

Hepatitis B Vaccination Histories in Persons With HIV Needing Revaccination

Minhee Kang, PhD,^a Triin Umbleja, MSc,^a Anchalee Avihingsanon, MD, PhD,^b
Sandra W. Cardoso, MD, PhD,^c Josphat Kosgei, MBChB,^d Karen J. Vigil, MD,^e
Ta Thi Dieu Ngan, MD, PhD,^f Unoda Chakalisa, MD, MSc,^g Stephanie Caruso, MBA,^h
Kenneth E. Sherman, MD, PhD,ⁱ and Kristen M. Marks, MD^j

Introduction: Past studies of hepatitis B vaccines in people with HIV (PWH) have shown mixed results about improving responses with increases in dose or dose frequency, leading to inconsistent guidelines and practice. We examined vaccine series completion and revaccinations in PWH lacking a seroprotective response.

Methods: Hepatitis B vaccination histories were evaluated as a retrospective study in 561 participants of A5379 trial (NCT04193189). Individuals in 41 sites in Africa, Asia, South America, and the United States qualified for the trial with antibody titers below the seroprotective level (<10 mIU/mL) despite past hepatitis B vaccinations. The primary measure of interest was the number of vaccines in the past vaccination records.

Results: Of the 1098 trial candidates, 561 (51%) did not have seroprotective titers at the time of screening and enrolled in A5379. Median age at the time of screening was 46 years (18–70 years), which varied across the regions: the lowest in Africa and the highest in the United States. The number of past hepatitis B vaccines varied widely across and within geographic regions. Twenty-four percent of the participants received ≥ 4 doses, up to 12, yet did not have seroprotective antibody titers.

Conclusions: Regardless of past vaccine records, antibody titers should be checked in PWH for revaccination needs. The recently approved long-acting and injectable antiretroviral treatment (ART) lacks protective effect against HBV, unlike tenofovir-based ART. As the long-acting ART becomes more widely used, we recommend reassessing serologies and offering the recommended CpG-adjuvanted vaccine series with promising response durability to individuals without seroprotection.

Key Words: hepatitis B, vaccination, HIV

(*J Acquir Immune Defic Syndr* 2026;101:534–540)

INTRODUCTION

Responses to hepatitis B vaccination in people with HIV (PWH) have been suboptimal in the past. Studies of conventional 3-dose series with an aluminum hydroxide adjuvant have reported 30%–80% rates of seroprotective response in PWH compared with 95% in people without HIV.^{1,2} The studies have used seroprotective response (SPR) defined as antibody titer against hepatitis B surface antigen (HBsAg) (anti-HBs) ≥ 10 mIU/mL. In PWH, low CD4⁺ T-cell count and HIV viremia have been reported as predictors of nonresponse to the conventional alum-adjuvanted vaccine, in addition to age, sex, race, body weight, and comorbidities such as diabetes.^{3–6} Studies with conventional alum-based vaccines before the availability of newer vaccines were conducted to improve responses with increases in dose or dose frequency,^{7–9}

Received for publication June 9, 2025; accepted November 20, 2025.

From the ^aCenter for Biostatistics in AIDS Research in the Department of Biostatistics, Harvard T.H. Chan School of Public Health, Boston, MA; ^bHIV-NAT, Thai Red Cross AIDS and Infectious Diseases Research Centre, and Center of Excellence in Tuberculosis, Chulalongkorn University, Bangkok, Thailand; ^cFundação Oswaldo Cruz (Fiocruz)—Instituto Nacional de Infectologia Evandro Chagas (INI), Rio de Janeiro, Brazil; ^dKenya Medical Research Institute/Walter Reed Project, Kericho, Kenya; ^eInfectious Diseases, McGovern Medical School, University of Texas, Houston, TX; ^fDepartment of Infectious Diseases, Hanoi Medical University, Hanoi, Vietnam; ^gBotswana Harvard Health Partnership Clinical Trials Unit, Gaborone, Botswana; ^hData Management Center, Frontier Science and Technology Research Foundation, Inc., Amherst, NY; ⁱGastroenterology Division, Massachusetts General Hospital-Harvard Medical School, Boston, MA; and ^jDivision of Infectious Diseases, Weill Cornell Medicine, New York, NY.

Supported by the National Institute of Allergy and Infectious Diseases of the National Institutes of Health under Award Numbers UM1 AI068634 (M.K., T.U., S.C.), UM1AI069419 (K.M.M.), UM1 AI068636, and UM1 AI106701 (K.E.S., K.M.M., A.A., S.W.C., J.K., K.J.V., T.T.D.N., U.C.). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. Dynavax Technologies provided the product for the trial.

