



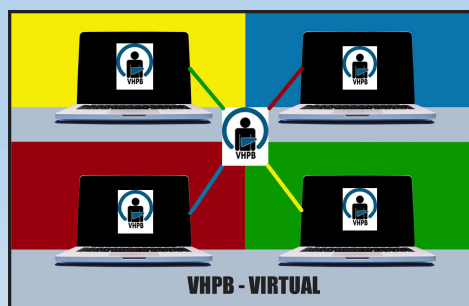
VHPB TECHNICAL MEETING

Treatment as Prevention (TAP) of Hepatitis B:

- (1) to prevent mother to child
transmission (MTCT) and**
- (2) to prevent liver disease progression**

Background document

22 October 2020 – 17h until 20h



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VHPB Secretariat

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MEETING OBJECTIVES

Viral hepatitis treatment as prevention (TAP)

- Give an overview of the scientific evidence to use treatment during pregnancy to avoid perinatal transmission of hepatitis B and C
- Discuss the new perinatal WHO recommendations on hepatitis B Prevention of mother to child transmission of hepatitis B focusing on the use of treatment during pregnancy
- Discuss the possible impact of treatment as prevention of perinatal transmission on the triple elimination goals.
- Review scientific evidence for treatment of all hepatitis B positives to prevent disease progression,
- Discuss if treatment to prevent disease progression could be a public health recommendation

PARTICIPANTS (± 35)

- Global scientists, opinion leaders, infectiologists, hepatologists, vaccinologists, paediatricians, and public health representatives who are experts in the field of viral hepatitis treatment and prevention
- Representatives of viral hepatitis or health organisations involved in the prevention and control of viral hepatitis.
- VHPB advisors

INTENDED IMPACT

Draft recommendations on how to address the use of viral hepatitis treatment as prevention.

OUTLINE OF THE MEETING

Presentations on selected topics about Hepatitis B and C TAP in risk groups and TAP for prevention of MTCT will be pre-recorded by the speakers and made available latest one week before the meeting. Both topics will be covered in separate 3h sessions, 1 week apart.

NOTE: This pre-meeting document contains general background information on the topic of the VHPB meeting. It contains a list of selected abstracts/references from a Pubmed MEDLINE search on different search terms depending on the topic discussed in a session of the meeting. The references are sorted by publication year (most recent first). This document should guide you in the preparation of the meeting, it should not be considered as complete literature review, but hopefully, it will give an overview of what has been published on the topics of the meeting. Because of the abundance of publications regarding “treatment as prevention for viral hepatitis”, only publications of the last 10 years are shown and the abstracts are included for publications of the last 5 years.

GENERAL BACKGROUND INFORMATION

[WHO Global Health Sector Strategy on Viral Hepatitis 2016-2021.](#)

[WHO Progress report on HIV, viral hepatitis and sexually transmitted infections 2019.](#)

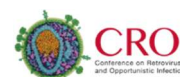
World Hepatitis Alliance: [Prevention, diagnosis, treatment of hepatitis B and C.](#)



S Chen, W Mao, L Guo, J Zhang, S Tang (2020). "[Combating hepatitis B and C by 2030: achievements, gaps, and options for actions in China.](#)" *BMJ Glob Health* 5(6).

China has the highest number of hepatitis B and C cases globally. Despite remarkable achievements, China faces daunting challenges in achieving international targets for hepatitis elimination. As part of a large-scale project assessing China's progress in achieving health-related Sustainable Development Goals using quantitative, qualitative data and mathematical modelling, this paper summarises the achievements, gaps and challenges, and proposes options for actions for hepatitis B and C control. China has made substantial progress in controlling chronic viral hepatitis. The four most successful strategies have been: (1) hepatitis B virus childhood immunisation; (2) prevention of mother-to-child transmission; (3) full coverage of nucleic acid amplification testing in blood stations and (4) effective financing strategies to support treatment. However, the total number of deaths due to hepatitis B and C is estimated to increase from 434 724 in 2017 to 527 829 in 2030 if there is no implementation of tailored interventions. Many health system barriers, including a fragmented governance system, insufficient funding, inadequate service coverage, unstandardised treatment and flawed information systems, have compromised the effective control of hepatitis B and C in China. We suggest five strategic priority actions to help eliminate hepatitis B and C in China: (1) restructure the viral hepatitis control governance system; (2) optimise health resource allocation and improve funding efficiency; (3) improve access to and the quality of the health benefits package, especially for high-risk groups; (4) strengthen information systems to obtain high-quality hepatitis epidemiological data; (5) increase investment in viral hepatitis research and development.

AF Luetkemeyer, DL Wyles (2019). "[CROI 2019: highlights of viral hepatitis.](#)" *Top Antivir Med* 27(1): 41-49.



At the 2019 Conference on Retroviruses and Opportunistic Infections (CROI), there was a major focus on hepatitis C virus (HCV) elimination and improving each component of the hepatitis C care cascade. Many interventions showed promising improvements in diagnosis and linkage to care. Settings with robust access to direct-acting antivirals (DAAs) continue to demonstrate the role of HCV treatment as prevention. However, substantial barriers to accessing curative therapy remain. Reinfection after treatment presents an important barrier to elimination, particularly in some populations of men who have sex with men (MSM). MSM without HIV infection are at an elevated risk for sexual acquisition of HCV, and several studies reported HCV rates that were as high as those seen in MSM living with HIV. There was also a focus on HCV and HBV in pregnant women. Rates of HCV infection in women of child-bearing potential have increased, making prenatal diagnosis a priority. In the first study of HCV treatment during pregnancy, sofosbuvir/ledipasvir started at 28 weeks of gestation led to cure in 8 pregnant women. Hepatitis B virus (HBV)-active antiretrovirals are generally effective in suppressing HBV but have low rates of surface antigen loss despite long term treatment. Initial results from novel laboratory assessments of intrahepatic HBV viral infection events were presented, hopefully paving the way for more effective HBV treatment strategies to control and potentially cure HBV.

EJ Aspinall, SJ Hutchinson, DJ Goldberg, H Valerio, A Mozalevskis, T Noori, E Duffell, L Tavoschi (2018). [Monitoring response to hepatitis B and C in EU/EEA: testing policies, availability of data on care cascade and chronic viral hepatitis-related mortality - results from two surveys \(2016\).](#) *HIV Med.* Feb;19 Suppl 1:11-15. doi: 10.1111/hiv.12599.

Objectives: The World Health Organization (WHO) developed a European Regional Action Plan (EAP) to fast-track action towards the goal of eliminating viral hepatitis. Robust monitoring is essential to assess

national programme performance. The purpose of this study was to assess the availability of selected monitoring data sources in European Union/European Economic Area (EU/EEA) Member States (MS).

Methods: Availability of data sources at EU/EEA level was assessed using two surveys distributed to 31 EU/EEA MS in 2016. The two surveys covered (A) availability of policy documents on testing; testing practices and monitoring; monitoring of diagnosis and treatment initiation, and; (B) availability of data on mortality attributable to chronic viral hepatitis.

Results: Just over two-thirds of EU/EEA MS responded to the surveys. 86% (18/21) reported national testing guidance covering HBV, and 81% (17/21) covering HCV; while 33% (7/21) and 38% (8/21) of countries, respectively, monitored the number of tests performed. 71% (15/21) of countries monitored the number of chronic HBV cases diagnosed and 33% (7/21) the number of people treated.

Corresponding figures for HCV were 48% (10/21) and 57% (12/21). 27% (6/22) of countries reported availability of data on mortality attributable to chronic viral hepatitis.

Conclusions: The results of this study suggest that sources of information in EU/EEA Member States to monitor the progress towards the EAP milestones and targets related to viral hepatitis diagnosis, cascade of care and attributable mortality are limited. Our analysis should raise awareness among EU/EEA policy makers and stimulate higher prioritisation of efforts to improve the monitoring of national viral hepatitis programmes.

V Soriano, B Young, N Reau (2018). "[Report from the International Conference on Viral Hepatitis - 2017](#)." *AIDS Rev* 20(1): 58-70.



The International Conference on Viral Hepatitis 2017 brought exciting news on the treatment of viral hepatitis. The most recent estimates of the burden for hepatitis B virus and hepatitis C virus (HCV) infections were presented. The current gaps and prospects for regional and global eradication of viral hepatitis were discussed on the light of the WHO roadmap until 2030. Debates focused on hepatitis C and expectations using the new approved HCV pan-genotypic, once daily, oral direct-acting antivirals (DAAs), glecaprevir-pibrentasvir, and sofosbuvir-velpatasvir-voxilaprevir. The management of difficult-to-cure HCV patients included individuals who had failed prior DAAs, people who inject drugs, patients with decompensated cirrhosis, or renal insufficiency. Special patient populations such as children, pregnant women, persons with acute hepatitis C, or HIV coinfection were addressed separately. The use of HCV treatment as prevention was subject to debate, balancing the benefits on halting transmission and the risk for HCV reinfections and high medication costs. Complementary efforts on behavioral interventions and harm reduction programs were highlighted. Data from both clinical trials and real-world experience (i.e., from the US Veterans) were compared. Further debates addressed hepatic conditions that may alter the management and outcome of viral hepatitis, such as hepatitis B reactivation, non-alcoholic fatty liver disease, liver transplantation, and hepatocellular carcinoma. Finally, the recent data on often neglected hepatitis D and E virus infections were reviewed.

V Soriano, B Young, N Terrault (2016). "[Report from the International Conference on Viral Hepatitis \(ICVH\), San Francisco, March 2016](#)." *AIDS Rev* 18(2): 81-88.

The International Conference on Viral Hepatitis 2016 brought exciting news on the treatment of viral hepatitis. The conference was mainly focused on the most recent estimates of burden for HBV and HCV; the current gaps and prospects for regional and global HCV eradication; the use of HCV treatment as prevention; and the management of difficult-to-cure hepatitis C patients, including individuals who fail on direct-acting antivirals, people who inject drugs, and those with decompensated cirrhosis or renal insufficiency. Special patient populations, such as children, pregnant women, HIV-coinfected and persons with acute hepatitis C, were addressed separately. Data from both clinical trials and real-world experience were discussed. Further debates focused on hepatic conditions that may alter the management and outcome of viral hepatitis, such as fatty liver disease, liver transplantation, and hepatocellular carcinoma.

EJ Aspinall, G Hawkins, A Fraser, S J Hutchinson, D Goldberg (2011). [Hepatitis B prevention, diagnosis, treatment and care: a review](#). *Occup Med (Lond)*. Dec;61(8):531-40. doi: 10.1093/occmed/kqr136.

1. Overview scientific evidence for TAP in pregnancy (HBV)

Al Awaidy, S. T. and S. Ezzikouri (2020). "[Moving towards hepatitis B elimination in Gulf Health Council states: From commitment to action.](#)" *J Infect Public Health* **13**(2): 221-227.

INTRODUCTION: In 2016, the World Health Assembly adopted the hepatitis B (HB) elimination strategy that aims at ending HB by 2030. In this descriptive review we provide the progress made and challenges to achieving hepatitis B elimination by 2030 in Gulf Health Cooperated (GHC) states. **METHODS:** Data record from relevant online databases and reliable resources were reviewed until the end of 2017. The analysis was based on the core indicators of the WHO monitoring and evaluation framework for viral hepatitis B and the targets of the global health sector strategy by 2016–2021. **RESULTS:** The states introduced HB vaccination, including birth-dose for those under 5 years old, with global coverage of more than 95%, in order to prevent mother-to-child transmission of HBV. The prevalence of HB antigens declined in children under age 5 to less than 1%. However, the rate of vaccination among the most-at-risk populations remains suboptimal. All states have implemented safe blood transfusions and injection safety policies as well as universal laboratory-based surveillance for acute HB. However, surveillance for chronic HB and sequelae as well as estimation methods of morbidity and mortality to evaluate impact are not established. Similarly, harm reduction for people who inject drugs and testing and treatment policies and protocols for people with chronic HB are suboptimal. **CONCLUSIONS:** Additional steps are required to strengthen immunisation among the most-at-risk populations, maintain high quality surveillance, use antiviral therapy to treat chronic HBV and stop unsafe injection practices for drug users. Establishing country-specific national hepatitis responses based on country priorities as well as the capacity of the home health sectors to address these needs are paramount. Achieving elimination targets will require a radical alteration in the current hepatitis response and this goal should be elevated to a higher priority in the public health arena.

P Boucheron, Y Lu, K Yoshida, T Zhao, A L Funk, F Lunel-Fabiani, A Guingané, E Tuaillon, J van Holten, R Chou, M Bulterys, Y Shimakawa (2020) [Accuracy of HBeAg to identify pregnant women at risk of transmitting hepatitis B virus to their neonates: a systematic review and meta-analysis.](#) *Lancet Infect Dis.* 2020 Aug 14;S1473-3099(20)30593-4. doi: 10.1016/S1473-3099(20)30593-4. Online ahead of print.

Background: Prevention of mother-to-child transmission (MTCT) of hepatitis B virus (HBV) involves neonatal immunoprophylaxis, with a birth dose of hepatitis B vaccine and immune globulin, and provision of peripartum antiviral prophylaxis in highly viraemic women. However, access to assays to quantify HBV DNA levels remains inadequate in resource-poor settings. This study was commissioned by WHO and aimed to identify the HBV DNA threshold for MTCT, to assess the sensitivity and specificity of hepatitis B e antigen (HBeAg) testing to identify pregnant women with HBV DNA levels above this threshold, and to predict MTCT of HBV infection on the basis of HBeAg testing.

Methods: For this systematic review and meta-analysis, we searched the PubMed, EMBASE, Scopus, CENTRAL, CNKI, and Wanfang databases for studies of pregnant women with chronic HBV infection without concurrent antiviral therapy, published between Jan 1, 2000, and April 3, 2019. Studies were eligible for inclusion if MTCT in mother-child pairs could be stratified by different levels of maternal HBV DNA during pregnancy, if maternal HBeAg status could be stratified by HBV DNA level, and if the MTCT status of infants could be stratified by maternal HBeAg status during pregnancy. Studies that selected pregnant women on the basis of HBeAg serostatus or HBV DNA levels were excluded. Aggregate data were extracted from eligible studies by use of a pre-piloted form; study authors were contacted to clarify any uncertainties about potential duplication or if crucial information was missing. To pool sensitivities and specificities of maternal HBeAg to identify highly viraemic women and to predict MTCT events, we used the DerSimonian-Laird bivariate random effects model. This study is registered with PROSPERO, CRD42019138227.

Findings: Of 9007 articles identified, 67 articles (comprising 66 studies) met the inclusion criteria. The risk of MTCT despite infant immunoprophylaxis was negligible (0.04%, 95% CI 0.00-0.25) below a maternal HBV DNA level of 5.30 log₁₀ IU/mL (200 000 IU/mL) and increased above this threshold. The pooled sensitivity of HBeAg testing to identify HBV DNA levels of 5.30 log₁₀ IU/mL or greater in pregnant women was 88.2% (83.9-91.5) and pooled specificity was 92.6% (90.0-94.5). The pooled sensitivity of HBeAg testing in predicting MTCT of HBV infection despite infant immunoprophylaxis was 99.5% (95% CI 91.7-100) and pooled specificity was 62.2% (55.2-68.7).

Interpretation: Maternal HBV DNA of 5-30 log₁₀ IU/mL or greater appears to be the optimal threshold for MTCT of HBV infection despite infant immunoprophylaxis. HBeAg is accurate to identify women with HBV DNA levels above this threshold and has high sensitivity to predict cases of immunoprophylaxis failure. In areas where HBV DNA assays are unavailable, HBeAg can be used as an alternative to assess eligibility for antiviral prophylaxis.

Funding: World Health Organization.

Cheung, K. W. and T. T. Lao (2020). "[Hepatitis B - Vertical transmission and the prevention of mother-to-child transmission](#)." *Best Pract Res Clin Obstet Gynaecol*.

Hepatitis B virus (HBV) infection is the commonest cause of chronic hepatitis, with an estimated global prevalence of 3.5%, and which leads to significant morbidity and mortality. Mother-to-child transmission (MTCT) during pregnancy is the leading form of transmission in endemic populations, and its interruption is thus crucial as the initial step in the elimination of HBV infection, notwithstanding the availability of potent antiviral medications. The risk of MTCT is dramatically reduced by timely neonatal HBV vaccination and the administration of hepatitis B immunoglobulin after birth in high-risk infants. Maternal HBV DNA quantification during pregnancy allows the assessment of the risk of newborn immunoprophylaxis failure (IF). Maternal antiviral treatment in highly viremic women can reduce the risk of IF. However, the optimal HBV DNA cutoff level for the initiation of antiviral treatment remains to be determined.

Ding, Y. and X. G. Dou (2020). "[[Commentary: evidence, evidence, always evidence. 2019 Chinese practice guidelines for the prevention and treatment of hepatitis B virus mother-to-child transmission](#)]." *Zhonghua Gan Zang Bing Za Zhi* **28**(2): 133-134.

Hu, Y. and H. Yu (2020). "[Prevention strategies of mother-to-child transmission of hepatitis B virus \(HBV\) infection](#)." *Pediatr Investig* **4**(2): 133-137.

Chronic hepatitis B virus (HBV) infection caused by mother-to-child transmission (MTCT, also known as vertical transmission) during the perinatal period is a major public health problem worldwide. Despite the availability of the combined active-passive immunization with a hepatitis B vaccine and hepatitis B immunoglobulin after birth, about 9% of newborns are still infected with HBV, especially those born to hepatitis B e antigen (HBeAg)-positive mothers. Currently, the management of HBV infection during pregnancy remains controversial. This article briefly reviews the recent advances in the epidemiology of HBV, immunization against it, and management strategies in the third trimester.

W Jing, J Liu, M Liu (2020). "[Eliminating mother-to-child transmission of HBV: progress and challenges in China](#)." *Front Med* **14**(1): 21-29.

China has the world's largest burden of hepatitis B virus (HBV) infection, but the country has made considerable progress in preventing its mother-to-child transmission (MTCT) in the past three decades. This feat is made possible due to the high coverage of birth-dose hepatitis B vaccine (HepB, > 95%), hepatitis B surface antigen (HBsAg) screening for pregnant women (> 99%), and hepatitis B immunoglobulin plus HepB for newborns whose mothers are HBsAg positive (> 99%). Studies on the optimal antiviral treatment regimen for pregnant women with high HBV-DNA load have also been conducted. However, China still faces challenges in eliminating MTCT of HBV. The overall HBsAg prevalence among pregnant women is considered an intermediate endemic. The prevalence of HBsAg among pregnant women from remote, rural, or ethnic minority areas is higher than that of the national level because of limited health resources and public health education for HBV. The coverage for maternal and child healthcare and immunization services should be improved, especially in western regions. Integration of current services to prevent MTCT of HBV with other relevant health services can increase the acceptability, efficiency, and coverage of these services, particularly in remote areas and ethnic minority areas. By doing so, progress toward key milestones and targets to eliminate hepatitis B as the main public health threat by 2030 can be achieved.

PM Khue, NTT Linh, VH Vinh, LV Dung, BN Van (2020) [Hepatitis B Infection and Mother-to-Child Transmission in Haiphong, Vietnam: A Cohort Study with Implications for Interventions](#). *Biomed Res Int*. 2020 Aug 20;2020:4747965. doi: 10.1155/2020/4747965. eCollection 2020.

Background: There is little data available on HBV infection and mother-to-child transmission (MTCT) in Vietnam.

Objective: This study is aimed at assessing the prevalence of HBV infection and the current situation of MTCT in Haiphong, Vietnam.

Methods: A transversal survey of 1721 pregnant women followed by an observational prospective cohort study of 183 HBV-infected women was conducted at Haiphong Gyneco-Obstetric Hospital. Women were followed up up to 12-month postpartum; use of prevention measures and the MTCT rate were evaluated. HBV infection in children was defined by a HBsAg-positive test at 12 months of age.

Results: At baseline, 183 of 1721 pregnant women (10.6%) tested HBsAg positive. Among them, 23.0% were HBeAg positive, 26.2% had a detectable load of HBV DNA, and 13.1% had a HBV DNA load \geq 200,000 IU/mL. All women underwent MTCT prevention antiviral therapy. At delivery, 98.9% of newborns receive a HBV vaccine birth dose, and 82% received HBIG. At 12 months of age, 94.7% have received the scheduled HBV vaccines. Eight percent of infants born from followed-up women were HBsAg positive. The mother's HBeAg-positive status was associated with a higher risk of HBV infection in infants.

Conclusion: The HBV prevalence and MTCT rates are high in Haiphong. A strong national plan to increase the access to preventive measures and to monitor results is needed in order to decrease this prevalence.

Kramvis, A. (2020). "[Challenges for hepatitis B virus cure in resource-limited settings in sub-Saharan Africa.](#)" *Curr Opin HIV AIDS* **15**(3): 185-192.

PURPOSE OF REVIEW: The aim of this article is to highlight the unique challenges for hepatitis B virus (HBV) cure faced in resource-limited settings (RLS) in sub-Saharan Africa (SSA), where access to disease prevention measures, medical testing, and treatment are limited. RECENT FINDINGS: SSA RLS face challenges, which need to be anticipated as HBV cure research advances. There is a paucity of data because of lack of HBV surveillance and limited access to laboratories. Interruption of transfusion-transmitted infections, perinatal mother-to-child-transmissions, and transmission in people-who-infect-drug networks has not been achieved fully. Although RLS in SSA are within the epicenter of the HIV pandemic, unlike for HIV, there is no population-based testing for HBV. Public health response to HBV is inadequate with concomitant political inertia in combatting HBV infection. SUMMARY: A functional HBV cure will improve the diagnosis/treatment cascade, decrease costs and accelerate HBV elimination. There is a concerted effort to find a HBV cure, which will be finite, not require life-long treatment, adherence, and continued monitoring. Increased research, improved financial, infrastructural and human resources will positively impact on implementation of HBV cure, when available. We can emulate major strides made in tackling HIV and the strength of advocacy groups in soliciting policymakers to take action.

SD Chao, CM Cheung, ET Chang, A Pei, SKS So (2019). "[Management of hepatitis B infected pregnant women: a cross-sectional study of obstetricians.](#)" *BMC Pregnancy Childbirth* **19**(1): 275.

BACKGROUND: Our study aims to describe how obstetricians manage pregnant women infected with chronic hepatitis B in a region with a large high-risk population. METHODS: We performed a cross-sectional study among practicing obstetricians in Santa Clara County, California. All obstetricians practicing in Santa Clara County were invited to participate in the study. Obstetricians were recruited in person or by mail to complete a voluntary, multiple choice survey on hepatitis B (HBV). Survey questions assessed basic HBV knowledge and obstetricians' self-reported clinical practices of the management of HBV-infected pregnant women. Pooled descriptive analyses were calculated for the cohort, as well as, correlation coefficients to evaluate the association between reported clinical practices and hepatitis B knowledge. RESULTS: Among 138 obstetricians who completed the survey, 94% reported routinely testing pregnant women for hepatitis B surface antigen (HBsAg) with each pregnancy. Only 60.9% routinely advised HBsAg-positive patients to seek specialist evaluation for antiviral treatment and monitoring and fewer than half (48.6%) routinely provided them with HBV information. While most respondents recognized the potential complications of chronic HBV (94.2%), only 21% were aware that chronic HBV carries a 25% risk of liver related death when left unmonitored and untreated, and only 25% were aware of the high prevalence of chronic HBV in the foreign-born Asian, Native Hawaiian and Pacific Islander population. Obstetricians aware of the high risk of perinatal HBV transmission were more likely to test pregnant women for HBV DNA or hepatitis B e-antigen in HBV-infected women ($r = 0.18$, $p = 0.033$). Obstetricians who demonstrated knowledge of the long-term consequences of untreated HBV infection were no more likely to refer HBV-infected women to specialists for care ($r = 0.02$, $p = 0.831$). CONCLUSION: Our study identified clear gaps in the practice patterns of obstetricians that can be readily addressed to enhance the care they provide to HBV-infected pregnant women.

KW Cheung, MTY Seto, TTH Lao (2019). "[Prevention of perinatal hepatitis B virus transmission.](#)" *Arch Gynecol Obstet* **300**(2): 251-259.

PURPOSE: Chronic hepatitis B virus (HBV) infection remains endemic and continues to cause significant morbidity and mortality. It is a global health issue and the World Health Organization aims to eradicate HBV by 2030. Since vertical transmission accounts for the majority of chronic HBV infection, pregnancy offers an excellent opportunity to achieve complete HBV eradication by providing effective immunization of the offspring. **METHODS:** We reviewed recent publications identified from PubMed database using a combination of the relevant keywords for HBV, pregnancy, vertical transmission, immunoprophylaxis failure and antiviral treatment. **RESULTS:** We summarized the evidence of factors associated with, and measures to reduce and prevent maternal to child transmission, including the use of antiviral treatment during pregnancy to prevent immunoprophylaxis failure. Evidence suggested that highly viremia mother can be offered antenatal antiviral treatment to prevent immunoprophylaxis failure. We elaborated the viral load threshold to start maternal antiviral treatment and the importance of timely neonatal vaccination. A clinical algorithm to manage HBV carriers during pregnancy was proposed. **CONCLUSION:** Eradication of HBV is achievable with optimal management of HBV carriers, especially during pregnancy by interruption of vertical transmission. Routine antenatal screening and neonatal immunoprophylaxis remain the key measures to reduce the global HBV burden, and additional antenatal antiviral treatment could further minimize the chance of persistent infection in newborns.

YB Zeng, ML Luo, HQ He, X Deng, SY Xie, Y Fang (2019). "[[Economic evaluation on strategy for preventing mother-to-child transmission of hepatitis B in Zhejiang Province](#)]." *Zhonghua Yu Fang Yi Xue Za Zhi* **53**(7): 706-712.

Objective: To evaluate the cost-benefit and cost-effectiveness of current strategy for preventing mother-to-child transmission (PMTCT) of hepatitis B virus. **Methods:** A decision tree model with the Markov process was developed and simulated over the lifetime of a birth cohort in Zhejiang Province in 2016. The current PMTCT strategy was compared with universal vaccination and non-vaccination. Costs were assessed from social perspective. Benefits were the savings from reduced costs associated with disease and effectiveness were measured by quality-adjusted of life-years (QALY) gained. The net present value (NPV), cost-benefit ratio (BCR) and incremental cost-effectiveness ratio (ICER) were calculated. Univariate and Probabilistic Sensitivity Analyses (PSA) were performed to assess parameter uncertainties. The parameters of costs and utilities value of hepatitis B-related disease came from the results of the field survey, which were obtained by face-to-face questionnaire survey combined with inpatient medical records, including eight county and municipal hospitals in Jinhua, Jiaxing and Taizhou. A total of 626 outpatients and 523 inpatient patients were investigated. The annual total costs of infection was calculated by combining the costs of outpatient and inpatient. **Results:** The PMTCT strategy showed a net-gain as 38 323.78 CNY per person, with BCR as 21.10, which was higher than 36 357.80 CNY per person and 13.58 respectively of universal vaccination. Compared with universal vaccination, the PMTCT strategy would save 2 787.07 CNY per additional QALY gained for every person, indicating that PMTCT would be cost-saving. The most important parameters that could affect BCR and ICER were the vaccine coverage rate and costs of hepatitis B related diseases respectively. The PSA showed the PMTCT strategy was preferable as it would gain more QALY and save costs. **Conclusions:** The PMTCT strategy appeared as highly cost-beneficial and highly cost-effective. High vaccination rate was a key factor of high economic value.

L Zhang, Y Tao, J Woodring, K Rattana, S Sovannarith, T Rathavy, K Cheang, S Hossain, L Ferradini, S Deng, C Sokun, C Samnang, M Nagai, YR Lo, N Ishikawa (2019). "[[Integrated approach for triple elimination of mother-to-child transmission of HIV, hepatitis B and syphilis is highly effective and cost-effective: an economic evaluation](#)]." *Int J Epidemiol* **48**(4): 1327-1339.

BACKGROUND: The Regional Framework for Triple Elimination of Mother-to-Child Transmission (EMTCT) of HIV, Hepatitis B (HBV) and Syphilis in Asia and the Pacific 2018-30 was endorsed by the Regional Committee of WHO Western Pacific in October 2017, proposing an integrated and coordinated approach to achieve elimination in an efficient, coordinated and sustainable manner. This study aims to assess the population impacts and cost-effectiveness of this integrated approach in the Cambodian context. **METHODS:** Based on existing frameworks for the EMTCT for each individual infection, an integrated framework that combines infection prevention procedures with routine antenatal care was constructed. Using decision tree analyses, population impacts, cost-effectiveness and the potential reduction in required resources of the integrated approach as a result of resource pooling and improvements in service coverage and coordination, were evaluated. The tool was assessed using simulated epidemiological data from Cambodia. **RESULTS:** The current prevention programme for 370,000 Cambodian pregnant women was estimated at USD\$2.3 (\$2.0-\$2.5) million per year, including the

duration of pregnancy and up to 18 months after delivery. A model estimate of current MTCT rates in Cambodia was 6.6% (6.2-7.1%) for HIV, 14.1% (13.1-15.2%) for HBV and 9.4% (9.0-9.8%) for syphilis. Integrating HIV and syphilis prevention into the existing antenatal care framework will reduce the total time required to provide this integrated care by 19% for health care workers and by 32% for pregnant women, resulting in a net saving of \$380,000 per year for the EMTCT programme. This integrated approach reduces HIV and HBV MTCT to 6.1% (5.7-6.5%) and 13.0% (12.1-14.0%), respectively, and substantially reduces syphilis MCTC to 4.6% (4.3-5.0%). Further introduction of either antiviral treatment for pregnant women with high viral load of HBV, or hepatitis B immunoglobulin (HBIG) to exposed newborns, will increase the total cost of EMTCT to \$4.4 (\$3.6-\$5.2) million and \$3.3 (\$2.7-\$4.0) million per year, respectively, but substantially reduce HBV MTCT to 3.5% (3.2-3.8%) and 5.0% (4.6-5.5%), respectively. Combining both antiviral and HBIG treatments will further reduce HBV MTCT to 3.4% (3.1-3.7%) at an increased total cost of EMTCT of \$4.5 (\$3.7-\$5.4) million per year. All these HBV intervention scenarios are highly cost-effective (\$64-\$114 per disability-adjusted life years averted) when the life benefits of these prevention measures are considered. CONCLUSIONS: The integrated approach, using antenatal, perinatal and postnatal care as a platform in Cambodia for triple EMTCT of HIV, HBV and syphilis, is highly cost-effective and efficient.

Y Chen, C Xie, Y Zhang, Y Li, S Ehrhardt, CL Thio, KE Nelson, Y Chen, CS Lin (2018). "[Knowledge regarding hepatitis B mother-to-child transmission among healthcare workers in South China.](#)" *J Viral Hepat* **25**(5): 561-570.

