APJAI
Asian Pacific Journal of
Allergy and Immunology

REVIEW ARTICLE

Lessons from Thailand's successful prevention of mother-to-child hepatitis B transmission: Advancing toward elimination by 2030

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Abstract

Thailand has achieved remarkable success in preventing and reducing hepatitis B virus (HBV) incidence through its nationwide newborn vaccination program, introduced in 1992 as part of the Expanded Program on Immunization (EPI). Before the vaccination era, HBV endemicity in Thailand was high, with a carrier rate of 6–8%, and mother-to-child transmission was a major route of infection. Early trials demonstrated the efficacy of hepatitis B vaccines, especially when administered within 12 hours of birth, followed by scheduled doses. The national vaccination program was initially piloted in two provinces in 1988 and expanded to full coverage by 1992. By 2024, carrier rates among children under 10 years dropped to less than 0.1%, meeting the WHO goal of zero mother-to-child transmission. Studies confirmed the vaccine's long-term protection, with no cases of chronic infection in vaccinated individuals with detectable anti-HBs over 20 years. Moreover, literature indicates that hepatitis B vaccination provides long-lasting protection more than 35 years. Additional measures, including antiviral use for high-risk mothers and expanded screening and treatment programs, have further supported HBV elimination. The program's impact has significantly reduced liver-related diseases and positioned Thailand as a model for HBV control. As the nation moves toward the 2030 hepatitis elimination goal, ongoing efforts focus on screening older populations with a high prevalence of infection and ensuring treatment access to achieve lasting eradication.

Key words: Prevention, Mother-to-Child Transmission (MTCT), Hepatitis B Virus, vaccine, Elimination, Thailand

Citation:
Poovorawan, Y., Inma, P., Nilyanimit, P., Kanokudom, S., Jullapetch, C. (2025). Lessons from Thailand's successful prevention of mother-to-child hepatitis B transmission: Advancing toward elimination by 2030.
Asian Pac J Allergy Immunol, 43(1), 1-9.
https://doi.org/10.12932/ap-220125-2021

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Summary: Key lessons learned and success factors for HBV elimination

Early vaccination is critical: Administering the hepatitis B vaccine within 12 hours of birth, followed by subsequent doses.

Importance of timely doses: Delaying the second dose of the vaccine increases the risk of mother-to-child transmission (MTCT), underscoring the need for adherence to the recommended vaccination schedule.

Long-term protection: The hepatitis B vaccine provides durable immunity for up to 20-35 years, making booster doses unnecessary for most individuals.

Antiviral therapy for high-risk mothers: Administering antiviral drugs like tenofovir during the last trimester of pregnancy to mothers with high viral loads further reduces MTCT risk to nearly zero.

Universal screening and treatment: Routine screening of pregnant women and high-risk groups, coupled with timely treatment, is essential for eliminating HBV.

Integration with national programs: Incorporating HBV vaccination into existing immunization programs (e.g., EPI) ensures high coverage rates and sustainability.

Strong policy commitment: Thailand's Ministry of Public Health (MOPH) demonstrated strong leadership by integrating HBV vaccination into the national immunization program and aligning with WHO goals.

Continuous monitoring and adaptation: Ongoing research and data collection enabled the program to adapt, such as adding a monovalent dose at 1 month for infants of carrier mothers.

Introduction

Before the 1980s, hepatitis B virus infection (HBV) was a significant global health issue, particularly in regions with high endemicity, such as East Asia, Southeast Asia, and Central Africa. It was a major cause of chronic hepatitis, cirrhosis, and liver cancer.[1] Similarly, in Thailand, the carrier rate of hepatitis B was exceedingly high, around 6-8%.[2] Males had a higher prevalence than females,[3] liver cancer caused by hepatitis B was the most common cancer among men and the third among females.[4]

The primary routes of HBV transmission involve exposure to infected body fluids such as blood, saliva, vaginal secretions, and semen. Examples include sharing sharp instruments, receiving contaminated blood transfusions or blood products, engaging in sexual contact, and mother-to-child transmission during childbirth.[5] It was estimated that about 50% of infections were caused by transmission from carrier mothers,[6] especially those who tested positive for both hepatitis B surface antigen (HBsAg) and hepatitis B e-antigen (HBeAg). Mother-to-child transmission of hepatitis B virus occurs in up to 90% of cases where the mother has a high viral load or is HBeAg positive.[7] Before the hepatitis B vaccine era, approximately 6% of pregnant women in Thailand were hepatitis B carriers, and of those 40% of them had high viral loads or tested positive for HBeAg.[2]

