Progress towards elimination of mother-to-child transmission of hepatitis B virus infection in China: a modelling analysis

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Objective To determine the projected burden of hepatitis B virus (HBV) in China, the intervention strategies that can eliminate mother-to-child transmission (MTCT) by 2030 or earlier and the measurable parameters that can be used to monitor progress towards this target.
Methods We developed a dynamic, sex- and age-stratified model of the HBV epidemic in China, calibrated using hepatitis B surface antigen (HBsAg) and e antigen (HBeAg) prevalence data from sequential national serosurveys (1979–2014) and the numbers of HBV-related cancer deaths (2012). We determined whether China can achieve elimination of MTCT of HBV by 2030 under current prevention interventions. We modelled various intervention scenarios to represent different coverage levels of birth-dose HBV vaccination, hepatitis B immunoglobulin to newborns of HBsAg-positive mothers and antiviral therapy (tenofovir) to HBeAg-positive pregnant women.
Findings We project that, if current levels of prevention interventions are maintained, China will achieve the elimination target by 2029. By modelling various intervention scenarios, we found that this can be brought forward to 2025 by increasing coverage of birth-dose vaccination, or to 2024 by the administration of tenofovir to HBeAg-positive pregnant women. We found that achievement of the target by 2025 would be predicted by a measurement of less than 2% MTCT in 2020.
Conclusion Our results highlight how high-quality national data can be combined with modelling in monitoring the elimination of MTCT of HBV. By demonstrating the impact of increased interventions on target achievement dates, we anticipate that other high-burden countries will be motivated to strengthen HBV prevention policies.

Abstracts in عربي, 中文, Français, Русский and Español at the end of each article.

Introduction

The global momentum towards the elimination of viral hepatitis is growing. The World Health Assembly adopted the first global viral hepatitis elimination target in 2016 in calling for a 90% reduction in new chronic hepatitis B virus (HBV) infections by 2030, and the *Global health sector strategy* outlined a target of achieving a childhood prevalence of hepatitis B surface antigen (HBsAg) of 0.1% by 2030.[1]

In China, the government have identified HBV as a significant health issue, and the virus is one of six major infectious diseases included in the latest 5-year Chinese national plan.[2] Substantial progress has been made over the past 20 years in implementing high national levels of coverage of interventions to prevent both horizontal transmission (infant HBV vaccination) and vertical transmission (birth-dose HBV vaccination within 24 hours of birth and hepatitis B immunoglobulin, Ig). The results of sequential national serosurveys in China reveal a reduction in the prevalence of HBsAg in children younger than 5 years from 9.7% in 1992, to 1.0% in 2006 and to 0.3% in 2014.[3]

Despite these public health efforts in China, there remains ongoing transmission of HBV. The major route is mother-to-child transmission (MTCT);[4] even with the use of birth-dose HBV vaccination and hepatitis B Ig, about 2–9% of mothers who test positive for hepatitis B e antigen (HBeAg) transmit HBV to their newborns.[5,6] There is now accumulating evidence, particularly from China, that the additional use of tenofovir during the final trimester of pregnancy is a safe and effective method of further reducing MTCT.[7–10] However, the impact of this strategy at a population level is unknown.

In 2017, the National Health Commission of the People's Republic of China (formerly the National Health and Family Planning Commission of China) and the World Health Organization (WHO) Western Pacific Region endorsed a framework for the triple elimination of MTCT of human immunodeficiency virus (HIV), HBV and syphilis by 2030.[11] The focus has now shifted from HBV control to the elimination of MTCT of HBV, the achievement of which by any country has not yet been validated by WHO. Elimination of MTCT is defined in China as an HBsAg prevalence of less than 0.1% in children aged 1–4 years, a directly measurable indicator in national serosurveys.

Given the global momentum and the available strategies to further reduce MTCT of HBV, there exists the real possibility of eliminating this route of transmission in China before 2030. Using a dynamic simulation model of the HBV epidemic in China, we aim to determine: (i) the current and projected burden of HBV nationwide; (ii) whether MTCT of HBV can be eliminated by 2030; (iii) which strategies could allow China to eliminate MTCT of HBV before 2030; and (iv) the indicators that can be used to measure progress towards this target.

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(*Submitted: 25 November 2019 – Revised version received: 10 September 2020 – Accepted: 14 September 2020 – Published online: 28 October 2020*)

Table 1. **Sources of transmission, calibration and intervention coverage data used to calibrate dynamic modelling of hepatitis B virus, China, 2019**