2. To determine the knowledge regarding hepatitis B virus (HBV) mother-to-child transmission (MTCT) and its prevention and treatment among healthcare workers (HCWs) in Guangdong Province, China, an HBV endemic area. An HBV knowledge questionnaire was administered to 900 HCWs from the 3rd Affiliated Hospital of Sun Yat-Sen University and 2 rural hospitals in Guangdong Province. The 27 items in the questionnaire fell into 3 sections: HBV MTCT general knowledge, respondents' practices of preventing HBV MTCT and awareness of the resources of preventing HBV MTCT. The data collected were coded and analysed using SPSS software version 20. In total, 503 of 900 HCWs responded to the survey (response rate: 55.9%). Eighty-four individuals responded correctly to all of the knowledge questions: 58 were doctors, and 26 were nurses ($P < .05$). Doctors more often performed practices than nurses ($t = 3.591$, $P < .01$). Participants from the infectious disease department demonstrated a significantly higher proportion of correct answers and resource utilization than other specialties ($\chi^2(2) = 14.052$, 7.998 , $P < .01$). In terms of the average knowledge score, t test or ANOVA showed that there were significant differences between the specialty groups ($t = 3.110$, $P < .01$), hospital level groups ($t = 2.337$, $P < .05$) and age groups ($F = 3.020$, $P < .05$). Respondents' initiative increased with hospital level and age ($t = 2.993$, 7.493 , $P < .01$). A considerable percentage of HCWs has misconceptions about HBV MTCT. Healthcare workers, in particular nurses, those working in noninfectious disease departments or township hospitals and younger medical staff, lack systematic and comprehensive knowledge about HBV MTCT and are in urgent need of HBV-related training.

Y Du, X Chi, C Wang, J Jiang, F Kong, H Yan, X Wang, J Li, NC Wu, L Dai, TH Zhang, S Shu, J Zhou, JM Yoshizawa, X Li, D Bhattacharya, TT Wu, J Niu, R Sun (2017). "[Quantifying perinatal transmission of Hepatitis B viral quasispecies by tag linkage deep sequencing.](#)" *Sci Rep* **7**(1): 10168.

Despite full immunoprophylaxis, mother-to-child transmission (MTCT) of Hepatitis B Virus still occurs in approximately 2-5% of HBsAg positive mothers. Little is known about the bottleneck of HBV transmission and the evolution of viral quasispecies in the context of MTCT. Here we adopted a newly developed tag linkage deep sequencing method and analyzed the quasispecies of four MTCT pairs that broke through immunoprophylaxis. By assigning unique tags to individual viral sequences, we accurately reconstructed HBV haplotypes in a region of 836 bp, which contains the major immune epitopes and drug resistance mutations. The detection limit of minor viral haplotypes reached 0.1% for individual patient sample. Dominance of "a determinant" polymorphisms were observed in two children, which pre-existed as minor quasispecies in maternal samples. In all four pairs of MTCT samples, we consistently observed a significant overlap of viral haplotypes shared between mother and child. We also demonstrate that the data can be potentially useful to estimate the bottleneck effect during HBV MTCT, which provides information to optimize treatment for reducing the frequency of MTCT.

I Gentile, E Zappulo, AR Buonomo, G Borgia (2014). "[Prevention of mother-to-child transmission of hepatitis B virus and hepatitis C virus.](#)" *Expert Rev Anti Infect Ther* **12**(7): 775-782.

NP Nelson, DJ Jamieson, TV Murphy (2014). "[Prevention of Perinatal Hepatitis B Virus Transmission.](#)" *J Pediatric Infect Dis Soc* **3 Suppl 1**: S7-s12.

I Vodkin, H Patton (2014). "[Management of Hepatitis B virus infection during pregnancy.](#)" *Minerva Gastroenterol Dietol* **60**(4): 205-214.

Xu H, Zeng T, Liu JY, Lei Y, Zhong S, Sheng YJ, Zhou Z, Ren H. (2014). "[Measures to reduce mother-to-child transmission of Hepatitis B virus in China: a meta-analysis.](#)" *Dig Dis Sci* **59**(2): 242-258.

KW Cheung, MTY Seto, SF Wong (2013). "[Towards complete eradication of hepatitis B infection from perinatal transmission: review of the mechanisms of in utero infection and the use of antiviral treatment during pregnancy.](#)" *Eur J Obstet Gynecol Reprod Biol* **169**(1): 17-23.

ML Giles, K Visvanathan, SR Lewin, J Sasadeusz (2012). "[Chronic hepatitis B infection and pregnancy.](#)" *Obstet Gynecol Surv* **67**(1): 37-44.

a) Hepatitis B vaccination & immunoglobulin treatment

Z Chen, M Zeng, D Liu, L Wu, L Zhang (2020). "[Antenatal administration of hepatitis B immunoglobulin and hepatitis B vaccine to prevent mother to child transmission in hepatitis B virus surface antigen positive pregnant women: A systematic review and meta-analysis.](#)" *Medicine (Baltimore)* **99**(16): e19886.

BACKGROUND: This study aims at evaluating the benefits and harms of hepatitis B immune globulin (HBIG) and hepatitis B vaccine (HBVac) in preventing mother to child transmission in HBV surface antigen (HBsAg) positive pregnant women during antenatal period. METHODS: Seven electronic databases including PubMed, Embase, Cochrane Library, China National Knowledge Infrastructure (CNKI), WanFang Database, Chinese Biomedical Literature Database (CBM), VIP Database for Chinese Technical Periodicals (VIP), and 3 clinical trial registry platforms were searched from inception date to December 2017. Only randomized controlled trials (RCTs) were included in this study. The Cochrane risk of bias tool was applied to assessing the risk of bias. The outcomes were analyzed by Review Manager 5.3 software. RESULTS: Sixteen RCTs involving 2440 HBsAg positive pregnant women were included in the meta-analysis. Compared with placebo group, HBIG and HBVac group had a significant decrease in the number of newborns who were HBsAg positive (relative risks [RR]: 0.2, 95% confidence interval [CI] [0.18, 0.40], $P < .00001$) and HBV-DNA positive (RR: 0.25, 95% CI [0.09, 0.71], $P = .010$), and had a significant increase in the number of anti-HBs positive newborns (RR: 3.95, 95% CI [3.11, 5.00], $P < .00001$). After 1-year follow up, the number of HBsAg positive newborns continued to decline (RR: 0.09, 95% CI [0.04, 0.20], $P < .00001$) and the number of anti-HBs positive newborns continued to increase in HBIG and HBVac group (RR: 1.30, 95% CI [1.22, 1.38], $P < .00001$). Compared with HBIG group, HBIG and HBVac group had no significant difference in the number of HBsAg positive newborns (RR: 1.68, 95% CI [0.66, 4.30], $P = .28$), and had a significant decrease in the number of HBsAg positive newborns (RR: 0.31, 95% CI [0.12, 0.84], $P = .02$). Additionally, only 1 study reported 2 swelling cases, 4 studies were reported no adverse events, and 11 studies were not report adverse reaction. CONCLUSIONS: HBIG and HBVac could be an effective alternative for HBsAg positive pregnant women to prevent mother to child transmission. However, due to the limitations of the study, the long-term efficacy and safety of HBIG and HBVac still need long-term and high-quality research to confirm.

PM Khue, NTT Linh, VH Vinh, LV Dung, BN Van (2020). "[Hepatitis B Infection and Mother-to-Child Transmission in Haiphong, Vietnam: A Cohort Study with Implications for Interventions.](#)" *Biomed Res Int* **2020**: 4747965.

BACKGROUND: There is little data available on HBV infection and mother-to-child transmission (MTCT) in Vietnam. OBJECTIVE: This study is aimed at assessing the prevalence of HBV infection and the current situation of MTCT in Haiphong, Vietnam. METHODS: A transversal survey of 1721 pregnant women followed by an observational prospective cohort study of 183 HBV-infected women was conducted at Haiphong Gyneco-Obstetric Hospital. Women were followed up up to 12-month postpartum; use of prevention measures and the MTCT rate were evaluated. HBV infection in children was defined by a HBsAg-positive test at 12 months of age. RESULTS: At baseline, 183 of 1721 pregnant women (10.6%) tested HBsAg positive. Among them, 23.0% were HBeAg positive, 26.2% had a detectable load of HBV DNA, and 13.1% had a HBV DNA load $\geq 200,000$ IU/mL. All women underwent MTCT prevention antiviral

therapy. At delivery, 98.9% of newborns receive a HBV vaccine birth dose, and 82% received HBIG. At 12 months of age, 94.7% have received the scheduled HBV vaccines. Eight percent of infants born from followed-up women were HBsAg positive. The mother's HBeAg-positive status was associated with a higher risk of HBV infection in infants. CONCLUSION: The HBV prevalence and MTCT rates are high in Haiphong. A strong national plan to increase the access to preventive measures and to monitor results is needed in order to decrease this prevalence.

M Guo, WW Luo, DZ Zhang (2019). "[\[Optimal cessation period of anti-HBV therapy to block mother-to-child transmission\]](#)." *Zhonghua Gan Zang Bing Za Zhi* **27**(2): 92-96.

Hepatitis B virus (HBV) carrier woman of childbearing age with high viral load is an important source of vertical transmission of hepatitis b virus from mother-to-child in China. Routine blockade with immunoglobulin combined with hepatitis B vaccine is used for neonates born to pregnant women with high viral load of hepatitis B virus, but in some cases, immunoprophylaxis fails. The main application of antiviral drugs in pregnancy is to reduce the serum viral load, thereby significantly improve the blocking rate of vertical transmission between mother and infant. Current evidence suggested that if the maternal age is less than 30 years old, with no obvious liver fibrosis or cirrhosis and there is no increase in ALT level >2ULN(upper limit of normal) during the treatment, the treatment with antiviral drugs can be stopped after delivery immediately. Additionally, ALT level should be examined at 4, 12 and 24 weeks after stopping the drug. Antiviral therapy for the occurrence of hepatitis attack should be given if criteria for HBV treatment are met.

AL McNaughton, J Lourenço, L Hattingh, E Adland, S Daniels, A Van Zyl, CS Akiror, S Wareing, K Jeffery, MA Ansari, P Klenerman, PJR Goulder, S Gupta, P Jooste, PC Matthews (2019). "[HBV vaccination and PMTCT as elimination tools in the presence of HIV: insights from a clinical cohort and dynamic model](#)." *BMC Med* **17**(1): 43.

BACKGROUND: Sustainable Development Goals set a challenge for the elimination of hepatitis B virus (HBV) infection as a public health concern by the year 2030. Deployment of a robust prophylactic vaccine and enhanced interventions for prevention of mother to child transmission (PMTCT) are cornerstones of elimination strategy. However, in light of the estimated global burden of 290 million cases, enhanced efforts are required to underpin optimisation of public health strategy. Robust analysis of population epidemiology is particularly crucial for populations in Africa made vulnerable by HIV co-infection, poverty, stigma and poor access to prevention, diagnosis and treatment. METHODS: We here set out to evaluate the current and future role of HBV vaccination and PMTCT as tools for elimination. We first investigated the current impact of paediatric vaccination in a cohort of children with and without HIV infection in Kimberley, South Africa. Second, we used these data to inform a new parsimonious model to simulate the ongoing impact of preventive interventions. By applying these two approaches in parallel, we are able to determine both the current impact of interventions, and the future projected outcome of ongoing preventive strategies over time. RESULTS: Existing efforts have been successful in reducing paediatric prevalence of HBV infection in this setting to < 1%, demonstrating the success of the existing vaccine campaign. Our model predicts that, if consistently deployed, combination efforts of vaccination and PMTCT can significantly reduce population prevalence (HBsAg) by 2030, such that a major public health impact is possible even without achieving elimination. However, the prevalence of HBV e-antigen (HBeAg)-positive carriers will decline more slowly, representing a persistent population reservoir. We show that HIV co-infection significantly reduces titres of vaccine-mediated antibody, but has a relatively minor role in influencing the projected time to elimination. Our model can also be applied to other settings in order to predict impact and time to elimination based on specific interventions. CONCLUSIONS: Through extensive deployment of preventive strategies for HBV, significant positive public health impact is possible, although time to HBV elimination as a public health concern is likely to be substantially longer than that proposed by current goals.

YP Qiao, M Su, Y Song, XY Wang, Z Li, YL Li, LX Dou, Q Wang, K Hann, GM Zhang, XN Huang, YN Yang, X Jin, AL Wang (2019). "[Outcomes of the national programme on prevention of mother-to-child transmission of hepatitis B virus in China, 2016-2017](#)." *Infect Dis Poverty* **8**(1): 65.

BACKGROUND: In addition to providing free hepatitis B vaccine (HBvacc) series to all infants in China since 2005, the national programme on prevention of mother-to-child transmission (PMTCT) of hepatitis B virus (HBV) started providing free hepatitis B immunoglobulin for all new-borns born to hepatitis B surface-antigen (HBsAg) positive mothers in 2010. However, few studies have evaluated the effectiveness of the PMTCT programme. Therefore, we aimed to investigate the outcomes of the programme and

identify associated factors. **METHOD:** Using a cross-sectional study design, we collected data on 4112 pairs of HBsAg-positive mothers and their children aged 7-22 months in four representative provinces through interviews and medical record review. We tested HBsAg and hepatitis B surface antibody (anti-HBs) of children by enzyme-linked immunosorbent assay at designated maternal and child hospital laboratories. We used logistic regression to analyse factors associated with child HBsAg and anti-HBs positivity. **RESULTS:** Thirty-five children were HBsAg positive, indicating the mother-to-child transmission (MTCT) rate was 0.9% (0.6-1.1%). The anti-HBs positive rate was 96.8% (96.3-97.4%). Children receiving HBvacc between 12 and 24 h of birth were 2.9 times more likely to be infected than those vaccinated in less than 12 h (adjusted odds ratio [aOR] = 2.9, 95% confidence interval [CI]: 1.4-6.3, P = 0.01). Maternal hepatitis B e-antigen (HBeAg) positivity was associated with higher MTCT rate (aOR = 79.1, 95% CI: 10.8-580.2, P < 0.001) and lower anti-HBs positive rate (aOR = 0.4, 95% CI: 0.3-0.6, P < 0.001). Children with low birth weight (LBW) were 60% less likely to be anti-HBs positive than those with normal birth weight (aOR = 0.4, 95% CI: 0.2-0.8, P = 0.01). **CONCLUSIONS:** The MTCT rate was lower than the 2030 WHO elimination goal, which implies the programme is on track to achieve this target. As earlier HBvacc birth dose (HBvcc-BD) was associated with lower MTCT rate, we suggest that the PMTCT programme work with the Expanded Programme on Immunization (EPI) to modify the current recommendation for early HBvcc-BD to a requirement. Our finding that LBW was associated with lower anti-HBs positivity points to the need for further studies to understand factors associated with these risks and opportunities for program strengthening. The programme needs to ensure providing essential test to identify HBeAg-positive mothers and their infants and provide them with appropriate medical care and follow-up.

Y Sasagawa, H Yamada, M Morizane, M Deguchi, To Shirakawa, I Morioka, K Tanimura (2019). "[Hepatitis B virus infection: Prevention of mother-to-child transmission and exacerbation during pregnancy.](#)" *J Infect Chemother* **25**(8): 621-625.

The aims of this study were to assess the effect of maternal screening for hepatitis B (HB) virus and a perinatal prevention program of mother-to-child transmission, and to identify clinical characteristics and findings associated with HB exacerbation during pregnancy. This prospective cohort study enrolled 3796 pregnant women and their neonates with informed consent. Pregnant women underwent maternal universal screening for HBs antigen (Ag) in the first trimester. If HBs Ag was positive, serum levels of HBe Ag, alanine transaminase (AST), aspartate aminotransferase (ALT), and HB virus (HBV) DNA were measured. All neonates delivered from HBs Ag-positive women were given HB immune globulin and HB vaccine based on the guidelines of the perinatal prevention program. Of the 3796 pregnant women, 40 (1.05%) tested positive for HBs Ag. Three (7.5%) of the 40 HBs Ag-positive women experienced exacerbation of HBV infection during pregnancy. Serum levels of AST (median 776 vs. 22 mIU/ml, p < 0.01), ALT (median 325 vs. 15 mIU/ml, p < 0.01), and HBV-DNA (median 9.1 vs. 5.4 log copies/ml, p < 0.05), and frequencies of HBe Ag-positive (100% vs. 29.7%, p < 0.05) and symptoms of itching or general fatigue (66.7% vs. 0%, p < 0.01) in three women with exacerbation of HBV infection were significantly higher than those in 37 women without exacerbation. There was no case of mother-to-child transmission, suggesting the perinatal HBV prevention program was effective. Levels of HBe Ag, liver enzymes, and HBV-DNA as well as symptoms of itching and general fatigue should be carefully monitored for HBs Ag-positive women during pregnancy and the postpartum period.

M Visser, CPB van der Ploeg, C Smit, CWPM Hukkelhoven, F Abbink, BHB van Benthem, ELM Op de Coul (2019). "[Evaluating progress towards triple elimination of mother-to-child transmission of HIV, syphilis and hepatitis B in the Netherlands.](#)" *BMC Public Health* **19**(1): 353.

BACKGROUND: In 2014 the World Health Organisation (WHO) established validation criteria for elimination of mother-to-child transmission (EMTCT) of HIV and syphilis. Additionally, the WHO set targets to eliminate hepatitis, including hepatitis B (HBV). We evaluated to what extent the Netherlands has achieved the combined WHO criteria for EMTCT of HIV, syphilis and HBV. **METHODS:** Data of HIV, syphilis and HBV infections among pregnant women and children (born in the Netherlands with congenital infection) for 2009-2015, and data required to validate the WHO criteria were collected from multiple sources: the antenatal screening registry, the HIV monitoring foundation database, the Perinatal Registry of the Netherlands, the national reference laboratory for congenital syphilis, and national HBV notification data. **RESULTS:** Screening coverage among pregnant women was > 99% for all years, and prevalence of HIV, syphilis and HBV was very low. In 2015, prevalence of HIV, syphilis and HBV was 0.06, 0.06 and 0.29%, respectively. No infections among children born in the Netherlands were reported in 2015 for all three diseases, and in previous years only sporadic cases were observed. In 2015, treatment of HIV positive pregnant women was 100% and HBV vaccination of children from HBV positive mothers was

> 99%. For syphilis, comprehensive data was lacking to validate WHO criteria. CONCLUSIONS: In the Netherlands, prevalence of maternal HIV, syphilis and HBV is low and congenital infections are extremely rare. All minimum WHO criteria for validation of EMTCT are met for HIV and HBV, but for syphilis more data are needed to prove elimination.

Y Wu, J Gao, J Qin, J He, A Wang, H Wang, Q Du, J Fang, X Sheng, R Wang, Z Wang, T Yang (2019). "[Mother-to-child transmission prevention of human immunodeficiency virus, syphilis and hepatitis B virus](#)." *Women Birth* **32**(6): 570-578.

BACKGROUND: China is the first country to initiate a nationwide program for prevention of mother-to-child transmission of human immunodeficiency virus, syphilis and hepatitis B virus by an integrated approach. However, the progress of this program remains unreported at national or local level for China. Therefore, we performed a hospital-based longitudinal study to assess the integrated prevention effect in Hunan, South-central China. METHODS: This study was conducted at 123 counties in Hunan and covered all local hospitals providing midwifery and antenatal care services from 2010 to 2016. We used the Cochran-Armitage test to examine the temporal changes of the indicators related with prevention of mother-to-child transmission. Besides, we used Spearman rank correlation analysis to assess the association between mother-to-child transmission rates and the process indicators related with prevention of mother-to-child transmission. RESULTS: After implementation of integrated prevention program, the indicators related with prevention of mother-to-child transmission are moving in the right direction. From 2010 to 2016, mother-to-child transmission rates significantly decreased from 19.4% to 9.6% for human immunodeficiency virus, and from 116.3 to 13.6 cases per 100,000 live births for syphilis. The proportion of children receiving hepatitis B immunoglobulin injection within 24h after birth increased from 95.2% to 98.9% among exposed neonates. Mother-to-child transmission rates were negatively associated with the process indicators related with prevention of mother-to-child transmission (all $P < 0.05$). CONCLUSIONS: Our prevention program of mother-to-child transmission for three diseases by an integrated approach proved to be viable and effective. Our model may be of interest to other countries.

T Chen, J Wang, H Qiu, Q Yu, T Yan, C Qi, F Cao, Z Tian, D Guo, N Yao, Y Yang, Y He, Y Zhao, J Liu (2018). "[Different interventional criteria for chronic hepatitis B pregnant women with HBeAg\(+\) or HBeAg\(-\): Epidemiological data from Shaanxi, China](#)." *Medicine (Baltimore)* **97**(27): e11406.

The seroprevalence of hepatitis B virus (HBV) and its impact on pregnancy outcomes of women from Shaanxi Province (China) was assessed. Risk factors for mother-to-child transmission (MTCT) were evaluated based on HBV-related seroprevalence data. Viral markers and biochemical parameters were assessed in HBsAg-positive mothers and their infants out of 13,451 cases recruited. A pretested and structured questionnaire was used to test the general HBV knowledge. Descriptive statistics and logistic regression analysis were done to reveal possible risk factors for MTCT. The overall prevalence of HBsAg in pregnant women was 7.07% (951/13,451), and a rate as high as 9.40% was observed. Among the HBsAg-positive pregnant women, 30.49% (290/951) were HBeAg-positive, 22.08% (210/951) had HBV DNA levels > 10 IU/mL and only 16.19% with a high risk of MTCT (34/210) had received antiviral treatment. The overall MTCT rate was 5.21%. Noteworthy, the risk ratio and 95% confidence interval (95% CI) of MTCT in HBeAg-negative mothers with HBV DNA levels > 2 x 10 IU/mL and HBsAg > 10 IU/mL was 26.062 (2.633-258.024), which was significantly higher than that of HBeAg-positive mothers with HBV DNA level > 10 IU/mL. Moreover, the awareness and knowledge about HBV transmission, risk factors, and intervention for MTCT were generally lacking among HBsAg-positive mothers. As a higher HBsAg seroprevalence and a higher MTCT rate among HBeAg-negative mothers with lower HBV DNA level was observed, our study emphasizes different interventional criteria for HBeAg-positive and HBeAg-negative mothers. Extensive health education, routine screening, and immunization against HBV during pregnancy are highly warranted to minimize the possibility of perinatal transmission.

P Wilson, JB Parr, R Jhaveri, SR Meshnick (2018). "[Call to Action: Prevention of Mother-to-Child Transmission of Hepatitis B in Africa](#)." *J Infect Dis* **217**(8): 1180-1183.

Hepatitis B virus (HBV) is a significant public health issue that has not been adequately addressed, especially in the high-prevalence region of Africa. Despite the incorporation of HBV vaccines into the Expanded Program on Immunization, children continue to be infected with HBV through maternal-to-child transmission (MTCT). The addition of a birth dose of HBV vaccine would be a cost-effective method to reduce MTCT. Birth-dose HBV vaccine policies have been adopted in the Western Pacific region but not yet in Africa. Even better protection against HBV MTCT can be achieved by treatment of pregnant

women with high HBV viral loads with tenofovir. Tenofovir is already widely used in prevention of HIV MTCT (PMTCT) programs. We suggest that existing HIV PMTCT programs could be expanded to deliver care for HBV-infected pregnant women. With appropriate adoption of birth-dose vaccination policies and expansion of PMTCT programs, elimination of HBV MTCT in Africa is achievable.

B Biot, N Laverdure, F Lacaille, A Lachaux (2017). "[\[Mother-to-child transmission of hepatitis B virus despite postexposure prophylaxis: A review of the literature and description of 11 observations\]](#)." *Arch Pediatr* **24**(2): 135-139.

Chronic hepatitis B virus (HBV) infection leads to a risk of developing cirrhosis and hepatocellular carcinoma. In France, where the prevalence of HBV is low, mother-to-child transmission is the cause of chronic infection in more than one-third of cases. After exposure, the risk of chronic infection is the highest for newborns (90 %). The World Health Organization implemented a global immunization program in 1991, applied in France in 1994. A significant number of children are infected each year, however, and failure of postexposure prophylaxis is reported in 4-10 % of newborns. We report 11 children with chronic HBV infection due to failure of serovaccination, followed up in two centers between 1993 and 2015. We discuss maternal screening, serovaccination, and follow-up conditions, as well as the role of maternal viral load, amniocentesis, and mode of delivery as risk factors. These observations confirm that serovaccination failures are related to the nonobservance of recommendations for maternal screening or postexposure prophylaxis, and to a high maternal viral load (>10⁶ copies/mL). We therefore recommend improving the screening strategy, with control of the hepatitis B antigen in early pregnancy, and discussion of treatment with a nucleoside analog during the last trimester of pregnancy. Serovaccination should be enforced. Its efficacy should be controlled when the child reaches 9 months of age, in order to organize the follow-up if infection occurs.

N Chamroonkul, T Piratvisuth (2017). "[Hepatitis B During Pregnancy in Endemic Areas: Screening, Treatment, and Prevention of Mother-to-Child Transmission](#)." *Paediatr Drugs* **19**(3): 173-181.

The proper management of pregnant women infected with hepatitis B virus (HBV) is necessary to prevent maternal and fetal morbidity and mortality and to protect the baby from HBV infection. In the majority of cases, vertical transmission can be prevented with a universal screening program, HBV vaccine immunoprophylaxis, and administration of hepatitis B immunoglobulin (HBIG) for babies born to mothers with HBV. However, in mothers with a high viral load (>200,000 or >1,000,000 IU/ml, depending on the guideline), the chance of immunoprophylaxis failure remains high. The standard recommendation is to give an antiviral agent during the third trimester in these patients. US FDA pregnancy category B agents such as tenofovir and telbivudine are allowed through all trimesters of pregnancy. Breastfeeding for patients who receive antiviral agents can be allowed after a risk-benefit discussion with the patient.

AC Eke, GU Eleje, UA Eke, Y Xia, J Liu (2017). "[Hepatitis B immunoglobulin during pregnancy for prevention of mother-to-child transmission of hepatitis B virus](#)." *Cochrane Database Syst Rev* **2**: Cd008545.

BACKGROUND: Hepatitis is a viral infection of the liver. It is mainly transmitted between people through contact with infected blood, frequently from mother to baby in-utero. Hepatitis B poses significant risk to the fetus and up to 85% of infants infected by their mothers at birth develop chronic hepatitis B virus (HBV) infection. Hepatitis B immunoglobulin (HBIG) is a purified solution of human immunoglobulin that could be administered to the mother, newborn, or both. HBIG offers protection against HBV infection when administered to pregnant women who test positive for hepatitis B envelope antigen (HBeAg) or hepatitis B surface antigen (HBsAg), or both. When HBIG is administered to pregnant women, the antibodies passively diffuse across the placenta to the child. This materno-fetal diffusion is maximal during the third trimester of pregnancy. Up to 1% to 9% infants born to HBV-carrying mothers still have HBV infection despite the newborn receiving HBIG plus active HBV vaccine in the immediate neonatal period. This suggests that additional intervention such as HBIG administration to the mother during the antenatal period could be beneficial to reduce the transmission rate in utero. **OBJECTIVES:** To determine the benefits and harms of hepatitis B immunoglobulin (HBIG) administration to pregnant women during their third trimester of pregnancy for the prevention of mother-to-child transmission of hepatitis B virus infection. **SEARCH METHODS:** We searched the The Cochrane Hepato-Biliary Group Controlled Trials Register, CENTRAL, MEDLINE Ovid, Embase Ovid, Science Citation Index Expanded (Web of Science), SCOPUS, African Journals OnLine, and INDEX MEDICUS up to June 2016. We searched ClinicalTrials.gov and portal of the WHO International Clinical Trials Registry Platform (ICTRP) in December 2016. **SELECTION CRITERIA:** We included randomised clinical trials comparing HBIG versus placebo or no intervention in pregnant women with HBV. **DATA COLLECTION AND ANALYSIS:** Two authors extracted

data independently. We analysed dichotomous outcome data using risk ratio (RR) and continuous outcome data using mean difference (MD) with 95% confidence intervals (CI). For meta-analyses, we used a fixed-effect model and a random-effects model, along with an assessment of heterogeneity. If there were statistically significant discrepancies in the results, we reported the more conservative point estimate. If the two estimates were equal, we used the estimate with the widest CI as our main result. We assessed bias control using the Cochrane Hepato-Biliary Group suggested bias risk domains and risk of random errors using Trial Sequential Analysis (TSA). We assessed the quality of the evidence using GRADE. MAIN RESULTS: All 36 included trials originated from China and were at overall high risk of bias. The trials included 6044 pregnant women who were HBsAg, HBeAg, or hepatitis B virus DNA (HBV-DNA) positive. Only seven trials reported inclusion of HBeAg-positive mothers. All 36 trials compared HBIG versus no intervention. None of the trials used placebo. Most of the trials assessed HBIG 100 IU (two trials) and HBIG 200 IU (31 trials). The timing of administration of HBIG varied; 30 trials administered three doses of HBIG 200 IU at 28, 32, and 36 weeks of pregnancy. None of the trials reported all-cause mortality or other serious adverse events in the mothers or babies. Serological signs of hepatitis B infection of the newborns were reported as HBsAg, HBeAg, and HBV-DNA positive results at end of follow-up. Twenty-nine trials reported HBsAg status in newborns (median 1.2 months of follow-up after birth; range 0 to 12 months); seven trials reported HBeAg status (median 1.1 months of follow-up after birth; range 0 to 12 months); and 16 trials reported HBV-DNA status (median 1.2 months of follow-up; range 0 to 12 months). HBIG reduced mother-to-child transmission (MTCT) of HBsAg when compared with no intervention (179/2769 (6%) with HBIG versus 537/2541 (21%) with no intervention; RR 0.30, TSA-adjusted CI 0.20 to 0.52; $I(2) = 36\%$; 29 trials; 5310 participants; very low quality evidence). HBV-DNA reduced MTCT of HBsAg (104/1112 (9%) with HBV-DNA versus 382/1018 (38%) with no intervention; RR 0.25, TSA-adjusted CI 0.22 to 0.27; $I(2) = 84\%$; 16 trials; 2130 participants; low quality evidence). TSA supported both results. Meta-analysis showed that maternal HBIG did not decrease HBeAg in newborns compared with no intervention (184/889 (21%) with HBIG versus 232/875 (27%) with no intervention; RR 0.68, TSA-adjusted CI 0.04 to 6.37; $I(2) = 90\%$; 7 trials; 1764 participants; very low quality evidence). TSA could neither support nor refute this observation as data were too sparse. None of the trials reported adverse events of the immunoglobulins on the newborns, presence of local and systemic adverse events on the mothers, or cost-effectiveness of treatment. AUTHORS' CONCLUSIONS: Due to very low to low quality evidence found in this review, we are uncertain of the effect of benefit of antenatal HBIG administration to the HBV-infected mothers on newborn outcomes, such as HBsAg, HBV-DNA, and HBeAg compared with no intervention. The results of the effects of HBIG on HBsAg and HBeAg are surrogate outcomes (raising risk of indirectness), and we need to be critical while interpreting the findings. We found no data on newborn mortality or maternal mortality or both, or other serious adverse events. Well-designed randomised clinical trials are needed to determine the benefits and harms of HBIG versus placebo in prevention of MTCT of HBV.

