Alignment of countries in the Americas with the latest WHO guidelines for hepatitis B virus (HBV) infection: a review

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Summary

Evidence is lacking on alignment of current guidance from the Region of the Americas (AMR) countries with the new guidelines for people with hepatitis B virus (HBV) infection published by the World Health Organization (WHO) in March 2024. We gathered the most updated guidance on HBV infection from organisations/societies and seven countries from AMR. Most guidelines were aligned with the new WHO recommendation to treat persons with elevated ALT and HBV-DNA levels ≥2,000 IU/ml or with HIV-coinfection, hepatocellular carcinoma family history, extra-hepatic manifestations, or immunosuppression. The new WHO 2024 guidelines introduced treatment for persistently abnormal ALT in the absence of HBV-DNA, with TDF and/or entecavir as first-line therapy. TDF in pregnant women with high HBV-DNA levels was recommended to prevent mother-to-child transmission (MTCT). These guidelines advised prophylaxis to pregnant women with positive HBsAg where HBV-DNA is unavailable. WHO 2024 and updated guidelines from most AMR countries had simplified and expanded criteria for HBV treatment and MTCT prevention.

Keywords: Hepatitis B; Treatment; Mother to child transmission; Non-invasive tests; Guidelines

Introduction

Chronic hepatitis B is a major health issue worldwide. Data from the World Health Organization (WHO) estimate that 254 million people were living with chronic hepatitis B virus (HBV) infection in 2022, with 1.1 million new infections and around 1 million deaths mostly due to cirrhosis or hepatocellular carcinoma (HCC).[1] The burden of HBV infection is highest in the WHO Western Pacific Region [prevalence of 7.1% (95% CI 6.3–7.9) and the WHO African Region [prevalence of 6.5% (95%CI 5.8–7.3)],[2] with about 5 million people with chronic hepatitis B in the WHO Region of Americas (AMR) [prevalence of 1.2% (95%CI 1.1–1.4)]. Approximately 21% of all people diagnosed by the end of 2022 received treatment.[1,2]

Not all people with HBV infection are eligible for treatment. Usually, an indication of treatment in people with chronic hepatitis B depends on the stage of liver fibrosis, transaminases and/or HBV-DNA levels. Clinical practice guidelines (CPGs) by the Pan American Health Organization (PAHO),[3] North/Latin American societies of Hepatology, such as the American Association for the Study of Liver Diseases (AASLD),[4] and the Asociación Latinoamericana para el Estudio del Hígado (ALEH)[5] were published in the last decade to provide recommendations about the benefits and downsides of best practice for management of people with HBV infection. In 2016, several countries signed an agreement with WHO aiming to define public health strategies to eliminate viral hepatitis by 2030, reducing new infections by 90% and global hepatitis-related mortality by 65%.[6] Most countries from Latin and Central America have developed National Programs to Eliminate Viral Hepatitis, including testing plans, policies and strategies for identification and care of people with viral hepatitis, and most AMR countries, societies and/or organisations have published their national guidance for HBV infection. However, management of HBV infection can vary between countries based on a range of factors, such as prevalence of the infection, income level, availability of technologies for diagnosis, prevention and treatment, and/or patient's values or preferences.

CPGs for the management of people with HBV infection need to be updated regularly based on current scientific knowledge.[7] Recent updates include developing point-of-care tests for HBV-DNA, validating non-invasive tests for fibrosis staging, and describing the safety and efficacy of tenofovir alafenamide fumarate (TAF). WHO first published guidelines on the prevention, care and treatment of people with HBV infection in 2015, with many countries updating their guidance regularly. Although considerable progress has been made toward eliminating HBV infection, simplifying HBV treatment criteria will be necessary to achieve the

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elimination goals.[8] WHO published new guidelines in 2024 for the management of people with HBV infection.[9] These guidelines (hereon referred to as WHO/2024) provide recommendations on simplified treatment criteria for adults and adolescents with chronic hepatitis B; expanded eligibility for antiviral prophylaxis for pregnant women to prevent mother-to-child transmission (MTCT) of HBV; and recommend the use of point-of-care HBV DNA viral load and reflex approaches to HBV DNA testing.[9]

According to the latest WHO Global Hepatitis Report (2024), Brazil, Colombia, Mexico and Peru are WHO focus countries from AMR for the viral hepatitis response.[1] The WHO focus countries represent diverse contexts in terms of their disease burden, sociopolitical situation, innovative program approaches and the country's commitment to the viral hepatitis response. However, there is a lack of evidence on the alignment of current guidance from most AMR countries with WHO/2024. Therefore, we aimed to compare the most updated guidance on prevention, care and treatment of people with HBV infection from international societies and official health departments from AMR countries with those recently proposed by the WHO.

Material and methods

We searched the most updated guidance on HBV infection from PAHO, hepatology international societies and countries from the AMR (Search strategy and selection criteria). Full-text versions of identified guidelines were assessed by a single investigator for extraction of the following data for this scoping review: "*who to test*" (screening of HBV infection) *and who to vaccinate*" (vaccination for HBV); "*who to treat*" (indications for start HBV treatment in adults); "*non-invasive tests* (NITs)" (type and thresholds of NITs to indications of treatment); "*first/second line therapy*" (drugs recommended for treatment); "*prophylaxis in pregnant women*" (recommendations to prevent MTCT); "*treatment indication for children/adolescents*" and "*who and how to test for HDV*" (screening for HDV infection). Data on these topics regarding the management of persons with HBV and prevention of MTCT from guidelines of the AMR organisations/societies/countries were described and compared to the new WHO directions for HBV infection. All data extracted from the guidelines and documents for this manuscript are open-source and website available for free at the links described in Supplementary Material.

Results

We identified guidelines for HBV management from PAHO,[3] AASLD,[4] ALEH[5] and seven Latin American countries (Argentina,[10] Brazil,[11] Chile,[12] Colombia,[13] Mexico,[14] Peru[15] and Uruguay[16]) (Supplementary Table S1). Among organisations/international societies, AASLD had the latest published guidelines (2018) followed by PAHO (2015) and ALEH (2011). Most countries had HBV guidance published on the website of their official health authorities (Brazil, Chile, Colombia, Peru and Uruguay), whereas recommendations from Argentina and Mexico were position papers from their national society of hepatology ("*Sociedad Argentina de Hepatologia*" and "*Asociación Mexicana de Hepatología*"). Brazil had the most updated guidelines (2023) followed by Uruguay (2022). Additionally, Argentina, Chile and Mexico published their guidance in 2021, followed by Peru in 2018 and Colombia in 2016.

