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ORIGINAL ARTICLE

Increasing Treatment Uptake for Chronic Hepatitis B in South America: A Comparative Analysis of Country-Specific and WHO 2024 Guidelines

Manuel Mendizabal[1] | Constanza D. Sabate[1] | Esteban González Ballerga[2] | Fernando Gruz[3] | Ezequiel Ridruejo[4] | Alejandro Soza[5] | Jaime Poniachik[6] | Grace Vergara[7] | Victoria Mainardi[8] | Gabriel Mezzano[9] | Fernando Bessone[10] | Margarita Anders[11] | Mario G. Pessoa[12] | Fernando Cairo[13] | Daniela Chiodi[14] | Melisa Dirchwolf[15] | Hugo Cheinquer[16] | Melina Susana[2] | Luis Rondeau[8] | Gabriel Rifrani[10] | Herman Aguirre[9] | Nelia Hernandez[14] | Carla Enrique[11] | Lucia Navarro[13] | Eugenia Labaronnie[15] | Patricia M. Zitelli[12] | Alexandre de Araujo[16] | Antonella Olivetti[2] | Daniela Simian[6] | Diego Giunta[7] | Marcelo Silva[1] | Sebastián Marciano[7]

[1]Unidad de Hígado y Trasplante Hepático, Hospital Universitario Austral, Pilar, Argentina | [2]Sección Hepatología, Hospital de Clínicas José de San Martín, Universidad de Buenos Aires, Ciudad Autónoma de Buenos Aires, Argentina | [3]Inmunología, Ciudad Autónoma de Buenos Aires, Buenos Aires, Argentina | [4]Sección Hepatología, Departamento de Medicina, Centro de Educación Médica e Investigaciones Clínicas Norberto Quirno "CEMIC", Ciudad Autónoma de Buenos Aires, Argentina | [5]Departamento de Gastroenterología, Pontificia Universidad Católica de Chile, Santiago, Chile | [6]Sección de Gastroenterología, Departamento de Medicina, Hospital Clínico de la Universidad de Chile, Santiago, Chile | [7]Sección Hepatología, Hospital Italiano de Buenos Aires, Ciudad Autónoma de Buenos Aires, Argentina | [8]Programa Nacional de Trasplante Hepático y Servicio de Hepatología, Hospital Central de Las Fuerzas Armadas, Montevideo, Uruguay | [9]Sección de Gastroenterología, Hospital del Salvador, Santiago, Chile | [10]Departamento de Gastroenterología, Facultad de Medicina, Hospital Provincial del Centenario, Universidad de Rosario, Rosario, Argentina | [11]Unidad de Hígado y Trasplante Hepático, Hospital Alemán, Ciudad Autónoma de Buenos Aires, Argentina | [12]Divisão de Gastroenterologia e Hepatologia, Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil | [13]Trasplante Hepático, Hospital El Cruce, Florencio Varela, Argentina | [14]Unidad Asistencial Gastroenterología, Facultad de Medicina, Hospital de Clínicas, UdelaR, Montevideo, Uruguay | [15]Unidad de Hígado, Hospital Privado de Rosario, Rosario, Argentina | [16]Departamento de Gastroenterología y Hepatología, Universidad Federal do Rio Grande do Sul e do Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil

Correspondence: Manuel Mendizabal (mmendiza@cas.austral.edu.ar)

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ABSTRACT

The 2024 WHO guidelines for chronic hepatitis B (CHB) aim to expand and simplify treatment eligibility. We aimed to estimate treatment eligibility and uptake according to country-specific guidelines and evaluate treatment expansion based on the WHO guidelines. Treatment-naïve CHB patients from Argentina, Brazil, Chile and Uruguay referred to evaluation between January 2010 and June 2024 were retrospectively included. Treatment candidacy was evaluated according to both country-specific and WHO guidelines. A total of 719 patients with CHB, treatment naïve, were included (67.1% male; median age: 50.4 years; HBeAg-positive: 36.3%). The median HBV-DNA level was 43,000 (IQR 633–110,000,000) IU/mL, median ALT was 41 (IQR 23–99) U/L, 47.0% had an APRI > 0.5 and 21.1% had cirrhosis. According to country-specific guidelines, 56.9% (95% CI: 53.2–60.5) met the criteria for treatment. Antiviral treatment was initiated in 84.3% of eligible patients. The proportion of patients meeting treatment criteria under the WHO guidelines increased to 67.3% (95% CI: 63.8–70.6), resulting in a 10.4% (95% CI: 8.1–12.8) increase in treatment candidacy. Treatment expansion was significantly higher in women (15.2%; 95% CI: 10.2–20.1) than in men (8.1%;