G Yonghao, D Pumei, Y Jianhui, X Jin, Z Yanyang, W Zhe (2017). "[A retrospective study of hepatitis B mother-to-child transmission prevention and postvaccination serological test results of infants at risk of perinatal transmission in two counties of middle China.](#)" *J Viral Hepat* **24**(8): 687-695.

Approximately, 240 million people have chronic hepatitis B worldwide, with mother-to-child-transmission (MTCT) accounting for most cases. Therefore, Henan Province, China launched a public health programme to prevent MTCT. To determine the efficacy of this health programme, a survey was carried out in Huixian and Xinan counties, which are located in northern and western Henan. All infants born in these two counties between January 1, 2013 and March 31, 2014 to a mother positive for hepatitis B surface antigen (HBsAg) were surveyed. In total, there were 438 mother-infant pairs. A blood sample was collected from all mothers and infants and the following Hepatitis B virus (HBV) markers, antibodies, and antigens were measured: HBsAg, anti-HBs, anti-HBc, HBeAg, anti-HBe, and HBV-DNA. All mothers and 5.3% (23/438) of the infants were HBsAg positive. All infants received three doses of the hepatitis B vaccine (HepB) and the postvaccination serological test (PVST) showed that the appropriate interval for PVST may be 1-8 months after the final HepB dose. Multivariable analysis showed that infants without a timely first and second dose of the HepB, with an HBeAg-positive mother and mothers who had not received hepatitis B immune globulin during pregnancy were implicated in MTCT. The stratified analysis using maternal HBeAg as a marker showed that maternal HBeAg may be a strong risk factor for MTCT. To prevent MTCT in middle China, several courses of action are recommended. The first is to optimize the screening method for the mother to allow HBeAg and HBsAg-positive mothers to receive medical treatment during pregnancy and a timely birth dose of the vaccine to all infants. Second, all infants with

an HBsAg-positive mother should be tested for anti-HBs and HBsAg at 7-14 months old and any anti-HBs-nonresponse infants should receive an additional three doses of the vaccine.

CP Liu, YL Zeng, M Zhou, LL Chen, R Hu, L Wang, H Tang (2015). "[Factors associated with mother-to-child transmission of hepatitis B virus despite immunoprophylaxis](#)." *Intern Med* **54**(7): 711-716.

OBJECTIVE: This study aimed to assess risk factors for mother-to-child transmission (MTCT) of hepatitis B virus (HBV) after immunoprophylaxis. METHODS: Risk factors for MTCT were assessed using a multivariate logistic regression model. PATIENTS: We enrolled 256 mother-child pairs with positive maternal hepatitis B surface antigens (HBsAg) between January 2010 and June 2013. All children received passive-active immunization after birth. The children were tested for HBsAg at birth and 6-12 months and/or 1-3 years of age. RESULTS: Among 256 children, 10 (3.9%) developed HBV infection, all of whom were born to hepatitis B e antigen (HBeAg)-positive mothers with a high HBV DNA level (median, 7.36; range, 6.75-8.00 log₁₀ IU/mL). A total of 20 mothers received antiviral treatment during pregnancy. The maternal viral load decreased from an average of 7.16 to 3.08 log₁₀ IU/mL ($p < 0.0001$) at delivery. The multivariate logistic regression analysis showed that a high maternal HBV DNA level [odds ratio (OR) for each log₁₀ IU/mL increase, 2.44; 95% confidence interval (CI), 1.13-5.29, $p = 0.023$] and vaginal delivery (OR=6.96, 95% CI, 1.80-26.93, $p = 0.005$) were risk factors for HBV immunoprophylaxis failure. CONCLUSION: Additional treatment strategies should be considered in HBeAg-positive mothers with an HBV DNA level above 6-7 log₁₀ IU/mL. In addition, our study supports the use of Cesarean section for infants born to HBsAg-positive mothers.

C Pande, SK Sarin, S Patra, A Kumar, S Mishra, S Srivastava, K Bhutia, E Gupta, CK Mukhopadhyay, AK Dutta, SS Trivedi (2013). "[Hepatitis B vaccination with or without hepatitis B immunoglobulin at birth to babies born of HBsAg-positive mothers prevents overt HBV transmission but may not prevent occult HBV infection in babies: a randomized controlled trial](#)." *J Viral Hepat* **20**(11): 801-810.

H Komatsu, A Inui, T Sogo, E Hiejima, A Tateno, P Klenerman, T Fujisawa (2010). "[Cellular immunity in children with successful immunoprophylactic treatment for mother-to-child transmission of hepatitis B virus](#)." *BMC Infect Dis* **10**: 103.

S Zhongjie, X Li, L Ma, Y Yang (2010). "[Hepatitis B immunoglobulin injection in pregnancy to interrupt hepatitis B virus mother-to-child transmission-a meta-analysis](#)." *Int J Infect Dis* **14**(7): e622-634.

b) Antiviral treatment: entecavir, tenofovir, lamivudine, adefovir, telbivudine

Y Ding, L Cao, L Zhu, Y Huang, C Lin, Y Wang, Y Liu, Q Sheng, S Wang, J Fan, R Chen, W Gan, B Chen, CQ Pan (2020) [Efficacy and safety of tenofovir alafenamide fumarate for preventing mother to child transmission of hepatitis B virus: a national cohort study](#). *Aliment Pharmacol Ther*. 2020 Aug 27. doi: 10.1111/apt.16043. Online ahead of print.

Background: Data on tenofovir alafenamide fumarate (TAF) therapy for preventing mother to child transmission of hepatitis B virus (HBV) are lacking.

Aims: To investigate the efficacy and safety of TAF therapy for preventing hepatitis B mother to child transmission.

Methods: Mothers with chronic HBV infection, positive for hepatitis B e-antigen and with HBV DNA >200 000 IU/mL received TAF for preventing mother to child transmission were enrolled retrospectively from multiple centres with data collection on mother-infant dyads up to postpartum week 24-28. Primary measurements were the mother to child transmission rate and infants' malformation rate. Secondary assessments included maternal HBV DNA reduction at delivery, and maternal or infant adverse events during follow up.

Results: Among 71 mothers enrolled, the mean (\pm SD) age was 30.3 (\pm 2.2) years. TAF therapy was initiated during the second or third trimester and continued to delivery with a mean (\pm SD) duration of 12.8 (\pm 4.0) weeks. At delivery, 85.9% (61/71) of the mothers achieved HBV DNA <200 000 IU/L. Seventy-three infants (two sets of twins) were born from mothers treated with TAF and none had congenital defects or malformations. All infants received HBV immunoglobulin and vaccine at birth with additional HBV vaccinations at one and six months. At age 24-28 weeks, all infants had negative hepatitis B surface

antigen and undetectable levels of HBV DNA (<100 IU/mL). Body weight, height, and head circumferences were comparable to national standards for physical development. No severe adverse effects were reported in either mothers or infants.

Conclusions: TAF for highly viraemic mothers effectively prevented mother to child transmission of hepatitis B. There were no safety concerns for either mothers or infants with 24-28 weeks of follow up.

Ergen, P. and F. Yilmaz Karadağ (2020). "[Approach to women who become pregnant while on tenofovir disoproxil fumarate for chronic B hepatitis: A report of two cases.](#)" *J Obstet Gynaecol Res* **46**(5): 779-783.

Mother-to-child transmission of hepatitis B virus can occur during the intrauterine, antenatal and postnatal periods, with an increased risk of perinatal transmission. Appropriate management of patients who are hepatitis B surface antigen positive during pregnancy can substantially reduce the rates of perinatal transmission. Herein, two pregnant women with chronic hepatitis B are presented; one became pregnant while receiving tenofovir disoproxil fumarate and continued the treatment during pregnancy, the other discontinued tenofovir disoproxil fumarate treatment on her own due to conception, but restarted at 26 weeks of pregnancy. At birth the newborns of both women were vaccinated and immunoglobulin was given, with no perinatal transmission. Whether pregnant women should receive antiviral therapy or immunoprophylaxis still remains controversial. In order to keep the mother's liver stable and to prevent perinatal transmission, it is of paramount importance to manage pregnant women in line with the current information and guidelines.

AL Funk, Y Lu, K Yoshida, T Zhao, P Boucheron, J van Holten, R Chou, M Bulterys, Y Shimakawa (2020). "[Efficacy and safety of antiviral prophylaxis during pregnancy to prevent mother-to-child transmission of hepatitis B virus: a systematic review and meta-analysis.](#)" *Lancet Infect Dis.*

BACKGROUND: To eliminate mother-to-child transmission (MTCT) of hepatitis B virus (HBV), peripartum antiviral prophylaxis might be required for pregnant women infected with HBV who have a high risk of MTCT despite infant immunoprophylaxis. We aimed to determine the efficacy and safety of peripartum antiviral prophylaxis to inform the 2020 WHO guidelines. METHODS: In this systematic review and meta-analysis, we searched PubMed, Embase, Scopus, CENTRAL, CNKI, and Wanfang for randomised controlled trials and non-randomised studies of peripartum antiviral prophylaxis versus placebo or no prophylaxis, with no language restriction, published from database inception until March 28, 2019. We used search terms covering HBV, antiviral therapy, and pregnancy. We included studies that enrolled pregnant women with chronic infection with HBV who received antiviral prophylaxis anytime during pregnancy; that included any of the following antivirals: adefovir, emtricitabine, entecavir, lamivudine, telbivudine, tenofovir alafenamide fumarate, and tenofovir disoproxil fumarate; and that reported the following outcomes: MTCT, indicated by infant HBsAg positivity or HBV DNA positivity, or both, at age 6-12 months, and any infant or maternal adverse events. Two reviewers independently extracted data. Our primary endpoint was MTCT based on infant HBsAg positivity. We assessed pooled odds ratios (ORs) of the efficacy of peripartum antiviral prophylaxis to reduce the risk of MTCT. We assessed safety of prophylaxis by pooling risk differences. The protocol for the systematic review was pre-registered in PROSPERO, CRD42019134614. FINDINGS: Of 7463 articles identified, 595 articles were eligible for full-text review and 129 studies (in 157 articles) were included. The following antivirals were assessed in the meta-analysis: tenofovir disoproxil fumarate 300 mg (19 studies, with 1092 mothers and 1072 infants), lamivudine 100-150 mg (40 studies, with 2080 mothers and 2007 infants), and telbivudine 600 mg (83 studies, with 6036 mothers and 5971 infants). The pooled ORs for randomised controlled trials were similar, at 0.10 (95% CI 0.03-0.35) for tenofovir disoproxil fumarate, 0.16 (0.10-0.26) for lamivudine, and 0.14 (0.09-0.21) for telbivudine. The pooled ORs in non-randomised studies were 0.17 (0.10-0.29) for tenofovir disoproxil fumarate, 0.17 (0.12-0.24) for lamivudine, and 0.09 (0.06-0.12) for telbivudine. We found no increased risk of any infant or maternal safety outcomes after peripartum antiviral prophylaxis. INTERPRETATION: Peripartum antiviral prophylaxis is highly effective at reducing the risk of HBV MTCT. Our findings support the 2020 WHO recommendation of administering antivirals during pregnancy, specifically tenofovir disoproxil fumarate, for the prevention of HBV MTCT. FUNDING: World Health Organization.

PW Hui, C Ng, KW Cheung, CL Lai (2020). "[Acceptance of antiviral treatment and enhanced service model for pregnant patients carrying hepatitis B.](#)" *Hong Kong Med J* **26**(4): 318-322.

INTRODUCTION: A service model was established for pregnant women with positive screening results for hepatitis B surface antigen (HBsAg) at Queen Mary Hospital in Hong Kong. All women were offered a blood test for hepatitis B virus (HBV) DNA level during the first antenatal visit. Women with HBV DNA

levels of $\geq 200\,000$ IU/mL received counselling from hepatologists regarding treatment with antenatal tenofovir disoproxil fumarate (TDF) 300 mg daily. **METHODS:** This retrospective review included women attending our antenatal clinic who exhibited positive HBsAg screening results from 15 May 2017 to 31 December 2019. The proportions of women with positive HBsAg, DNA test acceptance, hepatological review, and TDF acceptance during pregnancy were reviewed. **RESULTS:** In total, 375 (2.9%) of 13 082 pregnant women had positive HBsAg screening results. Blood tests for HBV DNA and hepatological reviews were offered to 273 women who had not undergone hepatological review prior to pregnancy; the acceptance rate was 97.8%. Sixty (22.6%) pregnant women were hepatitis B carriers with high viral loads of $\geq 200\,000$ IU/mL. Among 58 women with high viral loads, 57 received antenatal counselling regarding TDF and 56 (96.6%) agreed to take the drug; 92.9% of these 56 women had commenced TDF at or before 32 weeks of gestation. **CONCLUSIONS:** This study indicated broad acceptance of HBV DNA tests by pregnant women. Triage allowed early review and commencement of antiviral medication. This service model serves as a framework for enhanced antenatal service to prevent mother-to-child-transmission in public maternity units.

F Jia, F Deng, S Tong, S Li, H Ren, W Yin (2020). "[Efficacy of oral antiviral drugs to prevent mother-to-child transmission of hepatitis B virus: a network meta-analysis.](#)" *Hepatol Int* **14**(3): 338-346.

BACKGROUND: Hepatitis B is a serious global health problem. Mother-to-child transmission (MTCT) of hepatitis B virus (HBV) is a major risk factor in the endemicity of HBV infection. Oral antiviral drugs are recommended to highly viremic mothers to decrease MTCT of HBV. The present network analysis compared the efficacy of available treatments to prevent the MTCT of HBV. **METHODS:** The electronic databases of PubMed, Embase, Web of Science, Scopus, and Wanfang data were searched for eligible studies. Pair-wise meta-analysis and Bayesian network analysis were applied to compare the efficacy of antiviral drugs. **RESULTS:** Seventy-five studies involving 12,740 pregnant females were eligible for analysis. On pair-wise analysis, lamivudine (OR 0.15, 95% CI 0.09-0.25, I-squared = 0%), telbivudine (OR 0.07, 95% CI 0.05-0.10, I-squared = 0%) and tenofovir (OR 0.07, 95% CI 0.04-0.13, I-squared = 0%) significantly decreased the MTCT rate. Results of multiple comparisons with ranking probability based on Bayesian analysis showed that tenofovir (SUCRA = 96.83%) appeared more effective than the two other drugs. **CONCLUSION:** In addition to active and passive immunoprophylaxis, lamivudine, telbivudine and tenofovir in highly viremic mothers can further decrease MTCT of HBV. Based on direct and indirect evidence, tenofovir appears to be more effective than the two other drugs in the prevention of HBV MTCT.

Z Li, X Duan, Y Hu, M Zhou, M Liu, K Kang, H Cai, W Yi, D Fu, X Gao (2020). "[Efficacy and Safety of Lamivudine or Telbivudine in Preventing Mother-to-Child Transmission of Hepatitis B Virus: A Real-World Study.](#)" *Biomed Res Int* **2020**: 1374276.

BACKGROUND: There are few large sample studies evaluating the safety and efficacy of lamivudine (LAM) or telbivudine (LdT) in preventing hepatitis B mother-to-child transmission (MTCT) in highly viremic mothers in the third trimester of pregnancy in real-world settings. The purpose of this study was to analyze a large sample size of HBV-infected mothers to better understand the safety and efficacy of LAM and LdT under the aforementioned criteria. **METHODS:** During the period of November 2008 to November 2017, we retrospectively enrolled mothers with HBV DNA $> 1 \times 10^6$ IU/mL who received LAM or LdT during the third trimester of pregnancy and compared them to untreated mothers. All mothers were divided into the three following groups: the LAM group, the LdT group, and the control group. **RESULTS:** A total of 2624 HBV-infected mothers were enrolled in the study, with 363 in the LAM group, 1283 in the LdT group, and 978 in the control group. The MTCT rates were significantly lower in the LAM or LdT group than that in the control group (0.4% or 0.3% versus 9.0%, $P < 0.001$). Infants born to untreated mothers had a significantly higher risk of HBV infection (OR = 28.6, 95% CI: 10.4-78.7, $P < 0.001$). There were no significant differences in perinatal complications between the three groups ($P > 0.05$). There were also no differences for gestational age or infants' height, weight, Apgar scores, or birth defect rates. Postpartum discontinuation of antiviral therapy did not seem to increase the risk of postpartum alanine aminotransferase (ALT) flare. **CONCLUSION:** LAM or LdT treatment initiated in the third trimester for mothers with HBV DNA $> 1 \times 10^6$ IU/mL was equally safe and effective in preventing MTCT.

X Liang, P Liu, Z He, X Chen, X Xiao (2020). "[The effect of maternal use of telbivudine on neonatal CD4\(+\)CD25\(+\) regulatory T cells for the prevention of mother-to-child transmission of hepatitis B virus.](#)" *Clin Res Hepatol Gastroenterol* **44**(2): 195-203.

Antiviral treatment could block mother-to-child transmission (MTCT) of hepatitis B virus (HBV) effectively. We examined whether maternal use of telbivudine (LdT) could decrease the proportion of CD4(+)CD25(+) regulatory T cells and explored the immunological mechanism. A total of 89 pregnant women with HBsAg positive were enrolled, where 30 pregnant women with HBeAg negative (viral load <10(6) IU/ml) and the other 59 pregnant women with HBeAg positive (viral load ≥10(6) IU/ml) were followed in the study. The women with high viral load were divided to the LdT-treated group where they were prescribed with 600mg LdT daily (29 cases) during the third trimester of pregnancy or to the non-treated group (30 cases) on a voluntary basis. Samples of neonates were taken for analyzing CD4(+)CD25(+) Tregs with flow cytometric techniques. A more significant decrease in the proportion of CD4(+)CD25(+)Tregs in neonatal peripheral blood had been observed with maternal use of telbivudine ($2.8\% \pm 1.1\%$) than those without any treatment ($7.0\% \pm 1.6\%$, $P < 0.01$). None of the infants in the LdT-treated group were HBsAg positive at 7 months of age. In addition, neonates whose mothers received telbivudine had a significant improvement in cellular immune function, as indicated by the proportion of CD8(+) T cells. For HBV carriers with high viral load, maternal use of LdT may be useful in regulating neonatal immune function involved in mother-to-child transmission of hepatitis B virus.

C Ren, L Wang, W Sun, L Ma, Z Dong, A Hao, L Zhou, F Li, W Ma (2020). "[Efficacy and safety of telbivudine treatment for the prevention of HBV perinatal transmission.](#)" *Medicine (Baltimore)* **99**(24): e20583.

To observe the efficacy of telbivudine in chronic hepatitis B (CHB) women with high viral load during pregnancy and the long-term effects on intelligence, growth, and development of the newborns. A total of 87 patients were included. Forty-two patients received telbivudine orally 600mg per day and treatment initiated from 12 weeks after gestation until the 12th postpartum week. Forty-five patients were untreated according to principle of informed consent. All infants received injection of hepatitis B immune globulin (HBIG; 200 IU) and were vaccinated with recombinant HBV vaccine. Wechsler preschool intelligence scale was used to assess mental and neuropsychological developments of these children till they were 6 years old. Data including serum HBV DNA viral load, Apgar score, and scores of Wechsler preschool intelligence scale were analyzed and compared. Levels of both serum HBV DNA and ALT in patients who received telbivudine were significantly decreased at the 12th week after delivery, compared with baseline levels ($P < .01$). No significant changes were observed in patients not receiving telbivudine ($P > .05$). Serum HBV DNA and ALT levels at the 12th week after delivery in the telbivudine group were significantly lower than those of patients without telbivudine ($P < .01$). The serum HBsAg-positive rate in neonates 7 months of age was 0%, which was significantly lower than that in control group (11.11%) ($P < .05$). No statistical differences were observed between the 2 groups regarding maternal cesarean section rate, adverse pregnancy rate, postpartum bleeding rate, neonatal body mass, Apgar score, neonatal malformation incidence, or intelligence development of newborn. Telbivudine is effective to reduce the viral load in CHB mothers with high viral load and could lower the perinatal transmission rate. Both mental and physical development in neonates with exposure to telbivudine during perinatal period were similar to those without telbivudine exposure.

M Suoh, A Tamori, Y Amano Teranishi, T Nakai, M Enomoto, Y Kawasaki, K Kioka, N Kawada (2020). "[The Administration of Tenofovir Disoproxil Fumarate for Pregnant Japanese Women with Chronic Hepatitis B.](#)" *Intern Med* **59**(2): 205-210.

The appropriate management of hepatitis B virus (HBV) infection during pregnancy has not been established in Japan. We herein report five HBV-infected pregnant Japanese women who received tenofovir disoproxil fumarate (TDF). Two of them had been born after the introduction of nationwide immunoprophylaxis and were vertically infected with HBV, highlighting the need to address mother-to-child transmission further. In both entecavir-experienced and nucleoside/nucleotide analog-naïve mothers, TDF suppressed HBV replication without serious adverse events. All five children were free from congenital disorders, growth impairment, and HBV infection. TDF showed safety and efficacy for pregnant woman with chronic hepatitis B and might have helped prevent mother-to-child transmission.

Y Wu, J Liu, Y Feng, S Fu, F Ji, L Ge, N Yao, X Luo, Y Zhao, Y Chen, Y Yang, T Chen (2020). "[Efficacy and safety of antiviral therapy for HBV in different trimesters of pregnancy: systematic review and network meta-analysis.](#)" *Hepatal Int* **14**(2): 180-189.

BACKGROUND: Several antiviral agents licenced for blocking mother-to-child transmission (MTCT) of HBV, but their relative efficacy beginning from different trimesters has scarce been evaluated. We aimed to conduct a network meta-analysis to statistically differ the efficacy and safety of each antiviral agents initiating on different timings in preventing mother-to-infant transmission of HBV. METHODS: Studies

were included from PubMed, EMBASE, Web of Science, and Cochrane databases through July 1, 2019. Eligible studies recruited randomized controlled trials and nonrandomized studies reporting about infant or/and maternal efficacy and safety outcomes and were screened by two investigators independently. Extracted data were analyzed by pair-wised and network meta-analysis, respectively. RESULTS: 3 Randomized and 32 nonrandomized studies enrolling 6738 pregnant female were included. Using network analysis, any antiviral agent interrupted HBV vertical transmission much more effectively than placebo. No agent showed significant efficacy different from others, but a strong trend toward significance was found in telbivudine and tenofovir, of which had the highest probability of being ranked the first- or second-best treatment for reducing MTCT of HBV. The treatment applied in the first and second trimester had a similar efficacy in preventing MTCT. Compared with the initiation during the third trimester, lower rate of MTCT was revealed when antiviral therapy was administrated before third trimester, (RR = 0.045, 95% CI 0.0053 to 0.20); a similar effect at delivery on suppressing maternal HBV DNA level and converting serum HBeAg were achieved if the timing of antiviral treatment started prior, but an obvious improvement of normalizing ALT flare was calculated out; no statistically differences among maternal and fetal safety outcomes were found if mothers received antiviral agents before pregnant 28 weeks. CONCLUSION: This network meta-analysis recommended the earlier use of telbivudine or tenofovir, tends to be better to prevent MTCT of HBV in pregnancy with no increased adverse maternal or fetal outcomes.

LX Xiao, YR Chen, P Huang, YY Mei, CQ Pan, CS Lin (2020). "[The safety of antiviral therapy and drug withdrawal for the prevention of mother-to-child transmission of HBV during pregnancy.](#)" *J Med Virol*.

The efficacy of prenatal antiviral therapy (AVT) for preventing the vertical transmission of hepatitis B virus (HBV) is well demonstrated. However, data are limited regarding the safety of postpartum cessation of AVT, which may induce alanine aminotransferase (ALT) elevation. We aimed to investigate the necessity of prolonging maternal AVT after delivery. Chronic hepatitis B mothers at the immune-tolerant phase with HBV DNA levels $>6 \log(10)$ IU/mL were prospectively enrolled and received AVT during the third trimester until delivery. Patients were offered to discontinue AVT either at delivery or postpartum week (PPW) 6. In addition, mothers who deferred AVT during pregnancy served as the control group. All mothers were followed until PPW 52 for clinical and virological parameters of hepatitis flares. Among 118 mothers recruited, 91 received AVT with 53 (group A) and 24 (group B) discontinue their treatment at delivery and PPW 6, respectively. Twenty-seven mothers who deferred AVT during pregnancy were followed as the control (group C). A total of 104 of 118 mothers who completed the study, 50% (52/104) had postpartum-elevated ALT levels, which were mild and moderate except 6 of 104 (5.77%) of patients had levels ≥ 5 times the upper limit of normal; 70% (36/52) of the ALT flares occurred within 12 weeks after delivery. In subgroup analyses, the frequency of ALT elevation was similar among the groups A vs B vs C (50.9% [27/53] vs 58.3% [14/24] vs 40.7% [11/27], respectively; $P = .447$), as well as the mean peak ALT level (108.4/74.1/126.7 U/L in groups A/B/C, respectively; $P = .291$). Although postpartum ALT flares were common for mothers with or without AVT during pregnancy, most cases of ALT elevation were mild to moderate. Our study observed that extending AVT to PPW 6 did not affect maternal outcomes and ATV should be discontinued at birth. Close monitoring is warranted as severe flares rarely occurred.

X Yang, X Zhong, H Liao, Y Lai (2020). "[Efficacy of antiviral therapy during the second or the third trimester for preventing mother-to-child hepatitis B virus transmission: a systematic review and meta-analysis.](#)" *Rev Inst Med Trop Sao Paulo* **62**: e13.

For pregnant women with high viral load, antiviral therapy has been administered in addition to active and passive immune prophylaxis as a crucial adjunctive therapy to interrupt mother-to-child hepatitis B virus (HBV) transmission (MTCT). However, the time of antiviral therapy onset remains controversial. A systematic review and meta-analysis was conducted to compare the efficacy of antiviral therapy during the second or the third trimester for prevention of HBV vertical transmission. We searched nine databases for observational studies and randomized controlled trials that enrolled pregnant women with positive HBsAg treated with antivirals. The outcomes of interest were maternal HBV-DNA levels prior to delivery and the rates of HBV MTCT. We included nine studies that enrolled 1,502 pregnant women. The average HBV-DNA level before treatment was approximately $8 \log_{10}$ copies/mL. Compared to the onset of antiviral intervention in the third trimester, the beginning of treatment in the second trimester distinctly reduced maternal predelivery HBV-DNA levels. However, no significant difference in HBV MTCT was found between the second and third trimester groups. Furthermore, the subgroup analysis showed that there were no significant differences between groups beginning treatment at different times (second or third trimester) with regard to HBV MTCT or other evaluated endpoints. For pregnant women with

HBV-DNA levels less than or equal to 8 log₁₀ copies/mL, the beginning of antiviral treatment can be delayed until the third trimester.

J Yin, P Liang, G Chen, F Wang, F Cui, X Liang, G Zhuang (2020). "[Tenofovir prophylaxis for preventing mother-to-child hepatitis B virus transmission in China: A cost-effectiveness analysis](#)." *Int J Infect Dis* **95**: 118-124.

OBJECTIVES: This study aimed to evaluate whether tenofovir prophylaxis for mothers with high viral loads in late pregnancy is a cost-effective way to prevent mother-to-child hepatitis B virus (HBV) transmission in China. METHODS: A decision tree Markov model was constructed for a cohort of infants born to HBV surface antigen-positive mothers in China, 2016. The expected cost and effectiveness were compared between the current active-passive immunoprophylaxis strategy and the tenofovir prophylaxis strategy, and the incremental cost-effectiveness ratio was calculated. One-way and multi-way probabilistic sensitivity analyses were performed. RESULTS: For 100,000 babies born to mothers positive for hepatitis B surface antigen, tenofovir prophylaxis strategy will prevent 2213 perinatal HBV infections and will gain 931 quality-adjusted life years when compared with the current active-passive immunoprophylaxis strategy. The incremental cost-effectiveness ratio was ¥ 59,973 (\$9087) per quality-adjusted life years gained. This result was robust over a wide range of assumptions. CONCLUSIONS: Tenofovir prophylaxis for mothers with high viral loads in late pregnancy was found to be more cost-effective than the current active-passive immunoprophylaxis alone. Embedding tenofovir prophylaxis for mothers with high virus loads into the present hepatitis B prevention strategies should be considered to further prevent mother-to-child hepatitis B transmission in China.

P Zhao, X Qian, C Su, X Yang, X Bai (2020). "[Lamivudine vs placebo or no treatment in preventing the transmission of hepatitis B virus during pregnancy: a systematic review and meta-analysis](#)." *Trans R Soc Trop Med Hyg* **114**(2): 121-130.

BACKGROUND: Hepatitis B virus (HBV) infection is a severe health problem, especially in developing countries. Almost 45% of the population lives in highly endemic areas, where the most common form of transmission is mother to child transmission (MTCT). Administration of antiviral therapy has been established. Nevertheless, its efficacy still remains controversial. METHODS: We conducted the current study to fully evaluate the effectiveness of lamivudine in preventing the MTCT of HBV based on randomized controlled trials (RCTs). Four English electronic databases and four Chinese electronic databases were searched from the inception of each database to 26 September 2017. Studies were included if they (1) were human RCT studies, (2) indicated exposure to lamivudine, (3) explicitly indicated control to placebo or no treatment, (4) indicated the participants were pregnant women infected with HBV and (5) compared the outcome of interest as the MTCT. Extracted data were tabulated and analyzed using Review Manager. RESULTS: Eleven RCTs were included and analyzed. Compared with controls (placebo or no treatment), lamivudine significantly reduced the probability of MTCT, as indicated by newborn HBsAg seropositivity (RR=0.44, 95% CI 0.26 to 0.74, I²=41%), HBeAg seropositivity (RR=0.66, 95% CI 0.36 to 1.19, I²=0%) and HBV DNA seropositivity (RR=0.29, 95% CI 0.18 to 0.46, I²=0%) within 24 h after birth. Similar results were noted pertaining to infant HBsAg seropositivity and HBV DNA seropositivity within 6-7 and 12 mo. CONCLUSIONS: Lamivudine can significantly reduce the MTCT of HBsAg and HBV DNA of neonates during the third trimester of pregnancy without severe adverse events.

M Bierhoff, EJ Smolders, J Tarning, DM Burger, R Spijker, MJ Rijken, C Angkurawaranon, R McGready, NJ White, F Nosten, M van Vugt (2019). "[Pharmacokinetics of oral tenofovir disoproxil fumarate in pregnancy and lactation: a systematic review](#)." *Antivir Ther*.