Infants who receive the hepatitis B vaccine and immunoprophylaxis show no difference in infection rates regardless of the mode of delivery, whether normal labor or cesarean delivery.[8] However, some studies and data collection suggest that cesarean delivery may reduce the incidence of mother-to-child transmission of hepatitis B virus.[9] Nevertheless, the evidence is not conclusive. Therefore, for mothers who are carriers of the hepatitis B virus, there is no indication for cesarean delivery solely to prevent transmission. Similarly, when comparing breastfeeding with formula feeding, there is no difference in the transmission rate to infants born to hepatitis B carrier mothers.[10,11] The critical factor is the administration of the vaccine and immunoprophylaxis, and it is unnecessary to avoid breastfeeding in mothers who are hepatitis B carriers.

Hepatitis B Vaccines

The development of hepatitis B vaccines began in the early 1980s. Early studies showed that plasma-derived vaccines, made by inactivating the virus through heat or formalin, could stimulate immunity and prevent infection. Later, advances in recombinant DNA technology led to the production of hepatitis B surface protein using genetically engineered organisms.[12] These recombinant DNA vaccines, first used in the mid-1980s, were easier to produce, non-biological, highly immunogenic, and effective in preventing infection.[13] Alongside, hepatitis B immunoglobulin (HBIG) was developed for passive prophylaxis with significant efficacy in newborns with carrier mothers.[14] The vaccine and HBIG have been used worldwide.

Introduction of Hepatitis B Vaccination in Thailand

Early 1980's, plasma-derived hepatitis B vaccines (both formalin-inactivated and heat-inactivated types) were registered in Thailand, leading to further research, particularly on preventing mother-to-child transmission.[15,16] After the development of recombinant DNA hepatitis B surface protein vaccines, studies in Thailand began in 1986. The research focused on newborns of carrier mothers (HBsAg- positive), both HBeAg-positive and HBeAg-negative. Initial findings suggested that preventing transmission required both the vaccine and HBIG. However, our studies showed that vaccination alone, administered within 12 hours of birth and followed by doses at 1, 2 and 12 months, had a protective efficacy rate of 94% in neonates of HBeAg-positive mothers after one year. When compared to a three-dose schedule (at birth, 1, and 6 months), the result was similar. When the combination of vaccination 3 and 4 doses and HBIG, the efficacy remained similar, approximately 98%.[2,17-18] These findings underscored the effectiveness of hepatitis B vaccination programs.

Milestones and timelines Thailand hepatitis B elimination, research and implementation.

The timeline demonstrates key interventions and advancements aimed at preventing mother-to-child transmission and improving treatment access, ultimately targeting HBV elimination by 2030 (**Figure 1**). In 1988, initial implementation of HBV vaccination for newborns began as a pilot study to evaluate its feasibility and effectiveness. As a result, the HBV vaccine was incorporated into the Expanded Program on Immunization (EPI) and the nationwide vaccination program for all neonates born in 1992. This led to a significant reduction in new infections. In 2016, all mothers were routinely screened HBV carriers during prenatal cate or at delivery to identify HBV-positive mothers and ensure appropriate interventions, such as

