

Protection and Antibody Levels 35 Years after Primary Series with Hepatitis B Vaccine and Response to a Booster Dose



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Disclaimer

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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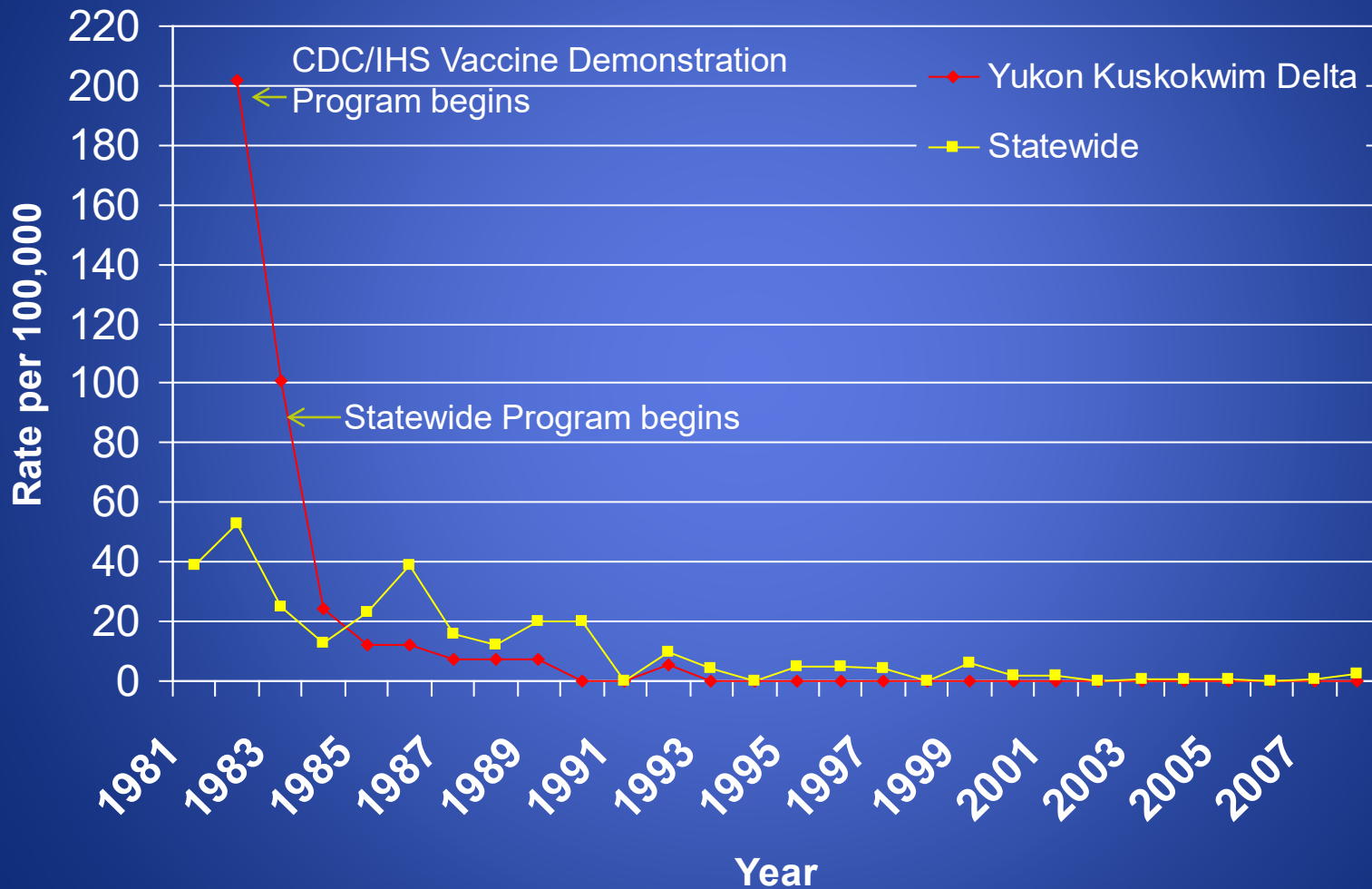
Collaboration between

