheng YC	2011	China	32	4	8/30	6/26	1.21 (0.36, 4.10)
Feng HF	2007	China	28	4	7/48	16/42	0.28 (0.10, 0.77)
Ge YL	2015	China	28-30	12	0/16	3/22	0.17 (0.01, 3.51)
Guo YZ	2008	China	28	0	3/70	13/40	0.09 (0.02, 0.35)
Han YP	2014	China	28	6	1/30	4/30	0.22 (0.02, 2.14)
Han ZH	2005	China	28	0	0/43	5/35	0.06 (0.00, 1.20)
Jackson V	2015	Ireland	32	0	0/21	1/6	0.09 (0.00, 2.39)
Ji YY	2015	China	28	4	2/65	12/65	0.14 (0.03, 0.65)
Jiang HX	2012	China	20-34	0	0/164	8/92	0.03 (0.00, 0.53)
Li G	2006	China	28	0	1/35	7/32	0.11 (0.01, 0.91)
Li WF	2006	China	24	0	1/36	7/44	0.15 (0.02, 1.29)
Li ZG	2015	China	28	6	1/25	4/25	0.22 (0.02, 2.11)
Ma J	2006	China	Pre-pregnancy	NR	0/18	9/16	0.02 (0.00, 0.41)
Pan CQ	2017	China	13-30	4	0/160	5/89	0.05 (0.00, 0.88)
Ren CJ	2016	China	28	0	2/67	10/72	0.19 (0.04, 0.91)
Ren YJ	2011	China	28	0	1/30	13/155	0.38 (0.05, 2.99)
Tang X	2009	China	33	4	0/17	4/24	0.13 (0.01, 2.59)
Tian XQ	2015	China	28	0	11/110	49/110	0.14 (0.07, 0.29)
Wakano Y	2018	Japan	28-32	4-8	0/3	2/3	0.09 (0.00, 3.10)
Wang DM	2016	China	28-30	12	1/42	5/20	0.07 (0.01, 0.68)
Wang EJ	2010	China	28	4	1/32	5/27	0.14 (0.02, 1.30)
Wang TM	2005	China	Pre-pregnancy	0	0/32	8/32	0.14 (0.02, 1.30,
Yang HW	2003	China	28	4	1/53	4/53	0.24 (0.03, 0.81)
Yuan QF	2014	China	27	4	1/32	3/32	0.24 (0.03, 2.18,
Zeng YM	2012	China	28	<del>4</del> 0 <b>-</b> 6	0/90	3/30	0.31 (0.03, 3.17)
Zeng rivi Zhang H	2013	China	28-30	4	0/90	10/352	0.04 (0.00, 0.87)
Zhang H Zhang YF	2014 2010a	China	28	4	3/50	16/50	
Znang 1F Zhu M	2010a	China	26	0	3/30 2/24	9/24	0.14 (0.04, 0.50)
		= 0.0%, p = 0.847)	26	U	2/24	9/24	0.15 (0.03, 0.80) 0.16 (0.12, 0.23)
Mixed HBeA	a positivi	itv					
Foaud HM	2019	Egypt	Anytime	NR	0/29	1/30	0.33 (0.01, 8.52)
Greenup AJ		Australia	32	2	0/43	2/10	0.04 (0.00, 0.89)
не Т	2018	China	1st Trimester	NR	0/29	4/34	0.11 (0.01, 2.23)
Xu WM	2009	China, Philippines		4	3/49	5/41	0.47 (0.11, 2.10)
		= 0.0%, p = 0.504)	55 07	•	5.70	<b>~</b>	0.26 (0.08, 0.82)
							<del></del>

### • LdT 600 mg by maternal HBeAg status at baseline

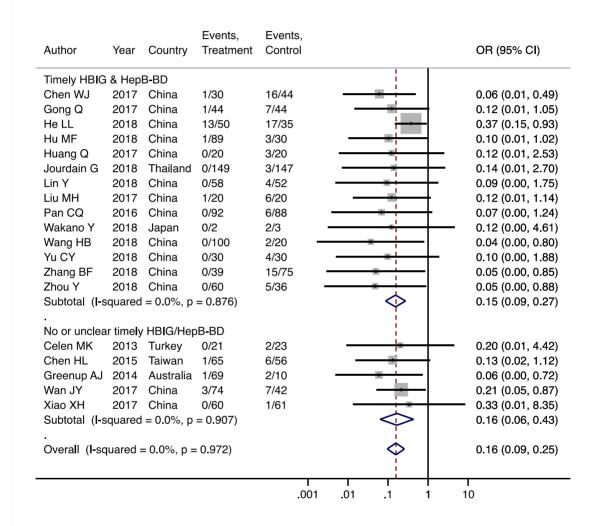
- HBeAg positive only (n=52): pooled OR= 0.11 (95% CI: 0.08-0.14), p<0.001,  $I^2=0\%$
- Mixed HBeAg positivity (n=6): pooled OR=0.09 (95%CI: 0.04-0.21), p<0.001,  $I^2=0\%$
- The p-value for heterogeneity between subgroups was 0.65



## Appendix N: Efficacy by infant immunoprophylaxis regimen

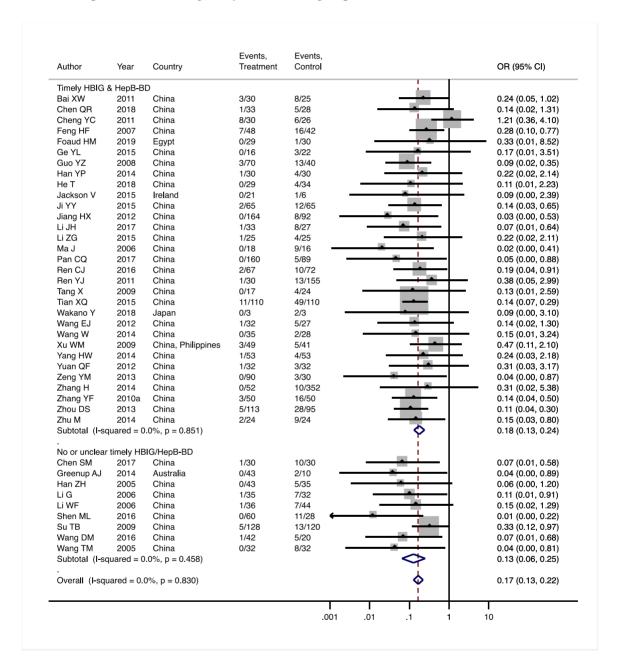
#### • TDF 300 mg by infant immunoprophylaxis regimens

- Timely HepB-BD & HBIG (n=14): pooled OR= 0.15 (95% CI: 0.09-0.27), p<0.001,  $I^2=0\%$
- No or unclear timely HepB-BD/HBIG (n=5): pooled OR=0.16 (95%CI: 0.06-0.43), p<0.001,  $I^2=0\%$
- The p-value for heterogeneity between subgroups was 0.89



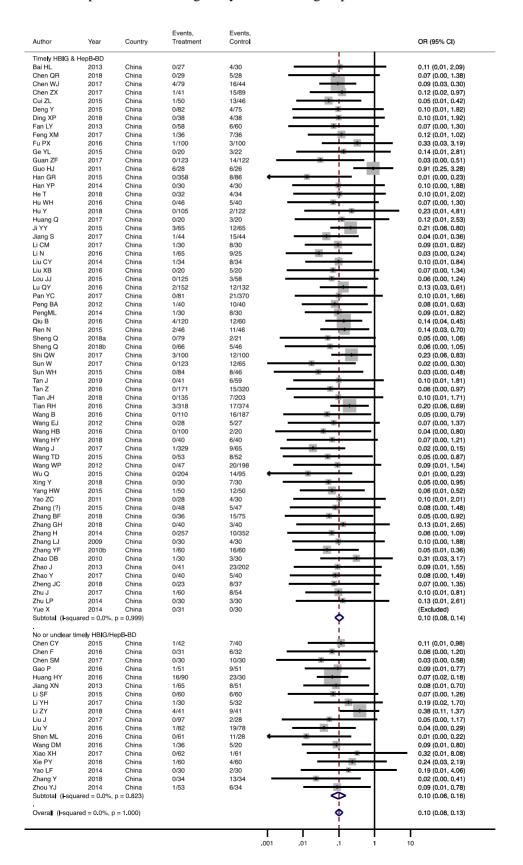
### • LAM 100-150 mg by infant immunoprophylaxis regimens

- Timely HepB-BD & HBIG (n=31): pooled OR= 0.18 (95%CI: 0.13-0.24), p<0.001,  $I^2=0\%$
- No or unclear timely HepB-BD/HBIG (n=9): pooled OR=0.13 (95%CI: 0.06-0.25), p<0.001,  $I^2$ =0%
- The p-value for heterogeneity between subgroups was 0.38



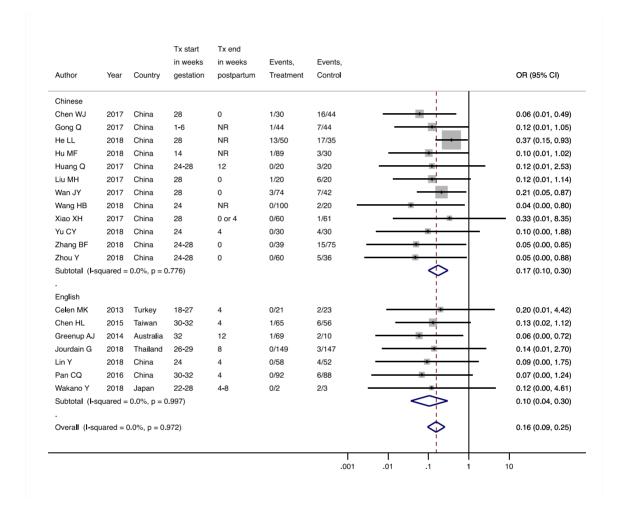
## • LdT 100-150 mg by infant immunoprophylaxis regimens

- Timely HepB-BD & HBIG (n=64): pooled OR= 0.10 (95% CI: 0.08-0.14), p<0.001,  $I^2=0\%$
- No or unclear timely HepB-BD/HBIG (n=18): pooled OR=0.10 (95%CI: 0.06-0.16), p<0.001,  $I^2=0\%$
- The p-value for heterogeneity between subgroups was 0.83



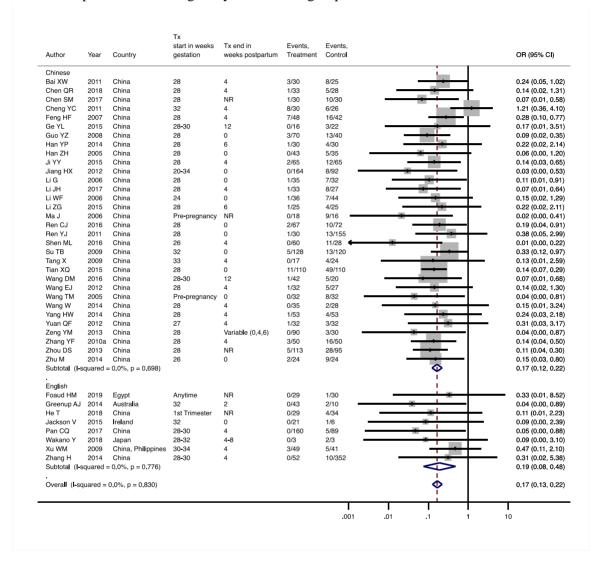
# Appendix O: Efficacy by language used for reporting (Chinese versus English)

- TDF 300 mg by language used for reporting (Chinese versus English)
- Chinese language (n=12): pooled OR= 0.17 (95% CI: 0.10-0.30), p<0.001,  $I^2=0\%$
- English language (n=7): pooled OR=0.10 (95% CI: 0.04-0.30), p<0.001,  $I^2$ =0%
- The p-value for heterogeneity between subgroups was 0.40



### • LAM 100-150 mg by language used for reporting (Chinese versus English)

- Chinese language (n=32): pooled OR= 0.17 (95% CI: 0.12-0.22), p<0.001,  $I^2=0\%$
- English language (n=8): pooled OR=0.19 (95%CI: 0.08-0.48), p<0.001,  $I^2$ =0%
- The p-value for heterogeneity between subgroups was 0.78



# • LdT 600 mg by language used for reporting (Chinese versus English)

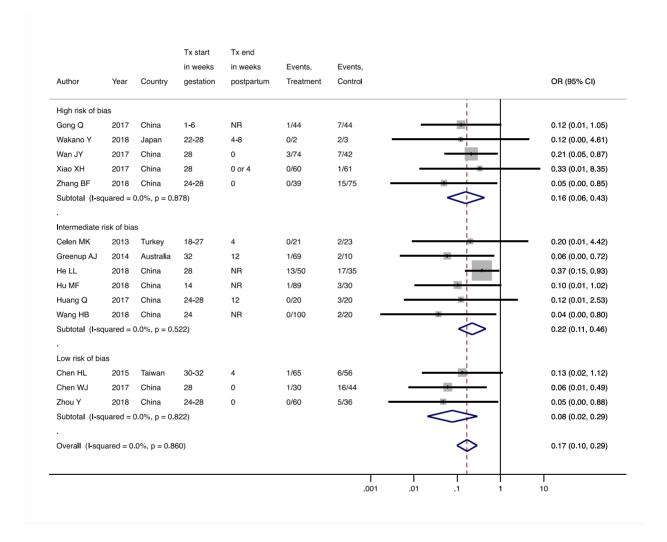
- Chinese language (n=72): pooled OR= 0.11 (95% CI: 0.08-0.14), p<0.001,  $I^2=0\%$
- English language (n=11): pooled OR=0.05 (95%CI: 0.02-0.11), p<0.001, I<sup>2</sup>=0%
- The p-value for heterogeneity between subgroups was 0.07