Abbreviations: ALT, alanine aminotransferase; APRI, AST to platelet ratio; AST, aspartate transaminase; CHB, chronic hepatitis B; FIB-4, fibrosis-4; HCC, hepatocellular carcinoma; WHO, World Health Organisation.

95% CI: 5.4–10.7). According to WHO guidelines, a considerable proportion of CHB patients who do not meet country-specific criteria are eligible for antiviral therapy. Implementing WHO criteria can enhance treatment rates and advance efforts toward CHB elimination.

1 | Introduction

Chronic hepatitis B (CHB) infection is a global public health concern, with an estimated 254 million people infected worldwide [1]. Despite extensive research efforts, there is still no cure for the disease. Oral antiviral medications are highly effective and well-tolerated, as they can suppress viral replication and protect most patients from developing liver complications, such as progression to cirrhosis, hepatocellular carcinoma (HCC) and death. In 2016, the World Health Organisation (WHO) provided a roadmap for eliminating hepatitis B and outlined clear elimination targets, including an 80% reduction in new chronic infections and a 65% reduction in mortality by 2030 [2]. In order to scale up the testing and treatment gap, WHO has recently released new CHB guidelines to simplify diagnostic approaches and treatment criteria [3]. These guidelines identified priority areas, such as simplified treatment criteria, and are primarily addressed to nonspecialist and specialist physicians and policymakers in health ministries, especially in low-income and middle-income countries.

Treatment indications for CHB vary by country according to local clinical practice guidelines. However, in general, the initiation of antivirals is based on a high viral load, elevated transaminases, and/or the presence of moderate to severe liver fibrosis. According to recent studies, between 22% and 29% of patients with CHB would be eligible to initiate antiviral treatment [4–6]. These reports did not reveal how many of the eligible patients actually initiated treatment. A similar study from Austria assessed treatment eligibility and linkage to therapy at their institution. The authors reported that 23%–29% of the patients met the treatment criteria, and approximately 80%–90% of those eligible for treatment began therapy [6].

To date, no specific studies are available on treatment eligibility among CHB patients in South America. Additionally, no regional study has reported on treatment eligibility according to the criteria of different clinical practice guidelines. This information would be valuable for understanding the burden of the disease and describing medical practices in the region. Based on these findings, strategies could be developed to define the best approach for these patients.

Thus, our study aimed to (i) estimate treatment eligibility and uptake according to country-specific guidelines and (ii) evaluate potential treatment expansion based on the new WHO guidelines in middle-and high-income countries of South America.

2 | Methods

2.1 | Study Design, Setting and Participating Centers

We conducted a multinational cross-sectional study that included consecutive patients with CHB from 16 centers across Argentina, Brazil, Chile and Uruguay who were referred to each participating institution between 1 January 2010 and 30 June 2024 (Table S1). Each Ethical Committee from all participating centers approved the study protocol (CIE N° P23-027). Additionally, the study followed institutional, national and international ethical standards, including those mandated by the Helsinki Declaration of 1975, as revised in 2008.