Who to test and who to vaccinate

Guidance for screening and HBV vaccination were reported by all reviewed guidelines, except for ALEH/2011. Most guidelines from the AMR countries/societies were aligned with WHO/2024 recommendations to test pregnant women and people at high risk for HBV infection. Only guidelines from Argentina (2021) recommended universal screening. WHO/2024 recommends HBV vaccination of all infants and target groups for catch-up vaccination including young adolescents; household and sexual contacts of people with chronic hepatitis B; and people at risk of acquiring HBV infection. HBV vaccination for pregnant women was recommended by WHO/2024 and all guidelines from the AMR. Interestingly, universal vaccination was recommended by AASLD/2018, Brazil/2023, Argentina/2021, Mexico/2021. Additionally, Uruguay/2022 and Chile/2021 recommended HBV vaccination for all adolescents <12 years and <19 years, respectively. Table 1 describes recommendations for screening and HBV vaccination.

Who to treat

Presence of cirrhosis was an indication of HBV treatment regardless of HBV-DNA and/or ALT levels by the new guidelines from WHO and all other reviewed guidelines. The main difference between WHO's and other guidelines was the definition of cirrhosis by an APRI >1.0. The new WHO directions for HBV infection recommend treatment for persistently elevated ALT (>ULN) associated with HBV-DNA levels ≥2000 IU/ml. Brazil (2023), Uruguay (2022), Argentina (2021) and Chile (2021) were aligned with this recommendation. Guidance form AASLD/2018 (if HBeAg negative), ALEH/2011, Mexico/2021 (if HBeAg negative) and Peru/2018 also recommended treatment using a 2000 IU/ml threshold for HBV-DNA, but with ALT levels > 2 × ULN. On the other hand, guidelines from PAHO (2015) and Colombia (2016) used ALT > ULN, but with an HBV-DNA levels >20,000 IU/ml for starting treatment. WHO/2024 innovated by recommending treatment for people with HBV infection and persistently abnormal ALT levels alone in the absence of HBV-DNA assay or HBeAg testing. None of the reviewed

	HBV screening	HBV vaccination
WHO 2024	Follow WHO recommendations on who to test (testing approaches) and how to test (testing strategies) from the 2017 WHO guidelines on hepatitis B and C testing **Summary:** **HBV testing for pregnant women** **HBV testing for people with high-risk for HBV infection:** household and sexual contacts of people with chronic hepatitis B, PLWH, PWID, MSM, sex workers, transgender people, prisoners, Indigenous peoples, blood and organ donors. Population-based screening is also recommended for migrants from endemic countries and in settings with a ≥2% or ≥5% seroprevalence of HBsAg.	**Vaccination of all infants** with the first dose administered as soon as possible after birth **Target groups** for catch-up vaccination and other preventive strategies include young adolescents; household and sexual contacts of people who are HBsAg-positive; and people at risk of acquiring HBV infection
ALEH 2011	**Not described**	**Not described**
PAHO 2015	**HBV testing for pregnant women** **HBV testing for people with high-risk for HBV infection:** household and sexual contacts of people with chronic hepatitis B, PLWH, PWID, MSM, sex workers, transgender people, prisoners, Indigenous peoples, blood and organ donors. Population-based screening is also recommended for migrants from endemic countries and in settings with a ≥2% or ≥5% seroprevalence of HBsAg	**HBV vaccination for pregnant women** **HBV vaccination for people with high-risk for HBV infection:** household and sexual contacts of people with chronic hepatitis B, PLWH, PWID, MSM, sex workers, transgender people, prisoners, Indigenous peoples, blood and organ donors. Population-based screening is also recommended for migrants from endemic countries and in settings with a ≥2% or ≥5% seroprevalence of HBsAg
AALSD 2018	**HBV testing for pregnant women** **HBV testing for people with high-risk for HBV infection:** Persons born in regions of high or intermediate HBV endemicity (HBsAg prevalence of >2%); U.S.-born persons not vaccinated as an infant whose parents were born in regions with high HBV endemicity (>8%); PWID; MSM; persons needing immunosuppressive therapy; individuals with elevated ALT or AST of unknown aetiology; donors of blood, plasma, organs, tissues, or semen; people with chronic kidney disease in haemodialysis; infants born to HBsAg-positive mothers; PLWH, people with HCV infection; household, needle-sharing, and sexual contacts of HBsAg-positive persons; persons seeking evaluation or treatment for a sexually transmitted disease; health care and public safety workers; residents and staff of facilities for developmentally disabled persons; travellers to countries with an intermediate or high prevalence of HBV infection*; unvaccinated persons with diabetes who are aged 19 through 59 years	Recommendations for vaccination are outlined in the Centers for Disease Control and Prevention and Advisory Committee on Immunization Practices guidelines – Recent recommendation for **universal vaccination** (since 2022) - https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/hepb.html
Brazil 2023	**HBV testing for pregnant women** **HBV testing at least once in life:** adults who were not vaccinated or those vaccinated without response (anti-HBs <10 mIU/ml); people living or immigrants from the Amazon region; infants born to HBsAg-positive mothers; household and sexual contacts of people with chronic hepatitis B; healthcare workers; Indigenous or people from riverside community; people with other sexual transmitted disease. **HBV testing regularly for high-risk populations:** PLWH, people with HCV infection who will receive DAA treatment; people with chronic kidney disease in haemodialysis; people with chronic liver disease; PWID; prisoners; MSM; transgender people; sex workers; people with multiple sex partners; individuals under PreP; persons needing immunosuppressive therapy and/or chemotherapy; blood, organ or semen donors	**Universal vaccination** (since 2016)
Uruguay 2022	**HBV testing for pregnant women** **HBV testing for people with high-risk for HBV infection:** healthcare workers/students; police officers/firefighters; sex workers; PWID; household and sexual contacts of people with chronic hepatitis B; MSM; transgender people; PLWH or HCV coinfection; prisoners; people with diabetes; people with chronic kidney disease in haemodialysis; people with organ transplantation or those who use immunosuppressors	**Vaccination for adolescents < 12 yrs** **Vaccination in people with high-risk for HBV infection:** healthcare workers/students; police officers/firefighters; sex workers; PWID; household and sexual contacts of people with chronic hepatitis B; MSM; transgender people; PLWH or HCV coinfection; prisoners; people with diabetes; people with chronic kidney disease in haemodialysis; people with organ transplantation or those who use immunosuppressors
Argentina 2021	**Universal screening** (at least once in life), **especially in pregnant women**, blood donors and people with high-risk for HBV infection (not detailed)	**Universal vaccination** (since 2012)
Chile 2021	**HBV testing for pregnant women** **HBV testing for people with high-risk for HBV infection:** immigrants from regions with intermediate/high prevalence of HBV infection; people from countries with HBV prevalence >2%; people with elevated ALT levels; PWID; MSM; PLWH or HCV coinfection; people with chronic kidney disease in haemodialysis; infants born to HBsAg-positive mothers; prisoners household and sexual contacts of people with chronic hepatitis B; blood or organ donors	**Vaccination for adolescents < 19 yrs** **Vaccination in people with high-risk for HBV infection:** adults (19–59 yrs) with diabetes; healthcare workers; infants born to HBsAg-positive mothers; immigrants from regions with intermediate/high prevalence of HBV infection; people from countries with HBV prevalence >2%; PWID; MSM; PLWH or HCV coinfection; people with chronic kidney disease in haemodialysis; people with multiple sex partners; prisoners; people with chronic liver disease

