Are Booster Doses of Hepatitis B Vaccine Necessary?

Current CDC Recommendations And Gaps in Knowledge

Division of Viral Hepatitis
Centers for Disease Control and Prevention, USA

Current United States Recommendations for Hepatitis B Vaccination

- Selective vaccination of children, adolescents, and adults at increased risk of infection (1982)
- Prevention of perinatal transmission through routine screening of pregnant women (1984)
- Routine vaccination of infants beginning at birth (1991)
- Routine vaccination of adolescents (11-12 yrs) (1995)
- Catch-up vaccination of unvaccinated children and adolescents (through 18 yrs) (1999)

Recommendations endorsed by the U.S. Advisory Committee on Immunization Practices (ACIP), American Academy of Pediatrics (AAP), American Academy of Family Physicians (AAFP), and American Medical Association (AMA).

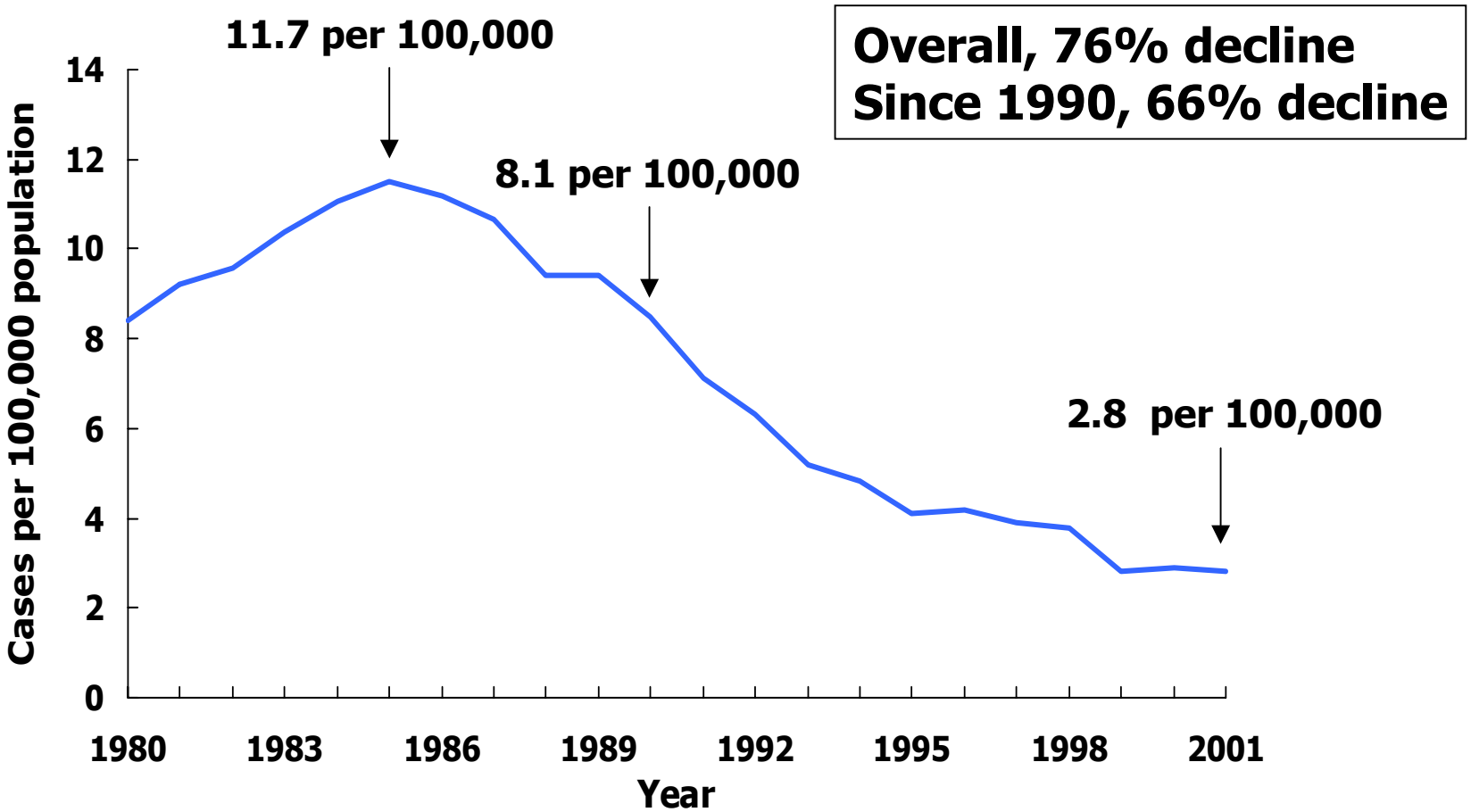
CDC

High-Risk Groups

- Injecting drug users
- Sexually active homosexual & bisexual men
- Heterosexual men and women with >1 sex partner
- Persons recently tx for another STD
- Sex contacts of persons with chronic hep B
- Household contacts of persons with chronic HBV infection
- Persons with occupational exposure (e.g., HCW's)
- Recipients of certain blood products (clotting factors)
- Clients and staff of institutions for developmentally disabled
- Chronic hemodialysis patients
- International travelers
- Inmates of long-term correctional facilities
- Adoptees from high HBV endemic countries