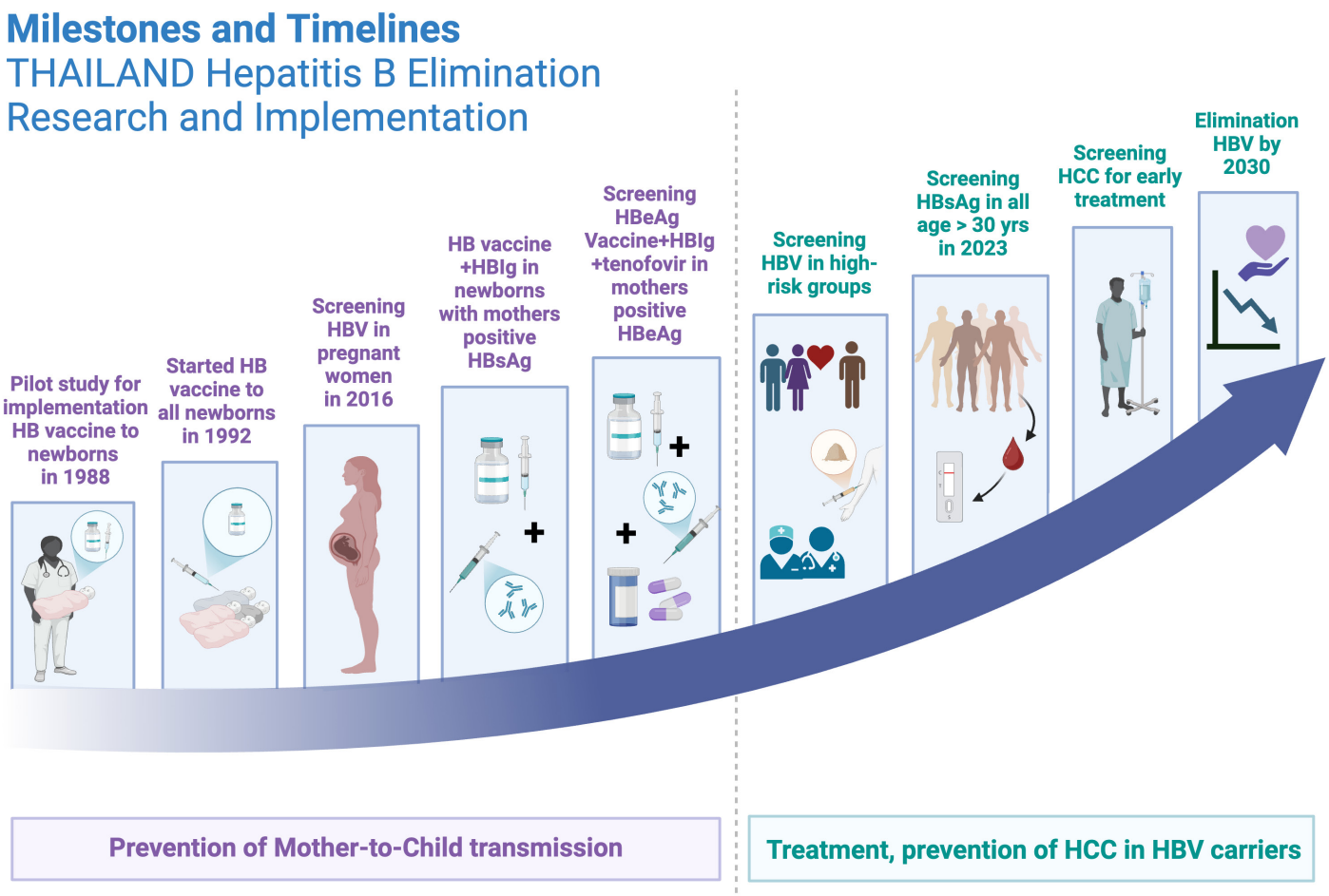

Figure 1. Milestones and timelines in Thailand's hepatitis B virus elimination efforts through research and implementation. (Created with Biorender.com)

timely vaccination and HBIG administration for newborns. Subsequently, the newborns of high-risk mother with HBeAg-positive was received the combination of HB vaccine, HBIG and tenofovir. Nationwide screening of high-risk groups, including healthcare workers and vulnerable communities, and the general population who aged over 30 years, was implemented in 2023. This initiative enabled the early detection and treatment of chronic liver diseases and hepatocellular carcinoma (HCC). Thailand is committed to eliminating HBV as a public health threat by 2030 through these comprehensive measures.

Introduction of the universal hepatitis B vaccination for infants in the National Immunization Program

The hepatitis B vaccine has proven highly effective in preventing infants from contracting the HBV from carrier mothers, with a safety profile, even for newborns. In preparation for implementing the national immunization program to prevent hepatitis B in newborns in 1988, the Ministry of Public Health (MOPH), in collaboration with the Program for Appropriate Technology in Health (PATH), the Australian International Development Assistance Bureau (AIDAB), and the Thai Red Cross Society, initiated a pilot project in Chiang Mai and Chonburi provinces. This project provided hepatitis B vaccines to all newborns alongside other vaccines in the EPI schedule at birth, 2 months, and 6 months of age. The vaccine schedule aligned with the EPI, providing three doses: at birth (monovalent HB vaccine), 2 months, and 6 months. The doses at 2 and 6 months were administered simultaneously with diphtheria, pertussis, and tetanus vaccines (DTPw) but in different injection sites for convenience.[19] Initially, healthcare personnel hesitated due to changes in the schedule, which traditionally administered doses at 1 and 6 months. However, unpublished studies demonstrated no difference in immunity levels between the two schedules (0, 1 and 6 vs 0, 2 and 6 months) after completing all three doses, leading to the adoption of the new schedule nationwide.

