Immunization Updates

New Shingles Vaccine

Perinatal Tdap

Influenza

Hepatitis Vaccines

CDPH Resources

Disclosures

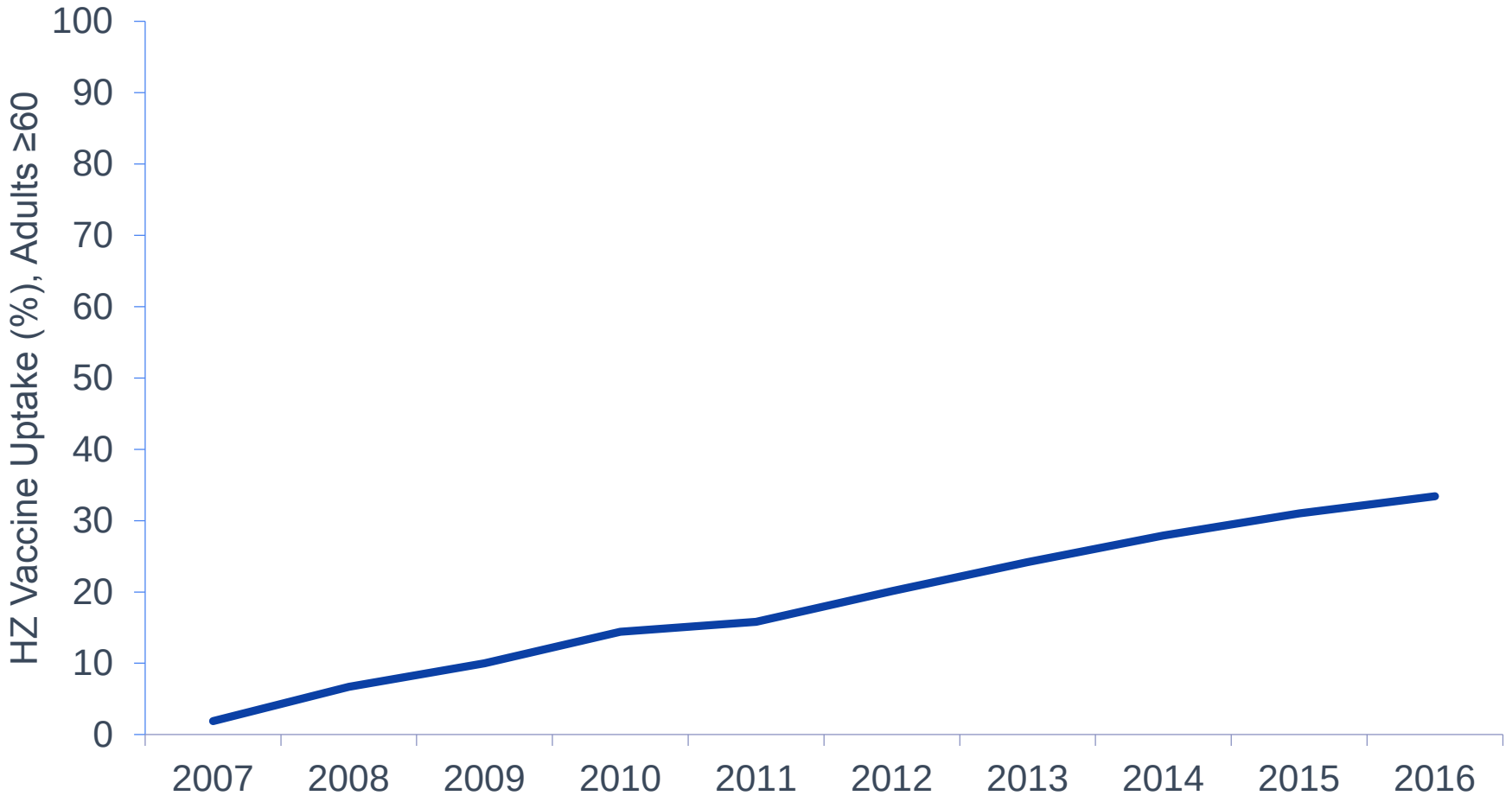
- I have no financial interests in immunizations discussed here
- I may discuss off-label use of licensed vaccines

Herpes Zoster (HZ) and Postherpetic Neuralgia (PHN) Epidemiology, United States

- ~1 million cases annually[1,2]
- Incidence of HZ and PHN increase with age[2,3,4]
- HZ (cases per 1,000 population)
  - Children: <1
  - 80 years and older: >15
- PHN
  - 50 years and older: 10-18% of HZ cases develop PHN
- Zoster Vaccine Live (ZVL, Zostavax) licensed in U.S. since 2006
  - 33% of individuals 60 years and older report receipt.[5]

1. Jumaan et al., JID, 2005, 191:2002-7
2. Yawn, et al., Mayo Clin Proc. 2007; 82:1341-9
3. Insinga et al., J Gen Intern Med. 2005, 20:748-53
4. Harpaz et al, IDWeek 2015
5. CDC, provisional unpublished data from NHIS

Vaccination Coverage of Zoster Vaccine Live, among Adults ≥60 yrs, United States, 2007-2016



* 2007: National immunization Survey (Lu et al, Vaccine 27:882-7); 2008-13: NHIS (Am J Prev Med 40:e1-6 & MMWR February 5, 2016 / 65(1);1–36), 2016 CDC, unpublished

