

# Post-licensure Safety Study of New-onset Immune-mediated Diseases, Herpes Zoster, and Anaphylaxis in Adult Recipients of HepB-CpG Vaccine Versus HepB-alum Vaccine

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## Background

- HepB-CpG (Heplisav-B®; Dynavax) is a licensed adjuvanted hepatitis B vaccine that requires only 2 doses compared to 3-dose HepB-alum vaccine (Engerix-B, GSK).
- As part of an FDA postmarketing commitment, we compared the incidence of new-onset immune-mediated diseases (IMD), herpes zoster (HZ), and anaphylaxis among HepB-CpG recipients versus HepB-alum recipients at Kaiser Permanente Southern California (KPSC).

## Results

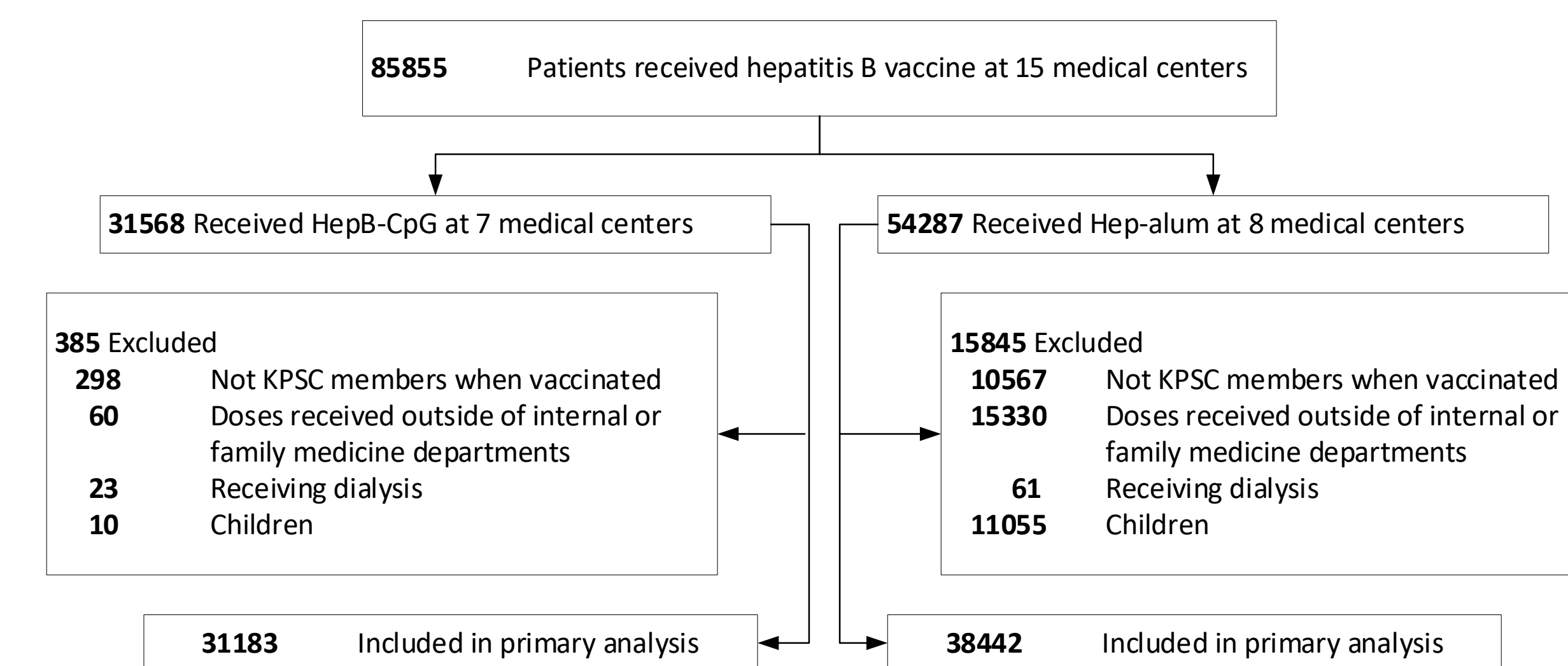
**Table 1: Demographic characteristics of HepB-CpG recipients and HepB-alum recipients**