By 1990, the national program expanded 10 more provinces to 12 provinces, and by April 1992, it covered all newborns nationwide (**Figure 2**). Subsequent studies revealed that most infants in Thailand are born in hospitals, facilitating the administration of the first dose at birth without barriers. The vaccine coverage rates were remarkably high, exceeding 90% for the full three-dose series, marking the program's exceptional success.[20]

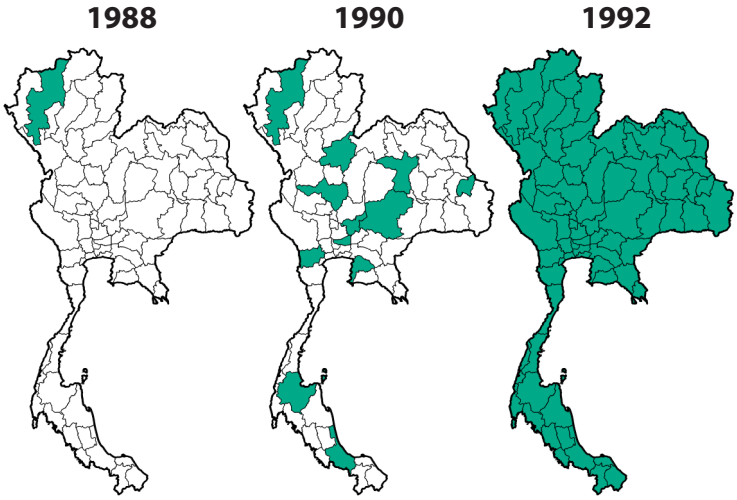

Figure 2. Implementation of the universal hepatitis B vaccine for newborns across various provinces, based on the year 1988-1992.

