

Long-term Protection from Hepatitis A Vaccine in Infants and Children: 3 Projects

Liver Disease and Hepatitis Program
Alaska Native Tribal Health
Consortium



Project A

Long-Term Immunogenicity and Protection from Hepatitis A Vaccine in Children: 3-dose Schedule

- Hepatitis A pre-licensure trial in children conducted in Alaska
 - This cohort is scheduled to be followed for 25 years post vaccination
 - 17 year data is now available

Project A: 3-dose study

- Children aged 3-6 years received 3 doses of 360 ELISA Units inactivated hepatitis A virus vaccine (HAVRIX™) in
- Randomized to 3 vaccination schedules
 - 0, 1, 2 months (A)
 - 0, 1, 6 months (B)
 - 0, 1, 12 months (C)

Project A: 3-dose study

17 Year Results: Persistence of Anti-HAV

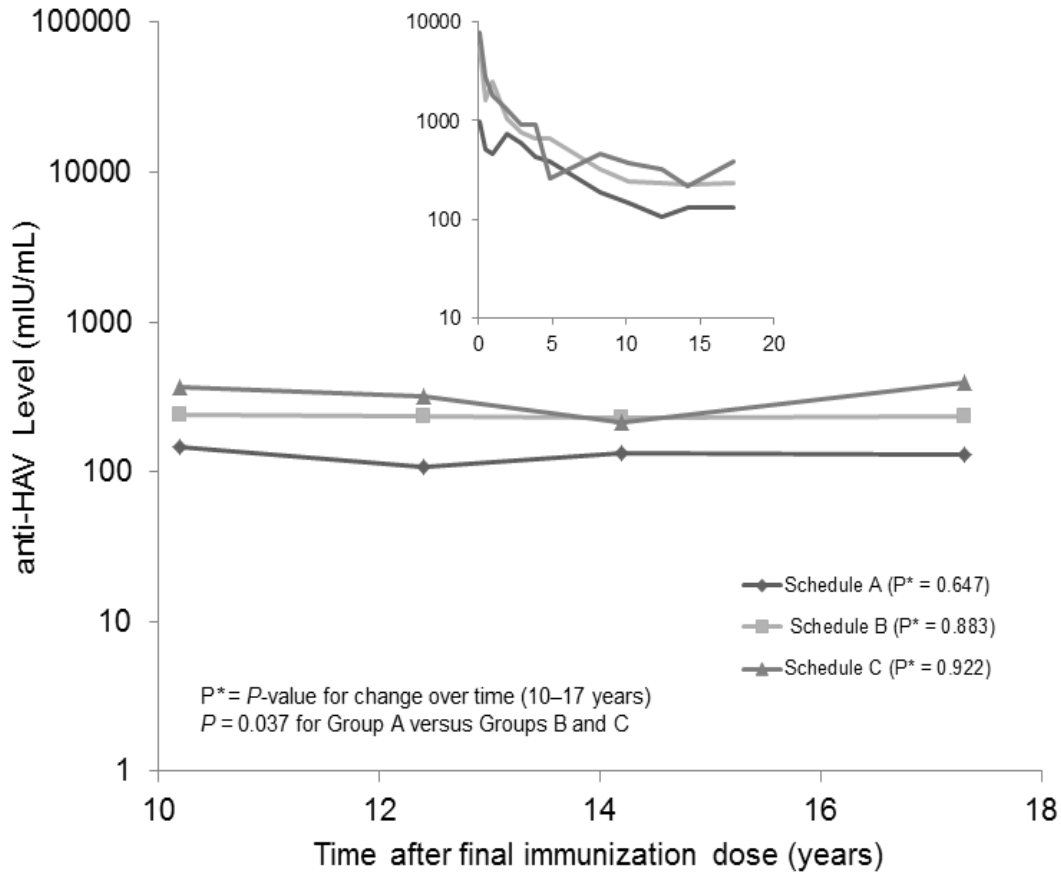
- Participants now ages 20-26 years
- Proportions with anti-HAV levels ≥ 20 mIU/ml
 - 87% of 0-1-2 schedule (similar to 12 (81%) and 14 (86%) year f/u)
 - 100% of 0-1-6 schedule
 - 95% of 0-1-12 schedule

Project A: 3-dose study

Anti-HAV GMC at 17 Years

- No significant decrease in GMC at 17 years in cohort compared with 12 and 14 years
- Anti-HAV GMC were significantly lower in 0, 1, 2 group than in the others ($P = 0.028$)
 - 0, 1, 2 GNC 129mIU/mL
 - 0, 1, 6 GNC 235mIU/mL
 - 0, 1, 12 GNC 391mIU/mL