Characteristic	HepB-CpG recipients	HepB-alum recipients	Standardized difference <sup>a</sup>
<b>Number of recipients</b>	31,183	38,442	
<b>Age (Years) at index dose, n (%)</b>			<b>0.0566</b>
18-29	4240 (13.6)	4754 (12.4)	
30-39	4315 (13.8)	5218 (13.6)	
40-49	7834 (25.1)	9518 (24.8)	
50-59	11354 (36.4)	14141 (36.8)	
60-69	2536 (8.1)	3543 (9.2)	
70-79	740 (2.4)	1052 (2.7)	
80+	164 (0.5)	216 (0.6)	
<b>Sex, n (%)</b>			<b>0.0077</b>
Female	15218 (48.8)	18909 (49.2)	
Male	15965 (51.2)	19533 (50.8)	
<b>Race/Ethnicity<sup>b</sup>, n (%)</b>			<b>0.3226</b>
Asian	4893 (15.7)	3987 (10.4)	
Black	2696 (8.6)	2768 (7.2)	
Hispanic	16423 (52.7)	18125 (47.1)	
White	5126 (16.4)	11188 (29.1)	
Other	1018 (3.3)	1266 (3.3)	
Unknown	1027 (3.3)	1108 (2.9)	
<b>Neighborhood median household income, n (%)</b>			<b>0.0963</b>
<\$40,000	3102 (9.9)	3198 (8.3)	
\$40,000-59,999	8676 (27.8)	9958 (25.9)	
\$60,000-79,999	8425 (27.0)	10184 (26.5)	
\$80,000-99,999	5228 (16.8)	7440 (19.4)	
\$100,000+	5700 (18.3)	7585 (19.7)	
Missing	52 (0.2)	77 (0.2)	