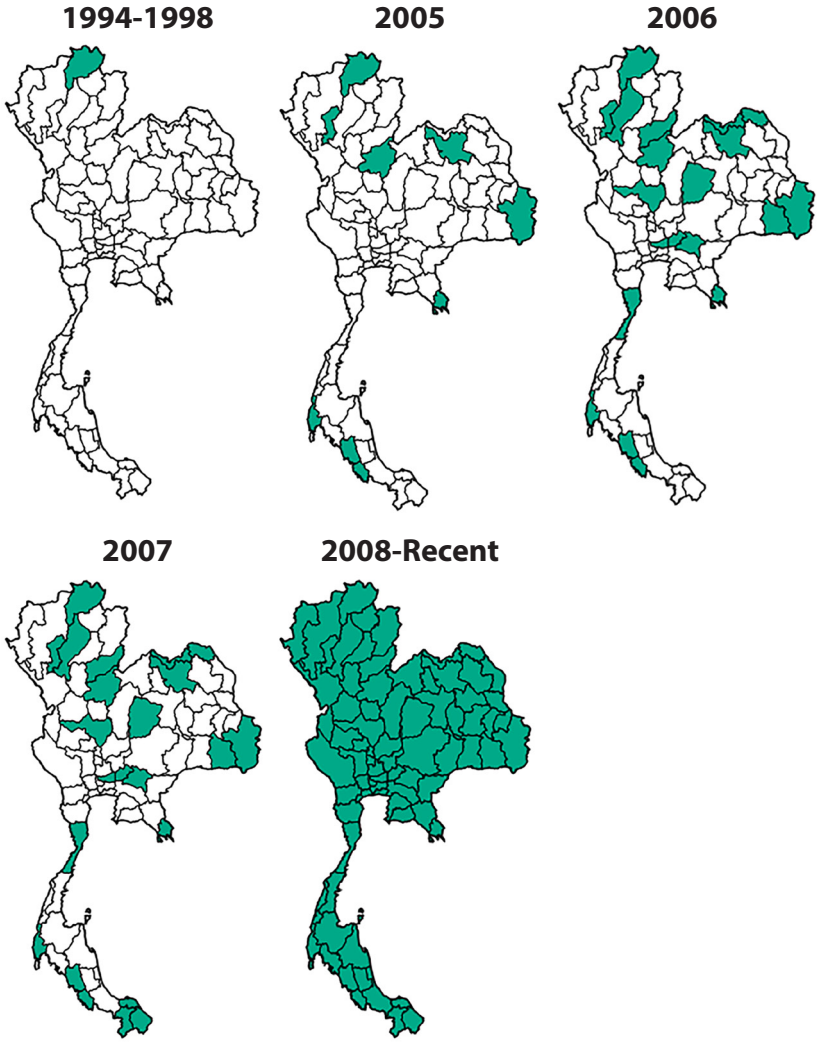

Figure 3. Administration of the hepatitis B vaccine as part of the combined DTPw-HB vaccine for infants in multiple provinces, since 1994-recent.

The introduction of combination vaccines

In 1994, following the development of a combined vaccine that included hepatitis B, diphtheria, pertussis, and tetanus (DTPw-HB) in a single shot, the MOPH piloted this approach in Chiang Rai province. The schedule included a monovalent hepatitis B vaccine at birth, followed by the combined DTPw-HB vaccine at 2, 4, and 6 months. Follow-up studies showed high efficacy in infants and maintained protection for up to 4 years.[21] Consequently, the MOPH transitioned from standalone vaccines at 2 and 6 months to the combined DTPw-HB vaccine starting in 1994 in Chiang Rai. By 2005, this program expanded to 10 provinces, achieving nationwide coverage by 2008. In 2018, the combination vaccine was further expanded to include five diseases: diphtheria, pertussis, tetanus, *Haemophilus influenzae* type B, and hepatitis B (DTPw-HB-Hib), which remained the standard afterward. (**Figure 3**)

Delayed second dose reduces prevention efficacy against mother-to-child transmission

In 2006, our research team, in collaboration with the MOPH, compared two vaccination schedules for infants born to HBV carrier mothers in Chiang Rai province. For the infants born to HBsAg-positive mothers, this was divided into two groups. In the first group, infants received a monovalent hepatitis B vaccine at birth, a second dose at 1 month, and three DTPw-HB combined doses at 2, 4, and 6 months, totaling five doses. In the second group, infants received a monovalent vaccine at birth, followed by the DTPw-HB combined vaccine at 2, 4, and 6 months, totaling four doses. Blood tests form the infants born to HBsAg-positive mothers conducted between 6 months and 2 years 5 months showed that delaying the second dose increased the risk of HBV transmission from mother to infant approximately threefold (1.44% vs. 4.58%).[22] As a result, since 2009, the MOPH mandated an additional monovalent hepatitis B vaccine dose at 1 month for infants born to HBV carrier mothers. This remains the current vaccination schedule in Thailand. Currently, the HBV vaccination schedule can be seen in the immunization program of the MOPH, Thailand, 2025 as described in **Table 1**.

Long-term effects of the hepatitis B vaccine

When administered in three or four doses within the first year of life, the hepatitis B vaccine provides long-term protection lasting up to 20 years. Studies indicate that a booster dose at age 5 is unnecessary, as long-term follow-ups show no significant differences in immunity. Antibody levels peak in the first year and gradually decline, with a steady drop in the first year and slower reductions in subsequent years. By age 10, antibody levels are generally low but remain effective in preventing infection for over 20-31 years.[23-27] Long-term studies of individuals vaccinated at birth and completing the series show no cases of chronic infection (HBsAg-positive), even after 20 years.[28] This is because the hepatitis B virus has a long incubation period of 1 to 6 months, during which the immune system can mount a protective memory response upon exposure. The findings were concordance to other study estimating that 86% vaccinees remained protective antibody for 35 years later.[29] This finding suggests that no need the booster doses in this age groups.

