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MAJOR ARTICLE

Observational Study Evaluating the Seroprotection of HepB-alum Vaccine and HepB-CpG Vaccine in People With HIV

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Background. Hepatitis B virus (HBV) vaccine seroprotection rates with conventional aluminum adjuvanted recombinant HBV vaccines, Engerix-B (HepB-alum) vaccine, among people with HIV (PWH) are varied. Heplisav-B (HepB-CpG) vaccine, a novel adjuvanted recombinant HBV vaccine, has shown higher seroprotection rates in immunocompetent patients but is not well studied in PWH. There are no published studies comparing seroprotection rates between HepB-alum and HepB-CpG in PWH. This study aims to evaluate and compare the seroprotection incidence of HepB-alum vs HepB-CpG in PWH at least 18 years of age.

Methods. This retrospective, observational cohort study included adults diagnosed with HIV who received a complete series of HepB-alum or HepB-CpG at a community health center in Phoenix, Arizona. Patients had a hepatitis B surface antibody <10 IU/L at the time of the first vaccine dose. The primary outcome was a comparison of seroconversion incidence between HepB-CpG and HepB-alum. Secondary outcomes included identifying factors associated with likelihood of response to HBV vaccination.

Results. A total of 120 patients were included in this study, 59 in the HepB-alum cohort and 61 in the HepB-CpG cohort. In the HepB-alum cohort, 57.6% achieved seroconversion, compared with 93.4% in the HepB-CpG cohort ($P < .001$). Those without diabetes were more likely to have response to a vaccine.

Conclusions. Among PWH at a single community health center, HepB-CpG provided a statistically higher incidence of seroprotection against HBV compared with HepB-alum.

Keywords. HIV; hepB-CpG; hepatitis B; vaccine.

It is estimated that 20 700 new cases of acute hepatitis B virus (HBV) occurred in the United States in 2019 and an estimated 880 000 to 1.89 million individuals are living with chronic HBV infection, despite HBV vaccines having been available in the United States since 1986 [1, 2]. The Advisory Committee on Immunization Practices (ACIP) recommends HBV vaccination in all infants at birth, children if not previously vaccinated, all adults aged 19–59 years, and adults aged ≥60 years at risk for infection by sexual exposure, percutaneous or mucosal exposure to blood, or traveling to a country where HBV is endemic [2–4]. The current single-antigen HBV vaccines available for adults 18 years of age and older in the United States are Recombivax HB, Engerix-B, Twinrix, and Heplisav-B. The older vaccines, Recombivax HB, Engerix-B, and Twinrix, are recombinant vaccines formulated with an aluminum adjuvant to increase immunogenicity. Twinrix is also co-formulated with inactivated hepatitis A virus. These vaccines, given as a 3-dose series at 0, 1, and 6 months, result in a modest seroprotection rate, between 75% and 90%, in immunocompetent adults. Seroprotection rates are much lower in immunocompromised individuals, such as those with diabetes mellitus, on hemodialysis, or diagnosed with HIV, and many require a "booster dose" after completing the initial series or receive a modified dosing regimen of double dose with each vaccine adminstration [3, 5]. The newest single-antigen HBV vaccine on the market, Heplisav-B (HepB-CpG), is also a recombinant hepatitis B vaccine but contains a novel adjuvant, CpG-ODN 1018, that binds to Toll-like receptor 9, which stimulates and enhances the immune response [4, 6, 7]. HepB-CpG is currently licensed as a 2-dose series, given at 0 and 1 month, and has been shown to lead to seroprotection in 90%–100% of individuals who completed the series in clinical trials [4]. Unfortunately, people with HIV (PWH) have been excluded from all major HBV vaccine trials. In a small single-center study, HepB-CpG was shown to have an 81% seroprotection rate after completion of 1 vaccination series in PWH [8]; however,

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no studies have been published comparing HepB-CpG and Engerix-B (HepB-alum) seroprotection rates in PWH. We hypothesize that HepB-CpG will provide greater seroprotection than HepB-alum in PWH.