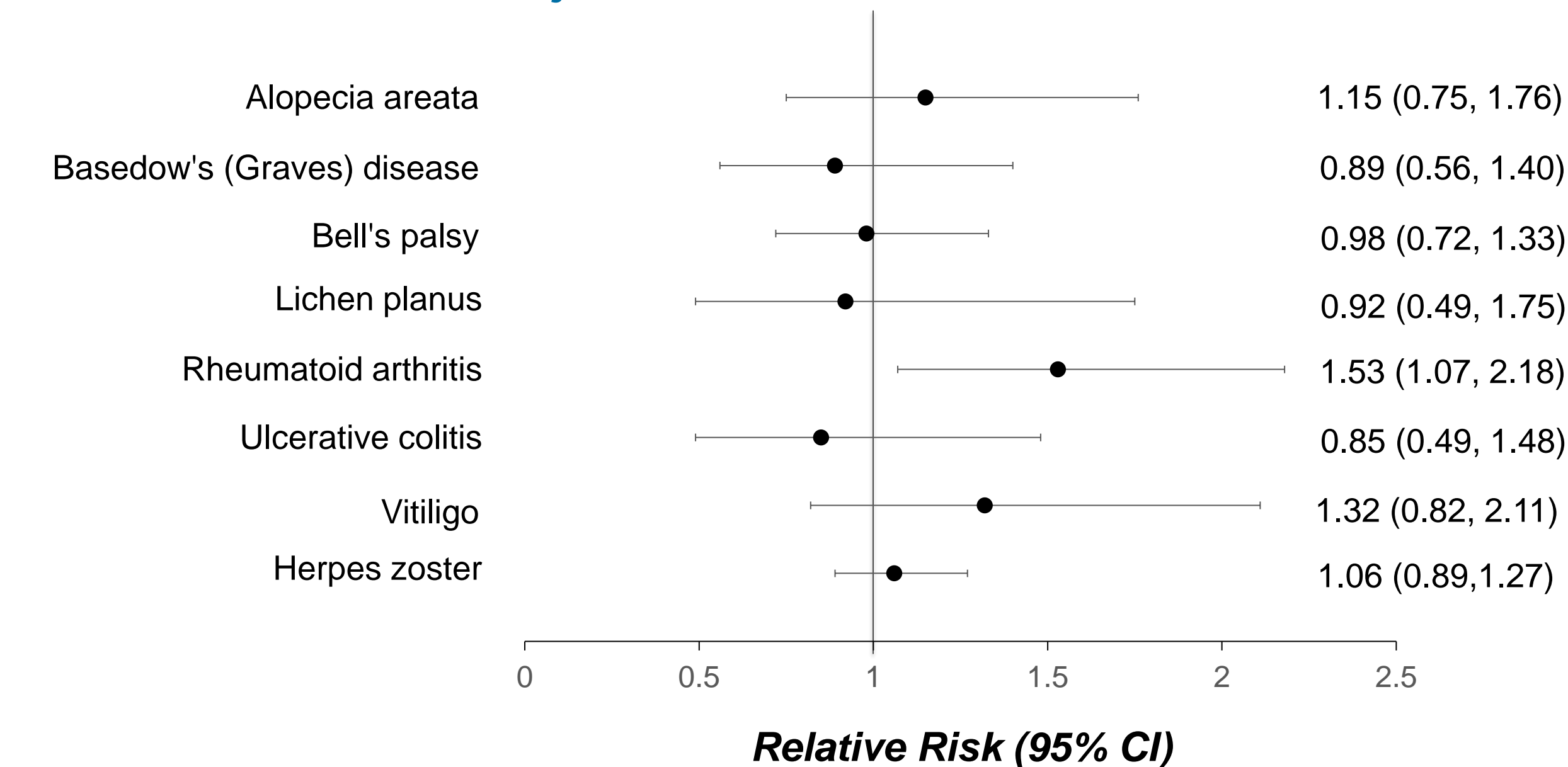
<sup>a</sup> Standardized difference = difference of means divided by the standard deviation of the difference before IPTW.

<sup>b</sup> Hispanic includes Hispanic of all races; other race groups only include non-Hispanic.

