



Strengthening vaccine confidence during the COVID-19 pandemic: A new opportunity for global hepatitis B virus elimination

Jeffrey V. Lazarus¹, Camila A. Picchio¹, Shevanthi Nayagam^{2,3}, Scott Ratzan⁴, Mark Thursz^{3,*}

¹Barcelona Institute for Global Health (ISGlobal), Hospital Clínic, University of Barcelona, Barcelona, Spain; ²Department of Metabolism, Digestion & Reproduction, Imperial College London, London, United Kingdom; ³MRC Centre for Infectious Disease Analysis, Department of Infectious Disease Epidemiology, Imperial College London, London, United Kingdom; ⁴Journal of Health Communication: International Perspectives, City University of New York (CUNY) Graduate School of Public Health & Health Policy, New York, USA

The SARS-CoV-2 virus responsible for the ongoing COVID-19 pandemic is expected to circulate for a long time to come and may even become endemic. Until an effective vaccine against the virus is developed, which could take years if it is achieved at all, our lives will be marked by the possibility of infection despite adopting measures to help diminish risk. As a result, the sudden public and policy focus on the broad and rapid benefits of vaccination for COVID-19 is unsurprising, and it would be remiss not to examine how this interest can be applied to improve vaccine coverage for other viruses, such as hepatitis B virus (HBV).

Vaccination is a high value investment in public health and is one of the most cost-effective ways of avoiding disease.¹ This worth has been repeatedly proven through the reduction in incidence of infectious diseases like polio, measles, diphtheria, yellow fever, and pertussis, for example, thanks to massive vaccination campaigns that strived to reach everyone in the world.

The HBV vaccine in particular has had a well-documented positive effect on the prevalence of HBV infection globally,² which currently affects an estimated 251 million people worldwide,³ and has reduced the HBsAg prevalence in under 5-year-olds to less than 2% among immunized child cohorts, including in highly endemic countries.⁴ It is estimated that HBV immunization in infants and newborns alone will avert 211 million deaths by 2030.⁵

Most countries have had national HBV vaccination programmes in place for more than 20 years and the global vaccine alliance Gavi provides immunization support to 76 resource-limited countries.⁶ From 2021, Gavi will support, conditional on its replenishment, the HBV birth dose vaccine, a change that is widely welcomed by the liver health community as it is expected to greatly increase infant vaccination coverage, which was only 38% in 2015.³

Current HBV vaccines are extremely safe and efficacious. Nevertheless, the recommended vaccination schedule calls for 3 doses, which can result in incomplete vaccination due to loss to

follow-up. Recently, a new 2-dose vaccine was approved for use in adults to address this.⁷ This development is particularly important as it can increase the likelihood of achieving a complete vaccination schedule in high-risk populations that have limited access to health services.

The value of vaccination, however, is being increasingly undermined by low coverage. In 2019, the World Health Organization named vaccine hesitancy – defined as a “delay in acceptance or refusal of vaccination despite availability of vaccination services” – as one of the top 10 global health threats.⁸ Vaccine hesitancy is a continuum, and ranges from an individual having some doubts about vaccination but still vaccinating to outright refusal for themselves or on behalf of a minor. Vaccine hesitancy is not a new phenomenon, despite only recently being defined, and has been described since the eighteenth century.⁹ However, the resurgence of infectious diseases such as measles has prompted renewed attention and energy focusing on how this alarming phenomenon has contributed to the spread of vaccine-preventable diseases in recent years.¹⁰

While a loss in vaccine confidence has been linked to decreasing HBV vaccination coverage^{11–13} in some cases, many health system barriers to achieving universal access to HBV vaccination exist, particularly in low- and middle-income countries. As a whole, the prevalence of HBV infection is 7.4-fold higher in low-income than high-income countries.¹⁴ Of most notable concern is that progress in improving timely birth dose coverage has been slow² and has been hindered by concerns regarding costs to individuals, logistical barriers, and healthcare service funding shortfalls.