Variable	Value (%)	Source
MTCT parameters		
HBeAg− mother, birth-dose vaccination	0	Lu et al.[12]
HBeAg+ mother, birth-dose vaccination	0.127	Ying et al. (2017, personal communication)
HBeAg− mother, birth-dose vaccination and hepatitis B Ig	0	Lu et al.[12]
HBeAg+ mother, birth-dose vaccination and hepatitis B Ig	0.056	Ying et al. (2017, personal communication)
HBeAg+ mother, birth-dose HBV vaccination, hepatitis B Ig and tenofovir	0.01	Hyun et al.[9] (to represent an 80% reduction in MTCT with addition of tenofovir)
Calibration data		
Prevalence of HBsAg by sex and age, years		
Male, 1–4	9.71	China CDC National Serosurvey 1979[13]
Male, 5–14	11.45–11.96	
Male, 15–59	7.38–11.55	
Male, 60–89	1.29–5.06	
Female, 1–4	7.92	
Female, 5–14	7.79–9.08	
Female, 15–59	5.72–7.76	
Female, 60–89	3.66–4.55	
Male, 1–4	9.18	China CDC National Serosurvey 1992[14]
Male, 5–14	10.89–11.94	
Male, 15–59	8.07–12.28	
Male, 60–64	11.76	
Female, 1–4	7.30	
Female, 5–14	7.88–9.07	
Female, 15–59	5.87–8.97	
Female, 60–64	14.81	
Male, 1–4	1.21	China CDC National Serosurvey 2006[15]
Male, 5–14	1.82–3.77	
Male, 15–59	8.48–10.91	
Female, 1–4	0. 93	
Female, 5–14	1.37–2.95	
Female, 15–59	5.79–7.47	
Male, 1–4	0.35	China CDC National Serosurvey 2014[16]
Male, 5–14	0.47–1.28	
Male, 15–29	2.82–6.32	
Female, 1–4	0.28	
Female, 5–14	0.70–1.43	
Female, 15–29	2.70–4.88	
Prevalence of HBeAg by sex and age, years		
Male, 1–4	70.75	China CDC National Serosurvey 2006[17]
Male, 5–14	66.38–70.54	
Male, 15–59	10.60–52.67	
Female, 1–4	66.20	
Female, 5–14	64.71–68.35	
Female, 15–59	11.86–56.79	
Male, 1–4	87.46	China CDC National Serosurvey 2014[3]
Male, 5–14	53.42–66.47	
Male, 15–29	37.03–59.38	
Female, 1–4	90.17	
Female, 5–14	32.97–61.37	
Female, 15–29	15.62–44.70	
Intervention coverage		Liu et al.,[18] WHO[19]
Infant vaccination, 1992–2018	32.6–99.49	
Birth-dose vaccination,1992–2018	23.5–96.05	

−: negative; +: positive; CDC: Centers for Disease Control and Prevention; HBeAg: hepatitis B e antigen; HBsAg: hepatitis B surface antigen; HBV: hepatitis B virus; Ig: immunoglobulin; MTCT: mother-to-child transmission; WHO: World Health Organization.

Table 2. **Main intervention scenarios considered in achieving the elimination of mother-to-child transmission of hepatitis B virus, China, from 2019**

Intervention scenario	% of relevant population covered		
	Birth-dose HBV vaccination of all newborns	Hepatitis B Ig to newborns of HBsAg+ mothers	Tenofovir to HBeAg+ pregnant women
Status quo (2016)	95.9	99.5	0.0
A: Increased birth-dose vaccination from 2019	99.0	99.5	0.0
B: Scenario A with increased hepatitis B Ig from 2019	99.0	99.9	0.0
C: Scenario B with tenofovir	99.0	99.9	50.0
D: Scenario B with tenofovir	99.0	99.9	70.0
E: Scenario B with tenofovir	99.0	99.9	90.0

+: positive; HBeAg: hepatitis B e antigen; HBsAg: hepatitis B surface antigen; HBV: hepatitis B virus; Ig: immunoglobulin.
Note: Infant vaccinations remain unchanged from status quo in all scenarios.

Methods

Model parameterization

We developed a dynamic, age- and sex-stratified simulation model of the HBV epidemic in China at a national level, incorporating the latest locally available epidemiological and demographic data. We based our dynamic model on a previously published transmission model that has been parameterized and calibrated to China-specific data (Table 1).[20] Our model is calibrated to HBsAg prevalence from four large nationally representative serosurveys (conducted in 1979, 1992, 2006 and 2014; available in the data repository),[3,13,17,21] HBeAg prevalence from 2006 and 2014, and the numbers of HBV-related cancer deaths in China (using overall liver cancer deaths[22] with a 70.0% HBV-attributable fraction applied).[23] We stratified MTCT percentages and the efficacy of prevention of MTCT (PMTCT) interventions by HBeAg status, and parameterized these with data from China (data repository;[21] Table 1). Regarding the efficacy of combined birth-dose HBV vaccination, hepatitis B Ig and tenofovir treatment for HBeAg-positive mothers, we assumed a residual transmission of 1.0%, consistent with an 80.0% transmission reduction compared with birth-dose vaccination and hepatitis B Ig only.[9]

We parameterized the historical coverage of infant and birth-dose vaccination by using annual national immunization programme data.[18] Hepatitis B Ig administration became national policy in 2010, and coverage was 91.2% in 2013 and 99.5% in 2016. The use of tenofovir by pregnant women with a high viral load (> 6–7 $\log_{10}$ international units per mL) to prevent MTCT of HBV is recommended by the Asian Pacific Association for the Study of the Liver 2015 guidelines,[24] but this intervention is usually limited to tertiary health-care centres and is not national policy. We assumed that historical population-level use of tenofovir during pregnancy was zero.

In all analyses, our primary outcome measure was whether China can achieve elimination of MTCT of HBV and the year of achieving that target. Our secondary outcome measure was the cumulative number of new infections averted under the different intervention scenarios.