What's new?
Recombinant Zoster Vaccine (RZV) - Shingrix

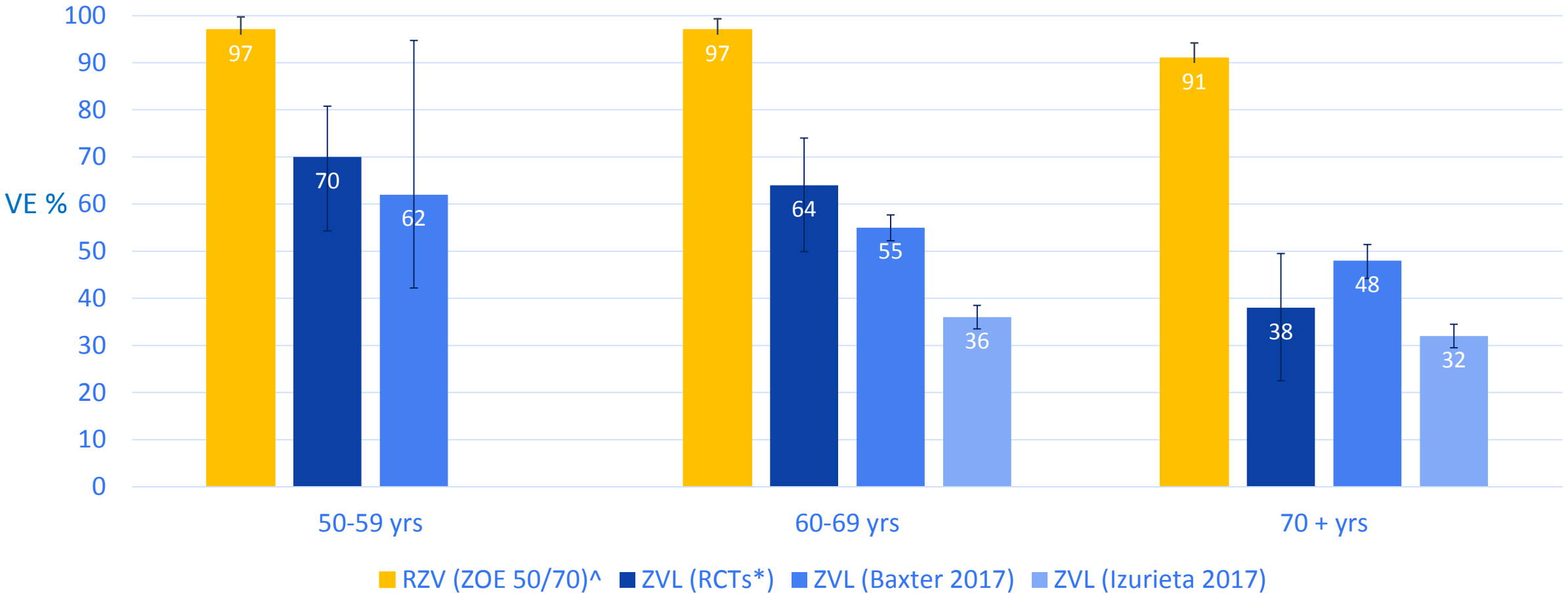
- 2 components
  - Glycoprotein E – recombinant protein
  - Adjuvant $ASO1_B$
- Efficacy & safety evaluated in 2-part, phase III RCT
  - >30,000 subjects
- FDA licensure on Oct 20, 2017
  - https://www.fda.gov/biologicsbloodvaccines/vaccines/approvedproducts/ucm581491.htm

Zoster vaccines – Important Differences!

Zoster vaccine	Storage	Route of injection	Doses in Series
RZV (Shingrix)	**Refrigerator**	IM	2
ZVL (Zostavax)	**Freezer**	SQ	1

Improperly stored vaccine is useless!

Herpes Zoster - Vaccine efficacy and effectiveness for RZV and ZVL, by age group, during the first 4‡ years following vaccination