- Arctic Investigations Program, CDC
- Division of Viral Hepatitis, CDC
- The Alaska Native Tribal Health Consortium (ANTHC)
- The Yukon Kuskokwim Health Corporation (YKHC)
- The Norton Sound Health Corporation (NSHC)

Hepatitis B in Alaska Natives

- 1970's
 - Highest rates of hepatitis B in the United States
 - Among the highest rates in the world
 - High rates of liver cancer and cirrhosis

Incidence of Symptomatic Hepatitis B in Alaska Native People, 1981- 2008



Long-term immunogenicity of Hepatitis B vaccination in Alaska

- Hepatitis B vaccine first used in Alaska in 1981
 - plasma-derived hepatitis B (HB) vaccine
- Studies of immunogenicity began at that time



Long-Term Immunogenicity & Efficacy Children & Adults

- Alaska HBV Vaccine Demonstration Project:
- 1530 children and adults immunized in 1981
 - Followed yearly for 11 years, at years 15, 22 and 30
 - No booster given at 1-11 and 15 years
 - % with anti-HBs levels ≥ 10 mIU/ml
 - 5 years: 81% (JAMA 1989)
 - 7 years: 74% (Arch Int Med 1991)
 - 15 years: 66% (Ann Int Med 2005)
 - 22 years: 60% (JID 2009)
 - 30 years: 51% (JID 2016)

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Objectives

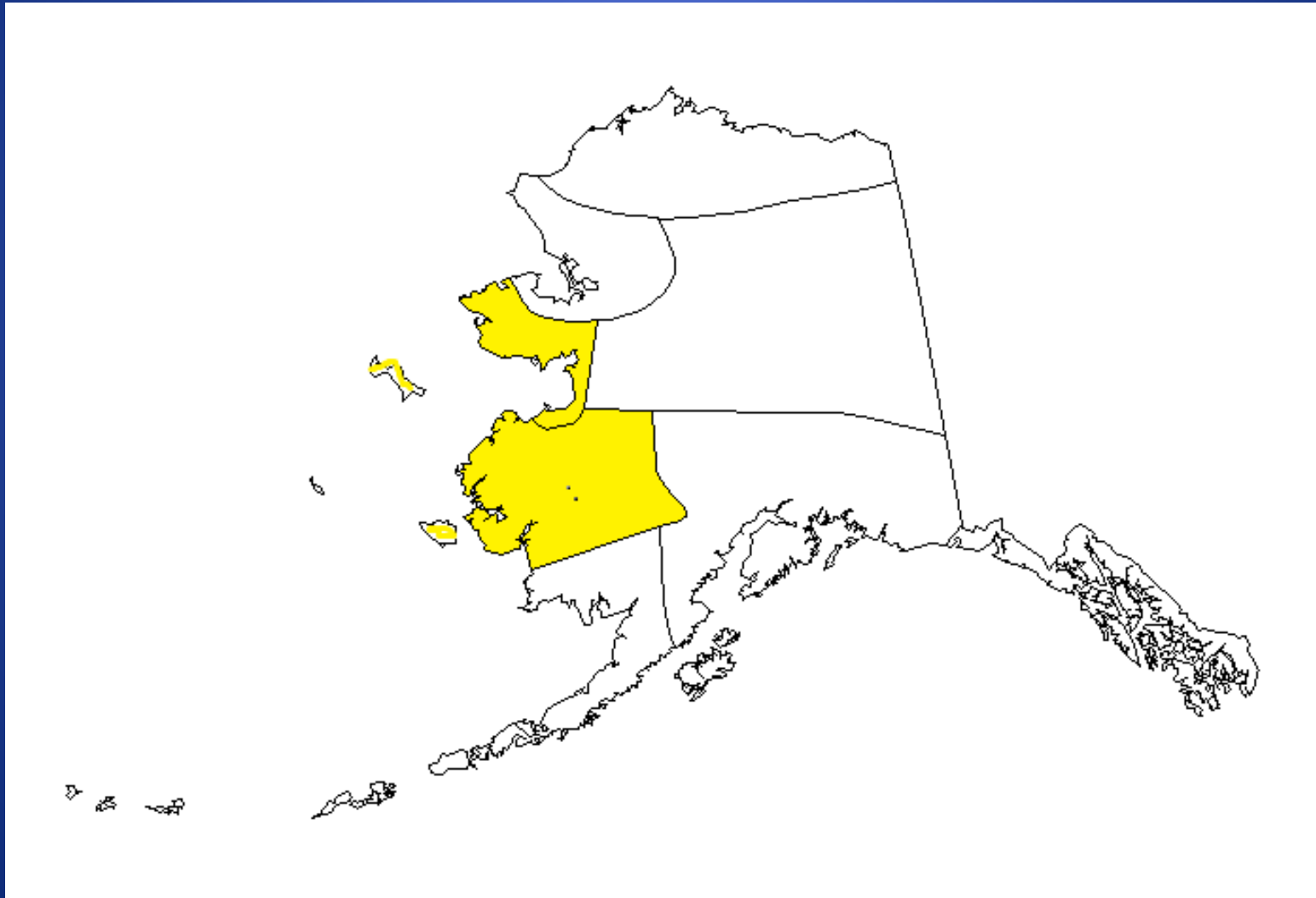
- Determine proportion of persons with anti-HBs \geq 10 mIU/mL 35 years after HB vaccine series
- Evaluate response to a booster dose of HB vaccine among those with anti-HBs $<$ 10mIU/ml
- Compare characteristics of persons with and without protective antibody levels