Intervention scenarios

We first modelled the epidemic under a status quo scenario, that is, intervention coverage remaining at current (2016) levels. We then modelled different scenarios to represent the various increases in and additions to this status quo intervention from 2019 (Table 2). In Scenario A, birth-dose vaccination is increased from 95.9% in 2016 to 99.0%. In Scenario B, in addition to the birth-dose vaccination increase in Scenario A, hepatitis B Ig is also increased from 99.5% in 2016 to 99.9%. Scenarios C–E represent Scenario B with the further addition of peripartum antiviral treatment, namely the administration of tenofovir to 50.0%, 70.0% and 90.0% of HBeAg-positive pregnant women, respectively. We used HBeAg status as a proxy for high viral load, as this is supported by data from China.[12]

Further analysis

Although elimination of MTCT of HBV is defined in China as a prevalence of HBsAg of less than 0.1% in children aged 1–4 years, there are alternative age ranges that can be used. We therefore also modelled the outcome of status quo interventions when changing the age group in which prevalence is measured to all children younger than 5 years and to children exactly 5 years.

We also performed a sensitivity analysis to explore how five different fertility projections would affect outcomes. These projections included three United Nations estimates of fertility at median, high and low levels,[25] and two hypothetical scenarios representing the relaxation of China's one-child policy (i.e. increased fertility) where fertility returned to 1965 levels for women (i) of all ages or (ii) older than 30 years.

Separately, we also evaluated the impact of (i) reducing HBV prevention interventions to 50.0% and 80.0% of current levels; and (ii) catch-up vaccination campaigns for children aged 2 years, 2–15 years and 12–13 years, in which 100.0% of unvaccinated and susceptible children in each age group were vaccinated (data repository).[21]

Finally, we also determined the cost of an intervention package that would allow a population strategy of peripartum tenofovir to be cost-effective. This cost represents the package required for the successful delivery of the intervention, and would include antiviral drugs for 4 months, diagnostics needed to select those in need of treatment (HBeAg status as a proxy for HBV viral load) and treatment monitoring costs. We used a cost–effectiveness threshold of United States dollars (US$) 4062 per disability-adjusted life year averted, which represents half the gross domestic product per capita of China, in line with current recommended international guidelines.[26]

Measuring progress

To monitor progress towards achieving elimination of MTCT of HBV, we considered the relation between MTCT values and the year in which the elimination prevalence target would be reached for both (i) all HBsAg-positive mothers and (ii) HBeAg-positive mothers only. For each of our five intervention scenarios, we plotted the projected MTCT in 2020 (the intervention having been scaled up in 2019) against the corresponding year of achievement of the elimination target.

Results

HBV burden

Our model estimates that in 2017 there were 78 million people living with chronic HBV infection, consistent with existing burden estimates.[27,28] At current levels of coverage, we project 198 000 new chronic infections and 7.7 million deaths between 2019 and 2030 (data repository).[21]

Status quo

By maintaining current intervention programmes, China is predicted to reach the elimination target of less than 0.1% HBsAg prevalence in children aged 1–4 years by 2029 (Fig. 1). This reduction in the epidemic at status quo levels of intervention is explained by the fact that, with time, the year in which a woman of child-bearing age was born corresponds to higher vaccination coverage levels at birth, and therefore lower HBsAg prevalence among pregnant women in future years (data repository).[21]

Intervention scenarios

Compared with the status quo, our model shows that by increasing coverage of birth-dose HBV vaccination from 95.9% in 2016 to 99.0% (Scenario A), 54 000 new chronic infections will be avoided by 2030 (Fig. 2) and the elimination target will be reached by 2025 (Fig. 3). The incremental impact of an increase in hepatitis B Ig coverage (Scenario B) is small as coverage is already very high, and does not change the year of target achievement (Fig. 4). The addition of tenofovir administration to pregnant women at 50.0%, 70.0% and 90.0% coverage levels (scenarios C, D and E, respectively) would avoid a further 37 000, 52 000 and 67 000 new chronic infections, respectively, compared with Scenario B (Fig. 2), and bring the year of elimination target achievement forward to 2024 in all cases (Fig. 4).

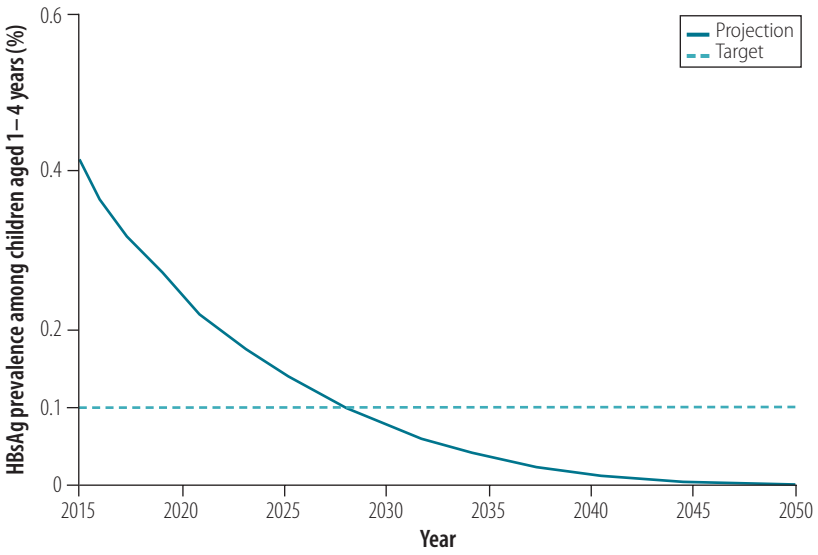
Further analysis

We show in data repository how the year of achieving the elimination target changes with the definition of elimination; if HBsAg prevalence of less than 0.1% in children aged 0–5 years or exactly 5 years is the target, this would be achieved in 2028 and 2030, respectively.[21]

Our different hypothetical fertility projections show that, if fertility levels return to pre-1965 levels in women of all ages or only in women older than 30 years, the projected fall in prevalence of HBsAg in children will slow. This reduced rate of prevalence decline would mean that the year of achieving the elimination target would be delayed to 2030 and 2032, respectively (data repository).[21] This result is due to the fact that HBsAg prevalence among older women is higher, as they are less likely to have benefitted from the vaccination programme.