T.U. reports grant supports from National Heart, Lung, and Blood Institute (NHLBI) and National Institute on Aging (NIA). A.A. reports research grants for HIV-NAT from Gilead Science, ViiV/GSK, Roche, MSD, Janssen Research & Development; transportation costs to attend meetings/conferences from Gilead Sciences; other nonfinancial interests (unpaid) for working with Strategic and Technical Advisory Group to WHO for HIV/hepatitis/STI, Thai AIDS Society Committee, and Thailand National ART, TB, HIV, Hepatitis Program Committee. K.J.V. reports personal fees from Gilead and ViiV, and research support from ViiV and Theratechnologies. K.E.S. reports that he has served as a site PI for studies sponsored by AbbVie, Gilead, Helio, Intercept, and Zydus, and as a consultant to CinRx and on safety monitoring boards associated with MedPace, Horizon-AMGEN, and Pliant. K.M.M. has been an expert witness for Gilead Sciences, is on a safety monitoring committee for Immorna and Noro Nordisk, and has received research funding paid to Weill Cornell Medicine from Gilead Sciences and Glaxo Smith Kline. The remaining authors have no conflicts of interest to disclose.

Correspondence to: Minhee Kang, PhD, Harvard T.H. Chan School of Public Health, 651 Huntington Avenue, Boston, MA 02115 (e-mail: mkang@hsph.harvard.edu).

Copyright © 2025 Wolters Kluwer Health, Inc. All rights reserved.

but the mixed results led to inconsistent guidelines and practice. A publication about a 2020 survey showed that the standard dose at 0, 1, and 6 months was preferred by clinicians over an increased dose or a 4-dose regimen for the initial vaccine series.¹⁰ The survey also showed that without seroconversion after the standard regimen, preference for repeat vaccination was split between standard-dose and double-dose series, with only a small number preferring a 4-dose regimen. Even if seroprotective response is achieved at the peak response time after the vaccination with conventional vaccines, immunity can wane over time.^{1,11}

Recent studies show superb responses with a recombinant HBsAg vaccine combined with cytosine phosphoguanine (CpG) 1018 adjuvant. A5379 trial (NCT04193189, B-Enhancement of Hepatitis B Vaccination in Persons with HIV, BEe-HIVe) in the Advancing Clinical Therapeutics Globally for HIV/AIDS and Other Infections (ACTG, formerly AIDS Clinical Trials Group) Network evaluated CpG-adjuvanted vaccine in PWH.^{12–14} Three-dose series of CpG-adjuvanted vaccines were administered intramuscularly at 0, 4, and 24 weeks, each containing 20 µg of recombinant HBsAg and 3000 µg of CpG 1018 adjuvant. The SPR result of 100% was reported in PWH who had not been vaccinated before.¹² Furthermore, SPR of 99% was reported in PWH without a seroprotective anti-HBs titer despite a history of vaccination with alum-based recombinant vaccine, demonstrating superior seroprotective humoral responses compared with the alum-adjuvanted hepatitis B vaccine.¹³ The CpG acts as a TLR9 agonist stimulating the response to HBsAg, inducing more robust immune responses that may overcome HIV-specific impairment.

Recently approved long-acting (LA) and injectable antiretroviral therapy (ART) lacks protective effect against HBV, unlike the tenofovir-based ART regimens. Switching from tenofovir-based ART to long-acting or 2-drug regimens without HBV activity may increase the risk of new HBV infections and reactivation of prior HBV in PWH as has been documented in several clinical trials of LA ART and case reports.^{15–21} As LA ART becomes more widely used, it is increasingly important to reassess hepatitis B immunity, especially given historically lower vaccine responses in PWH, and to consider vaccination or revaccination. A recent study demonstrated that the infrastructure developed for initiating LA ART can be leveraged to identify PWH lacking HBV seroprotection and facilitate vaccination.²²

Recognizing that vaccination practices may vary, we sought to improve our understanding of hepatitis B vaccination and revaccination practices in PWH around the world who are lacking a seroprotective response. We sought to characterize globally the hepatitis B vaccine histories of PWH who have been vaccinated but do not have seroprotective anti-HBs and compare by geographic region. We evaluated in participants who enrolled in A5379 with anti-HBs <10 mIU/mL despite previous conventional vaccinations.