Author	Year	Country	start in weeks gestation	in weeks postpartum	Events, Treatment	Events, Control		OR (95% CI)
Chinese								
Bai HL	2013	China	28-32	4	0/27	4/30		0.11 (0.01, 2.09)
Chen CY	2015	China	1st Trimester	NR	1/42	7/40		0.11 (0.01, 0.98)
Chen F	2016	China	Pre-pregnancy	NR	0/31	6/32		0.06 (0.00, 1.20)
Chen QR	2018	China	28	4	0/29	5/28	-	0.07 (0.00, 1.38)
Chen SM	2017	China	28	NR	0/30	10/30	<del></del>	0.03 (0.00, 0.58)
Chen WJ	2017	China	28	0	4/79	16/44		0.09 (0.03, 0.30)
Cui ZL	2015	China	28	4	1/50	13/46		0.05 (0.01, 0.42)
Deng Y	2015	China	24-36	4	0/82	4/75		0.10 (0.01, 1.82)
Ding XP	2018	China	28	4	0/38	4/38	-	0.10 (0.01, 1.92)
Fan LY	2013	China	28	24	0/58	6/60		0.07 (0.00, 1.30)
Feng XM	2017	China	28	4	1/36	7/36		0.12 (0.01, 1.02)
Fu PX	2016	China	24-28	4	1/100	3/100	<del></del>	0.33 (0.03, 3.19)
Gao P	2016	China	1st Trimester	0	1/51	9/51		0.09 (0.01, 0.77)
Ge YL	2015	China	28-30	12	0/20	3/22	- 12	0.14 (0.01, 2.81)
Guan ZF	2017	China	24	12	0/123	14/122		0.03 (0.00, 0.51)
Guo HJ	2011	China	28	4	6/28	6/26		0.91 (0.25, 3.28)
Han YP Hu WH	2014 2016	China China	28 28	6 28	0/30 0/46	4/30 5/40		0.10 (0.00, 1.88)
	2016	China	20	0	16/90	23/30		0.07 (0.00, 1.30)
Huang HY Huang Q	2017	China	24-28	12	0/20	3/20		0.07 (0.02, 0.18) 0.12 (0.01, 2.53)
Ji YY	2015	China	28	4	3/65	12/65		0.21 (0.06, 0.80)
Jiang S	2017	China	28	NR	1/44	15/44		0.04 (0.01, 0.36)
Jiang XN	2017	China	26-30	NR	1/65	8/51		0.04 (0.01, 0.30)
Li CM	2017	China	28	4	1/30	8/30		0.09 (0.01, 0.82)
Li N	2016	China	28	NR NR	1/65	9/25		0.03 (0.00, 0.24)
LiSF	2015	China	28	24	0/60	6/60		0.07 (0.00, 1.26)
LIYH	2017	China	28	~36	1/30	5/32	<del></del>	0.19 (0.02, 1.70)
Li ZY	2018	China	28	NR	4/41	9/41	<u> </u>	0.38 (0.11, 1.37)
Liu CY	2014	China	28	4	1/34	8/34	-	0.10 (0.01, 0.84)
Liu J	2017	China	30	NR	0/97	2/28	- <del> </del>	0.05 (0.00, 1.17)
Liu XB	2016	China	28-36	4	0/20	5/20		0.07 (0.00, 1.34)
Lou JJ	2015	China	28	4	0/125	3/58	-	0.06 (0.00, 1.24)
Lu QY	2016	China	28	0	2/152	12/132		0.13 (0.03, 0.61)
Pan YC	2017	China	32	0	0/81	21/370		0.10 (0.01, 1.66)
Peng BA	2012	China	28	0	1/40	10/40		0.08 (0.01, 0.63)
PengML	2014	China	28	NR	1/30	8/30		0.09 (0.01, 0.82)
Qiu B	2016	China	Pre-pregnancy	0	4/120	12/60	<del></del>	0.14 (0.04, 0.45)
Ren N	2015	China	28	24	2/46	11/46		0.14 (0.03, 0.70)
Shen ML	2016	China	26	4	0/61	11/28		0.01 (0.00, 0.22)
Shi QW Sun WH	2017 2015	China	24 12	0 12	3/100 0/84	12/100 8/46		0.23 (0.06, 0.83)
		China						0.03 (0.00, 0.48)
Tan J Tian JH	2019 2018	China China	28 Anytime	0 NR	0/41 0/135	6/59 7/203		0.10 (0.01, 1.81) 0.10 (0.01, 1.71)
Tian RH	2016	China	28	4	3/318	17/374		0.20 (0.06, 0.69)
Wang B	2016	China	28	4	0/110	16/187		0.05 (0.00, 0.79)
Wang DM	2016	China	28-30	12	1/36	5/20		0.09 (0.01, 0.80)
Wang EJ	2012	China	28	4	0/28	5/27		0.07 (0.00, 1.37)
Wang HB	2016	China	32	NB	0/100	2/20		0.04 (0.00, 0.80)
Wang HY	2018	China	12-14	24	0/40	6/40		0.07 (0.00, 1.21)
Wang J	2017	China	24-28	NR	1/329	9/65		0.02 (0.00, 0.15)
Wang TD	2015	China	28	4	0/53	8/52		0.05 (0.00, 0.87)
Wang WP	2012	China	28	0	0/47	20/198	-	0.09 (0.01, 1.54)
Xiao XH	2017	China	28	0 or 4	0/62	1/61		0.32 (0.01, 8.08)
Xie PY	2016	China	28	4	1/60	4/60		0.24 (0.03, 2.19)
Xing Y	2018	China	28	4	0/30	7/30		0.05 (0.00, 0.95)
Yang HW	2015	China	28	4	1/50	12/50		0.06 (0.01, 0.52)
Yao LF	2014	China	28-32	6	0/30	2/30		0.19 (0.01, 4.06)
Yao ZC	2011	China	28	4	0/28	4/30		0.10 (0.01, 2.01)
Zhang BF	2018	China	24-28	0	0/36	15/75	- 1	0.05 (0.00, 0.92)
Zhang GH	2018	China	28	4	0/40	3/40		0.13 (0.01, 2.65)
Zhang LJ	2009 2015	China	28-32	4 12	0/30 0/48	4/30 5/47		0.10 (0.00, 1.88)
Zhang X	2015 2018	China China	28 Bro prognancy	12 NR	0/48	5/47 13/34		0.08 (0.00, 1.48) 0.02 (0.00, 0.41)
Zhang Y Zhang YF	2018 2010b	China	Pre-pregnancy 28	NH 4	1/60	16/60		0.02 (0.00, 0.41)
Zhang TF Zhao DB	20100	China	28	4	1/30	3/30		0.31 (0.03, 3.17)
Zhao J	2010	China	20	0	0/41	23/202		0.01 (0.03, 3.17)
Zhao Y	2017	China	12	12	0/40	5/40	-	0.08 (0.00, 1.49)
Zheng JC	2018	China	28	4	0/23	8/37		0.07 (0.00, 1.35)
Zhou YJ	2014	China	1st Trimester	o o	1/53	6/34		0.09 (0.01, 0.78)
Zhu J	2017	China	28	0	1/60	8/54	<del>- 1</del>	0.10 (0.01, 0.81)
Zhu LP	2014	China	28	4	0/30	3/30		0.13 (0.01, 2.61)
Yue X	2014	China	Anytime	NR	0/31	0/30	<u> </u>	(Excluded)
Subtotal (I-squ	uared = 0.0%	, p = 0.999)					•	0.11 (0.08, 0.14)
							i l	
English							<u>:</u> 1	
Chen ZX	2017	China	13-32	NR	1/41	15/89	_	0.12 (0.02, 0.97)
Han GR	2015	China	28-32	NR	0/358	8/86	<del></del>	0.01 (0.00, 0.23)
He T	2018	China	1st Trimester	NR	0/32	4/34		0.10 (0.01, 2.02)
Hu Y	2018	China	28-32	3-4	0/105	2/122		0.23 (0.01, 4.81)
Liu Y	2016	China	4-27	4	1/82	19/78		0.04 (0.00, 0.29)
Sheng Q	2018a	China	24-32	4	0/79	2/21	-	0.05 (0.00, 1.06)
Sheng Q	2018b	China	24-28	0	0/66	5/46		0.06 (0.00, 1.05)
Sun W	2017	China	20-28	12	0/123	12/65		0.02 (0.00, 0.30)
Tan Z	2016	China	14-28	NR	0/171	15/320	-	0.06 (0.00, 0.97)
Wu Q	2015	China	24-32	0 or 4	0/204	14/95		0.01 (0.00, 0.23)
Zhang H	2014	China	28-30	4	0/257	10/352		0.06 (0.00, 1.09)
Subtotal (I-squ	uared = 0.0%	, p = 0.935)					$\sim$	0.05 (0.02, 0.11)
· Ovorall /l.ac···	arad = 0.00°	n = 1.000\						0.10 (0.00 0.10)
Overall (I-squa	areu = 0.0%,	p = 1,000)					Y I	0.10 (0.08, 0.13)
							1 1 1	
							001 .1 1	10

# Appendix P: Efficacy by risk of bias score for non-RCTs

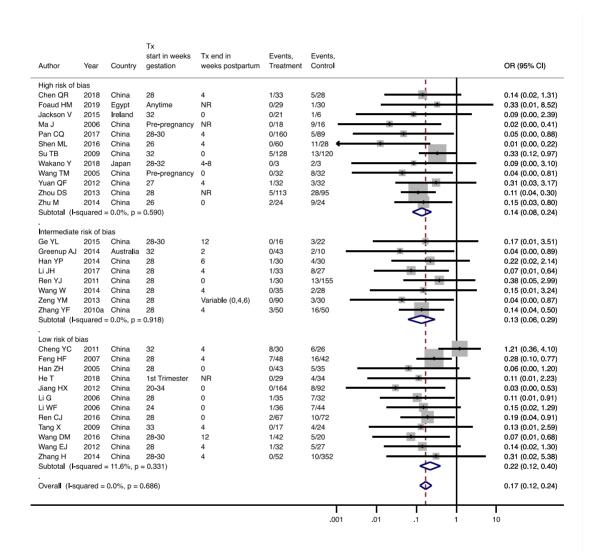
### • TDF 300 mg by risk of bias score for non-RCTs

- High risk (score of 6) (n=5): pooled OR= 0.16 (95% CI: 0.06-0.43), p<0.001,  $1^2$ =0%
- Intermediate risk (score of 7) (n=6): pooled OR=0.22 (95%CI: 0.11-0.46), p<0.001, I<sup>2</sup>=0%
- Low risk (score of 8-9) (n=3): pooled OR=0.08 (95% CI: 0.02-0.29), p<0.001,  $I^2$ =0%
- The p-value for heterogeneity between subgroups was 0.39



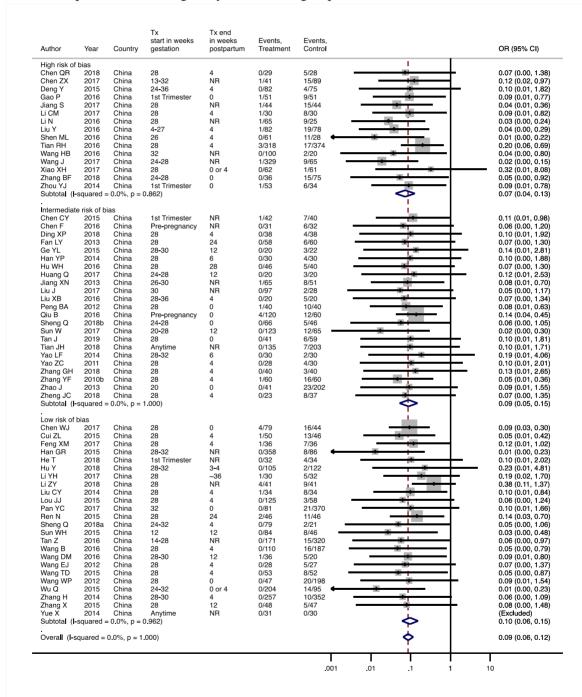
### • LAM 100-150 mg by risk of bias for non-RCTs

- High risk (score of 6) (n=12): pooled OR= 0.14 (95%CI: 0.08-0.24), p<0.001,  $I^2=0\%$
- Intermediate risk (score of 8) (n=8): pooled OR=0.13 (95%CI: 0.06-0.29), p<0.001, I<sup>2</sup>=0%
- Low risk (score of 8-9) (n=12): pooled OR=0.22 (95%CI: 0.12-0.40), p<0.001, I<sup>2</sup>=0%
- The p-value for heterogeneity between subgroups was 0.29



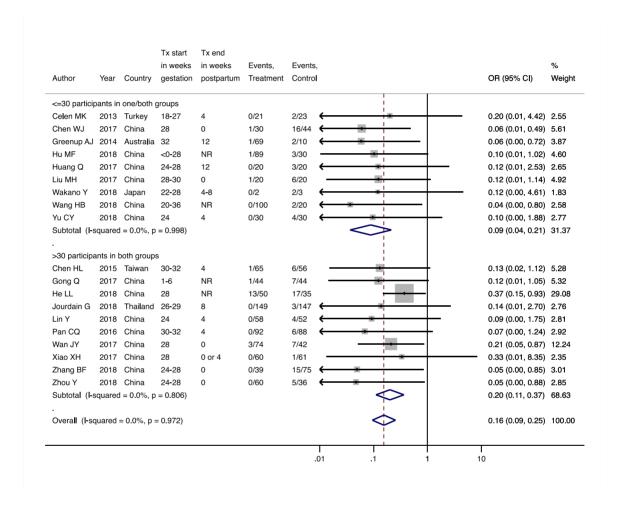
### • LdT 600 mg by risk of bias for non-RCTs

- High risk (score of 6) (n=15): pooled OR= 0.07 (95%CI: 0.04-0.13), p<0.001,  $I^2=0\%$
- Intermediate risk (score of 8) (n=23): pooled OR=0.09 (95%CI: 0.05-0.15), p<0.001,  $I^2$ =0%
- Low risk (score of 8-9) (n=24): pooled OR=0.10 (95%CI: 0.06-0.15), p<0.001, I<sup>2</sup>=0%
- The p-value for heterogeneity between subgroups was 0.75

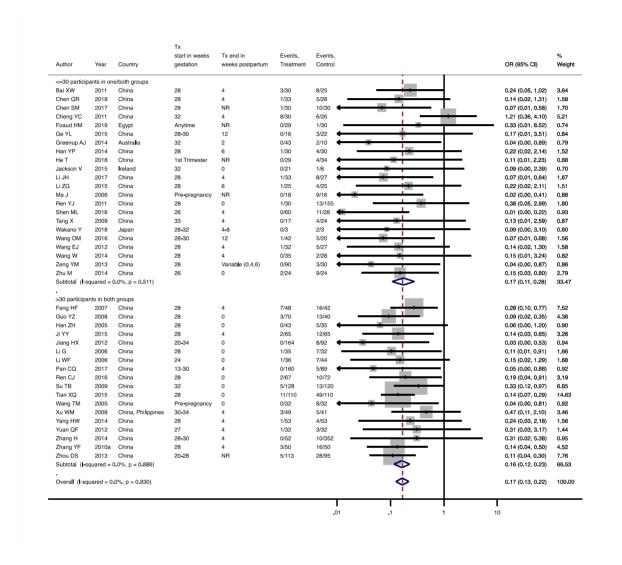


## Appendix Q: Efficacy by study sample size

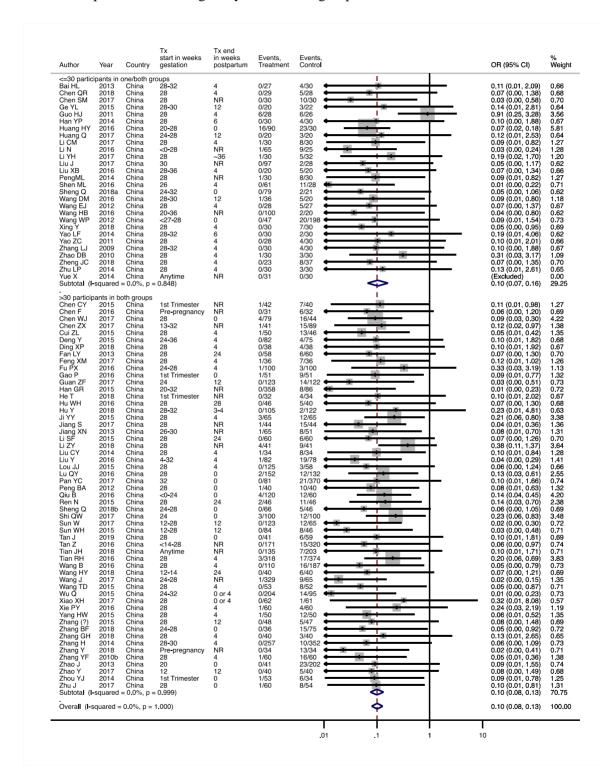
- TDF 300 mg by study sample size (<=30 participants in either group versus >30 participants in both groups)
  - The p-value for heterogeneity between subgroups was 0.131



- LAM 100-150 mg by study sample size (<=30 participants in either group versus >30 participants in both groups)
  - The p-value for heterogeneity between subgroups was 0.838

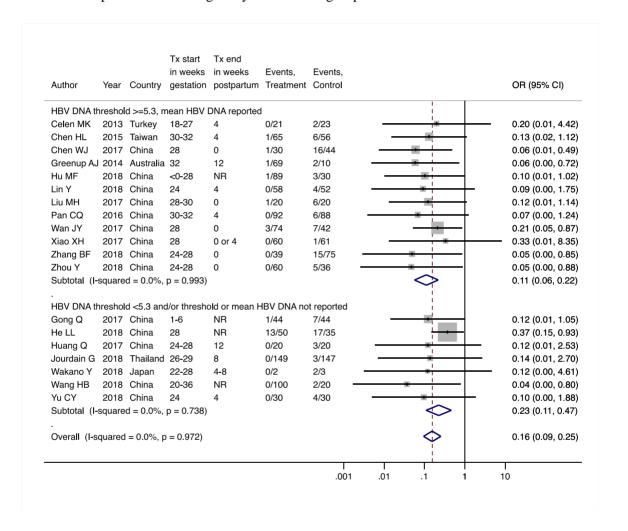


- LdT 600 mg by study sample size (<=30 participants in either group versus >30 participants in both groups)
- The p-value for heterogeneity between subgroups was 0.892

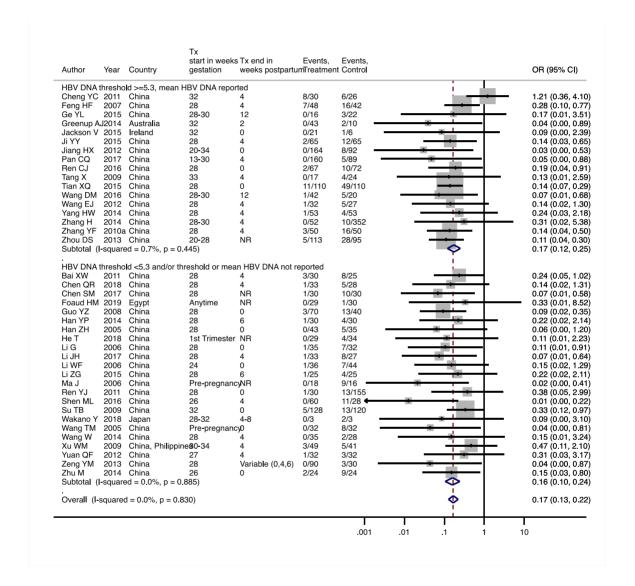


### Appendix R: Efficacy by maternal viral load criteria

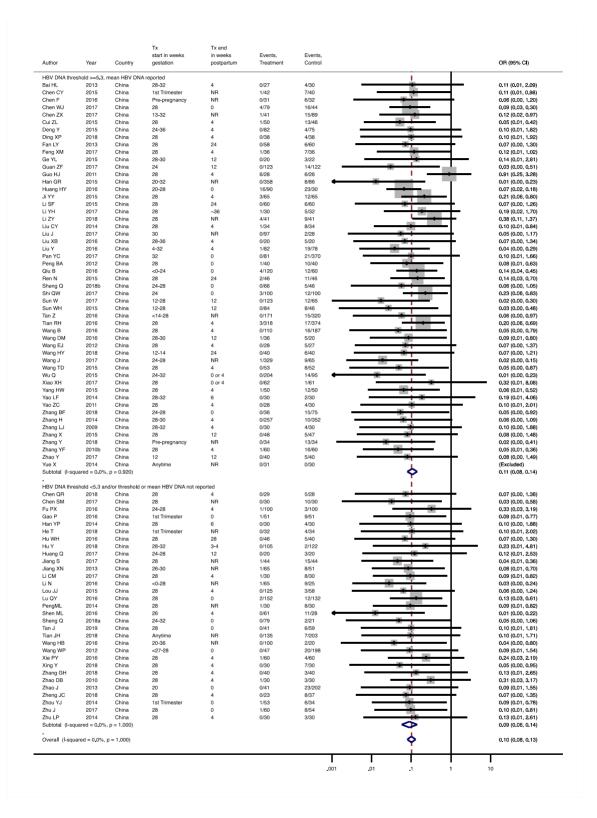
- TDF 300 mg by maternal viral load criteria (Pre-specified viral load threshold of ≥5.3 log10 IU/mL and mean HBV DNA level reported for participating women *versus* viral load threshold not specified or threshold was low (<5.3 log10 IU/ml) and/or HBV DNA level of participating women not reported)
  - The p-value for heterogeneity between subgroups was 0.161