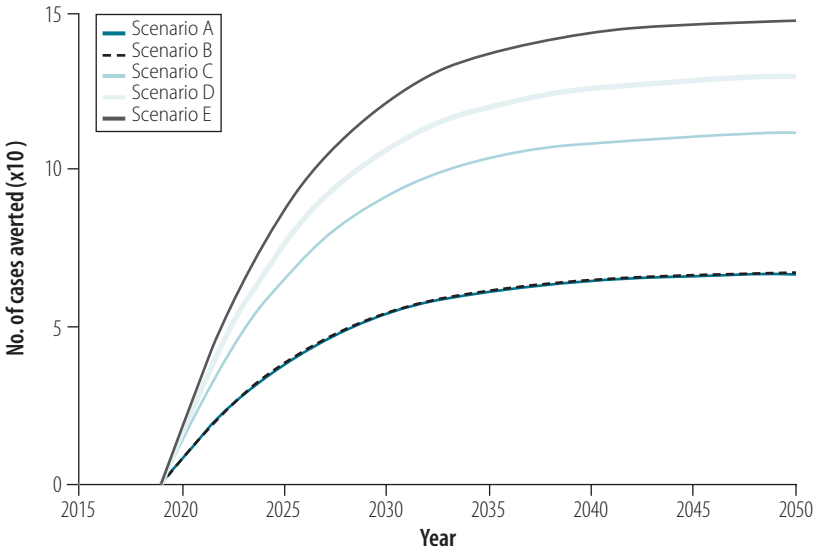
We show that a reduction in prevention interventions will slow down or even reverse the decline in HBsAg prevalence (data repository).[21] A reduction in coverage of birth-dose HBV vaccination to 80.0% or 50.0% of current levels would lead to 278 000 and 803 000

Fig. 1. **Projections of prevalence of hepatitis B surface antigen among children aged 1–4 years for current levels of interventions to prevent transmission of hepatitis B virus, China, 2015–2050**



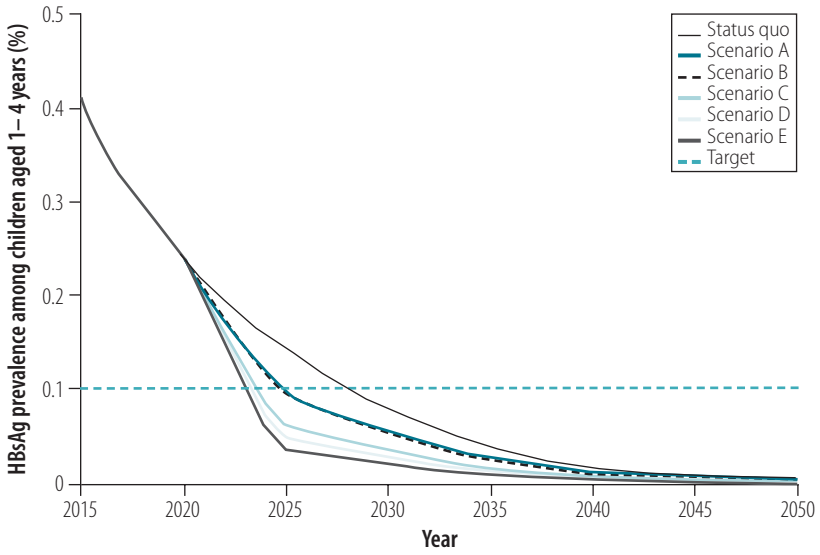
HBsAg: hepatitis B surface antigen.

Fig. 2. **Impact of intervention scenarios to prevent mother-to-child transmission of hepatitis B virus on the number of cases averted, China, 2015–2050**



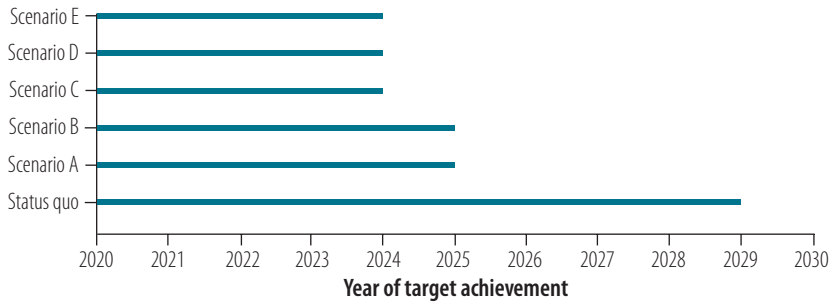
Note: As in Table 2, scenarios are defined as increased coverage of birth-dose vaccination (A), plus increased coverage of hepatitis B Ig (B), plus 50.0% (C), 70.0% (D) and 90.0% (E) coverage of tenofovir.

Fig. 3. **Impact of intervention scenarios to prevent mother-to-child transmission of hepatitis B virus on the prevalence of hepatitis B surface antigen among children aged 1–4 years, China, 2015–2050**



HBsAg: hepatitis B surface antigen.
Note: As in Table 2, scenarios are defined as increased coverage of birth-dose vaccination (A), plus increased coverage of hepatitis B Ig (B), plus 50.0% (C), 70.0% (D) and 90.0% (E) coverage of tenofovir.