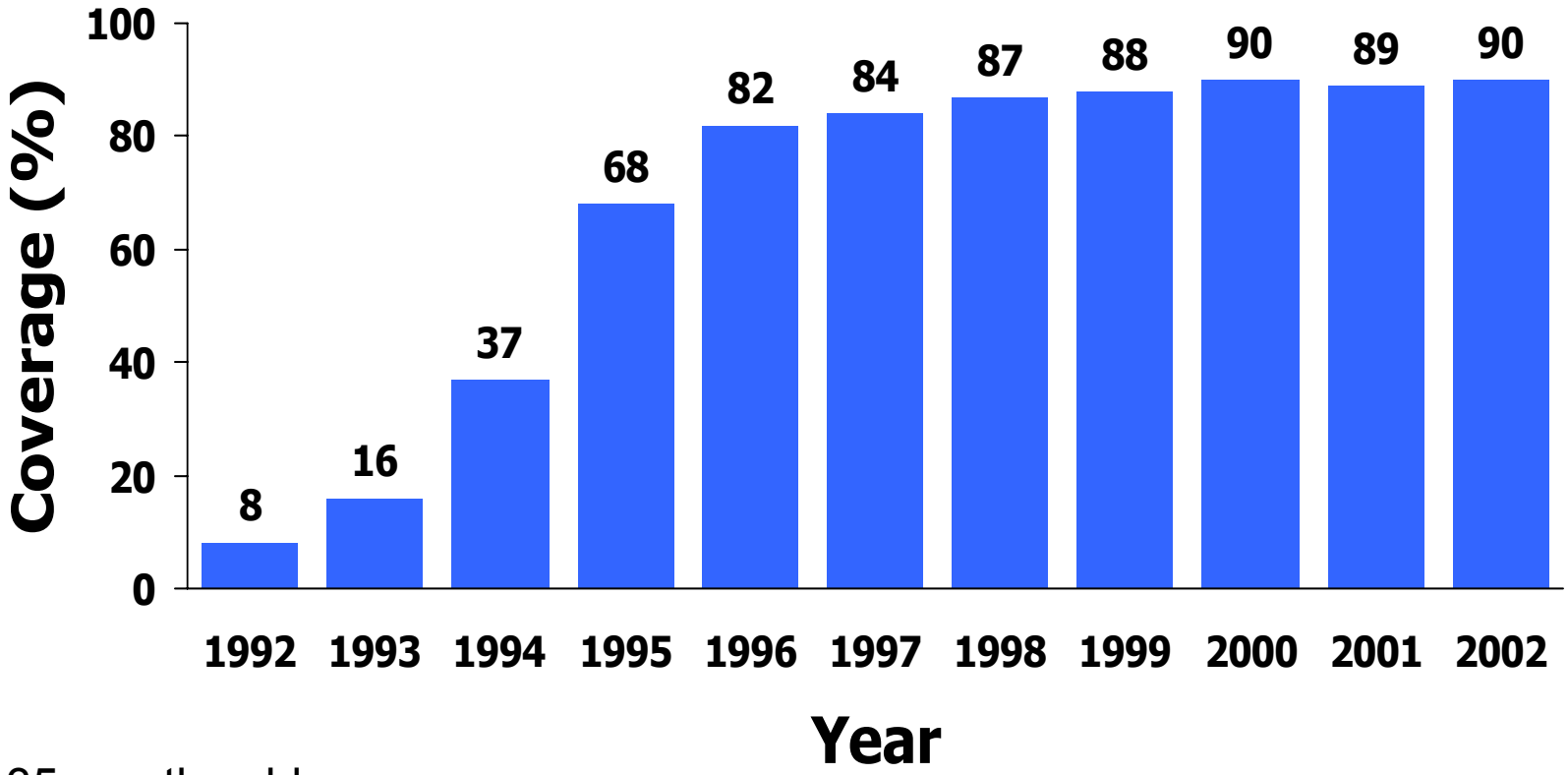
Hepatitis B Vaccination in the United States: Coverage and Impact

Incidence of Acute Hepatitis B, United States, 1980-2001



Source: CDC National Notifiable Diseases Surveillance System

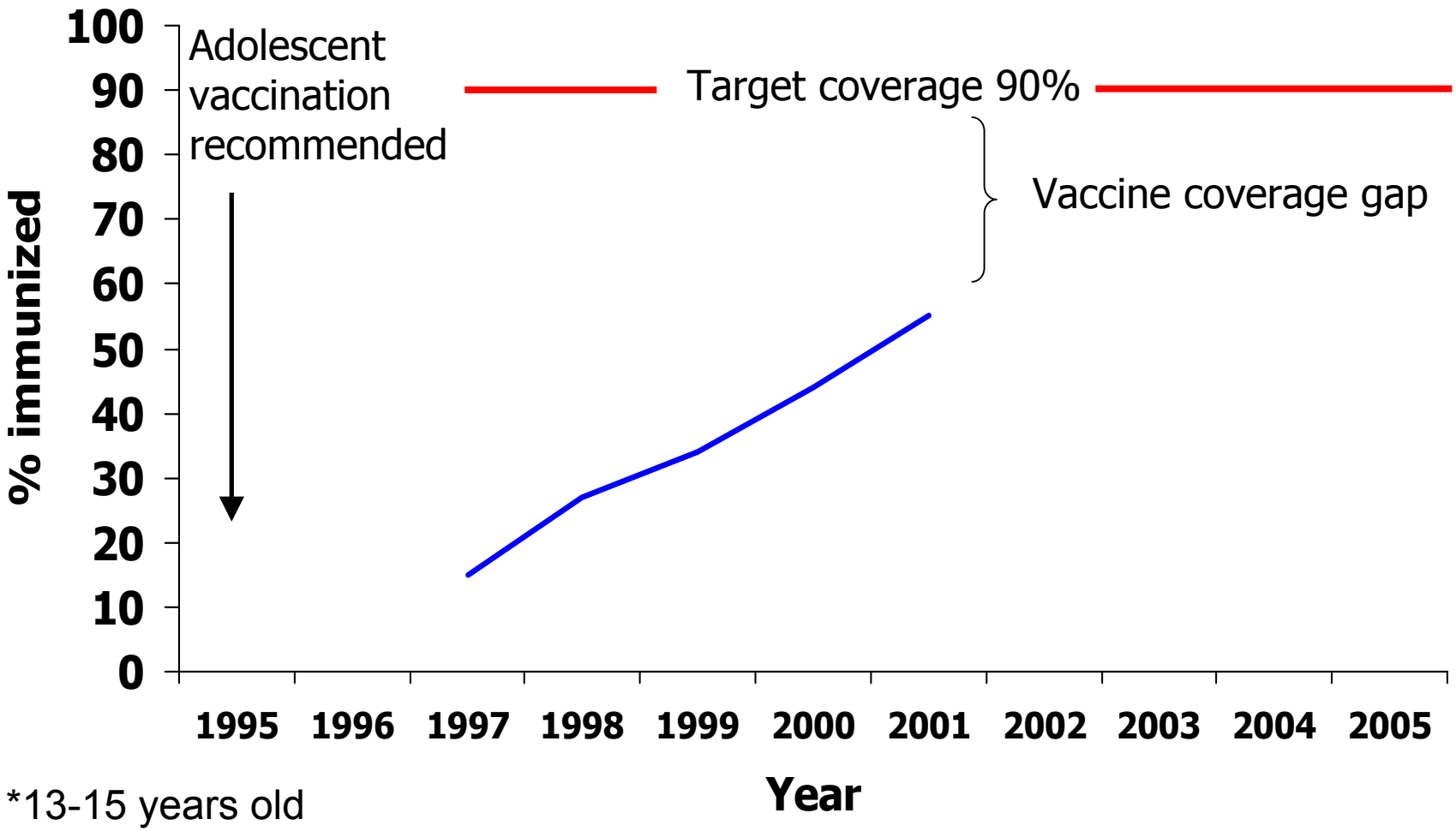
Hepatitis B Vaccination Coverage Among Children*, United States, 1990-2002