2.2 | Participants and Study Variables

We included patients older than 16 years old with CHB diagnosed according to each country-specific guideline (Table 1) and who were treatment-naïve at the first evaluation at the referral center. Patients with CHB were identified by the international classification of diseases (ICD-9/10) or equivalent. In those institutions with no access to electronic medical records, information regarding CHB status was obtained according to the resources of each center (i.e., CHB databases). The primary exclusion criteria were a previous history of the following: (i) solid organ transplantation; (ii) coinfection with human immunodeficiency virus and (iii) treatment evaluation in the context of pregnancy or immunosuppression treatment. Finally, we included patients with CHB with complete data available to evaluate treatment candidacy according to both guidelines. In the subgroup of patients in whom antiviral therapy was initiated, long-term outcomes regarding seroconversion, seroclearance, liver-related events and death were captured on the day of the last hospital visit.

2.3 | Assessment of Treatment Eligibility by Country-Specific Guidelines and WHO

Treatment eligibility was assessed according to country-specific guidelines based on HBeAg status, HBV-DNA and ALT levels and fibrosis staging [7–10] (Table 1). The eligibility for treatment was evaluated based on all available data obtained at the first referral to each participating centre. Then, we evaluated potential treatment expansion using the 2024 WHO CHB guidelines [3]. These guidelines expand eligibility for treatment with four options: (1) treat all individuals with fibrosis ≥ 2 (APRI score >0.5 or transient elastography >7 kPa); or (2) treat if HBV DNA is >2000 IU/mL and ALT is above the upper limit of normal; or (3) treat regardless of HBV DNA or ALT levels if there is the presence of any of the following: coinfections (e.g., HIV, HDV or HCV); a family history of HCC or cirrhosis; immune suppression; comorbidities (e.g., diabetes or metabolic dysfunction-associated steatotic liver disease); or extrahepatic manifestations; or (4) treat based on persistently abnormal ALT levels alone in settings where there is no access to HBV DNA testing. Our database was not designed to capture comorbidities such as diabetes or arterial hypertension. Therefore, we did not evaluate option 3.

TABLE 1 | Treatment indications for chronic hepatitis B according to the most recent recommendations from Argentina, Brazil, Chile and Uruguay guidelines.

Guideline (ref.)	HBeAg	HBV-DNA (UI/mL)	ALT	Fibrosis	Comments
Argentina [7]	(+) or (−)	> 2000	> ULN	Any	Age > 30 years
	(+) or (−)	Any	Any	≥ 2	Extrahepatic manifestations, family history of HCC
	(+) or (−)	Detectable	Any	Cirrhosis	
	(+)	> 20,000	Any	Any	
	(+) or (−)	Any	Any		
Brazil [8]	(+) or (−)	≥ 2000	> ULN[a]	≥ 2	Age > 30 years
	(+) or (−)	Any	Any	≥ 2	Extrahepatic manifestations, family history of HCC
	(+)	Any	Any	Cirrhosis	
	(+) or (−)	Any	Any	Any	
	(+) or (−)	Any	Any		
Chile [9]	(+) or (−)	> 2000	> ULN	Any	Age > 30 years
	(+) or (−)	> 2000	Any	≥ 2	Extrahepatic manifestations, family history of HCC
	(+) or (−)	Detectable or	Any	Cirrhosis	
	(+)	not detectable	Any	Any	
	(+) or (−)	> 2000,000	Any		
		Any			
Uruguay [10]	(+) or (−)	> 2000	> ULN	Any	Age > 30 years
	(+) or (−)	Any	Any	≥ 2	Extrahepatic manifestations, family history of HCC
	(+) or (−)	Detectable	Any	Cirrhosis	
	(+)	Any	Any	Any	
	(+) or (−)	Any	Any		
WHO [3]	(+) or (−)	Any	Any	APRI > 0.5,	Extrahepatic manifestations, family history of HCC, coinfections[c], cirrhosis, immunosuppression, comorbidities
	(+) or (−)	> 2000	> ULN[b]	TE > 7 kPa	
	(+) or (−)	Any	Any	Any	
	(+) or (−)	Not available	Persistently > ULN	Any	

Abbreviations: ALT, alanine aminotransferase; APRI, aspartate aminotransferase–platelet ratio index; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; TE, transient elastography; ULN, upper limit of normal; WHO, World Health Organisation.
[a] > 52 U/L men, > 34 U/L women.
[b] > 30 U/L men, > 19 U/L women.
[c] Human immunodeficiency virus, hepatitis C virus, hepatitis D virus 'e.g. diabetes or metabolic dysfunction-associated steatotic liver disease'.

