

Updates from the February 2023 ACIP Meeting

Melinda Wharton, MD, MPH

Executive Secretary, Advisory Committee on Immunization Practices

National Network of Immunization Coalitions

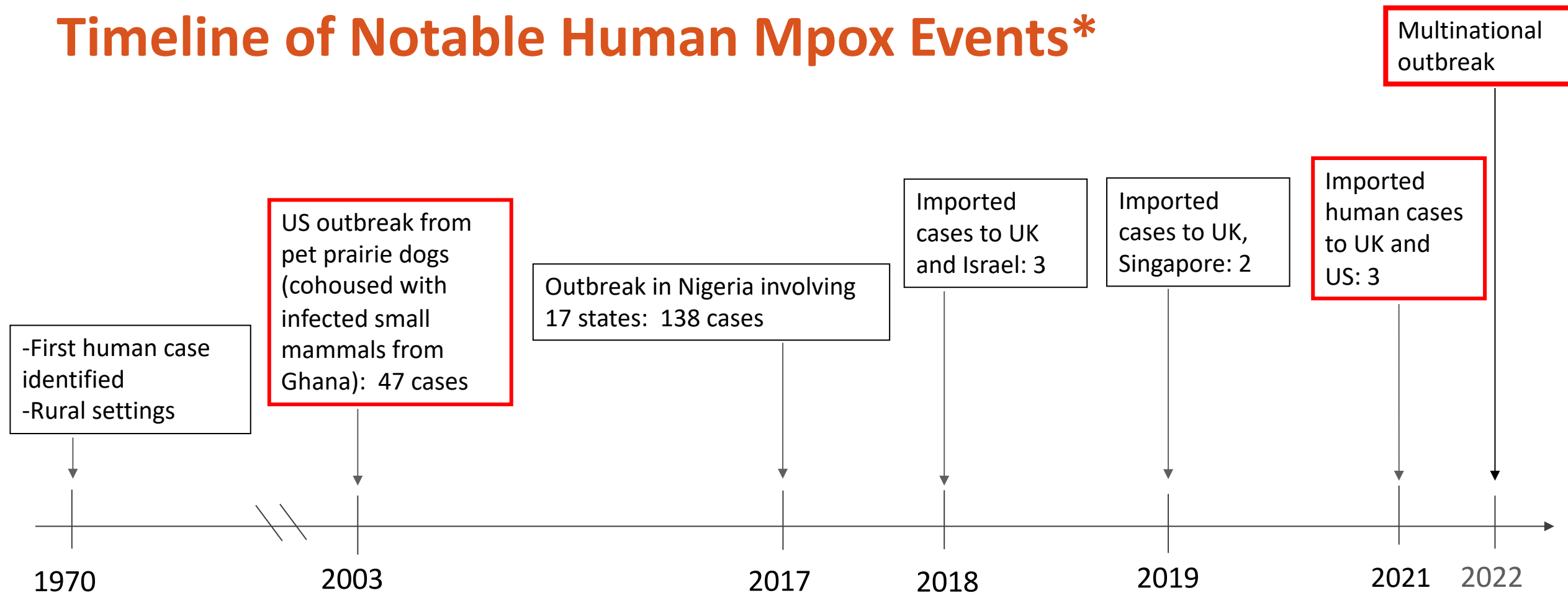
April 11, 2023

Mpox Vaccine

Mpox

- Rare, sometimes life-threatening infection
- Endemic in parts of west and central Africa
- Caused by monkeypox virus (which is an orthopoxvirus)
- Can spread from infected animals to people and then person-to-person
 - Respiratory secretions
 - Skin-to-skin contact with infected bodily fluids (e.g., fluid from lesions)
 - Fomites (e.g., shared towels, clothing, and bedding)

