SF Hep B Free—Bay Area Hepatitis ECHO
September 22, 2021

Hepatitis B Vaccination

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Learning Objectives

01

Understand the role of hepatitis B vaccine in hepatitis B elimination

02

Recognize the various hepatitis B vaccine options for persons susceptible to hepatitis B

03

Differentiate between waning immunity vs. a non-response to hepatitis B vaccine


SFhepBfree.org
HEP B FREE
SAN FRANCISCO
WHICH ONE DESERVES TO DIE?
1 in 10 Asian Americans is infected with hepatitis B,
the leading cause of liver cancer. But hepatitis B can be treated, even prevented.
Get the simple blood test. Stop liver cancer by stopping hepatitis B.
B A HERO. SEE A DOCTOR WHO TESTS FOR HEP B.

A victim among healers

Dr. Mark Lim, Internal Medicine physician, recent residency graduate

Diagnosed with hepatitis B during medical internship, told he was a "healthy" carrier

US (Chicago)-born, Chinese parents from Philippines

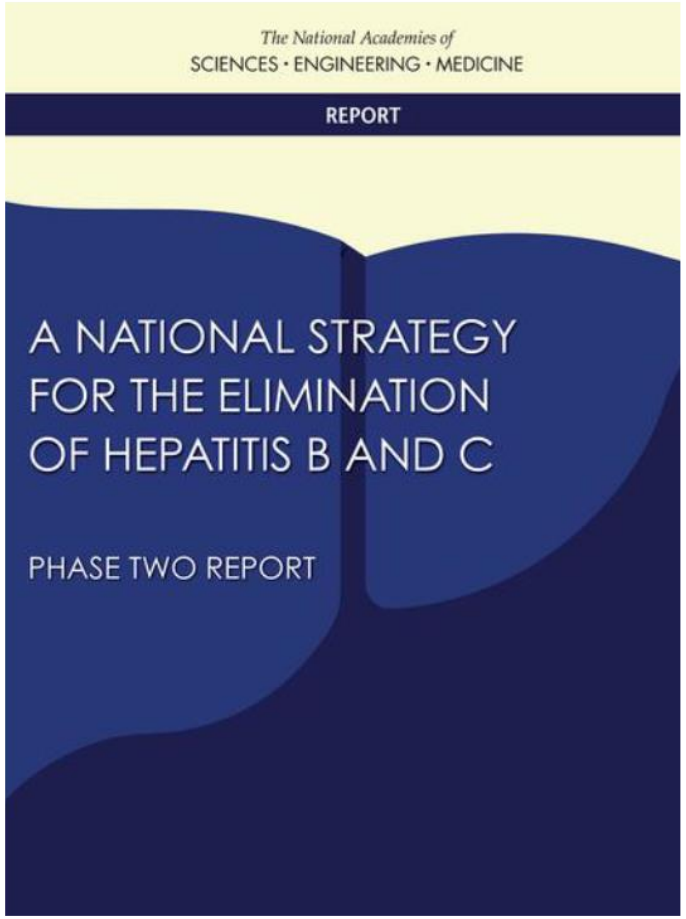
Part of a generation not vaccinated as children in the U.S. (U.S. began universal childhood vaccination in 1991)

Died of advanced liver cancer at age 31yo in 2002

"Only in a medical world that relies almost entirely on a Caucasian model for diagnosis and treatment could such a great health disparity exist" - Dr. Samuel So, Director of Stanford Asian Liver Center

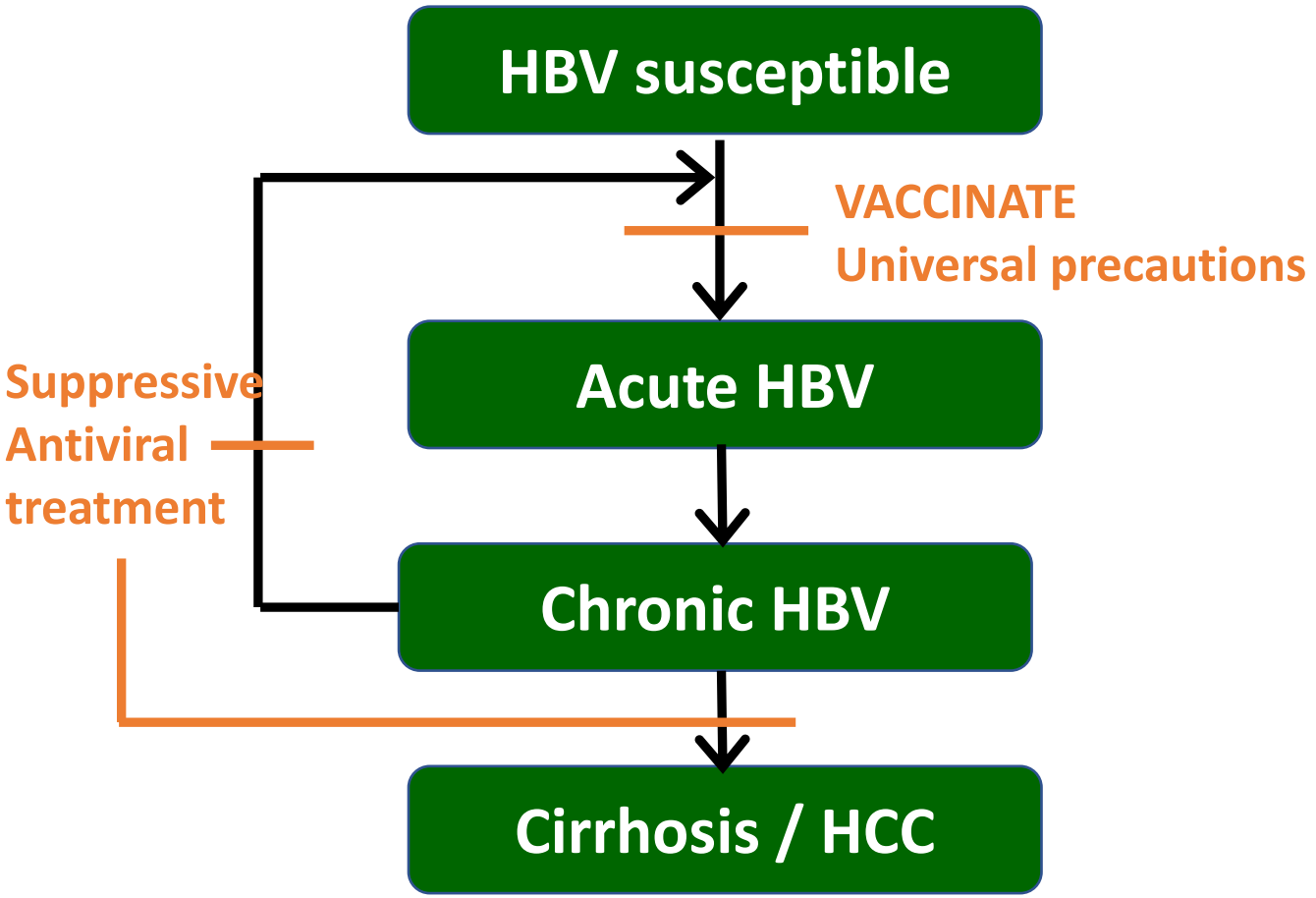
Engardio, JP. "Dying to Know" SF Weekly, 5/1/2002. https://www.sfweekly.com/news/dying-to-know/