(Table 1 continues on next page)

	HBV screening	HBV vaccination
(Continued from previous page)		
Mexico 2021	**HBV testing for pregnant women** **HBV testing for people with high-risk for HBV infection:** immigrants from regions with intermediate/high prevalence of HBV infection; PWID; MSM; PLWH or HCV coinfection; people with chronic kidney disease in haemodialysis; blood, organ or semen donors; healthcare workers; people with elevated ALT levels; people with multiple sex partners; people with a sexual partner with HBV infection	**Universal vaccination**
Peru 2018	**HBV testing for pregnant women** **HBV testing for people with high-risk for HBV infection:** household, needle-sharing, and sexual contacts of HBsAg-positive persons, immigrants from regions with intermediate/high prevalence of HBV infection; Indigenous people, PWID; MSM; transgender women; PLWH or HCV coinfection; people with chronic kidney disease in haemodialysis; persons needing immunosuppressive therapy; solid organ receptors; healthcare workers; persons with psychiatric diseases; people with oncology diseases; prisoners; elderly persons living in nursing homes; people with multiple sex partners; police officers, military force and/or firefighters	**Vaccination for newborns (first 12 h after birth)** **Vaccination in people with high-risk for HBV infection:** people from regions of high endemicity, healthcare students and workers, MSM, sex workers, Indigenous people, police officers, military force and/or firefighters
Colombia 2016	**HBV testing for pregnant women** **HBV testing for people with high-risk for HBV infection:** household and sexual contacts of HBsAg-positive persons, immigrants from regions with intermediate/high prevalence of HBV infection; PWID; MSM; PLWH or HCV coinfection; people with chronic kidney disease in haemodialysis; healthcare workers; elderly persons living in nursing homes; people with multiple sex partners; police officers, military force and/or firefighters	**Vaccination for newborns** **Vaccination in people with high-risk for HBV infection:** household and sexual contacts of HBsAg-positive persons, healthcare workers, PWID

AASLD, American Association for the Study of Liver Diseases; ALEH, Asociación Latinoamericana para el Estudio del Hígado; ALT, alanine aminotransferase; AST, aspartase aminotransferase; HBV, hepatitis B virus; HCV, hepatitis C virus; MSM, men who have sex with men; PAHO, Pan American Health Organization; PLWH, people living with HIV; PreP; Pre-exposure prophylaxis; PWID, people who inject drugs; ULN, upper limit of normal; WHO, World Health Organization. For links to guidelines see Supplementary Table S1.

Table 1: **Recommendations for HBV infection screening and vaccination.**

guidelines had this recommendation based on ALT levels alone.

All reviewed guidelines, with the exception of Mexico (2021), had an indication of treatment based on age (>30 or 40 years) with or without other criteria, such as positive HBeAg, high HBV-DNA and/or elevated ALT levels. Additionally, the indication of starting treatment in people with HBV-HIV coinfection was universally adopted in WHO/2024 and all reviewed guidelines from AMR. Treatment in people with HCC family history independently of HBV-DNA or ALT levels was recommended by WHO/2024 and by the recent guidelines from AASLD/2018, Brazil/2023, Uruguay/2022, Argentina/2021 and Chile/2021. Similarly, the presence of extra-hepatic manifestations of HBV infection, such as glomerulonephritis or vasculitis, was recommended for treatment by WHO/2024 and most recent guidelines from AMR (AASLD, Brazil, Uruguay, Argentina, Chile, Mexico and Peru). Additionally, except for PAHO/2015 and Colombia/2016, WHO/2024 and all other reviewed guidelines recommended HBV treatment as pre-emptive antiviral prophylaxis in people receiving immunosuppression or chemotherapy. Table 2 compares the indication of HBV treatment in the new WHO guidance with the AMR reviewed guidelines. WHO/2024 guidelines for HBV infection recommend starting HBV treatment in the presence of comorbidities, such as diabetes or metabolic-associated liver disease. Guidance on monitoring people who do not meet treatment eligibility are heterogenous across guidelines from the AMR. However, most guidelines considered the use of HBeAg testing, ALT and HBV-DNA levels to monitor untreated people with positive HBsAg at different intervals (Supplementary Table S2).

The use of non-invasive tests to indicate HBV treatment

The guidelines from PAHO/2015, AASLD/2018, Brazil/2023, Mexico/2021, Peru/2018 and Colombia/2016 agreed that treatment can be initiated based exclusively on results of NITs, especially with APRI > 2 or transient elastography (TE) by Fibroscan > 9–12 kPa. The use of new elastography technologies, such as p-SWE or 2D-SWE, can be an alternative to TE-Fibroscan in Brazil. Additionally, FIB-4 or FibroTest can be used to indicate treatment in AASLD/2018 and Mexico/2021. While the WHO/2024 guidelines reinforced the use of those NITs to start treatment, they recommended treatment based on lower thresholds of non-invasive methods, such as APRI >0.5 or TE-Fibroscan >7 kPa (Table 3).

First line therapy

The new WHO guidelines recommend the use of tenofovir disoproxil fumarate (TDF) or entecavir as first-