Fig. 4. **Impact of intervention scenarios to prevent mother-to-child transmission of hepatitis B virus on year of target achievement, China**



Note: The target is a prevalence of hepatitis B antigen less than 0.1% among children aged 1–4 years. As in Table 2, scenarios are defined as increased coverage of birth-dose vaccination (A), plus increased coverage of hepatitis B Ig (B), plus 50.0% (C), 70.0% (D) and 90.0% (E) coverage of tenofovir.

further new infections, respectively, during 2019–2030, and would push back the date of elimination target achievement to 2036 and 2040, respectively.

We project that catch-up vaccination campaigns will have a lower impact relative to the five main intervention scenarios. We estimate that 1800 new chronic infections will be averted by 2030 by targeting children aged 2–15 years, but this number is less than 500 if groups aged 2 or 12–13 years are targeted. We also project that catch-up programmes will not bring the year of elimination target achievement any closer (data repository).[21]

We estimate that administration of peripartum tenofovir would be cost-effective if the price of an intervention package falls between US$ 11 (for a 10% discount rate) and US$ 197 (for a 3% discount rate), assuming a long-term perspective.[29] However, if a population-level scale-up of antiviral treatment for those with chronic HBV infection became policy, the cost of the intervention package would need to be even lower to be cost-effective.

Measuring progress

We show how measured MTCT in a particular year can be used to predict the year in which the elimination target will be achieved. For example, if in 2020 we measure MTCT values of less than 2.1% among all HBsAg-positive mothers (Fig. 5) and of 6.5% in only HBeAg-positive mothers (data repository),[21] we can predict that the elimination target will be achieved by 2025.

Discussion

Our modelling study has shown that, at the current high levels of prevention interventions, China could be one of the high-burden countries to achieve elimination of MTCT of HBV before the 2030 global targets. However, our results also highlight that these high levels of prevention interventions must be maintained, as any reductions in coverage will delay the achievement of the elimination target.

Although we have also demonstrated that the addition of tenofovir treatment in pregnancy as an extra method of preventing MTCT will have a substantial impact on the trajectory of the epidemic in China, it must be noted that this result relies on certain assumptions about the population-based efficacy of tenofovir treatment. Our analysis provides projections of the possible impact under ideal conditions, including high levels of coverage and adherence to a peripartum antiviral therapy strategy. However, whether these conditions can be achieved in a real-world setting will also depend on the availability of good-quality health-care services, adherence of patients to HBV antiviral therapy during pregnancy and the availability of screening tests with high diagnostic performance. Our projections are also dependent on how the Chinese government can increase these prevention strategies by such a large scale, overcoming logistical barriers and increasing education among health-care workers and patients regarding the importance of PMTCT of HBV strategies. Implementation projects such as the Shield Project, which are piloting methods of increasing such interventions in China,[4] will provide much-needed real-world data on MTCT of HBV and on innovations to reduce vertical transmission in China. Such empirical data will help to refine our model projections, and can become part of the iterative process where applied modelling is used to help with programmatic support.

By using HBeAg status (an accurate marker of viral load, as confirmed in a recent global systematic review)[30] to determine which pregnant mothers require antiviral therapy, we also address the issue of limited access to HBV deoxyribonucleic acid testing in some areas of China. Further research into the most cost-effective method of scaling up tenofovir administration to pregnant women is needed, and the approach taken could be tailored by rural or urban areas depending on the availability of HBeAg or HBV viral load testing. Moving away from a one-size-fits-all solution in China might overcome differential logistical and financial barriers.

Over the last few years, the price of tenofovir has been successfully negotiated in China and has fallen dramatically from nearly US$ 1000 per patient per year in 2016 to US$ 10 per patient per year in 2020 (i.e. the drug cost alone meets our threshold for cost–effectiveness). However, although the cost of the antiviral drug alone should no longer be a barrier, the financing of a large-scale intervention providing tenofovir to pregnant women will still need careful consideration as there will also be associated diagnostic and monitoring costs.