Table 1. The vaccination schedule for newborns to children aged 4 years according to the immunization program of the Ministry of Public Health, Thailand, 2025

Age	Vaccine recommendation
Birth	BCG, HB
1 mo	HB (baby born to HBsAg+ve mother)
2 mos	DTPw-HB-Hib1, IPV1, Rota1
4 mos	DTPw-HB-Hib2, IPV2, Rota2
6 mos	DTPw-HB-Hib3, OPV3 (bivalents), Rota3 except RV1 (Rotarix)
9-12 mos	MMR1
12 mos	LA-JE1
18 mos	DTPw, OPV4 (bivalents), MMR2
30 mos	LA-JE2
4 yrs	DTPw5, OPV5 (bivalents)

Abbreviations: BCG, Bacillus of Calmette and Guérin (tuberculosis) vaccine; HB, Hepatitis B virus vaccine, DTPw, diphtheria-tetanus-whole-cell pertussis vaccine; HIB, Haemophilus influenzae type b vaccine; IPV; inactivated polio vaccine; Rota/RV, rotavirus vaccine; OPV, oral polio vaccine; MMR, measles, mumps vaccine, and rubella vaccine; LA-JE, Live attenuated Japanese Encephalitis vaccine.
(Source from: https://ddc.moph.go.th/dcd/journal_detail.php?publish=16667)

Eliminating mother-to-child transmission of hepatitis B in Thailand

Thailand has implemented policies to reduce the transmission of hepatitis B from mothers to infants to zero following the World Health Organization (WHO) policy.[30] This effort began in 1988 with the inclusion of the hepatitis B vaccine for newborns in the National Immunization Program, initially as a pilot project and later expanded nationwide. Screening of pregnant women was introduced, and infants born to carrier mothers received vaccine and HBIG to enhance prevention from 2018 onwards.[31] However, initial coverage rates for HBIG were not high. Later studies showed that administering the antiviral drug tenofovir to high-risk carrier mothers during the last trimester of pregnancy completely prevented hepatitis B transmission to their infants. Infants born to mothers who did not receive antivirals but were given the vaccine and HBIG had a 98% protection rate. Currently, if HBsAg is detected in pregnant women, additional tests for HBeAg or viral load are conducted. If the viral load exceeds 200,000 IU/mL or HBeAg is positive, antivirals (eg, Tenofovir) are administered

in the last trimester to achieve zero transmission risk.[32,33] Pregnant women are now routinely screened for hepatitis B carriers, and those who test positive. The neonates are offered both vaccines and HBIG to improve prevention effectiveness. Furthermore, current Thai guidelines recommend antiviral therapy, such as tenofovir, during the last trimester of pregnancy for carrier women with a high viral load exceeding 200,000 IU/mL or who are HBeAg-positive.[34] The effectiveness of preventing mother-to-child transmission of hepatitis B virus in mothers with HBeAg-positive using various preventive measures is shown in **Figure 4**.

Antibody response to hepatitis B in medical students born after the vaccination program

Our study of medical students, with an average age of 18 years and born after the introduction of hepatitis B vaccination under the national program, showed that most could not recall their vaccination history. However, it is assumed that over 90% received the complete vaccine series during infancy. Screening revealed that most (> 90%) had tested negative for antibody (anti-HBs levels below 10 mIU/mL), although many had low anti-HBs titer in the 3–<10 mIU/mL range. After extensive study, we advised that adolescents and young adults with anti-HBs levels ≥ 10 mIU/mL do not require booster doses. Those with low anti-HBs levels between 3 and < 10 mIU/mL in high-risk groups can receive a single booster dose, which rapidly and sufficiently increases immunity. For individuals with levels between 1 and < 3 mIU/mL, a single booster dose followed by testing one month later is recommended. If immunity remains low, the full three-dose series can be administered. Those with levels < 1 mIU/mL should immediately begin a new three-dose vaccine series without further testing.[35]

Impact of the national hepatitis B vaccination program

Since its pilot study in 1988, the national hepatitis B vaccination program for newborns has significantly reduced hepatitis B infections, especially among individuals under 35 years old. A 1999 study found a marked decrease