Public Health Significance of Hepatitis B and C Elimination in the United States



- Chronic HBV and HCV infections affect 3-5X more Americans than HIV; worldwide it is 10X more
- Viral hepatitis kills more people every year than HIV, road traffic injuries, or diabetes
- HBV and HCV account for ~80% of the world's liver cancer
  - Chronic HBV increased odds of liver cancer 50-100X, HCV 15-20X
  - Viral hepatitis is driving the 38% increase in liver cancer in the US

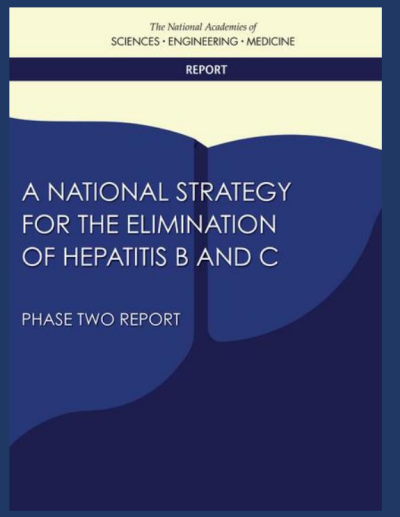
What does HBV elimination look like?



HBV is vaccine-preventative, but not curable
Suppressive treatment lowers risk of liver cancer and cirrhosis

From discovery to elimination

The Past, Present and Future of Hepatitis B



1965 HBV Discovered By Dr. Baruch Blumberg

1969 Dr. Blumberg and microbiologist Irving Millman develop first hepatitis B vaccine, heat-treated form of virus

1971 HBV test used to screen blood donations for HBV

1981 FDA approved a plasma-derived hepatitis B vaccine for human use

1986 Current 3-dose vaccine created, synthetically created from recombivant DNA

1988 Universal maternal HBV screening with HBsAg

1991 US begins universal vaccination of infants

1999 Catch up vaccination of children and adolescents

2005 Universal birth dose

2013 U.S. sets national targets for HBV and HCV elimination by 2030

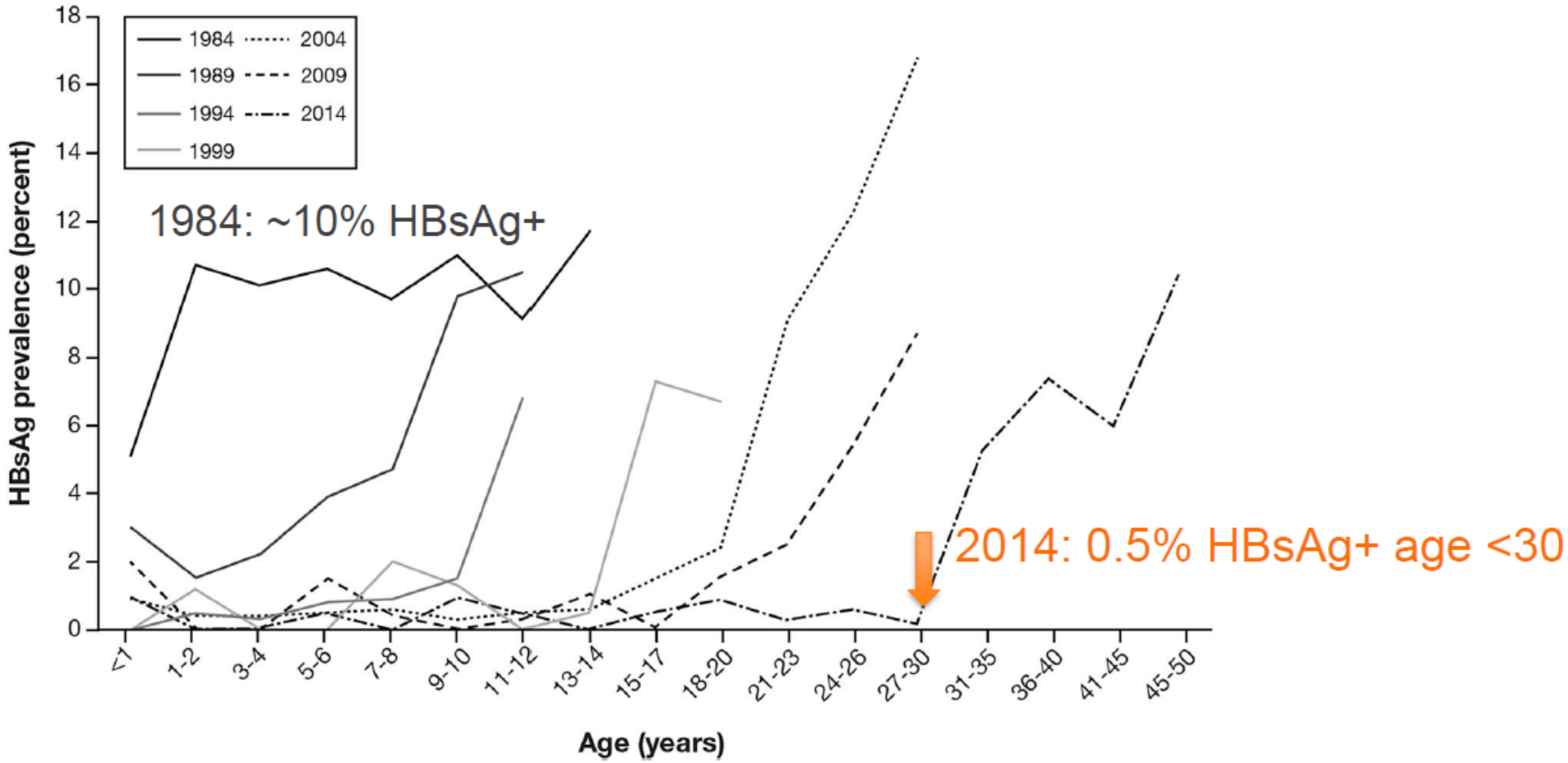
74% Birth dose (within 3d)
91% Vaccine completion among 19-35mo
93% Vaccine completion among 13-17yo
25% Adults
64% Health care workers