	WHO 2024	ALEH 2011	PAHO 2015	AALSD 2018	Brazil 2023	Uruguay 2022	Argentina 2021	Chile 2021	Mexico 2021	Peru 2018	Colombia 2016
Presence of cirrhosis regardless ALT and/or HBV-DNA levels	**Yes** APRI >1.0 or TE-Fibroscan >12.5 kPa	**Yes**	**Yes**	**Yes**	**Yes**	**Yes**	**Yes**	**Yes**	**Yes**	**Yes**	**Yes**
Persistent ALT elevation with HBV-DNA > 2000 IU/ml	**Yes** HBV-DNA ≥2000 IU/ml AND ALT > ULN In absence of HBV DNA assay, treatment if persistently abnormal ALT levels alone	**Yes** HBV-DNA ≥ 2000 IU/ml AND ALT > 2x ULN	**No** Age >30 yrs with ALT> 30 U/L for men or > 19 U/L in women; but HBV-DNA >20,000 IU/ml	**Yes** HBeAg negative AND HBV-DNA ≥2000 IU/ml AND ALT > 2x ULN If HBeAg positive: HBV-DNA ≥20,000 IU/ml AND ALT > 2x ULN	**Yes** HBV-DNA ≥2000 IU/ml AND mild ALT levels (≥52 U/L for men or ≥ 37 U/L for women)	**Yes** HBV-DNA ≥2000 IU/ml AND ALT > ULN	**Yes** HBV-DNA ≥2000 IU/ml AND ALT elevation	**Yes** HBV-DNA ≥2000 IU/ml AND ALT > ULN. If normal ALT: liver biopsy ≥ A2 or ≥ F2	**Yes** Negative HBeAg: ALT > 2 × ULN with HBV-DNA >2000 IU/ml Positive HBeAg: HBV-DNA >20,000 IU/ml	**Yes** HBV-DNA ≥2000 IU/ml AND ALT > 2x ULN If ALT < 2 × ULN: liver biopsy ≥ A2 or ≥ F2	**Yes/No** HBV-DNA ≥2000 IU/ml AND negative HBeAg AND ALT > ULN AND fibrosis HBV-DNA ≥20,000 IU/ml AND ALT > ULN
Treatment criteria based on age		**Yes** Age >40 years AND ALT 1–2 × ULN with ≥ A2 or ≥ F2 in liver biopsy	**Yes** Age >30 years with ALT> 30 U/L for men or >19 U/L in women AND HBV-DNA >20,000 IU/ml	**Yes** Age >40 years if HBV-DNA <2000 IU/ml (HBeAg negative) or < 20,000 IU/ml (HBeAg positive)	**Yes** Age >30 years with positive HBeAg	**Yes** Age >30 years with positive HBeAg	**Yes** Age >30 years with positive HBeAg and high levels of HBV-DNA	**Yes** Age >40 years with HBV-DNA ≥2000 IU/ml	**No**	**Yes** Age >30 years with HBV-DNA ≥2000 IU/ml AND positive HBeAg	**Yes/No** Age >30 years if unavailable HBV-DNA
HIV coinfection	**Yes** HIV, HCV or HDV co-infection	**Yes/No** Yes, when indicated c-ART (use TDF as part of c-ART); if non-indication of c-ART treat if liver biopsy > F2 OR similar to HBV mono-infected	**Yes**	**Yes**	**Yes** HIV, HCV or HDV co-infection	**Yes**	**Yes**	**Yes**	**Yes**	**Yes**	**Yes**
HCC history family	**Yes**	**No**	**No**	**Yes**	**Yes**	**Yes**	**Yes**	**Yes**	**No**	**Yes** HCC family history AND age >40 years with HBV-DNA ≥2000 IU/ml AND ALT 1–2 × ULN with ≥ A2 or ≥ F2 in liver biopsy.	**No**
Extra-hepatic manifestations	**Yes**	**No**	**No**	**Yes**	**Yes**	**Yes**	**Yes**	**Yes**	**Yes**	**Yes**	**No**

(Table 2 continues on next page)

	WHO 2024	ALEH 2011	PAHO 2015	AALSD 2018	Brazil 2023	Uruguay 2022	Argentina 2021	Chile 2021	Mexico 2021	Peru 2018	Colombia 2016
(Continued from previous page)											
Based exclusively on NIT results (regardless of HBV-DNA or ALT levels)	Yes APRI >0.5 or TE-Fibroscan >7 kPa	No	Yes APRI >2	Yes TE-Fibroscan, FibroTest or FIB-4 ≥ F2	Yes TE-Fibroscan >9 kPa if normal ALT or > 12 kPa if elevated ALT; p-SWE >1.8 m/s; 2D-SWE >10 kPa	Yes/No Fibrosis by TE-Fibroscan (no cut-off described)	No	Yes/No Fibrosis by TE-Fibroscan (no cut-off described) with HBV-DNA ≥2000 IU/ml	Yes FIB-4, FibroTest or TE-Fibroscan Thresholds not described	Yes APRI >2 or TE-Fibroscan >12 kPa	Yes APRI >2
Starting Immunosuppression or chemotherapy (pre-emptive antiviral prophylaxis)	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes Including HBV-HCV starting DAAs	Yes	Yes	No
Comorbidities (e.g., diabetes, metabolic dysfunction-associated steatotic liver disease)	Yes	No	No	No	No	No	No	No	No	No	No

AASLD, American Association for the Study of Liver Diseases; ALEH, Asociación Latinoamericana para el Estudio del Hígado; ALT, alanine transaminase; APRI, aspartate-to-platelet ratio index; DAAs, direct-acting agents; FIB-4, fibrosis-4 score; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; HDV, hepatitis Delta virus; NIT, non-invasive test; PAHO, Pan American Health Organization; TE, transient elastography; ULN, upper limit of normal; WHO, World Health Organization. For links to guidelines see Supplementary Table S1. Extrahepatic manifestations of HBV infection include polyarteritis nodosa, non-rheumatoid arthritis, non-Hodgkin lymphoma, cryoglobulinemia, uveitis, vasculitis and glomerulonephritis. Immunosuppression/chemotherapy includes cancer chemotherapy, checkpoint inhibitors, immunosuppressive therapies, bone marrow and stem cell treatment, newer anti-tumor necrosis factor immunobiologics, chimeric antigen receptor T-cell treatment and after treatment for coexistent hepatitis C.

Table 2: **Criteria for indication of treatment ("who to treat").**

line therapy for HBV infection. Additionally, TAF as first-line therapy would be restricted to persons with osteoporosis or impaired kidney function. TDF was universally recommended as first-line therapy by the reviewed AMR guidelines. Guidelines from Uruguay/2022, Argentina/2021, Chile/2021 and Mexico/2021 recommended TDF and/or TAF as first-line therapy; TAF can be used when there is a contraindication to TDF, as recommended by the Brazil/2023 guidelines. Alternative drugs as second-line therapy in most guidelines were adefovir, telvibudina, 3 TC and/or emtricitabine. Finally, PEG-IFN was recommended in specific cases by few guidelines (Table 4).