* 19-35 months old

Source: National Immunization Survey, CDC

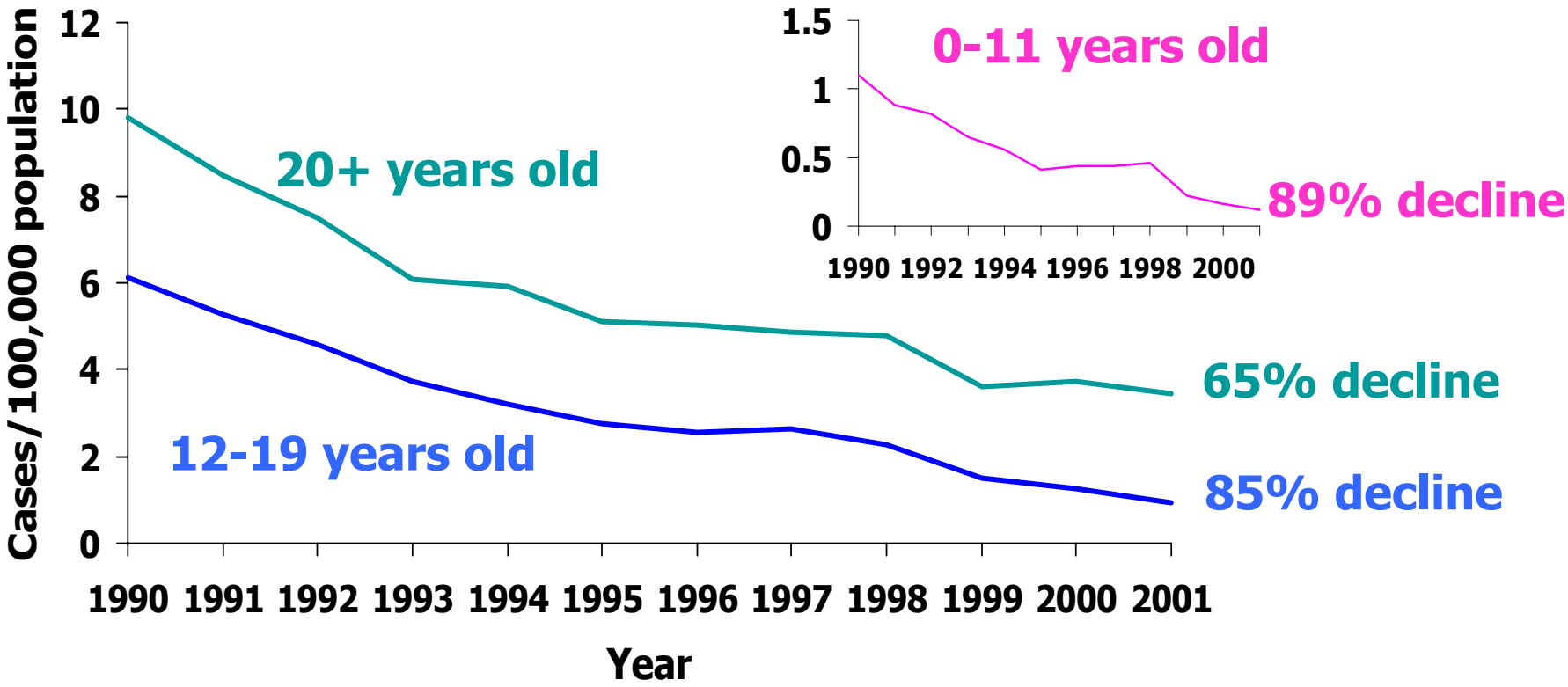
Hepatitis B Vaccination Coverage Among Adolescents*, United States



