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PERSPECTIVES

Now is the Time to Scale Up Birth Dose Hepatitis Vaccine in Low and Middle-Income Countries

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Globally, over 6 million children under the age of 5 are living with hepatitis B virus (HBV) infection that will increase their life-time risk of liver cancer and related morbidities. While hepatitis B birth-dose vaccine (HepB-BD) is effective at preventing mother-to-child transmission, it is not widely used. Only half of the world's infants have access to this life-saving and cancer-preventing vaccine[1,2]. A modeling analysis of hepatitis found that delays in scaling up HepB-BD in low and middle-income countries (LMICs) could contribute to 580,000 deaths among children born between 2020 and 2030.[3] Another global analysis found that expanding Gavi's coverage of HepB-BD would avert 70,000 deaths each year.[4] HepB-BD vaccinations

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have had a substantial impact on global health, decreasing perinatal HBV infections by 83% between 1985 and 2022.[4]

However, many Gavi-eligible countries lack national HBV prevention policies and do not provide HepB-BD[2,5]. In light of the urgent need to scale up HepB-BD and HBV testing in resource-constrained settings, the Gavi Board recommended supporting HepB-BD roll-out in LMIC countries in October 2018. Despite the support, persistent concerns about implementation challenges related to HepB-BD and the COVID-19 pandemic stalled Gavi-sponsored scale-up. However, four recent changes to the vaccine landscape, as outlined below, provide a unique opportunity to scale up HepB-BD in LMICs now.

First, there is a growing body of evidence to guide the implementation of HepB-BD in LMICs.[6] In order to be cost-effective, HepB-BD should be integrated into existing maternal-infant care at the policy level (incorporating HBV prevention into existing HIV PMTCT platforms[7]), the facility level (administration of HepB-BD alongside other birth-dose vaccines[8]) and the community level (education of local communities on the importance of vaccines in general and birth-dose vaccines specifically). The WHO Maternal Immunization and Antenatal Care Situation Analysis identified several strategies to enhance comprehensive maternal immunization programs in resource-constrained settings.[9] This approach aligns with broader global efforts towards triple elimination of mother-to-child HIV, HBV, and syphilis transmission (**Figure 1**).[10] Second, a large number of pregnant women in LMICs deliver in a maternal health facility. A recent study examining data from population-representative surveys in 37 countries from 2009-2018 across sub-Saharan Africa and Southeast Asia found that 71% of women delivered in hospitals or clinics, providing a strong anchor for birth-dose vaccination programs.[11] Third, an expanding literature demonstrates that HepB-BD is feasible and effective. For example, feasibility data from the Democratic Republic of Congo[7] and Burkina Faso[12] demonstrated the effective integration of HepB-BD delivery into existing perinatal care and vaccine delivery systems. HepB-BD is one of several essential vaccines (e.g., oral polio vaccine, BCG vaccine) that must be implemented alongside other critical health interventions (e.g., vitamin K) at birth (**Figure 1**). While experiences from existing birth-dose immunization programs can inform implementation efforts to a degree,[13] prospective implementing stakeholders should consider unique challenges related to HepB-BD within their particular context. In order to avert HBV MTCT effectively, HepB-BD must be administered within the first 24 hours after delivery and followed by the required subsequent doses. Timely administration is challenging especially in the case of home births; potential solutions could include leveraging community health workers and their reach/network or using out-of-cold-chain approaches.[6] Finally, from a COVID-19 perspective, disruptions to infrastructure, services, and supply chains have lessened, and the pandemic has highlighted the importance of multi-faceted solutions to public health problems. As we emerge from the global COVID epidemic, we are well-positioned to resume and re-energize vaccine-preventable disease campaigns in LMICs.[14]

We have the tools, the implementation pathways, and the vaccines necessary to ensure that all babies are born free of HBV. Each year the global community delays introduction of HepB-BD, tens of thousands of babies succumb to infection with an entirely preventable disease. This is unacceptable and contributes to health inequity on a global scale. Mother-to-child transmission of HIV has virtually been eliminated thanks to global action. Now is the time for a focus on HBV prevention, in accordance with the latest WHO recommendations for triple elimination.[10] With growing civil society engagement on hepatitis action,[15] now is the time to act and bring HepB-BD to scale in LMICs with a high burden of HBV.