Prevention of mother to child transmission

The new WHO guidelines recommend that TDF should be initiated from at least the second trimester of pregnancy (24–28 weeks) in pregnant women with high HBV-DNA levels (≥200,000 IU/ml) to prevent MTCT, with AASLD/2018, Brazil/2023, Uruguay/2022, Argentina/2021, Chile/2021, Mexico/2021 and Peru/2018 all aligned with this recommendation. Moreover, WHO/2024, Brazil/2023 and Uruguay/2022 were aligned stating that TDF can be initiated in pregnant women with positive HBeAg in the absence of HBV-DNA assay. Additionally, the new WHO directions innovated by recommending TDF as prevention of MTCT in pregnant women with positive HBsAg alone if HBV-DNA and HBeAg are not available. The new WHO recommendations suggest that TDF should be used at least after delivery or completion of the infant HBV vaccination series. Similarly, all AMR guidelines recommended discontinuing TDF 3–4 months after childbirth. Mothers have a potential risk of exacerbation or postpartum flare after TDF discontinuation, and therefore they need to be carefully monitored. Almost all guidelines agreed that there is no preference for the type of delivery and that newborns should receive the first dose of the HBV vaccine and immune globulin (HBIG) in the first 12–24 h of life to prevent MTCT. Additionally, guidelines agreed that breastfeeding is not contraindicated in mothers with HBV infection, although mothers should stop nursing temporarily if nipples and/or surrounding areola are cracked and/or bleeding. Table 5 describes recommendations for MTCT from WHO/2024 and AMR guidelines.

Treatment of children and/or adolescents

The new WHO guidelines recommend treatment of children and/or adolescents with similar criteria as those for adults with HBV infection. Few AMR guidelines are aligned with this recommendation (Brazil/2023, Argentina/2021, Chile/2021 and Colombia/2016) (Table 6). Guidelines from PAHO/2015 and international societies (ALEH/2021 and AASLD/2018) had more restricted criteria for initiating treatment in children and/or adolescents. A few guidelines required a

	WHO 2024	ALEH 2011	PAHO 2015	AALSD 2018	Brazil 2023	Uruguay 2022	Argentina 2021	Chile 2021	Mexico 2021	Peru 2018	Colombia 2016
Use of NITs for treatment indication in people with HBV	**Yes** APRI >0.5 or TE-Fibroscan >7 kPa	**Not described**	**Yes** APRI >2 TE-Fibroscan Cut-off?	**Yes** TE-Fibroscan, FibroTest or FIB-4 ≥ F2	**Yes** Liver elastography (Fibroscan, p-SWE or 2D-SWE) TE-Fibroscan >9 kPa if normal ALT or > 12 kPa if elevated ALT; p-SWE >1.8 m/s; 2D-SWE >10 kPa	**Not described**	**Not described**	**No** TE-Fibroscan only if HBV-DNA≥ 2000 UI/ml	**Yes** FIB-4, FibroTest or TE-Fibroscan	**Yes** APRI >2 or TE-Fibroscan >12 kPa	**Yes** APRI >2

AASLD, American Association for the Study of Liver Diseases; ALEH, Asociación Latinoamericana para el Estudio del Hígado; APRI, aspartate-to-platelet ratio index; FIB-4, fibrosis-4 score; NIT, non-invasive test; PAHO, Pan American Health Organization; SWE, shear-wave elastography; TE, transient elastography; WHO, World Health Organization. For links to guidelines see Supplementary Table S1.

Table 3: **Recommendation for HBV treatment based on non-invasive tests results regardless of HBV-DNA and/or ALT levels.**

liver biopsy to initiate treatment, especially for normal ALT levels. Guidelines from Uruguay (2022) recommended treatment in children and/or adolescents based on international guidelines and those from Mexico (2021) and Peru (2018) lacked recommendations for treatment of children and/or adolescents.

Who and how to test for HDV infection

The new WHO/2024 guidelines recommended universal HDV testing among people with chronic hepatitis B. However, where this approach may not be feasible, HDV testing should be prioritized in people at high-risk for hepatitis Delta. The guidelines from Chile (2021) supported universal testing for HDV infection, whereas those from AALSD/2018, Brazil/2023, Uruguay/2022 and Argentina/2021 recommended HDV testing for people with chronic hepatitis B at higher risk for HDV infection. WHO/2024 and most AMR guidelines (PAHO/2015, AASLD/2018, Brazil/2023, Argentina/2021 and Chile/2021) recommended screening with anti-HDV followed by HDV-RNA for anti-HDV positive individuals. Table 7 summarises recommendations on who and how to test for HDV infection.

Discussion

The new WHO HBV guidelines published in March 2024 provided updated evidence-based recommendations on key priority topics, including HBV screening and vaccination, expanded and simplified treatment criteria for adults and adolescents; use of simple NITs to indicate HBV treatment and expanded eligibility for antiviral prophylaxis for pregnant women to prevent MTCT of HBV. This review highlights that most updated recommendations for HBV treatment and MTCT prevention from AMR countries are aligned with those in WHO-2024.

Despite the global burden of chronic hepatitis B and new technologies available for diagnosis and advances in treatment, most people infected with HBV remain unaware of their infection (estimated as less than 5% in resource-limited settings). Additionally, region-specific

	WHO 2024	ALEH 2011	PAHO 2015	AALSD 2018	Brazil 2023	Uruguay 2022	Argentina 2021	Chile 2021	Mexico 2021	Peru 2018	Colombia 2016
First line therapy	TDF or entecavir TAF in persons with osteoporosis or impaired kidney function	TDF, entecavir or PEG-IFN	TDF or entecavir; PLWH should have c-ART with TDF or TAF associated with 3 TC or emtricitabine	TDF, TAF, entecavir or PEG-IFN	TDF	TDF, TAF or entecavir	TDF, TAF or entecavir; PLWH should have c-ART with TDF or TAF associated with 3 TC or emtricitabine	TDF, TAF or entecavir	TDF, TAF or entecavir	TDF	TDF or entecavir
Second line therapy	TDF + 3 TC or emtricitabine (if no access to TDF monotherapy)	adefovir, telvibudina and emtricitabine	adefovir	3 TC, adefovir, telvibudina	entecavir, TAF (if contraindication to TDF and entecavir)	3 TC, emtricitabine, PEG-IFN	Not described	3 TC, PEG-IFN	Not described	entecavir	3 TC, adefovir or telbivudine

AASLD, American Association for the Study of Liver Diseases; ALEH, Asociación Latinoamericana para el Estudio del Hígado; c-ART, combined antiretroviral therapy; PAHO, Pan American Health Organization; PEG-IFN, peg-interferon; PLWH, people living with HIV; TAF, tenofovir alafenamide; TDF, Tenofovir disoproxil fumarate; WHO, World Health Organization. For links to guidelines see Supplementary Table S1.