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Methods

- Study Design
 - Serologic survey
 - HB vaccine booster dose
- Study Setting
 - All 16 of the original villages in the YK Delta and Norton Sound
 - 3 visits X 16 villages = 48 visits
 - Anchorage for those who have moved since the start of the study

Map of Alaska Participating Regions



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Methods

- Study Population
 - All village residents (6 months or older) who received three doses of plasma-derived HB vaccine with a documented response of ≥ 10 mIU/mL or 10 SRU in the original study in 1981
 - Excluded persons who received a booster dose of HB vaccine anytime over the past 35 years

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Methods

- Visit 1 - initial blood draw, assess anti HBs levels
- Visit 2 - booster to persons anti-HBs <10 MIU/mL
- Visit 3 - post booster draw

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Preliminary Results

- Two Groups
 - Group 1: Persons who did not participate in the 22- or 30-year study
 - Group 2: Persons who participated in the 22- or 30-year study, but were not boosted

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Preliminary Results

- Two Groups
 - Group 1: Persons who did not participate in the 22- or 30-year study **Naïve Group**
 - Group 2: Persons who participated in the 22 or 30-year study, but were not boosted **Group biased toward higher antibody response**

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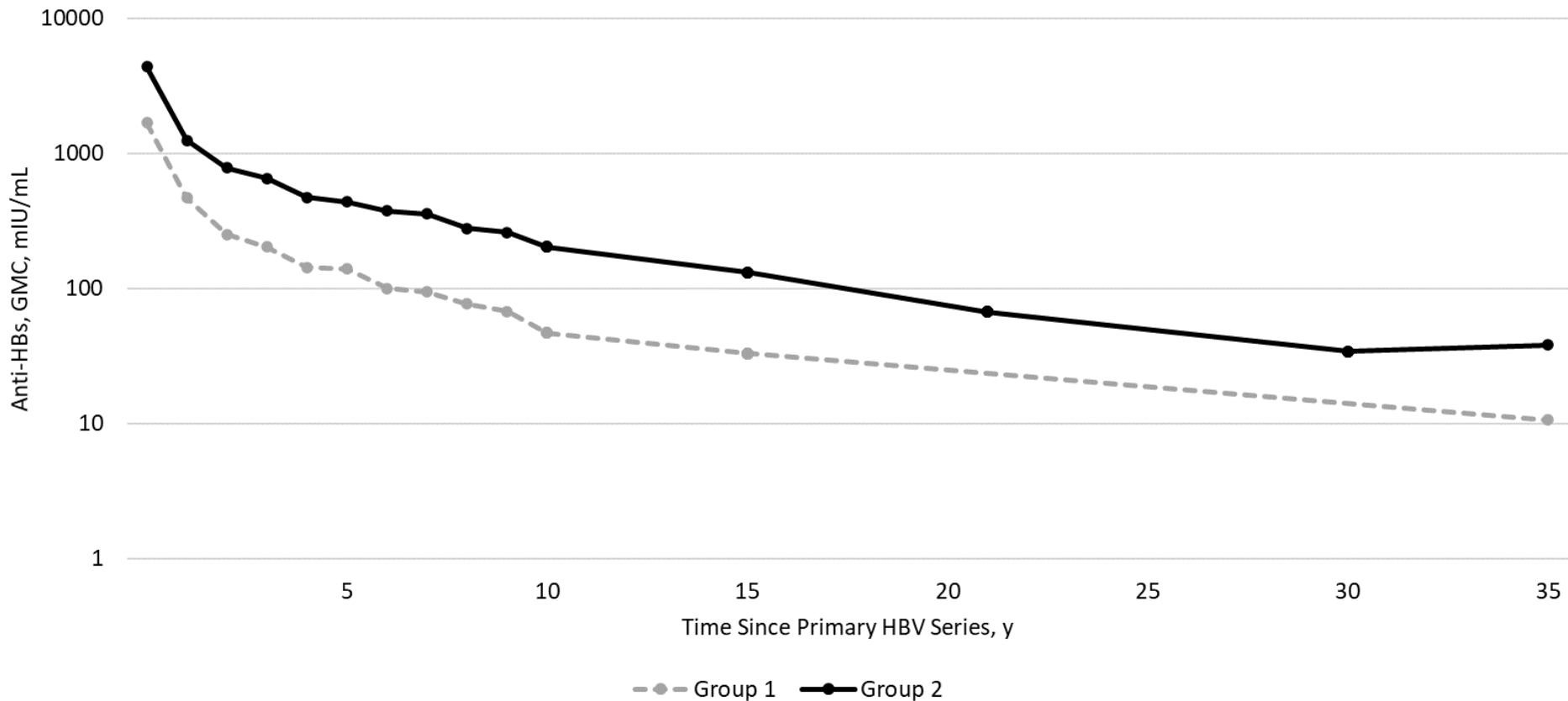
Visit 1

- Group 1: Naïve Group* (N=112)
 - 53 (47.3%) had anti-HBs \geq 10 mIU/ml

* Did not participate in the previous 22 or 30-year studies

Antibody Decline

Levels of antibody to hepatitis B surface antigen (anti-HBs) decline over 35 years among 2 groups in Alaska.