*13-15 years old

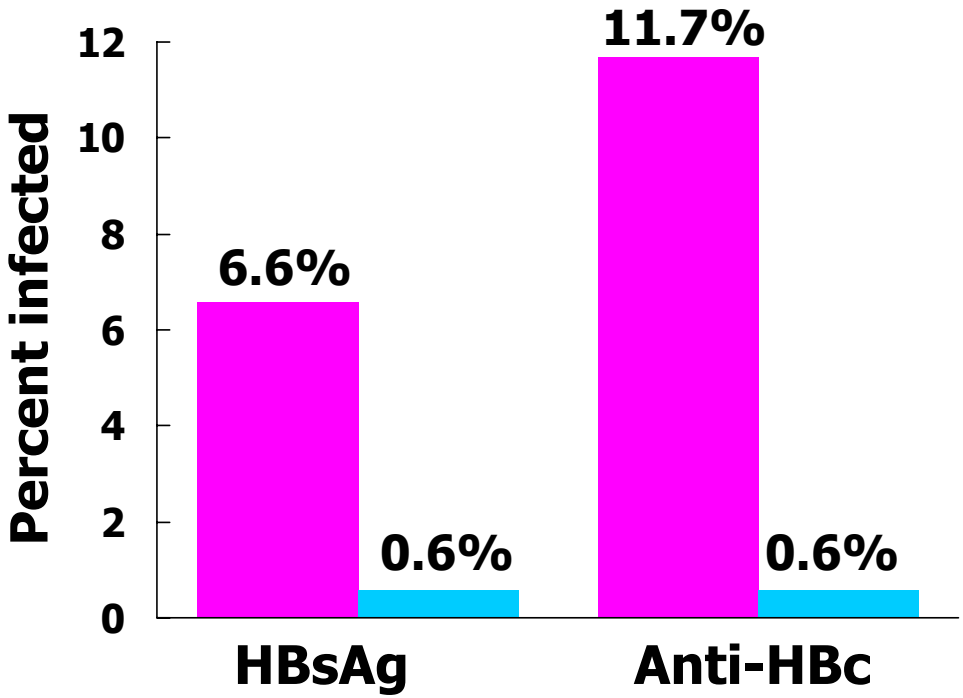
Source: National Health Interview Survey, CDC

Incidence of Acute Hepatitis B by Age, United States, 1990-2001



Source: National Notifiable Diseases Surveillance System, CDC

HBV Prevalence Among U.S. Born Children of Asian Immigrants, Atlanta, 1986 and 2002

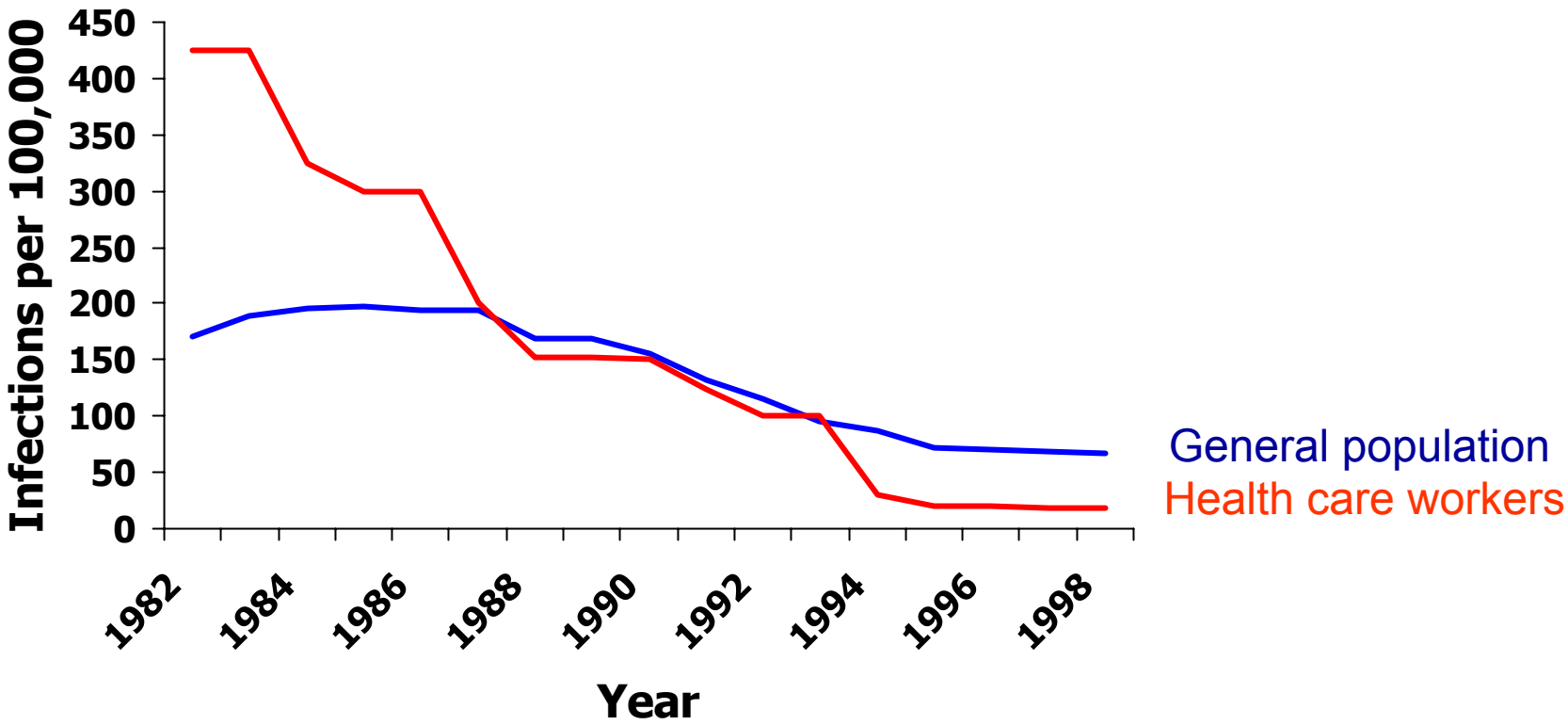


1986 (pre-vaccination; n=251)

2002 (vaccination coverage ≥3 doses=98%; n=157)

Sources: Franks. N Engl J Med. 1989; CDC and GA Department of Health, 2001-2002.

