L21

Evaluation of Medical Readiness and Operational Efficiencies Using a 2-Dose Versus 3-Dose Hepatitis-B Virus Vaccine Regimen in a Military Recruit Training Setting

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Background

- Hepatitis B virus (HBV) is a highly infectious blood-borne pathogen that can result in incurable liver disease.[1,2]
  - Globally, HBV has infected approximately 30% of the population.[3]
- The United States military combats infectious diseases such as HBV through the use of preventative vaccines during basic training.[4]
  - The US Advisory Committee on Immunization Practices recommends HBV vaccination for travelers to HBV-endemic regions and HBV immunization has been required for new US military recruits as a key part of medical readiness since 2002,[4,5] primarily because military personnel are at an increased likelihood of being exposed to the virus when deployed to countries where hepatitis is endemic.[6]
- Adult HBV vaccines are currently available as 2- and 3-dose series.
  - Three-dose HBV vaccines (HepB-Alum; GlaxoSmithKline, Research Triangle Park, NC) and combined HBV and hepatitis A virus (HAV) vaccines (HepA+HepB vaccine; GlaxoSmithKline, Research Triangle Park, NC) are available for administration on a 0-, 1-, and 6-month schedule.[7-9]
  - A 2-dose HepB-CpG vaccine (Dynavax Technologies, Emeryville, CA) is administered with a 1-month dose interval.[10]
  - Compared with a 3-dose vaccine, HepB-CpG vaccination induces earlier and higher seroprotection rates (SPRs) among healthy adults 18–70 years of age.[11-13]
- This novel HepB-CpG vaccine could help with increasing seroprotection and diminishing operational burden and inefficiencies associated with regimen completion requirements among military personnel.

Objective

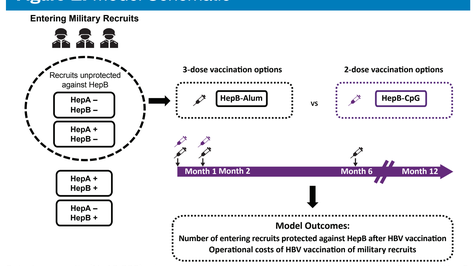
- **To investigate the health and cost impact associated with using the 2-dose HepB-CpG vs 3-dose HBV vaccines in a military recruit training setting**

Methods

Model Description and Outcome Measurements

- This model estimated the comparative value and number of protected US military recruits resulting from receipt of 2-dose HepB-CpG vs 3-dose HepB-Alum vaccination over a 12-month period (**Figure 1**).

Figure 1. Model Schematic



Entering recruits (N=10,000) who were antibody negative for both HepA and HepB or only HepB were considered unprotected against HepB. Unprotected military recruits in the base case scenario received either a 3-dose (HepB-Alum) or a 2-dose (HepB-CpG) vaccine series based on their age and vaccination status. Note that because HepB-CpG and HepA+HepB are only approved for individuals ≥18 years of age, those <18 years of age received HepB-Alum. HBV=hepatitis B virus; HepA=hepatitis A; HepB=hepatitis B.

- Model inputs are summarized in **Table 1**.
- Model outcomes included the number and percentage of military recruits protected against HBV and the operational costs of each vaccination program (ie, missed training time cost, administration cost).
  - Operational costs were adjusted for inflation using the consumer price list index and assumed 100% compliance.

Table 1. Model Inputs

	Vaccine Option[a]			
	3-Dose Vaccine (HepB-Alum)	2-Dose Vaccine (HepB-CpG)	3-Dose Vaccine (HepA + HepB)	2-Dose Vaccine (HepB-CpG + HepA)
Recruit age, %, y				
17	3	3	3	3
18	33	33	33	33
19	21	21	21	21
≥20	42	42	42	42
Vaccine SPR, %[b]				
Dose 1	4.2	22.0	17.9[c]	22.0[c]
Dose 2	24.0	95.7	61.2[c]	95.7[c]
Dose 3	79.5	N/A	95.1[c]	N/A
Recruits vaccinated by dose, %[d]				
Dose 1	0.8	0.8	0.8	0.8
Doses 1 and 2	1.2	99.2	1.2	99.2
Doses 1, 2, and 3	98.0	N/A	98.0	N/A
Effective SPR, %				
Dose 1	0.03	0.2	0.1	0.2
Dose 2	0.3	94.9	0.7	94.9
Dose 3	77.9	N/A	93.2	N/A
Total	78.2	95.1	94.0	95.1
Operational costs, $				
Missed training time[e]	154.00	154.00	154.00	154.00
Administration[f]	8.00	8.00	8.00	8.00
Vaccine (cost per dose)				
HepB-CpG	–	73.05	–	73.05
HepB-Alum pediatric	15.38[g]	15.38[g]	15.38[g]	15.38[g]
HepB-Alum adult	25.81	–	–	–
HepA+HepB vaccine	–	–	62.04	–
HepA vaccine pediatric	–	–	–	21.11[g]
HepA vaccine adult	–	–	–	32.86

