# Evaluating the Seroprotection of HepB-alum Vaccine and HepB-CpG Vaccine in Adults Living with HIV

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## Introduction

- Rate of reported acute hepatitis B (HBV) infections decreased 88.5% since the development of HBV vaccines, but an estimated 21,900 new cases of HBV occurred in the US in 2015[1]
- HBV vaccination is recommended for all infants at birth, children not previously vaccinated, all adults aged 19-59, and adults ≥ 60 years at risk for infection[1,2,3]
- Conventional HBV vaccines are co-formulated with an aluminum adjuvant (e.g., Engerix-B; HepB-alum); usually given as a 3-dose series and result in seroprotection rates of 75-90% in immunocompetent adults, but even lower in patients with certain comorbidities (e.g. diabetes, kidney disease)[1,4]
- HepB-CpG (Heplisav-B) is a newer, 2-dose series HBV vaccine using CpG-ODN 1018 as an adjuvant, which results in seroprotection rates of 90-100% in immunocompetent patients[2,5,6]
- People with HIV (PWH) were excluded from HepB-CpG clinical trials[2]
- A small, single-center study showed an 81% seroprotection incidence with HepB-CpG in PWH[7]
- There are no published studies comparing seroprotection incidence between HepB-alum and HepB-CpG in PWH

## Methods

**Study Objectives**:

- Primary: compare seroconversion incidence of HepB-CpG to HepB-alum
  - Seroconversion is defined as achievement of HBsAb ≥ 10 IU/L at least one month post vaccine series completion
- Secondary: identify factors associated with increased likelihood of response to HBV vaccination

**Study Design and Setting:**

- Retrospective, observational cohort study conducted at a community health center focusing on primary care for PWH
- Participants were identified for screening from vaccine billing records and HBsAb results performed at the clinic between January 1, 2015 through December 31, 2021
- HepB-CpG was introduced to the health center in March 2020
  - All participants receiving HepB-CpG were screened for study inclusion
- HepB-alum was previously the preferred vaccine at the health center
  - Participants receiving HepB-alum were randomly screened for inclusion until a sample size similar to the HepB-CpG cohort was met

**Statistical Analysis:**

- Sample size of 102 participants, 51 in each group, required to reach a 95% power based on an incidence of 60% and 90% in each group with alpha set to 0.05
- Fisher's exact test and student's t-test used to compare categorical and continuous variables between vaccine cohorts using BlueSky Statistics package (Chicago, IL)

## Methods

**Inclusion Criteria:**

- Adults aged ≥ 18 years
- Established HIV diagnosis
- HBsAb < 10 IU/L at the time of first vaccine dose
- Completed either a 2-dose series for HepB-CpG or 3-dose series for HepB-alum

**Exclusion Criteria:**

- No follow-up HBsAb titer
- Active HBV infection, defined as:
  - Positive HBV viral load OR Positive hepatitis B surface antigen
- Positive hepatitis B core antibody (HbcoreAb)
- Past medical history of solid organ transplant and/or stem cell transplant
- Pregnancy or breastfeeding at time of vaccine series administration
- Receipt of immunosuppressive therapy within 3 months of HBV vaccination
  - Chemotherapy, monoclonal antibodies, TNF inhibitors, steroids at dose equivalents of 20 mg/day prednisone for at least 3 weeks, or transplant anti-rejection medications

## Results

630 encounters screened for inclusion

510 encounters excluded:
- N = 248 did not complete vaccine series
- N = 220 no follow up HBsAb titer
- N = 18 no HIV diagnosis
- N = 12 HBsAb >10 IU/L at time of first vaccine dose
- N = 11 positive HbcoreAb
- N = 1 active HBV infection

120 encounters included:
N = 59 HepB-alum
N = 61 HepB-CpG

**Primary Outcome:**

- HepB-CpG group seroconversion: **93.4%**
- HepB-alum group seroconversion: **57.6%** ($p < 0.001$)

**Secondary Outcomes:**

- Univariate analysis conducted examining the following variables:
  - Sex at birth
  - Race
  - BMI
  - CD4 count
  - HIV RNA viral load
  - Diabetes
  - CKD
  - Liver disease
  - Tobacco use
  - Alcohol use
  - IVDU