Anti-HAV Levels over Time in Children who Received Hepatitis A 3 Dose Series between ages 3-6 years



Project A: 3-dose study

Summary

- High proportion of cohort has protective immunity at 17 years
- Anti-HAV levels declined initially but flattened out between years 10 and 17
- Immunogenicity may last longer than 26-32 years suggested by model developed at 15 years
- Reemphasizes importance of following this cohort as long as possible
 - 20 year follow up ongoing
 - Study approved for at least 25 years

Project B

Long-term Hepatitis A 2-dose Vaccine Study in Infants/Toddlers: Results of 10 year follow-up

- Three groups of infants randomized to receive two doses of hepatitis A vaccine* at the age of:
 - 6-12 months (Group 1)
 - 12-18 months (Group 2)
 - 15-21 months (Group 3)
- All groups stratified by maternal anti-HAV status (positive or negative)
- One small subgroup of mothers were immunized with hepatitis A vaccine prior to pregnancy
- Blood was drawn at 1 and 6 months, and at 3, 5, 7 and 10 years after second dose (also will be drawn at 12 and 15 years)

* SmithKline Beecham inactivated hepatitis A vaccine, 720 EL.U formulation, with 0.25 mg alum in 0.5 ml

Project B: 2-dose Infant/Toddler study

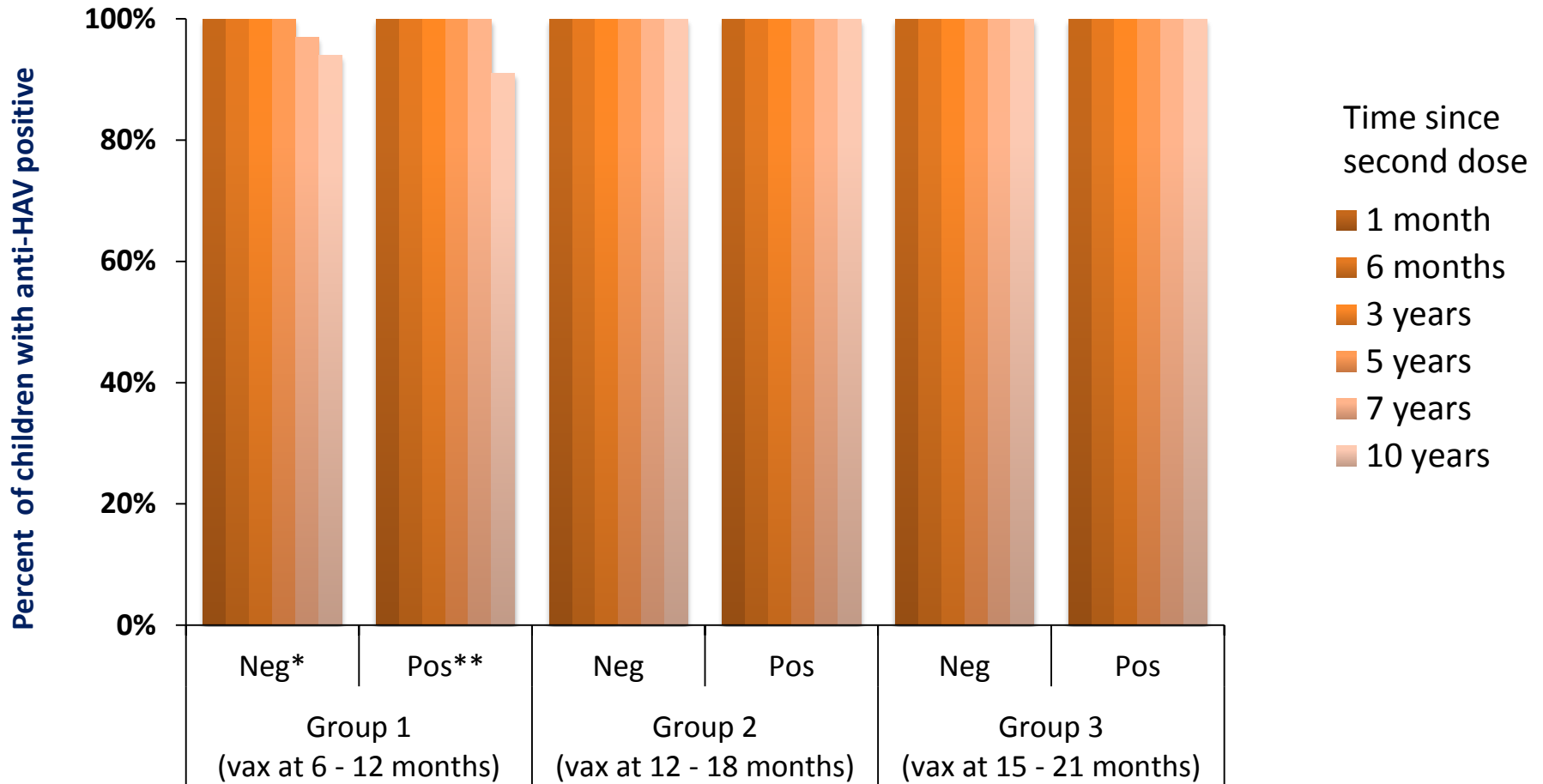
Anti-HAV GMC at 10 Years

		10 year f/u		
Ages at Vx	Maternal HAV	% anti-HAV+	GMC	95% CI
6-12 months	Negative	94%	45	33-65
6-12 months	Positive	91%	33	21-52
12-18 months	Negative	100%	97	61-155
12-18 months	Positive	100%	82	32-207
15-21 months	Negative	100%	100	66-151
15-21 months	Positive	100%	58	39-88

Project B: 2-dose Infant/Toddler study

Proportion of children anti-HAV-positive

by group, maternal anti-HAV status and year of follow up, 1999-2009



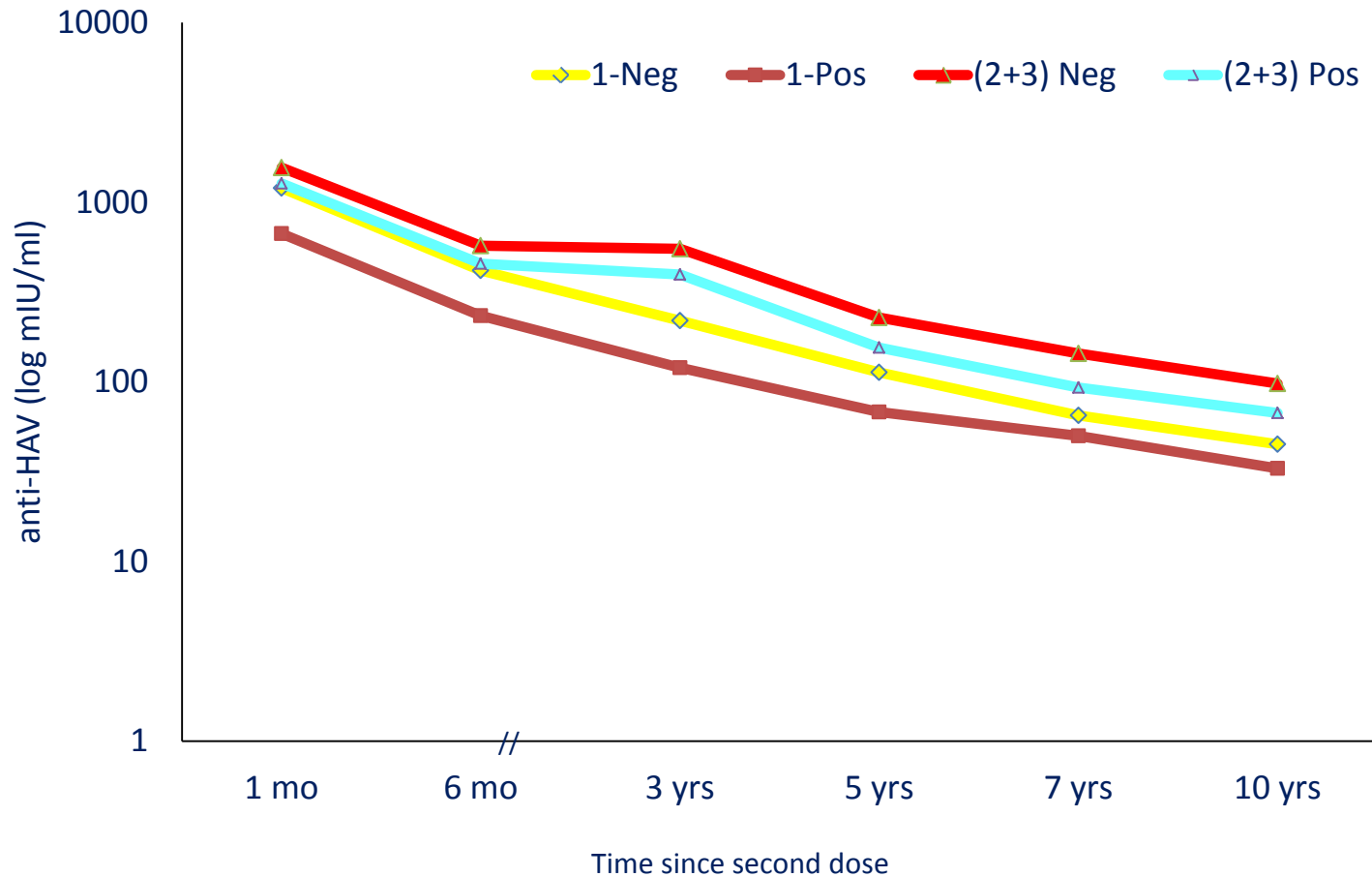
* Infants born to anti-HAV negative mothers