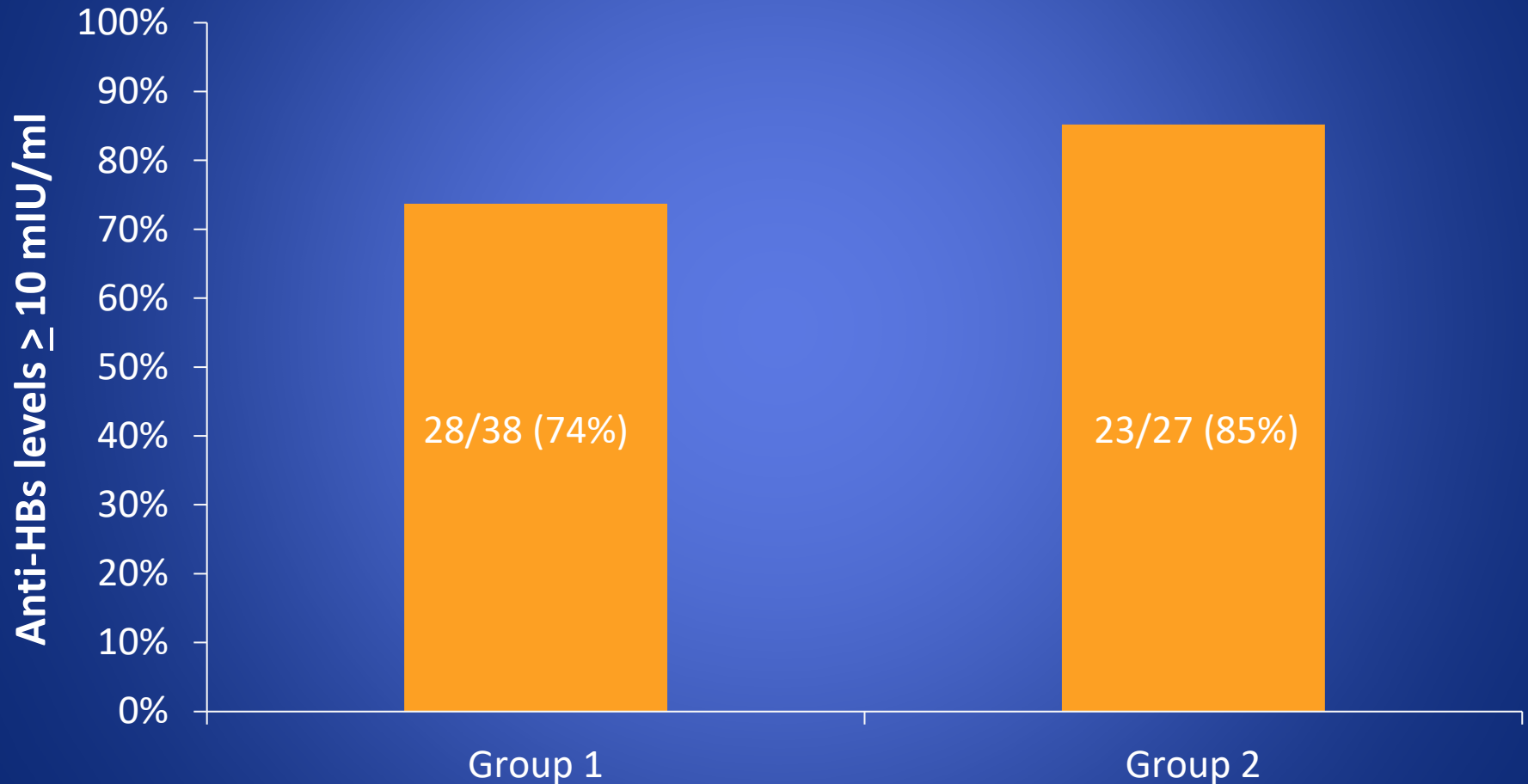
Group 1 persons had not participated in the 22 nor 30-year follow-up study.
Group 2 persons had participated in the 22 or 30-year follow-up participated but were not given an HBV booster dose.