2.4 | Study Variables

Variables collected included patients' age, sex and liver-related decompensation events such as ascites, encephalopathy, HCC and variceal bleeding. Routine laboratory tests included alanine aminotransferase (ALT), aspartate transaminase (AST), platelets and other baseline parameters. AST to platelet ratio (APRI) index and Fibrosis-4 (FIB-4) score were calculated according to published formulas. The liver fibrosis stage was recorded according to the last evaluation method by liver elastography, liver biopsy, serum markers or the presence of clinical signs of cirrhosis, as previously described [11]. On liver biopsy, cirrhosis was defined as METAVIR score F4. Liver stiffness measurements were recorded as a continuous variable in kilopascals (kPa) as obtained from liver elastography, and categorised according to international consensus guidelines (EASL-ALEH). Cutoff values for advanced fibrosis and cirrhosis were 9.5 and 12.5 kPa, respectively, with transient elastography. APRI score > 0.5 was considered significant fibrosis, > 1.0 advanced fibrosis and > 1.5 cirrhosis. When using FIB-4 score, a cutoff < 1.45 excluded advanced fibrosis, and a cutoff > 3.25 was considered advanced fibrosis. Cirrhosis could also be determined by the treating physician based on a combination of clinical signs of portal hypertension (e.g., presence of gastroesophageal varices on endoscopy), biochemical parameters (e.g., presence of a platelet count less than 100,000/mm^3) and/or radiologic findings consistent with cirrhosis (i.e., splenomegaly) [12].

2.5 | Sample Size Calculation and Statistical Analysis

The sample size was calculated for the primary objective: to estimate treatment eligibility and treatment uptake according to country-specific guidelines and to evaluate potential treatment expansion based on the new WHO guidelines. A literature review shows that approximately 80% of eligible patients start treatment in real-world settings [5, 6]. Considering this data and anticipating an event prevalence of 80% ± 3%, approximately 683 patients are needed to report a 95% confidence interval (CI). Considering that 10% of participants are expected to have missing data, we planned to include 750 patients. The estimation was performed with OpenEpi. Numerical variables are reported according to their distribution as means and standard deviation

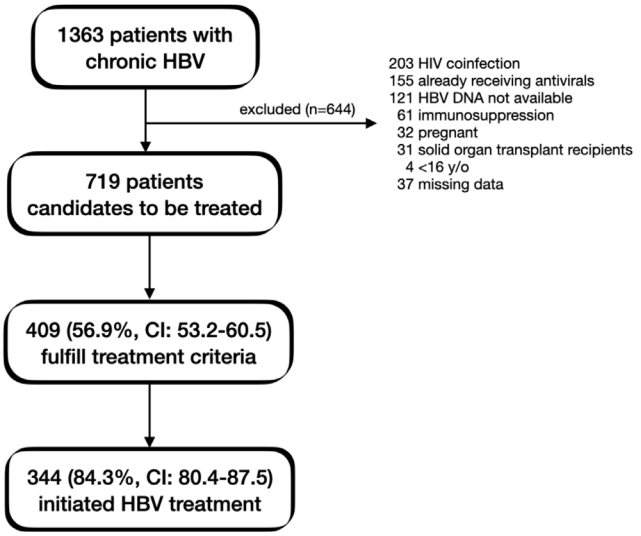

FIGURE 1 | Study patient flowchart.

(SD) or medians and 25%–75% percentiles (interquartile range, IQR). Only well-represented variables (less than 20% missing data in the record) were included in the study.