METHODS

Study Design and Participants

In this retrospective, observational cohort study, adults aged 18 years or older who were diagnosed with HIV and had a hepatitis B surface antibody (HBsAb) <10 IU/L at the time of the first vaccine dose were screened for inclusion. Participants received, at minimum, a 3-dose series of HepB-alum or a 2-dose series of HepB-CpG at a community health center in Phoenix, Arizona. The study was approved by the institutional review board within the health system. Due to its retrospective nature, the study was approved with a waiver of informed consent. Participants without follow-up HbsAb titers at least 1 month after the last vaccine dose was administered were excluded, as were participants with active HBV (as defined by either a positive HBV viral load or a positive hepatitis B surface antigen [HBsAg]), those with a positive hepatitis B core antibody (HBcoreAb), those with a past medical history of solid organ transplant and/or stem cell transplant, those who received immunosuppressive therapy within 3 months of HBV vaccination (specifically, chemotherapy, monoclonal antibodies, tumor necrosis factor [TNF] inhibitors, steroids at dose equivalents of at least 20 mg/d of prednisone for at least 3 weeks, or transplant antirejection medications), and those who were pregnant or currently breastfeeding.

Participants were screened from a list of patients who were either billed for HBV vaccine administration or had an HBsAb drawn between January 1, 2015, and December 31, 2021. HepB-CpG was introduced to the community health center in March 2020. Before this, HepB-alum (specifically, Engerix-B) was the only HBV vaccine available at the study site. Thus, all participants who received HepB-CpG since its introduction into the study site through December 31, 2021, were screened for inclusion. Participants in the HepB-alum cohort were randomly screened until a sample size similar to the HepB-CpG cohort was met. Clinical data were collected from the electronic medical record, including basic demographics, social determinants of health, medical history including comorbidities, laboratory values, HBV vaccination status and vaccine doses administered, and HBV serologic test results. Data on whether patients had an active prescription for antiretroviral therapy at any point during completion of vaccine series up to follow-up HbsAb titer were collected; those with an active prescription were considered to be on antiretroviral therapy. CD4 counts and HIV RNA viral loads collected were the values closest to the date of last dose of vaccine.

Outcomes Measures

The primary outcome was comparison of seroconversion incidence between vaccination with HepB-CpG and HepB-alum in PWH. Seroconversion was defined as achievement of a HBsAb ≥10 IU/L at least 1 month after completion of the vaccine series. Secondary outcomes included identification of factors associated with an increased likelihood of response to HBV vaccination, such as patient demographics, presence of diabetes mellitus, chronic kidney disease and prior liver disease, and use of tobacco, alcohol, and intravenous drugs.

Statistical Analysis

A sample size of 102 participants, 51 in each group, was calculated to reach a 95% power based on an incidence of 60% and 90% in each group. Alpha was set at .05. Contingency tables were constructed with 95% CIs to establish odds ratios and *P* values comparing odds of immunity response across patient characteristics. Continuous variable medians (body mass index [BMI], CD4 count, viral load, and age) were compared using a 2-sample Wilcoxon test with alpha set at 0.05% and 95% CIs. Normal distributions of continuous data were assessed using Shapiro Wilks tests. All statistical analyses were performed using BlueSky Statistics (Chicago, IL, USA), OpenEpi, and SAS 9.4.

RESULTS

Participant Demographics and Characteristics

Of the 630 encounters screened for inclusion, 120 were included in this study, 59 in the HepB-alum cohort and 61 in the HepB-CpG cohort. The most frequent reasons for study exclusion were incomplete vaccination series or lack of available follow-up HBsAb (Figure 1). Demographics are reported in Table 1. Among both groups, the median age was 41 years, 78% of participants identified as male, 78% identified as White, and 58% identified as Hispanic. Seven participants in the HepB-alum cohort had reported comorbid diabetes mellitus compared with none in the HepB-CpG cohort. Only 1 participant had documented cirrhosis, and they were included in the HepB-CpG cohort. A total of 8.6% had active hepatitis C infection in the HepB-alum cohort, while 3.3% had active hepatitis C in the HepB-CpG cohort. A total of 6.7% vs 3.4% had previous hepatitis C infection (defined as a positive hepatitis C antibody without a positive corresponding hepatitis C viral load) in the HepB-CpG and HepB-alum cohorts, respectively.