- LAM 100-150 mg by maternal viral load criteria (Pre-specified viral load threshold of ≥5.3 log10 IU/mL and mean HBV DNA level reported for participating women *versus* viral load threshold not specified or threshold was low (<5.3 log10 IU/ml) and/or HBV DNA level of participating women not reported)
  - The p-value for heterogeneity between subgroups was 0.781

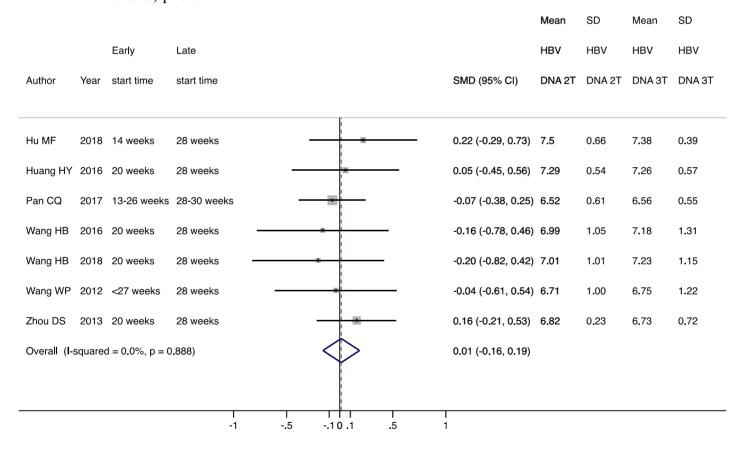


- LdT 600 mg by maternal viral load criteria (Pre-specified viral load threshold of ≥5.3 log10 IU/mL and mean HBV DNA level reported for participating women *versus* viral load threshold not specified or threshold was low (<5.3 log10 IU/ml) and/or HBV DNA level of participating women not reported)
  - The p-value for heterogeneity between subgroups was 0.546



# Appendix S: Viral load prior to treatment and prior to delivery in studies comparing second versus third trimester PAP initiation

- Standardized mean difference (SMD) of viral load AT START OF TREATMENT comparing participants starting PAP in the second ("experimental/treatment") versus third trimester ("control")
  - o 7/9 studies contributing (appropriate measures not provided by Liu Y, 2016 or Han GR 2015), SMD=0.01 (95%CI: -0.16-0.19) p=0.874



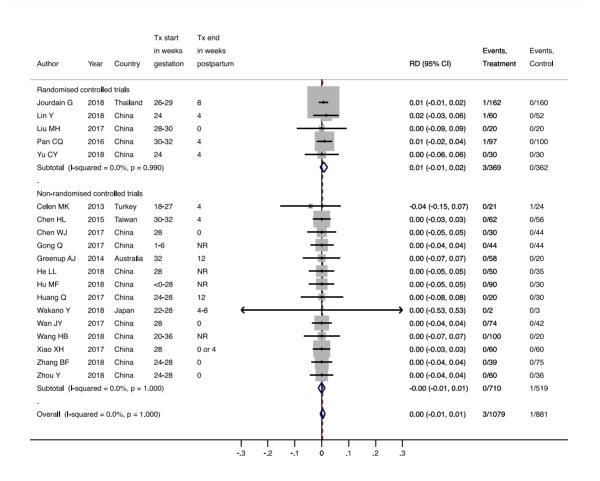
- Standardized mean difference (SMD) of viral load AT TIME OF DELIVERY comparing participants starting PAP in the second ("experimental/treatment") versus third trimester ("control")
  - o 7/9 studies contributing (not Liu Y, 2016 or Zhou DS 2013), SMD= -0.62 (95%CI: -0.77- -0.46) p<0.001

								Mean	SD	Mean	SD
		Treatment	Early	Late				HBV	HBV	HBV	HBV
Author	Year	type	start time	start time			SMD (95% CI)	DNA 2T	DNA 2T	DNA 3T	DNA 3T
Han GR	2015	LDT 600	20-27 weeks	28-32 weeks		=	-0.46 (-0.69, -0.23)	1.80	1.80	2.60	1.60
Hu MF	2018	TDF 300	14 weeks	28 weeks		-	-0.10 (-0.60, 0.41)	5.55	1.19	5.67	1.25
Huang HY	2016	LDT 600	20 weeks	28 weeks	-		-2.84 (-3.57, -2.12)	2.43	0.32	3.54	0.45
Pan CQ	2017	LAM 100	13 <b>-</b> 26 weeks	28-30 weeks		+	-0.59 (-0.91, -0.27)	3.42	1.02	3.98	0.90
Wang HB	2018	TDF 300	20 weeks	28 weeks			-0.84 (-1.49, -0.19)	2.22	0.36	2.63	0.59
Wang HB	2016	LDT 600	20 weeks	28 weeks	_		-1.00 (-1.66, -0.34)	2.63	0.70	3.41	0.85
Wang WP	2012	LDT 600	<27 weeks	28 weeks		-	-0.45 (-1.03, 0.13)	2.54	0.83	2.92	0.83
Overall (I-s	squared	d = 86.4%, p	= 0.000)			$\Diamond$	-0.62 (-0.77, -0.46)				
				-4	-3 -2	-1 0	I 1				

## Appendix T: Maternal safety 1. Fetal deaths

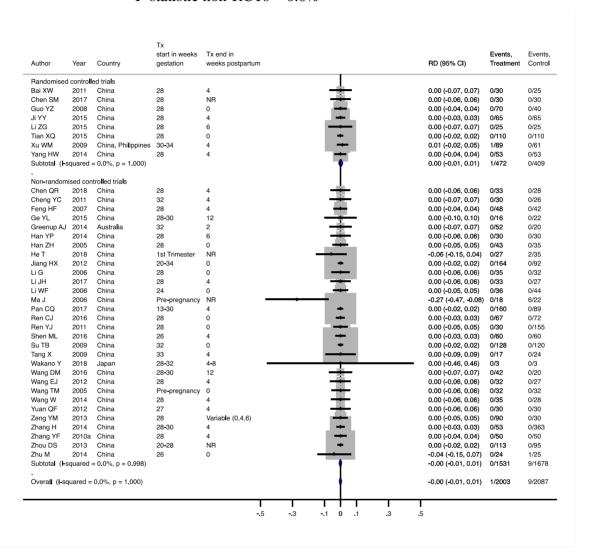
## • TDF 300 mg risk difference for fetal death

- $\circ$  Weighted pooled risk difference: 0.00 (95%CI: -0.01 0.01).
- $\circ$  I<sup>2</sup> statistic overall = 0%
  - $I^2$  statistic RCTs = 0%
  - $I^2$  statistic non-RCTs = 0%



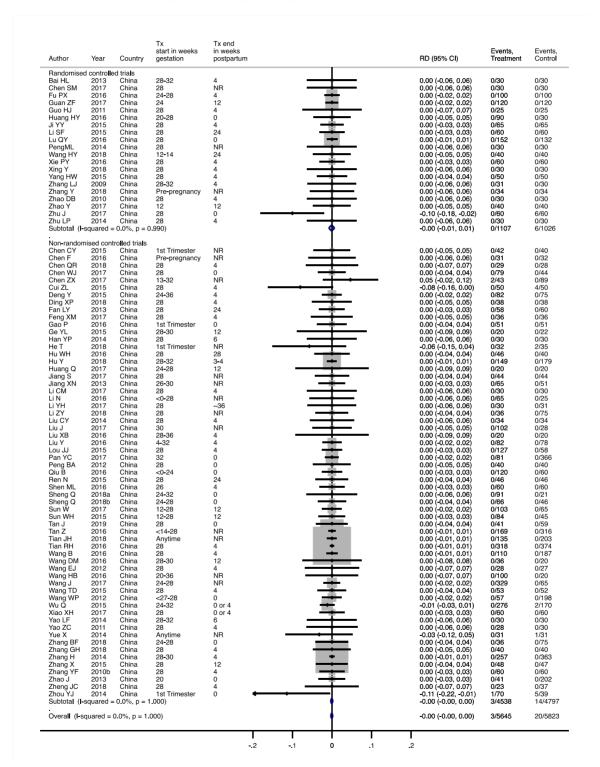
### • LAM 100-150 mg risk difference for fetal death

- $\circ$  Weighted pooled risk difference: 0.00 (95% CI: -0.01 0.01).
- $I^2$  statistic overall = 0.0%
  - $I^2$  statistic RCTs = 0.0%
  - $I^2$  statistic non-RCTs = 0.0%



#### • LdT 600 mg risk difference for fetal death

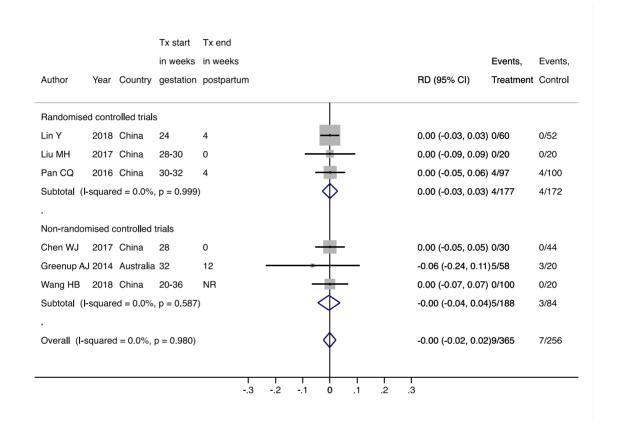
- Weighted pooled risk difference: 0.00 (95%CI: 0.00 0.00).
- $\circ$  I<sup>2</sup> statistic overall = 0.0%
  - $I^2$  statistic RCTs = 0.0%
  - $I^2$  statistic non-RCTs = 0.0%



# Appendix U: Maternal safety 2. Postpartum hemorrhage

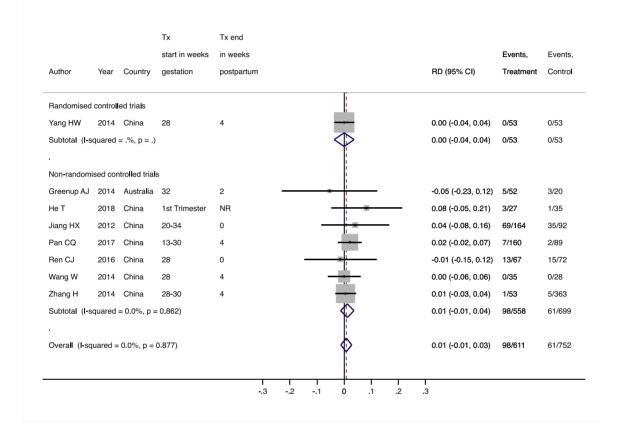
## • TDF 300 mg risk difference for postpartum hemorrhage

- $\circ$  Weighted pooled risk difference: 0.00 (95%CI: -0.02 0.02).
- $\circ$  I<sup>2</sup> statistic overall = 0.0%
  - $I^2$  statistic RCTs = 0.0%
  - $I^2$  statistic non-RCTs = 0.0%



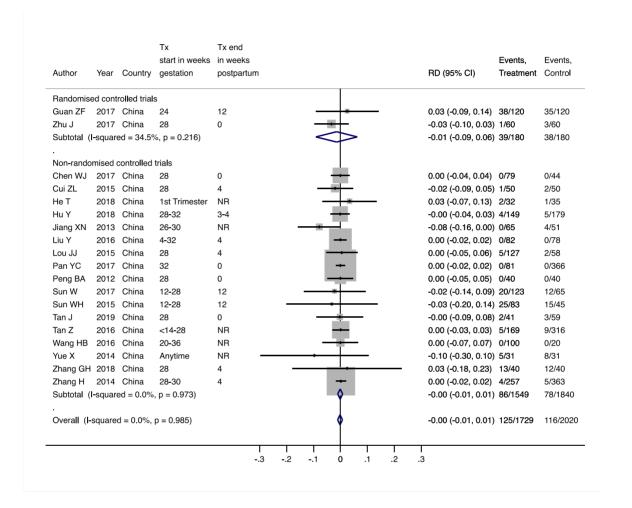
## LAM 100-150 mg risk difference for postpartum hemorrhage

- Weighted pooled risk difference: 0.01 (95%CI: -0.01 0.03).
- $I^2$  statistic overall = 0.0%
  - I<sup>2</sup> statistic RCTs = not enough studies
     I<sup>2</sup> statistic non-RCTs = 0.0%



### • LdT 600 mg risk difference for postpartum hemorrhage

- $\circ$  Weighted pooled risk difference: -0.001 (95%CI: -0.01 0.01).
- $\circ$  I<sup>2</sup> statistic overall = 0.0%
  - $I^2$  statistic RCTs = not enough studies
  - $I^2$  statistic non-RCTs = 0.0%



# Appendix V: Maternal safety 3. Postpartum hepatitis flare

• Table: Summary of postpartum hepatitis flare after discontinuation of PAP in treated group, and during the comparable period for control group

Study	Definition of flare	Timing of PAP discontinu -ation in treated group	Results	Include d in meta- analysis	Any very severe case (decompen- sation, death)?	Clinical course of flare cases
			TDF	Т		
Celen MK, 2013	None given (until 4 weeks postpartum)	4 weeks	No hepatic flare was observed in treated group until 4 weeks postpartum. No data reported for control group.	No (no control)	Unknown (not mentioned)	Unknown (not mentioned)
Chen HL, 2015	ALT >5 x ULN (evaluated at 1, 2, 4, and 6 months postpartum)	4 weeks	At 2 months postpartum (1 month after discontinuation) 1/62 in treated group and 8/56 in control group.	Yes	No case of hepatic decompens ation	Unknown (not mentioned)
Chen WJ, 2017	Hepatic insufficiency (no time-point specified)	At delivery	0/30 in treated, 0/44 in control	No (no time- point specified)	No hepatic insufficienc	N/A
Greenup AJ, 2014 (& Nguyen	Moderate: ALT ≥5 x ULN (i.e. ≥95 U/L) (within 24 weeks postpartum).	12 weeks	In Greenup, vague saying no correlation with flare. In Nguyen (subset n=43) it states 17/43 in treated group	Yes	No case of hepatic decompensation	8/15 in treated and 3/4 in control group spontaneously

V, 2014)*	Severe: ALT ≥20 x ULN (i.e. ≥380 U/L) (within 24 weeks postpartum)		and 4/14 in control group had post-partum flare. Severe flare was observed 2/17 in treated group and 2/4 in control group.			resolved. 6/15 in treated and 1/4 in control group resolved with antiviral therapy.
Jourdain G, 2018	ALT >300 IU/L (after the discontinuation of PAP)	8 weeks	9/154 in treated, 5/157 in control	Yes	No symptomat ic case	No women started or restarted TDF after flares that occurred within 6 months postpartum.
Lin Y, 2018	ALT >5 x ULN (no time-point specified)	4 weeks	2/60 in treated, 0/52 in control	No (no time- point specified)	Unknown (not mentioned)	Unknown (not mentioned)
Pan CQ, 2016	Severe: ALT 5-10 x ULN (no time-point specified). Serious: ALT >10 x ULN (after child delivery until 28 weeks postpartum).	4 weeks	5 severe and 1 serious = 6 total (6/97 in treated group); 6 severe and 3 serious = 9 total (9/100 in the control group). It is unclear whether "severe" flare included only those occurred postpartum or throughout the study period. We therefore used "serious flare" in the meta-analysis.	Yes	No case of hepatic decompen- sation	All cases of serious flare (1 in treated and 3 in control group) normalized their ALT levels after restarting/starting antiviral therapy.
Wakano Y, 2018	Elevation of ALT (no time-point specified)	4-8 weeks	No ALT elevation was observed in treated group. No data reported for control group.	No (no control)	Unknown (not mentioned)	Unknown (not mentioned)