BACKGROUND: Tenofovir Disoproxil Fumarate (TDF), the oral prodrug of Tenofovir (TFV), is advocated in pregnancy to for prevention of mother to child transmission (PMCT) with failure of hepatitis B immunoglobulin and vaccination. The pharmacokinetics of TDF monotherapy for PMCT-HBV is important if deployment is to emulate the success of multiple-ARVs for PMCT-HIV in resource constrained settings. METHODS: This systematic review followed a protocol and is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (PRISMA) guidelines. We included studies that enrolled pregnant women who received oral TDF therapy as monotherapy or in combination with other antiretrovirals (ARVs): irrespective of the reason for receiving the drug (e.g. HIV, HBV or pre exposure prophylaxis); and reported pharmacokinetics. RESULTS: The AUC, C_{max} and C_{last} of TFV were decreased in the second and third trimester compared to first trimester or post-partum. In none of the manuscripts was the non-pregnant HBV threshold of C_{max} of 300 ng/ml reached, but the EC₅₀ of TFV is lower for treatment of HBV compared to HIV. The TFV concentration in breastfed infants was 0.03% of the recommended infant dose. CONCLUSIONS: Most knowledge of pharmacokinetic of TFV in pregnancy

results from studies on HIV involving multiple antiretrovirals. Increased TFV clearance occurred in the second and third trimester when optimal TFV concentrations are required to maximize suppression of HBV in the window before birth. Dose or duration adjustments will be better conceptualized with concurrent analysis of the PK of TFV monotherapy and Hepatitis B pharmacodynamics in pregnancy.

M Cai, Y Hao, J Zhong, W Yao, X Cao, G Gu, G Qin (2019). ["Telbivudine Treatment during Late Pregnancy Prevents Mother-to-Child Transmission of Hepatitis B Virus: A Retrospective Study."](#) *Can J Gastroenterol Hepatol* 2019: 9046260.

Purpose: To investigate the efficacy of telbivudine (LdT) in blocking mother-to-child transmission (MTCT) of hepatitis B virus (HBV) during late pregnancy. Methods: A total of 651 pregnant women aged 18-40 in Nantong Third People's Hospital and Hospital affiliated to Nantong University with positive hepatitis B surface antigen (HBsAg) and HBV DNA were enrolled between January 2011 and December 2015. Patients with HBV DNA $\geq 10(6)$ copies/mL ($n=251$) received LdT during late pregnancy according to the patients' will, while 136 high viral patients with HBV DNA $\geq 10(6)$ copies/mL who did not take LdT therapy and 268 low viral patients with HBV DNA $< 10(6)$ copies/mL served as the controls. Results: At 7 months and 1 year postpartum, the basal HBV DNA serum level of treated patients declined significantly ($P < 0.001$), while no obvious decline was observed in the untreated high viraemic controls ($P < 0.05$) and untreated low viraemic controls ($P < 0.05$). Only 1 infant (0.4%) in LdT group was HBsAg positive at 7 months, while 14 (5.2%) were in the untreated low viraemic controls ($P < 0.001$) and 15 (11.0%) were in untreated high viraemic controls ($P < 0.001$). Conclusion: For pregnant women with HBV DNA $\geq 10(6)$ copies/mL, the use of LdT during late pregnancy could effectively reduce the MTCT rate of HBV.

KC Chang, MH Chang, CN Lee, CH Chang, JF Wu, YH Ni, WH Wen, MK Shyu, MW Lai, SM Chen, JJ Hu, HH Lin, JJ Hsu, SC Mu, YC Lin, CJ Liu, DS Chen, LH Lin, HL Chen Taiwan Study Group for the Prevention of Mother-to-Infant Transmission of HBV (PreMit Study) (2019). ["Decreased neonatal hepatitis B virus \(HBV\) viremia by maternal tenofovir treatment predicts reduced chronic HBV infection in children born to highly viremic mothers."](#) *Aliment Pharmacol Ther* 50(3): 306-316.

BACKGROUND: Maternal anti-viral treatment prevents mother-to-infant transmission of hepatitis B virus (HBV), but the role of neonatal viremia on subsequent HBV infection is not clear. AIMS: To investigate the effect of maternal anti-viral treatment on neonatal serum HBV DNA and hepatitis B surface antigen (HBsAg) in infants born to highly viremic mothers and the roles of neonatal markers in predicting chronic HBV infection in children. METHODS: Serum HBV DNA and HBsAg were tested in children. Of the 201 pregnant mothers, 110 received tenofovir during the third trimester. Chronic infection in children was defined by HBsAg seropositivity at 6 or 12 months lasting more than 6 months. RESULTS: The maternal HBV viral loads from baseline to delivery were 8.25 ± 0.48 to 4.29 ± 0.98 log(10) IU/mL; and 8.29 ± 0.49 to 8.12 ± 0.68 log(10) IU/mL in the tenofovir and control group respectively. Of the 208 children, those in the tenofovir group had a lower rate of neonatal HBV DNA seropositivity at birth (5.22% vs 30.11%, $P < 0.0001$) and HBsAg seropositivity at 6 months (1.74% vs 11.83%, $P = 0.003$) and 12 months (1.74% vs 10.75%, $P = 0.007$). In a first multivariate analysis, maternal HBV DNA level at delivery (odds ratio = 1.70, $P = 0.0172$) and neonatal HBsAg positivity (odds ratio = 19.37, $P < 0.0001$) were significantly associated with children's chronic HBV infection. In a second model, neonatal HBV DNA positivity was a strong independent influence variable (odds ratio = 61.89, $P = 0.0002$). CONCLUSIONS: Maternal tenofovir therapy decreased maternal viral load and neonatal viremia. Positive neonatal HBV DNA was highly correlated with chronic HBV infection in children. Clinical Trial Identifier: NCT01312012.

X Gao, X Duan, H Cai, Y Hu, M Liu, K Kang, M Zhou, D Fu, W Yi (2019). ["The safety and efficacy of tenofovir disoproxil fumarate used throughout pregnancy for mothers with chronic hepatitis B."](#) *Eur J Gastroenterol Hepatol*.

BACKGROUND: Antiviral therapy throughout pregnancy in women with chronic hepatitis B (CHB) during pregnancy has been suggested; however, the data of tenofovir disoproxil fumarate (TDF) are limited. The aim of this study was to evaluate the safety and efficiency in women with CHB. METHODS: It was a single-center, retrospectively study. Eighty-one women received TDF 300 mg/day before pregnancy. Sixty-three women did not receive antiviral treatment. All infants in both groups received immunoprophylaxis. Mothers and infants were followed at least postpartum 7 months. The primary endpoint was the safety of mothers and infants. The secondary endpoints were mother-to-child transmission (MTCT) rate and hepatitis B virus (HBV) DNA suppression. RESULTS: TDF was well tolerated in the mothers. The rates of neonatal congenital abnormalities were similar between the two groups (3.7% or 3/81 versus 3.3% or 2/63, $P = 1.000$). There were also no significant differences in infant length and weight, Apgar score (1 minute), rate of low birth weight, gestational age, or rate of cesarean section

between the two groups. TDF significantly reduced the viral load (3.4 ± 0.5 log IU/mL versus 6.3 ± 1.5 log IU/mL, $P < 0.001$) and the ALT levels (19.9 ± 10.2 versus 46.8 ± 44.8 U/L, $P < 0.001$) before delivery. At 7-month postpartum, the MTCT rate was 0% in the TDF-treated group when compared with 6.3% (4/63) in the untreated group ($P = 0.035$). CONCLUSION: TDF used throughout pregnancy can safely reduce the rate of MTCT.

LF Han, JM Zheng, LQ Zheng, HB Gao, LX Chen, QL Xu, YH Chai, X Zhang, C Pan, LF Yao (2019). "[Telbivudine can safely reduce mother-to-child transmission in chronic hepatitis B women after 12 weeks of gestation.](#)" *BMC Infect Dis* **19**(1): 614.

BACKGROUND: To evaluate the efficacy and safety of telbivudine in chronic hepatitis B women during the second and third trimesters of pregnancy. METHODS: The week 12-34 of pregnant women were screened in this prospective non-intervention study, with HBV DNA $> 10(6)$ IU/mL and alanine aminotransferase > 50 IU/L. The patients were received telbivudine treatment as a treatment group or without antiviral treatment as a control group. All infants were received recombinant hepatitis B vaccine 10 µg within 12 h of birth, at week 4 and week 24, immunoglobulin G within 12 h of birth and were detected HBV markers at the range from 7 to 12 months after delivery. RESULTS: A total of 241 patients were finally enrolled, 139 patients in telbivudine group and 102 patients in control group. HBsAg negative rate of infants was 99.3% (135/136) in telbivudine group and was 91.9% (91/99) in control group after 7 months ($P = 0.005$), respectively. The incidence of undetectable HBV DNA levels (47.5%) was significantly lower in telbivudine-treated mothers than that in the controls (0%), and 75.5% patients alanine aminotransferase returned to normal in telbivudine group, and 51% in control group at delivery ($P < 0.001$), respectively. CONCLUSIONS: Telbivudine can safely reduce mother-to-child transmission in chronic hepatitis B women after 12 weeks of gestation.

G Jourdain, N Ngo-Giang-Huong, W Khamduang (2019). "[Current progress in the prevention of mother-to-child transmission of hepatitis B and resulting clinical and programmatic implications.](#)" *Infect Drug Resist* **12**: 977-987.

There is currently no cure for hepatitis B chronic infections. Because new hepatitis B infections result mainly from perinatal transmission, preventing mother-to-child transmission is essential to reach by 2030 the goal of hepatitis B elimination set by the World Health Organization. The universal administration of hepatitis B vaccine to all infants, regardless of maternal status, starting with the birth dose, is the cornerstone of the strategy for elimination. Additional interventions, such as hepatitis B immune globulin administered to newborns and antiviral prophylaxis administered to hepatitis B infected pregnant women, may contribute to reaching the goal earlier. Hepatitis B immune globulin may remain out of reach of many pregnant women in low- and middle-income countries due to cost and logistic issues, but antivirals are cheap and do not require a cold chain for distribution. However, it has been observed that some viruses harbor mutations associated with escape from vaccine-elicited antibodies following immunization or administration of hepatitis B immune globulin. Also, resistance associated mutations have been described for several drugs used for treatment of hepatitis B infected patients as well as for the prevention of mother-to-child transmission. Whether these mutations have the potential to compromise the prevention of mother-to-child transmission or future treatment of the mother is a question of importance. We propose a review of important recent studies assessing tenofovir disoproxil fumarate for the prevention of mother-to-child transmission, and provides detailed information on the mutations possibly relevant in this setting.

J Li, XQ Dong, Z Wu, AL Ma, SB Xie, XQ Zhang, ZQ Zhang, DZ Zhang, WF Zhao, G Zhang, J Cheng, Q Xie, J Li, ZQ Zou, YX Liu, GQ Wang, H Zhao, Hepatitis B Related Fibrosis Assessment Research Group (2019). "[Unsatisfying antiviral therapeutic effect in patients with mother-to-child transmitted chronic hepatitis B virus infection: a prospective multi-center clinical study.](#)" *Chin Med J (Engl)* **132**(22): 2647-2656.

BACKGROUND: Few data are available regarding the progression of liver disease and therapeutic efficacy in chronic hepatitis B virus (HBV) carriers infected by mother-to-child transmission (MTCT). This study aimed to investigate these two aspects by comparing the adult chronic HBV carriers in MTCT group with those in horizontal transmission group. METHODS: The 683 adult chronic HBV patients qualified for liver biopsy including 191 with MTCT and 492 with horizontal transmission entered the multi-center prospective study from October 2013 to May 2016. Biopsy results from 217 patients at baseline and 78 weeks post antiviral therapy were collected. RESULTS: Patients infected by MTCT were more likely to have e antigen positive (68.6% vs. 58.2%, $\chi^2 = -2.491$, $P = 0.012$) than those with horizontal transmission. However, in patients with MTCT, levels of alkaline phosphatase (ALP) ($P = 0.031$), Fibroscan ($P = 0.013$), N-terminal propeptide of Type III procollagen (PIIINP) ($P = 0.014$), and Laminin (LN) ($P = 0.006$) were

high, in contrast to the patients with horizontal transmission for whom the levels of albumin (ALB) ($P = 0.041$), matrix metalloproteinase-3 (MMP-3) ($P = 0.001$) were high. The 47.2% of patients with MTCT and 36.8% of those with horizontal transmission had significant liver fibrosis ($P = 0.013$). Following antiviral therapy for 78 weeks, 21.2% and 38.0% patients with MTCT and horizontal transmission acquired hepatitis B e antigen (HBeAg) clearance, respectively ($P = 0.043$), and the virological response rates were 54.7% and 74.1% in the MTCT and horizontal groups, respectively ($P = 0.005$). MTCT was a risk factor for HBeAg clearance and virological response. CONCLUSION: Adult patients with MTCT were more prone to severe liver diseases, and the therapeutic efficacy was relatively poor, which underlined the importance of earlier, long-term treatment and interrupting perinatal transmission. TRIAL REGISTRATION: NCT01962155; <https://clinicaltrials.gov>.

X Liang, P Liu, Z He, X Chen, X Xiao (2019). "[The effect of maternal use of telbivudine on neonatal CD4\(+\)CD25\(+\) regulatory T cells for the prevention of mother-to-child transmission of hepatitis B virus.](#)" *Clin Res Hepatol Gastroenterol*.

Antiviral treatment could block mother-to-child transmission (MTCT) of hepatitis B virus (HBV) effectively. We examined whether maternal use of telbivudine (LdT) could decrease the proportion of CD4(+)CD25(+) regulatory T cells and explored the immunological mechanism. A total of 89 pregnant women with HBsAg positive were enrolled, where 30 pregnant women with HBeAg negative (viral load $< 10(6)$ IU/ml) and the other 59 pregnant women with HBeAg positive (viral load $\geq 10(6)$ IU/ml) were followed in the study. The women with high viral load were divided to the LdT-treated group where they were prescribed with 600mg LdT daily (29 cases) during the third trimester of pregnancy or to the non-treated group (30 cases) on a voluntary basis. Samples of neonates were taken for analyzing CD4(+)CD25(+) Tregs with flow cytometric techniques. A more significant decrease in the proportion of CD4(+)CD25(+)Tregs in neonatal peripheral blood had been observed with maternal use of telbivudine ($2.8\% \pm 1.1\%$) than those without any treatment ($7.0\% \pm 1.6\%$, $P < 0.01$). None of the infants in the LdT-treated group were HBsAg positive at 7 months of age. In addition, neonates whose mothers received telbivudine had a significant improvement in cellular immune function, as indicated by the proportion of CD8(+) T cells. For HBV carriers with high viral load, maternal use of LdT may be useful in regulating neonatal immune function involved in mother-to-child transmission of hepatitis B virus.

J Liu, J Wang, T Yan, D Du, C Qi, F Cao, N Yao, Y Yang, Y He, Z Tian, D Ren, L Zhu, T Chen, Y Zhao (2019). "[Efficacy and safety of telbivudine and tenofovir disoproxil fumarate in preventing hepatitis B vertical transmission: A real-life practice.](#)" *J Viral Hepat* **26**(10): 1170-1177.

Mother-to-child transmission (MTCT) is a major obstacle in the elimination of hepatitis B virus (HBV) infection. Telbivudine (LdT) and tenofovir disoproxil fumarate (TDF) are the two most common antiviral medicines for preventing MTCT. However, the efficacy and safety of LdT and TDF in preventing HBV vertical transmission during the second to third trimester have not been compared rigorously. Therefore, we carried out a prospective multicentre cohort study of chronic hepatitis B in mothers with HBV DNA $> 10(6)$ IU/mL, receiving LdT or TDF during the second to third trimester. Among the 893 mothers enrolled, 857 (LdT/TDF/untreated group (NTx) = 396/325/136) completed consecutive follow-up with 854 infants (LdT/TDF/NTx = 395/323/136). LdT and TDF treatment resulted in a similar decrease of HBV DNA in mothers at delivery. Multivariate analysis indicated that only HBsAg titre at the baseline correlated with viral DNA decrease ($P = 0.015$). With intention-to-treat analysis, MTCT rates in the LdT, TDF and NTx group were 4.41%, 2.42% and 22.08%, respectively. An increasing vertical transmission rate was found to be closely associated with higher HBsAg titre, 5.32% and 17.65% infection rate was estimated in infants born to mothers with HBsAg > 4 and $> 5 \log_{10}$ IU/mL, respectively. No serious side effects were reported in either mothers or infants. LdT and TDF treatments were well tolerated and showed comparable efficacy in reducing MTCT. Higher risk of MTCT was shown in pregnant women with HBsAg $> 4 \log_{10}$ IU/mL.

J Mokaya, EAO Burn, CR Tamandjou, D Goedhals, EJ Barnes, M Andersson, R Pinedo-Villanueva, PC Matthews (2019). "[Modelling cost-effectiveness of tenofovir for prevention of mother to child transmission of hepatitis B virus \(HBV\) infection in South Africa.](#)" *BMC Public Health* **19**(1): 829.

BACKGROUND: International sustainable development goals for the elimination of viral hepatitis as a public health problem by 2030 highlight the need to optimize strategies for prevention, diagnosis and treatment of hepatitis B virus (HBV) infection. An important priority for Africa is to have affordable, accessible and sustainable prevention of mother to child transmission (PMTCT) programmes, delivering screening and treatment for antenatal women and implementing timely administration of HBV vaccine for their babies. METHODS: We developed a decision-analytic model simulating 10,000 singleton

pregnancies to assess the cost-effectiveness of three possible strategies for deployment of tenofovir in pregnancy, in combination with routine infant vaccination: S1: no screening nor antiviral therapy; S2: screening and antiviral prophylaxis for all women who test HBsAg-positive; S3: screening for HBsAg, followed by HBeAg testing and antiviral prophylaxis for women who are HBsAg-positive and HBeAg-positive. Our outcome was cost per infant HBV infection avoided and the analysis followed a healthcare perspective. RESULTS: Based on 10,000 pregnancies, S1 predicts 45 infants would be HBV-infected at six months of age, compared to 21 and 28 infants in S2 and S3, respectively. Relative to S1, S2 had an incremental cost of \$3940 per infection avoided. S3 led to more infections and higher costs. CONCLUSION: Given the long-term health burden for individuals and economic burden for society associated with chronic HBV infection, screening pregnant women and providing tenofovir for all who test HBsAg+ may be a cost-effective strategy for South Africa and other low/middle income settings.

S Sali, M Darvishi, M GhasemiAdl, M Akhlaghdoust, A Mirzazadeh, SE Behjati, H Sheikh-Zeinolabedini, S Shokouhi, S Tavakolpour (2019). "[Comparing the Efficacy and Safety of Treating Chronic Hepatitis B Infection during Pregnancy with Lamivudine, Telbivudine, and Tenofovir: A Meta-analysis.](#)" *J Clin Transl Hepatol* **7**(3): 197-212.

Background and Aims: The perinatal transmission of hepatitis B virus (HBV) remains an important global health problem. Here, a systematic review and meta-analysis were conducted to evaluate the evidence regarding the efficacy and maternal/fetal safety of treating pregnant women with lamivudine, telbivudine (LdT), and tenofovir (TDF). Methods: A PubMed and Scopus search resulted in 1,076 records, which were reduced to 36, containing 7,717 pregnant women with chronic HBV infection and 7467 infants meeting the inclusion criteria. The latest search was in August 2019. Results: Treatment with LdT, but not lamivudine and TDF, could significantly reduce the hepatitis B virus surface antigen-positive rate (odds ratio (OR) = 0.37) in infants; it also led to higher rates of hepatitis B e antigen loss (OR = 12.14), hepatitis B e antigen seroconversion (OR = 8.93), and alanine aminotransferase normalization in mothers (OR = 1.49). Each of these treatments was able to significantly reduce HBV DNA positivity at birth (total OR = 0.19) and mother-to-child-transmission of HBV (total OR = 0.15), and to cause higher rates of HBV DNA suppression in mothers (total OR = 25.53). However, nucleos(t)ide analogues might also be involved in creatine kinase elevation (total OR = 7.48). In contrast, no significant association was found between nucleos(t)ide analogue therapy and preterm/premature births, congenital malformation, low birth weight, and abortion or fetal/infant death. The results suggested LdT's high capability of preventing mother-to-child-transmission. However, TDF failed to show significant associations to a reduced risk of mother-to-child-transmission, probably due to the low number of patients included. Conclusions: Although using either lamivudine, LdT, or TDF could lead to more favorable maternal/fetal outcomes, LdT seemed to show more potential in resolving certain infant- and maternal-related outcomes. More studies on the safety profile of such treatments are required.

N Salvadori, B Fan, W Teeyasoontranon, N Ngo-Giang-Huong, S Phanomcheong, A Luvira, A Puangsombat, A Suwannarat, U Srirompotong, C Putiyanun, TR Cressey, L Decker, W Khamduang, L Harrison, C Tierney, JA Shepherd, AP Kourtis, M Bulterys, GK Siberry, G Jourdain (2019). "[Maternal and Infant Bone Mineral Density 1 Year After Delivery in a Randomized, Controlled Trial of Maternal Tenofovir Disoproxil Fumarate to Prevent Mother-to-child Transmission of Hepatitis B Virus.](#)" *Clin Infect Dis* **69**(1): 144-146.

In a randomized, double-blind, placebo-controlled trial of tenofovir disoproxil fumarate (TDF) use from 28 weeks gestational age to 2 months postpartum to prevent mother-to-child transmission of hepatitis B virus, there was no significant effect of maternal TDF use on maternal or infant bone mineral density 1 year after delivery/birth. Clinical Trials Registration. NCT01745822.

J Song, F Yang, S Wang, S Tikande, Y Deng, W Tang, G Cao (2019). "[Efficacy and safety of antiviral treatment on blocking the mother-to-child transmission of hepatitis B virus: A meta-analysis.](#)" *J Viral Hepat* **26**(3): 397-406.

Nucleo(t)side analogues (NAs) have been administered as adjunctive therapy to interrupt the mother-to-child transmission (MTCT) of hepatitis B virus (HBV). The efficacy and safety of this method remain controversial. A meta-analysis was conducted to evaluate the efficacy and safety of NAs treatment during pregnancy. The differences among different agents and initiation trimesters were analysed. A total of 9228 mother-infant pairs in 59 studies (32 RCTs and 27 non-RCTs) were included in this meta-analysis. NAs significantly reduced the risk of MTCT, as indicated by seropositivity of hepatitis B surface antigen (HBsAg) (risk ratio (RR) = 0.51, 95% confidence interval (CI) 0.45-0.57) and HBV DNA in newborns (RR = 0.22, 95% CI 0.18-0.26). No differences in the efficacy of interrupting HBV MTCT were evident among lamivudine, telbivudine and tenofovir disoproxil fumarate. NA was more effective when administered from the second than from the third trimester as indicated by HBV DNA (RR: the second vs the third 0.08

vs 0.22, $P = 0.010$), but this effect was not evident as indicated by HBsAg (RR: the second vs the third 0.46 vs 0.53, $P = 0.596$). Antiviral treatment initiated from the second trimester did not confer a higher risk of safety problems in the newborns compared with treatment from the third trimester, as indicated by weight ($P = 0.064$), length ($P = 0.491$) and malformation rate ($P = 0.635$) of newborns. CONCLUSIONS: Lamivudine, telbivudine and tenofovir disoproxil fumarate are equally effective in blocking HBV MTCT. Antiviral treatment can be applied from the second trimester, without obvious safety concerns.

Sylvester-Armstrong, K. R. and P. Duff (2019). "[Evidence for Use of Tenofovir in Pregnancy to Prevent Perinatal Transmission of Hepatitis B Infection.](#)" *Clin Obstet Gynecol* **62**(4): 835-845.

Perinatal transmission of hepatitis B virus continues to be a serious global public health concern. Transmission failures are related to high maternal viremia. Several antiviral therapies reduce maternal viremia around the time of delivery and decrease maternal-to-child-transmission. This chapter is a review of current studies that, ultimately, have provided strong evidence for the efficacy and safety of 3 antiviral drugs in pregnancy-lamivudine, telbivudine and tenofovir. The latter drug is the particular focus of this chapter which will show that tenofovir is the preferred antiviral therapy in pregnant women because of its potency, safety profile, and low risk of resistance.

M Wang, Q Bian, Y Zhu, Q Pang, L Chang, R Li, BC Tiongson, H Zhang, CQ Pan (2019). "[Real-world study of tenofovir disoproxil fumarate to prevent hepatitis B transmission in mothers with high viral load.](#)" *Aliment Pharmacol Ther* **49**(2): 211-217.

BACKGROUND: Data on tenofovir disoproxil fumarate (TDF) therapy for preventing vertical transmission of hepatitis B virus (HBV) in the real-world setting are limited. AIM: To investigate TDF for preventing vertical transmission of HBV in real-world practice. METHODS: Hepatitis B e-antigen (HBeAg)-positive mothers with HBV-DNA $>6 \log_{10}$ IU/mL to receive TDF between gestational weeks 24-33 and delivery were prospectively enrolled and followed until post-partum week 28. All infants received immunoprophylaxis. Primary endpoints were safety of TDF use and mother-to-child transmission rates. Secondary outcomes were maternal HBV-DNA level suppression ($<200\ 000$ IU/mL) at delivery and HBeAg and hepatitis B surface antigen (HBsAg) serologic changes during the study. RESULTS: Among 147 mothers enrolled, 143 started TDF and 143/144 infants completed the study. At delivery, 93.7% (134/143) of the mothers achieved HBV-DNA $<200\ 000$ IU/L. On-treatment, alanine aminotransferase (ALT) flares were observed in 8.4% (12/143) of mothers. After TDF cessation, ALT increased in 7.7% (11/143) of the mothers and 2.8% (4/143) achieved HBeAg negativity, but none had HBsAg loss. At birth, HBsAg was detected in 13.9% (20/144) of newborns and none at post-partum week 28. Vertical transmission rates among infants were 0.7% (1/144, intention-to-treat) and 0% (per-protocol). No infants had birth defects. No serious adverse effects were reported in either mothers or infants. Breastfeeding did not increase the HBV infection rate among infants although mothers had viral rebound after TDF cessation. CONCLUSIONS: TDF for highly viraemic mothers was well tolerated and reduced vertical transmission of HBV in a real-world setting. There were no safety concerns during the postpartum 28-week follow-up. Registry number: Chinese Clinical Trial Registration No. ChiCTR-OIC-17010869.

J Xu, LL Tao, LX Ma (2019). "[Efficacy and safety of telbivudine to prevent mother-to-child transmission of hepatitis B virus in middle- and late-stage pregnancy with high viral loads.](#)" *J Med Virol* **91**(12): 2153-2157.

OBJECTIVE: To observe the efficacy and safety of telbivudine on mother-infant blockade in pregnant women with hepatitis B virus (HBV) DNA. METHODS: A total of 141 pregnant women between 24 and 28 weeks of gestation and chronic HBV carriers with HBV DNA $\geq 10^6$ copies/mL were enrolled, 105 in the treatment group and 36 in the control group. The treatment group was given telbivudine 600 mg/d oral, and the control group did not use antiviral drugs. Hepatitis B immunoglobulin 200 IU intramuscular injection and hepatitis B vaccine (HBVax) 10 mug subcutaneous injection were given to the infants in both groups within 12 hours after birth, and 10 mug of HBVax was subcutaneously injected when the infants were 1-month and 6-month old. Safety endpoints including HBV DNA quantification, liver function, CK were observed before treatment, 4 weeks after treatment, before delivery, and 24 weeks after delivery. RESULTS: There was no difference in HBV DNA levels between the two groups before treatment and 6 months after delivery ($P > .05$). The HBV DNA level in the treatment group was significantly lower than that in the control group before delivery ($P < .05$). Between the two groups, the HBV positive rate was statistically different between the two groups ($P < .05$), and the difference of serum HBsAg of infants had statistical significance ($P < .05$), but the safety of the telbivudine group was not significantly different from that of the control group ($P > .05$). CONCLUSION: The application of telbivudine antiviral therapy in the middle and late stage of pregnancy of HBV high-load pregnant

women can significantly reduce the HBV DNA level before delivery, reduce the mother-to-child transmission rate of HBV, and have excellent security.

M Zhao, H Zou, Y Chen, S Zheng, Z Duan (2019). "[Efficacy of antepartum administration of hepatitis B immunoglobulin in preventing mother-to-child transmission of hepatitis B virus.](#)" *J Viral Hepat* **26**(9): 1059-1065.

The aim of this study was to investigate the efficacy of antepartum administration of three doses of hepatitis B immunoglobulin (HBIG) in interrupting mother-to-child transmission (MTCT) of hepatitis B virus (HBV). In this trial, a total of 728 HBeAg-positive pregnant women with chronic HBV infection who had an HBV DNA level higher than 6log10 copies/mL were enrolled. They were divided into three groups based on individual preference. Subjects in group A and group B received 200 IU (unit) HBIG and 400 IU (unit) HBIG intramuscularly once a month at the third, second and first month before delivery, respectively. Subjects in the control group (C) received no special treatment. All the infants received passive-active immunoprophylaxis. The HBsAg-positive rate of all infants at 7-12 months of age was 5.1% (37/728). Specifically, the HBsAg-positive rate of infants was comparable in all three groups (5.3% vs 5.1% vs 5%, $P = 0.988$). No significant difference was found in anti-HBs levels between the infants aged 7-12 months in the three groups ($P = 0.469$). HBV DNA levels of the umbilical cord blood in the HBV-infected group were higher than those in the uninfected group (5.2 vs 3.4log10 copies/mL, $P < 0.001$), and these with family history of HBV infection were also higher (45.9% vs 28.5%, $P = 0.034$). To conclude, administration of passive-active immunoprophylaxis to infants contributed to effective prevention of the MTCT of HBV; extra antepartum administration of HBIG during pregnancy could not decrease the rate of MTCT or increase the anti-HBs levels of infants born to HBsAg-positive mothers with HBV DNA higher than 6log10 copies/mL.

P Zhao, X Qian, C Su, X Yang, X Bai (2019). "[Lamivudine vs placebo or no treatment in preventing the transmission of hepatitis B virus during pregnancy: a systematic review and meta-analysis.](#)" *Trans R Soc Trop Med Hyg*.

BACKGROUND: Hepatitis B virus (HBV) infection is a severe health problem, especially in developing countries. Almost 45% of the population lives in highly endemic areas, where the most common form of transmission is mother to child transmission (MTCT). Administration of antiviral therapy has been established. Nevertheless, its efficacy still remains controversial. **METHODS:** We conducted the current study to fully evaluate the effectiveness of lamivudine in preventing the MTCT of HBV based on randomized controlled trials (RCTs). Four English electronic databases and four Chinese electronic databases were searched from the inception of each database to 26 September 2017. Studies were included if they (1) were human RCT studies, (2) indicated exposure to lamivudine, (3) explicitly indicated control to placebo or no treatment, (4) indicated the participants were pregnant women infected with HBV and (5) compared the outcome of interest as the MTCT. Extracted data were tabulated and analyzed using Review Manager. **RESULTS:** Eleven RCTs were included and analyzed. Compared with controls (placebo or no treatment), lamivudine significantly reduced the probability of MTCT, as indicated by newborn HBsAg seropositivity (RR=0.44, 95% CI 0.26 to 0.74, $I^2=41\%$), HBeAg seropositivity (RR=0.66, 95% CI 0.36 to 1.19, $I^2=0\%$) and HBV DNA seropositivity (RR=0.29, 95% CI 0.18 to 0.46, $I^2=0\%$) within 24 h after birth. Similar results were noted pertaining to infant HBsAg seropositivity and HBV DNA seropositivity within 6-7 and 12 mo. **CONCLUSIONS:** Lamivudine can significantly reduce the MTCT of HBsAg and HBV DNA of neonates during the third trimester of pregnancy without severe adverse events.