N/A=not applicable; SPR=seroprotection rate.
[a]Options for the base case analysis were HepB-CpG and HepB-Alum; options for the scenario analysis were HepB-Alum, HepB-CpG, HepA+HepB vaccine, and HepB-CpG+HepA vaccine.
[b]SPRs for HepB-Alum and HepB-CpG were derived from 3 pivotal HepB-CpG clinical trials,[11-13] and SPRs for HepA+HepB vaccine were based on the prescribing information.[9]
[c]SPR values reflect protection against HBV only and does not take into account protection against HAV.
[d]Compliance rates were derived from the assumption that 98% of recruits receive all doses of the 3-dose vaccine regimens based on the opinion of a military expert.
[e]Adjusted for inflation using the CPI Inflation Calculator from the US Bureau of Labor Statistics (https://www.bls.gov/data/inflation_calculator.htm) and derived from an analysis of cost for every hour of training missed by soldiers in Advanced Individual Training while in clinic at Fort Sill.[14]
[f]Vaccination administration costs were $7.79 and then adjusted for inflation using the CPI Inflation Calculator from the US Bureau of Labor Statistics (https://www.bls.gov/data/inflation_calculator.htm) and taken from an analysis of a school-based hepatitis B vaccination program.[15] The analysis halved the school-based cost to account for large volumes and ease of contracting vaccines in the military. Administration costs were applied once for vaccines, which were assumed to be given at the same appointment.
[g]Recruits 17 years of age in the HepB-Alum, HepB-CpG, and HepA+HepB vaccine options were administered HepB-Alum pediatric. Those 17 years of age in HepB-CpG+HepA vaccine options were administered HepB-Alum pediatric and HepA pediatric.

Effective Seroprotection Rate

- Potential real-world efficacy after either HepB-CpG or HepB-Alum vaccination was assessed using the effective SPR (eSPR).
  - The eSPR used published vaccine compliance and SPRs to provide the potential real-word efficacy of adult HBV vaccines (**Table 1**).
  - The eSPR for each dose of HBV vaccine was determined by multiplying vaccine-specific compliance rates by the SPR for each dose. Total eSPR for each vaccine was calculated by summing the dose specific eSPRs.

Sensitivity Analyses

- One-way sensitivity analyses were conducted by assuming 15% higher or lower values than base-case inputs to examine the most influential variables (ie, age, administration costs, missed training time costs) affecting the cost difference of vaccination with either HepB-Alum or HepB-CpG (**Table 2**).
- A scenario analysis was conducted to evaluate the operational costs and number of military recruits protected assuming 75% of recruits needed only HBV vaccines (HepB-CpG or HepB-Alum) while 25% needed HBV and HAV vaccines (HepA+HepB vaccine or HepB-CpG and HepA vaccine [GlaxoSmithKline, Research Triangle Park, NC]; **Table 1**).