CDC model predicts 800-1000 infants infected/year

2017

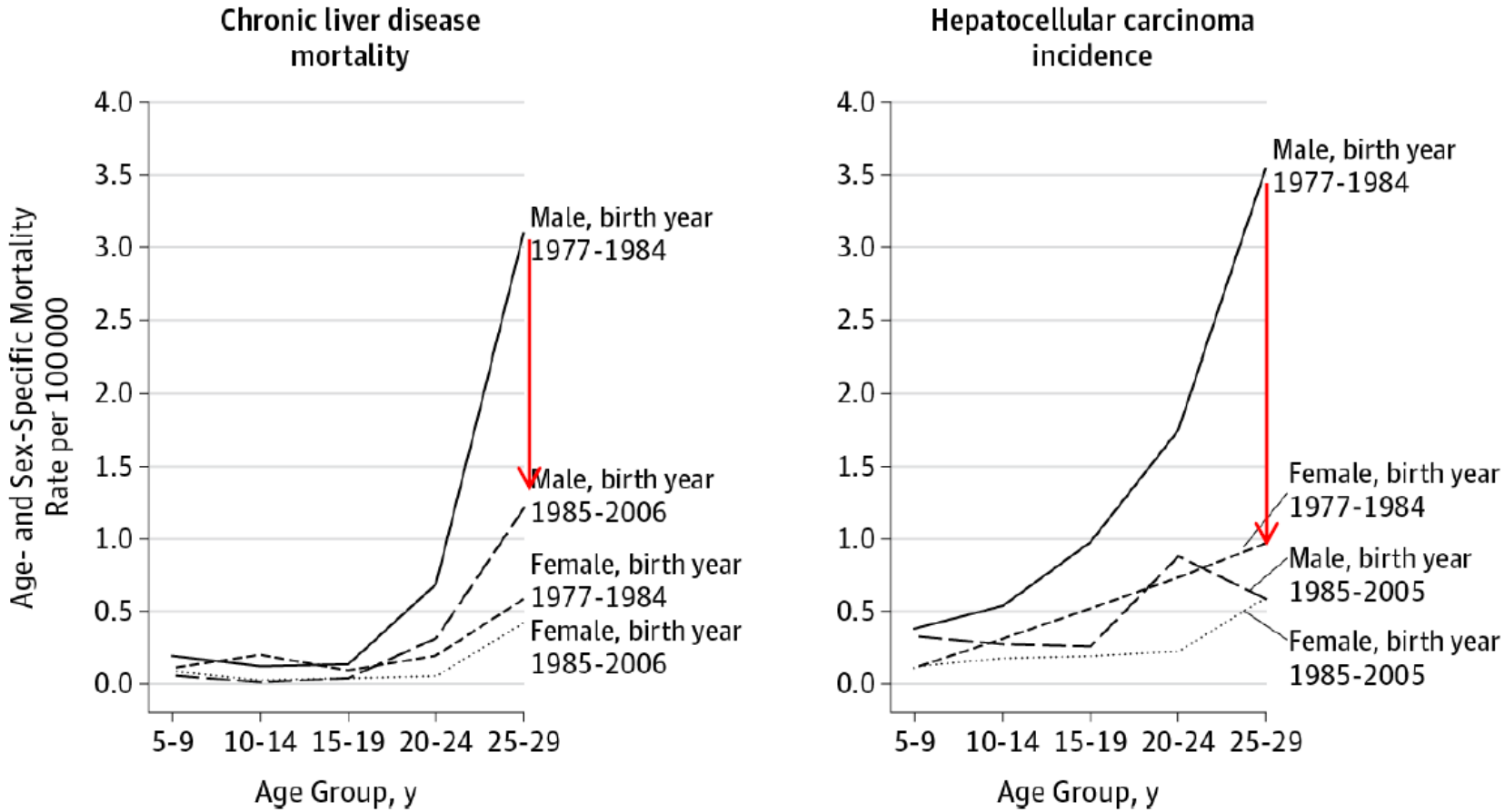
2030

Universal Newborn HBV Vaccine in Taiwan Decreased Prevalence of HBsAg in Persons <30 Years from 10% to 0.5%