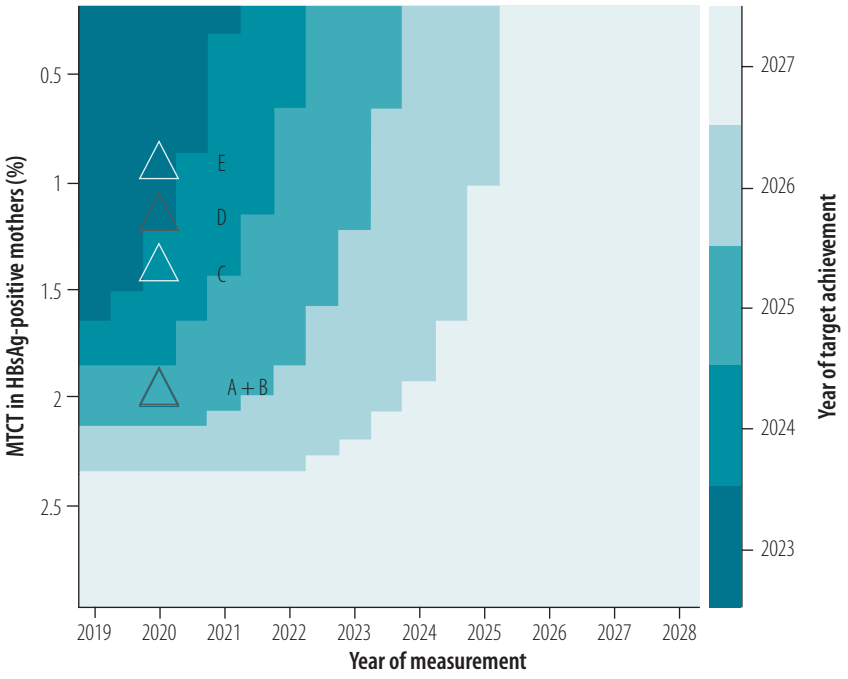
China is exceptional in having managed to achieve such high levels of hepatitis B Ig coverage to babies born to all HBsAg-positive mothers. In many low- and middle-income countries, the use of hepatitis B Ig is limited by cost, lack of availability, cold-chain requirements and the high numbers of births outside hospitals.[31] Data are emerging that show there is no residual transmission in HBeAg-negative mothers if a birth-dose HBV vaccination is received;[12] providing hepatitis B Ig only to babies born to HBeAg-positive mothers could therefore be a cheaper strategy with a potentially similar impact. Another strategy that might be useful for other countries with financial and logistical constraints to scaling up hepatitis B Ig is to adopt a PMTCT intervention based on birth-dose vaccination and tenofovir only. However, the efficacy of such a strategy is unknown; trials are currently ongoing in Lao People's Democratic Republic and Thailand.[32]

Our study benefitted from projections that used a dynamic model calibrated to the latest national data in China. Although previous models have attempted to quantify the HBV epidemic in China and the impact of vaccination,[33,34] they were not calibrated to the latest available data, did not evaluate the impact of the addition of hepatitis B Ig or tenofovir, or were not dynamic in nature. A further strength of our study is our proposal of a novel method to monitor HBV elimination targets both in the Western Pacific Region and globally. Our method, which combines measurable indicators on programmatic coverage and measured MTCT values with modelling, could overcome the reliance on expensive serosurveys that would otherwise be required. Antenatal screening combined with routine post-vaccination serological testing in babies born to HBsAg-positive mothers could be a useful method of measuring MTCT percentages and monitoring the effectiveness of intervention strategies. However, further research is needed on optimal and cost-effective methods of post-vaccination serological testing, and how these could be integrated into existing practices without overburdening health systems.

Our study had some limitations. We have taken a national perspective using national programme and sero-survey data; however, this may obscure heterogeneity on a more provincial level and does not consider the effect of migration or HIV coinfection on the projections (although the effect of the latter is expected to be small in China). Furthermore, we did not investigate the costs or the cost–effectiveness of alternative methods of implementing such a programme, or how non-adherence to tenofovir therapy during pregnancy would affect the trajectory towards elimination. All of these factors are important to policy-makers in deciding whether such a strategy should be adopted.

Our study highlights the important role of dynamic modelling combined with high-quality national data in validating country-level elimination of MTCT of HBV. To monitor progress on this path to elimination, we have proposed a unique framework for measurable indicators. Our results should motivate other high-burden countries that have not yet attained such high levels of PMTCT intervention coverage to not only strengthen their HBV prevention strategies, but also consider the provi-

Fig. 5. **Relationship between measured mother-to-child transmission in mothers positive for hepatitis B surface antigen and the year in which the elimination target will be achieved, China**



HBsAg: hepatitis B surface antigen; MTCT: mother-to-child transmission.
Note: (i) As in Table 2, scenarios are defined as increased coverage of birth-dose vaccination (A), plus increased coverage of hepatitis B Ig (B), plus 50.0% (C), 70.0% (D) and 90.0% (E) coverage of tenofovir. (ii) Triangles represent estimated mother-to-child transmission of hepatitis B in 2020 for intervention scenarios A–E.

sion of tenofovir to pregnant HBeAg-positive women and the establishment of effective monitoring systems. ■

Acknowledgements
Zheng Hui and Shevanthi Nayagam contributed equally to this work.

Funding: This work was supported by United Nations International Children's Emergency Fund (UNICEF) China office (grant number 602033) and the Chinese Ministry of Science and Technology Program for Important Infectious Diseases Control and Prevention (grant numbers 2017ZX10105015 and 2018ZX10721202).

Competing interests: None declared.

ملخص

التقدم الذي تم تحقيقه في سبيل القضاء على انتقال عدوى فيروس الالتهاب الكبدي "ب" من الأم إلى الطفل في الصين: تحليل لوضع النماذج

الغرض لتحديد العبء المتوقع لفيروس الالتهاب الكبدي "ب" (HBV) في الصين، واستراتيجيات التدخل التي يمكنها أن تقضي على انتقال العدوى من الأم إلى الطفل (MTCT) بحلول عام 2030 أو قبل ذلك، والمعايير القابلة للقياس التي يمكن استخدامها لرصد التقدم باتجاه هذا الهدف.