Treatment eligibility is reported as percentages according to both country-specific guidelines and WHO guidelines, along with their corresponding 95% CIs. Treatment expansion by WHO criteria was estimated by calculating the difference in treatment candidacy between WHO guidelines and country-specific guidelines, and it is reported with its 95% CI. WHO treatment expansion was estimated for the entire study population and stratified by the following variables: sex, age (< 40 vs. ≥ 40 years), HBeAg status, race (Hispanic vs. Asian), country (Argentina, Brazil, Chile and Uruguay) and the presence of steatosis on liver ultrasound. The 95% CIs were used to compare the stratified differences in treatment expansion. Data were analysed with STATA 13.0 (StataCorp, College Station, TX).

3 | Results

A total of 1363 patients with CHB were included in the database and 644 patients were excluded. The most common exclusion criteria were coinfection with human immunodeficiency virus ($n = 303$), patient already under antiviral therapy ($n = 155$), HBV DNA not available ($n = 121$) and patient receiving immunosuppressive regimen ($n = 61$). Finally, 719 individuals met the inclusion criteria and had complete data available to evaluate treatment candidacy according to both country-specific and WHO guidelines (Figure 1). Characteristics of the study population are summarised in Table 2. Overall, patients were predominantly male (67.1%) with a mean age of 50.4 years. Hepatitis D coinfection was detected in only one patient. Liver fibrosis evaluation is detailed in Table 3. Elastography was performed in 338 (47.0%) patients, and 157 (18.0%) underwent liver biopsy. A total of 338 patients (47.0%) had an APRI score > 0.5. Cirrhosis was diagnosed in 152 patients (21.1%). At the time of initial evaluation at the participating institution, 58 patients (8.1%) had at least one liver-related event, with HCC and ascites being the most common, affecting 44 and 21 patients, respectively.

TABLE 2 | Baseline characteristics of the overall final study cohort.

Variable	$n = 719$
Age, years mean (±SD)	50.4 ± 15.3
Sex, male *n* (%)	482 (67.1)
Race, *n* (%)	
Hispanic/Caucasian	580 (81)
Asian	109 (15.2)
African American	11 (1.5)
Others	19 (2.2)
ALT (U/L)[a]	41 (23–99)
AST (U/L)[a]	36 (22–78)
Platelets/mm^3[a]	202,000 (164,000–256,000)
Albumin g/dL[a]	4.1 ± 0.6
HCV coinfection, *n* (%)	16 (1.8)
HDV coinfection, *n* (%)	1 (0.1)
Hepatic steatosis in ultrasound? *n* (%)	193 (36.7)
Liver related events prior to first consult, *n* (%)	58 (8.1)
HCC	44 (6.1)
Ascites	21 (2.9)
Variceal bleeding	9 (1.3)
Encephalopathy	6 (0.8)
Other	3 (0.4)

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; HCC, hepatocellular carcinoma; HCV, hepatitis C virus, HDV, hepatitis delta virus.
[a]Median (IQR).

The median HBV DNA level was 43,000 IU/mL (IQR 633–110,000,000 IU/mL), 405 patients (56%) had HBV DNA > 2000 IU/mL and 67 patients (9.5%) had undetectable HBV DNA. The median ALT level was 41 [23–99] U/L. ALT levels were significantly higher in males (median 59 [IQR 27–125 U/L]) compared to females (median 27 U/L [IQR 18–54], $p < 0.001$). A total of 334 male patients (70%) and 164 female patients (69%) had ALT levels above 30 and 19 U/L, respectively.

Overall, 250 patients (36.3%) were HBeAg-positive. These patients tended to be younger (50.3 [IQR 35–63] vs. 53.0 [IQR 39–62] years; $p = 0.11$) and showed higher HBV DNA (10,000,000 [IQR 59,700—10,000,000] vs. 1550 [IQR 202–76,935] $p < 0.001$) and ALT levels (99 [IQR 56–196] vs. 29 [IQR 20–58 U/L]; $p < 0.001$) compared to HBeAg-negative patients.

TABLE 3 | Liver fibrosis evaluation in the study cohort.