Zhou Y, 2018	Impairment of liver function (during treatment)	At delivery	0/60 in treated group. No data reported for control group	No (no control)	No	N/A
			LAM			
Cheng YC, 2011	None given (after discontinuation of treatment)	4 weeks	7/30 in treated group, 5/26 in control group Note: in these cases there was elevation of ALT levels during treatment, but still <10×ULN	Yes	Unknown (not mentioned)	Resolved after restarting antiviral therapy.
Ge YL, 2015	Abnormality for liver function (during treatment)	3 months	0/16 in treated group. No data reported for control group.	No (no control)	No	N/A
Greenup AJ, 2014 (& Nguyen V, 2014)**	Moderate: ALT ≥5 x ULN (i.e. ≥95 U/L) (within 24 weeks postpartum). Severe: ALT ≥20 x ULN (i.e. ≥380 U/L) (within 24 weeks postpartum)	2 weeks	In the paper from Greenup et al., which had the full cohort, it was stated that there were 'no differences' in flare between the treated and nontreated group. In a subset presented in Nguyen et al., 22/44 in treated group and 4/14 in control group had postpartum flare.	Yes	Unknown (not mentioned)	15/20 in treated and 3/4 in control group spontaneously resolved. 5/20 in treated and 1/4 in control group resolved with antiviral therapy.
He T, 2018	ALT >2 x baseline (after child delivery)	All women continued treatment after child delivery, stop time not	0/27 in treated, 6/35 in control.  However, all women in treated group continued antiviral therapy after child delivery, so this is not used for the meta-analysis of flare.	No (treatmen t continued	Unknown (not mentioned)	All flare cases spontaneously resolved without antiviral therapy.

		mentioned.				
Jackson V, 2015	ALT >3 x ULN (postpartum following discontinuation of PAP)	At delivery	5/26 in treated. No data reported for control group.	No (no control)	Unknown (not mentioned)	Unknown (not mentioned)
Pan CQ, 2017	ALT >10 x ULN or >5 x baseline (after child delivery)	4 weeks	<ul> <li>1/147 in treated, 5/89 in control.</li> <li>13 mothers in treated group who continued treatment beyond postpartum week 4 were excluded from this analysis.</li> </ul>	Yes	No case of hepatic decompen- sation	One flare case in treated group improved ALT level without antiviral therapy. Five flare cases in control all started antiviral therapy.
Ren YJ, 2011	Impairment of liver function (before and after delivery)	At delivery	0/30 in treated group. No data reported for control group.	No (no control)	No	N/A
Wakano Y, 2018	Elevation of ALT (no time-point specified)	4-8 weeks	No ALT elevation was observed in treated group. No data reported for control group.	No (no control)	Unknown (not mentioned)	Unknown (not mentioned)
Wang DM, 2016	None given	12 weeks	1/42 in treated group.  No data reported for control group.  Note: in this one case there was elevation of ALT levels during treatment, but still <5×ULN	No (no control)	Unknown (not mentioned)	Transient, resolved spontaneously
Wang	Abnormality for	At delivery	0/30 in treated, $0/30$ in	No (no	No	N/A

TM,	liver function		control.	time-		
2005	(no time-point			point		
	specified)			specified)		
Wang W, 2014	Impairment of liver function (no time-point specified)	4 weeks	0/35 in treated, 0/28 in control.	No (no time- point specified)	No	N/A
Xu WM, 2009	ALT >3 x ULN (from postpartum week 4 to week 12)	4 weeks	16/83 in treated, 15/46 in control	Yes	No case of ALT elevations in association with signs of hepatic insufficienc	Unknown (not mentioned)
Yang	Impairment of liver function		0/53 in treated, 0/53 in	No (no time-		
HW, 2014	(no time-point specified)	4 weeks	control.	point specified)	No	N/A
Zeng YM, 2013	Elevated ALT and AST outside of the normal range (>50 U/L) (after child delivery)	At delivery, 4 weeks and 6 weeks	In treated group: I. discontinuation at delivery: 4/30 (1, 2 and 1 case at 1, 3 and 6 months after discontinuation, respectively); II. discontinuation at 4 weeks: 4/30 (1 and 3 cases at 1 and 3 months after discontinuation,	Yes	No case of ALT elevation with jaundice; No case of severe hepatitis	Unknown (not mentioned)

			respectively); III. discontinuation at 6 weeks: 5/30, (2 and 3 cases at 1 and 3 months after discontinuation, respectively) In control group: 5/30: (2 cases at 3 months after delivery, 3 cases at 6 months after delivery)			
Zhang H, 2014	ALT >10 x ULN or >5 x baseline (from postpartum week 4 to week 52)	4 weeks	0/53 in treated, 0/363 in control	Yes	No case of hepatic decompensation	N/A
Zhu M, 2014	Aggravation of liver function impairment (during pregnancy)	At delivery	0/24 in treated, 1/25 in control	No (not post- partum)	Unknown (not mentioned)	Unknown (not mentioned)
			LdT			
Chen CY, 2015	None given (no time-point specified)	Treatment continued after delivery, unless discontin- uation criteria met. Disaggregate d numbers not	1/41 in control group (severe hepatitis at 28 weeks of gestation). No data reported for treated group.	No (no data for treated group)	Unknown (not mentioned)	Unknown (not mentioned) (receiving treatment thereafter and dropping out)

		available.				
Chen WJ, 2017	Hepatic insufficiency (no time-point specified)	At delivery	0/79 in treated, 0/44 in control	No (no time- point specified)	No hepatic insufficiency	N/A
Chen QR, 2018	ALT elevation (during pregnancy)	4 weeks	1/29 in treated, 1/28 in control	No (not post- partum)	Unknown (not mentioned)	Both cases resolved spontaneously
Deng Y, 2015	Obvious abnormality for liver biochemical indicators (during treatment)	1 month	0/82 in treated group. No data reported for control group.	No (no control)	No	N/A
Ding XP, 2018	Impairment of liver function (during intervention)	1 month	0/38 in treated, 0/38 in control	No (no time- point specified)	No	N/A
Ge YL, 2015	Obvious abnormality for liver function (during treatment)	3 months	0/20 in treated group. No data reported for control group.	No (no control)	No	N/A
Fan LY, 2013	Severe impairment of liver function (after PAP discontinuation)	At least 6 months (9 in 60 pregnant women discontinued treatment 1 month after delivery)	0/9 pregnant women who discontinued antiviral treatment at 1 month after delivery.  No data reported for control group.	No (no control data)	No	N/A
Han GR,	Flare: ALT >5 x	Variable	In treated group: 3/236	No (no	No	6 of 46 with any

2015	ULN (after discontinuation of PAP). Severe: ALT >10 x ULN (after discontinuation of PAP).	(236 stopped at 4 weeks and 126 continued after 4 weeks)	had >5 x ULN, 0/236 with >10 x ULN.  126 mothers in treated group who continued treatment beyond postpartum week 4 were excluded from above.  No data reported for control group.	control)		ALT elevation had clinical therapies to reduce ALT levels and by 7-12 months post-partum, ALT of all mothers had returned to normal.
He T, 2018	ALT > 2 x baseline (after child delivery)	All women continued treatment after child delivery.	0/32 in treated, 6/35 in control.  However, all women in treated group continued antiviral therapy after child delivery, so this is not used for the metaanalysis of flare.	No (treatmen t continued	Unknown (not mentioned)	All flare cases spontaneously resolved without antiviral therapy.
Hu Y, 2018	ALT > 40 U/L (by the 7-14 months postpartum)	3-4 weeks	22/103 in treated, 25/124 in control	Yes	No case of elevated bilirubin or fulminant hepatitis.	ALT normalized within 2-4 weeks.
Jiang S, 2017	Abnormal liver function (no time-point specified)	None given	0/44 in treated group. No data reported for control group.	No (no control)	No	N/A
Jiang XN, 2013	Abnormal ALT (7 months after delivery)	All women continued treatment	0/65 in treated, 4/51 in control.	No (treatmen t	3/51 in control group	Unknown (not mentioned)

		after child delivery		continued )	progressed to severe hepatitis before delivery; 2/51 in control group developed ascites and liver	
Li N, 2016	None given (no time-point specified)	Not specified/ clarified	1/35 in treated group a     (re-bounce of ALT,     breakthrough during     treatment, due to antiviral         resistance)     2/30 in treated group b     (in one case, ALT elevated         to 416 U/L during         treatment and then     declined gradually to 102         U/L at delivery; in the     other case, ALT elevated to     336 U/L during treatment     and then declined to 86         U/L at delivery)	No (no control)	cirrhosis at 7 months after delivery  Unknown (not mentioned)	Transient for both cases in treated group b (treatment starting from 28 weeks of gestation); Unknown (not mentioned) for the case in treated group a (treatment starting before pregnancy)

			control group.			
Li YH, 2017	ALT elevation (no time-point specified)	Approximate ly 36 weeks postpartum (treatment started at 28 weeks gestation and went for 48 weeks)	1/30 in treated group.  No data reported for  control group.  Mild elevation of ALT levels at 34 weeks of gestation, ALT<5×ULN	No (no control)	Unknown (not mentioned)	Transient, resolved spontaneously without liver protecting drugs
Liu J, 2017	Elevation in ALT levels (1 month and 6 months postpartum)	Treatment continued after delivery, unless discontinuat ion criteria met (disaggregat ed numbers not available)	2/102 in treated, 1/28 in control at 1 month after delivery. 4/102 in treated, 1/28 in control at 6 months after delivery.	No (some continued treatment	Unknown (not mentioned)	Unknown (not mentioned)
Liu XB, 2016	Abnormality for liver biochemical indicators (during treatment)	1 month	0/20 in treated group. No data reported for control group.	No (no control)	No	N/A
Liu Y, 2016	ALT ≥2 x ULN (from discontinuation of PAP to postpartum	4 weeks	5/71 in treated, 1/78 in control. 11 mothers in treated group who continued	Yes	No case of ALT >8 x ULN.	Four flare cases in treated group restarted antiviral (entecavir).

	week 51)		treatment beyond postpartum week 4 were excluded from this analysis.			
Lou JJ, 2015	ALT between 2×ULN and 5×ULN (no time-point specified)	30 days	2/127 in treated group. No data reported for control group.	No (no control)	Unknown (not mentioned)	Active hepatitis, without obvious symptoms, stable after antiviral treatment with NA
Lu QY, 2016	Impairment of liver function (during and after treatment)	At delivery	0/152 in treated group. No data reported for control group.	No (no control)	No	N/A
Pan YC, 2017	High ALT levels (after child delivery)	At delivery	3/22 in treated group at 7 months after delivery. No data reported for control group.	No (no control)	Unknown (not mentioned)	All cases resolved spontaneously at 1 year after delivery
Peng BA, 2012	Abnormal liver function (no time-point specified)	At delivery	0/40 in treated group. No data reported for control group.	No (no control)	No	N/A
Qiu B, 2016	Abnormality for liver function indicators (until 48 weeks after discontinuation)	At delivery	0/120 in treated group (60 starting treatment before pregnancy and 60 starting treatment at 24 weeks of gestation). No data reported for control group.	No (no control)	No	N/A
Sheng Q, 2018a	ALT ≥2 x ULN (after	At delivery	3/87 in treated. 4 mothers in treated	No (no control)	No case of hepatic	All flare cases in treated group

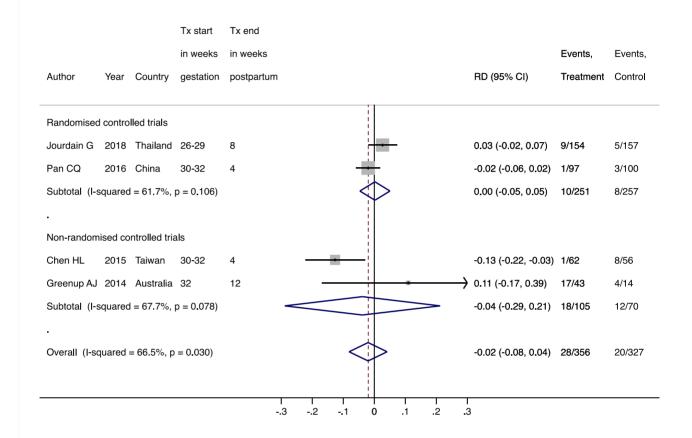
	discontinuation of PAP)		group who continued treatment after child delivery were excluded from the analysis. No data reported for control group.		decompen- sation	restarted antiviral and resolved.
Shi QW, 2017	Elevation in ALT levels (during treatment)	At delivery	3/100 in treated group. No data reported for control group.	No (no control)	Unknown (not mentioned)	Resolved spontaneously 1- 2 weeks after discontinuation
Tian JH, 2018	Unstable liver function (during treatment)	At least 1 month	0/135 in treated group. No data reported for control group.	No (no control)	No	N/A
Wang EJ, 2012	ALT elevation (no time-point specified)	4 weeks	1/28 in treated, 1/27 in control.  Mild elevation of ALT levels (ALT<5×ULN)	No (no time- point specified)	Unknown (not mentioned)	Transient, resolved spontaneously without use of liver protecting drugs
Wang WP, 2012	ALT elevation (no time-point specified)	At delivery	5/47 in treated group. No data reported for control group.	No (no control)	Unknown (not mentioned)	Resolved after liver protecting treatment
Yao LF, 2014	ALT elevation (during pregnancy)	6 weeks	7/30 in treated group. No data reported for control group.	No (no control group)	Unknown (not mentioned)	Resolved spontaneously without interventions, back to normal levels before delivery
Zhang H, 2014	Severe: ALT >10 x ULN or 5 x baseline (from postpartum week 4 to week 52)	4 weeks	0/257 in treated, 0/363 in control	Yes	No case of hepatic decompen- sation	N/A

Zhou YJ, 2014	Abnormal liver biochemical indicators (17 weeks of gestation)	Treatment continued after delivery, unless discontinuat ion criteria met (disaggregat ed numbers not available)	5/39 in control group. No data reported for treated group.	No (no data for treated group)	1 case of death (this woman received treatment from 17 weeks to delivery, she died of large hemorrhage (unspecified type) at delivery)	4 cases stopped pregnancy; 1 case of death (continuing pregnancy and receiving treatment from 17 weeks to delivery, die of massive hemorrhage at delivery)
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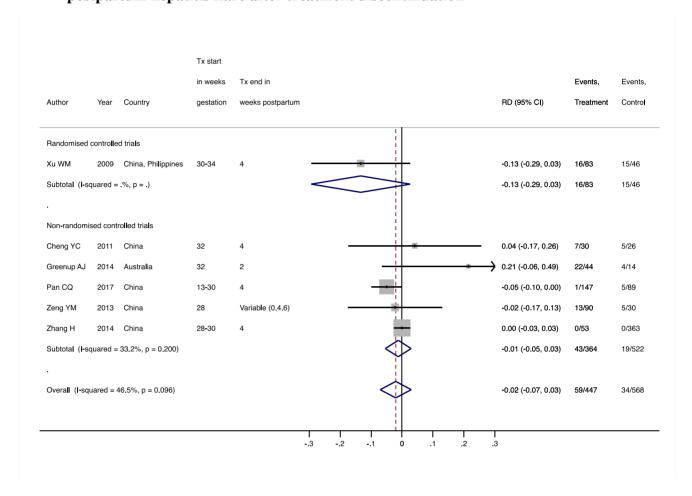
\* In Nguyen V, 2014, 12% (5/43) in the intervention group received LAM.