Mean CD4 counts (range) were 627 ± 245 (143–1238) cells/mm^3 in the HepB-alum cohort and 586 ± 314 (58–1307) cells/mm^3 in the HepB-CpG cohort. In the HepB-alum and HepB-CpG cohorts, 89.9% and 88.5%, respectively, had HIV RNA viral loads <40 copies/mL. Detectable HIV RNA viral loads ranged from 47 to 47 163 copies/mL in the HepB-alum cohort and from 44 to 356 709 copies/mL in the HepB-CpG cohort. No participants in either group were documented in provider notes to be either HIV elite controllers or HIV chronic nonprogressors. In both groups, 100% of participants were prescribed antiretroviral therapy during the course of vaccination.

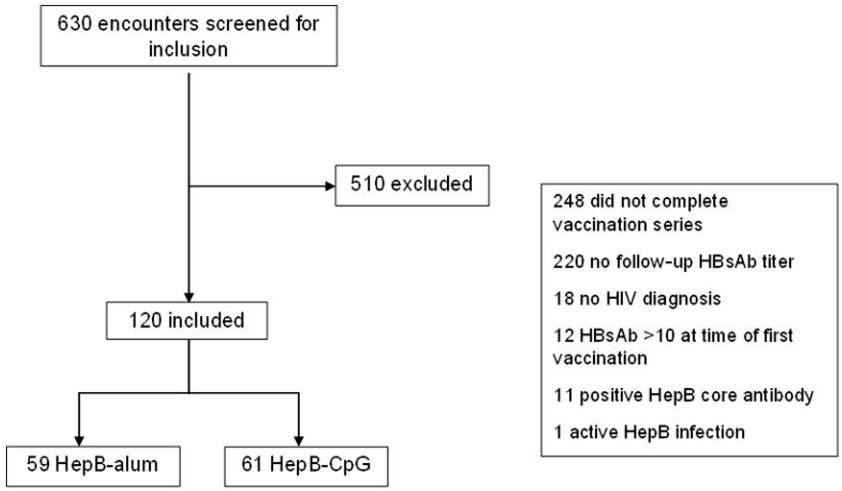

Figure 1. Participant screening for study inclusion and reasons for study exclusion. Abbreviations: HBsAb, hepatitis B surface antibody; HepB, hepatitis B; HepB-alum, Engerix-B; HepB-CpG, Heplisav-B.

In the HepB-CpG cohort, every participant received the standard dose (0.5 mL intramuscularly) of HepB-CpG. All participants received at least 2 doses of HepB-CpG before postvaccination serologic testing. The average time between the first and second vaccine doses was 9 weeks ± 10 weeks. The average time between the last vaccine dose and the follow-up titer was 22 weeks ± 17 weeks. One participant in the HepB-CpG cohort who did not seroconvert after 2 doses received a third dose of HepB-CpG 2 months after their second HepB-CpG dose. This participant had evidence of seroconversion 1.5 months after receiving the third dose.

In the HepB-alum cohort, 2 participants received a fourth HepB-alum vaccine dose. One patient received a double dose of vaccine (2 mL intramuscularly) for each of the 4 vaccine doses. Of the participants who received 3 doses of HepB-alum, 7 received double doses (2 mL intramuscularly per dose). The average time between the first and second vaccine doses was 2 months ± 2 months. The average time between the first and third vaccine doses was 7 months ± 2 months. The average time between the first and fourth vaccine doses was 7.5 months. The average time between the third vaccine dose and follow-up titer was 41 weeks ± 35 weeks. The average time between the fourth vaccine dose and follow-up titer was 19 weeks.