Variable	*n* = 719
Elastography performed, *n* (%)	338 (47.0)
Elastography value (kPa)[a]	6.1 (4.8–8.8)
Elastography fibrosis stage	
1–2	252 (74.6) 338
3	48 (14.2)
4	38 (11.2)
Liver biopsy performed, *n* (%)	157 (18.0)
Liver biopsy fibrosis stage	
1–2	107 (68.6)
3	32 (19.9)
4	18 (11.5)
FIB-4[a]	1.28 (0.8–2.4)
APRI > 0.5, *n* (%)	338 (47.0)
Cirrhosis, *n* (%)	152 (21.1%)

Abbreviations: APRI, aspartate aminotransferase–platelet ratio; FIB-4, fibrosis-4.
[a]Median (IQR).

3.1 | Hepatitis B Treatment Eligibility and Treatment Uptake

According to country-specific guidelines, 409 patients (56.9%; 95% CI: 53.2–60.5) met treatment criteria. Antiviral treatment was initiated in 344 eligible patients (84.3%; 95% CI: 80.4–87.5), with entecavir (63.1%), tenofovir disoproxil fumarate (25.9%), tenofovir alafenamide (5.8%) and pegylated interferon (4.4%). Median time from the first visit to treatment initiation was 75.5 (IQR 31.0–131.0) days. Treatment was not initiated in the remaining patients due to comorbidities (15%), health insurance issues (14%), social habits (13%) and other or unknown reasons (58%). Long-term treatment outcomes are described in Table S2.

Compared to country-specific guidelines, the proportion of patients meeting treatment criteria under the WHO guidelines increased to 484 (67.3%; 95% CI: 63.8–70.6), resulting in a 10.4% (95% CI: 8.1–12.8) increase in treatment candidacy (Table 4). Overall, 75 patients who were not eligible for antiviral therapy according to country-specific guidelines were included under the WHO recommendations.

Upon analysing treatment expansion based on WHO criteria, we found that 38 patients were reclassified under option 1 (treat all individuals with fibrosis ≥ 2), 28 patients under option 2 (treat if HBV DNA is > 2000 IU/mL and abnormal ALT), 6 patients under both options 1 and 2 and 3 patients under option 4 (persistently abnormal ALT levels and no access to HBV DNA testing) (Figure S1). We also evaluated treatment candidacy across different strata. Treatment expansion was significantly higher in women (15.2%; 95% CI: 10.2–20.1) compared to men (8.1%; 95% CI: 5.4–10.7) (Table 5).

TABLE 4 | Proportion of patients meeting treatment eligibility criteria according to country-specific guidelines and WHO criteria (*n* = 719).

		Eligible according to WHO guidelines		
		NO	YES	Total
Eligible according to country-specific guidelines	NO	235 (33%)[a]	**75 (10%)**[a]	310 (43%)
	YES	0 (0%)[a]	409 (57%)[a]	409 (57%)
	Total	235 (33%)	484 (67%)	719 (100%)

Note: Bold value indicates the patients not meeting treatment criter according to country specific guidelines but with treatment criteria acording to WHO recommendations.
Abbreviation: WHO, World Health Organisation.
[a]Total percentage of the study cohort.

4 | Discussion

In this large cohort of more than 700 real-world patients with CHB from South America, we evaluated treatment eligibility rates at baseline based on country-specific guidelines, immediate antiviral therapy initiation, and treatment expansion according to the new WHO guidelines. Approximately half of the patients were eligible for antiviral treatment at baseline, and 84% of patients who became eligible received treatment. At the time of their initial evaluation, nearly one in five patients had cirrhosis, and half presented with HBV DNA levels exceeding 2000 IU/mL. An assessment of the 2024 WHO guidelines for CHB treatment revealed a 10% increase in the proportion of patients eligible for antiviral therapy compared to country-specific guidelines. Notably, this expansion predominantly benefited women, with a 15% increase in eligibility compared to 8% in men. These revised eligibility criteria may have significant implications for improving CHB management and advancing hepatitis B elimination efforts in the region.