Hepatitis B Incidence Among Health Care Workers & General Population United States, 1982-1998



Source: Mahoney. Arch Intern Med. 1997; CDC

Current Booster Dose Recommendations

Current Recommendations for Booster Doses of Hepatitis B Vaccine

Booster doses of hepatitis B vaccine are not currently recommended

Recommendation based on:

- Long-term efficacy studies published to date
- Booster dose studies published to date
- U.S. surveillance data
  - of acute hepatitis B cases among children and adolescents, none report being vaccinated
  - suggests no breakthrough infections occurring among vaccinated infants and adolescents

Long-Term Protection Studies Among Vaccinated Infants

Country	Yrs f/u	n	Anti-HBs >10 mIU/m	Anti-HBc positive	HBsAg positive
China	15	52	50%	6%	2%
Alaska	15	119	61%	1%	0
The Gambia	14	175	64%	31%	2.8%
Hong Kong	12	148	74%	1%	0
Taiwan	12	951	37%	2.7%	--
Senegal	9-12	41	68%	27%	2%
Taiwan	10	805	85%	14%	0.4%
Taiwan	10	118	67%	12%	0
Italy	10	53	68%	0	0
Italy	10	474	68%	1%	0
Thailand	8-10	76	62%	9%	0

Liao Vaccine 1999; McMahon In press; Whittle BMJ 2002; Yuan Hepatology 1999; Lin JID 2003; Coursaget J Hepatol 1994; Wu JID 1999; Huang Hepatol 1999; Resti Vaccine 1997; Davilla Vaccine 1996; Poovorawan Ann Trop Med Parasit 2000.

Long-Term Protection Studies Among Vaccinated Adults

Country (Group)	Years of follow-up	n	Anti-HBs >10 mIU/m	Anti-HBc Positive	HBsAg Positive
Alaska (20-49 yo)	15	182	59%	<2%[1]	<0.2%[1]
Italy (HCW)	10	310	85%	0	0
U.S. (MSM)	10	127	91%	4%	0
Alaska[2]	9-10	1194	65-84%	0	1%
U.S. (MSM)	7-9	232	48%	7%	<1%

[1] Results for all 783 persons in study, not just those vaccinated at age 20-49 years.
[2] Includes vaccinated children.

McMahon in press 2004. Floreani Vaccine 2004 Stevens Peds 1992;Wainwright JID 1997; Hadler VHLD 1991.

Summary of Long-Term Protection Data

10-15 years after vaccination of infants, children and adults:

- Decline in detectable levels anti-HBs
  - 48-91% $\geq$10 mIU/ml
- Serologic evidence of HBV infection in some vaccinated persons
  - <1% to 37% (highest in Gambia & Senegal)
- No symptomatic infections
- Development of chronic infection very rare
- **Suggests despite decline in anti-HBs, protection persists**

Booster Doses Response Among Persons Vaccinated as Infants

Country	Known Responder	Years follow-up	n	Pre-boost anti-HBs >10 mIU/m	Post-boost anti-HBs >10 mIU/ml
Alaska	Yes	12.5	17	24%	76%
Alaska	Yes	12	16	31%	94%
Taiwan	Yes (?)	10	118	67%	100%
Italy	Yes	10	53	68%	100%
Samoa	No	9	41	39%	93%
Thailand	No	8	90	0[1]	95%

[1]Included only those with anti-HBs<10 mIU/ml

Peterson In prep 2004; Peterson In prep 2004; Huang Hepatol 1999; Resti Vaccine 1997; Williams PIDJ2003; Chongarisawat SE Asia J Trop Med Parasitol 2000.

Booster Doses Response Among Persons Vaccinated as Adults

Country (group)	Years follow-up	n	Pre-boost anti-HBs >10 mIU/m	Post-boost anti-HBs >10 mIU/ml
U.S. (adults)	13	7	71%	100%
Alaska (HCW)	3-13	59	0[1]	97-100%
Italy (HCW)	6	955	67% (3 dose)	97% (3 dose)
			94% (4 dose)	94% (4 dose)
Spain (adults, kids) [2,3]	6	182	64%[3]	96%[3]

[1] Included only those with anti-HBs<10 mIU/ml
[2] Average age: 30 years
[3] Used anti HBs ≥100 mIU/ml

Watson Vaccine 2001; Williams Vaccine 2001; Trivello Vaccine 1995; Ayerbe Eur J Epidemiol 2001.