Ni YH, Clin Gastroenterol Hepatol 2016; 14: 1324

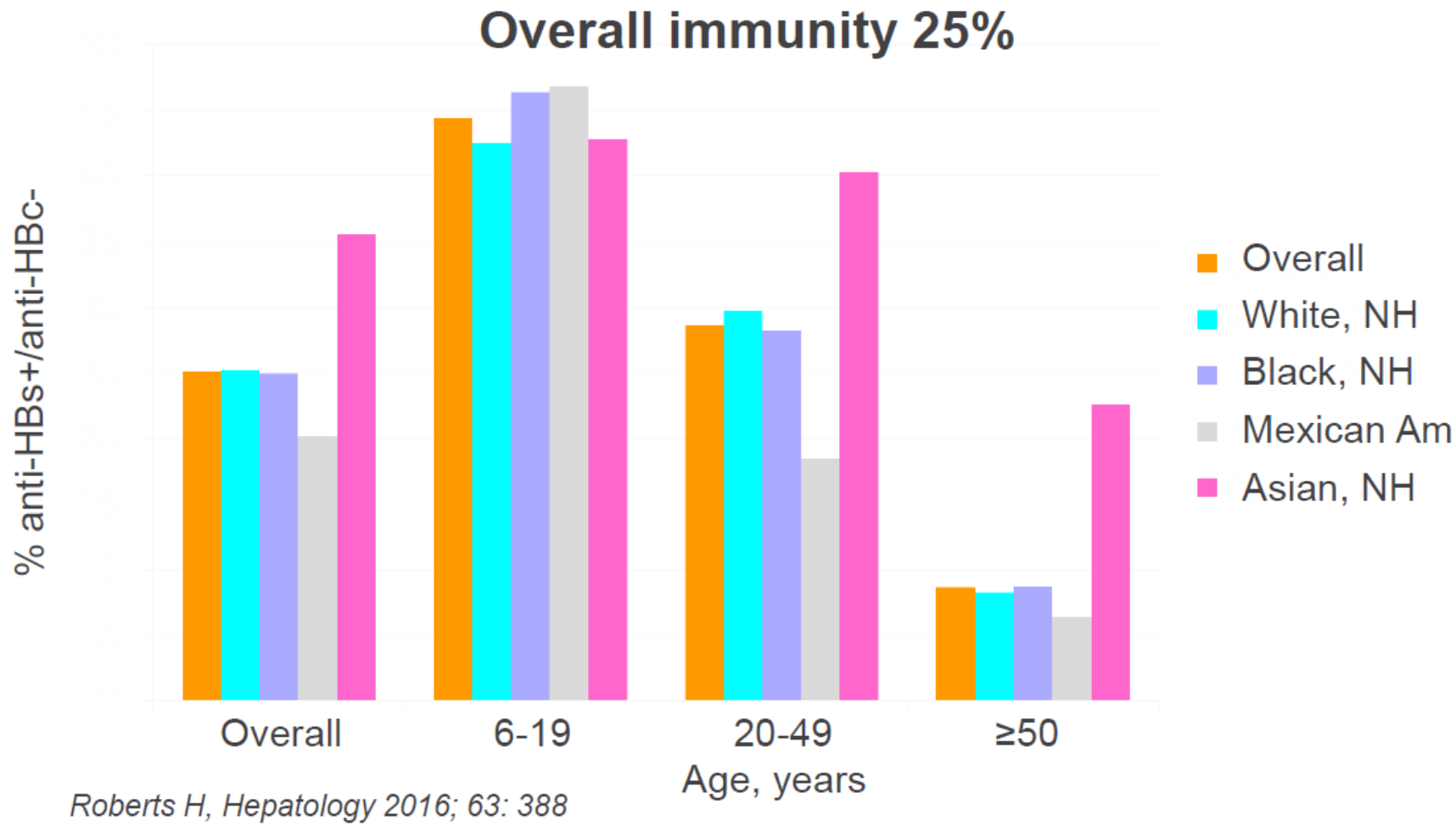
Impact of HBV Immunization Program on Chronic Liver Disease and HCC in Taiwan



Chronic liver disease and HCC mortality decreased by >90% and HCC incidence by >80%

Chiang CJ, JAMA 2013; 10: 974

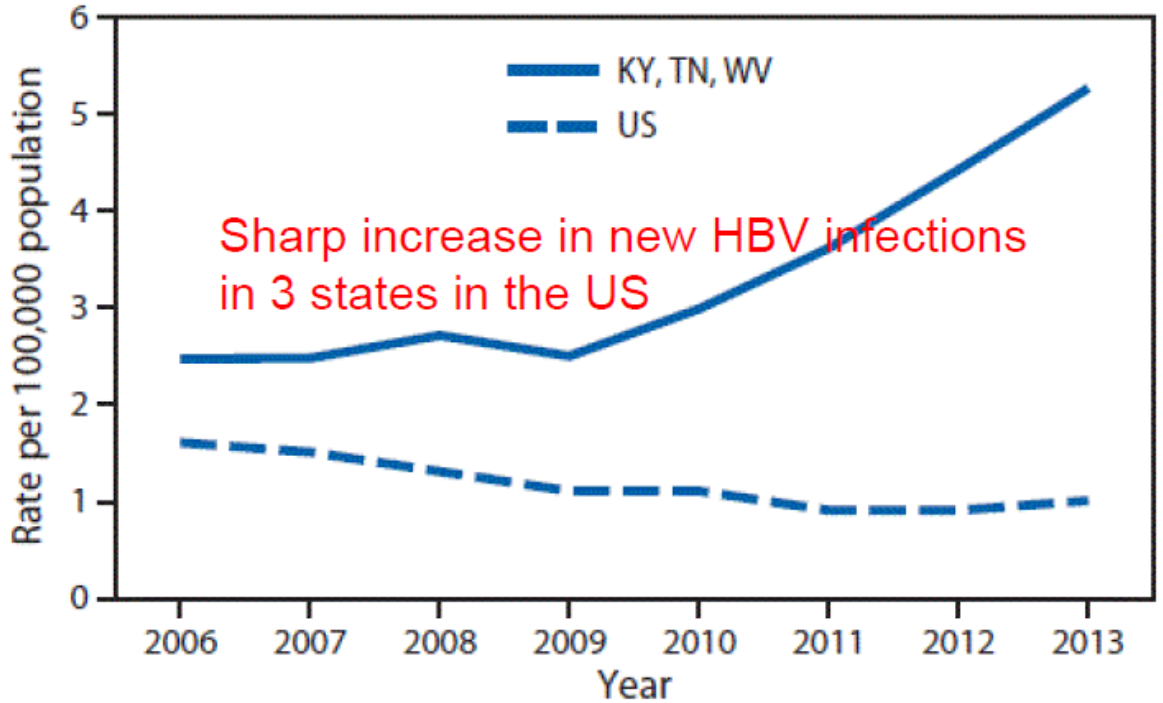
Prevalence of HBV Vaccine Immunity in the US, NHANES 2007-2012



Roberts H, Hepatology 2016; 63: 388

Outbreaks of Acute HBV in Persons Not Immune

- 3305 cases reported in Kentucky, Tennessee, and West Virginia 2006-2013
- 114% increase in incidence 2009-2013, mainly among whites, age 30-39, injection drug use



Harris AM, MMWR 2016; 65: 47

Clinical Scenario #1

37M US-born sexually active–HBV status checked as part of STD screening, HBV test shows HBV susceptible (HBsAg, anti-HBs, anti-HBc all negative), does not recall prior HBV vaccination.

What are your next steps?