FOOTNOTES

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References

1. Unicef & WHO. Progress towards global immunization goals -2019 [Internet]. 2020 [cited 2022 Dec 19]. Available from: https://cdn.who.int/media/docs/default-source/immunization/global_monitoring/slidesglobalimmunization.pdf?sfvrsn=25385c3b_7
2. Introduction of HepB birth dose [Internet]. [cited 2022 Dec 19]. Available from: https://immunizationdata.who.int/pages/vaccine-intro-by-antigen/hepb_bd.html?ISO_3_CODE=&YEAR=
3. Villiers MJ de, Nayagam S, Hallett TB. The impact of the timely birth dose vaccine on the global elimination of hepatitis B. Nat Commun. **2021**; 12(1):6223.
4. Razavi-Shearer D. The Impact of HBV Vaccination Programs in Gavi versus non-Gavi Countries. 2022.
5. CDA Foundation; Coalition for Global Hepatitis Elimination, Hepatitis Australia, Hepatitis Fund; Hepatitis B Foundation, Médecins Sans Frontières Access Campaign, PATH, TREAT

Asia/amfAR, The Foundation for AIDS Research, Union for International Cancer Control, World Hepatitis Alliance. Electronic address: contact@worldhepatitisalliance.org. An open letter to Gavi: hepatitis B birth dose vaccine can't wait. Lancet Gastroenterol Hepatol [Internet]. **2022**; . Available from: http://dx.doi.org/10.1016/S2468-1253(22)00422-8

6. Boisson A, Goel V, Yotebieng M, Parr JB, Fried B, Thompson P. Implementation approaches for introducing and overcoming barriers to hepatitis B birth-dose vaccine in sub-Saharan Africa. Glob Health Sci Pract [Internet]. Johns Hopkins School Bloomberg School of Public Health, Center for Communication Programs; **2022**; . Available from: http://www.ghspjournal.org/lookup/doi/10.9745/GHSP-D-21-00277
7. Thompson P, Morgan CE, Ngimbi P, et al. Arresting vertical transmission of hepatitis B virus (AVERT-HBV) in pregnant women and their neonates in the Democratic Republic of the Congo: a feasibility study. Lancet Glob Health [Internet]. **2021**; . Available from: http://dx.doi.org/10.1016/S2214-109X(21)00304-1
8. Boisson A, Morgan CE, Fried B, et al. Barriers and facilitators to timely birth-dose vaccines in Kinshasa Province, the DRC: a qualitative study. Journal of Global Health Reports [Internet]. Inishmore Laser Scientific Publishing Ltd; **2022**; 6. Available from: http://dx.doi.org/10.29392/001c.35449
9. WHO. Maternal Immunization and Antenatal Care Situation Analysis Report of the MIACSA project 2016–2019 [Internet]. World Health Organization; 2020. Available from: https://apps.who.int/iris/bitstream/handle/10665/331942/9789240004016-eng.pdf?sequence=1&isAllowed=y
10. Cohn J, Owiredu MN, Taylor MM, et al. Eliminating mother-to-child transmission of human immunodeficiency virus, syphilis and hepatitis B in sub-Saharan Africa. Bull World Health Organ. **2021**; 99(4):287–295.
11. Gage AD, Fink G, Ataguba JE, Kruk ME. Hospital delivery and neonatal mortality in 37 countries in sub-Saharan Africa and South Asia: An ecological study. PLoS Med. **2021**; 18(12):e1003843.
12. Guingané AN, Bougouma A, Sombié R, et al. 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. **2020**; 40(10):2367–2376.
13. Moturi E, Tevi-Benissan C, Hagan JE, et al. Implementing a Birth Dose of Hepatitis B Vaccine in Africa: Findings from Assessments in 5 Countries. Journal of immunological sciences. **2018**; Suppl(5):31–40.
14. Ho LL, Gurung S, Mirza I, et al. Impact of the SARS-CoV-2 pandemic on vaccine-preventable disease campaigns. Int J Infect Dis. **2022**; 119:201–209.
15. Kpokiri EE, Elasi D, Zhang TP, et al. Expanding community engagement and advocacy in chronic viral hepatitis. Lancet Gastroenterol Hepatol. **2022**; 7(10):902–904.