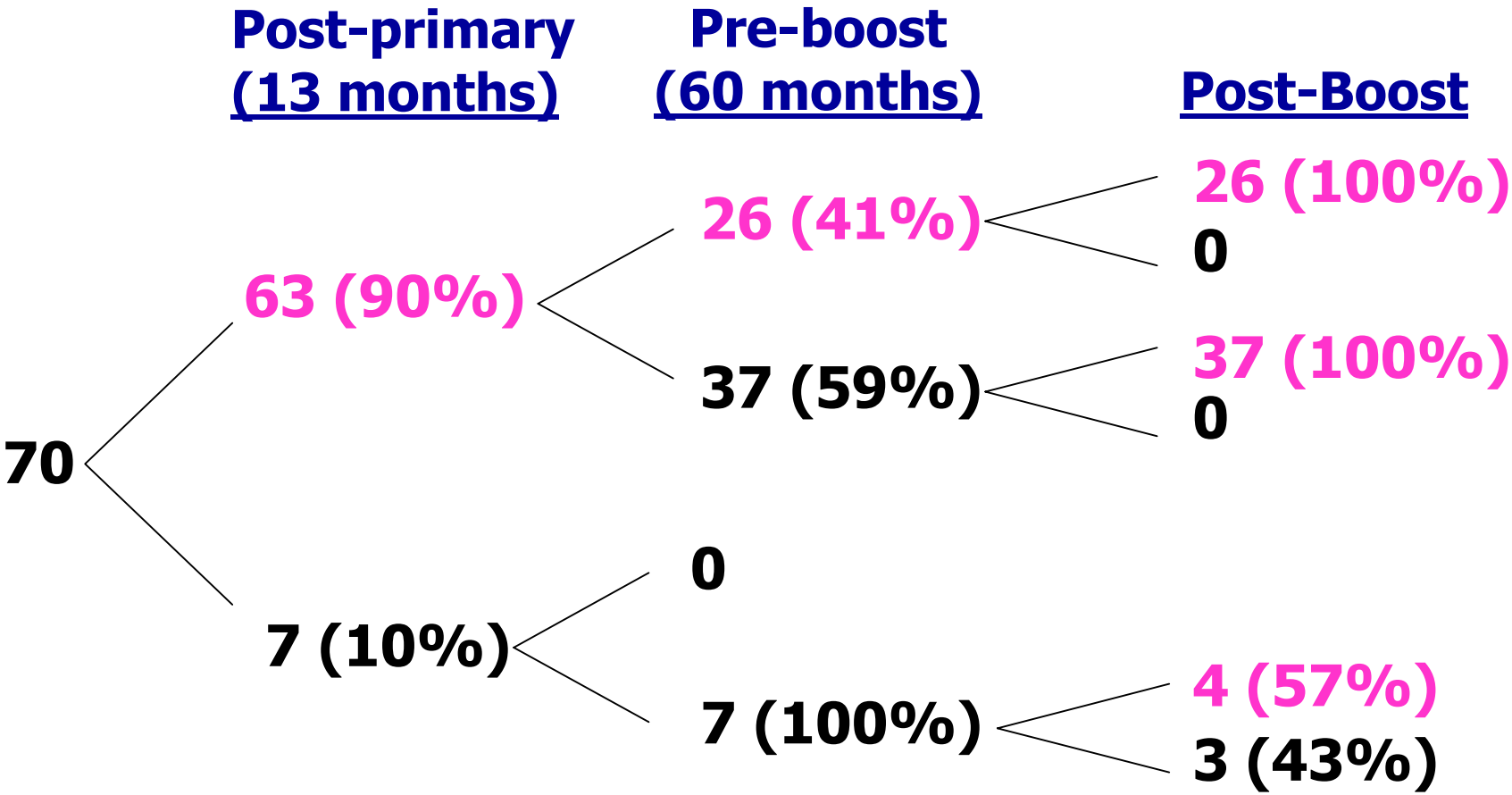
Summary of Booster Dose Studies

- Among vaccinated infants and adults who lose detectable levels anti-HBs
  - majority respond to booster doses of vaccine
  - among documented responders, 97-100% boost
- Suggests presence of immune memory despite loss of anti-HBs

CDC Booster Dose Study: American Samoa

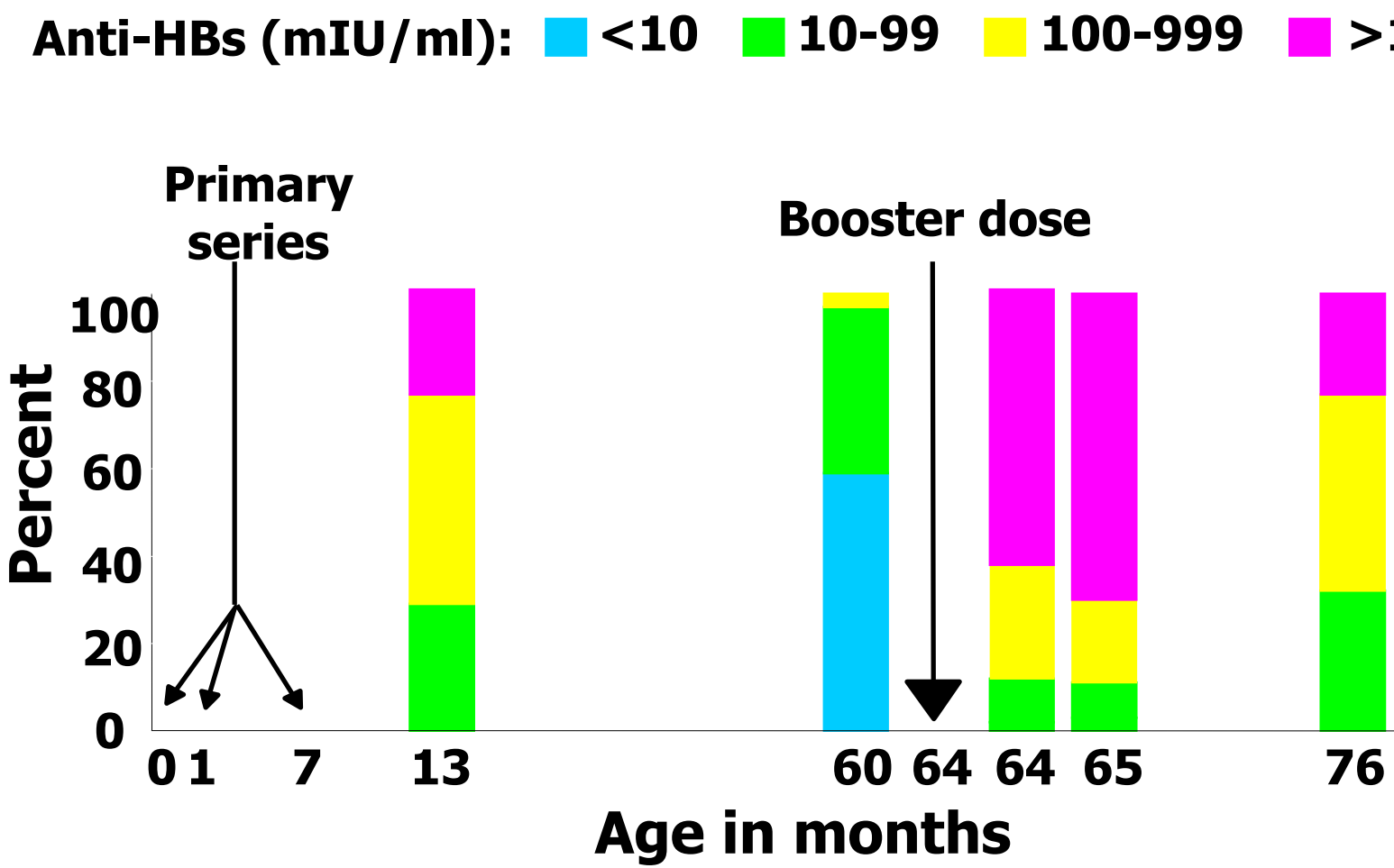
- 70 children born in 1991
- Received 3 doses recombinant hepatitis B vaccine at birth, 1, 6 months
- Tested for anti-HBs after primary series
- Received booster dose at 5 yrs old
- Anti-HBs testing at 2 wks, 4 wks, 1 yr post-boost