Based on the eligibility criteria outlined in various treatment guidelines, only a portion of individuals with CHB require treatment, and this proportion varies across populations, regions and settings [5, 6, 13, 14]. However, there are no available estimates of the percentage of CHB-infected individuals who meet these treatment criteria in South America. Compared to other cohorts, our study found nearly double the proportion of patients eligible for treatment. The reasons for this finding remain unclear. Genotype F, the most prevalent in our region, appears to follow a more aggressive disease course than other genotypes [15–18], it has been associated with higher viral loads, increased replication rates, and a greater frequency of liver disease-related deaths [17–19]. Additionally, our study was conducted at reference centers, primarily university hospitals, where individuals with more advanced liver disease might be overrepresented, leading to a two-fold greater likelihood of initiating treatment compared to those seen by primary care physicians only [14].

TABLE 5 | Stratified WHO treatment expansion candidacy.

Variable	Treatment candidacy according to country-specific guidelines, *n* (%)	Treatment candidacy according to WHO guidelines, *n* (%)	Country-specific NO and WHO NO, *n* (%)	Country-specific YES and WHO NO, *n* (%)	Country-specific YES and WHO YES, *n* (%)	Expansion by WHO criteria Country-specific guideline NO and WHO YES, *n* (%; 95% CI)
Sex						
Male, *n* = 482	317 (65.8)	356 (73.9)	126 (26.1)	0	317 (65.8)	39 (8.1; 5.4–10.7)
Female, *n* = 237	92 (38.8)	128 (54.0)	109 (46.0)	0	92 (38.8)	39 (15.2; 10.2–20.1)
Age						
≥40 years, *n* = 515	298 (57.9)	350 (68.0)	165 (32)	0	298 (57.9)	52 (10.1; 7.3–12.9)
<40 years, *n* = 203	111 (54.7)	134 (66.0)	69 (34)	0	111 (54.7)	23 (11.3; 6.5–15.1)
Liver steatosis on ultrasound						
Yes, *n* = 193	101 (52.3)	123 (63.7)	70 (36.3)	0	101 (52.3)	22 (11.4; 6.4–16.4)
No, *n* = 465	273 (58.7)	315 (67.7)	150 (32.3)	0	273 (58.7)	42 (9.0; 6.2–11.8)
Race[a]						
Hispanic, *n* = 580	330 (56.9)	387 (66.7)	193 (33.3)	0	330 (56.9)	57 (9.8; 72–12.4)
Asian, *n* = 109	66 (60.5)	79 (69.7)	33 (30.3)	0	66 (60.5)	10 (9.2; 2.8–15.5)
Country						
Argentina, *n* = 504	266 (52.8)	312 (61.9)	192 (38.1)	0	266 (52.8)	46 (9.1; 6.4–11.8)
Brazil, *n* = 38	24 (63.2)	30 (78.9)	8 (21.1)	0	24 (63.2)	6 (15.7; 1.5–30.0)
Chile, *n* = 127	89 (70.1)	102 (80.3)	25 (19.7)	0	89 (70.1)	13 (10.2; 4.2–16.3)
Uruguay, 49	29 (59.1)	39 (79.2)	10 (20.4)	0	29 (59.2)	10 (20.4; 7.1–33.7)
HBeAg						
Positive, *n* = 250	222 (88.8)	237 (94.8)	13 (85.2)	0	222 (88.8)	15 (6.0; 2.6–9.3)
Negative, *n* = 438	174 (39.7)	226 (51.6)	212 (48.5)	0	174 (39.7)	52 (11.8; 8.6–15.2)

Abbreviation: WHO, World Health Organisation.

[a]Patients of unknown race and those identified as Amerindian or African American were excluded from this stratified analysis (total = 27).