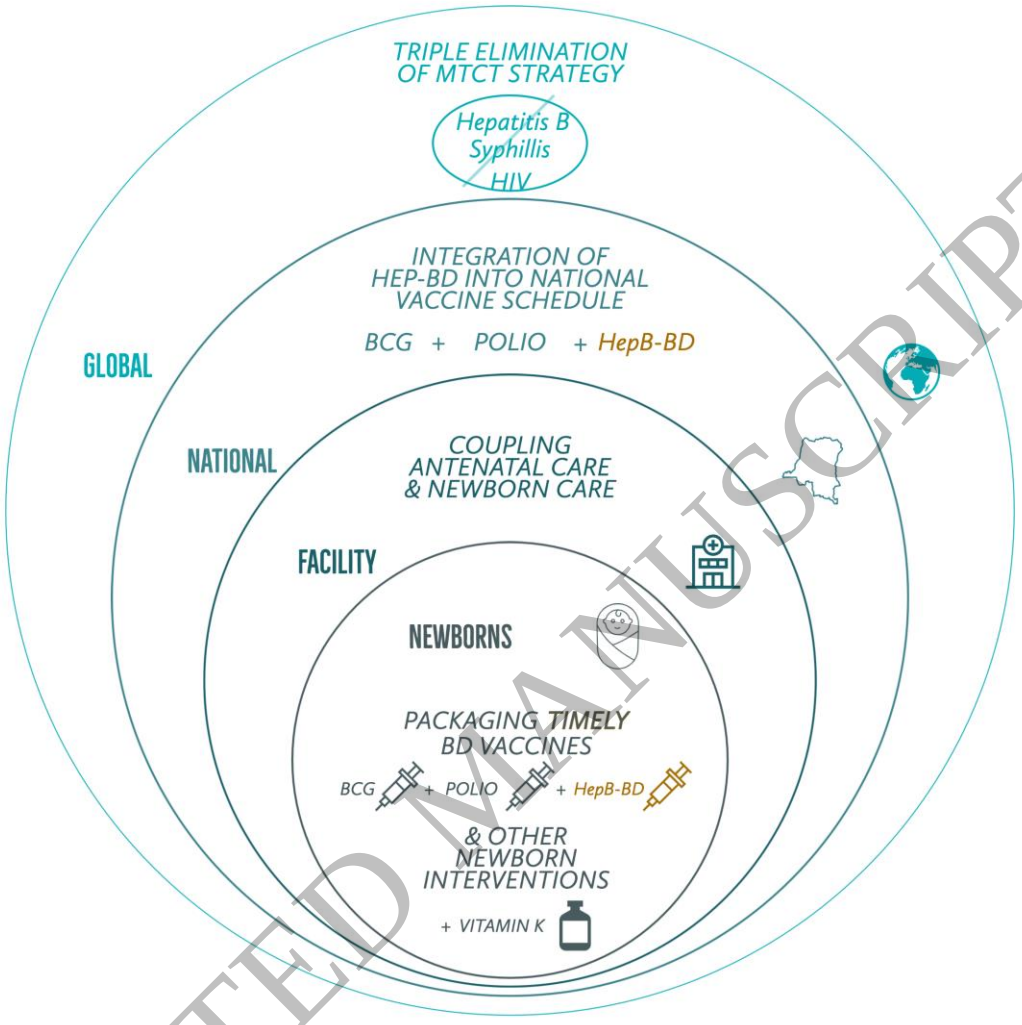

Figure 1
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