METHODS

Study Design and Population

We conducted a retrospective study using the completed A5379 trial, which recruited individuals ≥18 years of

age receiving ART for HIV-1 with CD4⁺ T-cell count ≥100 cells/µL and HIV RNA <1000 copies/mL. The participants (1) had known hepatitis B vaccination >168 days before trial entry and (2) did not have past or present serologic evidence of HBV or hepatitis B vaccine response, demonstrated by the presence of HBsAg, antibodies to hepatitis B core antigen, or anti-HBs ≥10 mIU/mL at or any time before screening. In addition to the trial follow-up data,¹² A5379 collected data about hepatitis B vaccinations before the A5379 entry from the trial participants, coded following the World Health Organization (WHO) drug classification as “HEPATITIS B VACCINE” or “HEPATITIS A VACCINE INACT; HEPATITIS B VACCINE RHBSAG (YEAST)” in the study database with receipt dates.

Analysis Variables

The primary measure of interest was the number of vaccines administered before A5379 anti-HBs screening. We also analyzed the ages at the first and the last hepatitis B vaccinations, and the time between the last hepatitis B vaccination and the screening test showing anti-HBs <10 mIU/mL.

Statistical Methods

Kruskal–Wallis tests were conducted to compare continuous variables across the geographic regions, and Fisher exact tests were applied for categorical variables. SAS software (version 9.4 for Linux; SAS Institute Inc.) was used.

RESULTS

Of the 1098 trial candidates, 561 (51%) did not have seroprotective titers at the time of screening and were enrolled in A5379 from December 2020 to February 2023. The participants enrolled at 41 sites in these regions: Africa (n = 117 from Botswana, Kenya, Malawi, South Africa, Uganda), Asia (n = 95 from Philippines, Thailand, Vietnam), North America (n = 312), and South America (n = 37, Brazil). Of the 537 who were not included in A5379, the most common screen failure reason was having anti-HBs ≥10 mIU/mL at or any time before screening for 335 individuals, with a higher proportion from Africa than from other regions (66% vs 12%, <1%, 21% in Asia, Brazil, and the United States, respectively). This likely reflects different prescreening practices and antibody assessments in different regions. The characteristics at study entry within 45 days of anti-HBs titer screening were presented previously.¹³ In brief, 36% were women, 13% had diabetes, 29% had body mass index (BMI) ≥30 kg/m², and 23% and 21% were current and former smokers, respectively. They were 42% Black, 35% White, 17% Asian; all from Africa were Black, and all from Asia were Asians. Median CD4⁺ count and CD4% were 638 cells/mm³ and 33%, respectively. Median nadir CD4 reported from 491 participants was 268 cells/mm³, 38% with <200 and 24% with ≥500 cells/mm³. All had HIV-1, and the duration with HIV ranged from <1 to 38 years, with a median of 13 years. Approximately 40% had been on the

TABLE 1. Demographics and Hepatitis B (HB) Vaccination History Characteristics by Region