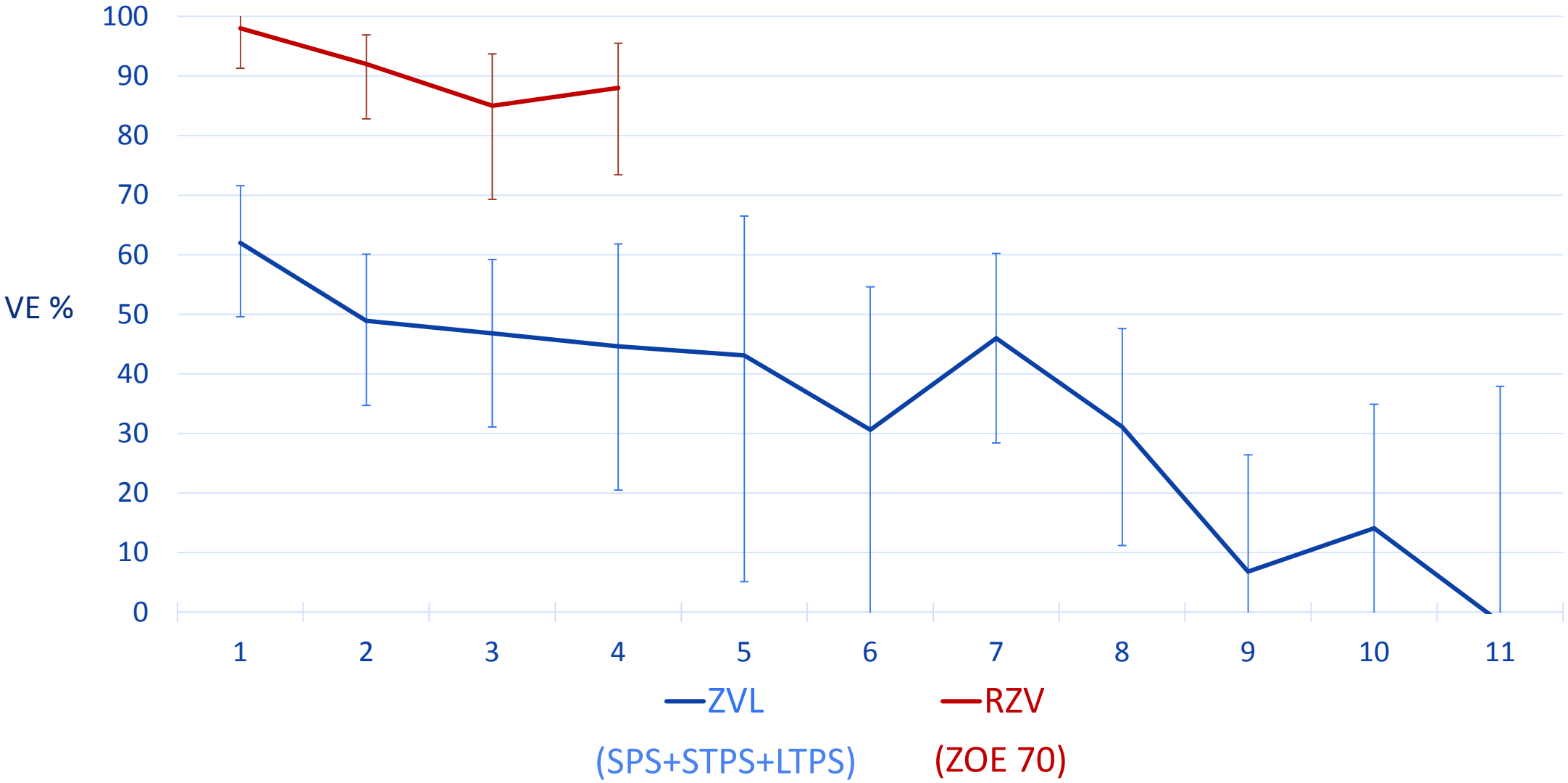


‡ Median follow up may be less than 3 yrs: Schmader 2012= 1.3 yrs

^ ZOE 50/70= 50-59 & 60-69yr: Lal 2015, 70+yrs: Cunningham 2016

* RCTs= 50-59 yrs: Schmader 2012, 60-69 and 70+ yrs: Oxman 2005,

Herpes Zoster - Vaccine efficacy for ZVL and RZV, by year following vaccination



Note: The Shingles Prevention Study, Short-term Persistence Study, and Long-term Persistence Study followed the same study population over time.

ACIP Recommendations
Zoster Vaccines – Recap

Age 50 years and older

- Administer 2 doses of RZV 2–6 months apart regardless of
  - past episode of herpes zoster, or
  - receipt of past doses of ZVL
    - wait at least 2 months after ZVL before dose of RZV.

Age 60 years or older

- Administer either RZV (preferred) or ZVL
  - wait at least 2 months after ZVL before dose of RZV

ACIP Recommendations
Zoster Vaccines – Co-morbidity

- Persons with chronic medical conditions (e.g., chronic renal failure, diabetes mellitus, rheumatoid arthritis, and chronic pulmonary disease) should receive RZV.

- Immunocompromised persons. No recommendations yet.
  - To be discussed as additional data become available.

RZV (Shingrix) Reactogenicity

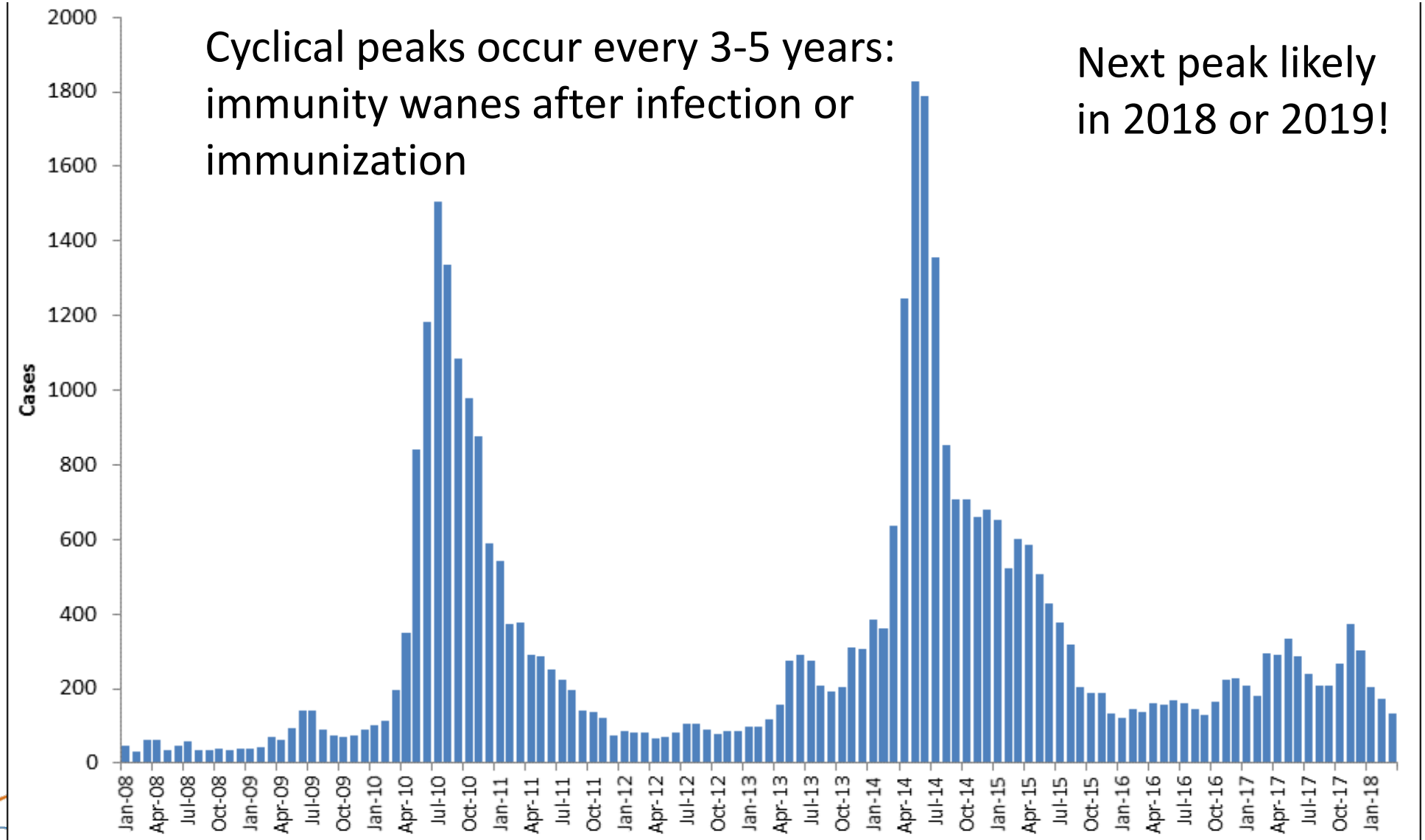
- Before vaccination, counsel about expected reactogenicity
  - pain (78%)
  - myalgia (45%)
  - fatigue (45%)
- Reactions to 1st dose did not predict reactions to 2nd dose
- Vaccine recipients should be encouraged to complete the series even if they experienced a grade 1–3 reaction to the first dose

