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A review of published data and comparison of Asia-Pacific and international guidelines on the use of quantitative HBsAg in the management of chronic hepatitis B

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Conclusions

- Overall, guidance on qHBsAg as a tool for predicting clinical outcomes is limited
- Most research on qHBsAg has been conducted in the Asia-Pacific region
- Compared with other regions, Asia-Pacific guidelines provide greater guidance on the use of qHBsAg in predicting HBsAg loss and in monitoring treated patients
- Harmonising recommendations would help support the most appropriate use of qHBsAg testing in the management of patients with CHB
- An international Delphi study is underway to obtain consensus on the use of qHBsAg testing in the areas identified in this literature review

Plain Language Summary

HBsAg is a protein produced by hepatitis B virus. Measuring the amount of this protein could guide the treatment of patients with CHB. However, most studies are small and guidelines differ on the best way to use this approach. There is clearer guidance from the Asia Pacific region than other regions. We are working with experts to determine the best ways of using HBsAg measurement in CHB.

Background

- qHBsAg is currently being studied for a variety of uses in the management of patients with CHB
- Potential uses include understanding disease progression[1,2], monitoring treatment progres[3,4], guiding the stopping of treatment[5,6], understanding the likelihood of HBsAg loss[7,8], and understanding the likelihood of clinical outcomes[9,10]

Aims

- We conducted a systematic literature search to summarise and evaluate evidence on the use of qHBsAg in CHB, as well as a scoping review of existing clinical guidelines and recommendations

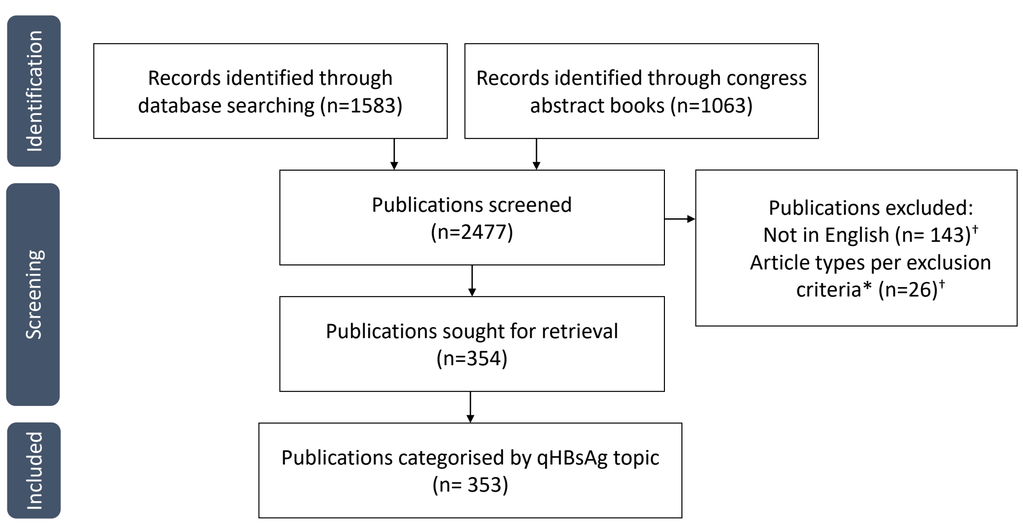
Methods

- Systematic literature search:
  - ProQuest search of Embase and Medline (conducted 31 October 2024; no cut-off date for inclusion)
  - Manual searches (October 2024) of published congress abstracts from recent international society meetings (AASLD 2022−2023, EASL 2024−2024, and APASL 2022−2024)
- Eligibility criteria:
  - Clinical trials or cohort studies conducted in people aged ≥16 years with CHB that reported qHBsAg measurements
- Exclusion criteria:
  - Focused on HBV prevention/vaccination
  - Focused on people with HIV, HCV or HDV coinfection
  - Not in English
- Studies were independently screened and categorised by two reviewers according to the use(s) of qHBsAg testing
- Professional society guidelines involving use of qHBsAg were also summarised and compared