	Total (N = 561)	Africa (N = 117)	Asia (N = 95)	Brazil (N = 37)	United States (N = 312)
Demographics and HIV-related characteristics					
Age at enrollment (yrs)					
Median (Q1, Q3)	46 (31, 56)	26 (21, 38)	33 (26, 47)	44 (26, 53)	53 (44, 59)
Min, Max	18, 70	18, 66	19, 62	20, 70	20, 70
Sex at birth					
Female	202 (36%)	79 (68%)	29 (31%)	11 (30%)	83 (27%)
Male	359 (64%)	38 (32%)	66 (69%)	26 (70%)	229 (73%)
Risk for HIV exposure per self-report					
Heterosexual contact	224 (40%)	64 (55%)	34 (36%)	15 (41%)	111 (36%)
Homosexual contact	201 (36%)	0 (0%)	33 (35%)	13 (35%)	155 (50%)
Perinatal transmission	58 (10%)	41 (35%)	13 (14%)	0 (0%)	4 (1%)
Injectable drug use	8 (1%)	0 (0%)	4 (4%)	1 (3%)	3 (<1%)
Transfusion	3 (<1%)	0 (0%)	1 (1%)	1 (3%)	1 (<1%)
Other exposure	3 (<1%)	1 (<1%)	0 (0%)	0 (0%)	2 (<1%)
Multiple exposures	6 (1%)	0 (0%)	3 (3%)	1 (3%)	2 (<1%)
Unknown	55 (10%)	11 (9%)	7 (7%)	6 (16%)	31 (10%)
Not reported	3 (<1%)	0 (0%)	0 (0%)	0 (0%)	3 (<1%)
Age at HIV diagnosis (yrs)					
Median (Q1, Q3)	31 (23, 38)	21 (7, 29)	26 (20, 31)	32 (26, 45)	35 (29, 43)
Min, Max	0, 63	0, 53	0, 53	19, 63	0, 61
ART regimen class					
NRTI + INSTI	376 (67%)	102 (87%)	49 (52%)	29 (78%)	196 (63%)
NRTI + NNRTI	80 (14%)	6 (5%)	44 (46%)	3 (8%)	27 (9%)
NRTI + PI	12 (2%)	5 (4%)	1 (1%)	4 (11%)	2 (<1%)
Other NRTI-containing	71 (13%)	4 (3%)	1 (1%)	0 (0%)	66 (21%)
NRTI-sparing	22 (4%)	0 (0%)	0 (0%)	1 (3%)	21 (7%)
CD4 ⁺ count (cells/mm ³)					
Median (Q1, Q3)	638 (477, 856)	755 (581, 989)	596 (469, 769)	613 (494, 865)	621 (442, 852)
HIV-1 RNA (copies/mL)					
<40	526 (94%)	112 (96%)	91 (96%)	37 (100%)	286 (92%)
40+	35 (6%)	5 (4%)	4 (4%)	0 (0%)	26 (8%)
Hepatitis B vaccination history					
Number of previous vaccine doses					
1–2 doses	124 (22%)	45 (38%)	22 (23%)	6 (16%)	51 (16%)
3 doses	304 (54%)	72 (62%)	69 (73%)	15 (41%)	148 (47%)
4–12 doses	133 (24%)	0 (0%)	4 (4%)	16 (43%)	113 (36%)
Age at first HB vaccination (yrs)					
Median (Q1, Q3)	36 (24, 45)	3 (0, 37)	29 (19, 38)	37 (21, 48)	41 (33, 48)
Min, Max	0, 66	0, 66	0, 62	0, 65	0, 64
0–<1	94 (17%)	58 (50%)	18 (19%)	5 (14%)	13 (4%)
1–12	13 (2%)	3 (3%)	3 (3%)	3 (8%)	4 (1%)
13–18	10 (2%)	2 (2%)	2 (2%)	1 (3%)	5 (2%)
19–39	220 (39%)	30 (26%)	51 (54%)	15 (41%)	124 (40%)
40–59	213 (38%)	21 (18%)	19 (20%)	12 (32%)	161 (52%)
60+	11 (2%)	3 (3%)	2 (2%)	1 (3%)	5 (2%)
Age at last HB vaccination (yrs)					
Median (Q1, Q3)	38 (26, 47)	4 (1, 37)	29 (20, 38)	37 (23, 49)	44 (35, 50)
Min, Max	0, 66	0, 66	0, 62	0, 65	0, 66
0–<1	80 (14%)	52 (44%)	17 (18%)	4 (11%)	7 (2%)
1–12	18 (3%)	9 (8%)	3 (3%)	4 (11%)	2 (<1%)
13–18	8 (1%)	1 (<1%)	2 (2%)	1 (3%)	4 (1%)
19–39	194 (35%)	31 (26%)	52 (55%)	13 (35%)	98 (31%)
40–59	242 (43%)	21 (18%)	19 (20%)	13 (35%)	189 (61%)
60+	19 (3%)	3 (3%)	2 (2%)	2 (5%)	12 (4%)

TABLE 1. (Continued) Demographics and Hepatitis B (HB) Vaccination History Characteristics by Region