Primary Outcome

In the HepB-CpG cohort, 93.4% achieved seroconversion, compared with 57.6% in the HepB-alum cohort ($P < .001$). In the HepB-CpG cohort, none of the participants with detectable HIV RNA viral loads failed to achieve seroconversion. In the HepB-alum cohort, 4 out of 6 participants with detectable HIV RNA viral loads failed to achieve seroconversion. Of the 2 participants in the HepB-alum cohort who received a fourth vaccine dose, both achieved seroconversion. Of the 7 participants who received 3 doses of double-dose HepB-alum, 5 achieved seroconversion. Overall, a 35.8% difference in seroconversion incidence between the HepB-alum and HepB-CpG cohorts was found ($P < .0001$) (Table 2).

Secondary Outcomes

On post hoc bivariate analysis, no statistically significant differences were identified in achievement of seroconversion among vaccine cohorts with respect to the presence or absence of chronic kidney disease, fatty liver disease, cirrhosis, active or cured hepatitis C infection, level of alcohol use, tobacco use, or intravenous drug use. Standard vs nonstandard vaccine doses administered also did not show significant differences, with P values >.05 (Table 2, column P). A higher incidence of seroconversion was found in individuals without diabetes than those with diabetes, with an odds ratio >1, which was found to be statistically significant (Table 2). Table 2 further summarizes associated 95% CIs, odds ratios, and P values.

Table 3 summarizes associated summary statistics of continuous variables. Of these variables, only CD4 count was found to be fairly normally distributed [9]. Supplementary Table 1 summarizes the results of Shapiro-Wilks tests. As CD4 count data were the only numeric variable to be mostly normally distributed, the mean value is reported. BMI, viral load, and time in months between completion of vaccination series and titer illustrated skewed distributions, so medians were analyzed and reported. The median body mass index and HIV RNA viral loads were not significantly different between immune and nonimmune cohorts. Similarly, the CD4 count mean was also not found to differ between immune status cohorts. Continuous variables were further examined between vaccine cohorts to include subgrouping of ages above and below 65

Table 1. Demographics

	120 Participants	
	HepB-alum (n = 59)	HepB-CpG (n = 61)
Sex assigned at birth, No. (%)		
Male	48 (81.4)	51 (83.6)
Female	11 (18.6)	10 (16.4)
Gender identity, No. (%)		
Male	44 (74.6)	49 (80.3)
Female	15 (25.4)	12 (19.7)
Age		
Mean ± SD, y	40 ± 11	42 ± 11
Range, y	21–65	19–62
Race/ethnicity, No. (%)[a]		
White	44 (74.5)	50 (81.9)
Hispanic	30 (50.8)	40 (65.6)
Black	13 (22)	8 (13.1)
American Indian or Alaska Native	0 (0)	0 (0)
Asian	0 (0)	0 (0)
Native Hawaiian or other Pacific Islander	0 (0)	1 (1.6)
Body mass index		
Mean ± SD, kg/m^2	29.2 ± 7.1	28.1 ± 7.6
Range	19.9–55.4	18.2–58.6
Diabetes mellitus, No. (%)		
	7 (11.9)	0 (0)
HbA1c		
Mean ± SD	7.3 ± 2.1	N/A
Range	5.7–11.8	N/A
Chronic kidney disease, No. (%)	2 (3.4)	3 (4.9)
End-stage renal disease on HD, No. (%)	0 (0)	0 (0)
Fatty liver disease, No. (%)	1 (1.7)	5 (8.2)
Active hepatitis C infection, No. (%)	5 (8.5)	2 (3.3)
Prior hepatitis C infection, No. (%)	2 (3.4)	4 (6.6)
Cirrhosis, No. (%)	0 (0)	1 (1.6)
Tobacco use, No. (%)		
Never	33 (55.9)	28 (46)
Current	22 (37.3)	31 (50.8)
Quit	4 (6.8)	2 (3.3)
Alcohol use,[b] No. (%)		
Never	32 (54.2)	27 (44.3)
Moderate	26 (44.1)	32 (52.5)
Heavy	1 (1.7)	2 (3.3)
Current intravenous drug use, No. (%)		
Yes	0 (0)	2 (3.2)
No	59 (100)	59 (96.8)
CD4 count		
Mean ± SD, cells/mm^3	627 ± 245	586 ± 314
Range, cells/mm^3	143–1238	58–1307
HIV RNA viral load		
Undetectable, No. (%)	53 (89.8)	54 (88.5)
Detectable range, copies/mL	47–47 163	44–356 709
Prescribed antiretroviral therapy, No. (%)		
Yes	59 (100)	61 (100)
No	0 (0)	0 (0)