Results

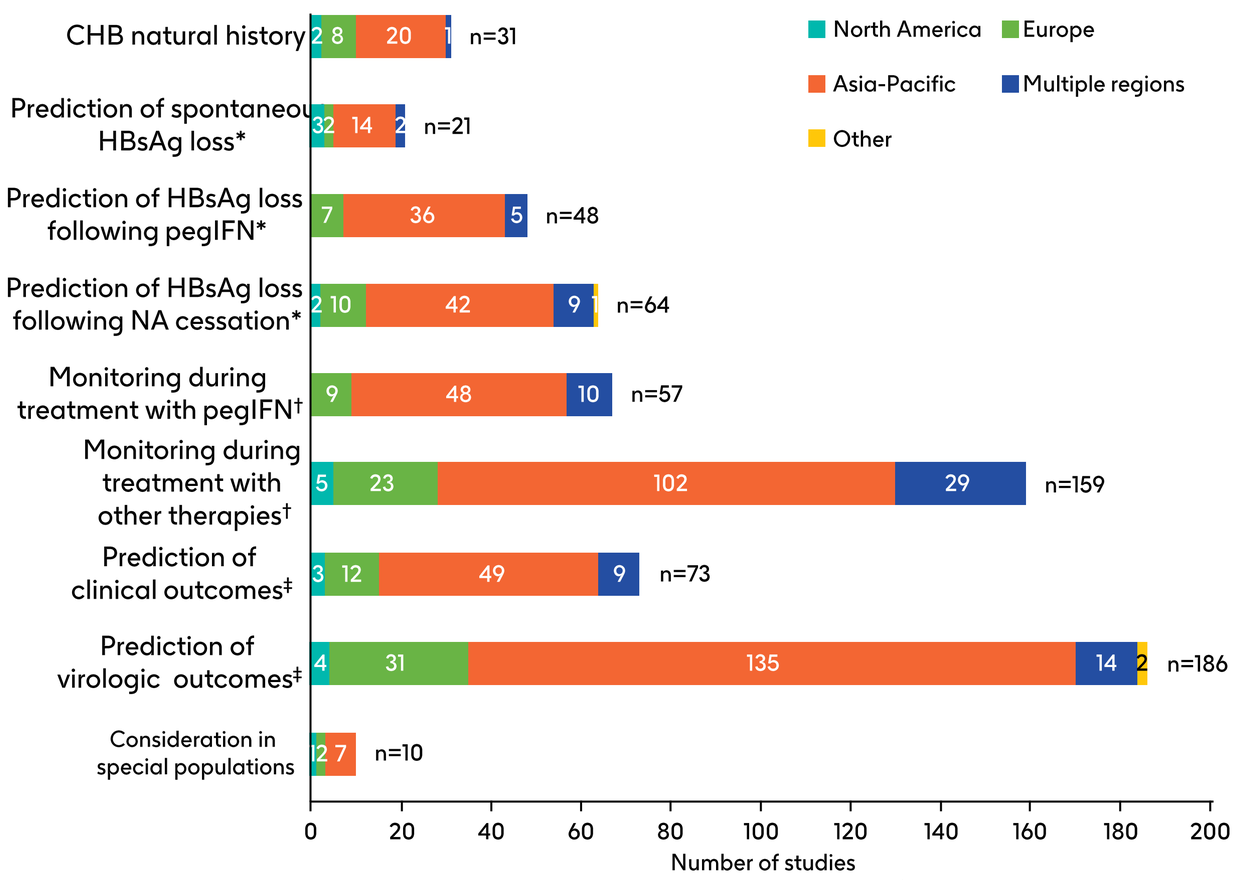
- In total, 2477 publications were identified; 353 were included as relevant (Figure 1) with most studies from the Asia-Pacific region (Figure 2)
- Most studies were cohort studies of small-to-medium size. Apart from monitoring during treatment with pegIFN, where most relevant studies were multicentre, most studies across topics were conducted at a single centre
- At least three out of five studies included in each topic originating from the Asia-Pacific region; the majority of the remaining studies originating from North America and Europe. Other regions were poorly represented (Figure 2)
- Guidelines from 4 Asia-Pacific-based societies and 6 other national and international societies were compared (Table 1)
  - The topics covered varied between regions, with organisations outside of the Asia-Pacific region being more likely to mention predicting risk with qHBsAg
- Asia-Pacific guidelines were more likely to:
  - Have been updated since 2020
  - Include guidance on the role of qHBsAg in predicting HBsAg loss
  - Include guidance on the role of qHBsAg in monitoring treated patients, particularly for those receiving antiviral therapy
- This literature review is limited by the following:
  - Conclusions are based on guidelines as they stood at the end of 2024. Updates to guidelines are expected in 2025, including those from AASLD, CASL and EASL
  - It only on focuses on chronic CHB management in the absence of HIV co-infection
  - It only includes studies published in English. Additionally, regions such as Africa have less data available. As such, it is not possible to comment on the use of qHBsAg in these places