Table 4: **First and second line therapies for chronic HBV infection recommendations.**

	WHO 2024	ALEH 2011	PAHO 2015	AALSD 2018	Brazil 2023	Uruguay 2022	Argentina 2021	Chile 2021	Mexico 2021	Peru 2018	Colombia 2016
Positive HBsAg alone if HBV-DNA assay or HBeAg testing not available	**Yes** TDF from at least second trimester of pregnancy until at least after delivery	**No**	**No**	**No**	**No**	**No**	**No**	**No**	**No**	**No**	**No**
Pregnant women with HBV-DNA ≥ 200,000 IU/ml.	**Yes** TDF from at least the second trimester of pregnancy (W28) until at least after delivery or completion of the infant HBV vaccination series Alternative if HBV-DNA not available: positive HBeAg	**Not described**	**No**	**Yes** TDF must be initiated at W24–W28 of gestation.	**Yes** TDF must be initiated at W24–W28 of gestation. Treatment can be stopped 3 months after childbirth Alternative if HBV-DNA not available: positive HBeAg	**Yes** TDF must be initiated at W24–W28 of gestation. Treatment can be stopped 3 months after childbirth Alternative if HBV-DNA not available: positive HBeAg	**Yes** The week of start is not described TDF Treatment can be stopped 3 months after childbirth	**Yes** TDF must be initiated at W24–W28 of gestation. Treatment can be stopped 3 months after childbirth	**Yes** TDF must be initiated at W24–W28 of gestation. Treatment can be stopped 3 months after childbirth	**Yes** TDF must be initiated at W24–W28 of gestation. Treatment can be stopped 4 months after childbirth	**No** There is no recommendation for TDF to prevent MTCT
Preferred type of delivery	Not described	Not described	Not described	Not described	No	No	Not described	No	Not described	No	Not described
Vaccination for newborn	Yes, First 24 h	Not described	Yes, First 24 h	Yes, First 12 h	Yes, First 12 h	Yes First 12 h	Yes First 12 h	Yes	Not described	Yes	Not described
Immune globulin (HBIG) for newborn	Not described	Not described	Yes, First 24 h	Yes, First 12 h	Yes, First 12–24 h	Yes, First 12 h	Yes, First 12 h	Yes First 12 h	Yes First 12 h	Yes	Not described
Contraindication to breastfeeding	No (among women taking TDF)	Not described	No	No	No	No	No	No	No	No	Not described

AASLD, American Association for the Study of Liver Diseases; ALEH, Asociación Latinoamericana para el Estudio del Hígado; HBIG, immune globulin; MTCT, mother-to-child transmission; PAHO, Pan American Health Organization; TDF, Tenofovir disoproxil fumarate; W, week; WHO, World Health Organization. For links to guidelines see Supplementary Table S1.

Table 5: **Recommendations to prevent mother-to-child transmission (MTCT) of HBV infection.**

estimates of HBV screening remain extremely variable.[17] These findings might be explained by limited availability of testing facilities and services, ineffective testing policies, weak or non-existent national hepatitis surveillance programs, high costs of diagnostic assays, and limited laboratory capacity and infrastructure[18]

The most recent WHO/2024 recommendations expanded eligibility criteria for HBV treatment regardless of HBV-DNA and ALT levels, such as based on the presence of cirrhosis or coinfections, results of NITs, HCC family history, extra-hepatic manifestations and when starting immunosuppression. The main WHO/2024 innovation was the indication of treatment in people with persistently elevated ALT levels [at least two ALT values > ULN (30 U/L for men and 19 U/L for women) for a 6–12-month period] in settings where HBeAg and HBV-DNA testing are not available. We acknowledge that there is no consensus for ALT ULN. A recent meta-analysis including data from more than 400,000 individuals showed ALT ULN levels of 32 U/L in people without metabolic diseases and 40 U/L among the overweight/obese.[19] Most guidelines from the AMR countries/societies recommended using ALT ULN from 30 to 40 U/L as an eligibility criterion for HBV treatment (Supplementary Table S3). Additionally, WHO/2024 recommends treatment in people with comorbidities, such as diabetes and/or metabolic dysfunction-associated steatotic liver disease (MASLD), regardless of HBV-DNA or ALT levels. Recent studies have shown a high burden of MASLD in AMR countries,[20] which might lead to more people with HBV infection being eligible for treatment.

A modelling study by the Polaris Observatory Hepatitis B Collaborators estimated that only 5% of eligible people with HBV infection received antiviral treatment in 2016.[21] However, there has been notable global progress toward hepatitis treatment. A recent study that used data reported by WHO countries and regional offices showed that up to 23% of those diagnosed with hepatitis B received treatment in 2019, compared to 8% in 2015.[22] The expanded eligibility criteria for HBV treatment described in WHO/2024 will probably

	WHO 2024	ALEH 2011	PAHO 2015	AALSD 2018	Brazil 2023	Uruguay 2022	Argentina 2021	Chile 2021	Mexico 2021	Peru 2018	Colombia 2016
Presence of clinical or ultrasound signs of cirrhosis	**Yes**	**No**	**Yes** Alternative: liver biopsy ≥ A2	**No**	**Yes**	**Yes/No** Based on international guidelines	**Yes**	**Yes**	**Not described**	**Not described**	**Yes**
HBV-DNA ≥ 2000 UI/ml AND ALT elevation	**Yes** HBV-DNA ≥2000 IU/ml AND ALT > ULN In absence of HBV DNA assay, treatment if persistently abnormal ALT levels alone (defined as two ALT values above the ULN at unspecified intervals during a 6- to 12-month period)	**Yes** HBV-DNA ≥2000 IU/ml AND negative HBeAg AND liver biopsy > A1-F1 Alternative: positive HBeAg with HBV-DNA >20,000 IU/ml	**No**	**Yes/No** HBeAg-positive with ALT > 1.3 × ULN AND HBV-DNA ≥10,000 IU/ml	**Yes** HBV-DNA ≥2000 IU/ml with ALT ≥1.3 × ULN for more than 6 months; if ALT between 1.0–1.3 × ULN treat if liver biopsy with ≥A2 or ≥ F2	**Yes/No** Based on international guidelines	**Yes**	**Yes** HBV-DNA ≥ 2000 IU/ml AND ALT > ULN. If normal ALT: liver biopsy ≥ A2 or ≥ F2	**Not described**	**Not described**	**Yes/No** HBV-DNA ≥ 2000 IU/ml AND negative HBeAg AND ALT > ULN AND fibrosis HBV-DNA ≥ 20,000 IU/ml AND ALT > ULN
HIV coinfection	**Yes**	**No**	**Yes**	**Yes**	**Yes**	**No**	**Yes**	**Yes**	**Not described**	**Not described**	**Yes**
HCC history family	**Yes**	**No**	**No**	**No**	**Yes**	**No**	**Yes**	**Yes**	**Not described**	**Not described**	**No**
Extra-hepatic manifestations	**Yes**	**No**	**No**	**No**	**Yes**	**No**	**Yes**	**Yes**	**Not described**	**Not described**	**No**
Starting immunosuppression or chemotherapy (pre-emptive antiviral prophylaxis)	**Yes**	**No**	**No**	**No**	**Yes**	**No**	**Yes**	**Yes**	**Not described**	**Not described**	**No**
Comorbidities (e.g., diabetes, metabolic dysfunction-associated steatotic liver disease)	**Yes**	**No**	**No**	**No**	**No**	**No**	**No**	**No**	**No**	**No**	**No**

AASLD, American Association for the Study of Liver Diseases; ALEH, Asociación Latinoamericana para el Estudio del Hígado; ALT, alanine transaminase; APRI, aspartate-to-platelet ratio index; DAAs, direct-acting agents; FIB-4, fibrosis-4 score; HCC, hepatocellular carcinoma; PAHO, Pan American Health Organization; ULN, upper limit of normal; WHO, World Health Organization. For links to guidelines see Supplementary Table S1.