Adults recommended to receive HepB vaccine (CDC/ACIP 2018)

Sexual exposure risk

- Sex partners of hepatitis B surface antigen (HBsAg)–positive persons
- Sexually active persons who are not in a long-term, mutually monogamous relationship (e.g., persons with more than one sex partner during the previous 6 months)
- Persons seeking evaluation or treatment for a sexually transmitted infection
- Men who have sex with men

Percutaneous or mucosal exposure to blood risk

- Current or recent injection-drug users
- Household contacts of HBsAg-positive persons
- Residents and staff of facilities for developmentally disabled persons
- Health care and public safety personnel with reasonably anticipated risk for exposure to blood or blood-contaminated body fluids
- Hemodialysis patients and predialysis, peritoneal dialysis, and home dialysis patients
- Persons with diabetes aged 19–59 years; persons with diabetes aged ≥60 years at the discretion of the treating clinician

Other

- International travelers to countries with high or intermediate levels of endemic hepatitis B virus (HBV) infection (HBsAg prevalence of ≥2%)
- Persons with hepatitis C virus infection
- Persons with chronic liver disease (including, but not limited to, persons with cirrhosis, fatty liver disease, alcoholic liver disease, autoimmune hepatitis, or an alanine aminotransferase [ALT] or aspartate aminotransferase [AST] level greater than twice the upper limit of normal)
- Persons with HIV infection
- Incarcerated persons
- **All other persons seeking protection from HBV infection**

Schillie S, Vellozzi C, Reingold A, et al. Prevention of Hepatitis B Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices. MMWR Recomm Rep 2018;67(No. RR-1):1–31. DOI: http://dx.doi.org/10.15585/mmwr.rr6701a1external icon.

HBV Vaccines

3-dose recombivant (Engerix-B, Recombivax-HB)

- May be given to all ages, and safe for pregnancy
- 3 doses given over 6 months (at 0, 1, and 6 months)

2-dose recombivant adjuvanted (Heplisav-B)

- For 18 and older, non-pregnant adults
- 2 doses given 1 month apart

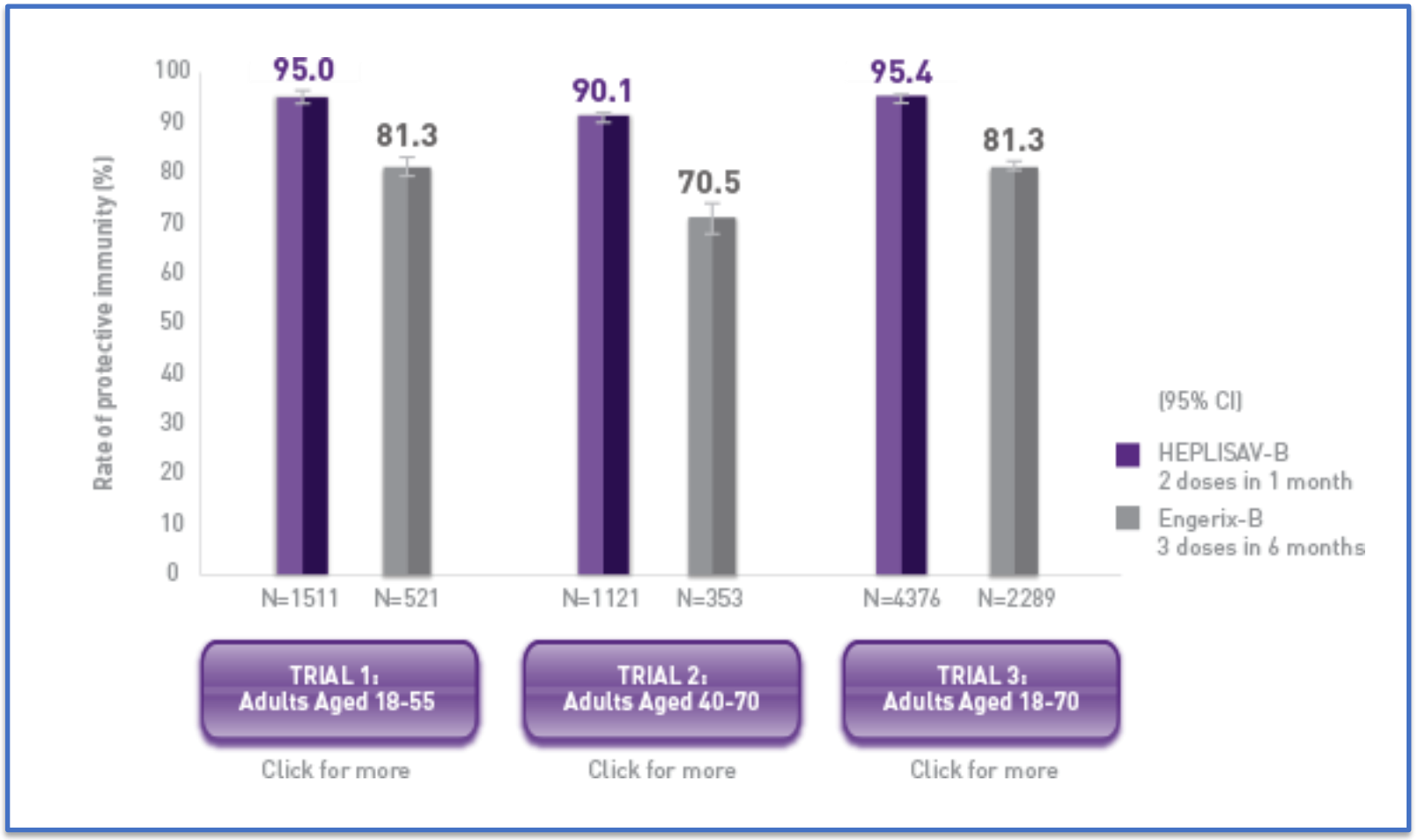
Combo pentavalent and hexavalent (Pediarix, Vaxelis)

- Given in pediatrics protects against 5 or 6 diseases including DTaP-IPV-HepB+/- HiB
- 3 doses given following birth dose HBV vaccine

3-dose combo HAV/HBV vaccine (Twinrix)