JR Chandran, SV Raj (2018). "[Efficacy of Antiviral Therapy in HBsAg-Positive Pregnant Women to Reduce Mother-to-Infant Transmission of Hepatitis B Virus.](#)" *J Obstet Gynaecol India* **68**(5): 355-359.

Background and Objectives: Hepatitis B is a major health concern in Asia. Chronic hepatitis B virus (HBV) infection may cause hepatic cirrhosis and liver cancer. HBV is transmitted horizontally through blood and blood products and vertically from mother to infant. Perinatal infection is the main route of transmission in regions with high prevalence of hepatitis B surface antigen (HbsAg) carriage, and perinatal transmission leads to high rates of chronic infection. Therefore, it is important to prevent mother-to-child transmission (MTCT) of HBV1. The present study aims at comparing the use of antivirals (lamivudine vs tenofovir) in reducing MTCT. **Materials and Methods:** A total of 60 HbsAg-positive pregnant women were enrolled in the prospective study to test the efficacy of antiviral (lamivudine vs tenofovir-category B drug) to reduce mother-to-child transmission and monitor hepatitis B viral status in infant. HbsAg-positive pregnant women aged 18-43 years at gestational age between 28 and 32 weeks were followed up. They were tested for HBsAg, liver function test and HBeAg. In whom HbeAg was positive, HBV viral load was tested. Sixty patients with high viral load (>6 log copies/ml) were recruited in the study. Alternate

patients were randomized into two groups. Group A comprised 31 subjects treated with lamivudine 100 mg daily starting from 28 to 32 weeks of gestation (third trimester) and continued to 1 month after delivery. Group B comprised 29 pregnant women who were treated with tenofovir 300 mg daily from 28 to 32 weeks of gestation and continued to 1 month post-partum. The newborn babies were given HBIG within 24 h after delivery and HBV vaccines at 0, 1 and 6 months. HBsAg infectivity was tested in the infant at 1 year after birth. Results: Antivirals, lamivudine/tenofovir treatment in HBV carrier mothers from 28 weeks of gestation along with active and passive immunization of new born may interrupt MTCT of HBV efficiently. Tenofovir, category B drug, is more effective in preventing transmission of HBV infection to infants ($p = 0.004$).

F Cui, J Woodring, P Chan, F Xu (2018). "[Considerations of antiviral treatment to interrupt mother-to-child transmission of hepatitis B virus in China.](#)" *Int J Epidemiol* **47**(5): 1529-1537.

Background: Treating high-risk women with antivirals in their third trimester is a promising intervention to further reduce perinatal transmission in neonates born to hepatitis B surface antigen positive [HBsAg(+)] mothers. Methods: We estimated the number of perinatal infections based on coverage and effectiveness of hepatitis B immunization. We compared cost-effectiveness of different approaches to identify high-risk women for antiviral treatment, by region and urban/rural residence. Results: Of the 16.59 million live births in 2015, 1.04 million infants (6.3%) were born to HBsAg(+) mothers and 268 201 infants (1.6%) to HBsAg(+) and HBeAg(+) dual-positive mothers. Despite immunoprophylaxis, 51 478 perinatal hepatitis B virus (HBV) transmissions were estimated to have occurred from HBsAg and HBeAg dual-positive mothers in 2015. Using HBeAg or HBV viral load testing to identify high-risk pregnant women and to treat them with Tenofovir, the incremental cost ranged from US\$68.2 million to US\$90.3 million. Assuming HBV viral load testing is available and used to guide treatment and all women with HBV viral loads > 200 000 IU/ml are treated, 25 912 infections would be averted at a projected cost of US\$3500 per infection averted. Conclusions: Identifying high-risk pregnant women and providing them with antiviral treatment is feasible and cost-effective to interrupt perinatal HBV transmissions. Policy options should be urgently explored in order for China to reach the HBV elimination goal of 0.1% prevalence among children by 2030.

T He, Y Bai, H Cai, X Ou, M Liu, W Yi, J Jia (2018) "[Safety and efficacy of lamivudine or telbivudine started in early pregnancy for mothers with active chronic hepatitis B.](#)" *Hepatol Int* **12**(2): 118-125.

BACKGROUND: Few data exist regarding use of nucleos(t)ide analogs started in early pregnancy for mothers with active chronic hepatitis B (CHB). We assessed the safety and efficacy of lamivudine/telbivudine initiated in the first trimester versus no treatment in mothers with active CHB. METHODS: We retrospectively enrolled 94 mothers newly diagnosed with active CHB in the first trimester of pregnancy. Patients with or without antiviral therapy were followed until postpartum week 28. All newborns received immunoprophylaxis. The primary endpoint was the safety of mothers and infants. The secondary endpoints were hepatitis B virus (HBV) DNA suppression and mother-to-child transmission (MTCT) rate. RESULTS: Fifty-nine of the 94 mothers initiated lamivudine/telbivudine (27/32) in the first trimester of pregnancy; 35 received no treatment. At delivery, the viral load reduction was similar between lamivudine and telbivudine. Early initiation of lamivudine/telbivudine significantly increased the proportion of mothers achieving HBV DNA <10(6) copies/ml compared with those with no treatment (100 versus 42.42 %, $p < 0.001$). At postpartum week 28, the MTCT rate was significant lower in the treated group than in the control group (0/61 or 0 versus 4/34 or 11.76 %, $p = 0.028$). Lamivudine and telbivudine were well tolerated in the mothers except mild creatine kinase (CK) elevation. There existed no differences in gestational age, infant length and weight, Apgar score, adverse events, or birth defect rates between infants from treated and untreated mothers. CONCLUSIONS: Treatment with lamivudine or telbivudine for active CHB in early pregnancy appears to be safe and effective for controlling maternal disease as well as interrupting MTCT.

KI Seo, SH Bae, PS Sung, CH Park, HL Lee, HY Kim, HJ Kim, BH Jang, JW Jang, SK Yoon, JY Choi, IY Park, J Lee, HS Lee, SJ Kim, JH Kwon, UI Chang, CW Kim, SH Jo, Y Lee, F Tekle, JH Kim (2018). "[Effect of antiviral therapy in reducing perinatal transmission of hepatitis B virus and maternal outcomes after discontinuing them.](#)" *Clin Mol Hepatol* **24**(4): 374-383.

BACKGROUND/AIMS: There have been numerous efforts to reduce mother-to-child transmission (MTCT) of hepatitis B virus (HBV) with antiviral agents during pregnancy. However, there are limited data regarding the outcomes of pregnant women after delivery. This study was performed to evaluate the efficacy of antiviral agents in preventing MTCT of HBV and maternal long-term outcomes. METHODS:

The HBV-infected pregnant women treated with antiviral agents to prevent MTCT were retrospectively reviewed. Forty-one pregnant women who received telbivudine or tenofovir during late pregnancy (28-34 week) were analyzed. Hepatitis B virus surface antibody (HBsAb) positivity was tested in 43 infants after 7 months of birth. Eleven mothers were followed > 1 year after delivery. RESULTS: The mean HBV DNA titer before antiviral therapy was 8.67 (6.60-9.49) log copies/mL, and the median age at delivery was 32 years (range, 22-40). Eleven patients were treated with tenofovir and 30 with telbivudine. The median duration was 57 days (range, 23-100), and the median HBV DNA titer at birth was 5.06 log copies/mL (range, 2.06-6.50). Antiviral treatments were associated with significant HBV DNA reduction ($P < 0.001$). Among 43 infants (two cases of twins), HBsAb was not detected in two, subsequently confirmed to have HBV infection. Biochemical flare was observed in two of 11 mothers followed > 12 months, and an antiviral agent was administered. CONCLUSION: Antiviral treatment during late pregnancy effectively reduced MTCT. Long-term follow-up should be required in such cases. In addition, given that maternal biochemical flare occurred in 18% of mothers, re-administration of antiviral agents might be required.

Q Sheng, Y Ding, B Li, C Han, Y Li, C Zhang, H Bai, J Wang, L Zhao, T Xia, Z An, M Zhang, X Dou (2018). ["Efficacy and safety of nucleos\(t\)ide analogues to prevent hepatitis B virus mother-to-child transmission in pregnant women with high viremia: real life practice from China."](#) *Int J Med Sci* **15**(8): 796-801.

Purpose: To evaluate the efficacy and safety of nucleos(t)ide analogues, especially telbivudine (LdT) for the prevention of mother-to-child transmission (MTCT) of hepatitis B virus (HBV) in women with high viremia. Methods: We conducted a prospective, open-label, multicenter study of LdT for treating pregnant women having high viral loads of hepatitis B virus (HBV DNA $> 5 \log_{10}$ IU/mL) but normal levels of alanine aminotransferase (ALT). Maternal HBV DNA, HBV serologic status and ALT were measured at baseline, 4 weeks after therapy, before delivery, 4 weeks after delivery, and 12 weeks after delivery. Infant HBV serologic status and HBV DNA levels were measured at 7 months. We calculated the MTCT rate of LdT-treated and LdT-untreated groups and analyzed the efficacy and safety of LdT. Results: Ninety-one women (the treatment group) were treated with LdT, and twenty-one patients (the observation group) did not undergo antiviral therapy. The baseline HBV DNA levels were $8.15 \pm 0.82 \log_{10}$ IU/mL in the treatment group, and $8.09 \pm 1.04 \log_{10}$ IU/mL in the observation group. The MTCT rate was 0% in the treatment group, and 9.5% in the observation group ($p = 0.042$). In the treatment group, HBV DNA levels were $5.02 \pm 0.74 \log_{10}$ IU/mL at one month after therapy, and $3.95 \pm 0.94 \log_{10}$ IU/mL before delivery. Both groups had significant differences from baseline levels in HBV DNA levels ($p < 0.001$). In total, five patients had elevated ALT levels but without evidence of decompensate liver function. No severe adverse events or complications were observed in women or infants. Conclusions: For pregnant women with HBV DNA greater than $5 \log_{10}$ IU/mL, LdT therapy was effective in reducing HBV MTCT. If serum HBV DNA was detectable at delivery, discontinuation of LdT immediately was found to be safe and rarely induced off-treatment hepatitis flare.

S Tavakolpour, M Darvishi, HS Mirsafaei, M Ghasemiadl (2018). ["Nucleoside/nucleotide analogues in the treatment of chronic hepatitis B infection during pregnancy: a systematic review."](#) *Infect Dis (Lond)* **50**(2): 95-106.

BACKGROUND: Women of childbearing age who have developed chronic hepatitis B (CHB) infection, especially HBeAg-positive highly viraemic pregnant women, are largely responsible for the familial transmission of the infection. Therefore, choosing the most effective and safest antiviral medications to manage pregnant CHB patients is of crucial importance. MATERIALS AND METHODS: The PubMed and Scopus databases were searched through September 2017, for all the journal articles possessing original results regarding treatment of CHB pregnant women with any nucleos(t)ide analogue (NA) therapies, including lamivudine (LAM), adefovir (ADV), entecavir (ETV), telbivudine (LdT), and tenofovir (TDF). RESULTS: After the primary search, 882 studies were recognized, and updating the searching results, 41 journal articles with original data were investigated, involving 3874 newborn infants from mothers with CHB, and their mothers completed follow-up until the delivery. The most important basic data and results regarding the efficacy of drugs, the rate of vertical transmission, safety issues associated with pairs of mothers and infants, median levels of HBV DNA, breastfeeding data, and rate of vaccination success were collected. Moreover, possible key conclusion, recommendations, and learned lessons were discussed. Among the evaluated NAs, all LAM was efficient and safe. LdT was found to be very effective but had some safety concerns. In contrast, TDF had the advantages of both effectiveness and safety. CONCLUSION: According to data in the literature, initiation of TDF at the trimester of pregnancy in combination with immunoprophylaxis to prevent mother-to-child transmission (MTCT) of CHB infection is strongly recommended as well as successful immunization of CHB pregnant women by anti-HBV vaccines.

Y Wakano, T Sugiura, T Endo, K Ito, M Suzuki, H Tajiri, Y Tanaka, S Saitoh (2018). "[Antiviral therapy for hepatitis B virus during second pregnancies.](#)" *J Obstet Gynaecol Res* **44**(3): 566-569.

Mother-to-child transmission of the hepatitis B virus (HBV) is a major concern for infected mothers, especially after their first child has become an HBV carrier despite immunoprophylaxis. Eight mothers whose first child had become an HBV carrier despite immunoprophylaxis were referred for antiviral therapy during the subsequent pregnancy. All pregnant women were seropositive for both the hepatitis B surface antigen and hepatitis B e antigen. In the treatment group (three receiving lamivudine and two receiving tenofovir), mother-to-child transmission of the HBV was successfully prevented in all infants (5/5). On the other hand, two of three infants became HBV carriers in the untreated group. There were no significant adverse effects in either mothers or infants. Antiviral therapy using lamivudine and tenofovir during the second pregnancy successfully prevented mother-to-child transmission of the HBV for high-risk mothers.

J Yin, P Liang, G Chen, F Wang, F Cui, X Liang, G Zhuang (2018). "[Efficacy of tenofovir in preventing perinatal transmission of HBV infection in pregnant women with high viral loads.](#)" *Sci Rep* **8**(1): 15514.

Mother-to-child transmission is the major cause of chronic hepatitis B virus (HBV) infection. This double-blind trial tested the effect of tenofovir disoproxil fumarate (TDF) in preventing vertical transmission. Pregnant women who were HBsAg/HBeAg-positive with a HBV DNA titer $\geq 2 \times 10^6$ IU/mL were randomly assigned to the control (n = 60) and TDF-treated (n = 60) groups. TDF treatment (oral dose 300 mg/day) was initiated at 24 weeks of gestation and continued to 4 weeks after delivery. The subjects were followed up to 28 weeks postpartum. The effects of TDF on vertical transmission, outcomes of the mothers and infants and virological changes were monitored. TDF dynamically reduced the serum HBV DNA level of the mothers, particularly during the first 4 weeks of treatment. The lower viral loads were maintained in the pregnancies until delivery. Approximately 90% and 33.9% of the TDF-treated mothers had viral loads ≤ 2000 IU/mL after delivery and at 28 weeks postpartum, respectively. No cervical transmission or adverse effects were observed in the TDF-treated individuals, whereas 13.5% of the infants were infected with HBV in the control group. We conclude that TDF treatment initiated at 24 weeks of gestation in high-viremia, HBsAg/HBeAg-positive mothers efficiently prevents mother-to-child HBV transmission without adverse events in mothers and infants.

BF Zhang, ML Cheng, Q Zhang, XK Zhao, L Yu, J Yang, KS Deng, LS Zhang, J Wang, YX Hu (2018). "[\[Clinical study on blocking mother-to-child transmission of hepatitis B virus with high viral load and HBeAg positivity during pregnancy in Guizhou province\]](#)." *Zhonghua Gan Zang Bing Za Zhi* **26**(12): 945-950.

Objective: To observe the efficacy and safety related measures by blocking mother-to-child transmission of hepatitis B virus with high viral load and HBeAg positivity during pregnancy in Guizhou province. Methods: Outpatient and inpatient cases of the Department of Infectious Diseases and Obstetrics of Guizhou Medical University Affiliated Hospitals from May 2016 to July 2017 were retrospectively divided into intervention group, non-intervention group and non-hepatitis B pregnant women group; with 75 cases in each group. HBsAg and HBeAg were positive in the intervention group. Pregnant women with HBV DNA $\geq 10^6$ IU/ml were treated with anti-HBV therapy for 24 to 28 weeks of gestation until delivery. According to oral drugs, they were divided into tenofovir (TDF) group or telbivudine (LDT) group, non-intervention group (HBsAg and HBeAg positive), HBV DNA positive pregnant women, pregnant women with no anti-HBV drugs, non-hepatitis B pregnant women (normal pregnant women without HBV infection). Infants and young children born to the three groups of women were immunized with the national viral hepatitis B action plan. The gestational weeks and Apgar scores at birth, delivery mode, feeding mode, sex and 7-months-old age were observed and counted. Serum hepatitis B markers (HBVM) and HBV DNA were quantitatively detected. HBVM was detected by time-resolved fluorescence immunoassay (TRFIA), and HBV DNA was detected by real-time PCR (FQ-PCR). The changes of liver parameters, HBsAg, HBeAg, HBV DNA, adverse drug reactions and treatment response of pregnant intervention group before medication (12-24 weeks of gestation), 4 weeks of medication (28-32 weeks of gestation), 36-40 weeks of gestation (36-40 weeks of gestation) were statistically calculated. A t-test was used to compare the data between the measurements. Data measurements within the groups were analyzed using rank-sum test. Results: In the intervention group, therapeutic medications showed no differences in demographic and clinical characteristics between TDF group and LDT group, including liver parameters, HBsAg, HBeAg and log₁₀HBV DNA level. Compared with pre-treatment (TDF group: 4.84 ± 2.01 ; LDT group: 5.08 ± 1.99), TDF and LDT were significantly lower at the end of pregnancy (TDF group: 3.06 ± 0.66 ; LDT group: 3.51 ± 1.20). $P < 0.05$; and the treatment response rate was 100%.

There were no serious adverse events in the intervention group. Infants and young children (7-months-old) in the intervention group had negative HBsAg, HBeAg and HBV DNA. The mother-to-child transmission rate of HBV was zero, with blocking rate of 100%. In addition, both infants and young children had different degrees of hepatitis B protective antibodies (anti-HBs, M: 144.33), and their antibody titers were higher than that of non-intervention group (anti-HBs, M: 65.91) and non-hepatitis B pregnant women (anti-HBs, M: 58.43). The difference was statistically significant ($P < 0.05$), and there was no significant correlation between the use of antiviral and the way of delivery and feeding. Outcomes of mother-to-child transmission of HBV infection in infants and young children (7-months-old) delivered by three groups of pregnant women in the non-intervention groups had 20.0% (15/75)/ 17.3% (13/75) HBsAg/HBeAg positivity rate, and 17.3% (13/75) HBV DNA positivity rate. Overall, mother-to-child transmission rate of HBV infection was 20% (15/75). Furthermore, the relationship between mother's HBV DNA load and infant HBV infection in the non-intervention group showed mother's HBV DNA $\geq 10^6$ IU/ml. Conclusion: In the non-intervention group, mother-to-child transmission of HBV occurred, and infected mothers HBV DNA was $\geq 10^6$ IU/ml before delivery. This suggests that HBeAg positive and high load HBV DNA replication were independent risk factors for mother-to-child transmission of hepatitis B. Therefore, prenatal drug intervention and postpartum standard immune blockade are necessary for high-risk pregnant women with hepatitis B to achieve zero mother-to-child transmission of hepatitis B in real- clinical practice.

N Chotun, W Preiser, CJ van Rensburg, P Fernandez, GB Theron, D Glebe, MI Andersson (2017). "[Point-of-care screening for hepatitis B virus infection in pregnant women at an antenatal clinic: A South African experience.](#)" *PLoS One* **12**(7): e0181267.

BACKGROUND & AIMS: Elimination of HIV and syphilis mother-to-child transmission (MTCT) has received much attention but little consideration has been given to the possibility of elimination of HBV MTCT. In sub-Saharan Africa, HBV vertical transmission continues to be reported and it remains an important public health problem. This study aimed to assess the feasibility of screening pregnant women for HBV using a point-of-care (POC) test and implementing interventions to prevent HBV MTCT. **METHODS:** In this observational prospective cohort study, HIV-uninfected pregnant women who consented to testing were screened for HBV using a rapid POC test for HBsAg. Positive results were laboratory-confirmed and tested for HBV DNA and serological markers. Women with viral loads $\geq 20\,000$ IU/ml received tenofovir (TDF) treatment and all infants received birth-dose HBV vaccine. Two blood samples collected six months apart from HBV-exposed infants within their first year of life were tested for HBV DNA. **RESULTS:** Of 144 women who were approached, 134 consented to participating (93% acceptance rate of HBV POC test). Six women tested positive for HBsAg (4.5%; 95% CI 0.99%-8.01%), all confirmed by laboratory testing. Two mothers, M1 and M4, were treated with TDF during their third trimester of pregnancy. Six HBV-exposed infants received the HBV vaccine within 24 hours of birth, of whom two were lost to follow-up and four (including the two born to M1 and M4) had undetectable levels of HBV DNA when tested at the two time points. **CONCLUSION:** We found that HBV screening using POC testing fulfilled the criteria considered necessary for implementation. It has acceptable performance, is inexpensive, reliable, and was well accepted by the study participants. Screening pregnant women as part of the HBV MTCT prevention strategy is therefore feasible in a South African clinical setting.

GR Han, HX Jiang, CM Wang, Y Ding, GJ Wang, X Yue, L Zhou, W Zhao (2017). "[Long-term safety and efficacy of telbivudine in infants born to mothers treated during the second or third trimesters of pregnancy.](#)" *J Viral Hepat* **24**(6): 514-521.

Telbivudine, an FDA pregnancy category B drug, has been found to reduce hepatitis B virus (HBV) perinatal transmission with no safety concerns in infants aged up to 1 year. This study evaluated the long-term efficacy and safety of telbivudine in 214 infants born to 210 pregnant women with chronic hepatitis B infection who were treated with telbivudine during pregnancy (weeks 20-32 of gestation). The infants were followed for up to 5 years after birth. The efficacy endpoint was the rate of perinatal transmission, which was established by HBsAg and HBV DNA levels at 7 and 12 months. Safety endpoints included head circumference, weight, height, congenital abnormality and hospitalization rates. In addition, the Denver Developmental Screening Test was performed in 92 randomly selected infants. None of the 214 infants born to these women were infected with HBV, and all had effective serum hepatitis B surface antibody (HBsAb) levels. Compared with Chinese standard values, there were few differences in the infants' mean head circumference, weight, and height values. No birth defects were diagnosed, and the congenital abnormality rate was 0.934%. Serious adverse events requiring

hospitalization occurred in 20 infants (9.35%). The qualified Denver Developmental Screening Test rate in 92 infants was 97.82%, which was comparable to a rate of 92% in normal Chinese children. Thus, treatment with telbivudine during the second or third trimesters of pregnancy safely blocked perinatal transmission of HBV. Infants born to telbivudine-treated mothers showed normal growth and development during long-term follow-up of up to 5 years.

MH Hyun, YS Lee, JH Kim, JH Je, YJ Yoo, JE Yeon, KS Byun (2017). "[Systematic review with meta-analysis: the efficacy and safety of tenofovir to prevent mother-to-child transmission of hepatitis B virus.](#)" *Aliment Pharmacol Ther* **45**(12): 1493-1505.

BACKGROUND: Preventing mother to child transmission of chronic hepatitis B infection in the setting of a high maternal viral load is challenging. The idea has emerged from antepartum tenofovir treatment with combination immunoprophylaxis. AIMS: To demonstrate the efficacy and safety of tenofovir to prevent mother to child transmission of hepatitis B virus. METHODS: PubMed, EMBASE, and Cochrane databases were searched through August 16, 2016. Comparative trials of second or third trimester tenofovir administration vs. controls for patients with chronic hepatitis B infection and non-comparative case series assessing mother to child transmission rates and evaluating maternal and foetal safety outcomes were included. RESULTS: Ten studies (one randomised controlled trial, four non-randomised controlled trials and five case series) that enrolled 733 women were included. The pooled results from comparative trials (599 pregnancies) showed that tenofovir significantly reduced the risk of infant hepatitis B surface antigen seropositivity by 77% (odds ratio=0.23, 95% confidence intervals=0.10-0.52, $P=0.0004$) without heterogeneity ($I^2=0\%$). In the case series analysis (134 pregnancies), only two cases (1.5%) of mother to child transmission with extremely high maternal viral load and non-compliance to treatment were identified. Maternal and foetal safety parameters including congenital malformation and foetal death were re-assuring. CONCLUSIONS: For pregnant women with high hepatitis B virus DNA levels, tenofovir administration in the second or third trimester can prevent mother to child transmission when combined with hepatitis B immunoglobulin and the hepatitis B vaccine. Tenofovir is safe and tolerable for both the mother and foetus.

CQ Pan, W Yi, M Liu, G Wan, YH Hu, MF Zhou (2017). "[Lamivudine therapy during the second vs the third trimester for preventing transmission of chronic hepatitis B.](#)" *J Viral Hepat* **24**(3): 246-252.

There are little data on the timing of initiating lamivudine therapy for preventing transmission of hepatitis B in highly viremic mothers. Between May 2008 and January 2015, we retrospectively enrolled mothers with HBV DNA $>6 \log_{10}$ copies/mL who received lamivudine during pregnancy, and we compared them to untreated mothers. The primary measurement was the vertical transmission rate. The secondary outcomes were the mothers' and infants' safety. Among 249 consecutive mothers enrolled, 66 and 94 received lamivudine during the second and third trimesters, respectively, and 89 were untreated. At delivery, maternal mean HBV DNA levels were significantly lower in mothers who received lamivudine ($4.45 \log_{10}$; vs $7.16 \log_{10}$ copies/mL; $P<0.001$). Lamivudine treatment was well tolerated. However, early treatment during the second trimester did not significantly increase the percentage of mothers achieving HBV DNA levels of $<6 \log_{10}$ copies/mL compared to those treated during the third trimester (98.5% vs 94.7%; $P=0.40$). At the age of 28 weeks, the vertical transmission rates were significantly lower in the lamivudine-treated mothers vs in the untreated mothers (0% [0/160] vs 5.62% [5/89]; $P<0.001$), but the rates were similar when comparing the two subgroups treated with lamivudine (0% [0/66] vs 0% [0/94], $P>0.05$). The birth defect rates and mothers' and infants' adverse events were similar among the groups. Lamivudine treatment initiated in the second or third trimester for mothers with HBV DNA levels below $9 \log_{10}$ copies/mL was equally safe and effective in preventing vertical transmission. Thus, lamivudine should be deferred until the third trimester to minimize foetal exposure and drug resistance.

J Shang, Q Wen, CC Wang, K Liu, L Bai, H Tang (2017). "[Safety and efficacy of telbivudine for chronic hepatitis B during the entire pregnancy: Long-term follow-up.](#)" *J Viral Hepat* **24 Suppl 1**: 43-48.

The management of hepatitis B virus (HBV) infection in pregnancy is a unique issue. Telbivudine (LdT) is recommended to block HBV mother-to-child transmission (MTCT) in the third trimester. However, the safety of LdT treatment during the entire pregnancy for the long-term growth of infants is unclear. The aim of this study was to evaluate the efficacy and long-term safety of LdT for the entire pregnancy period. This retrospective cohort study included 40 pregnant women and 43 children from 2011 to 2017. The antiviral effects and maternal abnormalities were evaluated. In addition, adverse events regarding infants at delivery and HBV vaccination outcomes were recorded. The status of physical development in the children during follow-up was also evaluated. Among pregnant women, the rates of HBV DNA flare

were 5.00% during pregnancy and 7.50% postpartum, and the HBeAg seroconversion rates were 7.50% during pregnancy and 7.50% postpartum. No severe maternal abnormalities were observed. Regarding the infants, no one was positive for HBsAg, and only one infant was negative for anti-HBs in children over 7 months of age. Furthermore, no birth defects or severe adverse events were observed at delivery, and 97.67% normal height and 93.02% normal weight in children were observed on follow-up until 5 years of age. In conclusion, LdT use for the entire pregnancy is both effective for treating pregnant women and blocking HBV MTCT. Moreover, LdT is safe for women and infants. Most importantly, the long-term follow-up indicated that LdT is safe and does not affect the growth of children.

W Yi, MH Li, Y Xie, J Wu, YH Hu, D Zhang, Y Zhang, WH Cao (2017). "[Prospective cohort study on the efficacy and safety of telbivudine used throughout pregnancy in blocking mother-to-child transmission of hepatitis B virus.](#)" *J Viral Hepat* **24 Suppl 1**: 49-56.

Women with chronic hepatitis B should maintain nucleotide analogue treatment to prevent disease progression during pregnancy. The aim of this study was to prospectively evaluate the efficacy and safety of telbivudine used throughout pregnancy for preventing hepatitis B virus (HBV) mother-to-child transmission (MTCT). From January 2012 to June 2014, women who were receiving telbivudine therapy and became pregnant were enrolled in group A at 28 weeks of gestation. Pregnant women with an HBV DNA level >10(6) IU/mL were enrolled in either group B (telbivudine started at 28 weeks of gestation) or group C (control group without treatment). MTCT was defined as infants who were positive for serum hepatitis B surface antigen at 7 months after birth. There were 41, 179 and 177 pregnant women (397 infants) enrolled in groups A, B and C, respectively. The HBV DNA load at 28 weeks of gestation and delivery was 1.50 +/- 0.62 vs 1.45 +/- 0.61, 8.05 +/- 0.37 vs 4.24 +/- 0.89 and 7.94 +/- 0.62 vs 7.86 +/- 0.73 log10 IU/mL in groups A, B and C, respectively. The rate of MTCT in group C was 4.60%, which was significantly higher than the rates in groups A and B (0% and 0.6%, respectively) (P = .043). The difference between group A and group B was not significant. The rates of neonatal congenital abnormalities were 2.4%, 0.6% and 2.3% in groups A, B and C, respectively, and there were no significant differences (P = .140). Telbivudine used throughout pregnancy may be safe and effective for mothers and infants, but it may not enhance the efficacy of an HBV MTCT block compared with treatment starting at 28 weeks of gestation (NCT02253485).

G Jourdain, N Ngo-Giang-Huong, TR Cressey, L Hua, L Harrison, C Tierney, N Salvadori, L Decker, P Traisathit, W Sirirungsri, W Khamduang, C Bowonwatanuwong, T Puthanakit, GK Siberry, DH Watts, TV Murphy, J Achalapong, S Hongsiwong, V Klinbuayaem, S Thongsawat, RT Chung, S Pol, N Chotivanich (2016). "[Prevention of mother-to-child transmission of hepatitis B virus: a phase III, placebo-controlled, double-blind, randomized clinical trial to assess the efficacy and safety of a short course of tenofovir disoproxil fumarate in women with hepatitis B virus e-antigen.](#)" *BMC Infect Dis* **16**: 393.