	Total (N = 561)	Africa (N = 117)	Asia (N = 95)	Brazil (N = 37)	United States (N = 312)
Time between first vaccine and HIV diagnosis (yrs)					
Median (Q1, Q3)	21.4 (9.0, 29.5)	−1.9 (−14.4, 25.3)	20.4 (4.3, 25.4)	27.0 (15.8, 34.8)	22.6 (13.5, 32.5)
Min, Max	−27.2, 58.9	−26.3, 52.0	−19.2, 51.6	−0.8, 58.9	−27.2, 58.1
Time between first and last HB vaccination (yrs)					
Median (Q1, Q3)	0.5 (0.2, 1.8)	0.2 (0.1, 0.6)	0.5 (0.1, 0.5)	0.5 (0.5, 1.3)	0.9 (0.5, 4.9)
Min, Max	0.0, 27.3	0.0, 1.8	0.0, 27.3	0.0, 8.8	0.0, 25.5
Time between last vaccine dose and anti-HBs testing (yrs)					
Median (Q1, Q3)	8.5 (3.2, 15.7)	18.0 (2.4, 21.9)	9.7 (2.0, 10.7)	7.7 (2.6, 12.5)	8.2 (3.9, 13.7)
Min, Max	0.5, 35.6	0.5, 27.7	0.5, 31.6	0.6, 23.1	0.5, 35.6
0–<2	79 (14%)	22 (19%)	23 (24%)	6 (16%)	28 (9%)
2–<5	123 (22%)	29 (25%)	17 (18%)	11 (30%)	66 (21%)
5–<10	122 (22%)	4 (3%)	17 (18%)	7 (19%)	94 (30%)
10–<20	142 (25%)	16 (14%)	22 (23%)	7 (19%)	97 (31%)
20+	95 (17%)	46 (39%)	16 (17%)	6 (16%)	27 (9%)
Received 3 doses in 6 mo	127 (23%)	35 (30%)	51 (54%)	5 (14%)	36 (12%)
Received 3 doses in 1 yr	264 (47%)	67 (57%)	69 (73%)	13 (35%)	115 (37%)

Frequency (%) for categorical measures; median with lower and upper quartiles (Q1, Q3), minimum and maximum (Min, Max), for continuous measures.

same ART regimen for ≥ 3 years, 4% on ART without a nucleoside reverse transcriptase inhibitor (NRTI).

The median age at the time of anti-HBs screening was 46 years (18–70 years), which varied across the regions ($P < 0.0001$): the lowest median was 26 years in Africa and the highest median was 53 years in the United States (Table 1). The median age at HIV diagnosis was 31 years (birth to 63 years). The proportions of women varied across regions as well ($P < 0.0001$) with a higher proportion in Africa than the others.

The number of past hepatitis B vaccines ranged from 1 to 12, where most received 3 doses (54%), 24% received ≥ 4 , and 22% received 1–2 doses. Although none in Africa received ≥ 4 , 4% in Asia, 43% in Brazil, and 36% in the United States did ($P < 0.0001$). The age at the first hepatitis B vaccination varied across regions ($P < 0.0001$). The first vaccination age was < 1 year for 50% in Africa, compared with 19%, 14%, and 4% in Asia, Brazil, and the United States, respectively, reflecting that the younger participants in Africa were more likely to have been vaccinated as infants. The median time between the last hepatitis B vaccination and the anti-HBs test for screening was 8.5 years; < 5 years for 36%, and ≥ 10 years for 42%. Although the median was 18 years in Africa, about twice as high compared with the other regions, the statistical evidence of difference in the distributions of the time between the last vaccination and the anti-HBs screening across the regions was weak ($P = 0.13$).

Figure 1 presents when hepatitis B vaccinations occurred for each participant and their ages at the time of anti-HBs testing. The age at the time of HIV diagnosis on record for 545 participants is also shown; 27% had hepatitis B vaccination within a year after the diagnosis, whether it be the first in the vaccine series or revaccination. Receipt of 3 doses for 6 months is shown in the 3-dose panels as a 6-month blue interval. The proportions of participants who received 3 doses

for a 6-month interval without additional vaccinations were 30%, 54%, 14%, and 12% in Africa, Asia, Brazil, and the United States, respectively (Table 1). This mostly occurred during infancy in Africa, where the participants were younger. Overall, participants who were vaccinated as infants were younger than 33 years, in line with when the WHO guidelines were introduced in the 1990s. There was the most heterogeneity in the time span of the 3-dose series and in the number of vaccines in the United States, which enrolled the most participants and older individuals.

DISCUSSIONS

Among the individuals who qualified for the BEE-HIVE trial with anti-HBs < 10 mIU/mL despite past hepatitis B vaccinations, the number of vaccines varied widely, particularly in the United States and Brazil. Administration of doses spanned up to 27 years, and 24% of the participants received 4 or more doses. Fifteen percent of the participants received ≥ 5 doses, up to 12, yet did not have seroprotective antibody titers. In 1992, the WHO set a goal for all countries to introduce hepatitis B vaccine into national routine infant immunization programs by 1997,²³ and this was reflected in our data where infant vaccinations were observed in participants mostly younger than 30 years. Our review of the vaccination history relative to the reported HIV diagnosis date suggests that there was a missed opportunity to revaccinate: only 27% had hepatitis B vaccination within a year after the HIV diagnosis. Although past recommendations delayed vaccinating PWH until CD4⁺ counts were higher, the latest WHO guidelines recommend vaccinating PWH as early as possible. Our data suggest that variation in vaccination practices, related to the timing and availability of guidance in different regions, may require regionally guided revaccination policies.