Abbreviations: HD, hemodialysis; HepB-alum, Engerix-B; HepB-CpG, Heplisav-B; NIAAA, National Institute on Alcohol Abuse and Alcoholism.

[a]Race data not available for 4 patients (n = 2 in HepB-alum group, n = 2 in HepB-CpG group).

[b]Per NIAAA: moderate alcohol use was defined as ≤2 drinks/d for men or ≤1 drink/d for women. Heavy alcohol use was defined as 4+ drinks/d or 14+ drinks/wk for men or 3+ drinks/d or 7+ drinks/wk for women.

Table 2. Odds Ratios, Confidence Intervals, and *P* Values Comparing Odds of Immunity Response Across Patient Characteristics

Variable	Responder (Immune/Not Immune)	95% CI	*P* Value	Odds Ratio
Vaccine				
HepB-alum[a]	34/25	3.36–32.69	<.0001	10.48
HepB-CpG	57/4			
Sex assigned at birth				
Male	76/23	0.46–3.80	.603	1.322
Female[a]	15/6			
Chronic kidney disease				
No	87/27	0.34–13.53	.405	2.148
Yes[a]	3/2			
Diabetes mellitus				
No	87/25	0.97–22.11	.037	4.64
Yes[a]	3/4			
Tobacco use				
Never[a]	45/16	0.116–10.885	(ref)	(ref)
Current	42/11	0.566–3.257	.493	1.358
Quit	4/2	0.119–4.262	.708	0.711
Active hepatitis C infection				
No	86/26	0.521–11.80	.241	2.481
Yes[a]	4/3			
Prior hepatitis C infection				
No	85/27	0.273–9.073	.609	1.574
Yes[a]	4/2			
Alcohol use[b,c]				
Never[a]	40/19	(ref)		(ref)
Moderate	48/10	0.432–12.962	>.999	2.28
Heavy	3/0	n/a	n/a	n/a
Fatty liver disease				
No	85/28	0.173–80.618	>.999	0.607
Yes[a]	5/1			
Cirrhosis[b]				
No	89/29	n/a	>.999	n/a
Yes	1/0			
Race				
White/Hispanic[a]	77/21	0.822–0.136	(ref)	(ref)
Black	13/8	0.266–48.651	.106	0.443
Native Hawaiian or other Pacific Islander	1/1	n/a	n/a	n/a
Current intravenous drug use[c]				
No	87/29	n/a	>.999	n/a
Yes[a]	2/0			
Standard vaccine Dose				
No	6/2	0.181–5.00	>.999	0.952
Yes[a]	85/27			

Abbreviations: HepB-alum, Engerix-B; HepB-CpG, Heplisav-B; NIAAA, National Institute on Alcohol Abuse and Alcoholism.

[a]Reference category for the calculation of odds ratios.

[b]Per NIAAA: moderate alcohol use was defined as ≤2 drinks/d for men or ≤1 drink/d for women. Heavy alcohol use was defined as 4+ drinks/d or 14+ drinks/wk for men or 3+ drinks/d or 7+ drinks/wk for women.

[c]Odds ratio could not be calculated, as 1 of the counts is <1.

years, BMI above and below 30, CD4 count above and below 200, and detectable viral loads. Of note, there was only 1 individual with a CD4 count <200 within the HepB-alum arm, so analysis could not be completed. Similarly, only 2 individuals age >65 were identified, both belonging to the HepB-alum arm, which limited ability for any comparisons. No statistically significant differences were found between these subgroupings between the vaccine arms.