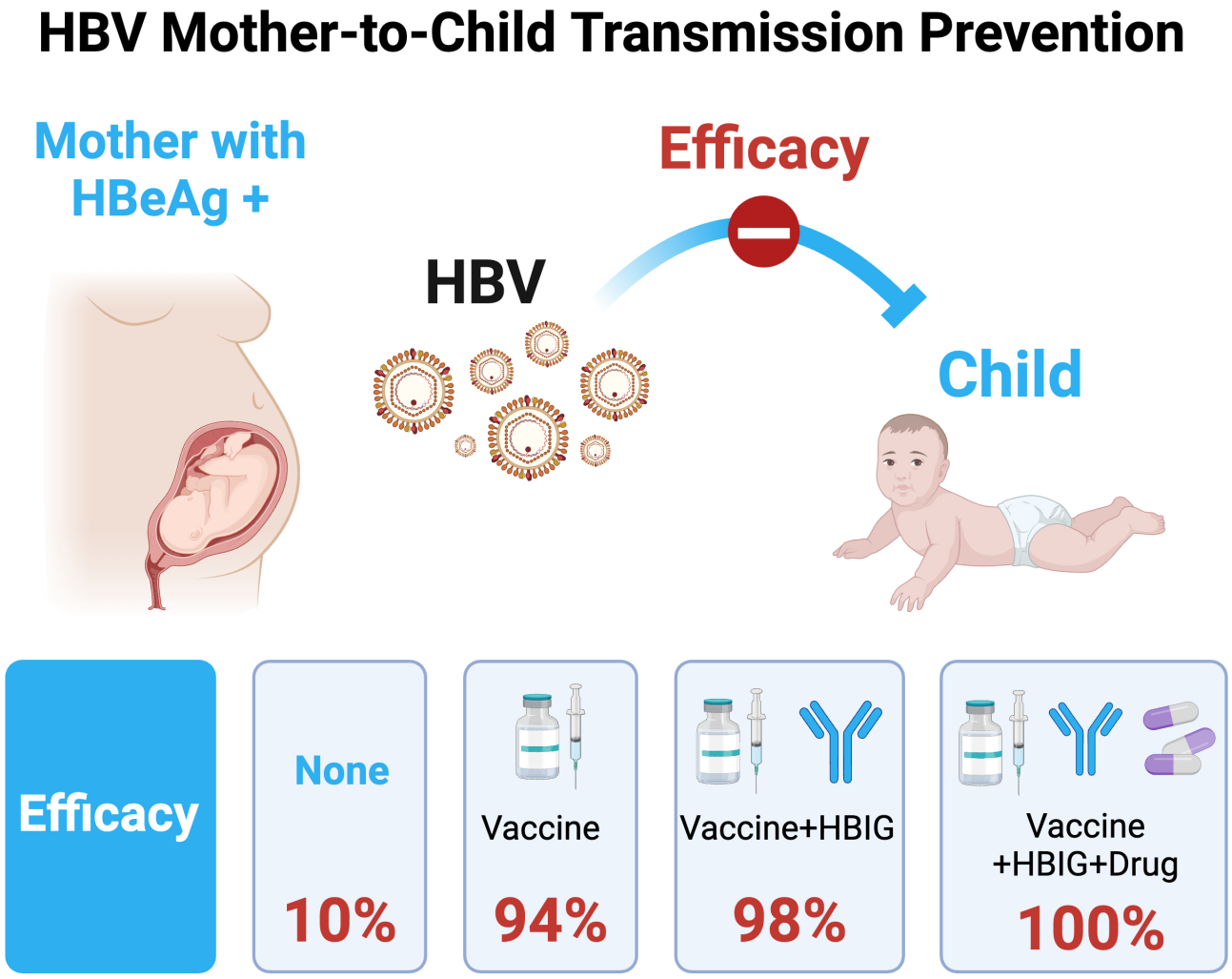

Figure 4. Percentage of mother-to-child transmission prevention of hepatitis B virus infection among HBeAg-positive mothers under different implementation strategies. (Adapted from references 7, 18, and 33, and generated with Biorender.com)