BACKGROUND: Chronic hepatitis B virus (HBV) infection is complicated by cirrhosis and liver cancer. In Thailand, 6-7 % of adults are chronically infected with HBV. The risk of mother-to-child transmission (MTCT) of HBV has been estimated to be about 12 % when mothers have a high hepatitis B viral load, even if infants receive passive-active prophylaxis with HBV immunoglobulin (HBIG) and initiate the hepatitis B vaccine series at birth. We designed a study to assess the efficacy and safety of a short course of maternal tenofovir disoproxil fumarate (TDF) among women with a marker of high viral load for the prevention of MTCT of HBV. **METHODS:** The study is a phase III, multicenter (17 sites in Thailand), placebo-controlled, double-blind, randomized 1:1, two-arm clinical trial of TDF 300 mg once daily versus placebo among pregnant women from 28 weeks' gestation through 2-month post-partum. All infants receive HBIG at birth, and a hepatitis B (HB) vaccination series according to Thai guidelines: birth, and age 1, 2, 4 and 6 months. Participant women at study entry must be age >=18 years, hepatitis B surface antigen (HBsAg) and e-antigen (HBeAg) positive, have alanine aminotransferase (ALT) level < 30 IU/L at screening (confirmed < 60 IU/L pre-entry), negative hepatitis C serology, creatinine clearance >50 mL/min, and no history of anti-HBV antiviral treatment. The target sample size of 328 mother/infant pairs assumed 156 evaluable cases per arm to detect a >=9 % difference in MTCT transmission (3 % experimental arm versus 12 % placebo arm) with 90 % power. Mothers and infants are followed until 12 months after delivery. The primary infant endpoint is detection of HBsAg, confirmed by detection of HBV DNA at six months of age. Secondary endpoints are maternal and infant adverse events, acute exacerbations of maternal hepatitis B disease (ALT >300 IU/L, defined as a "flare") following discontinuation of study treatment, infant HBV infection status and growth up to 12 months of age. **DISCUSSION:** The results of this randomized trial will clarify the efficacy and safety of a short course of

antiviral treatment to prevent mother-to-child transmission of HBV and inform international guidelines.
TRIAL REGISTRATION: ClinicalTrials.gov Identifier NCT01745822 .

M Pawlowska, A Pniewska, M Pilarczyk, D Koziulewicz, K Domagalski (2016). "[Prophylaxis of vertical HBV infection.](#)" *Expert Opin Drug Saf* **15**(10): 1361-1368.

INTRODUCTION: An appropriate management of HBV infection is the best strategy to finally reduce the total burden of HBV infection. Mother-to-child transmission (MTCT) is responsible for more than one third of chronic HBV infections worldwide. Because HBV infection in infancy or early childhood often leads to chronic infection, appropriate prophylaxis and management of HBV in pregnancy is crucial to prevent MTCT. AREAS COVERED: The prevention of HBV vertical transmission is a complex task and includes: universal HBV screening of pregnant women, administration of antivirals in the third trimester of pregnancy in women with high viral load and passive-active HBV immunoprophylaxis with hepatitis B vaccine and hepatitis B immune globulin in newborns of all HBV infected women. EXPERT OPINION: Universal screening of pregnant women for HBV infection, early identification of HBV DNA level in HBV-infected mothers, maternal treatment with class B according to FDA antivirals and passive/active anti-HBV immunoprophylaxis to newborns of HBV-positive mothers are crucial strategies for reducing vertical HBV transmission rates. Consideration of caesarean section in order to reduce the risk of vertical HBV transmission should be recommend in HBV infected pregnant women with high viral load despite antiviral therapy or when the therapy in the third trimester of pregnancy is not available.

T Piratvisuth, GR Han, S Pol, Y Dong, A Trylesinski (2016). "[Comprehensive review of telbivudine in pregnant women with chronic hepatitis B.](#)" *World J Hepatol* **8**(9): 452-460.

AIM: To achieve an evidence-based conclusion regarding the safety and efficacy of telbivudine during pregnancy. METHODS: A pooled analysis of data from a literature search reported 1739 pregnancy outcomes (1673 live births) from 1725 non-overlapping pregnant women treated with telbivudine. The prevalence of live birth defects (3.6/1000) was similar to that of the non-antiviral controls (3.0/1000) and not increased as compared with overall prevalence (14.5 to 60/1000). No target organ toxicity was identified. The prevalence of spontaneous abortion in pregnant women treated with telbivudine (4.2/1000) was not increased compared with the overall prevalence (16/1000). The mother-to-child transmission rate was significantly reduced in pregnant women treated with telbivudine (0.70%) compared to those treated with the non-antiviral controls (11.9%; $P < 0.0001$) or compared to the historical rates of hepatitis B virus (HBV)-infected population without antiviral treatment (10%-15%). RESULTS: Cumulatively 489 pregnancy cases have been reported in the telbivudine pharmacovigilance database (with a cut-off date 31 August 2014), of those, 308 had known pregnancy outcomes with 249 cases of live births (239 cases of live birth without congenital anomaly and 10 cases of live birth with congenital anomaly). In the latest antiretroviral pregnancy registry report (1 January 1989 through 31 January 2015) of 27 patients exposed to telbivudine during pregnancy (18, 6 and 3 during first, second and third trimester, respectively) 19 live births were reported and there were no cases of birth defects reported. CONCLUSION: Telbivudine treatment during pregnancy presents a favorable safety profile without increased rates of live birth defects, spontaneous abortion or elective termination, or fetal/neonatal toxicity. Exposure to telbivudine in the first, second and third trimester of pregnancy has been shown to significantly reduce the risk of HBV transmission from mother to child on the basis of standard immune prophylaxis procedure.

Z Tan, Y Yin, J Zhou, L Wu, C Xu, H Hou (2016). "[Telbivudine treatment of hepatitis B virus-infected pregnant women at different gestational stages for the prevention of mother-to-child transmission: Outcomes of telbivudine treatment during pregnancy.](#)" *Medicine (Baltimore)* **95**(40): e4847.

This prospective study evaluated the viability of telbivudine for blocking mother-to-child transmission (MTCT) of hepatitis B virus (HBV) infection. Pregnant women positive for the hepatitis B surface antigen began telbivudine treatment before 14 weeks of gestation (i.e., early), between 14 and 28 weeks of gestation (late), or not at all (control). In the late-treatment group, 55 women terminated telbivudine therapy within puerperium. All neonates underwent routine hepatitis B immunoglobulin plus vaccination. Mothers and infants were followed for 7 months after birth. Pregnancy outcomes were similar among the 3 groups. HBV MTCT rates in the early and late treatment and control groups were 0, 0, and 4.69%, respectively. The rates of infant vaccination success among the 3 groups were similar, as were neonatal outcomes including birth weights, asphyxia, hyperbilirubinemia, Apgar score, birth defects, and weight and height at 7 months. Puerperal discontinuation of telbivudine did not increase the alanine transaminase value at 7 months after birth, but increased serum HBV DNA levels, and rates of positive

hepatitis Be-antigen. Telbivudine treatment in HBV-infected pregnant women was associated with lower serum HBV DNA levels and reduced rates of HBV MTCT; there were no associated changes in pregnancy or neonatal outcomes at birth or 7 months after birth, or in the rate of infant vaccination success. Puerperal drug withdrawal after short-term antiviral therapy will not influence hepatic function, but may increase virus replication.

H Zhuang (2016). "[[Prevention of mother-to-child transmission of hepatitis B virus](#)]." *Zhonghua Gan Zang Bing Za Zhi* **24**(12): 881-884.

Mother-to-child transmission (MTCT) is a major mode of hepatitis B virus (HBV) transmission, especially in high endemic areas. Administration of hepatitis B immunoglobulin (HBIG) and hepatitis B vaccine to infants at birth, followed by completion of the vaccine series, prevented approximately 95% of HBV transmission from HBsAg-positive mothers to their infants. However, immunoprophylaxis failure was still observed in 5~10% infants born to mothers with high levels of viremia. It was demonstrated that antiviral nucleot(s)ide analogues (NUCs) provided to pregnant women with high viral loads in late pregnancy further reduced MTCT. This paper discussed criteria of antiviral treatment for prevention of MTCT including threshold of HBV DNA level in pregnant women, time of starting treatment, time of stopping treatment, and kind of NUCs. The route of hepatitis B vaccine administration was also discussed.

MO El Agheb, JD Grange (2015). "[[Prevention of mother to child transmission of hepatitis B](#)]." *Pan Afr Med J* **20**: 316.

V Jackson, W Ferguson, TB Kelleher, M Lawless, M Eogan, U Nusgen, S Coughlan, J Connell, JS Lambert (2015). "[[Lamivudine treatment and outcome in pregnant women with high hepatitis B viral loads](#)]." *Eur J Clin Microbiol Infect Dis* **34**(3): 619-623.

Perinatal transmission is the most common mode of hepatitis B virus (HBV) transmission and is a leading cause of chronic infection worldwide. Maternal treatment with lamivudine (LAM) can result in a rapid and significant reduction in HBV viral load (VL) and, thus, mitigate the risk of mother-to-child transmission (MTCT). The aim of this study was to retrospectively evaluate the safety of LAM treatment administered in the third trimester of pregnancy and determine the influence, if any, on infant outcome. The medical charts of all HBV surface antigen (HBsAg)-positive women eligible for treatment with LAM and who registered for antenatal care between 2007 and 2012 were retrospectively reviewed. During the 6-year period, 45 women met the criteria for LAM treatment. Thirty-six women (80 %) accepted treatment; the remaining women declined treatment (5), defaulted from care (3) or transferred to another maternity unit (1). The median duration of treatment was 11.4 weeks (range 5.3-17.4) and the median baseline VL was $1.4 \times 10(8)$ IU/mL (range $1.8 \times 10(7)$ - $1.7 \times 10(8)$). The median VL at delivery was $2.3 \times 10(5)$ IU/mL and 60 % of women achieved a VL reduction $>2 \log_{10}$ IU/mL before delivery. No cases of perinatal transmission occurred in the infants born to mothers who received treatment; however, one infant, born to a mother who defaulted from care, was HBV-infected at 8 months. The results suggest that LAM therapy in highly viraemic HBV-infected pregnant women could lower the rate of vertical transmission.

JR Lamberth, SC Reddy, JJ Pan, KJ Dasher (2015). "[[Chronic hepatitis B infection in pregnancy](#)]." *World J Hepatol* **7**(9): 1233-1237.

There are no standard guidelines to follow when a patient with chronic hepatitis B infection becomes pregnant or desires pregnancy. Topics to consider include which patients to treat, when to start treatment, what treatment to use and when to stop treatment. Without any prophylaxis or antiviral therapy, a hepatitis B surface antigen and E antigen positive mother has up to a 90% likelihood of vertical transmission of hepatitis B virus (HBV) to child. Standard of care in the United States to prevent perinatal transmission consists of administration of hepatitis B immune globulin and HBV vaccination to the infant. The two strongest risk factors of mother to child transmission (MTCT) of HBV infection despite immunoprophylaxis are high maternal HBV viral load and high activity of viral replication. The goal is to prevent transmission of HBV at birth by decreasing viral load and/or decreasing activity of the virus. Although it is still somewhat controversial, most evidence shows that starting antivirals in the third trimester is effective in decreasing MTCT without affecting fetal development. There is a growing body of literature supporting the safety and efficacy of antiviral therapies to reduce MTCT of hepatitis B. There are no formal recommendations regarding which agent to choose. Tenofovir, lamivudine and telbivudine have all been proven efficacious in decreasing viral load at birth without known birth defects, but final decision of which antiviral medication to use will have to be determined by physician and patient. The

antivirals may be discontinued immediately if patient is breastfeeding, or within first four weeks if infant is being formula fed.

JF Lu, YL Liu, LN Ma, ZH Cao, ZM He, Y Jin, SB Zhang, XY Chen (2015). "[Efficacy of combination antiviral therapy following childbirth in pregnant HBV carriers receiving telbivudine for prevention of mother-to-child transmission](#)." *Zhonghua Gan Zang Bing Za Zhi* **23**(11): 821-825.

OBJECTIVE: To observe the clinical efficacy of combination therapy with peg-IFN α and adefovir (CPIA) in women who were hepatitis B virus (HBV) carriers and had just given birth and received telbivudine (LdT) during pregnancy for prevention of mother-to-child transmission. METHODS: One-hundred-and-fifty third trimester-pregnant women who were HBV carriers with highly-viremic were treated with LdT until time of birth. After delivery, those women with alanine aminotransferase (ALT) level exceeding two times the upper limit of normal and HBV DNA level that had decreased more than 31 gIU/mL or hepatitis B e antigen (HBeAg) titer that had decreased more than 50% were switched to CPIA for 96 weeks. RESULTS: Following delivery, 45 of the women were switched to the CPIA treatment, of which 91.1% (41/45) achieved virological response, 55.6% (25/45) achieved HBeAg clearance or seroconversion, and 26.7% (12/45) achieved hepatitis B surface antigen (HBsAg) clearance or seroconversion. The immediate post-delivery (and pre-CPIA) levels of HBeAg and HBV DNA were negatively associated with HBeAg clearance. Ninety-eight of the total study participants stopped the LdT treatment and there were no cases of significant deterioration of liver function. CONCLUSION: Pregnant women who are HBV carriers and receive LdT for protection against mother-to-child transmission, and who show significant ALT elevation and decreased HBeAg titer and/or reduced HBV DNA after delivery, may be good candidates for the CPIA therapy following delivery.

P Sogni (2015). "[Pregnancy and viral hepatitis B and C](#)." *Presse Med* **44**(6 Pt 1): 654-659.

The screening for HBsAg is a medical obligation in France during pregnancy. A serovaccination with antiHBs immunoglobulins (100 IU) and a 1st dose of vaccine (10 mug) has to be realized during the first 12 hours of life when the mother is HBsAg+. The serovaccination failures are related to high maternal viral load (HBV-DNA >7 log IU/mL). In this case, a treatment with analogue (tenofovir) associated with serovaccination could be performed during the last trimester of pregnancy. The risk of mother-to-child transmission of virus C is around 3 to 5% in case of HCV-RNA positive without co-infection with HIV. The mode of delivery is unchanged in case of maternal HBV or HCV. Breast-feeding is not contra-indicated in case of maternal HBV or HCV infection.

W Sun, L Ma, A Hao, W Liu, M Song, M Li, Y Xin (2015). "[Predictive value of telbivudine in preventing mother-to-infant transmission of hepatitis B virus in pregnant women with high viremia](#)." *Zhonghua Gan Zang Bing Za Zhi* **23**(3): 180-183.

OBJECTIVE: To investigate the efficacy and safety of telbivudine for blocking mother-to-child transmission of hepatitis B virus (HBV) in pregnant women with high viremia. METHODS: A total of 128 pregnant women with high HBV load (HBV DNA $\geq 1.0 \times 10^7$ copies/ml and positive for hepatitis B surface antigen (HBsAg)) were enrolled in the study from January 2009 to January 2013 and divided into the following three groups: group A (n=42) treated with telbivudine at 12 weeks of gestation until postpartum 12 weeks; group B (n=41) treated with telbivudine at 20 to 28 weeks of gestation until postpartum 12 weeks; group C (n=45; control group) with no telbivudine treatment. All study participants were given compound gilyeyrhizin for liver protection. All infants born to the women from the three groups were vaccinated with hepatitis B immunoglobulin (200 IU) and the HBV vaccine (20 tg) after birth. The mother-to-infant transmission of HBV was indicated by the presence of HBsAg in infants at 7 months after birth. The maternal HBV DNA levels of the women in the three groups were statistically compared with the HBsAg positive rates in their neonates. RESULTS: There were no significant differences in the HBV DNA levels between the three groups before treatment (P more than 0.05). The pre-delivery level of HBV DNA in group A (0.553 \pm 1.588 log₁₀ copies/ml) and in group B (0.486 \pm 1.429 log₁₀ copies/ml) was significantly decreased compared to that in group C (7.698 \pm 0.255 log₁₀ copies/ml) (both P < 0.01). The post-delivery (12 weeks) level of HBV DNA in group A (0.381 \pm 1.116 log₁₀ copies/ml) and in group B (0.335 \pm 1.073 log₁₀ copies/ml) was significantly decreased compared to that in group C (7.728 \pm 0.277 log₁₀ copies/ml) (both P < 0.01). There were no significant differences in the HBV DNA levels between group A and group B (P > 0.05). No infants in group A or group B were HBsAg-positive, while the HBsAg-positive rate was 17.4% in group C (P=0.012; P=0.015). CONCLUSIONS: Telbivudine treatment starting from the 12th week of gestation or from the 20-28th week of gestation

can significantly decrease the serum HBV DNA level in peripheral blood of pregnant women with high viremia and reduce the infection rate of HBV in their neonates.

AL Wang, YP Qiao, LH Wang, LW Fang, F Wang, X Jin, J Qiu, XY Wang, Q Wang, JL Wu, SH Vermund, L Song (2015). "[Integrated prevention of mother-to-child transmission for human immunodeficiency virus, syphilis and hepatitis B virus in China.](#)" *Bull World Health Organ* **93**(1): 52-56.

PROBLEM: China continues to face challenges in eliminating mother-to-child transmission of human immunodeficiency virus (HIV), syphilis and hepatitis B virus (HBV). APPROACH: In 2010, a programme that integrated and standardized prevention of mother-to-child transmission (PMTCT) efforts for HIV, syphilis and HBV was implemented in 1156 counties. At participating antenatal care clinics, pregnant women were offered all three tests concurrently and free of charge. Further interventions such as free treatment, prophylaxis and testing for mothers and their children were provided for HIV and syphilis. LOCAL SETTING: China's national PMTCT HIV programme started in 2003, at which time there were no national programmes for perinatal syphilis and HBV. In 2009, the rate of maternal-to-child transmission of HIV was 8.1% (57/702). Reported congenital syphilis was 60.8 per 100,000 live births. HBV infection was 7.2% of the overall population infected. RELEVANT CHANGES: Between 2010 and 2013 the number of pregnant women attending antenatal care clinics with integrated PMTCT services increased from 5.5 million to 13.1 million. In 2013, 12.7 million pregnant women were tested for HIV, 12.6 million for syphilis and 12.7 million for HBV. Mother-to-child transmission of HIV fell to 6.7% in 2013. Data on syphilis transmission are not yet available. LESSONS LEARNED: Integrated PMTCT services proved to be feasible and effective, and they are now part of the routine maternal and child health services provided to infected women. The services are provided through a collaboration between maternal and child health clinics, the national and local Centers for Disease Control and Prevention, and general hospitals.

YP Lu, XJ Liang, XM Xiao, SM Huang, ZW Liu, J Li, B Hoher, YP Chen (2014). "[Telbivudine during the second and third trimester of pregnancy interrupts HBV intrauterine transmission: a systematic review and meta-analysis.](#)" *Clin Lab* **60**(4): 571-586.

H Zhang, CQ Pan, Q Pang, R Tian, M Yan, X Liu (2014). "[Telbivudine or lamivudine use in late pregnancy safely reduces perinatal transmission of hepatitis B virus in real-life practice.](#)" *Hepatology*.

MH Liu, YJ Sheng, JY Liu, HD Hu, Q Zhang, H Ren (2013). "[Efficacy of telbivudine on interruption of hepatitis B virus vertical transmission: a meta-analysis.](#)" *Ann Saudi Med* **33**(2): 169-176.

HX Xu, LJ Wang, YX Yu, YP Wu, YF Xu, XX Liu, Y Chen (2012). "[\[Efficacy and safety of telbivudine treatment to block mother-to-child transmission of hepatitis B virus: a meta-analysis\]](#)." *Zhonghua Gan Zang Bing Za Zhi* **20**(10): 755-760.

L Han, HW Zhang, JX Xie, Q Zhang, HY Wang, GW Cao (2011). "[A meta-analysis of lamivudine for interruption of mother-to-child transmission of hepatitis B virus.](#)" *World J Gastroenterol* **17**(38): 4321-4333.

C Buchanan, TT Tran (2010). "[Management of chronic hepatitis B in pregnancy.](#)" *Clin Liver Dis* **14**(3): 495-504.

Z Shi, Y Yang, L Ma, X Li, A Schreiber (2010). "[Lamivudine in late pregnancy to interrupt in utero transmission of hepatitis B virus: a systematic review and meta-analysis.](#)" *Obstet Gynecol* **116**(1): 147-159.

2. Guidelines and recommendations for TAP in pregnancy

(2020). "[Screening for Hepatitis B Virus Infection in Pregnant Women: Recommendation Statement.](#)" *Am Fam Physician* **101**(2): 112-114.

A Guingané, A Bougouma, R Sombié, R King, N Nagot, N Meda, P Van de Perre, E Tuaillon (2020). "[Identifying gaps across the cascade of care for the prevention of HBV mother-to-child transmission in Burkina Faso: Findings from the real world.](#)" *Liver Int.*

BACKGROUND: Prevention of mother-to-child transmission (PMTCT) is a challenge for controlling the hepatitis B epidemic. In Sub-Saharan countries, pilot interventions including the screening of pregnant women for HBsAg, implementation of anti-HBV therapy and infant immunization within 24 hours of life are initiated and need to be evaluated. This pilot study aimed to describe the cascade of care for hepatitis B PMTCT in a real life situation, and to identify sociodemographic factors associated with adequate management of pregnant women and infants. **METHOD:** The study was conducted from October 1st, 2014 to February 28th, 2016 in the antenatal clinics (ANCV) of Baskuy district which comprises nine first-level public health centres. Univariate and multivariate logistic regression analysis were used to identify sociodemographic factors associated with the likelihood of retention in the cohort, HBV DNA testing, birth dose delivery and HBsAg testing of the children at 6 months of age; $P < .05$ was selected as cut off for significance. **RESULTS:** In this prospective cohort study, of 5200 pregnant women consulting for the antenatal visit, 2261 (43.5%) were proposed pre-test counselling and HBsAg screening and 2220 (98.2%) have agreed to screening. Among 1580 (71.2%) women that came back for the post-counselling interview, 75 were positive for HBsAg (4.8%), 73 (97.3% of the women provided HBsAg result) consented to medical consultation with hepatogastroenterologists and 53 (72.6%); performed the HBV DNA testing. Forty-seven out of 60 (78.3%; 65.8-87.9) children born alive were immunized for HBV within 24 hours of life. Retention in care was associated with the level of education of the infant's father, secondary school or higher was associated with a better retention in care of the women (OR: 6.6; $P = .03$). **CONCLUSION:** Our study shows large gaps in HBV PMTCT. Resources for hepatitis B screening, care and prevention including universal access to the vaccine birth dose should be allocated to reduce infection in HBV exposed infants born in Burkina Faso.

JF Liu, TY Chen, YL Chen, YR Zhao (2020). "[\[Reply to the comments on 2019 Chinese guidelines for the prevention and treatment of mother-to-child transmission of hepatitis B virus\]](#)." *Zhonghua Gan Zang Bing Za Zhi* **28**(1): 27-30.

Obstetrics group, Chinese Society of Obstetrics and Gynecology, Chinese Medical Association; Society of Perinatal Medicine, Chinese Medical Association (2020). "[\[Clinical guidelines on prevention of mother-to-child transmission of hepatitis B virus \(2020\)\]](#)." *Zhonghua Fu Chan Ke Za Zhi* **55**(5): 291-299.

YH Zhou, T Li, H Zhuang (2020). "[\[Comments on 2019 Chinese practice guideline for the prevention and treatment of hepatitis B virus mother-to-child transmission\]](#)." *Zhonghua Gan Zang Bing Za Zhi* **28**(1): 24-26.

Recently, the Society of Infectious Diseases of Chinese Medical Association and Chinese GRADE Center jointly released the "2019 Chinese practice guideline for the prevention and treatment of hepatitis B virus mother-to-child transmission". We concerned several issues in the Guideline, including the improper citation of some references, no recommendations for some key strategies for the prevention of hepatitis B virus mother-to-child transmission, insufficient or even lack of evidence for some recommendations and others. Based on the principle of academic contention, we present in this article our comments on the Guideline to discuss these issues with the Guideline's authors and readers.

A Arora, A Kumar, AC Anand, P Puri, RK Dhiman, SK Acharya, K Aggarwal, N Aggarwal, R Aggarwal, YK Chawla, VK Dixit, A Duseja, CE Eapen, B Goswami, K Gujral, A Gupta, A Jindal, P Kar, K Kumari, K Madan, J Malhotra, N Malhotra, G Pandey, U Pandey, RD Puri, RR Rai, PN Rao, SK Sarin, A Sharma, P Sharma, KT Shenoy, KR Singh, SP Singh, V Suri, N Trehanpati, M Wadhawan (2019). "[Indian National Association for the Study of the Liver- Federation of Obstetric and Gynaecological Societies of India Position Statement on Management of Liver Diseases in Pregnancy](#)." *J Clin Exp Hepatol* **9**(3): 383-406.

Liver diseases occurring during pregnancy can be serious and can progress rapidly, affecting outcomes for both the mother and fetus. They are a common cause of concern to an obstetrician and an important reason for referral to a hepatologist, gastroenterologist, or physician. Liver diseases during pregnancy can be divided into disorders unique to pregnancy, those coincidental with pregnancy, and preexisting liver diseases exacerbated by pregnancy. A rapid differential diagnosis between liver diseases related or unrelated to pregnancy is required so that specialist and urgent management of these conditions can be carried out. Specific Indian guidelines for the management of these patients are lacking. The Indian National Association for the Study of the Liver (INASL) in association with the Federation of Obstetric and Gynaecological Societies of India (FOGSI) had set up a taskforce for development of consensus guidelines for management of patients with liver diseases during pregnancy, relevant to India. For development of these guidelines, a two-day roundtable meeting was held on 26-27 May 2018 in New Delhi, to discuss, debate, and finalize the consensus statements. Only those statements that were unanimously approved by most members of the taskforce were accepted. The primary objective of this

review is to present the consensus statements approved jointly by the INASL and FOGSI for diagnosing and managing pregnant women with liver diseases. This article provides an overview of liver diseases occurring in pregnancy, an update on the key mechanisms involved in its pathogenesis, and the recommended treatment options.

X Hu, L Wang, F Xu (2019). ["Guides concerning tenofovir exposure via breastfeeding: A comparison of drug dosages by developmental stage."](#) *Int J Infect Dis* **87**: 8-12.

Tenofovir disoproxil fumarate (TDF) is a prodrug of tenofovir, and after being administered orally, it converts to tenofovir in the blood. With the increasing use of TDF in women for treatment and prevention of mother-to-child transmission (MTCT) of both human immunodeficiency virus (HIV) and hepatitis B virus (HBV), or the pre-exposure prophylaxis (PrEP) for HIV, many nursing mothers have to understand the risk of exposure to tenofovir via breastmilk and make the decision about breastfeeding while on TDF treatment. Despite the safety record of TDF in pregnancy, some guidelines recommend against its use during breastfeeding. In this paper, we compared the dosage levels of tenofovir exposure in fetuses, breastfed infants, and children receiving tenofovir treatment. We found that breastfed infants were exposed to only 0.5%-16% of the tenofovir dosage that fetuses experienced via placental transfer, and 0.01-0.04% of the recommended weight-adjusted therapeutic dose. The assessment of toxicity risk from the dose perspective is an important and natural way of addressing safety concerns about exposure to tenofovir via breastfeeding. Based on the safety data from fetuses and children with tenofovir exposure, and the comparatively negligible exposure dosage from breastfeeding, our study supports mothers on TDF treatment should be encouraged to breastfeed.

J Hou, F Cui, Y Ding, X Dou, Z Duan, G Han, J Jia, Q mao, J Li, Z Li, Z Liu, L Wei, Q Xie, X Yang, H Zhang, H Zhang (2019). ["Management Algorithm for Interrupting Mother-to-Child Transmission of Hepatitis B Virus."](#) *Clin Gastroenterol Hepatol* **17**(10): 1929-1936.e1921.

In areas where hepatitis B virus (HBV) is endemic, mother-to-child transmission (MTCT) is the major route of infection of children. Blocking MTCT of HBV therefore would reduce its prevalence. The China Foundation of Hepatitis Prevention and Control organized a team of specialists in infectious diseases, hepatology, immunology, obstetrics, and public health to develop an algorithm for interrupting MTCT of HBV, based on the most recent hepatitis B guidelines and latest evidence. This algorithm comprises 10 steps and has been adopted in clinical practice in China. Four aspects (screening, antiviral intervention during pregnancy, immunoprophylaxis, and postvaccination serologic testing) are the core components of preventing MTCT. Although the combination of passive and active immunization in newborns of hepatitis B surface antigen-positive mothers reduces MTCT of HBV, this immunoprophylaxis cannot completely eradicate MTCT. In the past decade, administration of antiviral agents to pregnant women has been shown to be safe and effective in reducing MTCT of HBV in combination with immunoprophylaxis. Aiming to achieve zero MTCT, this algorithm recommends the use of antivirals during pregnancy by women with high viral loads. Preventing MTCT is key to achieving the goal of eliminating HBV as a public health threat by 2030. Implementation and enhancement of the standardized algorithm for pregnant women with chronic HBV infection and their infants is urgently needed to prevent MTCT.

J Woodrington, R Pastore, A Brink, N Ishikawa, Y Takashima, RA Tohme (2019). ["Progress Toward Hepatitis B Control and Elimination of Mother-to-Child Transmission of Hepatitis B Virus - Western Pacific Region, 2005-2017."](#) *MMWR Morb Mortal Wkly Rep* **68**(8): 195-200. CDC

Hepatitis B vaccine (HepB), which has been available since 1982, provides lifelong protection against hepatitis B virus (HBV) infection and the associated 20%-30% increased lifetime risk for developing cirrhosis or hepatocellular carcinoma among >95% of vaccine recipients (1). Before HepB introduction into national childhood immunization schedules, the estimated hepatitis B surface antigen (HBsAg) prevalence in the World Health Organization (WHO) Western Pacific Region (WPR)* was >8% in 1990 (2). In 2005, the WPR was the first WHO region to establish a hepatitis B control goal, with an initial target of reducing HBsAg prevalence to <2% among children aged 5 years by 2012. In 2013, the WPR set more stringent control targets to achieve by 2017, including reducing HBsAg prevalence to <1% in children aged 5 years and increasing national coverage with both timely HepB birth dose (HepB-BD) (defined as administration within 24 hours of birth) and the third HepB dose (HepB3) to ≥95% (3). All WPR countries/areas endorsed the Regional Action Plan for Viral Hepatitis in the Western Pacific Region 2016-2020 in 2015 (4) and the Regional Framework for the Triple Elimination of Mother-to-Child Transmission of human immunodeficiency virus (HIV), Hepatitis B and Syphilis in Asia and the Pacific 2018-2030 (triple

elimination framework) in 2017 (5). These regional targets and strategies are aligned with program targets established by the WHO Global Health Sector Strategy on Viral Hepatitis 2016-2021 that aim to reduce HBsAg prevalence among children aged 5 years to $\leq 1\%$ by 2020 and to $\leq 0.1\%$ by 2030 (6). This report describes progress made to achieve hepatitis B control in the WPR and the steps taken to eliminate mother-to-child transmission (MTCT) of HBV during 2005-2017. During this period, regional timely HepB-BD and HepB3 coverage increased from 63% to 85% and from 76% to 93%, respectively. As of December 2017, 15 (42%) countries/areas achieved $\geq 95\%$ timely HepB-BD coverage; 18 (50%) reached $\geq 95\%$ HepB3 coverage; and 19 (53%) countries/areas as well as the region as a whole were verified to have achieved the regional and global target of $< 1\%$ HBsAg prevalence among children aged 5 years. Continued implementation of proven vaccination strategies will be needed to make further progress toward WPR hepatitis B control targets. In addition to high HepB-BD and HepB3 coverage, enhanced implementation of complementary hepatitis B prevention services through the triple elimination framework, including routine HBsAg testing of pregnant women, timely administration of hepatitis B immunoglobulin to exposed newborns, and antiviral treatment of mothers with high viral loads, will be needed to achieve the global hepatitis B elimination target by 2030.