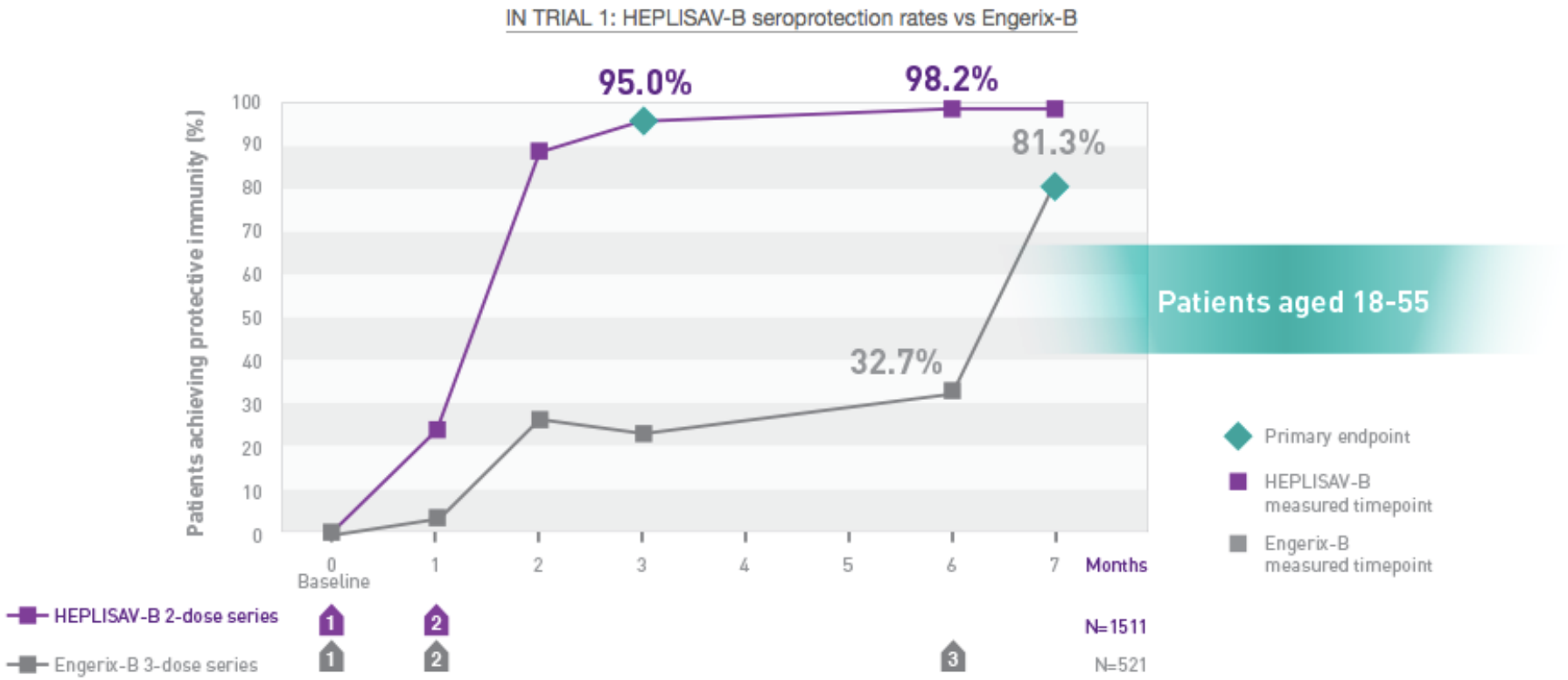
- May be given to all ages
- 3 doses given over 6 months (at 0, 1, and 6 months)

Heplisav-B vs. Engerix-B



Heplisav-B vs. Engerix-B

2 doses of HEPLISAV-B provided earlier (3 months vs 7 months) and higher levels of protective immunity than 3 doses of Engerix-B® in patients aged 18-55[1,16]



Heplisav-B vs. Engerix-B

HEPLISAV-B DELIVERED PROTECTION FOR PATIENTS WITH FACTORS THAT TYPICALLY AFFECT IMMUNE RESPONSE

IN TRIAL 3: 2 doses of HEPLISAV-B provided statistically significantly higher rates of protective immunity vs 3 doses of Engerix-B®

	Peak rates of protective immunity[1,16]	
	HEPLISAV-B	Engerix-B
Total trial population (N=6665)	95.4%	81.3%
Patients with diabetes (N=961)	90.0%	65.1%
Aged 40-70 (N=5434)	94.6%	78.7%
Male (N=3353)	94.5%	78.8%
Obesity (N=3241)	94.7%	75.4%
Smokers (N=2082)	95.9%	78.6%

Recommendations of the Advisory Committee on Immunization Practices for Use of a Hepatitis B Vaccine with a Novel Adjuvant

Weekly / April 20, 2018 / 67(15);455–458

Sarah Schillie, MD[1]; Aaron Harris, MD[1]; Ruth Link-Gelles, PhD[1]; José Romero, MD[2]; John Ward, MD[1]; Noele Nelson, MD[1]

Interchangeability and dosing schedule.

- Data are limited on the safety and immunogenicity effects when HepB-CpG is interchanged with HepB vaccines from other manufacturers. When feasible, the same manufacturer's vaccines should be used to complete the series (*10*). However, vaccination should not be deferred when the manufacturer of the previously administered vaccine is unknown or when the vaccine from the same manufacturer is unavailable (*10*).
- The 2-dose HepB vaccine series only applies when both doses in the series consist of HepB-CpG. Series consisting of a combination of 1 dose of HepB-CpG and a vaccine from a different manufacturer should consist of 3 total vaccine doses and should adhere to the 3-dose schedule minimum intervals of 4 weeks between dose 1 and 2, 8 weeks between dose 2 and 3, and 16 weeks between dose 1 and 3. Doses administered at less than the minimum interval should be repeated. However, a series containing 2 doses of HepB-CpG administered at least 4 weeks apart is valid, even if the patient received a single earlier dose from another manufacturer.

Discussion Question:

How do your respective organizations utilize standing orders for HBV vaccination?

Clinical Scenario #2

Your patient with chronic inactive hepatitis B is now pregnant with her first child. She asks about how to prevent her infant from getting hepatitis B.

How do you counsel her?

Universal HBV Birth Dose and Hep B Immune Globulin

Universal HBV Birth Dose

- HBV vaccine given within 24h of birth, regardless of maternal HBV status
- Minimize risk of HBV infection from mothers with unclear status or caregivers/contacts prior to vaccination.