\*\* In Nguyen V, 2014, 18% (8/44) in the the intervention received TDF. group

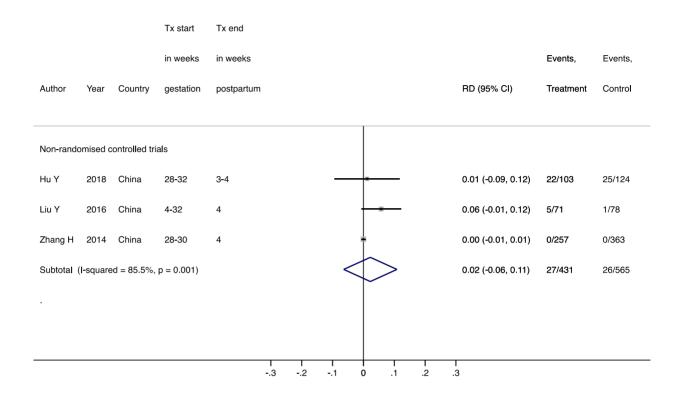
# • Figure: Forest plot for TDF 300 mg weighted risk difference of postpartum hepatitis flare after treatment discontinuation



# • Figure: Forest plot for LAM 100-150 mg weighted risk difference of postpartum hepatitis flare after treatment discontinuation

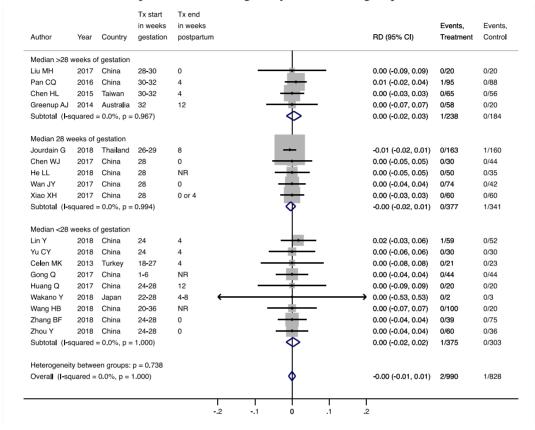


# • Figure: Forest plot for LdT 600 mg weighted risk difference of postpartum hepatitis flare after treatment discontinuation

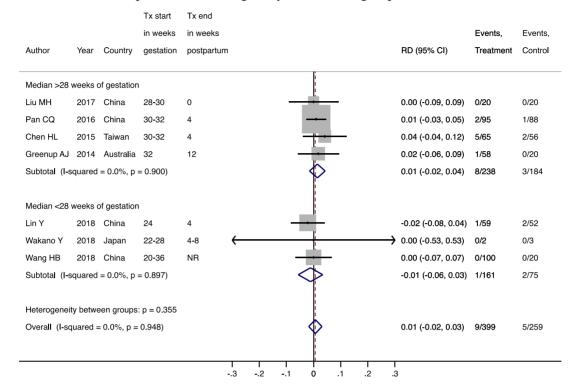


#### **Appendix W: Maternal and Infant Safety Subgroup Analysis**

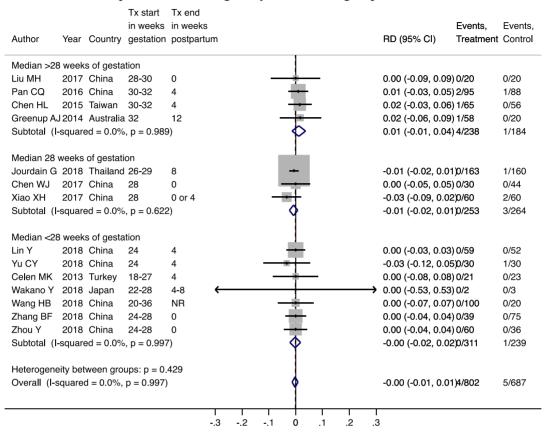
# • TDF 300 mg risk difference of neonatal death by timing of treatment initiation



### • TDF 300 mg risk difference of preterm birth by timing of treatment initiation



# • TDF 300 mg risk difference of congenital abnormalities by timing of treatment initiation

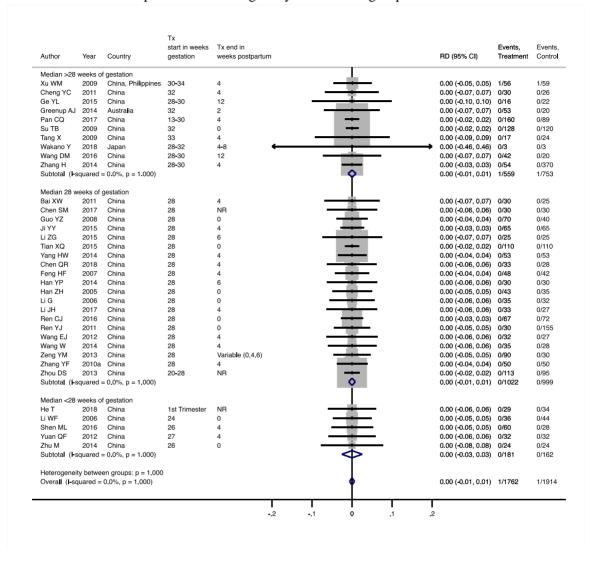


#### • TDF 300 mg risk difference of foetal death by timing of treatment initiation

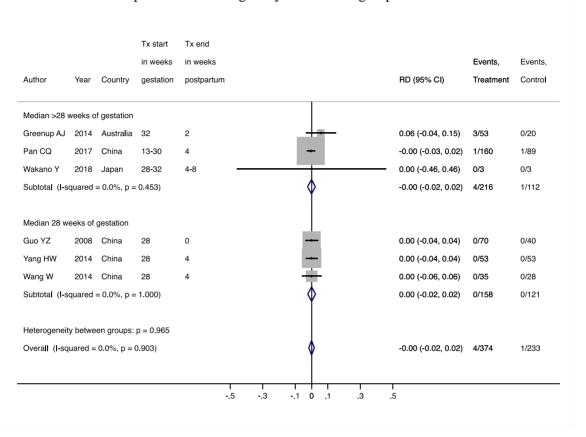
Author	Year	Country	Tx start in weeks gestation	Tx end in weeks postpartum	RD (95% CI)	Events, Treatment	Events, Control
Median >28	weeks o	f gestation					
Liu MH	2017	China	28-30	0	0.00 (-0.09, 0.09)	0/20	0/20
Pan CQ	2016	China	30-32	4	0.01 (-0.02, 0.04)	1/97	0/100
Chen HL	2015	Taiwan	30-32	4	0.00 (-0.03, 0.03)	0/62	0/56
Greenup AJ	2014	Australia	32	12	0.00 (-0.07, 0.07)	0/58	0/20
Subtotal (I-s	quared :	= 0.0%, p =	0.967)	<b>•</b>	0.01 (-0.01, 0.03)	1/237	0/196
Median 28 w	eeks of	gestation					
Jourdain G	2018	Thailand	26-29	8 -	0.01 (-0.01, 0.02)	1/162	0/160
Chen WJ	2017	China	28	0	0.00 (-0.05, 0.05)	0/30	0/44
He LL	2018	China	28	NR —	0.00 (-0.05, 0.05)	0/50	0/35
Wan JY	2017	China	28	0	0.00 (-0.04, 0.04)	0/74	0/42
Xiao XH	2017	China	28	0 or 4	0.00 (-0.03, 0.03)	0/60	0/60
Subtotal (I-s	quared :	= 0.0%, p =	0.995)	•	0.00 (-0.01, 0.02)	1/376	0/341
Median <28	weeks o	f gestation					
Lin Y	2018	China	24	4	0.02 (-0.03, 0.06)	1/60	0/52
Yu CY	2018	China	24	4	0.00 (-0.06, 0.06)	0/30	0/30
Celen MK	2013	Turkey	18-27	4	-0.04 (-0.15, 0.07)	0/21	1/24
Gong Q	2017	China	1-6	NR ——	0.00 (-0.04, 0.04)	0/44	0/44
Huang Q	2017	China	24-28	12	0.00 (-0.08, 0.08)	0/20	0/30
Wakano Y	2018	Japan	22-28	4-8	→ 0.00 (-0.53, 0.53)	0/2	0/3
Wang HB	2018	China	20-36	NR —	0.00 (-0.07, 0.07)	0/100	0/20
	2018	China	24-28	0	0.00 (-0.04, 0.04)	0/39	0/75
Zhang BF		China	24-28	0	0.00 (-0.04, 0.04)	0/60	0/36
•	2018			$\overline{\Phi}$	0.00 (-0.02, 0.02)	1/376	1/314
Zhang BF Zhou Y Subtotal (I-s		= 0.0%, p =	0.998)	T T	,		
Zhou Y	quared :	.,	,		(,,		

- TDF 300 mg risk difference of postpartum hemorrhage by timing of treatment initiation
  - o Too few studies for subgroup analysis
- TDF 300 mg risk difference of postpartum hepatitis flare by timing of treatment initiation
  - o Too few studies for subgroup analysis

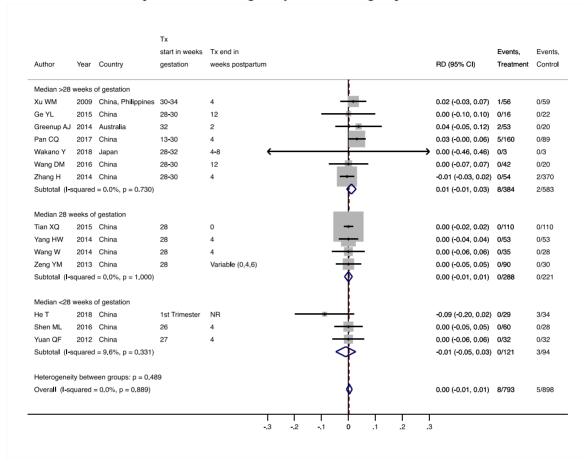
# • LAM 100-150 mg risk difference of neonatal death by timing of treatment initiation



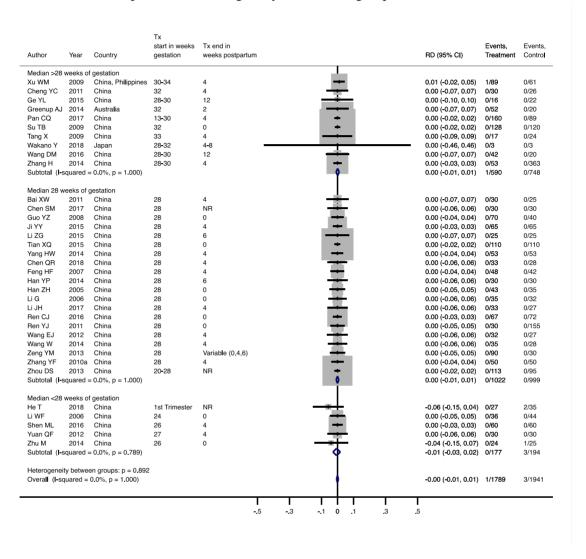
# • LAM 100-150 mg risk difference of preterm birth by timing of treatment initiation



# • LAM 100-150 mg risk difference of congenital abnormalities by timing of treatment initiation

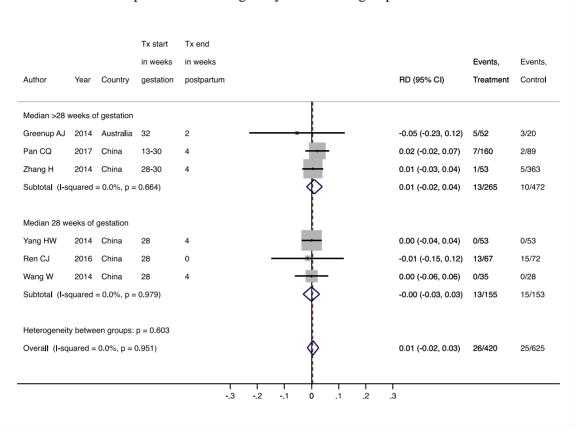


# • LAM 100-150 mg risk difference of foetal death by timing of treatment initiation



# • LAM 100-150 mg risk difference of postpartum hemorrhage by timing of treatment initiation

o The p-value for heterogeneity between subgroups was 0.603



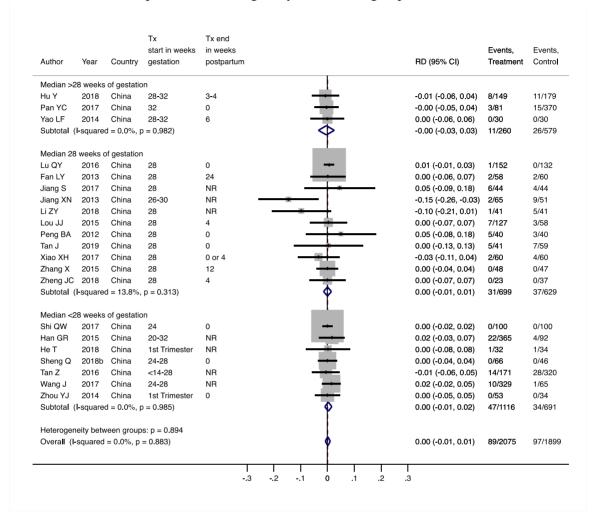
# • LAM 100-150 mg risk difference of postpartum flare by timing of treatment initiation

o Too few studies for subgroup analysis

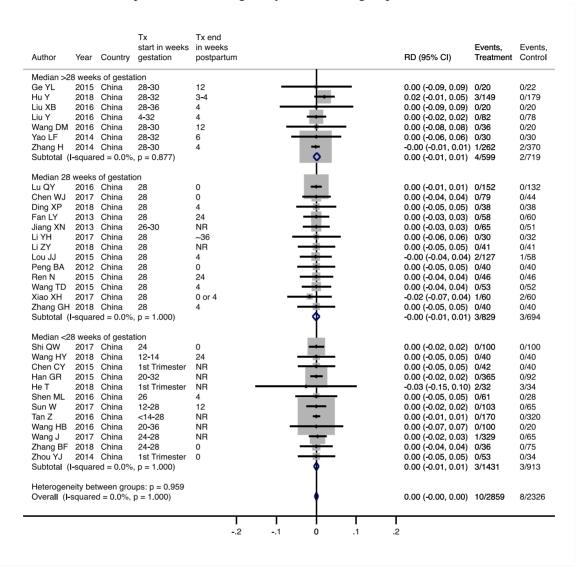
# • LdT 600 mg risk difference of neonatal death by timing of treatment initiation

author Year	Country	start in weeks gestation	in weeks postpartum	RD (95% CI)	Events, Treatment	Events, Control
Median > 28 weeks of lai HL 2013 2009 lei YL 2015 tu Y 2016 liu XB 2016 liu XB 2016 liu Y 2016 liu	China	28-32 28-32 28-30 28-32 30 28-36 4-32 32 28-30 28-32 28-30 1.000)	4 4 12 3-4 NR 4 4 0 12 6 4	0.00 (-0.06, 0.06) 0.00 (-0.08, 0.06) 0.00 (-0.09, 0.09) 0.00 (-0.01, 0.01) 0.00 (-0.05, 0.05) 0.00 (-0.02, 0.02) 0.00 (-0.02, 0.02) 0.00 (-0.02, 0.02) 0.00 (-0.06, 0.06) 0.00 (-0.01, 0.01)	0/30 0/31 0/31 0/20 0/149 0/104 0/20 0/82 0/81 0/36 0/30 0/262 0/845	0/30 0/30 0/30 0/22 0/179 0/28 0/20 0/78 0/370 0/20 0/30 0/370 0/1177
Median 28 weeks of githen SM 2017 2015 2011 i YY 2015 i SF 2015 u QY 2016 eing M 2017 2016 ing Y 2018 ang HW 2015 that DB 2010 that DB 2010 that DB 2010 ing Y 2018 ing Y 2018 ing Y 2018 ing Y 2018 ing Y 2017 that DF 2018 ing Y 2019 ing R 2016 ing Y 2019	China	28 28 28 28 28 28 28 28 28 28 28 28 28 2	NR 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4	0.00 (-0.06, 0.06) 0.00 (-0.07, 0.07) 0.00 (-0.03, 0.03) 0.00 (-0.01, 0.01) 0.00 (-0.03, 0.03) 0.00 (-0.01, 0.01) 0.00 (-0.06, 0.06) 0.00 (-0.06, 0.06) 0.00 (-0.06, 0.06) 0.00 (-0.06, 0.06) 0.00 (-0.06, 0.06) 0.00 (-0.07, 0.07) 0.00 (-0.06, 0.06) 0.00 (-0.07, 0.07) 0.00 (-0.08, 0.06) 0.00 (-0.07, 0.07) 0.00 (-0.07, 0.07) 0.00 (-0.07, 0.07) 0.00 (-0.05, 0.05) 0.00 (-0.07, 0.07) 0.00 (-0.05, 0.05) 0.00 (-0.07, 0.07) 0.00 (-0.05, 0.05) 0.00 (-0.05, 0.06) 0.00 (-0.05, 0.06) 0.00 (-0.05, 0.06) 0.00 (-0.05, 0.06) 0.00 (-0.05, 0.06) 0.00 (-0.05, 0.06) 0.00 (-0.05, 0.06) 0.00 (-0.05, 0.06) 0.00 (-0.05, 0.06) 0.00 (-0.05, 0.06)	0/30 0/28 0/65 0/66 0/152 0/30 0/60 0/152 0/30 0/60 0/30 0/50 0/30 0/60 0/30 0/50 0/38 0/36 0/36 0/30 0/46 0/44 0/44 0/44 0/45 0/30 0/46 0/41 0/34 0/41 0/34 0/41 0/31 0/34 0/110 0/28 0/53 0/60 0/28 0/40 0/48 0/40 0/48	0/30 0/26 0/66 0/66 0/60 0/132 0/30 0/60 0/30 0/50 0/30 0/50 0/20 0/46 0/38 0/46 0/38 0/40 0/41 0/34 0/48 0/48 0/48 0/48 0/48 0/49 0/49 0/49 0/49 0/49 0/49 0/49 0/49
Median <28 weeks of u PX 2016 u PX 2016 Juan ZF 2017 Juang HY 2016 Juan HY 2016 Juan HY 2016 Juan HY 2017 Juang HY 2015 Juan HY 2016 Juang HB 2016 Ju	China	o = 1.000	4 12 0 0 24 112 NR 0 NR 12 4 0 12 12 12 NR NR NR 10 12 12 12 NR 0 0 10 11 12 12 12 12 12 12 12 14 15 16 16 16 16 16 16 16 16 16 16 16 16 16	0.00 (-0.02, 0.02) 0.00 (-0.05, 0.05) 0.00 (-0.06, 0.06) 0.00 (-0.09, 0.09) 0.00 (-0.09, 0.09) 0.00 (-0.00, 0.05) 0.00 (-0.01, 0.01) 0.00 (-0.01, 0.01) 0.00 (-0.01, 0.01) 0.00 (-0.02, 0.02) 0.00 (-0.02, 0.02) 0.00 (-0.04, 0.04) 0.00 (-0.02, 0.02) 0.00 (-0.04, 0.04) 0.00 (-0.02, 0.02) 0.00 (-0.04, 0.04) 0.00 (-0.05, 0.05) 0.00 (-0.01, 0.01)	0/100 0/123 0/90 0/100 0/40 0/40 0/40 0/42 0/51 0/66 0/103 0/84 0/171 0/100 0/329 0/57 0/36 0/41 0/53 0/1739	0/100 0/122 0/30 0/40 0/40 0/40 0/51 0/28 0/46 0/20 0/65 0/46 0/20 0/65 0/46 0/320 0/40 0/34 0/20 0/65 0/40 0/34 0/20 0/65 0/40 0/34 0/20 0/65 0/40 0/34 0/20 0/65 0/40 0/34 0/20 0/65 0/40 0/65 0/40 0/65 0/40 0/65 0/40 0/65 0/40 0/65 0/40 0/65 0/40 0/65 0/40 0/65 0/40 0/65 0/40 0/65 0/40 0/65 0/40 0/65 0/40 0/20 0/65 0/40 0/20 0/20 0/20 0/20 0/20 0/20 0/20