DISCUSSION

Literature has shown increased seroprotection rates in immunocompetent individuals vaccinated with HepB-CpG compared with HepB-alum, but no published studies have compared seroconversion rates or incidence in PWH [10]. Multiple studies have evaluated seroprotection rates in PWH vaccinated with HepB-alum and have observed a wide range of seroprotection rates, from 18% to 71% [11]. However, there

Table 3. Confidence Intervals and *P* Values Calculated Using Independent *T* Test for CD4 Mean and Wilcoxon Two-Sample Test Statistic to Compare Medians of Age, BMI, Viral Load, and Time to Titer in Months

	Vaccine										Wilcoxon 2-Sample Rank-Sum 2-Sided *P* With T-Approximation
	HepB-alum					HepB-CpG					
	No.	Mean	Median	Min	Max	No.	Mean	Median	Min	Max	
Age all	59	44.62	42.85	25.35	68.58	61	43.1	43.19	20.72	63.17	.5978
BMI	59	29.17	27.76	19.92	55.42	57[a]	28.07	26.38	18.19	58.58	.2354
BMI <30	44	25.91	25.75	19.92	29.86	44	24.89	25.61	18.19	29.29	.1524
BMI >30	15	38.74	38.45	30.24	55.42	13	38.84	35.05	30.57	58.58	1
Time, mo	59	8.81	6	1	43	61	5	4	1	21	.0032
CD4 count	59	626.51	600	143	1238	61	586.15	527	58	1307	.2188
CD4 count >200	58	634.8	600	227	1238	53	652.9	580	201	1238	.8594
HIV viral load detectable and undetectable	59	817.78	0	0	47 163	61	5859.2	0	0	356 709	.846
HIV viral load detectable	6	8041.5	264	47	47 163	7	515 059	98	44	356 709	.7308

Abbreviations: BMI, body mass index; HepB-alum, Engerix-B; HepB-CpG, Heplisav-B.

[a]BMI data missing for n = 4 participants in the HepB-CpG group

are limited data on the efficacy of HepB-CpG in PWH. To date, only 2 other studies have thus far been reported in PWH.

The AIDS Clinical Trials Group (ACTG) study A5379[12] is an ongoing prospective, open-label study evaluating the efficacy of various HBV vaccination strategies in PWH. The trial compares 2-dose series of HepB-CpG vs 3-dose series of HepB-CpG vs 3-dose series of HepB-alum. In the 3-dose HepB-CpG group, patients received HepB-CpG at study entry, week 4, and week 24. Preliminary single-arm evaluation of this 3-dose HepB-CpG group showed an observed seroconversion rate of 100% at 28 weeks after receipt of the third dose, compared with rates of 87% at 8 weeks after the second dose, which increased to 94.4% at 12 weeks and 98.5% at 24 weeks (ie, before the third HepB-CpG dose). The 12- and 24-week results after 2 doses in the A5379 study were comparable to our result of 93.4% at a median of 22 weeks of follow-up. Therefore, it is likely that our seroconversion incidence of 93.4% appears higher after 2 doses as compared with results from A5379 at week 8 due to the timing of dose administration and/or follow-up titers within our cohort.

While an A1C of <9% was required for study inclusion in A5379, little information otherwise is available in the preliminary results on incidence of comorbidities within the cohort [12]. Additionally, preliminary data comparing 2-dose HepB-CpG vs 3-dose HepB-CpG vs HepB alum have not yet been released; therefore, our study provides the only data directly comparing HepB-CpG with HepB-alum in PWH at this time.

A second single-site retrospective cohort study by Schnittman et al. [8] found a seroconversion rate of 81% in PWH vaccinated with HepB-CpG [8], which is lower than the seroconversion incidence of 93.4% in the HepB-CpG arm of our study. Most patients (63 out of 64) in the Schnittman et al. cohort received 2 doses of HepB-CpG, with 1 patient receiving only 1 dose. Their study did not compare seroconversion rates between the HepB-CpG vaccines and any other HBV vaccine.