RZV (Shingrix) Clinical Guidance

- RZV may be co-administered with other vaccines
  - RZV+ QIV (Fluarix) – no interference or safety problems
  - RZV+ PPSV23 (Pneumovax23) or Tdap (Boostrix) – studies ongoing
  - RZV+ Fluad – have not been studied

https://www.fda.gov/biologicsbloodvaccines/vaccines/approvedproducts/ucm581491.htm

Pertussis Cases by Onset Date, CA, 2008-2018



*2018 case numbers will increase due to reporting delays

*Reported to CDPH as of 4/2/2018

Pertussis in Infants <4 months of Age

- Most severe disease and deaths occur in infants <4 months of age
  - 2017: 119 cases (1/1000 births)
  - Infants born to mothers with Medi-Cal coverage had >2 times the risk of pertussis compared to privately insured*
- Prenatal Tdap is the focus of pertussis control
  - Tdap at earliest opportunity between 27-36 weeks gestation of every pregnancy
- Administer first dose of DTaP vaccine to infants promptly at 6-8 weeks of age
  - A dose as early as 6 weeks will help protect infants sooner if their mothers did not receive Tdap during pregnancy

*2013-14. K. Winter. PIDJ, 2018.

Figure 1. *Receipt of Tdap vaccine during pregnancy among women with a live birth in 2016, in California, by maternal characteristics, MIHA 2016**

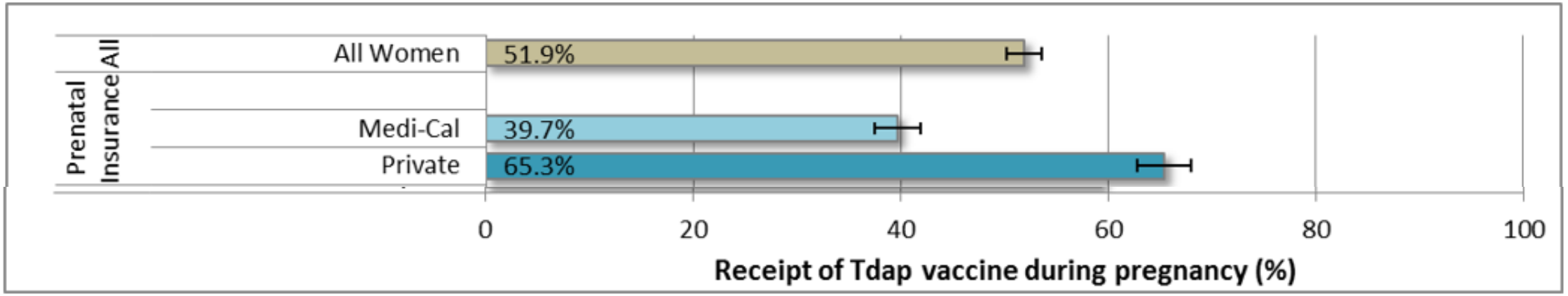


Figure 4. *Receipt of influenza vaccine during pregnancy among women with a live birth in 2016, in California, by maternal characteristics, MIHA 2016‡*