Table 6: **Recommendations to treat children and/or adolescents.**

	Who to test for HDV infection	How to test for HDV infection
WHO 2024	**Universal HDV testing approach** among people with chronic hepatitis B **Where this approach may not be feasible because of limited laboratory capacity, HDV testing should be prioritised in specific HBsAg-positive populations or settings with well-established higher prevalence of HDV infection**: people born in HDV-endemic countries and regions; people at higher risk of acquiring HDV (PWID, MSM, sex workers, people living with HCV or HIV, and haemodialysis recipients); children and family members of people with HDV infection and people with advanced liver disease	**Serological assay to detect total anti-HDV followed by a NAT to detect HDV RNA and active (viraemic) infection among those who are anti-HDV positive** Reflex testing is recommended for anti-HDV antibody testing following a positive HBsAg test result and also for HDV RNA testing (where available) following a positive anti-HDV antibody test result
ALEH 2011	**Not described**	**Not described**
PAHO 2015	**Not described**	**Screening with IgG and IgM anti-HDV followed by HDV-RNA for those who are anti-HDV positive** However, HDV diagnostics are not widely available, and there has also been limited standardisation of HDV RNA assays
AALSD 2018	**High-risk populations for HDV infection:** PLWH, PWID, MSM, people with multiple sexual partners, immigrants from areas of high HDV endemicity	**Screening with total anti-HDV followed by HDV-RNA for those who are anti-HDV positive**
Brazil 2023	**Specific populations**: people with HBsAg positive living or born in the Amazon region[a] or people with chronic hepatitis B under treatment having decompensation of the liver disease with an unknown aetiology	**Screening with total anti-HDV followed by HDV-RNA for those who are anti-HDV positive** People with HBsAg positive living in the Amazon region should be tested for anti-HDV annually. Those with positive anti-HDV with undetectable HDV-RNA should repeat HDV-RNA every 6 months during the first year. Thereafter, HDV-RNA annually
Uruguay 2022	**Not described** According to the guidance, HDV infection should be suspected in people with HBsAg positive who have severe inflammatory activity not related to high HBV-DNA levels, those HBsAg positive with acute hepatitis (high ALT elevation) and/or rapid fibrosis progression	**HDV antibody test (screening) and HDV-RNA are not available in Uruguay**
Argentina 2021	**Specific patients:** people with HBsAg positive who have severe inflammatory activity not related to high HBV-DNA levels, those HBsAg positive with acute hepatitis (high ALT elevation) and/or rapid fibrosis progression	**Screening with total anti-HDV followed by HDV-RNA for those who are anti-HDV positive**
Chile 2021	**All individuals with HBV infection should be tested for HDV at least once** **High-risk populations for HDV infection:** PWID, immigrants from areas of high HDV endemicity, people with HBsAg positive who have severe inflammatory activity not related to high HBV-DNA levels	**Screening with total anti-HDV followed by HDV-RNA for those who are anti-HDV positive**
Mexico 2021	**Not described**	**Not described**
Peru 2018	**Not described** Recommendation for HDV testing for those with a diagnosis of chronic hepatitis B	**Not described**
Colombia 2016	**Not described** Recommendation for HDV testing for those with a diagnosis of chronic hepatitis B	**Not described**

[a]Federative Units of the Brazilian Amazon region: Amazonas (AM), Acre (AC), Roraima (RR), Rondônia (RO), Amapá (AP), Pará (PA), Tocantins (TO), Maranhão (MA) e Mato Grosso (MT).

Table 7: **Testing for HDV infection in patients with chronic hepatitis B.**

capture a higher proportion (at least 50%) of all HBsAg-positive people compared to the previous criteria. Recent guidelines from the Chinese Society of Hepatology together with the Chinese Society of Infectious Diseases (Asia–Pacific Region) propose expanded HBV treatment criteria based on ALT levels and qualitative HBV-DNA assays instead of quantitative thresholds of HBV-DNA levels. Additionally, these guidelines recommend that people older than 30 years with detectable HBV-DNA should be treated regardless of normal ALT levels.[23] Moreover, few studies have proposed treatment for all people with detectable HBV-DNA ("treat all strategy" for HBV infection).[24,25] Simplifying treatment for all patients with chronic hepatitis B can reduce the complexity and costs of testing and monitoring for eligibility, increase access to treatment, decrease the risk of transmission, and help to destigmatize the need for HBV treatment. However, treating people with chronic hepatitis B in the "immune tolerant phase" (high levels of HBV-DNA with normal

ALT) remains controversial and it is not advocated by the guidelines. Further studies are needed to validate the strategy "treat-all" for HBV and to better understand the impact of simplifying treatment criteria on the long-term outcomes of patients with chronic hepatitis B.

A study from the US estimated that treating all HBV infections would be highly cost-effective at an annual treatment cost of $2000, and cost saving, with a positive return on investment before 2050 at an annual treatment cost of $750.[26] These estimates might vary across AMR countries; for example the monthly treatment cost with TDF 300 mg (30 tablets) is US$ 5.22 (US$ 63 per year) in Brazil and US$ 9.60 in Colombia (US$ 115 per year).[1] More recently, simplifying and expanding HBV treatment was confirmed to be cost-effective in different countries and regions. Despite a significant increase in the number of individuals treated, the savings from preventing end-stage liver disease and simplifying diagnostic processes make these scenarios consistently cost-effective, and sometimes even cost-saving.[27]

The new WHO guidelines indicate antiviral treatment in people with HBV infection based on NITs at lower thresholds (APRI >0.5 or TE-Fibroscan >7 kPa). The recent AASLD guidelines for the use of NITs to stage liver fibrosis supported a higher accuracy for liver elastography than serological biomarkers, such as APRI or FIB-4, for detection of advanced fibrosis and cirrhosis.[28,29] Furthermore, different ultrasound-based elastography methods that have excellent accuracy for detecting cirrhosis (F = 4) are recommended for patients with HBV infection. However, TE-Fibroscan or other liver elastography technologies, such as p- or 2D-SWE, are expensive and not widely available. On the other hand, APRI uses simple parameters (AST and platelet count) and is easy to calculate. Serological biomarkers, such as APRI and FIB-4, are better to exclude than to detect significant/advanced fibrosis (thresholds with high specificity).[29] Nevertheless, the use of simple and worldwide NITs, especially at a low cut-off (i.e., APRI >0.5 with higher sensitivity) will provide access to treatment to more people with positive HBsAg.