One possible explanation for the difference in seroconversion incidence could be the longer time interval between doses and between the last dose and follow-up titers in our study. Another possible explanation could be the differences in cohort comorbidities, as our HepB-CpG cohort did not have any patients with diabetes mellitus, whereas in the Schnittman et al. study 19% of included patients had diabetes mellitus. Overall, the cohort within our study had a low incidence of comorbidities, and with 1 exception, we did not find any of the comorbidities to be associated with increased likelihood of response to vaccine. On bivariate analysis, individuals without diabetes were found to be more likely to respond to vaccine; however, this finding is reflective of HepB-alum, as all the included patients with diabetes had received HepB-alum. Thus, this finding does not provide any additional information to elucidate vaccine response in PWH receiving HepB-CpG.

Also of note is the relatively high incidence of seroconversion in current smokers identified on bivariate analysis, which was found to be comparable to the rate in those who have quit. This is challenging to interpret without more information regarding reported pack-years. Alcohol use cohorts also displayed interesting results in that moderate consumers reached high levels of seroconversion, above that of never consumers with similar sample sizes. Only 3 individuals included in this study self-reported as heavy drinkers, and thus this information is reported with caution due to such a small percentage. Moreover, the odds ratios for these categories were not statistically significant.

Regardless of study differences, all 3 studies, ours, the Schnittman et al. [8] study, and A5379 [12], all suggest high incidence of seroconversion with HepB-CpG in PWH. Further, pending the full results from A5379, our study is thus far the only study to directly compare HepB-CpG with HepB-alum, which aligns with the findings in immunocompetent hosts that HepB-CpG provides better protection against HBV in PWH.

There are limitations to this study. The sample size is relatively small compared with the number of encounters screened for inclusion. The most common reason for exclusion of HepB-CpG participants was lack of follow-up HBsAb titers due to inconsistent evaluation of postvaccination serologic titers despite being recommended by ACIP [3]. Another common reason for exclusion for the HepB-alum participants was failure to complete the 3-dose series, with the majority missing the third vaccine dose. The exclusion of patients without follow-up HBsAb titers and those who did not complete the vaccination series may have led to the generation of bias, as those who had follow-up titers and who completed the vaccine series may have better adherence overall. It is possible that having improved adherence, particularly with antiretroviral therapy, could lead to different immune responses to vaccination.

Additionally, quantitative HBsAb results were not reported by the laboratory and could not be assessed. All HbsAb results >9.9 IU/L were reported as positive by the laboratory. Another limitation is the low rates of comorbidities, which limited our ability to find any factors that influenced seroconversion or assess the impact of multiple disease states on seroconversion. Further studies will be needed to clarify the magnitude or effect of comorbidities on seroconversion rates in PWH. Also, our study population largely identified as White or Hispanic, while the majority of new HIV diagnoses in the United States are among Black/African Americans, followed by Hispanic/Latinos and Whites [13]. Multicenter studies may be able to capture a racially diverse study population. Lastly, larger studies will also be able to better assess seroconversion in persons with various comorbid conditions and in persons who are not virally suppressed or have lower CD4 counts than observed in this study.

As HepB-CpG has only been Food and Drug Administration approved since 2017, we are not yet able to assess the durability of the vaccine. It is known that HepB-alum immunity can wane over time in both immunocompetent and immunocompromised individuals [5, 14, 15]. Larger prospective studies are warranted to assess waning of HepB-CpG immunity in both the general population and PWH. A5379 is designed to follow patients for 72 weeks, and thus should be able to provide information on durability of vaccine response in PWH once final results are available [12].

Among PWH at a single community health center, HepB-CpG provided statistically higher incidence of seroprotection against HBV compared with HepB-alum. In this study, the higher seroprotection incidence in the HepB-CpG cohort vs the HepB-alum cohort was not observed to be due to differences in group demographics or reported comorbidities, though this observation was limited by the small sample size and low incidence of comorbidities. HepB-CpG may be preferred over HepB-alum in PWH due to apparent increased seroprotection and a more convenient dosing regimen.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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Patient consent. This study was approved by the institutional review board at Valleywise Health with a waiver of informed consent.

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