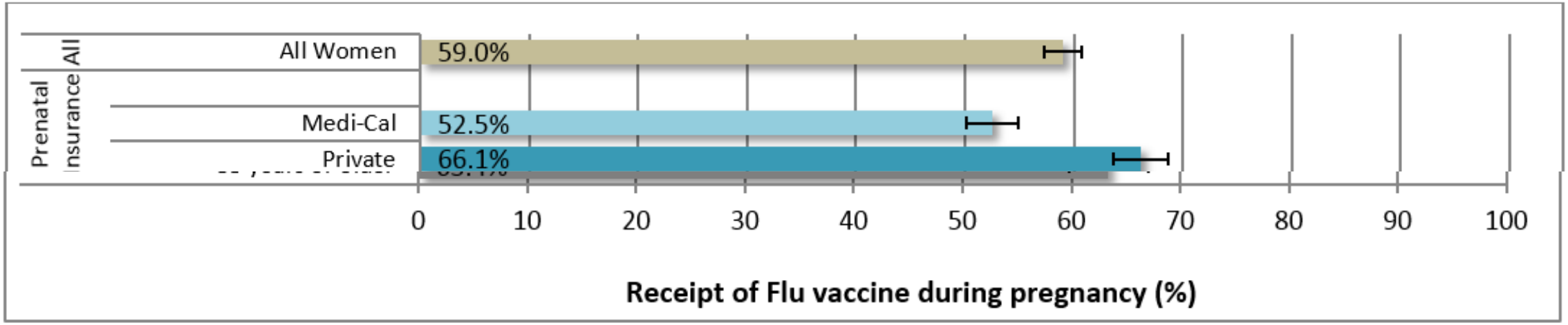
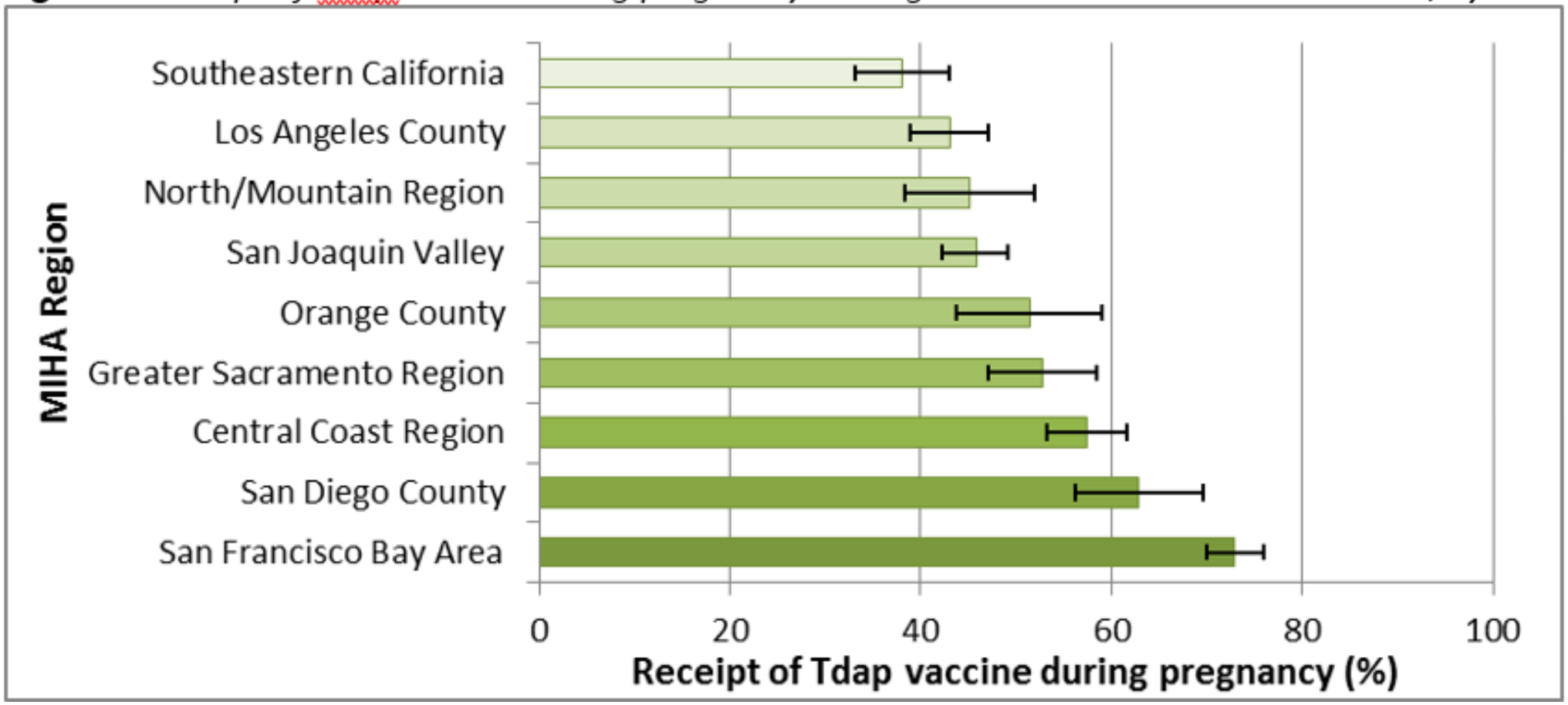


Figure 2. *Receipt of Tdap vaccine during pregnancy among women with a live birth in 2016, by MIHA region[10], 2016[†]*



Influenza – 2/18 ACIP Meeting

- Live attenuated influenza vaccine returns as an one of many vaccine options for 2018-2019 influenza season
- 2017-18 (A/Slovenia) vs. 2015-16 (A/Bolivia) H1N1 strains
  - Increased reproduction in human cells, more immunogenic
  - No effectiveness data yet
- License indication unchanged: healthy, 2-49 years of age

Influenza vaccine 2018-2019 season

- WHO recommends that vaccines for use in the 2018-2019 northern hemisphere influenza season contain:

Trivalent

- A/Michigan/45/2015 (**H1N1**)pdm09-like virus;
- A/Singapore/INFIMH-16-0019/2016 (**H3N2**)-like virus - **CHANGE**
- B/Colorado/06/2017-like virus (**B/Victoria**/2/87 lineage) – **CHANGE**