Hepatitis B Immune Globulin (HBIG)

- Given within 12h of birth
- Not HBV vaccine, contains large amounts of hepatitis B antibodies taken from donated human blood
- Given when immediate protection against HBV is needed (e.g. post-exposure prophylaxis)
- Protection is short-term

Vaccine Schedules for Infants Born to Mothers who have Hepatitis B

For infants < 1 year of age

Vaccine	Dose 1 "Birth Dose"	Dose 2	Dose 3	Dose 4
 **3-dose vaccine series** U.S. brand names: Engerix-B, Recombivax HB Brands may vary outside the U.S.	Within 24 hours of birth (Hepatitis B vaccine + HBIG (if available))	1 month after dose 1	6 months after dose 1	
 **4-dose combination vaccine series (pentavalent or hexavalent)** Brand names : Vaxelis, Pediarix	Within 24 hours of birth (Hepatitis B vaccine + HBIG (if available))	6 weeks of age (Combination vaccine)	14 weeks of age (Combination vaccine)	24 weeks of age (Combination vaccine)

Key

= Monovalent hepatitis B vaccine (protection against hepatitis B only)

= Hepatitis B Immunoglobulin (HBIG)

= Combination vaccine (protection against hepatitis B + other diseases)

Clinical Scenario #3

25F US-born, starting nursing school, has documentation of completed HBV-vaccination series as a child. Her school requires anti-HBs titer to evaluate for immunity. Her results come back as follows:

- **HBsAg negative**
- **Anti-HBs negative (<10 IU/mL)**
- **Anti-HBc (total) negative**

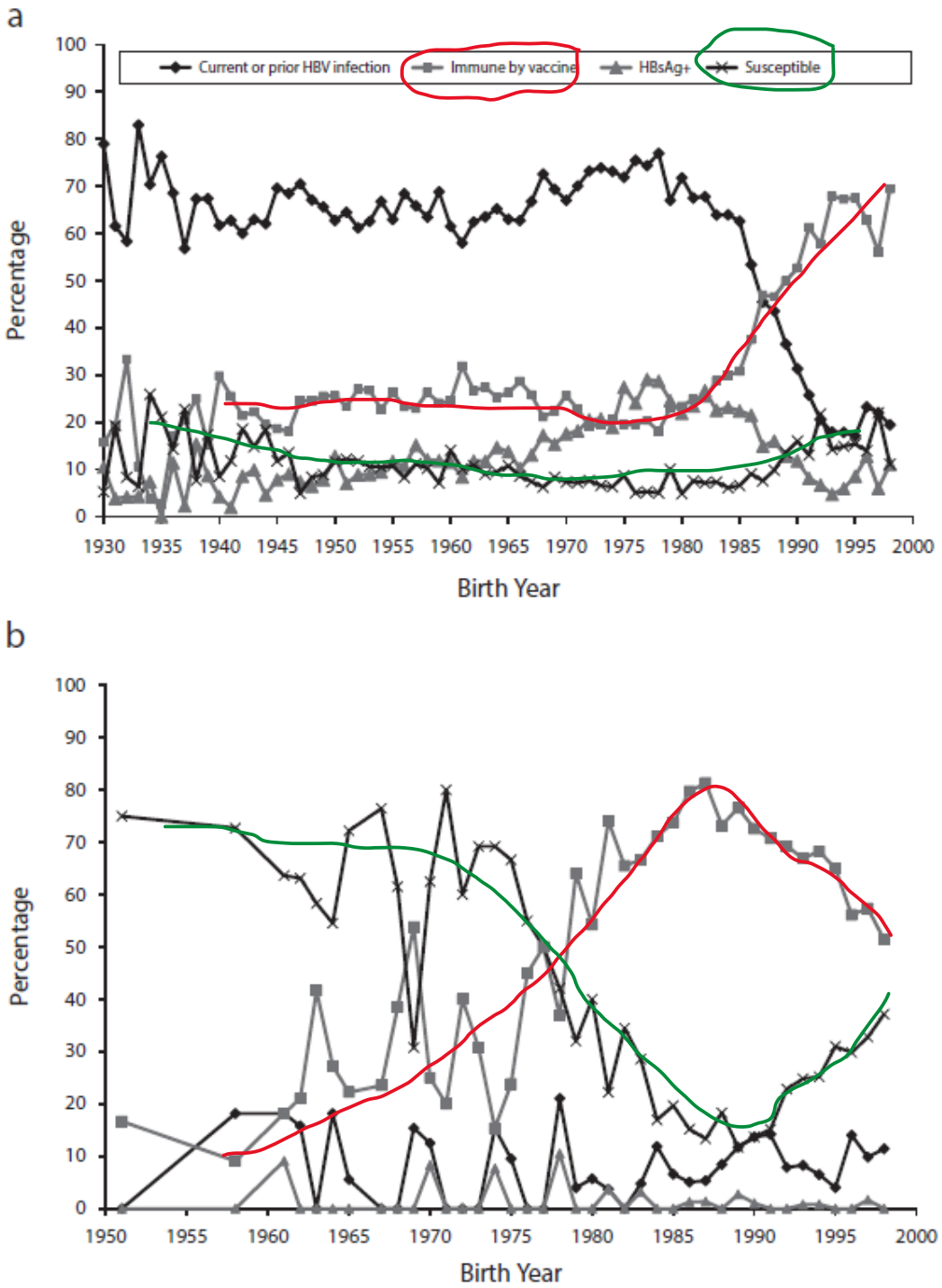
What are your next steps

A. Give a booster HBV dose
B. Give a full HBV series
C. Do nothing
D. Give a booster HBV dose and recheck anti-HBs 1-2 months later to evaluate for a response

How to differentiate vaccine non-responders from those with waning immunity?