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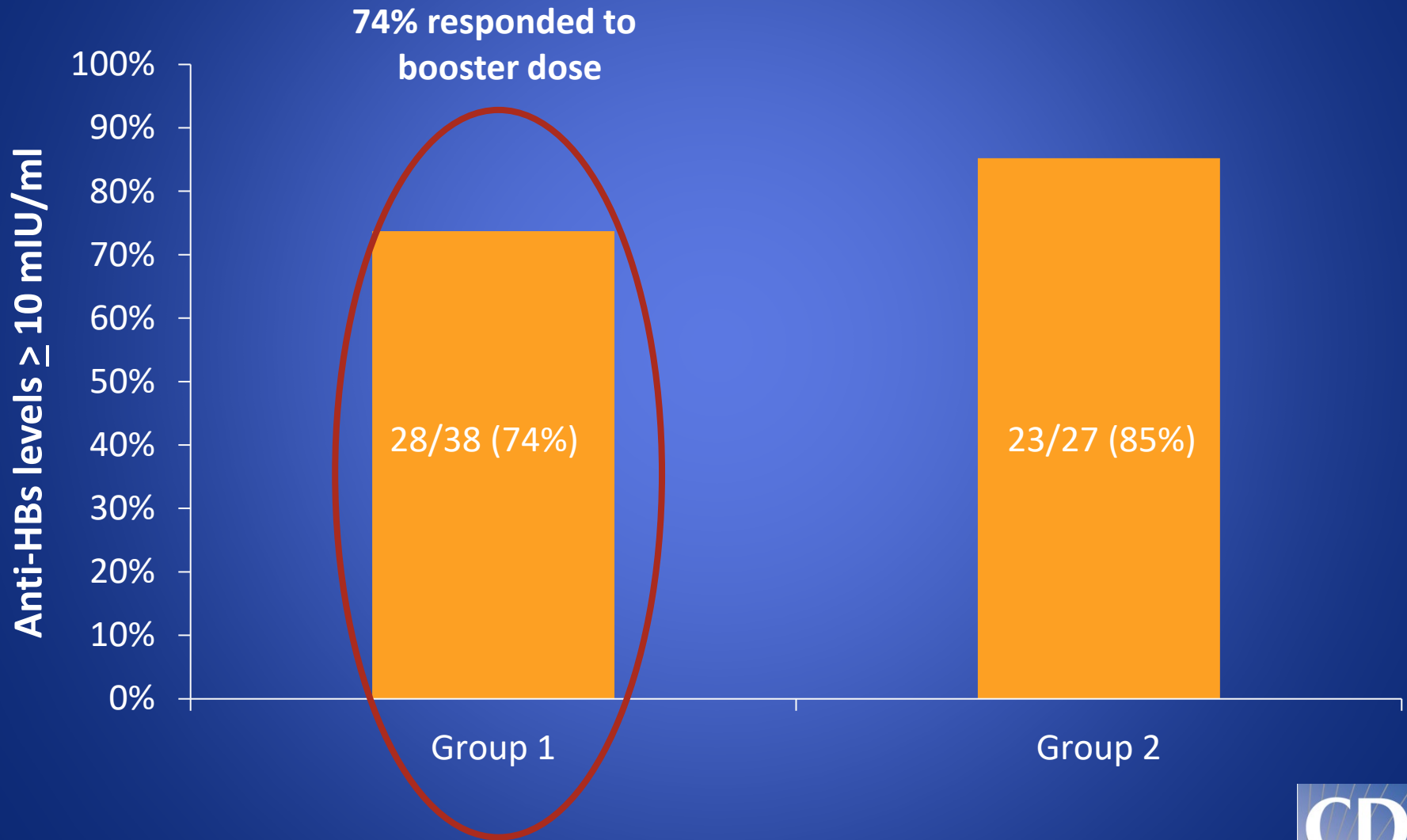
Visit 3 (Booster follow-up)

- Booster doses were given only to persons (Groups 1 and 2) who had anti-HBs < 10 mIU/ml

Proportion who Responded to booster dose with anti-HBs ≥ 10 mIU/ml at 35 years



Proportion who Responded to booster dose with anti-HBs ≥ 10 mIU/ml at 35 years



Anti-HBs level 35 years after Hepatitis B Vaccination, by Post-vaccination Antibody level after Primary Series Alaska (Group 1)

	Anti-HBs after Primary Series	N	> 10 MIU at 35 years	P-value
Anti-HBs after Primary Series	10 - 199 mIU/ml	17	6% (1)	<0.0001
	200 - 499 mIU/ml	16	13% (2)	
	500 – 999 mIU/ml	10	20% (2)	
	≥1000 mIU/ml	69	70% (48)	

- No association between protective antibody level and:
Age, gender, BMI, Diabetes, or comorbidities associated with poor immune response