Yu, S. Z. (2019). "[[Facilitating the continuous decline on the incidence rates of hepatitis B and liver cancer through cutting off the mother-to-child viral transmission, based on the "prevention first" strategy, in China](#)]." *Zhonghua Liu Xing Bing Xue Za Zhi* 40(12): 1650-1653.

There have been 6-10 million reported patients with chronic hepatitis B virus (HBV) infection worldwide, and the United Nations (UN) called for a "90% reduction by 2030" strategy. Since the wide practice of HBV vaccination, the numbers of HBV cases have been reduced by 85% and the incidence of hepatocellular carcinoma has also decreased by 50%. As formulated by the UN in 2015, the sustainable development agenda for the eradication of hepatitis B included the success rate of preventing mother-to-child viral transmission by 95%, together with the reduction of new hepatitis B infections by 90% in 2030. In order to achieve the agenda, we proposed a strategy to achieve the "three 96%" goals derived from the Shanghai experience. In brief, hepatitis B vaccine should cover for 96% newborns within 24 h, and the vaccination boosting rate should reach 96% for both one and six months after birth. If cutting off the mother-to-child viral transmission strategy can be successfully achieved, the future of hepatitis B prevention will be promising, and the task of eliminating hepatitis B and controlling hepatocellular carcinoma can be completed ahead of 2030, time proposed by the UN.

(2018). "[[Consensus on clinical management of hepatitis B virus- infected women of childbearing age](#)]." *Zhonghua Gan Zang Bing Za Zhi* 26(3): 204-208.

The mother-to-child transmission(MTCT) of hepatitis B virus (HBV) is the dominant cause of chronic HBV infection. In order to achieve the goal of "zero" MTCT before pregnancy, during pregnancy, and after pregnancy; standardized management for hepatitis HBV infection in women of childbearing age should be regulated. The content of this consensus includes: screening and treatment of HBV in pregnant women and women of childbearing age, treatment of hepatitis B during pregnancy, preventive measures and evaluation of combined immunization of hepatitis B immunoglobulin and hepatitis B vaccine in newborns, anti-viral therapy for all pregnant women with a high HBV DNA level and post-partum period related management. In addition, 16 recommendations were formed for clinicians to standardize the clinical management of HBV infection in women of child-bearing age.

CM Espinosa, R Jhaveri (2018). "[[Update on the management of hepatitis B and C infections in the neonatal period](#)]." *Semin Perinatol* 42(3): 185-190.

Hepatitis B virus and hepatitis C virus have received a significant amount of attention in recent years, and both viruses share a significant amount of similarities with one another beyond just that they both primarily target the liver. In recent years, cases of both infections have been fueled by a nationwide epidemic of injection drug use. Most relevant to this audience, they are both transmitted from mother to child. The increased cases in young adults combined with mother to child transmission translate into more exposed infants that will need to be managed and followed. Screening of pregnant women for hepatitis B infection coupled with appropriate treatment and prophylaxis measures are incredibly effective to preventing transmission. Prevention of hepatitis C infection is not yet possible, but advances in antiviral therapy make interruption of transmission a future possibility.

P Hu, H Ren (2017). "[[Interpretations of EASL 2017 clinical practice guidelines on the management of hepatitis B virus infection](#)]." *Zhonghua Gan Zang Bing Za Zhi* 25(6): 415-418.

The European Association for the Study of the Liver recently released the updated Clinical Practice Guidelines on the management of hepatitis B virus infection at the International Liver Congress(TM) 2017 in Amsterdam. The latest clinical practice guideline integrated the latest scientific advances on diagnosis and therapy of hepatitis B, thereby providing optimize the management of patients with either acute or chronic HBV. The latest clinical practice guideline includes new definitions of disease phases, expanded indications for initiating treatment, prevention of mother-to-child transmission, new stopping rules for antiviral therapy. Future treatment strategies to achieve 'cure' of disease and new biomarkers are discussed.

J Woodring, N Ishikawa, M Nagai, M Malarski, Y Takashima, H Sobel, YR Lo (2017). "[Integrating HIV, hepatitis B and syphilis screening and treatment through the Maternal, Newborn and Child Health platform to reach global elimination targets.](#)" *Western Pac Surveill Response J* 8(4): 1-5.

Every year, an estimated 180 000 babies in the Western Pacific Region are infected by hepatitis B, 13 000 by syphilis and 1400 by HIV through mother-to-child transmission. (1) These infections can be largely prevented by antenatal screening, treatment and timely vaccination for newborns. Despite challenges in controlling each disease, major achievements have been made. National immunization programmes have reduced the regional hepatitis B prevalence from over 8% in 1990 to 0.93% among children born in 2012. In addition, HIV testing and treatment have helped keep the regional prevalence of HIV infections at 0.1%. In contrast, the number of maternal syphilis cases is still high in the Western Pacific Region, with an estimated 45 million cases in 2012. Elimination of mother-to-child transmission of these infections cannot be achieved through vertically applied programming and require using and augmenting to the shared Maternal, Newborn and Child Health platform to coordinate, integrate and enable cost efficiencies for these elimination efforts. The Regional Framework for Triple Elimination of Mother-to-Child Transmission of HIV, Hepatitis B and Syphilis in Asia and the Pacific 2018-2030 offers such a coordinated approach towards achieving the triple elimination of mother-to-child transmission of HIV, hepatitis B and syphilis and provides guidance for decision-makers, managers and health professionals working in programmes addressing maternal, newborn and child health, HIV, hepatitis, sexually transmitted infections and immunization.

JC Dunkelberg, EMF Berkley, KW Thiel, KK Leslie (2014). "[Hepatitis B and C in pregnancy: a review and recommendations for care.](#)" *J Perinatol* 34(12): 882-891.

TREATMENT AS PREVENTION TO PREVENT LIVER DISEASE PROGRESSION

Dunn R, Musabaev E, Razavi H, Sadirova S, Bakieva S, Razavi-Shearer K, Brigida K, Kamili S, Averhoff F, Nasrullah M. Progress [Toward Hepatitis B and Hepatitis C Elimination Using a Catalytic Funding Model - Tashkent, Uzbekistan](#), December 6, 2019-March 15, 2020. MMWR Morb Mortal Wkly Rep. 2020 Aug 28;69(34):1161-1165.

In 2016, the World Health Organization (WHO) set hepatitis elimination targets of 90% reduction in incidence and 65% reduction in mortality worldwide by 2030 (1). Hepatitis B virus (HBV) and hepatitis C virus (HCV) infection prevalences are high in Uzbekistan, which lacks funding for meeting WHO's targets. In the absence of large financial donor programs for eliminating HBV and HCV infections, insufficient funding is an important barrier to achieving those targets in Uzbekistan and other low- and middle-income countries. A pilot program using a catalytic funding model, including simplified test-and-treat strategies, was launched in Tashkent, Uzbekistan, in December 2019. Catalytic funding is a mechanism by which the total cost of a program is paid for by multiple funding sources but is begun with upfront capital that is considerably less than the total program cost. Ongoing costs, including those for testing and treatment, are covered by payments from 80% of the enrolled patients, who purchase medications at a small premium that subsidizes the 20% who cannot afford treatment and therefore receive free medication. The 1-year pilot program set a target of testing 250,000 adults for HBV and HCV infection and treating all patients who have active infection, including those who had a positive test result for hepatitis B surface antigen (HBsAg) and those who had a positive test result for HCV core antigen. During the first 3 months of the program, 24,821 persons were tested for HBV and HCV infections. Among those tested, 1,084 (4.4%) had positive test results for HBsAg, and 1,075 (4.3%) had positive test results for HCV antibody (anti-HCV). Among those infected, 275 (25.4%) initiated treatment for HBV, and 163 (15.2%) initiated treatment for HCV, of whom 86.5% paid for medications and 13.5% received medications at no cost. Early results demonstrate willingness of patients to pay for treatment if costs are low, which can offset elimination costs. However, improvements across the continuum of care are needed to recover the upfront investment. Lessons learned from this program, including the effectiveness of using simplified test-and-treat guidelines, general practitioners in lieu of specialist physicians, and innovative financing to reduce costs, can guide similar initiatives in other countries and help curb the global epidemic of viral hepatitis, especially among low- and middle-income countries.

A Koffas, J Petersen, PT Kennedy (2020). "[Reasons to consider early treatment in chronic hepatitis B patients.](#)" *Antiviral Res* 177: 104783.

In spite of a decrease in the prevalence and incidence seen in recent years, chronic hepatitis B (CHB) still remains a major healthcare challenge, prevalent mostly in developing but also in developed regions. CHB is associated with significant morbidity and mortality, secondary to the complications of disease progression; cirrhosis and hepatocellular carcinoma (HCC). Historically, antiviral treatment has been restricted to patients with active hepatitis, established liver disease, fibrosis or cirrhosis and/or the risk of HCC development. As a result, patients with hepatitis B 'e' antigen (HBeAg) -positive chronic infection, formerly referred to as the 'immune tolerant' disease phase, have been excluded from treatment, since immune tolerant CHB had been considered 'benign' with no ostensible progressive liver disease. However, recent advances in 'decoding' the immunopathogenesis of CHB challenged the accuracy of this classical perception: it is now well-recognised that HBeAg-positive chronic infection is not characterized by immunological tolerance and that events associated with tumourigenesis are already present during this early disease phase. These findings have led to a paradigm shift: in 2017, the European Association for the Study of the Liver (EASL) recommended a change in the nomenclature and clinical categorisation of CHB and proposed lowering the threshold for antiviral treatment to include patients with HBeAg-positive chronic infection. It is anticipated that this could delay or even prevent disease progression and the development of HCC, alongside the potential to achieve functional cure (hepatitis B 'surface' antigen loss with or without development of hepatitis B 'surface' antibody). The current article reviews relevant literature and discusses the reasons for considering early treatment in CHB.

L Lapointe-Shaw, H Chung, L Holder, JC Kwong, B Sander, PC Austin, HLA Janssen, JJ Feld (2020). "[Diagnosis of Chronic Hepatitis B Peri-Complication: Risk factors and Trends over Time.](#)" *Hepatology*.

BACKGROUND & AIMS: Hepatitis B virus (HBV) is a major cause of chronic liver disease, which can progress to cirrhosis, hepatocellular carcinoma, and death. A timely diagnosis allows for antiviral treatment, which can prevent liver-related complications. Conversely, a late diagnosis signals a missed opportunity for earlier care and treatment. Our objective was to measure the proportion of chronic HBV diagnoses that are made within 6 months of presentation with a liver disease-related complication and

examine associated factors and trends over time. **APPROACH & RESULTS:** We used provincial laboratory data to identify patients with chronic HBV diagnosed from 2003 to 2014. We measured the proportion who experienced a liver disease complication (decompensated cirrhosis, hepatocellular carcinoma, or liver transplant) within +/- 6 months of their HBV diagnosis date. A multivariable logistic regression model was used to identify factors associated with HBV diagnosis peri-complication. Of 18,434 patients with chronic HBV, 1,279 (6.9%) developed an HBV-related complication during the follow-up period. Among these, 570 (44.6%) had a first diagnosis peri-complication. HBV diagnosis peri-complication did not decrease over time and was independently associated with older age at HBV diagnosis, rural residence, alcohol use, and moderate to high levels of comorbidity. Female patients, immigrants, and those with more outpatient physician visits were less likely to have an HBV diagnosis peri-complication. **CONCLUSIONS:** A high proportion of patients with HBV-related complications are first diagnosed with HBV peri-complication. These signal missed opportunities for earlier detection and treatment. Our findings support expansion of HBV screening.

TG Maponga, AL McNaughton, M van Schalkwyk, S Hugo, C Nwankwo, J Taljaard, J Mokaya, DA Smith, C van Vuuren, D Goodhals, S Gabriel, MI Andersson, W Preiser, C van Rensburg, PC Matthews (2020). "[Treatment advantage in HBV/HIV coinfection compared to HBV mono-infection in a South African cohort.](#)" *J Infect* **81**(1): 121-130.

OBJECTIVES: Prompted by international targets for elimination of hepatitis B virus (HBV), we set out to characterise individuals with HBV mono-infection vs. those coinfected with HBV/HIV, to evaluate the impact of therapy and to guide improvements in clinical care. **METHODS:** We report observational data from a real world cross-sectional cohort of 115 adults with chronic hepatitis B infection (CHB), at a university hospital in Cape Town, South Africa. HIV coinfection was present in 39 (34%) subjects. We recorded cross-sectional demographic, clinical and laboratory data. **RESULTS:** Compared to those with HIV coinfection, HBV mono-infected adults were less likely to be HBeAg-positive ($p=0.01$), less likely to have had assessment with elastography ($p<0.0001$), and less likely to be on antiviral treatment ($p<0.0001$); they were more likely to have detectable HBV viraemia ($p=0.04$), and more likely to have features of liver disease including moderate/severe thrombocytopenia ($p=0.007$), elevated bilirubin ($p=0.004$), and elevated APRI score ($p=0.02$). Three cases of hepatocellular carcinoma all arose in HBV mono-infection. **CONCLUSIONS:** Our data demonstrate that individuals with HBV mono-infection may be disadvantaged compared to those with HIV coinfection, highlighting potential systematic inequities in referral, monitoring and treatment.

S Nayagam, P Chan, K Zhao, E Sicuri, X Wang, J Jia, L Wei, N Walsh, LE Rodewald, G Zhang, W Ailing, L Zhang, JH Chang, WW Hou, Y Qiu, B Sui, Y Xiao, H Zhuang, MR Thursz, F Scano, D Low-Beer, B Schwartländer, Y Wang, TB Hallet (2020). "[Investment Case for a Comprehensive Package of Interventions Against Hepatitis B in China: Applied Modeling to Help National Strategy Planning.](#)" *Clin Infect Dis.*

BACKGROUND: In 2016, the first global viral hepatitis elimination targets were endorsed. An estimated one-third of the world's population of individuals with chronic hepatitis B virus (HBV) infection live in China and liver cancer is the sixth leading cause of mortality, but coverage of first-line antiviral treatment was low. In 2015, China was one of the first countries to initiate a consultative process for a renewed approach to viral hepatitis. We present the investment case for the scale-up of a comprehensive package of HBV interventions. **METHODS:** A dynamic simulation model of HBV was developed and used to simulate the Chinese HBV epidemic. We evaluated the impact, costs, and return on investment of a comprehensive package of prevention and treatment interventions from a societal perspective, incorporating costs of management of end-stage liver disease and lost productivity costs. **RESULTS:** Despite the successes of historical vaccination scale-up since 1992, there will be a projected 60 million people still living with HBV in 2030 and 10 million HBV-related deaths, including 5.7 million HBV-related cancer deaths between 2015 and 2030. This could be reduced by 2.1 million by highly active case-finding and optimal antiviral treatment regimens. The package of interventions is likely to have a positive return on investment to society of US\$1.57 per US dollar invested. **CONCLUSIONS:** Increases in HBV-related deaths for the next few decades pose a major public health threat in China. Active case-finding and access to optimal antiviral treatment are required to mitigate this risk. This investment case approach provides a real-world example of how applied modeling can support national dialog and inform policy planning.

Tovo CV, Ahlert M, Panke C, de Mattos ÂZ, de Mattos AA. [Treatment of hepatitis B virus infection in chronic infection with HBeAg-positive adult patients \(immunotolerant patients\): a systematic review](#). Eur J Gastroenterol Hepatol. **2020** Sep 15.

Recently, a controversial approach suggesting the early treatment of chronic infection with hepatitis B "e" antigen-positive patients with hepatitis B virus (HBV) infection, has been proposed. The objective of this study is to systematically review medical literature regarding treatment of HBV infection in adult chronic infection with HBeAg-positive patients. A systematic review was performed according to the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis statement. Original studies that evaluated the effect of antivirals in adult chronic infection with HBeAg-positive patients were included. The outcomes of interest were viral load suppression, the loss/seroconversion of HBeAg, the loss/seroconversion of hepatitis B surface antigen, and the development of cirrhosis or hepatocellular carcinoma. The search for eligible studies was performed in Excerpta Medica dataBASE, PubMed and Cochrane databases until January 2020, without language or date restriction. The risk of bias was evaluated using the Newcastle-Ottawa Scale for observational studies and the Revised Cochrane Risk-of-Bias Tool for randomized controlled trials. Two hundred ninety-six articles were retrieved. After analyzing titles and abstracts, 287 articles were excluded and nine were considered potentially eligible. From these, five were excluded after full-text analysis. Finally, four articles were included. Only two were randomized controlled trials. All studies were carried out in Asian patients. Results were variable with regard to viral load, negatization/seroconversion of HBeAg and HBsAg. One study demonstrated that treated patients developed cirrhosis or hepatocellular carcinoma less frequently than untreated individuals. Overall, the studies were of poor quality. In conclusion, the present systematic review demonstrated that, at present, there is not enough evidence to recommend treating this population of patients.

S Yalaki, MS Yalcin (2020). "[Does regression in treatment-induced liver fibrosis reflect noninvasive tests? Assessing treatment results of hepatitis B patients who took potent antiviral drugs for 5 years](#)." *Niger J Clin Pract* **23**(2): 226-231.

BACKGROUND: Chronic liver disease may be reversed through treatment, and it is crucial to have a definitive diagnosis of liver fibrosis for this treatment. **Aims:** In this study, we aimed to determine whether regression of liver fibrosis in naive patients undergoing strong antiviral therapy is reflected in noninvasive tests. **MATERIALS AND METHODS:** We systematically reviewed and monitored medical records of patients with chronic hepatitis B who underwent liver biopsy for patient qualification. We selected patients with a liver fibrosis score of two or more who had not previously received antiviral treatment. We used previously described formulas to compute the indirect indicators of fibrosis for the patients and noted the values of Aspartate aminotransferase (AST) to alanine aminotransferase (ALT) ratio (AAR), age-platelet index (API), fibrosis index-based 4 factor (FIB-4), AST-platelet ratio index (APRI), mean platelet volume (MPV) and platelet count (PLT). **RESULTS:** We found a significant difference between the three measurements for APRI, AAR and FIB-4 scores and MPV and PLT distributions in patients who were administered entecavir and tenofovir (Friedman $P < 0.05$). In the post-hoc binary comparison for both entecavir and tenofovir, we found significant differences between the baseline measurements and the 3(rd)- and 5(th)-year measurements in terms of APRI, AAR, FIB-4, MPV, and PLT. **CONCLUSION:** Liver biopsy is considered the gold standard for the treatment and follow-up of hepatitis B but may not be appropriate in all cases. Non-invasive tests may be effective in monitoring antiviral therapy. We demonstrated that non-invasive tests improved with antiviral therapy, which may be a reflection of treatment-regression in liver histopathology.

TC Yip, HW Lee, VWS Wong, GLH Wong, YK Tse, GCY Lui, SH Ahn, HLY Chan (2020). "[Factors associated with improvement in MELD score after antiviral treatment in patients with chronic hepatitis B](#)." *J Gastroenterol Hepatol* **35**(9): 1610-1618.

BACKGROUND AND AIMS: Improvement in Model for End-Stage Liver Disease (MELD) score during antiviral treatment is associated with reduced hepatic decompensation and death in patients with chronic hepatitis B (CHB)-related cirrhosis. We aimed to identify factors associated with transplant-free survival and on-treatment MELD score improvement. **METHODS:** We identified patients with CHB-related cirrhosis and MELD score ≥ 15 at the start of entecavir and/or tenofovir disoproxil fumarate treatment between 2005 and 2017. The primary endpoint was transplant-free survival at month 6. The secondary endpoints at month 6 were transplant-free survival with > 5 -point improvement in MELD score and transplant-free survival with MELD score < 15 . **RESULTS:** Of 999 cirrhotic CHB patients, 605 (60.6%) achieved transplant-free survival at month 6. Proportion of transplant-free survival at month 6 stabilized

at 10% in patients with high MELD. Patients who achieved transplant-free survival at month 6 were younger, had lower MELD score, lower alanine aminotransferase (ALT), and higher albumin at baseline. Of 605 patients with transplant-free survival, 276 (45.6%) achieved > 5-point improvement in MELD score; 183 (30.2%) had 1-point to 5-point improvement in MELD score; 146 (24.1%) had no improvement or a worsened MELD score. Also, 321 (53.1%) patients with transplant-free survival had a MELD score < 15 at month 6. CONCLUSION: On top of lower MELD score, patients with CHB-related cirrhosis who are younger, have higher albumin, and lower ALT are more likely to achieve transplant-free survival after 6 months of antiviral treatment.

H Gao, Z Kuang, CX Zhong, XE Liang, R Fan, KF Wang, WY Lin, JL Hou, J Sun (2019). "[[Prevalence and risk factors of nonalcoholic fatty liver disease in patients with chronic hepatitis B receiving antiviral therapy](#)]." *Zhonghua Gan Zang Bing Za Zhi* **27**(5): 347-351.

Objective: To investigate the prevalence and risk factors of non-alcoholic fatty liver disease (NAFLD) in patients with chronic hepatitis B (CHB) receiving antiviral treatment. Methods: The cross-sectional study included 3 477 cases with CHB who received antiviral therapy. The prevalence of NAFLD was investigated, and then the risk factors were screened and analyzed by stepwise regression method in CHB patients with NAFLD as the dependent variable and the related influencing factors as independent variables. Results: The prevalence of NAFLD was 24.1% in CHB patients who received antiviral therapy. After adjusting for age and gender, central obesity (OR: 7.44, 95%CI: 6.06 ~ 9.14), hypertension (OR: 1.74, 95%CI: 1.51 ~ 2.20), and triglyceride (OR: 1.52, 95%CI: 1.18 ~ 1.96) were positively associated with NAFLD, and cirrhosis was negatively associated with NAFLD (OR: 0.42, 95%CI: 0.34 ~ 0.53). Patients with long-term antiviral therapy had increased risk of NAFLD. Conclusion: A significant proportion of CHB patients receiving antiviral therapy have suffered from NAFLD. Therefore, CHB patients receiving long-term antiviral treatment should pay more attention to the prevalence of NAFLD.

HA Osman, AA Ghweil, AM Sabry RE Mahdy, A Khodeary (2019). "[Management Of Patients With Hepatitis B Virus Reactivation Post-DAA Treatment Of Chronic Hepatitis C Virus Infection In HCV-HBV Coinfected Patients With Pretreatment HBeAg Seroconversion And Early Degree Of Hepatic Fibrosis](#)." *Infect Drug Resist* **12**: 3067-3073.

BACKGROUND AND AIM: Hepatitis C virus (HCV)-HBV coinfection is a significant health problem with rapid progression of liver disease without precise diagnosis and treatment. We aimed in this study to identify if there were any role of HBV antiviral therapy in patients with HBV reactivation after direct-acting antiviral therapy in HCV-HBV coinfecting patients. METHODS: A prospective random study was carried out on 140 patients presenting with chronic HCV and chronic HBV coinfection. All patients had pretreatment HBeAg seroconversion, HBV DNA <2,000 IU/mL, normal liver enzymes, and F0/F1 hepatic fibrosis. They treated with sofosbuvir 400 mg and daklatasvir 60 mg once daily for 3 months. All patients underwent pretreatment hepatic fibrosis assessment using Fibro Scan and laboratory investigations: platelet count, liver-function tests, quantitative HCV PCR, HBsAg, HBc IgG, HBeAg, and HBeAb. All patients were followed up at 1, 3, 6, and 12 months from the start of HCV therapy. RESULTS: The study enrolled 140 HCV-HBV coinfecting patients: 55% were F0 and the rest F1. All our patients had negative HCV PCR at 1 month posttreatment and had achieved sustained virologic response with negative HCV PCR 3 months after treatment end. Four patients showed HBV reactivation with raised HBV DNA PCR and liver enzymes. Their mean age was 23.7±2.7 years, and three were male. Regarding patients with HBV reactivation, at 12 months posttreatment they showed significant decreases in liver enzymes, bilirubin, and INR, with increased platelet count (P=0.001), each with undetectable HBV PCR (P=0.001). CONCLUSION: HBV-HCV coinfecting patients with no/mild hepatic fibrosis, HBeAg seroconversion, and HBV DNA <2,000 IU/mL can complete direct-acting antiviral therapy without HBV antiviral treatment with close monitoring.

DH Sinn (2019). "[[Natural History and Treatment Indications of Chronic Hepatitis B](#)]." *Korean J Gastroenterol* **74**(5): 245-250.

HBV is the most common etiology of both liver cirrhosis and hepatocellular carcinoma in Korea. Despite much progress made, the currently available antiviral therapies cannot eradicate or eliminate this virus. Hence, the benefits and risks of antiviral therapy should be carefully evaluated on an individual basis and within the context of the clinical situation. The ultimate goals of treatment are to decrease the mortality from liver disease. The benefits of antiviral therapy come from prevention of progression of liver disease. Understanding the natural history of chronic HBV infection is a key step in the decision making process to treat patients with chronic HBV infection. Generally, chronic hepatitis B patients in the immune tolerant phase and immune inactive phase are not recommended to undergo antiviral treatment, except

for those patients in special conditions (e.g., immunosuppression or anticancer chemotherapy). Chronic hepatitis B patients in the immune active phase are recommended for antiviral therapy. For patients with liver cirrhosis, treatment should be considered when serum HBV DNA is detectable regardless of the serum level of ALT.

D Sinn, SE Kim, BK Kim, JH Kim, MS Choi (2019). "[The risk of hepatocellular carcinoma among chronic hepatitis B virus-infected patients outside current treatment criteria.](#)" *J Viral Hepat* **26**(12): 1465-1472.

We assessed the incidence of hepatocellular carcinoma (HCC) in those outside of current treatment recommendations and risk factors associated with HCC development. A multi-centre, retrospective cohort of 3624 patients who were monitored without antiviral treatment was analysed. Incident HCC risk according to the Asian Pacific Association for the study of the Liver (APASL), the American Association for the Study of Liver Disease (AASLD) and the European Association for the Study of the Liver (EASL) treatment recommendations was assessed. A risk score was developed using independent factors associated with HCC development among patients who were outside current treatment criteria. During a median follow-up of 4.6 years, incident HCC was diagnosed in 161 (4.4%) patients. The proportions of patients who developed HCC outside treatment recommendation according to APASL, AASLD and EASL criteria were 64.0%, 46.0% and 33.5%, respectively. The 5-year cumulative HCC incidence rate was 13.9% for cirrhotic patients with low-level viremia and 6.1 ~ 7.3% for chronic hepatitis patients with elevated HBV DNA levels plus mildly elevated alanine aminotransferase levels. Among patients who were outside treatment recommendation, age, sex, hepatitis B e antigen, cirrhosis, alanine aminotransferase and platelet levels were independent factors associated with HCC development. When these factors were used to calculate the risk score for each patient, those with a score ≥ 8 had a higher HCC incidence rate (14.3% at 5-year), although they were currently outside treatment recommendations. Thus, HCC was observed among patients who were outside current treatment criteria indicating that careful monitoring for HCC and efforts to identify patients at risk are required.

T Wilkins, R Sams, M Carpenter (2019). "[Hepatitis B: Screening, Prevention, Diagnosis, and Treatment.](#)" *Am Fam Physician* **99**(5): 314-323.

Hepatitis B virus (HBV) is a partly double-stranded DNA virus that causes acute and chronic liver infection. Screening for hepatitis B is recommended in pregnant women at their first prenatal visit and in adolescents and adults at high risk of chronic infection. Hepatitis B vaccination is recommended for medically stable infants weighing 2,000 g or more within 24 hours of birth, unvaccinated infants and children, and unvaccinated adults requesting protection from hepatitis B or who are at increased risk of infection. Acute hepatitis B is defined as the discrete onset of symptoms, the presence of jaundice or elevated serum alanine transaminase levels, and test results showing hepatitis B surface antigen and hepatitis B core antigen. There is no evidence that antiviral treatment is effective for acute hepatitis B. Chronic hepatitis B is defined as the persistence of hepatitis B surface antigen for more than six months. Individuals with chronic hepatitis B are at risk of hepatocellular carcinoma and cirrhosis, but morbidity and mortality are reduced with adequate treatment. Determining the stage of liver disease (e.g., evidence of inflammation, fibrosis) is important to guide therapeutic decisions and the need for surveillance for hepatocellular carcinoma. Treatment should be individualized based on clinical and laboratory characteristics and the risks of developing cirrhosis and hepatocellular carcinoma. Immunologic cure, defined as the loss of hepatitis B surface antigen with sustained HBV DNA suppression, is attainable with current drug therapies that suppress HBV DNA replication and improve liver inflammation and fibrosis. Pegylated interferon alfa-2a, entecavir, and tenofovir are recommended as first-line treatment options for chronic hepatitis B.

LSY Tang, E Covert, E Wilson, S Kottlil (2018). "[Chronic Hepatitis B Infection: A Review.](#)" *Jama* **319**(17): 1802-1813.

IMPORTANCE: More than 240 million individuals worldwide are infected with chronic hepatitis B virus (HBV). Among individuals with chronic HBV infection who are untreated, 15% to 40% progress to cirrhosis, which may lead to liver failure and liver cancer. OBSERVATIONS: Pegylated interferon and nucleos(t)ide analogues (lamivudine, adefovir, entecavir, tenofovir disoproxil, and tenofovir alafenamide) suppress HBV DNA replication and improve liver inflammation and fibrosis. Long-term viral suppression is associated with regression of liver fibrosis and reduced risk of hepatocellular carcinoma in cohort studies. The cure (defined as hepatitis B surface antigen loss with undetectable HBV DNA) rates after treatment remain low (3%-7% with pegylated interferon and 1%-12% with nucleos[t]ide analogue therapy). Pegylated interferon therapy can be completed in 48 weeks and is not associated with the development of resistance; however, its use is limited by poor tolerability and adverse effects such as

bone marrow suppression and exacerbation of existing neuropsychiatric symptoms such as depression. Newer agents (entecavir, tenofovir disoproxil, and tenofovir alafenamide) may be associated with a significantly reduced risk of drug resistance compared with older agents (lamivudine and adefovir) and should be considered as the first-line treatment. CONCLUSIONS AND RELEVANCE: Antiviral treatment with either pegylated interferon or a nucleos(t)ide analogue (lamivudine, adefovir, entecavir, tenofovir disoproxil, or tenofovir alafenamide) should be offered to patients with chronic HBV infection and liver inflammation in an effort to reduce progression of liver disease. Nucleos(t)ide analogues should be considered as first-line therapy. Because cure rates are low, most patients will require therapy indefinitely.

TCF Yip, HLY Chan, YK Tse, KLY Lam, GCY Lui, VWS Wong, GLH Wong (2018). "[On-Treatment Improvement of MELD Score Reduces Death and Hepatic Events in Patients With Hepatitis B-Related Cirrhosis](#)." *Am J Gastroenterol* **113**(11): 1629-1638.