Figure 1: Inclusions and exclusions of the conducted systematic literature search



*Case studies, corrections, editorials, etc; †Overlapping categories.

Figure 2: Number of studies on different key research topics relating to the use of qHBsAg in CHB by region



*Includes studies which discuss specific threshold values that are predictive of HBsAg loss; †Includes studies which discuss recording values to monitor the response to treatment; ‡Includes patients who are on and off treatment.

Table 1: Guidance from international and national societies relating to the use of qHBsAg in CHB management

Organisation	Last updated	qHBsAg as a tool to predict HBsAg loss	qHBsAg as a tool for monitoring CHB treatment	qHBsAg as a tool for predicting risk of clinical outcomes
Asian Pacific Association for the Study of the Liver (**APASL**)[11,12]	2015 (main guideline) 2021 (NA cessation)	Extensive discussion; recommended thresholds if considering NA cessation or add-on pegIFN (2021)	Recommended during pegIFN and NA (2021)	Discussion of general utility; no thresholds discussed (2015)
National Institute for Health and Care Excellence (**NICE**)[13]	2017	Potential of qHBsAg discussed, but no specific thresholds recommended	Recommended during pegIFN and NA	Not included
European Association for the Study of the Liver (**EASL**)[14]	2017	Discussion as part of a composite score in the context of pegIFN only	Recommended during pegIFN	Discussion of general utility; no thresholds discussed
Canadian Association for the Study of the Liver (**CASL**)[15]	2018	Discussion of baseline HBsAg and HBsAg level changes as predictors	Discussion of stopping rule for pegIFN	Suggested thresholds for better/worse outcomes
American Association for the Study of Liver Diseases (**AASLD**)[16]	2018	Discussion of HBsAg changes as potential indicator of successful NA cessation	Discussion of potential use; not recommended as routine	Discussion of general utility; no thresholds discussed
Indian National Association for Study of the Liver (**INASL**)[17]	2018	Not included	Recommended during pegIFN	Not included
Japanese Society of Hepatology (**JSH**)[18]	2020	Predictive threshold for HBsAg loss listed	Recommended alongside HBV DNA monitoring during antiviral treatment	Not included
Chinese Society of Hepatology / Chinese Society of Infectious Diseases (**CSH/CSID**)[19]	2022	Predictive thresholds for HBsAg loss listed	Recommended during pegIFN and NA	Not included
Gastroenterological Society of Australia (**GESA**)[20]	2022	Predictive thresholds for HBsAg loss listed	Recommended during pegIFN	Discussion of general utility; no thresholds discussed
World Health Organization (**WHO**)[21]	2024	Discussion of EOT HBsAg as a potential predictor	Routine monitoring recommended	Suggested threshold for improved outcomes

Key: qHBsAg guidance provided | Discussion of potential use of qHBsAg | Discussion of potential, limited use of qHBsAg | Not included

Abbreviations

AASLD, American Association for the Study of Liver Diseases; APASL, Asian Pacific Association for the Study of the Liver; CHB, chronic hepatitis B; EASL, European Association for the Study of the Liver; HBV, hepatitis B virus; HBsAg, hepatitis B surface antigen; qHBsAg, quantitative HBsAg; HCV, hepatitis C virus; HDV, hepatitis D virus; HIV, human immunodeficiency virus.

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Digital poster (left)
Narrated summary (right)

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