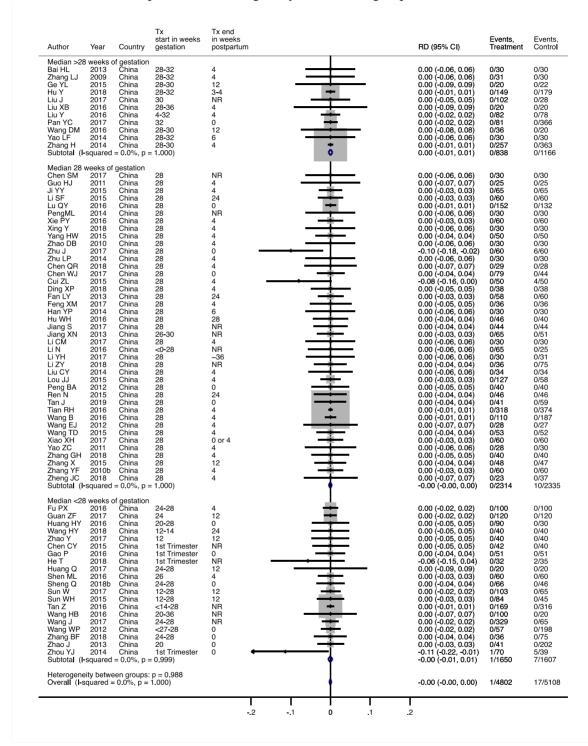
#### • LdT 600 mg risk difference of preterm birth by timing of treatment initiation



# • LdT 600 mg risk difference of congenital abnormalities by timing of treatment initiation

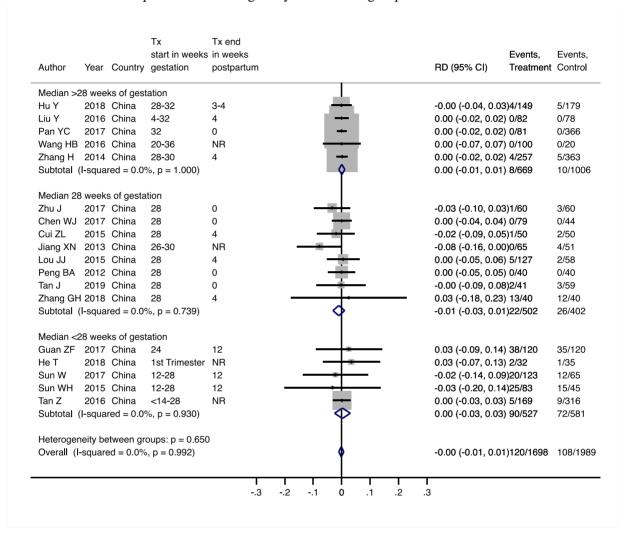


#### • LdT 600 mg risk difference of foetal death by timing of treatment initiation



# • LdT 600 mg risk difference of postpartum hemorrhage by timing of treatment initiation

o The p-value for heterogeneity between subgroups was 0.650



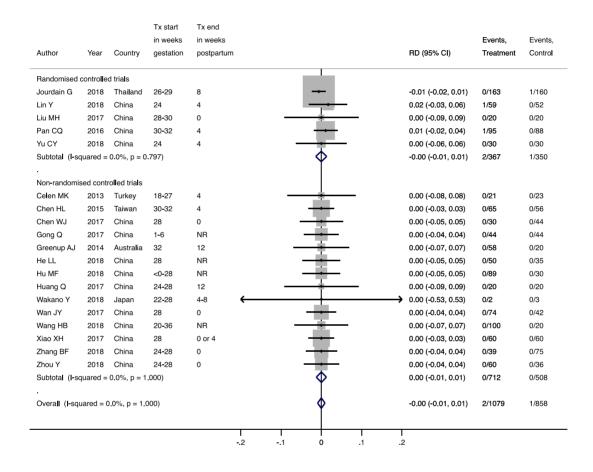
# • LdT 600 mg risk difference of postpartum flare by timing of treatment initiation

o Not enough studies for subgroup analysis

### Appendix X: Infant safety 1. Neonatal deaths

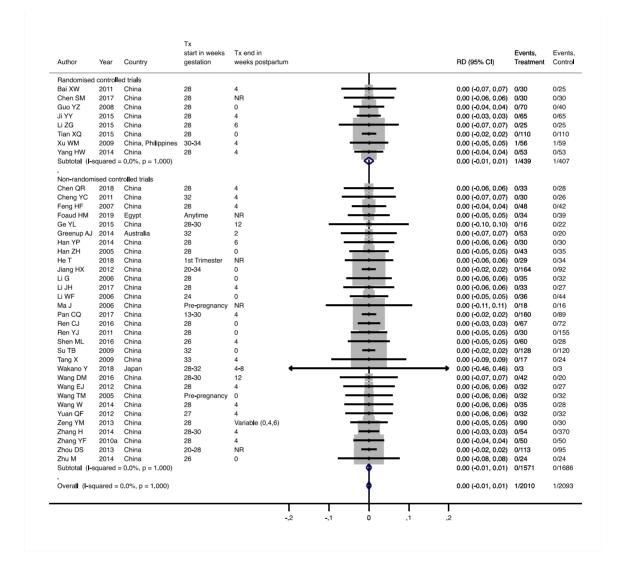
#### • TDF 300 mg risk difference for neonatal death

- $\circ$  Weighted pooled risk difference: 0.00 (95%CI: -0.01 0.01).
- $\circ$  I<sup>2</sup> statistic overall = 0.0%
  - $I^2$  statistic RCTs = 0.0%
  - $I^2$  statistic non-RCTs = 0.0%



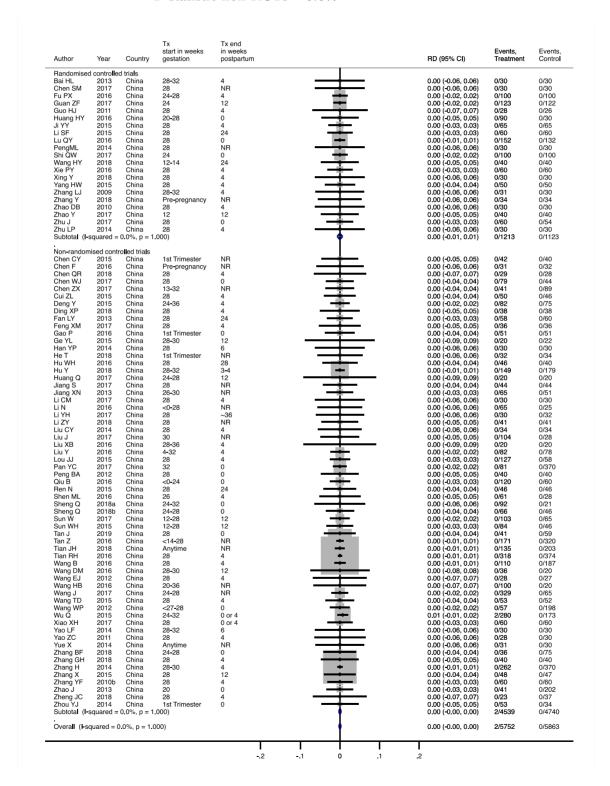
#### • LAM 100-150 mg risk difference for neonatal death

- $\circ$  Weighted pooled risk difference: 0.00 (95% CI: -0.01 0.01).
- $\circ$  I<sup>2</sup> statistic overall = 0.0%
  - $I^2$  statistic RCTs = 0.0%
  - $I^2$  statistic non-RCTs = 0.0%



#### • LdT 600 mg risk difference for neonatal death

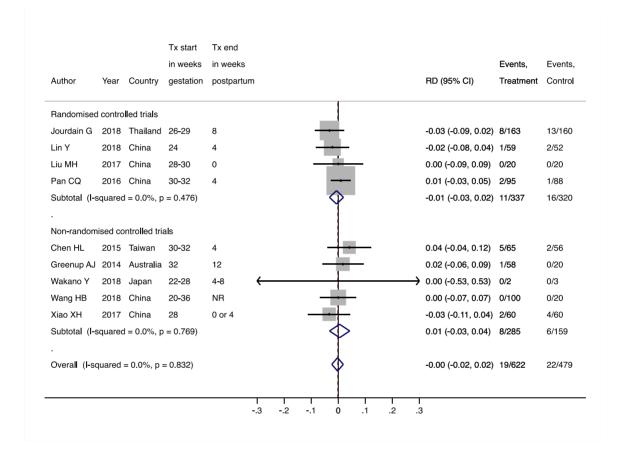
- $\circ$  Weighted pooled risk difference: 0.00 (95% CI: -0.00 0.00).
- $I^2$  statistic overall = 0.0%
  - $I^2$  statistic RCTs = 0.0%
  - $I^2$  statistic non-RCTs = 0.0%



### Appendix Y: Infant safety 2. Preterm birth

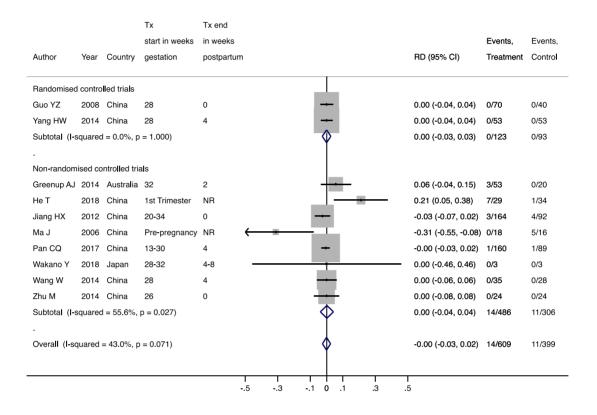
#### • TDF 300 mg risk difference for preterm birth

- $\circ$  Weighted pooled risk difference: 0.00 (95%CI: -0.02 0.02).
- $I^2$  statistic overall = 0.0%
  - $I^2$  statistic RCTs = 0.0%
  - $I^2$  statistic non-RCTs = 0.0%



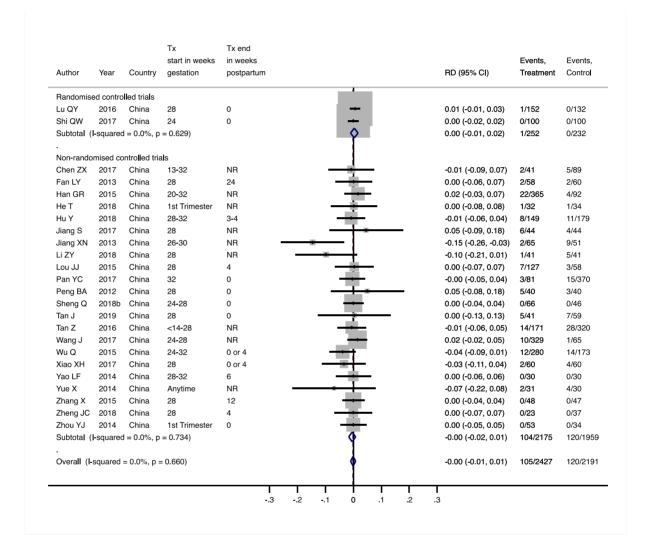
#### • LAM 100-150 mg risk difference for preterm birth

- $\circ$  Weighted pooled risk difference: 0.00 (95% CI: -0.03 0.02).
- $\circ$  I<sup>2</sup> statistic overall = 43.0%
  - $I^2$  statistic RCTs = not enough studies
  - $I^2$  statistic non-RCTs = 55.6%



#### • LdT 600 mg risk difference for preterm birth

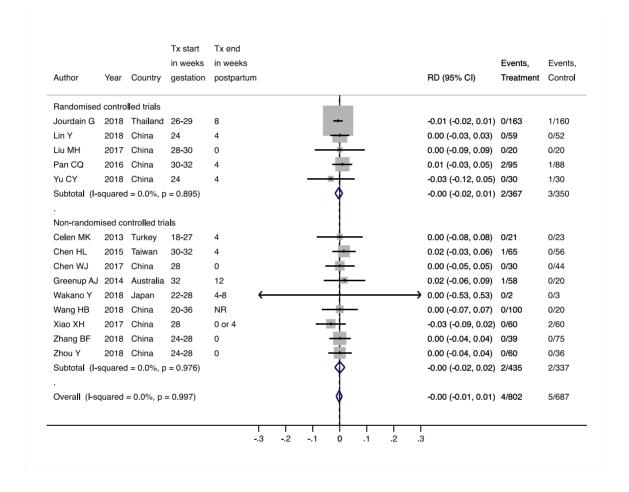
- $\circ$  Weighted pooled risk difference: 0.00 (95% CI: -0.01 0.01).
- $\circ$  I<sup>2</sup> statistic overall = 0.0%
  - $I^2$  statistic RCTs = not enough studies
  - $I^2$  statistic non-RCTs = 0.0%



### Appendix Z: Infant safety 3. Congenital abnormalities

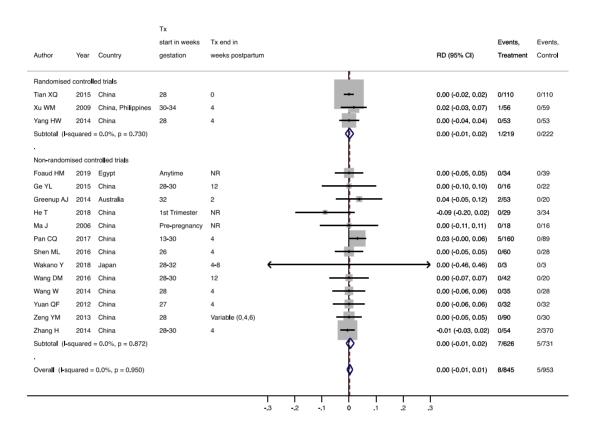
#### • TDF 300 mg risk difference for congenital abnormalities

- $\circ$  Weighted pooled risk difference: -0.00 (95%CI: -0.01 0.01).
- $\circ$  I<sup>2</sup> statistic overall = 0.0%
  - $I^2$  statistic RCTs = 0.0%
  - $I^2$  statistic non-RCTs = 0.0%



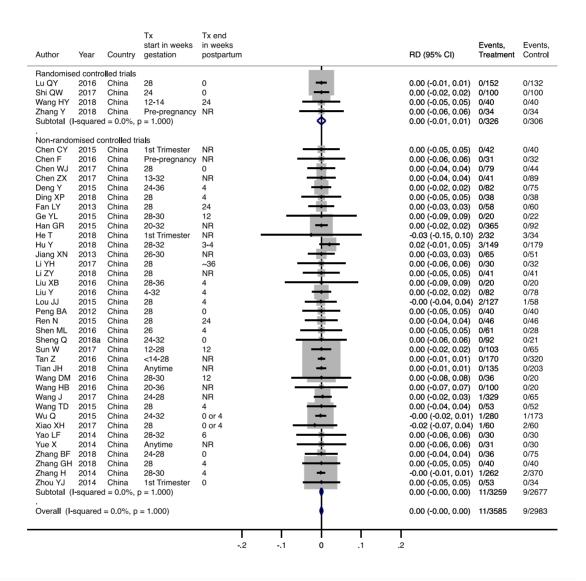
#### • LAM 100-150 mg risk difference for congenital abnormalities

- Weighted pooled risk difference: 0.00 (95% CI: -0.01 0.01).
- $\circ$  I<sup>2</sup> statistic overall = 0.0%
  - $I^2$  statistic RCTs = 0.0%
  - $I^2$  statistic non-RCTs = 0.0%



#### • LdT 600 mg risk difference of congenital abnormalities

- Weighted pooled risk difference: 0.00 (95% CI: -0.00 0.00).
- $\circ$  I<sup>2</sup> statistic overall = 0.0%
  - $I^2$  statistic RCTs = 0.0%
  - $I^2$  statistic non-RCTs = 0.0%