Both antiviral prophylaxis of pregnant women with positive HBsAg with high HBV-DNA levels as well as hepatitis B vaccination in the first 24 h in children are cornerstones in preventing MTCT of HBV infection. The most recent AMR guidelines are aligned with WHO/2024 in recommending TDF from the second trimester of pregnancy (24–28 weeks) in pregnant women with HBV-DNA levels >200,000 IU/ml, and early newborn HBV vaccination (12–24 h of life) to prevent MTCT. A systematic review/meta-analysis including 19 studies (1092 mothers and 1072 infants) showed that antiviral prophylaxis with TDF was highly effective at reducing the risk of HBV MTCT (pooled ORs were 0.10 (95% CI 0.03–0.35) for randomised controlled trials and 0.17 (0.10–0.29) in non-randomised studies).[30] As of 2018, 25 countries in the Latin America region had introduced the universal hepatitis B vaccine for neonates in the first 24 h of life.[31] Brazil has a low incidence of MTCT of HBV infection (0.5 per 1000 living births in 2021)[32] and the incidence of HBV infection has decreased in Colombia after implementation of vaccination at birth.[33]

Many challenges remain for the prevention of MTCT of HBV infection. The regional coverage of the timely hepatitis B vaccine first dose in Latin America has declined from 87% in 2015 to 79% in 2018.[31] An international survey performed in 2019 with HBV experts from 63 countries reported that 44% of countries did not screen for viral hepatitis during pregnancy, and 46% did not provide third-trimester antiviral therapy for highly viraemic pregnant mothers. Additionally, the first vaccine dose was given at more than 24 h in 36% of the total countries and the recommended birth dose was unavailable for outborn neonates in 45% of the total countries, including 50% of Latin American countries/regions.[34] The new WHO guidelines intend to expand access to antiviral prophylaxis to a higher proportion of pregnant women with HBV infection. The cost and availability of HBV-DNA were major barriers to access to treatment in Africa.[35] A high accuracy for the use of dried blood spots for HBV-DNA[36] and alternative techniques, such as loop-mediated isothermal amplification (LAMP) assay, to diagnose high viremia (≥200,000 IU/ml)[37] has been described. However, manufacturers must standardise technical guidance, as experience in the use of these techniques/tools for hepatitis testing across a wide range of settings in low and middle-income countries remains limited. Therefore, one of the main innovative recommendations by WHO/2024 was the implementation of prophylaxis with TDF in all women with positive HBsAg when HBV-DNA or HBeAg testing are not available. This recommendation will probably lead to a higher proportion of pregnant women with HBV infection under TDF-prophylaxis, especially in resource-limited settings. The best way to monitor mothers after discontinuation of TDF postpartum remains a research gap.

This review has limitations. We are aware of the burden of HBV-HDV coinfection in endemic areas of South American countries (prevalence up to 54% in several regions). A systematic review estimated a pooled anti-HDV prevalence of 22% in South America.[38] Despite the clinical relevance of hepatitis Delta, several reviewed guidelines from the AMR did not include their local recommendations for HDV screening or how to test for hepatitis Delta [ALEH/2011), Mexico/2021), Peru/2018) and Colombia/2016)]. Secondly, a few HBV infection guidelines were published more than 5 years ago. The older guidelines, especially ALEH/2011 and PAHO/2015, lacked some of the currently used recommendations, such as treatment based on NITs, HCC family history or extrahepatic manifestations and the use of TDF as prevention of MTCT, probably due to lack of evidence by the time of writing. However, those were

Search strategy and selection criteria

For this scoping review, we searched for the most updated guidance on HBV infection from PAHO and two international societies of hepatology (AASLD and ALEH) from WHO-Region of Americas. Additionally, we searched the websites of Ministries of Health and/or National Viral Hepatitis Programs of 11 countries in Latin America (Argentina, Bolivia, Brazil, Chile, Colombia, Ecuador, Mexico, Paraguay, Peru, Uruguay and Venezuela), to assess data on recommendations for management of patients with HBV infection. We also manually searched for publications, statements, or position papers on the management of HBV infection by National Societies of Hepatology from those countries. We used terms to identify guidelines in Portuguese language for Brazil ("Hepatite"; "Hepatite B"; "Protocolo Clínico"; "Protocolo Clínico Hepatite B") and in Spanish for other countries ("Hepatitis"; "Hepatitis B"; "Guía de Práctica Clínica"; "Guía Clínica Hepatitis B"). The most recent guidelines publication was retained if more than one version were available. Data were extracted from the identified documents by a single investigator.

the last versions available. Additionally, differences among guidelines might be explained by the fact that WHO considers a broader scenario, especially in the absence of more complex procedures (i.e., HBV-DNA assay), while national guidelines must account for the local context for public health strategies, such as HBV management. Finally, despite searching the sites of local health departments with specific terms in local languages, we could not identify national guidelines for HBV infection from four South American countries (Bolivia, Ecuador, Paraguay and Venezuela). The major strength of this review was the comparison of the recently published recommendations by WHO with the last updated multi-societies (AASLD/2018, ALEH/2011 and PAHO/2015) and national guidelines for the management of HBV infection from many AMR countries (Argentina/2021, Brazil/2023, Chile/2021, Colombia/2016, Mexico/2021, Peru/2018 and Uruguay/2022). Furthermore, we focused on major key points, such as HBV screening, who to treat, first/second-line therapies, non-invasive assessment of liver disease, MTCT prevention and HDV testing.

In conclusion, the main innovative recommendations of WHO/2024 were the indication of treatment based on low thresholds of NITs and the possibility of treatment based on isolated ALT elevation and/or antiviral prophylaxis to MTCT in people with positive-HBsAg in the absence of HBeAg testing or HBV-DNA assays. Despite the absence of these new recommendations, most AMR countries' guidelines had simplified and expanded criteria for HBV treatment and prevention of MTCT of HBV infection. Therefore, the last updated AASLD guidelines and the current national guidance of most AMR countries are aligned with those recently proposed by the WHO.

Contributors

Hugo Perazzo: study concept and design; data collection, interpretation of data; drafting and critical revision of the manuscript; **Estevão Portela Nunes & Sandra Wagner Cardoso:** data collection, interpretation of data; critical revision of the manuscript; **Valdilea Gonçalves Veloso & Beatriz Grinsztejn:** study concept and design; interpretation of data and critical revision of the manuscript.

Declaration of interests

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lana.2024.100925.

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