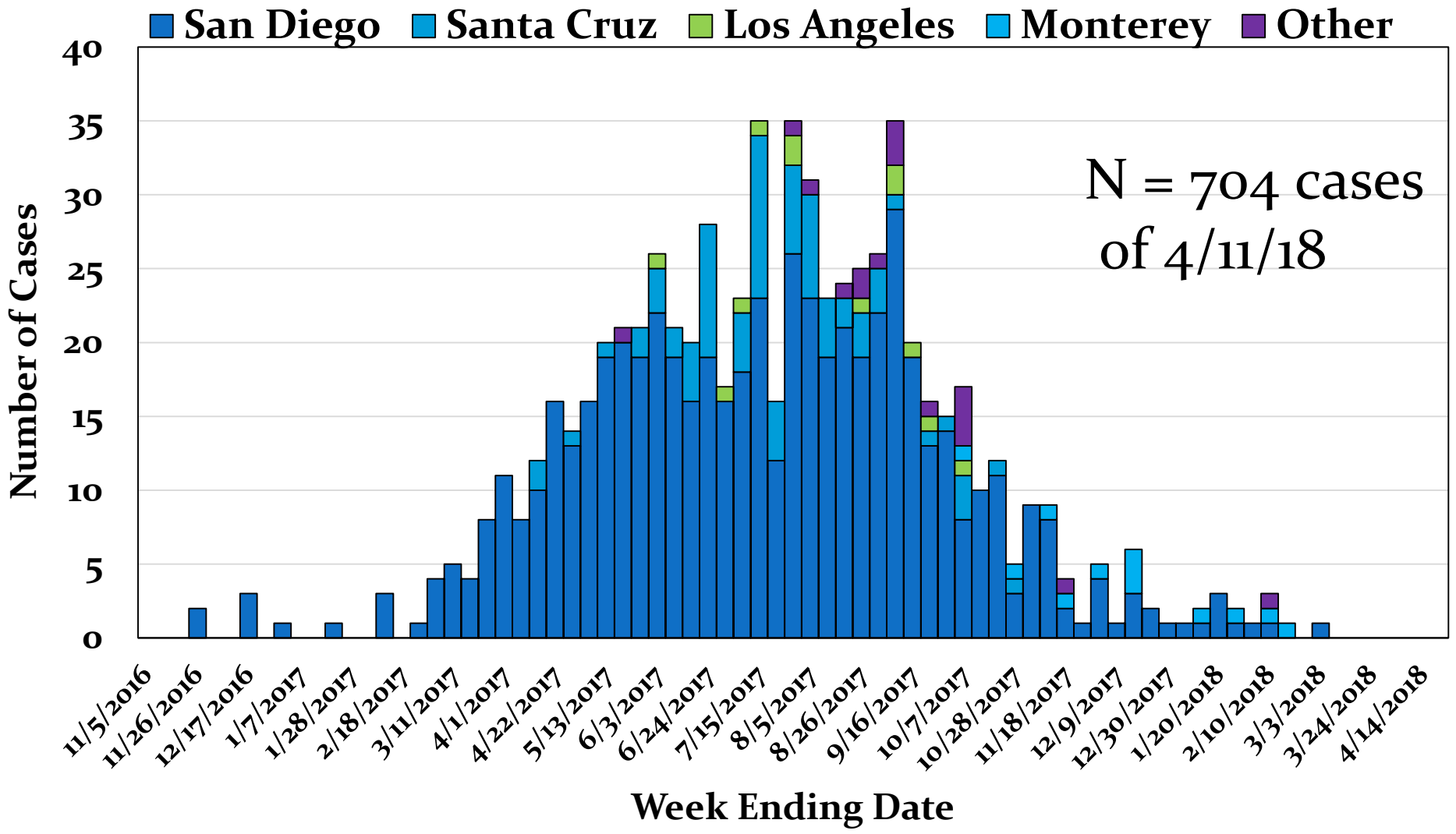
Quadrivalent – above +

- B/Phuket/3073/2013-like virus (**B/Yamagata**/16/88 lineage)

http://www.who.int/influenza/vaccines/virus/recommendations/2018_19_north/en/

CDPH

Hepatitis A Outbreak, California, 2016-2018



Hepatitis A Outbreak Cases as of 11/10/17
Hospitalization or Death for Persons with CLD

	San Diego	Santa Cruz	Los Angeles
Start of outbreak	11/2016	4/2017	9/2017
Cases	546	76	11
Deaths	20	1	0
Homeless or illicit drug use (%)	69%	81%	55%
Hospitalized (%)	68%	43%	73%
HCV or HBV coinfection (%)	19%	39%	-
Male (%)	68%	63%	91%
Median age (years)	43	37	40

Low coverage rates, HAV + HBV vaccines

2014 and 2015 National Health Interview Surveys
Adults aged ≥ 18 years self-reporting receipt of vaccines

HAV

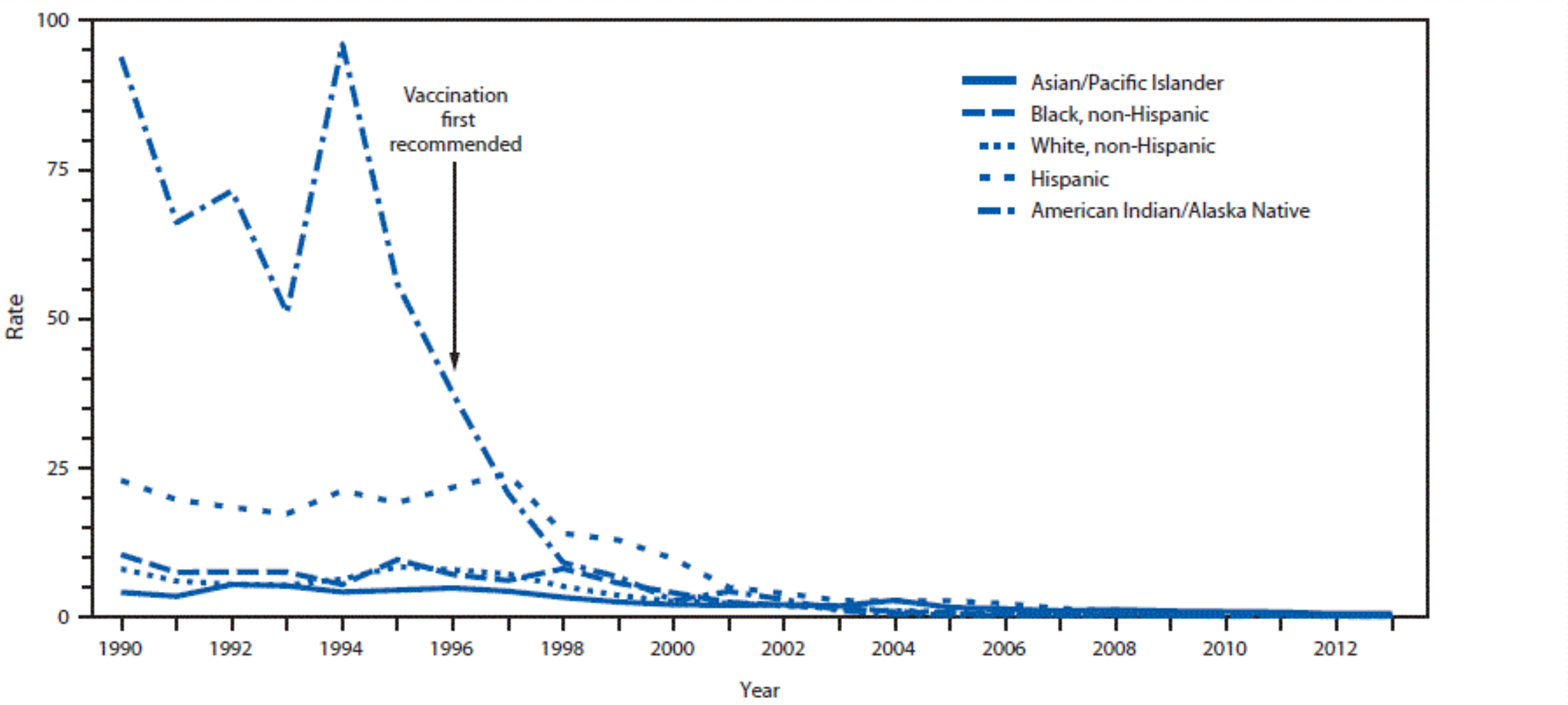
- 19% ≥1 dose 12% ≥2 doses Chronic Liver Disease (CLD)
- 15% ≥1 dose 9% ≥2 doses No CLD