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Results

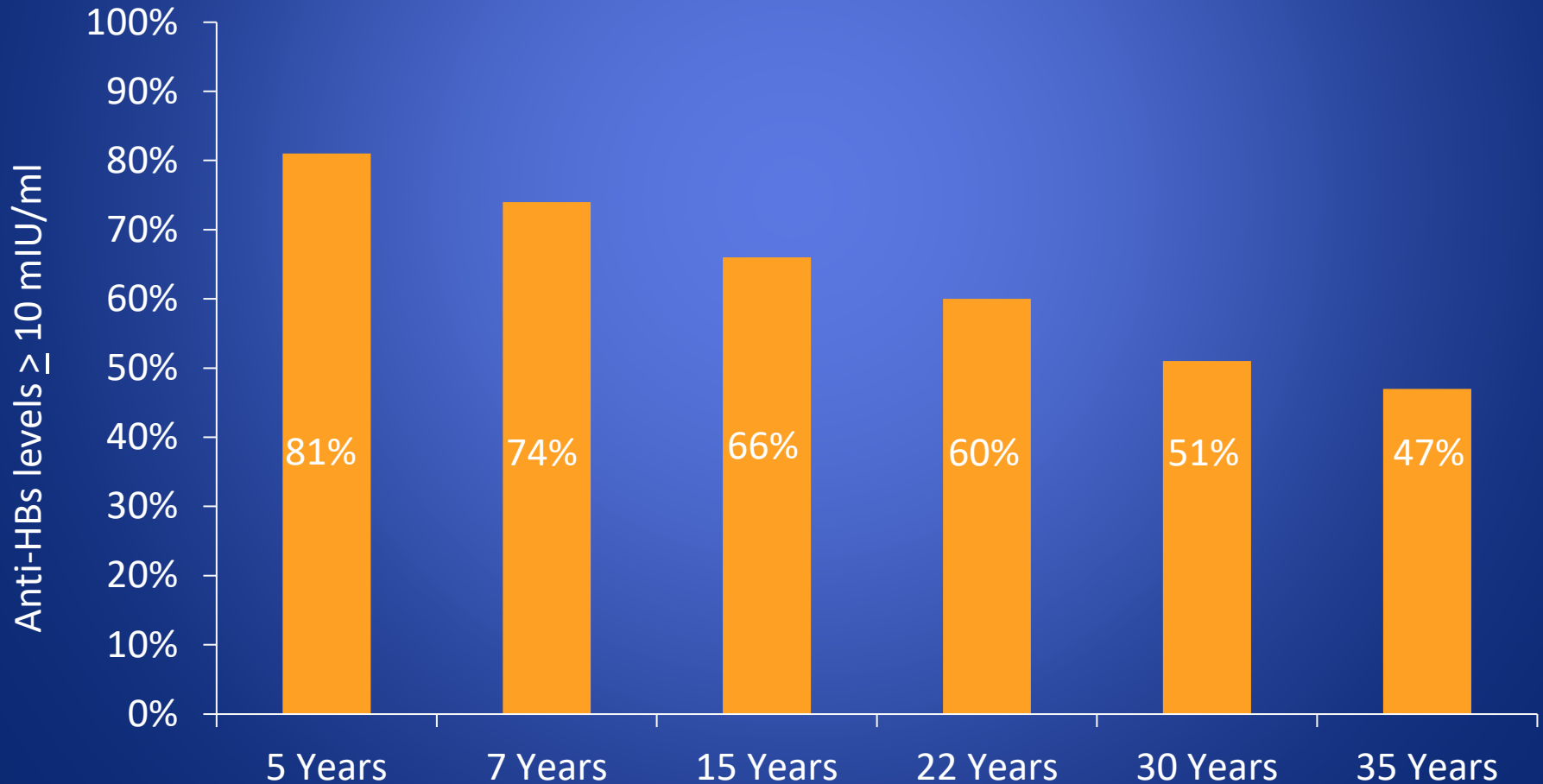
- 8 persons were anti-HBc positive
 - 4 not previously identified
 - All HBV DNA-negative
 - In the 35-year period, 27 persons had detectable anti-HBc breakthrough infection
 - None had clinical hepatitis or developed chronic HBV

Limitations

- Loss to follow-up over 35 years
- Participants in our study received the primary hepatitis B vaccination series with the plasma-derived vaccine, which is no longer used in the United States

Vax Demo 35 Summary

- Antibodies have continued to decline over the past 35 years



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Summary I

- 47% had anti-HBs level ≥ 10 mIU/ml at 35 years
- 74% boosted to ≥ 10 mIU/mL
- Overall, **86%** had evidence of immunity: either boosted or had anti-HBs ≥ 10 mIU/mL at 35 years
- Protection by primary immunization with plasma-derived Hep B vaccine lasts at least 35 years
 - Booster doses not needed

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Summary II

- Our study findings likely apply to populations currently using the recombinant vaccine
 - ACIP closely follows data from the Alaska cohort
 - No recommendation for booster at this time
- Higher anti-HBs after primary series was associated with protective antibody levels at 35 years

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