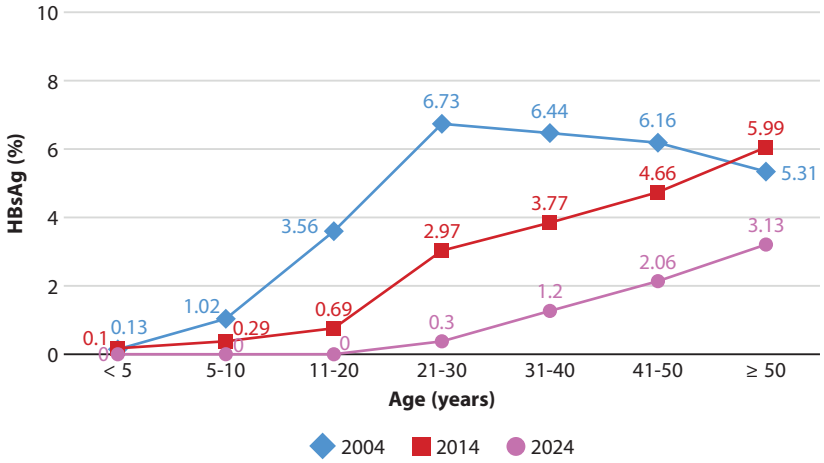

Figure 5. Highlights the prevalence of hepatitis B virus carriers across age groups in 2004, 2014, and 2024, demonstrating a substantial reduction, particularly among children in 2024.

in hepatitis B carrier rates among children born after the vaccination program compared to those born before its implementation.[36] Large national surveys conducted in 2004, 2014, and 2024, each involving approximately 6,000 participants from representative provinces across Thailand's four regions, demonstrated a significant decline in hepatitis B carrier rates over time. The age range of participants varied, spanning from 6 months to 60 years in 2004 and 2014, and from 6 months to 80 years in 2024. The hepatitis B carrier rate decreased from 4.0% in 2004 to 3.8% in 2014 and further to 1.6% in 2024[37-40] By 2024, the carrier rate among children under 10 years of age was less than 0.1% (**Figure 5**), demonstrating the success of preventing zero mother-to-child transmission as per WHO goals.

Thailand's achievement in implementing universal hepatitis B vaccination is the result of the well-planned strategies, strong governmental support, and efficient public health execution. The country's robust healthcare infrastructure, including village health volunteers and the very high rate of hospital births. Furthermore, other countries, such as Taiwan, have also successfully implemented the hepatitis B vaccination program for newborns, leading to evidenced by the significant decline in the hepatitis B incidence. Notably, the incidence of liver cancer has also decreased significantly.[41-42]

Eliminating hepatitis by 2030

The 2015 Glasgow Summit declared the goal of viral hepatitis elimination by 2030, which the WHO adopted in 2016. Thailand aligned with this policy, aiming to reduce new hepatitis infections by 90%, screen 90% of the general population, treat 80% of those infected, and decrease liver-related mortality by 65% by 2030.[40] The Department of Disease Control, MOPH, has implemented measures, starting with screening high-risk groups, the general population, and infected individuals to ensure timely treatment. Since 2019, Phetchabun Province has served as a pilot project for a "simplify test-to-treat strategy" or Phetchabun Model approach for hepatitis B and C, which will serve as a model for other provinces.[43-45] The approach designed to make HBV and HCV diagnosis and treatment more accessible, efficient, and patient-friendly. This strategy aims to eliminate unnecessary steps, reduce the time between diagnosis and treatment initiation, and expand access to care, especially in resource-limited settings. This approach initially involves screening with a rapid diagnostic test or strip test, followed by confirmation of positive sera using qualitative nucleic acid testing (NAT) or HCV core antigen detection. Furthermore, patients are referred to general practitioners for appropriate treatment with antiviral drugs.

Conclusion

Thailand has achieved remarkable success in reducing hepatitis B incidence through its newborn vaccination program over the past 35 years. This effort has transitioned Thailand from a high-endemicity area to a low-endemicity area for hepatitis B. Related conditions such as liver cirrhosis and liver cancer have significantly declined. Mother-to-child transmission has been virtually eliminated. Moving forward, screening for hepatitis B among individuals over 30 years old and ensuring treatment for carriers will further support the elimination of hepatitis B by 2030.

Acknowledgment

The authors would like to thank the Health Systems Research Institute (HSRI), the MK Restaurant Group, the Aunt Thongkham Foundation, and the BJC Big C Foundation, the Education and Public Welfare Foundation for funding and supporting the Center of Excellence in Clinical Virology. In addition, the authors sincerely appreciate the staff of the Center of Excellence in Clinical Virology, Chulalongkorn University & Hospital for their support in this study. Pornjarim Nilyanimit received support from the Second Century Fund (C2F) fellowship at Chulalongkorn University.

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