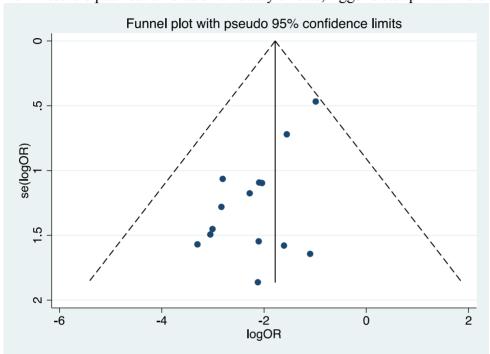


# **Appendix AA: Publication Bias Assessment (Funnel Plots)**Efficacy (HBsAg)

TDF 300 mg

### MTCT indicated by HBsAg positivity at 6-12 months, non-RCTs

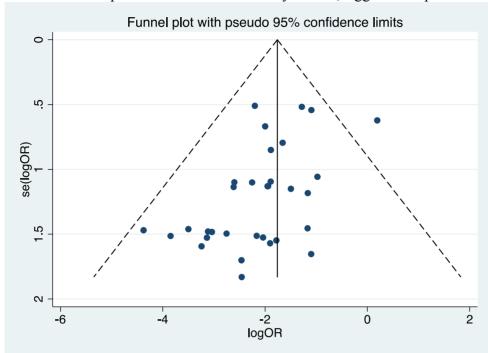
o Possible publication bias/small study effects, Egger's test p-value=0.002



# LAM 100-150 mg

MTCT indicated by HBsAg positivity at 6-12 months, non-RCTs

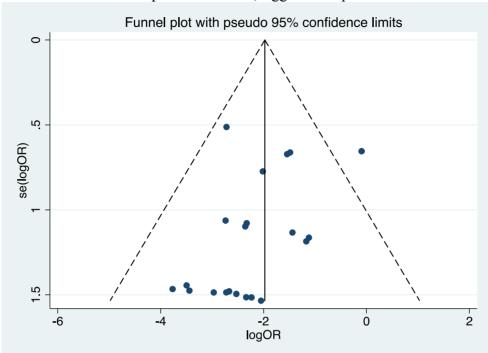
o Possible publication bias/small study effects, Egger's test p-value=0.002



### LdT 600 mg

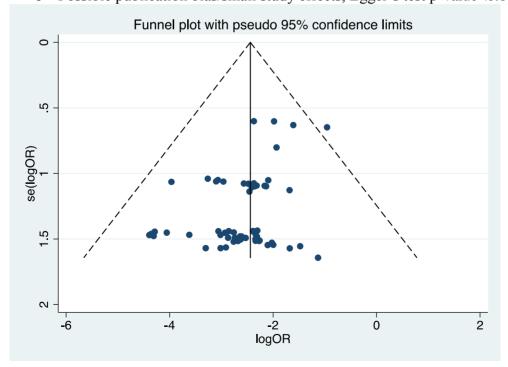
### MTCT indicated by HBsAg positivity at 6-12 months, RCTs

o No evidence of publication bias, Egger's test p-value=0.119



### MTCT indicated by HBsAg positivity at 6-12 months, non-RCTs

o Possible publication bias/small study effects, Egger's test p-value<0.001

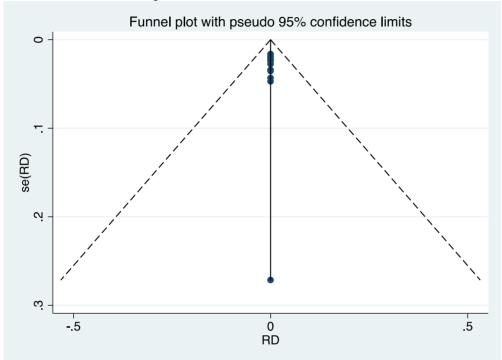


# Safety outcomes

# TDF 300 mg

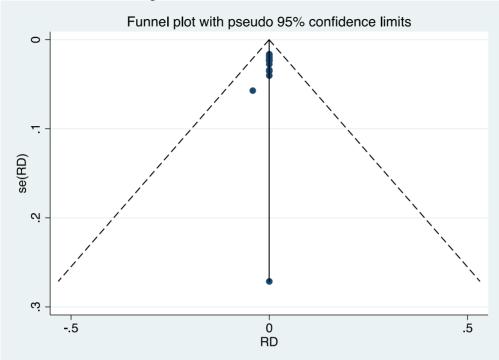
### Neonatal deaths, non-RCTs

No evidence of publication bias



# Fetal deaths, non-RCTs

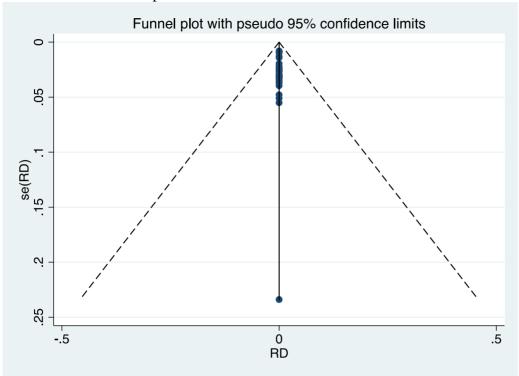
No evidence of publication bias



# LAM 100-150 mg

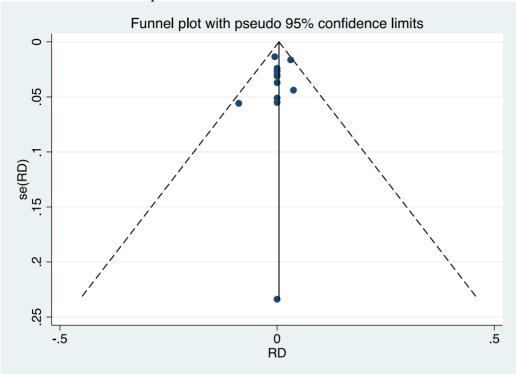
Neonatal deaths, non-RCTs

○ No evidence of publication bias



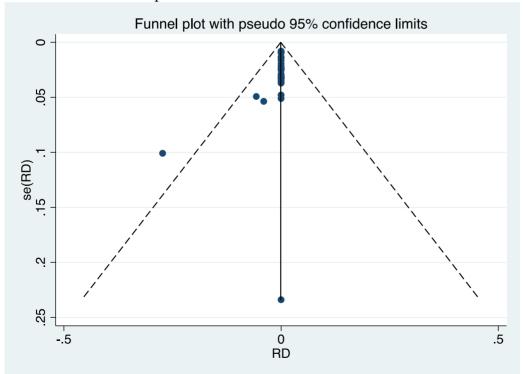
### Congenital abnormalities, non-RCTs

No evidence of publication bias



# Fetal deaths, non-RCTs

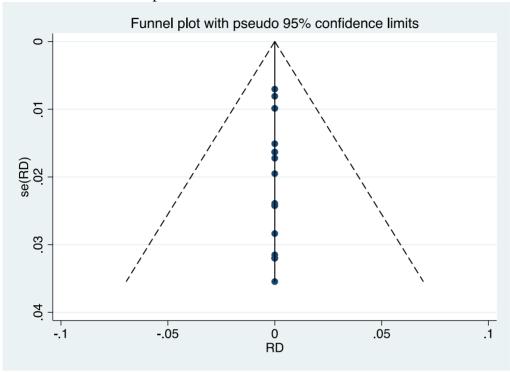
o No evidence of publication bias



# LdT 600 mg

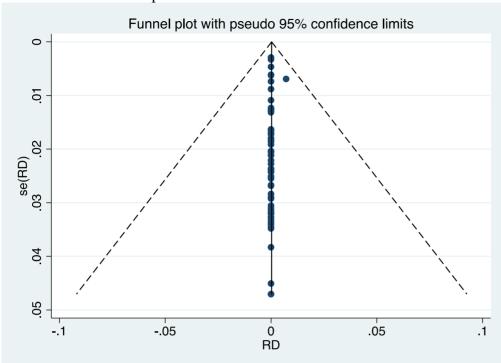
Neonatal deaths, RCTs

○ No evidence of publication bias



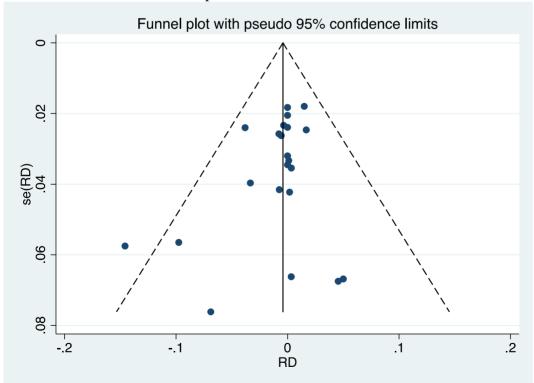
### Neonatal deaths, non-RCTs

o No evidence of publication bias



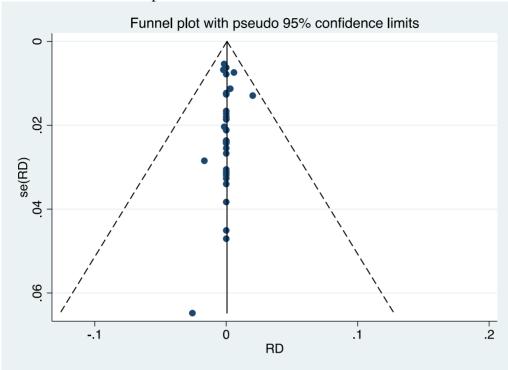
# Prematurity, non-RCTs

o Unclear/no evidence of publication bias



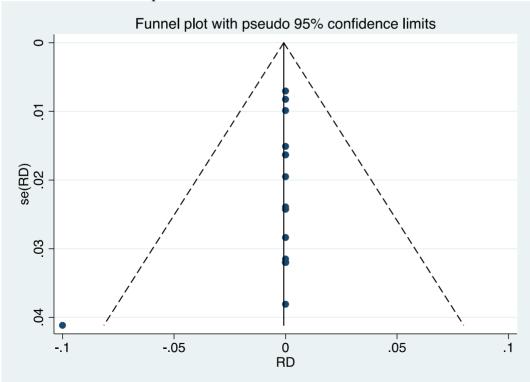
### Congenital abnormalities, non-RCTs

No evidence of publication bias



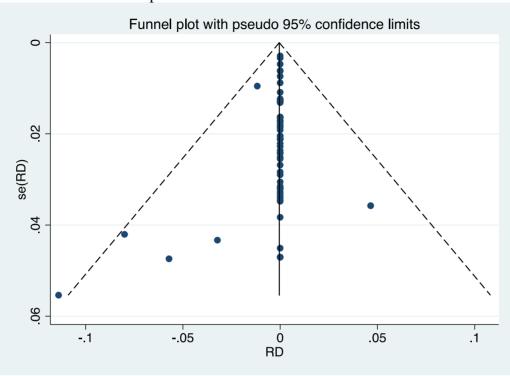
# Fetal deaths, RCTs

o No evidence of publication bias



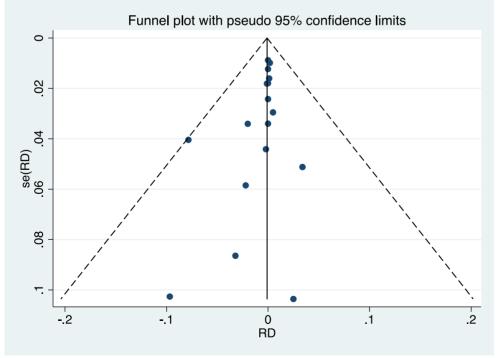
### Fetal deaths, non-RCTs

o No evidence of publication bias



### Postpartum hemorrhage, non-RCTs

No evidence of publication bias



## **Appendix AB: GRADE Evidence Profiles**

## **GRADE** review process methods

For each examined treatment comparison, the quality of the evidence studied was evaluated using the Grading of Recommendations Assessment, Development and Evaluation methodology (GRADE). We used this tool to evaluate the risk of bias, inconsistency (high heterogeneity), imprecision (confidence intervals), indirectness (use of surrogate outcomes), reporting and publication bias, and other factors, within each intervention group (i.e. antiviral treatment used as the intervention) from which the evidence was summarized within the review. This eventually gave a score of high (further research is very unlikely to change the effect estimate), moderate, low or very low (all estimates are very uncertain). Decisions for the complex judgments within the GRADE table were made through study group consensus. The study group reviewers were supported in the process of completing this GRADE template through discussion and advice from a WHO-designated methodological expert, (RC). For this specific meta-analysis, the following rules were used to determine whether or not a group of studies had no serious, serious, or very serious issues with regards to GRADE criteria:

**Limitations** – this was rated as 'no serious' only in the following circumstances: for RCTs, if multiple studies (>=2) were of high quality with low risk of bias for the majority of criteria; for non-RCTs, if >50% of studies had a 'low risk of bias' assessment as per the Newcastle-Ottawa risk of bias assessment tool

*Inconsistency*–  $I^2$ <30%='no serious',  $I^2$ >=30&<60%='serious',  $I^2$ >60%='very serious'

*Indirectness* – all studies were considered to have 'no serious' issues as this was guaranteed by the PICO question specifications

**Imprecision** – for odds ratios, an absolute range in the 95% confidence intervals of 0.5 was considered as 'no serious', a range  $\geq$ =0.5 and  $\leq$ 1.0 was considered as 'serious', and a range of  $\geq$ =1 was considered as 'very serious'. For risk difference estimates, an absolute range in the 95% confidence intervals of  $\leq$ 0.01 (i.e.  $\leq$ 10/1000) was allowed for a set of studies to be considered as having 'no serious' limitations in this area.

If the absolute range of the risk difference was >=0.01 and <0.1 then it was considered as having 'serious' limitations, and if it was >=0.1 (i.e. 100 per 1000) then it was considered as having 'very serious' limitations. Note: wherever odds ratios were available, the range of this estimate was used to define imprecision; if no odds ratio was available then risk difference range was used.

**Publication bias** – An Eggers test with p-value of <0.05 led to assumption of 'possible evidence of publication bias or small study effects' if odds ratios had been estimated. Where risk difference estimates, only, were estimated, an obviously asymmetrical funnel plot led to the same assumption.

*Other* – a non-RCT study set could be upgraded for 'magnitude of effect' if the protective odds ratio was <0.5 and was not considered as imprecise.

TDF 300 mg

				Quality a	ssessment			Number o	f patients	Eff	fect	
Numbe r of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Publication Bias	Other	AVT (%)	No AVT (%)	OR (95%CI	Absolut e (95%CI	Quality
		•	•	HB	sAg positiv	ity at 6-12	months		•	•		
5	Randomize d controlled trials	No serious	No serious	No serious	No serious	Not able to examine publication bias.	N/A	1/349 (0.3)	23/337 (6.8)	<b>0.10</b> (0.03- 0.35)	80 fewer per 1000 (10-140 fewer)	High <sup>a</sup>
14	Non- randomized controlled trials	No serious	No serious	No serious	No serious	Evidence of possible publication bias/small study effects	Magnitude of the effect.	21/723 (2.9)	88/499 (17.6)	<b>0.17</b> (0.10-0.29)	140 fewer per 1000 (80-200 fewer)	Low <sup>b</sup>
		•	•	HBV	<b>DNA</b> posit	ivity at 6-1	2 months		•	•		
4	Randomize d controlled trials	No serious	No serious	No serious	No serious	Not able to examine publication bias.	N/A	1/319 (0.3)	20/307 (6.5)	<b>0.11</b> (0.03- 0.43)	70 fewer per 1000 (0-150 fewer)	High <sup>c</sup>
7	Non- randomized controlled trials	No serious	No serious	No serious	No serious	Not able to examine publication bias.	Magnitude of the effect.	0/451 (0.0)	38/308 (12.3)	<b>0.06</b> (0.02-0.19)	110 fewer per 1000 (50-170 fewer)	Moderat e <sup>d</sup>
	•			In	fant safety	neonatal d	leaths		•		, , , , , , , , , , , , , , , , , , ,	
5	Randomize d	No serious	No serious	No serious	Serious	Not able to examine publication	N/A	2/367 (0.5)	1/350 (0.3)	-	<b>0</b> (10	Moderat e <sup>e</sup>

	controlled					bias.					fewer -	
	trials										10 more)	
14	Non- randomized controlled trials	No serious	No serious	No serious	Serious	No evidence of publication bias	None	0/712 (0.0)	0/508 (0.0)	,	0 (10 fewer - 10 more)	Very low <sup>f</sup>
					Infant safe	ty: prematu	rity					
4	Randomize d controlled trials	No serious	No serious	No serious	Serious	Not able to examine publication bias.	N/A	11/337 (3.3)	16/320 (5.0)	-	10 fewer (30 fewer – 20 more)	Moderat e <sup>g</sup>
4	Non- randomized controlled trials	No serious	No serious	No serious	Serious	Not able to examine publication bias.	None	8/285 (2.8)	6/159 (3.8)	-	10 more (30 fewer to 40 more)	Very low <sup>h</sup>
	<del>.</del>			Infant	safety: con	genital abn	ormalities	3			•	
5	Randomize d controlled trials	No serious	No serious	No serious	Serious	Not able to examine publication bias.	N/A	2/367 (0.5)	3/350 (0.9)	-	0 (20 fewer - 10 more)	Moderat e <sup>i</sup>
9	Non- randomized controlled trials	No serious	No serious	No serious	Serious	Not able to examine publication bias.	None	2/435 (0.5)	2/337 (0.6)	-	0 (20 fewer - 20 more)	Very low <sup>j</sup>
	,			Infa	nt safety: b	one mineral	density		,		1	1
1	Randomize d controlled trials	No serious	N/A	No serious	Serious	Not able to examine publication bias.	N/A	N/A	N/A	-	-0.006 g/cm2 (-0.019 to 0.007 g/cm <sup>2</sup> ); P =0.38)	Low <sup>k</sup>
				Materna	ıl safety: m	iscarriage a	nd stillbii	th				