In addition to the aforementioned challenges in maintaining vaccination coverage, global infectious disease outbreaks like the ongoing COVID-19 pandemic can derail routine vaccination efforts, which could have serious consequences. This has already been shown in a recent report quantifying the effects of disruptions due to COVID-19 for HIV, TB, and malaria services.¹⁵ Maintaining childhood and birth dose HBV vaccination coverage during the COVID-19 pandemic is critical¹⁶ if we are to stay on track for viral hepatitis elimination. A modelling study in China, for example, found that any future drops in newborn and childhood vaccination coverage would quickly reverse the remarkable national progress that has been made

Keywords: Hepatitis B; Liver cancer; Vaccine hesitancy; COVID-19.

Received 2 June 2020; accepted 5 June 2020; available online 27 July 2020

* Corresponding author. Address: Digestive Disease Division, Department of Metabolism, Digestion & Reproduction, St Marys Hospital, London W2 1NY, UK. Tel.: +44 203 312 6454.

E-mail address: m.thursz@imperial.ac.uk (M. Thursz).

<https://doi.org/10.1016/j.jhep.2020.06.008>



ELSEVIER

and delay the elimination of mother-to-child HBV transmission in the country.

Nevertheless, we believe that the current pandemic offers important opportunities to strengthen the resolve to develop and use vaccines to prevent disease, despite some reported mistrust promulgated by a highly vocal minority. Given the tremendous limitations that COVID-19 control measures place on populations coupled with the promise of a successful vaccine in alleviating these measures, one would expect near-unanimous support for COVID-19 vaccination. The success of a vaccination programme must, however, go beyond the biological and immunological individual benefit and offer support at the social, political, and community levels.

There is already a global cry for the scientific community to rapidly develop a vaccine, which has led to some 80 confirmed COVID-19 vaccine candidates actively being researched at the exploratory or preclinical stages, and 37 additional candidates under consideration.¹⁷ Although there is some scepticism about a COVID-19 vaccine, both in terms of its efficacy, safety and developmental timescale, there is now a unique opportunity to address recent erosion in vaccine confidence by promoting the benefits of a COVID-19 vaccine specifically, in addition to broader vaccine literacy¹⁸ efforts. Efforts that increase fundamental support for vaccination and confidence¹⁹ can demonstrate the importance of prevention and build trust in the entire healthcare delivery system. The consequences of the current pandemic and potentially equally virulent future infections are now understood, and we need to remind the public of earlier immunization successes; for example, this year marks 40 years since the eradication of smallpox.

To carry this momentum into HBV elimination, clinicians, policymakers, community leaders, and others must stress that HBV vaccination prevents a viral infection that can require life-long treatment and can lead to liver cancer.²⁰ Although overall HBV vaccination coverage rates are increasing, in the absence of a cure (functional or otherwise) we must not lose focus on maintaining high vaccination coverage rates where this has already been achieved, in addition to increasing access to birth dose vaccination in high prevalence settings like South-East Asia and sub-Saharan Africa. There is an urgent need to keep working with healthcare professionals and the public on eliminating vaccine hesitancy, as it can be a significant impediment to implementing one of the most effective tools we have for HBV control worldwide. The COVID-19 pandemic has taught the world the importance of international collaboration, solidarity and the need for renewed efforts to address infectious diseases. While there are possible collateral effects of the pandemic, including disruption of health systems, diverted attention, and reduced donor funding, let it also be the start for a renewed effort to reach the 2030 goal to eliminate viral hepatitis as a public health threat.

Financial support

MT & SN acknowledge the support of NIHR Imperial Biomedical Research Centre.

JVL is supported by a Spanish Ministry of Science, Innovation and Universities Miguel Servet grant (Instituto de Salud Carlos III/ESF, European Union [CP18/00074]) and further acknowledges

support from the Spanish Ministry of Science, Innovation and Universities through the “Centro de Excelencia Severo Ochoa 2019-2023” Programme (CEX2018-000806-S), and from the Government of Catalonia through the CERCA Programme.

Conflict of interest

The authors who have taken part in this study declared that they do not have anything to disclose regarding funding or conflict of interest with respect to this manuscript.

Please refer to the accompanying [ICMJE disclosure](#) forms for further details.

Authors' contributions

MT, JVL – Conceptualization, writing and editing. CP, SN & SR, writing & editing.

Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jhep.2020.06.008>.