HBV

- 36% ≥1 dose 29% ≥3 doses CLD
- 30% ≥1 dose 25% ≥3 doses No CLD

Yue X et al., Vaccine 2018;36:1183 https://doi.org/10.1016/j.vaccine.2018.01.033

Incidence* of reported acute hepatitis A cases, by race/ethnicity — National Notifiable Diseases Surveillance System, U.S., 1990–2013



* Rate per 100,000 population.

CDC, 2016: https://www.cdc.gov/mmwr/volumes/65/su/su6501a6.htm

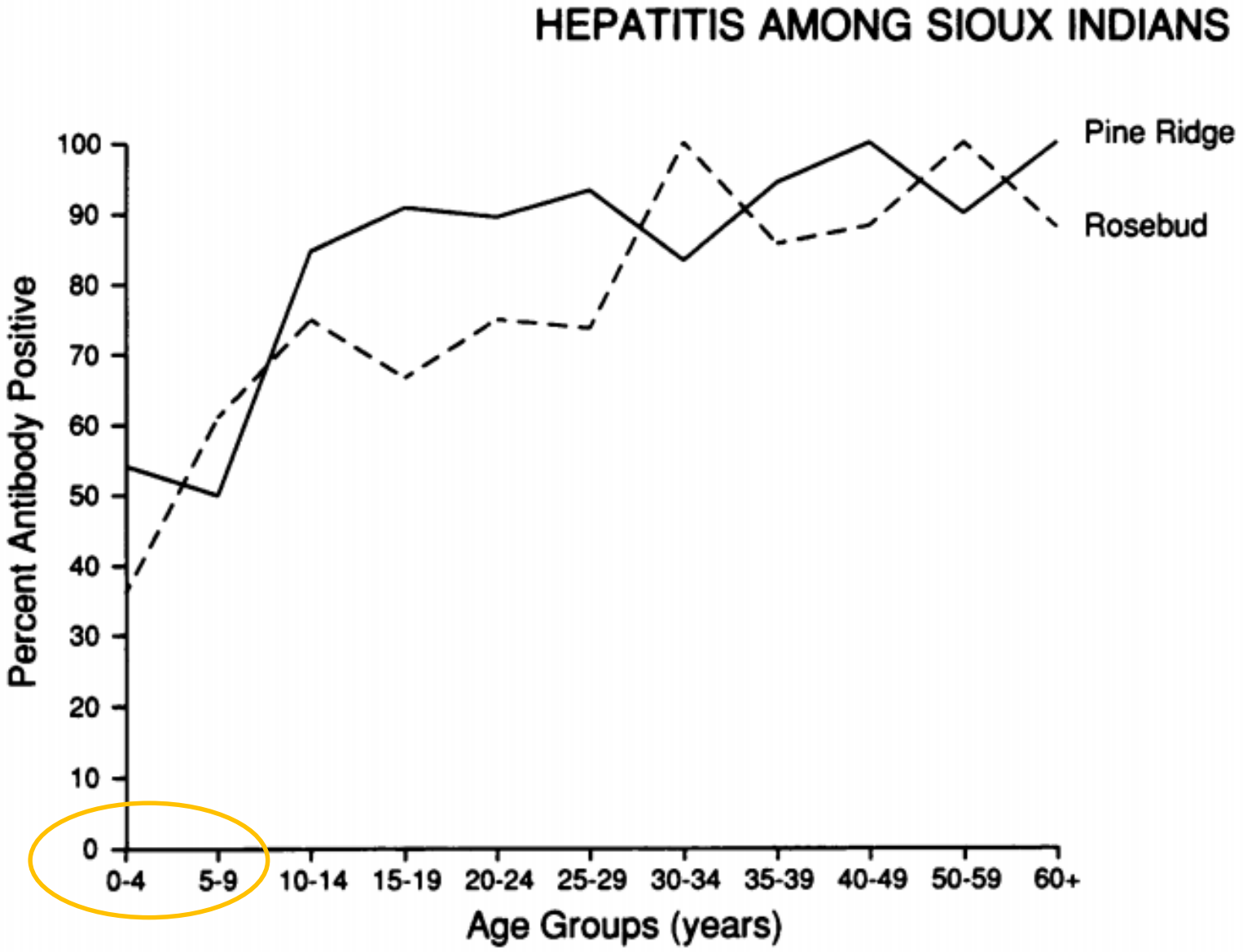


FIGURE 3—Anti-HAV Prevalence by Age Group, Pine Ridge and Rosebud Reservations, South Dakota, June 1985

Shaw FE et al. Am J Public Health. 1990 September; 80(9): 1091–1094.