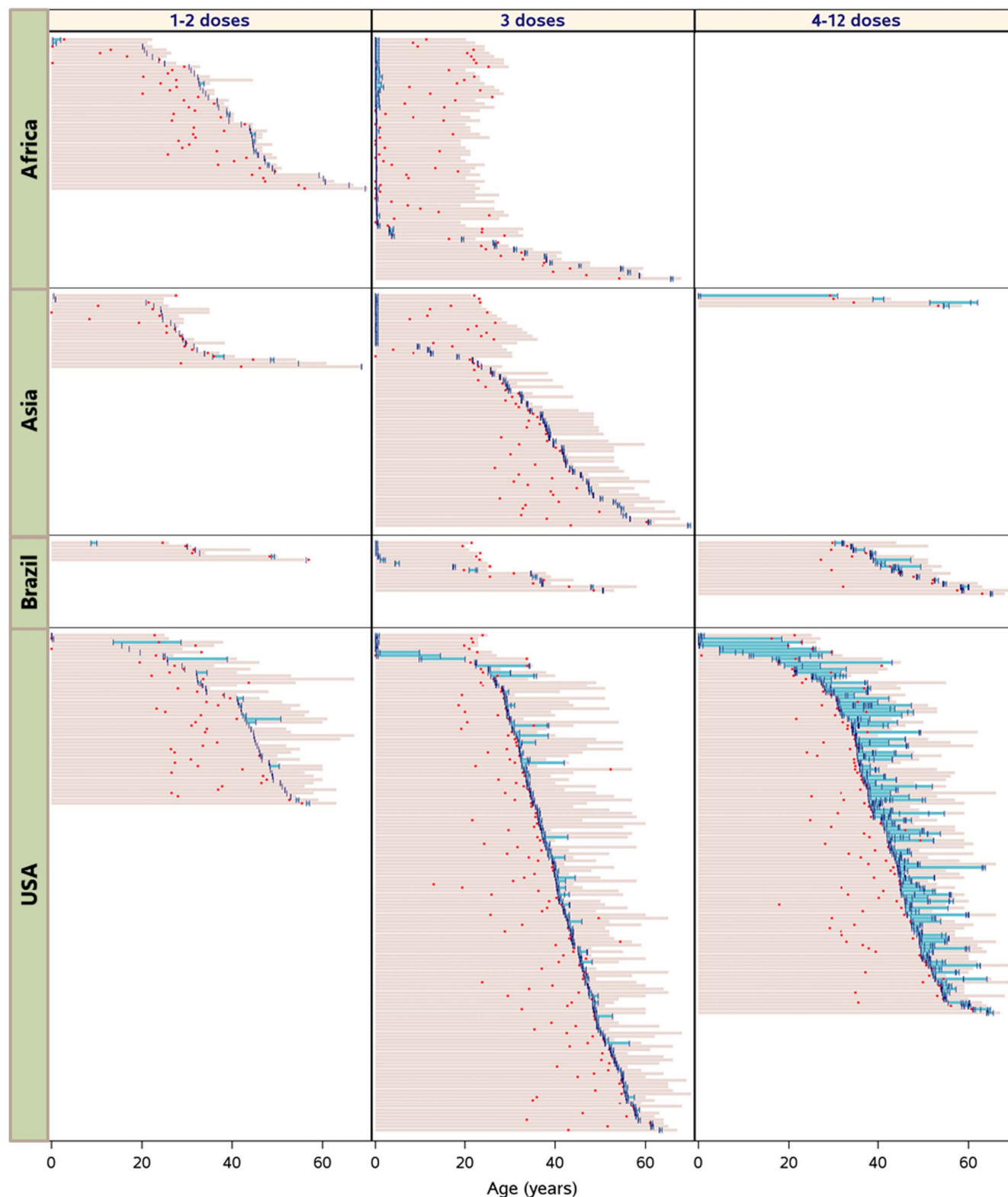


FIGURE 1. Hepatitis B vaccination histories of A5379 BEe-HIVE participants. Each tan line represents the time from birth to the participant's age at the time of anti-HBs test for trial eligibility. Ages when hepatitis B vaccination occurred for each participant are marked in blue (●), and multiple vaccine doses are connected by a blue line (—). Age at HIV diagnosis is marked in red (●). Participants are grouped by geographic region and the number of hepatitis B vaccines received before trial entry.