Table 2. Inputs for 1-Way ±15% Sensitivity Analysis

Factor Changed	Base Case	–15% Number	+15% Number
Cost, $			
Missed training time	153.95	131.00	177.00
Administration	7.79	6.62	8.96
Age group, %, y			
17	3	3.89	2.87
18	33	33.18	33.52
19	21	20.89	21.11
≥20	42	42.05	42.49

Results

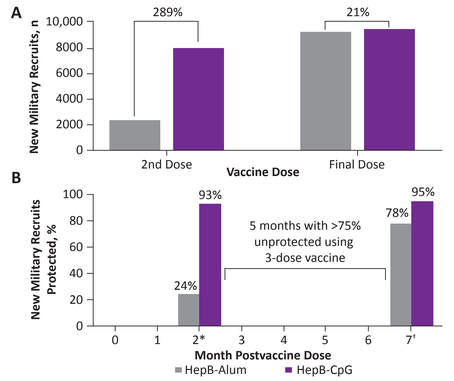
Protection Rates After Vaccination

- The estimated number of recruits protected after receiving each dose of either HepB-CpG or HepB-Alum is shown in **Table 3**.
- HepB-CpG was estimated to provide protection 5 months earlier than HepB-Alum, with 9270 military recruits protected after 2 doses of HepB-CpG, an increase of 289% in protection compared with HepB-Alum (**Figure 2**).
  - On series completion, HepB-CpG was estimated to protect an additional 21% of military recruits compared with HepB-Alum (**Figure 2**). During the additional 5-month interval required for completing the 3-dose HepB-Alum regimen, >75% of military recruits were unprotected from HBV.

Table 3. Estimated Number of Military Recruits Protected With HepB-Alum vs HepB-CpG

	New Military Recruits N=10,000	
	HepB-Alum	HepB-CpG
After 1st dose, n (%)	420 (4.2)	2140 (21.4)
After 2nd dose, n (%)	2384 (23.8)	9270 (92.7)
Increase in recruits protected with HepB-CpG, %	–	289%
After all doses, n	7823 (78.2)	9454 (94.5)
Increase in recruits protected with HepB-CpG, %	–	21%

Figure 2. Estimated (A) Number Protected and (B) Percentage Protected Among Military Recruits After Vaccination With Either HepB-CpG or HepB-Alum

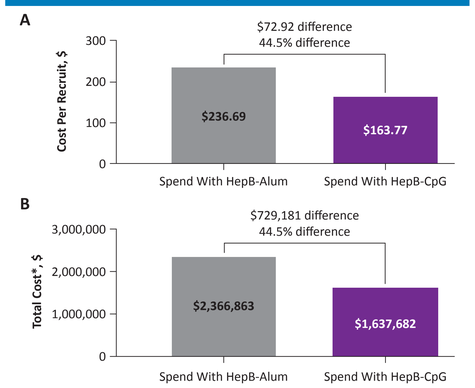


*After 2 doses.
†After final dose.

Operational Costs After Vaccination

- The operational costs of vaccinating military recruits with either HepB-Alum or HepB-CpG are summarized in **Figure 3**.
- Assuming the missed training time and administration costs are $154 and $8, respectively, the cost per recruit was approximately $70 less with HepB-CpG compared with HepB-Alum.
- Assuming 10,000 new military recruits are unprotected against HBV, there would be a 44.5% cost decrease and a total cost saving of $729,181 with HepB-CpG vs a 3-dose vaccine.

Figure 3. Costs (A) Per Recruit and (B) In Total Among Military Recruits After Vaccination With Either HepB-CpG or HepB-Alum

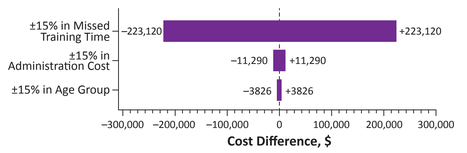


*Based on 10,000 military recruits.

Sensitivity Analyses

- The 1-way sensitivity analysis between HepB-Alum and HepB-CpG determined that the incremental cost was most sensitive to the missed training time cost (**Figure 4**).
- The scenario sensitivity analysis, assuming 75% of recruits needed only HBV vaccines whereas 25% needed HBV and HAV vaccines, showed a 26.8% difference in costs from the base case scenario (base case: $729,181; sensitivity analysis: $534,158; difference=$195,023) and a –24.3% difference in the number of protected recruits (N, base case: 1631; sensitivity analysis: 1235).

Figure 4. One-Way ±15% Sensitivity Analysis on Influential Variables



Conclusions

- **Modeling showed that vaccinating military recruits with HepB-CpG provided earlier and greater protection in more individuals compared with HepB-Alum.**
- **HepB-CpG was also more cost-effective, reducing operational burdens and associated downrange costs compared with HepB-Alum.**

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