5	Randomize d controlled trials	No serious	No serious	No serious	Serious	Not able to examine publication bias.	N/A	3/372 (0.8)	0/362 (0.0)	-	10 more (10 fewer - 20 more)	Moderat e <sup>l</sup>
14	Non- randomized controlled trials	No serious	No serious	No serious	Serious	No evidence of publication bias	None	0/570 (0.0)	1/520 (0.2)	-	0 (10 fewer - 10 more)	Very low <sup>m</sup>
				Materna	al safety: po	ostpartum l	nemorrha	ge				
3	Randomize d controlled trials	Serious	No serious	No serious	Serious	Not able to examine publication bias.	N/A	4/177 (2.3)	5/172 (2.9)	-	0 (30 fewer - 30 more)	Low <sup>n</sup>
3	Non- randomized controlled trials	No serious	No serious	No serious	Serious	Not able to examine publication bias.	None	5/188 (2.7)	3/84 (3.6)	-	0 (40 fewer - 40 more)	Very low <sup>o</sup>
		Ma	ternal safe	ty: postpar	tum hepati	tis flare aft	er treatm	ent discon	tinuatio	n		
2	Randomize d controlled trials	No serious	Serious I <sup>2</sup> =43.7%	No serious	Serious	Not able to examine publication bias.	N/A	10/251 (4.0)	8/257 (3.1)	-	2 more (47 fewer - 51 more)	Low <sup>p</sup>
2	Non- randomized controlled trials	No serious	Very serious I <sup>2</sup> =80.6%	No serious	Very serious	Not able to examine publication bias.	None	18/105 (17.1)	12/70 (17.1)	-	38 fewer (289 fewer - 212 more)	Very low <sup>q</sup>

<sup>&</sup>lt;sup>a</sup>No downgrading
<sup>b</sup>Downgrading due to possible publication bias/small study effects, upgrading due to magnitude of effect.
<sup>c</sup>No downgrading
<sup>d</sup>Upgrading due to magnitude of effect.
<sup>e</sup>No downgrading

<sup>f</sup>No upgrading or downgrading <sup>g</sup>Downgrading due to imprecision of risk difference estimate

<sup>h</sup> Downgrading due to imprecision of risk difference estimate

<sup>i</sup>No downgrading

<sup>j</sup>No upgrading or downgrading

<sup>k</sup>Downgrading due to inability to examine certain elements (e.g. inconsistency), and for imprecision due to the fact that there was only one RCT included.

No downgrading

<sup>m</sup>No upgrading or downgrading

"Downgrading due to 'serious' study design limitations (the majority of RCTs had <=4 of 8 criteria with low risk of bias, the rest being unclear or high), downgrading due to imprecision.

<sup>o</sup>Downgrading due to imprecision (OR absolute range >1.0)

<sup>p</sup>Downgrading due to inconsistency, downgrading due to imprecision

<sup>q</sup>Downgrading due to inconsistency, downgrading due to imprecision

## LAM 100-150 mg

Number				Quality a	ssessment			Number of	f patients	Ef	fect	
Number of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Publication Bias	Other	AVT (%)	No AVT (%)	OR (95%C I)	Absolute (95%CI)	
				HBs	Ag positivi	ty at 6-12 n	nonths					
8	Randomized controlled trials	Serious	No serious	No serious	No serious	Not possible to examine publication bias.	N/A	25/432 (5.8)	105/38 9 (27.0)	<b>0.16</b> (0.10-0.26)	190 fewer per 1000 (90-280 fewer)	Moderate a
32	Non- randomized controlled trials	No serious	No serious	No serious	No serious	Evidence of possible publication bias/small study effects	Magnitude of the effect.	41/1575 (2.6)	233/16 55 (14.1)	<b>0.17</b> (0.12-0.24)	140 fewer per 1000 (110-180 fewer)	Low <sup>b</sup>
				HBV	DNA positi	vity at 6-12	months					
5	Randomized controlled trials	Serious	Serious I <sup>2</sup> =39.8%	No serious	No serious	Not possible to examine publication bias.	N/A	21/312 (6.7)	73/269 (27.1)	<b>0.22</b> (0.10-0.47)	fewer per 1000 (320 fewer to 4 more)	Low <sup>c</sup>
18	Non- randomized controlled trials	No serious	No serious	No serious	No serious	No evidence of publication bias.	Magnitude of the effect.	22/1014 (2.2)	137/10 57 (13.0)	<b>0.14</b> (0.09-0.23)	140 fewer per 1000 (90 - 190 fewer)	Moderate d
				Inf	fant safety:	neonatal d	eaths					

8	Randomized controlled trials	Serious	No serious	No serious	Serious	Not possible to examine publication bias.	N/A	1/439 (0.2)	1/407 (0.2)	-	0 (10 fewer - 10 more)	Low <sup>e</sup>
31	Non- randomized controlled trials	No serious	No serious	No serious	Serious	No evidence of publication bias.	None	0/1571 (0.0)	0/1686 (0.0)	-	0 (10 fewer - 10 more)	Very low <sup>f</sup>
				Iı	nfant safet	y: prematur	rity					
2	Randomized controlled trials	Serious	No serious	No serious	Serious	Not possible to examine publication bias.	N/A	0/123 (0.0)	0/93 (0.0)	-	0 (30 fewer - 30 more)	Low <sup>g</sup>
8	Non- randomized controlled trials	Serious	Serious $I^2 = 55.6\%$	No serious	Serious	Not possible to examine publication bias.	None	14/486 (2.9)	11/306 (3.6)	-	0 (40 fewer - 40 more)	Very low <sup>h</sup>
				Infant s	afety: cong	genital abno	rmalities					
3	Randomized controlled trials	Serious	No serious	No serious	Serious	Not possible to examine publication bias.	N/A	1/219 (0.5)	0/222 (0.0)	-	0 (10 fewer - 20 more)	Low <sup>i</sup>
13	Non- randomized controlled trials	No serious	No serious	No serious	Serious	No evidence of publication bias.	None	7/626 (1.1)	5/953 (0.5)	-	0 (10 fewer - 20 more)	Very low <sup>j</sup>
				Maternal	safety: mis	scarriage an	d stillbirt					
8	Randomized controlled trials	Serious	No serious	No serious	Serious	Not possible to examine publication bias.	N/A	1/472 (0.2)	0/409 (0.0)	-	<b>0 more</b> (10 fewer - 10	Low <sup>k</sup>

											more)	
31	Non- randomized controlled trials	No serious	No serious	No serious	Serious	No evidence of publication bias.	None	0/1531 (0.0)	9/1678 (0.5)	-	0 (10 fewer - 10 more)	Very low <sup>l</sup>
Maternal safety: postpartum hemorrhage												
1	Randomized controlled trials	Serious	Not applicable	No serious	Serious	Not possible to examine publication bias.	N/A	0/53 (0.0)	0/53 (0.0)	-	0 (40 fewer - 40 more)	Very low <sup>m</sup>
7	Non- randomized controlled trials	No serious	No serious	No serious	Serious	Not possible to examine publication bias.	None	98/558 (17.6)	61/699 (8.7)	-	<b>10 more</b> (10 less - 40 more)	Very low <sup>n</sup>
		Mat	ternal safet	y: postpart	um hepatit	is flare afte	r treatme	nt discont	inuation	ļ		
1	Randomized controlled trials	Serious	Not applicable	No serious	Very serious	Not possible to examine publication bias.	N/A	16/83 (19.3)	15/46 (32.6)	-	130 less (290 fewer - 30 more)	Very low <sup>o</sup>
5	Non- randomized controlled trials	No serious	Serious $I^2 = 33.2\%$	No serious	Serious	Not possible to examine publication bias.	None	43/364 (11.8)	19/522 (3.6)	-	10 fewer (50 fewer -30 more)	Very low <sup>p</sup>

<sup>&</sup>lt;sup>a</sup>Downgrading due to 'serious' study design limitations (all RCTs had <=4 of 8 criteria with low risk of bias, the rest being unclear or high).

<sup>&</sup>lt;sup>b</sup>Downgrading due to evidence of possible publication bias, however, upgrading due to magnitude of effect.

Downgrading due to 'serious' study design limitations (all RCTs had <=4 of 8 criteria with low risk of bias, the rest being unclear or high), downgrading due to inconsistency >30%.

<sup>&</sup>lt;sup>d</sup>Upgrading due to magnitude of effect.

<sup>&</sup>lt;sup>e</sup>Downgrading due to 'serious' study design limitations (all RCTs had <=4 of 8 criteria with low risk of bias, the rest being unclear or high).

<sup>&</sup>lt;sup>f</sup>No upgrading or downgrading

<sup>&</sup>lt;sup>g</sup>Downgrading due to 'serious' study design limitations (all RCTs had <=4 of 8 criteria with low risk of bias, the rest being unclear or high), downgrading due to imprecision

<sup>&</sup>lt;sup>h</sup>Downgrading due to 'serious' study design limitations (the majority of non-RCTs had a score of 6 on the Newcastle-Ottawa scale), downgrading due to inconsistency >30%, downgrading due to imprecision

Downgrading due to 'serious' study design limitations (all RCTs had <=4 of 8 criteria with low risk of bias, the rest being unclear or high).

<sup>j</sup>No upgrading or downgrading

<sup>k</sup>Downgrading due to 'serious' study design limitations (all RCTs had <=4 of 8 criteria with low risk of bias, the rest being unclear or high).

<sup>1</sup>No upgrading or downgrading

<sup>m</sup>Downgrading due to 'serious' study design limitations (all RCTs had <=4 of 8 criteria with low risk of bias, the rest being unclear or high), downgrading due to inability to examine certain elements (e.g. inconsistency) due to the fact that there was only one RCT included, downgrading due to imprecision.

<sup>n</sup>Downgrading due to imprecision.

<sup>o</sup>Downgrading due to 'serious' study design limitations (all RCTs had <=4 of 8 criteria with low risk of bias, the rest being unclear or high), downgrading due to inability to examine certain elements (e.g. inconsistency) due to the fact that there was only one RCT included, downgrading due to serious imprecision.

<sup>p</sup>Downgrading due to some inconsistency >30%, downgrading due to imprecision

## LdT 600 mg

Numbe				Quality a	ssessment			Number	of patients	E	ffect		
r of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Publication Bias	Other	AVT (%)	No AVT (%)	OR (95%C I)	Absolute (95%CI)	Quality	
				H	BsAg positi	vity at 6-12	months						
21	Randomize d controlled trials	Serious	No serious	No serious	No serious	No evidence of publication bias	N/A	36/1209 (3.0)	175/112 3 (15.6)	<b>0.14</b> (0.09-0.21)	150 fewer per 1000 (100-200 fewer)	Moderat e <sup>a</sup>	
62	Non- randomized controlled trials	No serious	No serious	No serious	No serious	Evidence of possible publication bias/small study effects	Magnitude of the effect.	34/4762 (0.7)	521/467 4 (11.1)	<b>0.09</b> (0.06-0.12)	130 fewer per 1000 (110-150 fewer)	Low <sup>b</sup>	
	HBV DNA positivity at 6-12 months												
8	Randomize d controlled trials	Serious	No serious	No serious	No serious	Not possible to examine publication bias.	N/A	6/382 (1.6)	58/374 (15.5)	<b>0.12</b> (0.05-0.26)	<b>160 fewer</b> per 1000 (60 to 250 fewer)	Moderat e <sup>c</sup>	
45	Non- randomized controlled trials	No serious	No serious	No serious	No serious	Evidence of possible publication bias/small study effects	Magnitude of the effect.	18/3648 (0.5)	377/336 7 (11.2)	<b>0.07</b> (0.05-0.10)	130 fewer per 1000 (100 - 150 fewer)	Low <sup>d</sup>	
				I	nfant safety	y: neonatal	deaths						
21	Randomize d controlled trials	Serious	No serious	No serious	Serious	No evidence of publication bias	N/A	0/1213 (0.0)	0/1123 (0.0)	-	<b>0 per</b> <b>1000</b> (10 fewer - 10 more)	Low <sup>e</sup>	
61	Non-	No	No	No	No	No evidence of publication	None	2/4539	0/4740	-	0 per	Low <sup>f</sup>	

	randomized controlled trials	serious	serious	serious	serious	bias		(0.0)	(0.0)		1000 (2 fewer - 3 more)		
					Infant saf	ety: premat	urity						
2	Randomize d controlled trials	Serious	No serious	No serious	Serious	Not possible to examine publication bias.	N/A	1/252 (0.4)	0/232 (0.0)	-	0 per 1000 (10 fewer - 20 more)	Low <sup>g</sup>	
22	Non- randomized controlled trials	No serious	No serious	No serious	Serious	No evidence of publication bias	None	104/217 5 (4.8)	120/195 9 (6.1)	1	0 per 1000 (20 fewer - 10 more)	Very low <sup>h</sup>	
Infant safety: congenital abnormalities													
4	Randomize d controlled trials	Serious	No serious	No serious	Serious	Not possible to examine publication bias.	N/A	0/326 (0.0)	0/306 (0.0)	-	0 per 1000 (10 fewer - 10 more)	Low <sup>i</sup>	
36	Non- randomized controlled trials	No serious	No serious	No serious	No serious	No evidence of publication bias	None	11/3529 (0.3)	9/2677 (0.3)	-	0 per 1000 (4 fewer – 4 more)	Low <sup>j</sup>	
				Matern	al safety: n	niscarriage :	and stillb	irth					
20	Randomize d controlled trials	Serious	No serious	No serious	Serious	No evidence of publication bias	N/A	0/1107 (0.0)	6/1026 (0.6)	-	1 fewer per 1000 (8 fewer - 6 more)	Low <sup>k</sup>	
61	Non- randomized controlled	No serious	No serious	No serious	No serious	No evidence of publication bias	None	3/4538 (0.1)	14/4797 (0.3)	-	0 per 1000 (3 fewer -	Low <sup>1</sup>	

	trials										2 more)			
	Maternal safety: postpartum hemorrhage													
2	Randomize d controlled trials	Serious	Serious I <sup>2</sup> =34.5%	No serious	Serious	Not possible to examine publication bias.	N/A	39/180 (21.7)	38/180 (21.1)	-	<b>10 fewer</b> (90 fewer - 60 more)	Very low <sup>m</sup>		
17	Non- randomized controlled trials	No serious	No serious	No serious	Serious	No evidence of publication bias	None	86/1549 (5.6)	78/1840 (4.2)	-	1 fewer (10 less - 8 more)	Very low <sup>n</sup>		
		M	aternal saf	ety: postpa	rtum hepa	titis flare af	ter treatn	nent disco	ntinuatior	1				
3	Non- randomized controlled trials	No serious	Very serious I <sup>2</sup> =85.5%	No serious	Very serious	Not possible to examine publication bias.	N/A	27/431 (6.3)	26/565 (4.6)	-	20 less (60 fewer -110 more)	Very low <sup>o</sup>		

<sup>&</sup>lt;sup>a</sup>Downgrading due to 'serious' study design limitations (all RCTs had <=4 of 8 criteria with low risk of bias, the rest being unclear or high).

<sup>&</sup>lt;sup>b</sup>Downgrading due to possible evidence of publication bias/small study effects, upgrading due to magnitude of effect.

Downgrading due to 'serious' study design limitations (all RCTs had <=4 of 8 criteria with low risk of bias, the rest being unclear or high.

<sup>&</sup>lt;sup>d</sup> Downgrading due to possible evidence of publication bias/small study effects, upgrading due to magnitude of effect.

<sup>&</sup>lt;sup>e</sup>Downgrading due to 'serious' study design limitations (all RCTs had <=4 of 8 criteria with low risk of bias, the rest being unclear or high).

<sup>&</sup>lt;sup>f</sup>No upgrading or downgrading

<sup>&</sup>lt;sup>g</sup>Downgrading due to 'serious' study design limitations (all RCTs had <=4 of 8 criteria with low risk of bias, the rest being unclear or high).

<sup>&</sup>lt;sup>h</sup>No upgrading or downgrading

Downgrading due to 'serious' study design limitations (all RCTs had <=4 of 8 criteria with low risk of bias, the rest being unclear or high).

<sup>&</sup>lt;sup>j</sup>No upgrading or downgrading

<sup>\*</sup>Downgrading due to 'serious' study design limitations (all RCTs had <=4 of 8 criteria with low risk of bias, the rest being unclear or high).

No upgrading or downgrading

<sup>&</sup>lt;sup>m</sup>Downgrading due to 'serious' study design limitations (all RCTs had <=4 of 8 criteria with low risk of bias, the rest being unclear or high), downgrading due to 'serious' inconsistency (I<sup>2</sup>>30%), downgrading due to imprecision.

<sup>&</sup>lt;sup>n</sup>Downgrading due to 'very serious' inconsistency (1<sup>2</sup>>60%), downgrading due to imprecision, downgrading due to evidence of possible publication bias/small study effects.

<sup>°</sup>Downgrading due to 'very serious' inconsistency (I²>60%), downgrading due to imprecision