No statistical differences were identified in cohort demographics or comorbidities between groups. Preliminary analyses were limited to categorical and continuous comparisons using Fisher's exact test and student t-tests, respectively

## Results

**Demographics:** (values are no. [%] unless otherwise noted)

| | HepB-alum n=59 | HepB-CpG n=61 |
|---|---|---|
| **Sex Assigned at Birth** | | |
| **Male** | 48 (81.4) | 51 (83.6) |
| **Female** | 11 (18.6) | 10 (16.4) |
| **Gender Identity** | | |
| **Male** | 44 (74.6) | 49 (80.3) |
| **Female** | 15 (25.4) | 12 (19.7) |
| **Age (years)** | | |
| **Mean ± SD** | 40 ± 11 | 42 ± 11 |
| **Race** | | |
| **White/Hispanic** | 46 (78) | 52 (85.3) |
| **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 (BMI) (kg/m$^2$)** | | |
| **Mean ± SD** | 29.2 ± 7.1 | 28.1 ± 7.6 |
| **Diabetes** | | |
| | 7 (11.9) | 0 (0) |
| **HbA1c Mean ± SD** | 7.3 ± 2.1 | N/A |
| **Chronic Kidney Disease (CKD)** | 2 (3.4) | 3 (4.9) |
| **End Stage Renal Disease on Hemodialysis** | 0 (0) | 0 (0) |
| **Fatty Liver Disease** | 1 (1.7) | 5 (8.2) |
| **Active Hepatitis C Infection** | 5 (8.5) | 2 (3.3) |
| **Prior Hepatitis C Infection** | 2 (3.4) | 4 (6.6) |
| **Cirrhosis** | 0 (0) | 1 (1.6) |
| **Tobacco Use** | | |
| **Never** | 33 (55.9) | 28 (46) |
| **Current** | 22 (37.3) | 31 (50.8) |
| **Quit** | 4 (6.8) | 2 (3.3) |
| **Alcohol Use$^{\alpha}$** | | |
| **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 (IVDU)** | | |
| **Yes** | 0 (0) | 2 (3.2) |
| **No** | 59 (100) | 59 (96.8) |
| **Prescribed Antiretroviral Therapy** | | |
| **Yes** | 59 (100) | 61 (100) |
| **No** | 0 (0) | 0 (0) |
| **CD4 count (cells/mm$^3$)** | | |
| **Mean ± SD** | 627 ± 245 | 586 ± 314 |
| **Range** | 143-1238 | 58-1307 |
| **HIV RNA Viral Load (copies/mL)** | | |
| **Undetectable$^{\Delta}$** | 53 (89.8) | 54 (88.5) |
| **Detectable Range** | 47-47,163 | 44-356,709 |

$^{\alpha}$ Per NIAAA: Moderate alcohol use was defined as ≤2 drinks/day for men or ≤1 drink/day for women. Heavy alcohol use was defined as 4+ drinks/day or 14+ drinks/week for men or 3+ drinks/day or 7+ drinks/week for women

$^{\Delta}$ Undetectable as reported by the lab was <40 copies/mL

## Discussion

- An increased seroconversion incidence was found in literature using HepB-CpG compared to using HepB-alum, but no published studies thus far comparing seroconversion incidence in PWH[8]
- Single center study found 81% seroconversion incidence with HepB-CpG in PWH, however the study did not compare HepB-CpG to HepB-alum[7]
- Current study found a statistically higher seroconversion incidence associated with HepB-CPG compared to seroconversion with HepB-alum in PWH
- Limitations include the small sample size and low incidence of comorbidities
  - Comorbidities such as diabetes and kidney disease are known to affect seroconversion to HBV vaccination[1,4]
  - Further studies needed to clarify magnitude of effect of comorbidities on seroconversion in PWH
- Future directions include
  - Expanding the sample size to include significant variation in demographics and comorbidities to build logistic regression models and assess for covariance in order to allow assessment of the impact of chronic diseases, substance use and vaccine type on seroprotection status in PWH
- HBV immunity from HepB-alum vaccine can wane over time in both immunocompetent and immunocompromised individuals[4,10,11]
  - Further studies are needed to assess for waning of immunity from HepB-CpG in both the general population and in PWH
- Overall, this study suggests that HBV vaccination in PWH with HepB-CpG leads to higher incidence of seroconversion compared to vaccination with HepB-alum

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