الطريقة قمنا بتطوير نموذج ديناميكي وفقاً للجنس والعمر، لوباء فـيروس الالتهاب الكبدي ب في الصين، تمت معايرته باستخدام مستضد الالتهاب الكبدي "ب" السطحي (HBsAg)، وبيانات انتشار المستضد الإلكتروني (HBeAg) من المسوح المصلية الوطنية المتسلسلة (الفترة من 1979 إلى 2014)، وأعداد وفيات مصابي السرطان المرتبطة بفيروس الالتهاب الكبدي "ب" (2012). لقد حددنا ما إذا كان بإمكان الصين تحقيق القضاء على انتقال عدوى فيروس الالتهاب الكبدي الوبائي "ب" بحلول عام 2030 بموجب تدخلات الوقاية الحالية. قمنا بوضع نماذج لسيناريوهات تدخل مختلفة لتمثيل مستويات تغطية مختلفة لجرعة التطعيم ضد فيروس الالتهاب الكبدي "ب" عند الولادة، والجلوبولين المناعي ضد الالتهاب الكبدي "ب" لحديثي الولادة من أمهات تم تشخيصهم بإيجابية HBsAg، والعلاج المضاد للفيروسات (تينوفوفير) لنساء حوامل تم تشخيصهم بإيجابية HBeAg.

النتائج نحن نتوقع أنه في حالة الحفاظ على المستويات الحالية من التدخلات الوقائية، سوف تحقق الصين هدف القضاء بحلول عام 2029. وعن طريق وضع نماذج لسيناريوهات التدخل المختلفة، وجدنا أنه يمكن تقديم ذلك إلى عام 2025 عن طريق زيادة تغطية التطعيم بجرعة الولادة، أو إلى عام 2024 عن طريق إعطاء تينوفوفير (tenofovir) للنساء الحوامل تم تشخيصهم بإيجابية HBeAg. وجدنا أنه سيتم توقع تحقيق الهدف بحلول عام 2025 عن طريق قياس أقل من 2% من انتقال العدوى من الأم إلى الطفل في عام 2020.

الاستنتاج تركز النتائج لدينا على كيفية الجمع بين البيانات الوطنية ذات الجودة العالية، مع وضع النماذج في مراقبة القضاء على انتقال عدوى فيروس الالتهاب الكبدي "ب" من الأم إلى الطفل. عن طريق إظهار تأثير التدخلات المتزايدة على تواريخ الإنجاز المستهدفة، نتوقع أن يكون لدى البلدان الأخرى ذات العبء الثقيل الحافز لدعم سياسات الوقاية من فيروس الالتهاب الكبدي ب.

摘要

中国在消除母婴传播乙型肝炎病毒感染方面的进展：建模分析

目的 旨在确定中国预计的乙型肝炎病毒 (HBV) 负担、可在 2030 年或更早之前消除母婴传播 (MTCT) 的干预策略，以及可用于监测实现这一目标进展的可衡量参数。

方法 我们针对中国的乙型肝炎病毒 (HBV) 流行情况，建立了按性别和年龄分层的动态模型，采用来自全国血清流行病学调查（1979 年至 2014 年）的乙型肝炎表面抗原 (HBsAg) 和乙型肝炎病毒 e 抗原 (HBeAg) 患病率数据以及乙型肝炎病毒 (HBV) 相关癌症死亡人数（2012 年）进行了校准。我们确定了中国通过目前的预防干预是否能够在 2030 年之前实现消除乙型肝炎病毒 (HBV) 的母婴传播 (MTCT)。我们对各种干预方案进行了建模，以体现不同出生接种剂量的乙型肝炎病毒 (HBV) 疫苗、对乙型肝炎表面抗原 (HBsAg) 阳性母亲的新生儿的乙型肝炎免疫球蛋白和对乙型肝炎病毒 e 抗原 (HBeAg) 阳性孕妇的抗病毒治疗（替诺福韦）的覆盖程度。

结果 我们预计，如果维持目前的预防干预程度，中国将在 2029 年之前实现消除目标。通过对各种干预方案进行建模，我们发现可以通过扩大出生接种剂量疫苗的覆盖范围将这一目标提前到 2025 年实现，或者通过让乙型肝炎病毒 e 抗原 (HBeAg) 阳性孕妇服用替诺福韦将这一目标提前到 2024 年实现。我们发现，由于 2020 年母婴传播 (MTCT) 的衡量值低于 2%。，因此预计会在 2025 年之前实现目标。

结论 我们的结果突显出如何将高质量的国家数据与建模相结合，以监测消除乙型肝炎病毒 (HBV) 母婴传播 (MTCT) 的进展。通过证明增加干预对目标实现日期的影响，我们预计其他负担沉重的国家将会有动力加强乙型肝炎病毒 (HBV) 预防政策。

Résumé

Progrès accomplis dans l'élimination de la transmission de l'infection au virus de l'hépatite B de la mère à l'enfant en Chine: analyse par modélisation

Objectif Déterminer la charge exercée par le virus de l'hépatite B (VHB) en Chine, les stratégies d'intervention qui pourraient éliminer la transmission de la mère à l'enfant (TME) d'ici 2030 au plus tard, et les paramètres mesurables pouvant être utilisés pour suivre les progrès réalisés dans ce domaine.

Méthodes Nous avons développé, pour l'épidémie de VHB en Chine, un modèle dynamique stratifié selon l'âge et le sexe. Nous l'avons calibré à l'aide des données de prévalence de l'antigène de surface (HBsAg) et de l'antigène e (HBeAg) de l'hépatite B, issues des enquêtes sérologiques nationales de type séquentiel (1979–2014) et du nombre de décès par cancer associés au VHB (2012). Nous avons établi si les interventions de prévention actuelles permettraient à la Chine d'éliminer la TME du VHB d'ici 2030. Nous avons modélisé plusieurs scénarios d'intervention pour représenter différents niveaux de couverture de vaccination contre le VHB à la naissance, d'injection d'immunoglobuline aux enfants nés de mères HBsAg-positives, et de traitement antiviral (ténofovir) administré aux femmes enceintes HBeAg-positives.