Complex treatment guidelines from liver societies may contribute to undertreatment in primary and specialty care settings. Evidence suggests that patients with CHB in the "grey zone" remain at significant risk for liver-related events such as HCC and death [20]. Simplified CHB guidelines, like those proposed by Wong et al., suggest increasing treatment eligibility from 6.7% under current AASLD criteria to 14.1%–33.5%. In this context, the WHO new CHB guidelines aimed at radically simplifying treatment eligibility, particularly in low- and middle-income countries, potentially resulting in a three- to four-fold increase in treatment rates [3]. In our population, we observed a 10% treatment expansion rate. These results contrast with a recent large cohort study from China, where WHO treatment eligibility nearly doubled from 23%–28% to 63% compared to EASL, AASLD and APASL guidelines [21]. However, in our South America cohort we observed a similar proportion of patients meeting treatment criteria under the WHO guidelines (67%). This may be explained by the higher baseline CHB treatment indication rate in our cohort compared to the 14%–29% reported in studies from the U.S., Europe and China [5, 6, 14, 21]. Furthermore, according to the World Bank, the countries participating in this study are classified as middle- to high-income countries, and our database did not capture the new metabolic dysfunction-associated steatotic liver disease criteria, preventing a full evaluation of WHO's third treatment option [22]. Whether the coexistence of steatotic liver disease and CHB accelerates the progression of chronic liver disease is still controversial [23–25]. Further research is needed to assess the impact of these guidelines across diverse clinical settings globally.

To better understand the impact of the WHO guidelines in our population, we analysed the different treatment expansion options in each group. We observed a higher proportion of treatment-eligible patients under the 2024 WHO guidelines in women compared to men, which was expected due to the lower (and sex-specific) ALT thresholds applied for treatment initiation in the WHO guidelines. Additionally, WHO guidelines adopt a more aggressive approach to reducing the liver fibrosis threshold, with the APRI diagnostic cutoff value lowered to >0.5. Consequently, most of the patients in our study were included due to the lowering of the fibrosis threshold. The benefits of expanding treatment criteria beyond reducing hepatic complications of CHB are that increasing the number of patients eligible for treatment is also cost-effective. Previous studies have shown that expanding treatment coverage can reduce the incidence of decompensated cirrhosis, HCC and liver-related deaths [26].

Strengths of our study include the large, multicenter cohort from four South American countries, which provides a representative snapshot of CHB management in the region. Additionally, we utilised robust data collection methods and evaluated both WHO and country-specific guidelines, offering a comprehensive analysis of treatment eligibility and uptake. However, some limitations should be noted. First, the study's cross-sectional design limits our ability to assess changes in HBV DNA, ALT and fibrosis over time, which could affect treatment eligibility. Second, the participating centres are mostly university hospitals where patients with advanced liver disease are often referred, which may not fully represent the broader national landscape. Third, althouth we analysed eligibility under WHO guidelines, our database did not capture certain comorbidities (e.g., diabetes) that may influence treatment candidacy. Finally, external factors such as insurance coverage and healthcare access, which may impact treatment uptake, were not thoroughly examined.

In conclusion, the expansion of treatment eligibility under the 2024 WHO guidelines has the potential to significantly increase antiviral therapy coverage among CHB patients in South America, especially among women. In our study, the main reasons for expanding treatment indications were a fibrosis score ≥ 2 and HBV DNA >2000 IU/mL with elevated ALT. Future studies should explore the long-term outcomes of patients treated under these expanded criteria and rigorously assess the feasibility of implementing the WHO recommendations according to the country resource levels and national health priorities. Additionally, efforts should focus on addressing barriers to treatment access, such as healthcare infrastructure, economic impact and patient education, to fully realise the benefits of expanded eligibility.

Author Contributions

All authors contributed to conceptualisation (Manuel Mendizabal and Sebastian Marciano), data curation (all authors), formal analysis and visualisation (Sebastián Marciano, Diego Giunta and Manuel Mendizabal), writing of the original draft (Manuel Mendizabal and Sebastian Marciano), reviewing and editing (all authors) and supervision (Manuel Mendizabal).

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The authors have nothing to report.

Disclosure

ChatGPT was used for grammar and spelling check.

Conflicts of Interest Statement

The authors declare no conflicts of interest regarding this study. Outside the submitted work, the authors declare the following potential conflicts of interest: M.M. has served as a speaker for Biosidus, Gador, Gilead Sciences and Knight; and received grants/research support from AstraZeneca, Gador and Roche.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.