** Infants born to anti-HAV positive mothers

Vax = vaccinated

Project B: 2-dose Infant/Toddler study

GMC* of anti-HAV by Group and Maternal Anti-HAV Status, 1999-2009



Vaccination: Group-1 = 6-12 mos; Group-2 = 12-18 mos; Group-3 = 15-21 mos

* Geometric mean concentration; Neg = children born to anti-HAV negative mothers; Pos = children born to anti-HAV positive mothers; (2+3) = Group 2 and 3 combined

Project B: 2-dose Infant/Toddler study

Summary of 10 year Follow-up

- 100% of children vaccinated at 12 and 15 months of age (Group 2 and 3) anti-HAV-positive at 10 years
- 91-94% of children vaccinated at 6 months of age (Group 1) anti-HAV-positive at 10 years
- Using repeated measures linear model we estimate anti-HAV levels will last for 15-17 years

Project C

Long-term f/u of Children who Received Current 2-dose Hepatitis A Vaccination Schedule

- Objectives:
 - Determine long-term immunogenicity of current licensed 2-dose regimen of hepatitis A vaccine when given in childhood among a convenient sample of young adults
 - Compare long-term immunogenicity of the 2-dose regimen to the long-term immunogenicity in children who received pre-licensure 3-dose schedule and are participating in a long-term study of hepatitis A vaccine immunogenicity (Project A)

Project C

2-dose study

- Inclusion criteria:
 - Current age: 10-20 years
 - Participant in long-term Hep B vaccine study
 - Received in childhood two doses of 720 EU GSK HAV vaccine given ≥ 5 months apart
 - Initial dose ≥ 5 years ago
- 101 participants were enrolled

Project C: 2-dose study

Anti-hepatitis A GMC (95% CI) by age at first dose and duration of follow-up

Follow-up since 2 nd dose	Age at First Dose (n=101)			P-value (comparing 3 age groups)
	1-2 years	3-6 years	7+ years	
< 7.5 yrs	-	-	148	
≥ 7.5 - < 9 yrs	48	115 (12, 1114)	125 (11, 1358)	0.688
≥ 9 - < 11 yrs	144 (78, 263)	160 (94, 271)	201 (117, 343)	0.634
≥ 11 – 13 yrs	98 (66, 147)	298 (51, 1749)	211 (112, 397)	0.054
≥ 13 – 15 yrs	21 (6, 77)	80 (40, 159)	81	0.081
≥ 15 yrs	-	43	-	
Overall	88 (63-124)	155 (86,277)	196 (141, 271)	0.007

Comparison 3-dose (Project A) vs 2-dose (Project C)

Includes only those vaccinated at age 3-6 years

Anti-hepatitis A GMC (n) (95% CI) by duration of follow-up

Follow-up since 2 nd dose	Vaccine schedule		P-value
	3-dose group	2-dose group	
≥ 7.5 - < 9 yrs	293 (66) (214, 400)	115 (3) (12, 1114)	0.212
≥ 9 - < 11 yrs	232 (62) (165, 327)	160 (7) (94, 271)	0.467
≥ 11 – 13 yrs	201 (49) (135, 300)	298 (8) (51, 1749)	0.496
≥ 13 – 15 yrs	183 (56) (128, 261)	80 (5) (40, 159)	0.175
≥ 15 yrs	219 (59) (142, 339)	43 (1)	-

Conclusions

- 3-dose study indicated persistence of anti-HAV levels for 17 years;
 - May persist longer than 26-32 years based on 15 yr analysis
 - Represents longest follow up period for a vaccinated cohort
- 2-dose infant/toddler study indicated persistence anti-HAV levels at 10 years
- Comparison 3-dose to 2-dose shows no significant difference in anti-HAV levels out to 15 years post-vaccination



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Alaska Native Tribal Health Consortium

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