The observed patterns we describe are subject to several limitations. First, our data may not be generalizable because these are clinical trial participants, although the trial had limited eligibility criteria. There were regional differences in the demographics, which likely reflect the HIV populations and the variability in HBV risk exposure in different parts of the world. Second, past vaccination records were reported without the specifics on the formulation, dose amount, and the prescribed number of doses in the series. Therefore, our descriptions do not include how the HIV providers prescribed hepatitis B vaccine series, if the dose amounts were increased, or if the increased numbers were intentional. Third, the time of HIV diagnosis on record may not accurately reflect when HIV was acquired, and the delay in the record could have varied widely across the regions. Fourth, the past vaccine records may not be complete; if so, the number of doses is underestimated.

For PWH, guidelines recommend HBV screening and vaccination of all nonimmune individuals, followed by confirmation of serologic response and revaccination if anti-HBs <10 mIU/mL.²⁴ Based on the BEe-HIVE data, they recommend the CpG-adjuvanted vaccine for PWH, because it has been shown to induce seroprotective levels in 100% of recipients of 3-dose series at 4 weeks after series and 97% at 1 year after the series (with 94% at 8 weeks after second dose).¹² They also recommend the CpG-adjuvanted vaccine for PWH and prior vaccine nonresponse.^{13,25} They acknowledge waning immunity stating that some experts check anti-HBs annually and give a booster dose (or revaccination series) if levels fall <10 mIU/mL, particularly in those with risk factors for acquiring HBV and not receiving tenofovir. Based on our findings, we conclude that anti-HBs titers should be checked regardless of the number of vaccine doses administered in PWH. Of the screened individuals whom the sites identified as potential candidates for A5379, 51% did not have seroprotective titers at the time of screening, which led to enrollment. This percentage is probably enriched by prescreening, but there were also other criteria that led to ineligibility,¹³ suggesting that up to 50% may need revaccination.

Long-acting ART regimens do not provide the same protection against HBV as tenofovir-based therapies, and switching to HBV-inactive regimens has been linked to both new HBV infections and reactivation of prior HBV in PWH. Before initiating or switching, guidelines recommend assessing HBsAg, anti-HBs, and anti-HBc unless evaluated within 3 months.²⁴ Our findings taken with the previously reported BEe-HIVE trial results support reassessing serologies and offering a CpG-adjuvanted vaccine series to individuals without seroprotection, particularly those initiating LA ART. Although CpG-adjuvanted vaccines show promising durability, further data are needed to guide long-term anti-HBs monitoring strategies.

ACKNOWLEDGMENTS

The authors are grateful to the volunteers and participants in the ACTG A5379 (BEe-HIVE) trial and the individuals at the participating clinical research sites who

contributed to the study. The authors also acknowledge the contributions of all A5379 protocol team members.