Résultats Nous estimons que si les interventions de prévention actuelles sont maintenues, la Chine atteindra l'objectif d'élimination prévu d'ici 2029. En modélisant divers scénarios d'intervention, nous avons découvert que cet objectif pourrait même être concrétisé pour 2025 en augmentant la couverture de vaccination à la naissance, voire 2024 en administrant du ténofovir aux femmes enceintes HBeAg-positives. Nous avons également constaté qu'un taux de TME inférieur à 2% en 2020 préfigurait la réalisation de l'objectif pour 2025.

Conclusion Nos résultats mettent en lumière la façon dont des données nationales de qualité peuvent être combinées à des modèles pour surveiller l'élimination de la TME du VHB. En démontrant l'impact de l'accroissement des interventions sur les échéances des objectifs, nous espérons motiver d'autres pays durement touchés à renforcer leurs politiques de prévention du VHB.

Резюме

Прогресс в предотвращении передачи вируса гепатита B от матери ребенку в Китае: модельный анализ

Цель Определить прогнозируемое бремя вируса гепатита B (HBV) в Китае, стратегии вмешательства, которые могут исключить его передачу от матери ребенку (ПМР) к 2030 году или раньше, а также измеряемые параметры, которые можно использовать для мониторинга прогресса в достижении этой цели.

Методы Авторы разработали динамическую, стратифицированную по полу и возрасту модель эпидемии HBV в Китае, откалиброванную с использованием данных о распространенности поверхностного антигена вируса гепатита B (HBsAg) и e-антигена вируса гепатита B (HBeAg), полученных в результате последовательных национальных серологических обследований (1979–2014 гг.), а также ряда связанных с HBV смертельных случаев среди больных раком (2012 г.). Авторы определили, сможет ли Китай добиться ликвидации передачи HBV от матери ребенку к 2030 году при соблюдении текущих профилактических мер. Были смоделированы различные сценарии вмешательства, представляющие разные уровни охвата: вакцинация против HBV при рождении, иммуноглобулин против гепатита B для новорожденных от HBsAg-положительных матерей и противовирусная терапия (тенофовир) для HBeAg-положительных беременных женщин.

Результаты Авторы прогнозируют, что при сохранении текущего уровня профилактических мер Китай достигнет цели по ликвидации передачи HBV от матери ребенку к 2029 году. Моделируя различные сценарии вмешательства, авторы обнаружили, что поставленная цель может быть достигнута к 2025 году в случае увеличения охвата вакцинацией при рождении или к 2024 году в случае назначения тенофовира HBeAg-положительным беременным женщинам. Авторы определили, что достижение поставленной цели к 2025 году можно спрогнозировать, если в 2020 году показатель передачи вируса от матери ребенку составит менее 2%.

Вывод Полученные результаты подчеркивают, как высококачественные общенациональные данные можно объединить с моделированием для мониторинга ликвидации передачи HBV от матери ребенку. Авторы надеются, что демонстрация влияния расширенных мер вмешательства на сроки достижения поставленных целей послужит стимулом для других стран с высоким бременем этой болезни усилить политику профилактики HBV.

Resumen

Avances en la eliminación de la transmisión maternofilial de la infección por el virus de la hepatitis B en China: un análisis de modelos

Objetivo Determinar la carga prevista del virus de la hepatitis B (VHB) en China, las estrategias de intervención que pueden eliminar la transmisión maternofilial (TMT) para 2030 o antes y los parámetros mensurables que se pueden aplicar para vigilar los avances logrados en la consecución de este objetivo.

Métodos Se elaboró un modelo dinámico, estratificado por sexo y edad, de la epidemia del VHB en China, que se calibró mediante el uso de datos de prevalencia del antígeno HBs y del antígeno HBe obtenidos a partir de encuestas serológicas nacionales secuenciales (1979-2014) y de la cantidad de muertes por cáncer causadas por el VHB (2012). Se determinó si China puede lograr la eliminación de la TMT del VHB para 2030 con las actuales intervenciones de prevención. Se elaboraron varios escenarios de intervención para representar diferentes niveles de cobertura de la vacunación contra el VHB en dosis al nacer, de la inmunoglobulina de la hepatitis B a los recién nacidos de madres con pruebas positivas para el antígeno HBs y de la terapia antivírica (tenofovir) a las mujeres embarazadas con pruebas positivas para el antígeno HBe.

Resultados Se prevé que, si se mantienen los niveles actuales de intervenciones de prevención, China logrará el objetivo de eliminación para 2029. Mediante la elaboración de modelos de varios escenarios de intervención, se descubrió que este objetivo se puede adelantar para 2025 al aumentar la cobertura de la vacunación de dosis al nacer o para 2024 al administrar tenofovir a las mujeres embarazadas que

den positivo en la prueba del antígeno HBe. Además, se observó que el logro del objetivo para 2025 se podría predecir mediante la medición de menos del 2 % de la TMT en 2020.

Conclusión Los resultados de este análisis destacan cómo se pueden combinar los datos nacionales de alta calidad con la elaboración de modelos para vigilar la eliminación de la TMT del VHB. Al demostrar el impacto del aumento de las intervenciones en las fechas de cumplimiento de los objetivos, se prevé que otros países con una gran carga del VHB estarán motivados para reforzar las políticas de prevención de este virus.

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