Anti-HBs Response to Primary Series and Booster Dose: American Samoa

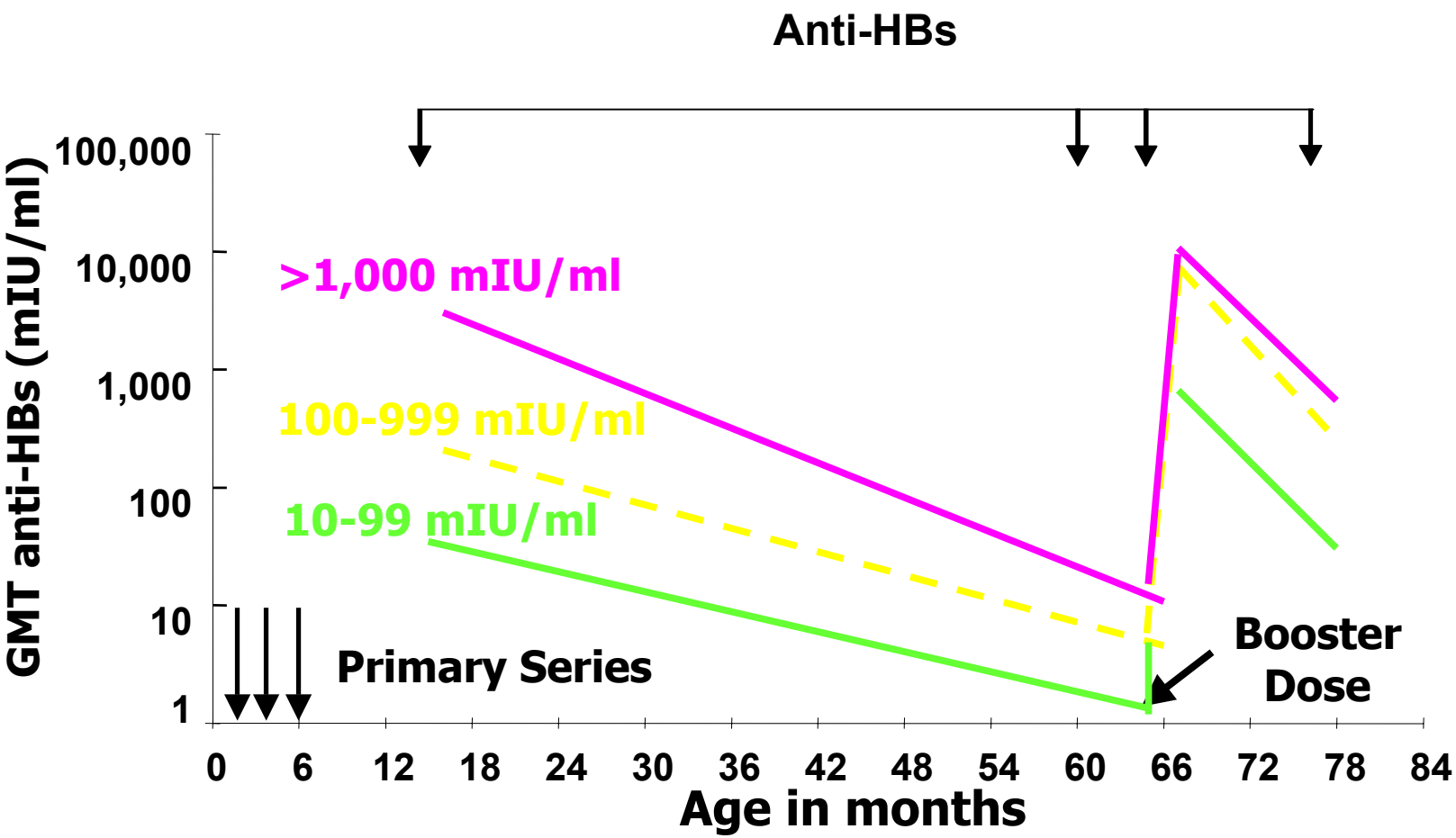


Anti-HBs ≥10 mIU/ml
Anti-HBs <10 mIU/ml

Distribution of Anti-HBs in Response to Booster Dose of Vaccine: Samoa



Booster Doses Response Among Persons Vaccinated in Infancy: Samoa



Unanswered Questions and Gaps in Knowledge

Unanswered Questions

Of the various determinants of duration of protection, which are the most important?