True vaccine non-response is shown with an anti-HBs level < 10 mIU/mL between 1-2 months after last dose of vaccine series

A negative anti-HBs performed several years after last dose could indicate waning immunity (more likely in US born < 30) vs. HBV vaccine non-response (more likely if anti-HBs tested closer to vaccine completion)



Long lasting protection of HBV vaccine

- 243 persons in Alaska, responded to primary HBV vaccine series in 1981, reassessed 30 years later
  - 51% anti-HBs ≥10 mIU/mL
  - 88% of those with anti-HBs <10 mIU/mL responded to 1 booster dose within 30 days
- Results suggest ≥90% had evidence of protection 30 years after vaccination

Bruce MG, J Infect Dis 2016; 214: 16

CDC Recommendations for Hepatitis B Vaccine Non-Responders

- Persons who do not respond to the primary hepatitis B vaccine series (i.e., anti-HBs <10 mIU/mL) should complete a second vaccine series or be evaluated to determine if they are HBsAg-positive. For the second series, a different brand of vaccine should be administered. For adults in the U.S., the second series can be given using the traditional 3-dose vaccine or the 2-dose vaccine (Heplisav-B™).
- Persons who do not respond to an initial 3-dose vaccine series have a 30%--50% chance of responding to a second 3-dose series. The 2-dose vaccine might provide greater seroprotection, which can mean a greater antibody response, especially in adults who may be older, obese or live with type 2 diabetes. If you have not responded to a primary hepatitis B vaccine series, talk to your doctor about whether the 2-dose vaccine is an option for you.
- Revaccinated persons should be retested to check antibody response at the completion of the second vaccine series, 1-2 months following the last dose of the series.
- Persons exposed to HBsAg-positive blood or body fluids who are known not to have responded to a primary vaccine series should receive a single dose of hepatitis B immunoglobulin (HBIG) and restart the hepatitis B vaccine series with the first dose of the hepatitis B vaccine as soon as possible after exposure. Alternatively, they should receive two doses of HBIG, one dose as soon as possible after exposure, and the second dose 1 month later.
- The option of administering one dose of HBIG and restarting the vaccine series is preferred for non-responders who did not complete a second 3-dose vaccine series. For persons who previously completed a second vaccine series but failed to respond, two doses of HBIG are preferred.
- **Hepatitis B vaccine “non-responders” test negative for hepatitis B infection and do not respond after revaccination** are at risk for being infected and should be counseled regarding how to prevent a hepatitis B infection and to seek immediate medical care to receive a dose of hepatitis B immunoglobulin (HBIG) if they have been exposed to potentially infected blood.

Postvaccination serologic testing

Assessment of the response to HBV vaccination with a post-vaccination serologic test of anti-HBs between 1 and 2 months after the final dose of vaccine should be obtained in all of the following adult groups at high risk for HBV transmission:

- Health care personnel
- Sexual and household contacts of HBsAg(+) persons
- Hemodialysis patients
- Persons with HIV and other immunocompromising conditions

Clinical Scenario #4

55M from China HBV tests as follows:

- **HBsAg negative**
- **Anti-HBs negative**
- **Anti-HBc (total) positive**

5. What are your next steps in management for this patient?

a. Check HBV DNA level for occult hepatitis B Only if immunocompromised or HIV-positive
b. Counsel on likely prior HBV infection and risk of HBV reactivation If immunocompetent
c. Repeat HBV screening panel to check for possible false positive anti-HBc
d. Recommend HBV vaccine Consider HBV vaccination for persons with no known risk factors or persons not from an area of intermediate or high endemicity as this may represent a false-positive anti-HBc result. The rate of false positive anti-HBc is less than 2 per 1,000 tests using current assays.

Immunosuppressive Drugs and HBV Reactivation Risk

Risk group	HBVr drug risk estimates (HBsAg positive or anti-HBc positive)	Potential disorders for treatment
High-risk group (>10%)	B cell–depleting agents such as rituximab and ofatumumab ◦ HBsAg positive/anti-HBc positive: 30%–60% (A) ◦ HBsAg negative/anti-HBc positive: >10% (A)	Lymphoma/leukemia, rheumatoid arthritis, idiopathic thrombocytopenic purpura, cryoglobulinemia
	Anthracycline derivatives such as doxorubicin and epirubicin ◦ HBsAg positive/anti-HBc positive: 15%–30% (A)	Breast, ovarian, uterine, and lung cancers; lymphoma and leukemias; transarterial chemoembolization
	Corticosteroid therapy for ≥4 wk ◦ HBsAg positive/anti-HBc positive: >10% (B) (moderate/high dose[a])	Inflammatory bowel disease, vasculitis, sarcoidosis, autoimmune disorders
Moderate-risk group (1%–10%)	TNF-α inhibitors: etanercept, adalimumab, certolizumab, infliximab ◦ HBsAg positive/anti-HBc positive: 1%–10% (B) ◦ HBsAg negative/anti-HBc positive: 1% (C)	Inflammatory bowel disease, rheumatoid arthritis, ankylosing spondylitis
	Other cytokine inhibitors and integrin inhibitors: abatacept, ustekinumab, natalizumab, vedolizumab ◦ HBsAg positive/anti-HBc positive: 1%–10% (C) ◦ HBsAg negative/anti-HBc positive: 1% (C)	Plaque psoriasis, inflammatory bowel disease
	Tyrosine kinase inhibitors: imatinib, nilotinib ◦ HBsAg positive/anti-HBc positive: 1%–10% (B) ◦ HBsAg negative/anti-HBc positive: 1% (C)	Chronic myelogenous leukemia, gastrointestinal stromal tumors
	Corticosteroid therapy for ≥4 wk ◦ HBsAg positive/anti-HBc positive: 1–10% (C) (low dose[a]) ◦ HBsAg negative/anti-HBc positive: 1–10% (C) (moderate/high dose[a])	Inflammatory bowel disease, vasculitis, sarcoidosis, autoimmune disorders
	Anthracycline derivatives: doxorubicin and epirubicin ◦ HBsAg negative/anti-HBc positive: 1%–10% (C)	Breast, ovarian, uterine, and lung cancers; lymphoma and leukemias; transarterial chemoembolization

Perillo RP et al. Gastroenterology 2015; 148:221-244

Can a HBV vaccine booster help decrease risk of HBV reactivation in persons with isolated anti-HBc 2/2 prior infection?

A HBV vaccine booster may convert anti-HBs from negative to positive in persons with isolated anti-HBc but there is not evidence to show that this reduces their changes of HBV reactivation

Hep B/C Elimination Advocacy and Policy

California AB 789 (Low/Gibson) Hep B and C Screening and Referral to Care

- This bill would require routine hep B and C screening in certain healthcare settings and referral to care as appropriate
- This bill has made it through the State legislature and is awaiting the Governor's signature (or veto)

ACIP to consider recommendation for universal hepatitis B vaccination for adults Sept 2021, public comments invited

Questions?

Are there materials for patients around co-administration of hep B vaccines with COVID vaccines?