REFERENCES

- Farooq PD, Sherman KE. Hepatitis B vaccination and waning hepatitis B immunity in persons living with HIV. *Curr HIV/AIDS Rep*. 2019;16:395–403.
- Mohareb AM, Kim AY. Hepatitis B vaccination in people living with HIV-If at first you don't succeed, try again. *JAMA Netw Open*. 2021;4:e2121281.
- Anthony DD, Umbleja T, Aberg JA, et al. Lower peripheral blood CD14+ monocyte frequency and higher CD34+ progenitor cell frequency are associated with HBV vaccine induced response in HIV infected individuals. *Vaccine*. 2011;29:3558–3563.
- Van der Wielen M, Van Damme P, Chlibek R, et al. Hepatitis A/B vaccination of adults over 40 years old: comparison of three vaccine regimens and effect of influencing factors. *Vaccine*. 2006;24:5509–5515.
- Overton ET, Sungkanuparph S, Powderly WG, et al. Undetectable plasma HIV RNA load predicts success after hepatitis B vaccination in HIV-infected persons. *Clin Infect Dis*. 2005;41:1045–1048.
- Schillie SF, Spradling PR, Murphy TV. Immune response of hepatitis B vaccine among persons with diabetes: a systematic review of the literature. *Diabetes Care*. 2012;35:2690–2697.
- Launay O, van der Vliet D, Rosenberg AR, et al. Safety and immunogenicity of 4 intramuscular double doses and 4 intradermal low doses vs standard hepatitis B vaccine regimen in adults with HIV-1: a randomized controlled trial. *JAMA*. 2011;305:1432–1440.
- Rey D, Piroth L, Wendling MJ, et al. Safety and immunogenicity of double-dose versus standard-dose hepatitis B revaccination in non-responding adults with HIV-1 (ANRS HB04 B-BOOST): a multicentre, open-label, randomised controlled trial. *Lancet Infect Dis*. 2015;15:1283–1291.
- Overton ET, Kang M, Peters MG, et al. Immune response to hepatitis B vaccine in HIV-infected subjects using granulocyte-macrophage colony-stimulating factor (GM-CSF) as a vaccine adjuvant: ACTG study 5220. *Vaccine*. 2010;28:5597–5604.
- Hastie E, Wooten D. Hepatitis B virus screening and vaccination in patients with HIV: a survey of clinicians' current practices. *Open Forum Infect Dis*. 2021;8:ofab270.
- McMahon BJ, Bruden DL, Petersen KM, et al. Antibody levels and protection after hepatitis B vaccination: results of a 15-year follow-up. *Ann Intern Med*. 2005;142:333–341.
- Marks KM, Kang M, Umbleja T, et al. Immunogenicity and safety of Hepatitis B virus (HBV) vaccine with a toll-like receptor 9 agonist adjuvant in HBV vaccine-naïve people with human immunodeficiency virus. *Clin Infect Dis*. 2023;77:414–418.
- Marks KM, Kang M, Umbleja T, et al. HepB-CpG vs HepB-Alum vaccine in people with HIV and prior vaccine nonresponse: the BEe-HIVE randomized clinical trial. *JAMA*. 2025;333:295–306.
- Kang M, Marks KM, Cox AL, et al. An efficient vaccine clinical trial: ACTG A5379 hepatitis B vaccine trial in persons with HIV. *Vaccine*. 2025;55:127028.
- Mizushima D, Takano M, Aoki T, et al. Effect of tenofovir-based HIV pre-exposure prophylaxis against HBV infection in men who have sex with men. *Hepatology*. 2023;77:2084–2092.
- Vasishta S, Dieterich D, Mullen M, et al. Brief report: hepatitis B infection or reactivation after switch to 2-Drug antiretroviral therapy: a case series, literature review, and management discussion. *J Acquir Immune Defic Syndr*. 2023;94:160–164.
- Pintado C, Delaugerre C, Molina JM. Acute hepatitis B infection after a switch to long-acting cabotegravir and rilpivirine. *Open Forum Infect Dis*. 2020;7:ofaa367.
- Abdullahi A, Popoussi OM, Torimiro J, et al. Hepatitis B virus (HBV) infection and Re-activation during nucleos(t)ide reverse transcriptase inhibitor-sparing antiretroviral therapy in a High-HBV endemicity setting. *Open Forum Infect Dis*. 2018;5:ofy251.
- Kaya A, Benke D, Swan T, et al. Use of dual antiretroviral therapy in individuals with different serological patterns for hepatitis B: what are the risks? What are the clinical implications? *HIV Med*. 2025;26:1317–1320.
- Denyer RV, Tate JP, Benator DA, et al. 1026. Hepatitis B reactivation in persons with HIV with positive hepatitis B core antibody after switching to antiretroviral therapy without hepatitis B activity. *Open Forum Infect Dis*. 2023;10(suppl 2):ofad500.057.

21. Todesco E, Valantin MA, Akhavan S, et al. Acute hepatitis B infections among PWH treated with 2-drug regimen: can we trust the vaccination status? *AIDS*. 2025;39:1845–1847.
22. Ochieng E, Robinson V, Anderson E, et al. Enhancing hepatitis B virus vaccine uptake and immunity through long-acting antiretroviral therapy programmatic synergy in the US south. *Open Forum Infect Dis*. 2025;12: ofaf096.
23. Centers for Disease Control and Prevention CDC. Global progress toward universal childhood hepatitis B vaccination, 2003. *MMWR Morb Mortal Wkly Rep*. 2003;52:868–870.
24. Panel on Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV. *Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV*. National Institutes of Health, HIV Medicine Association, and Infectious Diseases Society of America; 2025. Available at: <https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-opportunistic-infection>. Accessed November 3, 2025.
25. Marks KM, Kang M, Umbleja T, et al. HepB-CpG vaccine in people with HIV and prior nonresponse to HBV vaccine: the BEe-HIVe trial end-of-study results. *JAMA*. 2025;334:910–912.