References

- [1] Ratzan S, Bloom B, El-Mohandes A, Fielding J, Gostin LO, Hodge JG, et al. The Salzburg Statement on vaccine acceptance. *J Health Commun* 2019;5:581–583.
- [2] Nayagam S, Shimakawa Y, Lemoine M. Mother-to-child transmission of hepatitis B: what more needs to be done to eliminate it around the world? *J Hepatol* 2020;27(4):342–349.
- [3] World Health Organization. Global Health Sector Strategy (GHSS) on viral hepatitis. Geneva, Switzerland: WHO; 2016–2021.
- [4] Kane MA, Roudot-Thoraval F, Guerin N, Papaevangelou V, Van Damme P, Viral Hepatitis Prevention Board. Global process in the control of viral hepatitis and acceptable delay in hepatitis B immunization. *Hum Vaccin Immunother* 2016:1–4.
- [5] Nayagam S, Thursz M, Sicuri E, Conteh L, Wiktor S, Low-Beer D, et al. Requirements for global elimination of hepatitis B: a modelling study. *Lancet Infect Dis* 2016;16(12):1399–1408.
- [6] Gavi supported countries. Available at: <https://www.gavi.org/programmes-impact/country-hub>. [Accessed 18 March 2020].
- [7] A two-dose hepatitis B vaccine for adults (Heplisav-B). *Med Lett Drugs Ther* 2018;60(1539).
- [8] World Health Organization. Ten threats to global health in 2019. Available at: www.who.int/news-room/feature-stories/ten-threats-to-global-health-in-2019. [Accessed 18 February 2020].
- [9] Wolfe RM, Sharp LK. Anti-vaccinationists past and present. *BMJ* 2002;325:430–432.
- [10] Gowda C, Dempsey AF. The rise (and fall?) of parental vaccine hesitancy. *Hum Vaccin Immunother* 2013;9(8):1755–1762.
- [11] World Health Organization. Assessment of the viral hepatitis response in Ukraine Mission report, 2017. Available at: http://www.euro.who.int/__data/assets/pdf_file/0007/372697/ukr-hepatitis-report-eng.PDF?ua=1. [Accessed 1 July 2020].
- [12] Denis F, Cohen R, Martinot A, Stahl JP, Lery T, Le Danvic M, et al. Evolution of hepatitis B vaccine coverage rates in France between 2008 and 2011. *Med Mal Infect* 2013;43:272–278.
- [13] Li X, Wiesen E, Diorditsa S, Toda K, Duong TH, Nguyen LH, et al. Impact of adverse events following immunization in Viet Nam in 2013 on chronic hepatitis B infection. *Vaccine* 2016;34(6):869–873.
- [14] World Health Organization. Global Hepatitis Report 2017. 2017. Available at: <https://apps.who.int/iris/bitstream/handle/10665/255016/9789241565455-eng.pdf?sequence=1>. [Accessed 1 July 2020].
- [15] Hogan A, Jewell B, Sherrard-Smith E, Vesga J, Watson OJ, Whittaker C, et al. Report 19- The potential impact of the COVID-19 epidemic on HIV, TB, and malaria in low-and middle-income countries. London: Imperial College London; 2020.
- [16] World Health Organization. Protecting lifesaving immunization services during COVID-19: new guidance from WHO. 2020. Available at: <https://>

- www.who.int/immunization/news_guidance_immunization_services_during_COVID-19/en/. [Accessed 21 May 2020].
- [17] The COVID-19 vaccine development landscape. *Nature reviews*. 2020. Available at: <https://www.nature.com/articles/d41573-020-00073-5> [Accessed 1 July 2020].
- [18] Ratzan SC. Vaccine literacy: a new shot for advancing health. *J Health Commun* 2011;16(3):227–229.
- [19] European Union. State of vaccine confidence in the EU 2018. Available at: https://ec.europa.eu/health/sites/health/files/vaccination/docs/2018_vaccine_confidence_en.pdf. [Accessed 18 May 2020].
- [20] Song C, Lv J, Liu Y, Chen JG, Ge Z, Zhu J, et al. Associations between hepatitis B virus infection and risk of all cancer types. *JAMA Netw Open* 2019;2(6):e195718.