ACIP Updates – Adult Hepatitis B Prevention

- Reminder to vaccinate persons with chronic liver disease
  - Hepatitis C virus [HCV] infection
  - Cirrhosis
  - Fatty liver disease
  - Alcoholic liver disease
  - Autoimmune hepatitis
  - ALT or AST level greater than twice the upper limit of normal

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

New Hepatitis B Vaccine for Adults

- Single-antigen HepB (HEPLISAV-B, Dynavax Technologies Corp.)
- 11/2017: Licensed by FDA for persons ≥ 18y years of age
- 2/2018: ACIP voted to recommend – published recommendations to follow
- Joins other inactivated HBV vaccines in U.S
  - Engerix-B, Recombivax HB, Pediarix, Twinrix

- Yeast-derived recombinant HBsAg
- 1018 adjuvant
  - 22-mer oligonucleotide sequence containing CpG that binds Toll-like receptor 9 to stimulate directed immune response
- 2 doses given at least 1 month apart

Heplisav-B – Seroprotection and Safety

- Immunogenicity
  - Healthy: 90%–100% vs. 71%–90% (3 doses Engerix-B)
  - Diabetes Type II: 90% vs. 65% (3 doses Engerix-B)
  - Chronic kidney disease: 90% (3 doses) vs. 81% (4 double doses Engerix-B)
- Safety and reactogenicity
  - Mild adverse events 46% vs. 46% (Engerix-B)
  - Serious adverse events 5% vs. 6% (Engerix-B)
  - Cardiovascular events 0.27% vs. 0.14% (Engerix-B)
  - Potentially immune-mediated events (e.g., granulomatosis + polyangiitis, Graves' disease) 0.1%–0.2% vs. 0%–0.7% (Engerix-B)

Jackson S, Lentino J, Kopp J, et al. Immunogenicity of a two-dose investigational hepatitis B vaccine, HBsAg-1018, using a toll-like receptor 9 agonist adjuvant compared with a licensed hepatitis B vaccine in adults. Vaccine 2017; 36:668-74

Janssen R, Bennett S, Namini H, et al. Immunogenicity and Safety of Two Doses of Investigational Heplisav Compared to Three Doses of Licensed Hepatitis B Vaccine (Engerix-B) in Two Phase 3 Trials. Journal of Hepatology 2013; 58(Suppl 1):S574

HEPLISAV-B™ [Hepatitis B Vaccine (Recombinant), Adjuvanted] package insert. https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM584762.pdf

Meningococcal Vaccines–High-risk Populations

Different vaccines protect against different serogroups.

Risk groups:
- **Exp. Increased Exposure to meningococcal serogroups covered by vaccines** (due to outbreaks[1], travel to affected areas [e.g. the Hajj], lab exposure)
- **CD. Persistent Complement component Deficiencies** (including persons taking eculizumab [Soliris®])
- **Asp. Functional or Anatomic Asplenia** (including sickle cell disease)
- **HIV. HIV Infection**

Age at first dose	Exp	CD	Asp	HIV	1) MenACWY vaccines[2]	Boosters for those who remain at increased risk
2–6 months	✓	✓	✓	✓	2 months: **ACWY-CRM** Menveo® → 4 months: **ACWY-CRM** Menveo® → 6 months: **ACWY-CRM** Menveo® → 12–15 months: **ACWY-CRM**[3] Menveo®	
7–23 months	✓	✓	✓	✓	**ACWY-CRM** Menveo® → 3 months → **ACWY-CRM**[3] Menveo®	If primary dose(s) given when younger than 7 years: 3 years → **ACWY-CRM or -D**[6] Menveo® or Menactra® → Every 5 years → **ACWY-CRM or -D** Menveo® or Menactra®
9–23 months	✓	✓			**ACWY-D**[4,5,6] Menactra® → 3 months → **ACWY-D**[3,6] Menactra®	
2 years and older		✓	✓[5]	✓[5]	**ACWY-CRM or -D**[5,6] Menveo® or Menactra® → 2 months → **ACWY-CRM or -D**[6] Menveo® or Menactra®	If primary dose(s) given at age 7 years or older: Every 5 years → **ACWY-CRM or -D** Menveo® or Menactra®
	✓				**ACWY-CRM or -D**[5,6] Menveo® or Menactra®	

2) Also give MenB vaccine—may be given at same time as MenACWY vaccine. Use the same brand for each dose in the series.

10 years and older	✓	✓	✓		1st dose **MenB-4C** Bexsero® → 1 month → 2nd dose **MenB-4C** Bexsero®	**OR** 1st dose **MenB-FHbp** Trumenba® → 1–2 months → 2nd dose **MenB-FHbp** Trumenba® → 6 months between 1st and 3rd dose → 3rd dose **MenB-FHbp** Trumenba®

http://eziz.org/assets/docs/IMM-1218.pdf

CDPH

Pneumococcal Vaccine Timing–For Children

A. Chronic conditions:

- **Diabetes**
- **Heart Disease** (particularly failure or cyanotic disease)
- **Lung disease** (excluding asthma, unless immunocompromised by prolonged high-dose oral corticosteroids – see below)

PPSV 23 Pneumovax® 23

Children younger than 6 years of age should have received the standard or catch-up doses of PCV13 described above before receiving PPSV23.

B. Immunocompromised (including HIV infection or immunosuppressive treatments), **Hemoglobinopathy** (including sickle cell disease), **Asplenia, Chronic renal failure, or Nephrotic syndrome**

PCV 13 → 8 weeks → PPSV 23 → 5 years → PPSV 23

C. CSF leaks or Cochlear implants

PCV 13 → 8 weeks → PPSV 23

eziz.org/assets/docs/IMM-1159.pdf

CDPH CDPH

HPV Vaccine – 2 or 3 Doses?

9-14 YEARS[1] — 2 DOSES

Routine: 11-12 years

As early as 9 years
Catch-up at 13-14 years

HPV9 Gardasil-9® → 6–12 months[2] → HPV9 Gardasil-9®

15+ YEARS[4] OR COMPROMISED IMMUNE SYSTEM[3] — 3 DOSES

15–26 years[4]

OR

9–14 years with a compromised immune system[3]

HPV9 Gardasil-9® → 1–2 months[5] → HPV9 Gardasil-9® → 6 months between 1st and 3rd dose → HPV9 Gardasil-9®

http://eziz.org/assets/docs/IMM-1254.pdf

Thank you - Questions?

Many thanks to following CDC staff for sharing their slides:

- Kathleen Dooling, MD MPH – Zoster
- David Kim, MD – Hepatitis B

EXTRAS