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hepatitis B in the United States are identified and in care and treatment. [3] Although country of birth (COB) could assist with identifying additional infections, this information is not consistently collected. Many of those on the front line of screening for hepatitis B are smaller primary care practices that are not equipped to do so. Additionally, collecting COB can be sensitive for both health care staff and patients, [4] and there is considerable concern about possible discrimination associated with such questions. [5] This is especially true now with concerns of stigma and harassment of immigrants and anti-Asian racism.

Although machine learning might be able to identify high-risk people, there are significant challenges to its widespread implementation. Overall, universal screening followed by linkage to care is the single best way to ensure that people living with chronic hepatitis B in the United States are diagnosed and can access care and treatment to prevent cirrhosis and liver cancer. Universal screening offers a cost-effective, simplified, and nonstigmatizing way to identify people with hepatitis B. Additionally, universal screening with the threetest panel (HBsAg, HBsAb, HBcAb) will identify people who would benefit from vaccination as well as those at risk for reactivation. We strongly advocate for universal screening as the most effective and equitable testing strategy toward eliminating hepatitis B in the United States by 2030.

# CONFLICT OF INTEREST

Nothing to report.

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# Reply

We thank Dr. Cohen and colleagues for their interest in our manuscript, and for highlighting important issues surrounding HBV screening and advocating for universal screening. [1] Our manuscript was motivated by a desire to improve the status quo regarding HBV screening. Existing recommendations endorsed by the

Centers for Disease Control are cumbersome and include stigmatizing information including illicit drug use history, human immunodeficiency virus status, and country of birth. We agree that the failures of risk-based screening are clear and may contribute to HBV infection underdiagnosis.<sup>[2]</sup>

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While universal screening for HBV is easily understandable and may identify infection in those without apparent risk factors, the cost-effectiveness of universal screening remains controversial. This is largely due to limited literature, as most cost-effectiveness studies focused on higher HBV seroprevalence groups. [3] The well-conducted study by Toy et al., which found that universal HBV screening is cost-effective, was not published when we wrote our manuscript. [4] As with all cost-effectiveness studies, it makes assumptions including excellent linkage to care and adherence to recommended HBV monitoring and treatment, whereas in real-world studies both linkage and adherence are suboptimal. [2,5]

Cohen et al. had several specific comments on our study. First, they note that place of birth may be sensitive information. Our model only asks whether someone is born in the USA, and not a specific country of birth, which is still less stigmatizing than existing screening guidelines. Second, they raised questions about implementing a machine learning model. One could create a web-based calculator or a phone app in which one inputs the required data and is given an estimated risk of HBV infection and recommendation for whether screening is warranted. These are frequently used to compute other scores within hepatology such as Fibrosis-4. It may even be possible to program a calculator into the electronic medical record directly.

In summary, we share the concerns of Cohen et al. about the existing state of HBV screening and hope that our models may improve screening practices.

# **CONFLICT OF INTEREST**

Dr. Nguyen consults and received grants from Exact Sciences and Gilead. She consults for Intercept, GlaxoSmithKline, Eli Lilly, Laboratory of Advanced Medicine, and Janssen. She received grants from Pfizer, Enanta, Vir, Healio Health, NCI, Glycotest, and BK Kee Foundation.

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# Letter to the editor: Evidence on the use of L-ornithine L-aspartate in overt HE—But does it really improve prognosis?

To the editor.

We read with great interest the study by Jain et al. investigating L-ornithine L-aspartate (LOLA) in combination with lactulose and rifaximin for the treatment of patients with overt HE (OHE) grades 3 and 4.<sup>[1]</sup> The

authors have to be congratulated on conducting this important and elaborate study that adds to the growing body of evidence indicating an important role of LOLA for the treatment of OHE. The main finding of this study was that adding LOLA to a combination therapy of