OBJECTIVES: Antiviral treatment modifies the natural history of chronic hepatitis B (CHB)-related cirrhosis as reflected by improving Model for End-Stage Liver Disease (MELD) score over time. We evaluated the impact of on-treatment change of MELD score on clinical outcomes in patients with CHB-related cirrhosis. METHODS: Cirrhotic CHB patients who received entecavir and/or tenofovir disoproxil fumarate for at least 6 months in Hong Kong between 2005 and 2016 were identified. The primary outcome was all-cause mortality; secondary outcomes were hepatocellular carcinoma (HCC), and hepatic events including ascites, spontaneous bacterial peritonitis, variceal bleeding, hepatorenal syndrome, hepatic encephalopathy, and liver transplantation. RESULTS: We identified 1743 cirrhotic CHB patients. Their mean MELD score decreased from 12.3 ± 5.5 at baseline to 11.0 ± 4.7 at month 6. At a median (interquartile range) follow-up of 3.9 (1.9-6.0) years, 290 (16.6%) patients died; 201 (11.5%) developed HCC. Among 1140 patients without prior hepatic events, 150 (13.2%) developed hepatic events. Among 464 patients with baseline MELD score ≥ 15 , the 6-year cumulative mortality was 72.8, 36.7, and 23.1% for unchanged or increased MELD score, 1-5 point improvement in MELD score, and >5 point improvement in MELD score at month 6, respectively (log-rank test, $P < 0.001$); the corresponding 6-year cumulative incidence of hepatic events was 52.7, 30.5, and 23.9% in the three subgroups (Gray's test, $P = 0.004$). Patients with MELD score < 15 at month 6 had lower risk of mortality and hepatic events (all $P < 0.001$). CONCLUSIONS: On-treatment improvement of MELD score correlates with reduced risk of mortality and hepatic events in cirrhotic CHB patients.

J Liu, T Chen, Y Zhao (2017). "[Telbivudine therapy for gravidas with chronic hepatitis B infection and patients at risk of renal impairment](#)." *J Viral Hepat* **24 Suppl 1**: 6-11.

Hepatitis B virus infection is currently the most important cause of chronic viral hepatitis worldwide and is one of the most frequent causes of end-stage liver disease. With the international implementation of the hepatitis B vaccine and combined prophylaxis for infants born to HBsAg(+) mothers, the prevalence of hepatitis B has decreased remarkably. However, intra-uterine transmission has become a critical bottleneck for eliminating hepatitis B infection. The efficacy of nucleos(t)ide analogs on inhibiting hepatitis B replication has been widely confirmed, and the quality of life and the survival of individuals with chronic hepatitis B (CHB) have improved to a great degree. However, with the availability of long-term antiviral treatment and the ever increasing ageing population, renal disorders should be considered when choosing antiviral medicines. The antiviral efficacy and safety of telbivudine (LdT) have been shown in patients with CHB infection, and LdT is approved as a class B drug for pregnancy. Furthermore, the renal protective function of LdT has been demonstrated recently. In this review, we will focus on the efficacy and safety of LdT in gravidas with CHB infection, as well as the renal protective function of LdT in CHB patients. LdT might provide physicians with a solid option for effectively treating patients with CHB, especially gravidas or those either with or at risk of renal impairment.

C Stasi, E Salomoni, U Arena, G Corti, P Montalto, F Bartalesi, F Marra, G Laffi, S Milani, AL Zignego, M Pinzani (2017). "[Non-invasive assessment of liver fibrosis in patients with HBV-related chronic liver disease undergoing antiviral treatment: A preliminary study](#)." *Eur J Pharmacol* **806**: 105-109.

In chronic hepatitis B (CHB) patients, fibrosis assessment during antiviral treatment is a key step in the clinical management. Aim of this study was to evaluate the performance of elastography in assessing fibrosis stage in CHB before and after two years of nucleoside/nucleotide analogues (NUC) treatment in comparison with indirect serum markers. CHB diagnosis was made according to standard criteria. A clinical and virological evaluation was performed at baseline and again at 3, 6, 9, 12, 18, and 24 months during treatment. Fibrosis was evaluated by liver biopsy, elastography and indirect serum markers. Of 75 patients, 50 had CHB, HBeAg negative and were deemed eligible for this study. Of these, 22 underwent

liver biopsy. Mean histo-morphometric values of fibrotic tissue differed significantly in the stage < S3 vs. stage ≥S3: $2.01 \pm 2.62\%$ vs. $12.85 \pm 7.31\%$ ($p=0.03$), respectively. At 18 and 24 months, stiffness values were statistically reduced from those previously observed ($P=0.03$ and $P<0.001$). At 24 months the values of APRI, FIB-4 and LOK were not different from baseline values, while the value of FORNS score at 24 months was the only one statistically reduced. In two patients with fibrosis stage S3 and S6, respectively, fibrosis regressed to stage S2 and S5. In conclusion, the results of the present study show that liver histology, stiffness and FORNS score improve significantly during a long-term follow-up of HBV patients successfully treated with NUC. These results strongly suggest that the non-invasive evaluation of liver fibrosis represents a key step in the management and treatment of chronic HBV hepatitis.

CL Lin, HC Yang, JH Kao (2016). "[Hepatitis B virus: new therapeutic perspectives.](#)" *Liver Int* **36 Suppl 1**: 85-92.

Current antiviral therapies have dramatically improved the long-term outcomes of patients with chronic hepatitis B virus (HBV) infection. Both interferon (IFN) and nucleos(t)ide analogue (NA) treatments have been shown to reduce the progression of liver disease in chronic hepatitis B (CHB) patients. However, persistent covalently closed circular DNA (cccDNA) can result in a viral relapse after discontinuation of antiviral treatment. On the basis of extensive research on the HBV lifecycle and virus-host interactions, several new agents focusing on viral and host targets are under development to cure HBV. New polymerase inhibitors, tenofovir alafenamide and besifovir provide effective and safer treatment for CHB patients. Agents targeting cccDNA, such as engineered site-specific nucleases and RNA interference therapeutics could eliminate cccDNA or silence cccDNA transcription. Inhibitors of HBV nucleocapsid assembly suppress capsid formation and prevent synthesis of HBV DNA. The HBV entry inhibitor, Myrcludex-B, has been shown to effectively inhibit amplification of cccDNA as well as the spread of intrahepatic infection. Agents targeting host factors that enhance innate and adaptive immune responses, including the lymphotoxin-β receptor agonist, toll-like receptor agonist, immune checkpoint inhibitors and adenovirus-based therapeutic vaccine, could play a critical role in the elimination of HBV-infected cells. With all of these promising approaches, we hope to reach the ultimate goal of a cure to HBV in the near future.

SH Ou, YP Chen, RL Jiang, J Peng (2016). "[\[Prognostic analysis of acute-on-chronic liver failure after withdrawal of nucleos\(t\)ide analogues for antiviral treatment of chronic hepatitis B\]](#)." *Zhonghua Gan Zang Bing Za Zhi* **24**(4): 252-257.

OBJECTIVE: To investigate the prognostic factors for acute-on-chronic liver failure (ACLF) after the withdrawal of nucleos(t)ide analogues (NAs) for the antiviral treatment of chronic hepatitis B (CHB). METHODS: The clinical data of 67 hospitalized patients with ACLF after withdrawal of NAs for the antiviral treatment of CHB were analyzed retrospectively. RESULTS: The HBeAg status before initial treatment and after recurrence, course of the antiviral treatment, duration from the withdrawal of NAs to recurrence, and type of NAs before and after withdrawal were not associated with the prognosis of ACLF. The Cox univariate regression analysis showed that serum bilirubin, international normalization ratio, serum creatinine, model of end-stage of liver disease (MELD) score, hepatic encephalopathy, and concurrent infection were associated with the 12-week death. The Cox multivariate regression analysis showed that MELD score and hepatic encephalopathy were independent predictors for 12-week death. The area under the receiver operating characteristic curve for the MELD score to predict 12-week death was 0.906, with an optimal cutoff value of 32, a sensitivity of 82.9%, a specificity of 88.5%, a positive predictive value of 91.9%, and a negative predictive value of 76.7%. CONCLUSION: MELD score and hepatic encephalopathy are closely associated with the prognosis of patients with ACLF after withdrawal of NAs for the antiviral treatment of CHB.

YQ Zhang, LJ Peng, YR Cao, ZP Zeng, YJ Wu, H Shi, SY Cheng, JY Wang, SC Friedman, JJ Sninsky, JS Guo (2016). "[Risk Factors for Hepatocellular Carcinoma in Cirrhotic Patients with Chronic Hepatitis B.](#)" *Genet Test Mol Biomarkers* **20**(9): 535-543.

AIMS: To investigate the clinical and genetic risk factors associated with hepatocellular carcinoma (HCC) in cirrhotic patients with chronic hepatitis B (CHB). METHODS: Nine hundred forty-nine Chinese Han patients with CHB were studied, including noncirrhotic patients without HCC ($N = 234$), cirrhotic patients without ($N = 281$) and with HCC ($N = 434$). Patients were genotyped for 10 candidate single nucleotide polymorphisms (SNPs) by the polymerase chain reaction (PCR)-ligase detection reaction (LDR) method. RESULTS: By multivariate logistic regression analysis adjusted for Child-Pugh scores, noneffective antiviral treatment, drinking history, family history of HCC, and age ≥50 years old were associated with HCC risk (odds ratio [OR] = 5.923, 2.456, 2.241, 1.955, respectively). Sixty-two of 170 cirrhotic patients who

achieved sustained virological suppression by antiviral treatment developed HCC, with fatty liver disease, family history of HCC, and family history of hepatitis B virus (HBV) infection as the risk factors (OR = 11.646, 3.339, 2.537, respectively). The SNPs associated with HCC risk in patients with cirrhosis and CHB were rs11536889 in TLR4 and rs2853744 in SPP1. Polymorphisms of TLR4 rs2149356, AP3S2 rs2290351, STXBP5L rs2169302, MLEC rs7976497, and SOCS3 rs4969168 were associated with HCC risk in specific stratified analyses with gender, age, and drinking history in the cirrhotic patients. CONCLUSIONS: Inadequate antiviral treatment, family history of HCC, drinking history, and age ≥ 50 years old are risk factors for HCC. Sustained suppression of HBV does not eliminate the risk of HCC. Specific host genetic factors may impact HCC development in Han Chinese cirrhotic patients with CHB, including SNPs in TLR4, SPP1, AP3S2, STXBP5L, MLEC, and SOCS3, which warrant further validation in additional cohorts.

SH Han, TT Tran (2015). "[Management of Chronic Hepatitis B: An Overview of Practice Guidelines for Primary Care Providers.](#)" *J Am Board Fam Med* **28**(6): 822-837.

Despite the introduction of hepatitis B virus (HBV) vaccination programs, chronic hepatitis B (CHB) remains an important disease burden worldwide and in the United States. A number of clinical practice guidelines are available to assist in the clinical management of CHB by providing recommendations regarding screening and diagnosis, treatment indications, and the choice, duration, and monitoring of treatment. Adherence to these guidelines has proven beneficial in terms of better treatment compliance, improved clinical outcomes, and lower likelihoods of emergency admission. This review summarizes current recommendations from the major clinical CHB practice guidelines and presents a simple algorithm for the treatment of patients with CHB to help primary care providers make informed choices in clinical practice. In general, antiviral treatment should be initiated in patients with CHB who have a high risk of liver-related morbidity and who are likely to respond to treatment, that is, patients with persistently elevated serum HBV DNA and either increased serum alanine aminotransferase concentrations or advanced liver disease. In patients who are eligible for antiviral therapy, treatment should be initiated with one of the recommended first-line therapies (pegylated interferon- α , entecavir, or tenofovir), and treatment efficacy should be monitored regularly for serum HBV DNA, alanine aminotransferase, and serologic responses. Patients who are not immediately considered for treatment should be monitored and started on antiviral therapy in case of disease progression. A number of issues in CHB management remain controversial or unresolved, such as identifying treatment candidates, managing partial or nonresponders, and predicting treatment response; we discuss some of the latest evidence around these topics.

JL Hou, D Xu, G Shi, M Wan, Z Goodman, D Tan, Q Xie, C Chen, L Wei, J Niu, Q Wang, H Ren, Y Wang, Jia, W Bao, Y Dong, A Trylesinki, NV Naoumov (2015). "[Long-Term Telbivudine Treatment Results in Resolution of Liver Inflammation and Fibrosis in Patients with Chronic Hepatitis B.](#)" *Adv Ther* **32**(8): 727-741.

INTRODUCTION: The long-term goal of chronic hepatitis B (CHB) treatment is improvement of liver disease and prevention of cirrhosis. The aim of this study was to assess whether prolonged telbivudine treatment improves liver inflammation and fibrosis. The primary objective was to evaluate the proportion of patients with absence/minimal inflammation (Knodel necroinflammatory score ≤ 3) on liver biopsy at Year 5. METHODS: Fifty-seven patients aged 16-70 years with a clinical history of CHB and active viral replication (38 hepatitis B e antigen [HBeAg] positive and 19 HBeAg negative) were followed for 6 years: 33 received telbivudine 600 mg/day continuously for 5 years; 24 received lamivudine 100 mg/day for 2 years and then telbivudine for 3 years. Liver biopsies were taken pre-treatment and after 5 years of treatment. RESULTS: At baseline, mean (standard deviation) serum hepatitis B virus (HBV) DNA load was 8.5 (1.7) log₁₀ copies/mL, Knodel necroinflammatory score was 7.6 (2.9), and Ishak fibrosis score was 2.2 (1.1). After antiviral treatment (median duration: 261 weeks), liver histology improved with increased proportions of patients with absence/minimal liver inflammation (Knodel necroinflammatory score ≤ 3), from 16% (9/57) at baseline to 98% (56/57), and absence/minimal fibrosis (Ishak score ≤ 1), from 25% (14/57) at baseline to 84% (48/57). At Year 5, HBV DNA load was <300 copies/mL for all patients; cumulative HBeAg loss and seroconversion rates were 88% and 77%, respectively. At Year 6, 95% of patients with abnormal baseline glomerular filtration rate (60-90 mL/min/1.73 m²) improved to normal GFR (>90 mL/min/1.73 m²). CONCLUSION: Long-term telbivudine treatment with profound and durable viral suppression significantly improved liver histology, thus achieving the long-term goals of CHB treatment. FibroScan(®) results after 5 and 6 years of treatment (in almost 20% of patients) were consistent with this information. FUNDING: Novartis and National Science and Technology Major Project (2012ZX10002003). TRIAL REGISTRATION: ClinicalTrials.gov # NCT00877149.

I Rapti, S Hadziyannis (2015). "[Risk for hepatocellular carcinoma in the course of chronic hepatitis B virus infection and the protective effect of therapy with nucleos\(t\)ide analogues.](#)" *World J Hepatol* 7(8): 1064-1073.

Hepatocellular carcinoma (HCC) is a major health problem worldwide, representing one of the leading causes of death. Chronic hepatitis B virus (HBV) infection (CHB) is the most important etiologic factor of this tumor, accounting for the development of more than 50% of the cases in the world. Primary prevention of HCC is possible by hepatitis B vaccination conferring protection from HBV infection. However, according to the World Health Organization Hepatitis B Fact sheet N° 204 (update of July 2014) globally there exists a large pool of > 240 million people chronically infected with HBV who are at risk for development of HCC. These individuals represent a target population for secondary prevention both of cirrhosis and of HCC. Since ongoing HBV replication in CHB is linked with the progression of the underlying liver disease to cirrhosis as well as with the development of HCC, effective antiviral treatment in CHB has also been evaluated in terms of secondary prevention of HCC. Currently, most patients with active CHB are subjected to long term treatment with the first line nucleos(t)ide analogues entecavir and tenofovir. These compounds are of high antiviral potency and have a high barrier to HBV resistance compared to lamivudine, adefovir dipivoxil and even telbivudine. Many studies have shown that patients under antiviral treatment, especially those in virological remission, develop less frequently HCC compared to the untreated ones. However, the risk for development of HCC cannot be eliminated. Therefore, surveillance for the development of HCC of patients with chronic hepatitis B must be lifelong or until a time in the future when new treatments will be able to completely eradicate HBV from the liver particularly in the early stages of CHB infection. In this context, the aim of this review is to outline the magnitude of the risk for development of HCC among patients with CHB, in the various phases of the infection and in relation to virus, host and environmental factors as evaluated in the world literature. Moreover, the benefits of antiviral treatment of CHB with nucleos(t)ide analogs, which have changed the natural history of the disease and have reduced but not eliminated the risk of HCC are also reviewed.

M Ringelhan, T O'Connor, U Protzer, M Heikenwalder (2015). "[The direct and indirect roles of HBV in liver cancer: prospective markers for HCC screening and potential therapeutic targets.](#)" *J Pathol* 235(2): 355-367.

Chronic hepatitis B virus (HBV) infection remains the number one risk factor for hepatocellular carcinoma (HCC), accounting for more than 600 000 deaths/year. Despite highly effective antiviral treatment options, chronic hepatitis B (CHB), subsequent end-stage liver disease and HCC development remain a major challenge worldwide. In CHB, liver damage is mainly caused by the influx of immune cells and destruction of infected hepatocytes, causing necro-inflammation. Treatment with nucleoside/nucleotide analogues can effectively suppress HBV replication in patients with CHB and thus decrease the risk for HCC development. Nevertheless, the risk of HCC in treated patients showing sufficient suppression of HBV DNA replication is significantly higher than in patients with inactive CHB, regardless of the presence of baseline liver cirrhosis, suggesting direct, long-lasting, predisposing effects of HBV. Direct oncogenic effects of HBV include integration in the host genome, leading to deletions, cis/trans-activation, translocations, the production of fusion transcripts and generalized genomic instability, as well as pleiotropic effects of viral transcripts (HBsAg and HBx). Analysis of these viral factors in active surveillance may allow early identification of high-risk patients, and their integration into a molecular classification of HCC subtypes might help in the development of novel therapeutic approaches.

M Toy, DW Hutton, SK So (2015). "[Cost-Effectiveness and Cost Thresholds of Generic and Brand Drugs in a National Chronic Hepatitis B Treatment Program in China.](#)" *PLoS One* 10(11): e0139876.

Chronic liver disease and liver cancer associated with chronic hepatitis B (CHB) are leading causes of death among adults in China. Although newborn hepatitis B immunization has successfully reduced the prevalence of CHB in children, about 100 million Chinese adults remain chronically infected. If left unmanaged, 15-25% will die from liver cancer or liver cirrhosis. Antiviral treatment is not necessary for all patients with CHB, but when it is indicated, good response to treatment would prevent disease progression and reduce disease mortality and morbidity, and costly complications. The aim of this study is to analyze the cost-effectiveness of generic and brand antiviral drugs for CHB treatment in China, and assessing various thresholds at which a highly potent, low resistance antiviral drug would be cost-saving and/or cost-effective to introduce in a national treatment program. We developed a Markov simulation model of disease progression using effectiveness and cost data from the medical literature. We measured life-time costs, quality adjusted life years (QALYs), incremental cost-effectiveness ratios (ICERs), and clinical outcomes. The no treatment strategy incurred the highest health care costs (\$12,932-\$25,293) per patient, and the worst health outcomes, compared to the antiviral treatment strategies. Monotherapy with either entecavir or tenofovir yielded the most QALYs (14.10-19.02) for both HBeAg-

positive and negative patients, with or without cirrhosis. Threshold analysis showed entecavir or tenofovir treatment would be cost saving if the drug price is \$32-75 (195-460 RMB) per month, highly cost-effective at \$62-110 (379-670 RMB) per month and cost-effective at \$63-120 (384-734 RMB) per month. This study can support policy decisions regarding the implementation of a national health program for chronic hepatitis B treatment in China at the population level.

Y Zhang, L Peng, Y Cao, Z Zeng, Y Wu, H Shi, S Chen, J Guo (2015). "[Analysis of the risk factors of hepatocellular carcinoma in cirrhotic patients with chronic hepatitis B](#)." *Zhonghua Gan Zang Bing Za Zhi* **23**(7): 512-516.

OBJECTIVE: To identify risk factors of hepatocellular carcinoma (HCC) in cirrhotic patients with chronic hepatitis B (CHB). METHODS: A total of 715 cirrhotic patients with CHB were recruited from the Zhongshan Hospital Affiliated to Fudan University and enrolled in this case-control study between January 2009 and September 2014. All participants were Chinese Han residing in Shanghai and the surrounding areas. The patients were divided into a cirrhosis group (n = 281) and a HCC group (n = 434). History of hepatitis B infection and HCC, as well as clinical data from serological, imaging and pathological examinations were collected for analysis. SPSS software, version 19.0, was used for all statistical comparisons. RESULTS: Single factor analysis indicated that development of HCC in cirrhotic patients with CHB was significantly associated with male sex, age of 50 years or more, family history of HCC, alcohol consumption, fatty liver, detectable levels of hepatitis B virus (HBV) DNA, and history of HBV infection without effective antiviral treatment. Multivariate logistic regression analysis indicated that age of 50 years or more (P = 0.005, odds ratio [OR] = 1.766), history of alcohol consumption (P = 0.002, Or = 2.570), family history of HCC (P = 0.014, Or = 2.268), fatty liver (P = 0.023, Or = 3.390), and history of HBV infection without effective antiviral treatment (P < 0.001, Or = 5.389) were risk factors of HCC. The risk factors for development of HCC in cirrhotic patients with hepatitis B after achieving sustained virologic suppression (SVS) were family history of HBV infection (P = 0.014, Or = 2.537), family history of HCC (P = 0.037, Or = 3.339) and fatty liver (P = 0.018, Or = 11.646). CONCLUSION: Risk factors of HCC in cirrhotic patients with CHB include age, drinking history, family history of HCC, fatty liver, and ineffective antiviral treatment of CHB. Family history of HBV infection or HCC, and fatty liver disease, were significantly associated with HCC development after SVS in patients with hepatitis B-related cirrhosis.

ZG Zhou, XR Zheng, Q Zhou, M Shi, YJ Zhang, RP Guo, YF Yuan, MS Chen, XJ Lin, XM Lao, SP Li (2015). "[Impact of oral anti-hepatitis B therapy on the survival of patients with hepatocellular carcinoma initially treated with chemoembolization](#)." *Chin J Cancer* **34**(5): 205-216.

INTRODUCTION: Most hepatocellular carcinomas (HCC) develop in a background of underlying liver disease including chronic hepatitis B. However, the effect of antiviral therapy on the long-term outcome of patients with hepatitis B virus (HBV)-related HCC treated with chemoembolization is unclear. This study aimed to evaluate the survival benefits of anti-HBV therapy after chemoembolization for patients with HBV-related HCC. METHODS: A total of 224 HCC patients who successfully underwent chemoembolization were identified, and their survival and other relevant clinical data were reviewed. Kaplan-Meier and Cox regression analyses were performed to validate possible effects of antiviral treatment on overall survival (OS). RESULTS: The median survival time (MST) was 15.9 [95% confidence interval [CI], 9.5-27.7] months in the antiviral group and 9.6 [95% CI, 7.8-13.7] months in the non-antiviral group (log-rank test, P = 0.044). Cox multivariate analysis revealed that antiviral treatment was a prognostic factor for OS (P = 0.008). Additionally, a further analysis was based on the stratification of the TNM tumor stages. In the subgroup of early stages, MST was significantly longer in the antiviral-treatment group than in the non-antiviral group (61.8 months [95% CI, 34.8 months to beyond the follow-up period] versus 26.2 [95% CI, 14.5-37.7] months, P = 0.012). Multivariate analysis identified antiviral treatment as a prognostic factor for OS in the early-stage subgroup (P = 0.006). However, in the subgroup of advanced stages, MST of the antiviral-treated group was comparable to that of the non-antiviral group (8.4 [95% CI, 5.2-13.5] months versus 7.4 [95% CI, 5.9-9.3] months, P = 0.219). Multivariate analysis did not indicate that antiviral treatment was a significant prognostic factor in this subgroup. CONCLUSION: Antiviral treatment is associated with prolonged OS time after chemoembolization for HCC, especially in patients with early-stage tumors.

J Yang, G Chen, X Chen, H Zhang, D Jian, G Yang (2015). "[Initial combination anti-viral therapy with lamivudine and adefovir dipivoxil decreases short-term fatality rate of hepatitis-B-virus-related acute-on-chronic liver failure](#)." *Virol J* **12**: 97.

BACKGROUND: Acute-on-chronic liver failure (ACLF) is a common serious hepatitis B virus (HBV)-related disease and has a poor prognosis. Until recently, initial combination antiviral treatment in ACLF patients

was rarely reported. This study evaluated the effect of initial combination treatment with lamivudine and adefovir dipivoxil on the prognosis of HBV-related ACLF. **METHODS:** In this retrospective study, 131 eligible ACLF patients, including 61 treated with 100 mg lamivudine and 10 mg adefovir dipivoxil daily and 70 not treated with any nucleoside analogs (NAs), were selected and assigned into the NA and non-NA groups. All the patients received standard medicinal therapy. At weeks 0-4 and 12, serum markers for hepatic and renal functions were measured in all patients and accumulated fatality rates were calculated. Statistical analyses, including Student's t test, χ^2 test and unconditional logistic regression analysis, were performed using SPSS version 17.0 software. **RESULTS:** Clinical data indicated that improvement of hepatic function was better in the NA than in the non-NA group. The accumulated fatality rate in the NA group was lower than in the non-NA group at weeks 2-4 and 12, and these differences were significant. Univariate analysis showed that age, prothrombin activity, model of end-stage liver disease (MELD) score, and treatment without NAs were risk factors for short-term survival of ACLF. Further research by unconditional logistic regression analysis identified that older age, high MELD score and treatment without NAs were independent risk factors for short-term survival of ACLF. **CONCLUSIONS:** Initial combination antiviral treatment is effective in decreasing short-term fatality of HBV-related ACLF.

M Bhat, P Ghali, M Deschenes, P Wong (2014). "[Prevention and Management of Chronic Hepatitis B.](#)" *Int J Prev Med* **5**(Suppl 3): S200-207.

P Hu, GD Zhao, H Li, T Gao, ST Li, WL Tang, HJ Zhou, H Wang, Q Xie (2014). "[Effects of oral antiviral agents on long-term outcomes of treatment-naïve patients with HBV-related decompensated cirrhosis: a retrospective cohort study](#)." *Zhonghua Gan Zang Bing Za Zhi* **22**(11): 806-811.

JS Koskinas, M Deutsch, S Adamidi, M Skondra, M Tampaki, A Alexopoulou, S Manolakopoulos, D Pectasides (2014). "[The role of tenofovir in preventing and treating hepatitis B virus \(HBV\) reactivation in immunosuppressed patients. A real life experience from a tertiary center.](#)" *Eur J Intern Med* **25**(8): 768-771.

A Perrella, AG Lanza, D Pisaniello, G DiCostanzo, F Calise, O Cuomo (2014). "[Telbivudine prophylaxis for hepatitis B virus recurrence after liver transplantation improves renal function.](#)" *Transplant Proc* **46**(7): 2319-2321.

CM Tang, TO Yau, J Yu (2014). "[Management of chronic hepatitis B infection: current treatment guidelines, challenges, and new developments.](#)" *World J Gastroenterol* **20**(20): 6262-6278.

A Perrakis, T Förtsch, A Del Medico, RS Croner, N Vassos, S Yedibela, C Lohmüller, S Zopf, W Hohenberger, V Müller (2013). "[Liver transplantation for hepatitis B-induced liver disease: long-term outcome and effectiveness of antiviral therapy for prevention of recurrent hepatitis B infection.](#)" *Transplant Proc* **45**(5): 1953-1956.

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Part II Treatment as prevention (TAP)

2. Treatment as to prevent perinatal mother to child transmission (MTCT) of hepatitis B – Liver disease progression

Introduction of the participants

VHPB secretariat

- 16:30-16h:45** Welcome and opening of the meeting
- Welcome and opening
 - Introduction of the participants

1. Treatment as to prevent perinatal mother to child transmission (MTCT) of hepatitis B


Session 2.1.1: Overview TAP in MTCT

Chairs: Antons Mozalevskis and Mark Kane

- Conclusions of Pre-recorded presentation
- 16h:45-16:55** **Who to treat**
Prevention of perinatal hepatitis B virus transmission.
Pre recorded
Kelvin Cheung
- 16h:55-17:10** **Efficacy and Safety of TAP In pregnancy**
Efficacy and safety of antiviral prophylaxis during pregnancy to prevent mother-to-child transmission of hepatitis B virus: a systematic review and meta-analysis.
LIVE
Yusuke Shimakawa
- Cost-effectiveness (see later)**

Session 2.1.2: Guidelines and recommendation for TAP in MTCT

- 17h:10-17:25** **Pre-recorded Lessons learnt from Treatment as prevention in real world (Western Pacific)**
Progress Toward Hepatitis B Control and Elimination of Mother-to-Child Transmission of Hepatitis B Virus - Western Pacific Region, 2005-2017.
Pre recorded
Rania Tohme
- 17:25-17:40** New recommendations on HBV prevention of mother-to-child transmission and the use of NUCs as an additional PMTCT intervention.
LIVE
Antons Mozalevskis

17:40-17:55	Cost-effectiveness Mother-to-child transmission of hepatitis B: What more needs to be done to eliminate it around the world  <i>Shevanthi Nayagam</i>
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Session 2.1.3: Groups discussion: hepatitis treatment as prevention

17:55-18:35	<p>Groups discussion: hepatitis TAP be included in guidelines and recommendations</p> <p>Questions to be answered:</p> <ol style="list-style-type: none"> 1. Are the new WHO recommendations on HBV prevention of perinatal transmission, including TAP and added value to reach the hepatitis elimination goals? <p>Chair: Vana Papaevangelou</p> <ol style="list-style-type: none"> 2. In low endemic countries (Europe) should we focus on Screening and TAP in pregnant women or on Birth dose vaccination or both? <p>Chair: Silvia Bino</p>
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Pagina-einde

2. Treatment to prevent liver disease progression

Session 2.2.1: Overview treatment to prevent liver disease progression in HbsAg positives

18:35-18:50	<p>Conclusions of <u>Pre-recorded</u> presentation</p> <p>Evidence for application of treatment to prevent liver disease progression in hepatitis B</p>  <i>Homie Razavi</i>
	<p>Country example Uzbekistan</p> <p>Toward Hepatitis B and Hepatitis C Elimination Using a Catalytic Funding Model - Tashkent, Uzbekistan,</p>  <i>Shakhlo Sadirova</i>

Session 2.2.2: Groups discussion: hepatitis treatment as prevention liver disease progression

18:50-19:30

Groups discussion: hepatitis TAP be included in guidelines and recommendations
Questions to be answered:

1. Is there enough scientific evidence to recommend treatment to prevent liver disease progression in the context of public health

Chair: John Ward

2. Is treatment for all patients who tested positive for Hepatitis B feasible (resources)

Chair: Daniel Shouval

PARTICIPANTS LIST

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Speakers		
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Kojouharova	Mira	Bulgaria
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Reic	Tatjana	Croatia
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