- Age at vaccination
  - birth
  - later infancy
  - childhood
  - adulthood
- GMC post primary series
- Receipt of HBIG
- Vaccine type: plasma-derived vs. recombinant
- Infection pressure: endemicity, maternal HBV status, vaccination coverage
- Natural boosting

Natural Boosting and Infection Pressure

Is natural boosting important?
Is infection pressure important?
What is the relationship between the two?

- High vs. low endemic areas
- Areas with catch-up vaccination of older children, adolescents, adults (i.e., Alaska)
- Implications for movement to from low to high endemic areas and potential for exposure

Protection from Infection: Infection Pressure vs. Natural Boosting

Continued infection pressure

↓

Persistent natural boosting

↓

Persistent protection

↓

No infection: Protected

Example: China
- Infant vaccination
- No catch-up vaccination
- More HBsAg/HBeAg among adults

No infection pressure

↓

No natural boosting

↓

Not protected

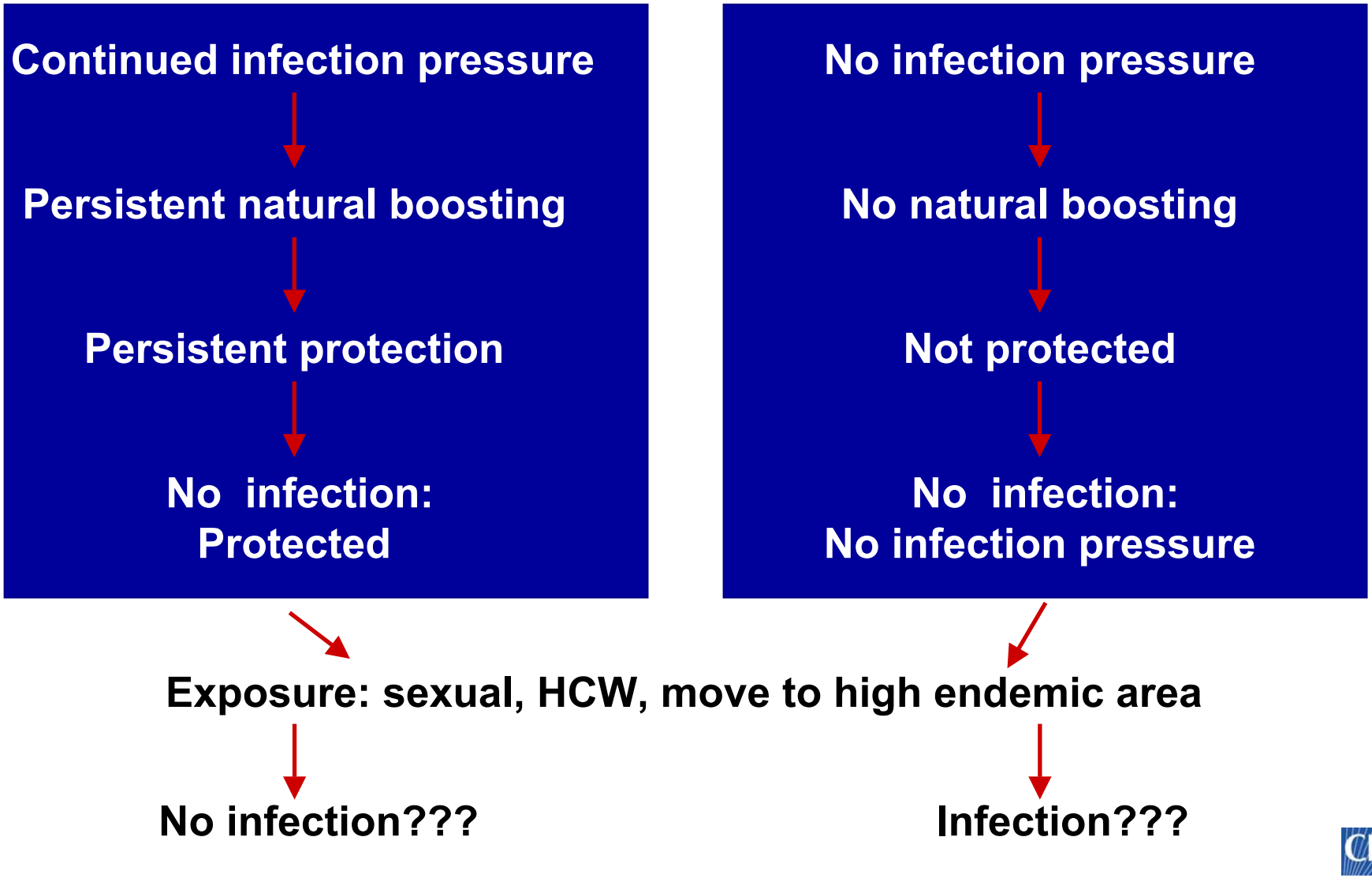
↓

No infection: No infection pressure

Example: Alaska
- Infant vaccination
- Catch-up of all susceptibles
- Less HBsAg/HBeAg among adults

Example: U.S. and W Europe
- low endemicity

Protection from Infection: Infection Pressure vs. Natural Boosting



Ongoing CDC Long-Term Protection and Booster Dose Studies

Palau (high endemic)

- Adolescents (9-10 yrs) vaccinated at birth with recombinant vaccine

Alaska (Anchorage, low endemic)

- Children (5-7 yrs) and adolescents (10-13 yrs) vaccinated at birth with recombinant vaccine

Alaska (villages, high endemic) (Vax Demo)

- 22-23 year follow-up of infants (>6 months), children, and adults vaccinated with plasma-derived vaccine