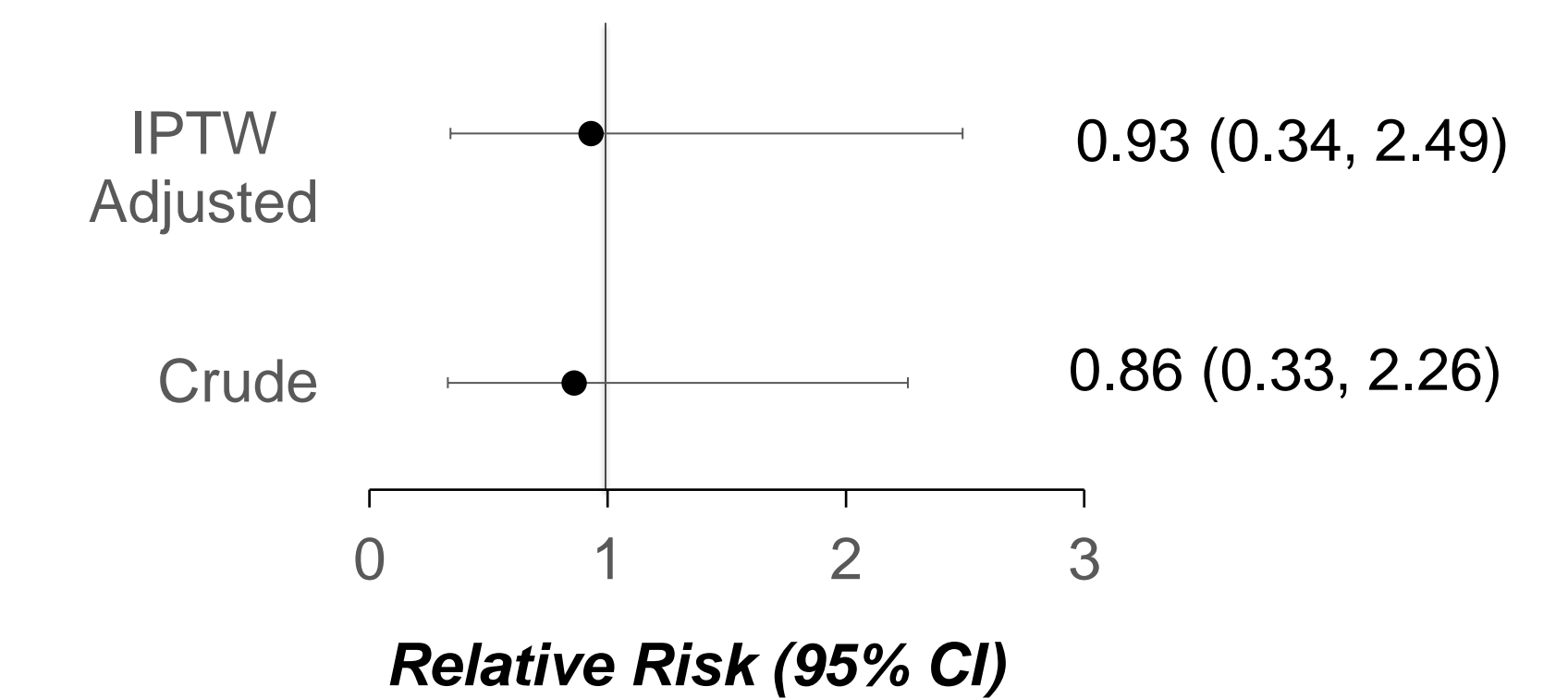
**Figure 1: Cohort formation, inclusion and exclusion**



**Figure 2: Immune-mediated diseases, HZ, and anaphylaxis IPTW-adjusted relative risk estimates**



**Figure 3: Relative risk of chart-confirmed rheumatoid arthritis**



## Discussion

- Among all IMD occurring frequently enough for formal comparison, only rheumatoid arthritis had a lower 95% CI greater than 1
- The risk of chart-confirmed new-onset RA among HepB-CpG recipients was similar to that among HepB-alum recipients
- The risk of HZ was not increased following HepB-CpG compared to HepB-alum
- No cases of anaphylaxis following HepB-CpG were observed, suggesting a low risk of occurrence
- Continued monitoring of immune-mediated events after vaccination is important, particularly among vaccines containing novel adjuvants

**Acknowledgements:** Special thanks to the KPSC study team and Dynavax Technologies.

## Conclusion

**No safety concerns were observed for HepB-CpG compared to HepB-alum for selected immune-mediated diseases, HZ, or anaphylaxis in this observational study of over 69,000 hepatitis B vaccine recipients.**

## Methods

- Cohort:** Adults not on dialysis who received  $\geq 1$  dose of hepatitis B vaccine in family or internal medicine departments from 8/7/2018 to 10/31/2019
- Exposure:** HepB-CpG administered routinely in 7 of 15 KPSC medical centers; HepB-alum was administered at the other 8 medical centers
- Follow-up time:** 13 months after receipt of the first hepatitis B vaccine dose during accrual period
- Outcomes:** New-onset IMD, HZ, and anaphylaxis identified using diagnosis codes
- Analysis:** Incidence rates were compared using Poisson regression with inverse probability of treatment weighting (IPTW) when there was 80% power to detect a relative risk (RR) of 5 for anaphylaxis and a RR of 3 for all other outcomes