Timeline of Notable Human Mpox Events*

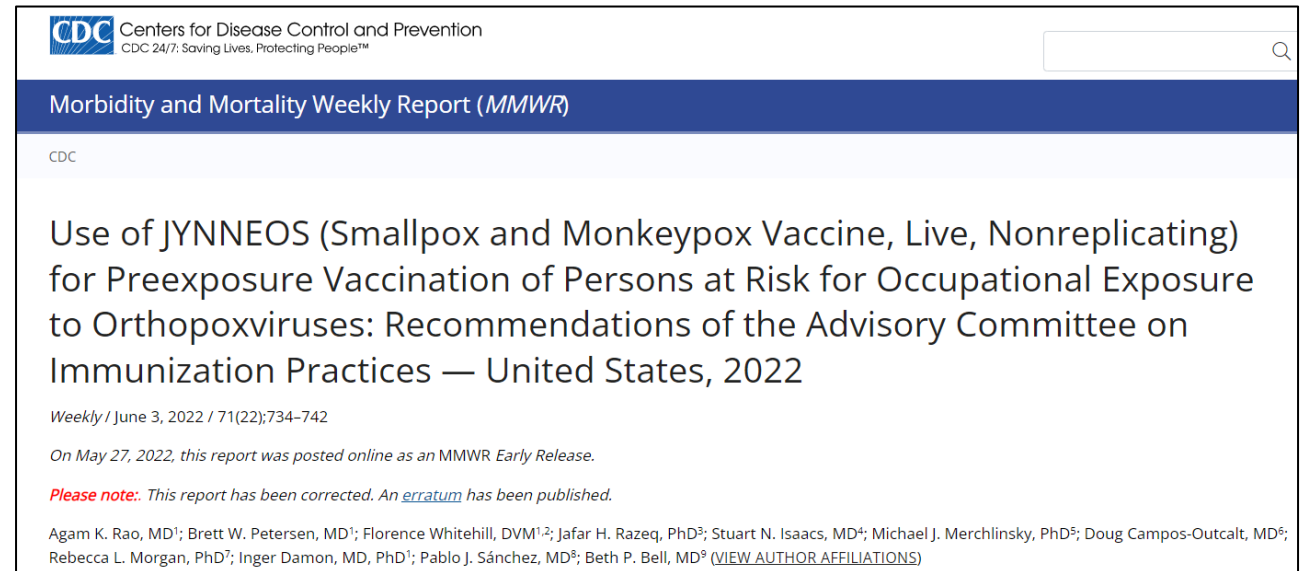


*During 1970-2021, mpox was known to be endemic in 9 African countries: Cameroon, Central African Republic, Cote d'Ivoire, Democratic Republic of Congo, Gabon, Liberia, Nigeria, Republic of Congo, and Sierra Leone; during recent years, there has been a re-emergence of human cases after decades of no reported cases

2021 ACIP Orthopoxvirus Vaccine Vote

- Use of orthopoxvirus vaccine, JYNNEOS, (licensed in 2019) for pre-exposure vaccination of people at occupational risk for orthopoxvirus exposures
- 2-dose series, subcutaneous administration
- Recommendations published June 3, 2022*

**Currently no ACIP
recommendation for use of
JYNNEOS during outbreaks**

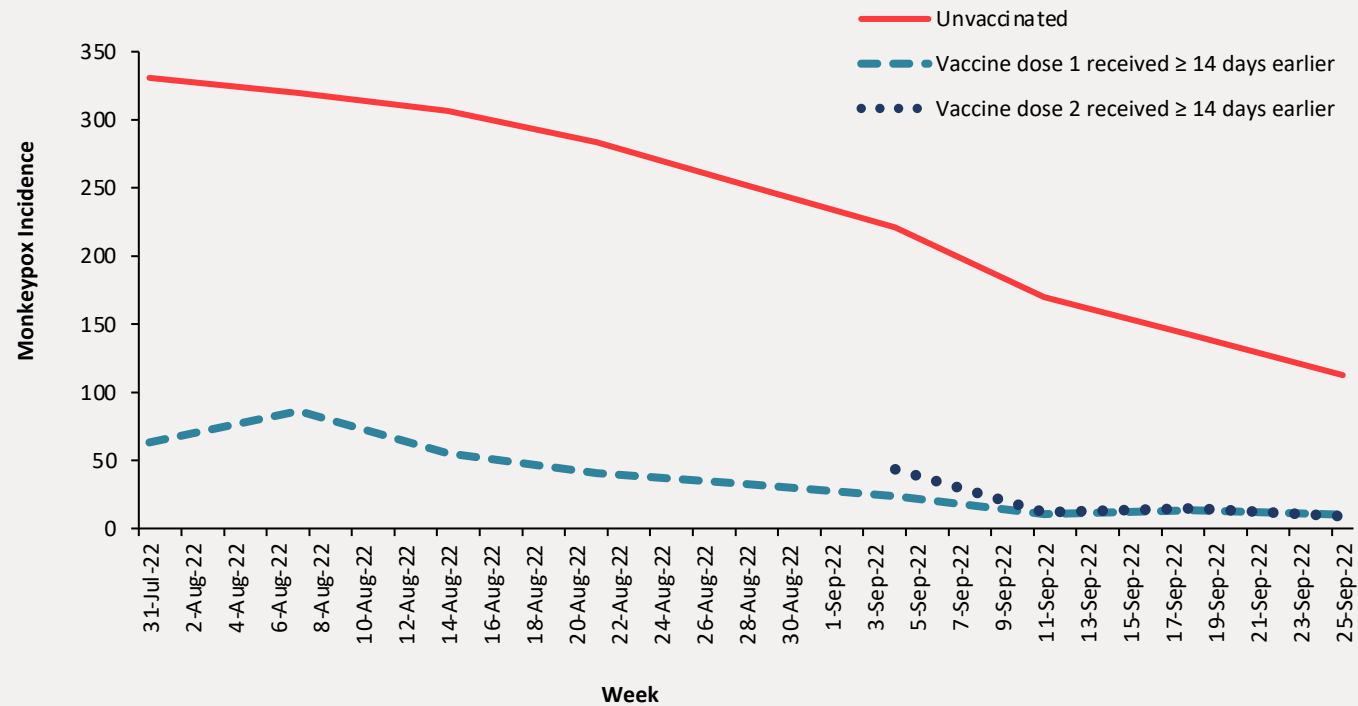


The screenshot shows the CDC website header with the logo and tagline "CDC 24/7: Saving Lives. Protecting People™". Below the header is a blue bar with the text "Morbidity and Mortality Weekly Report (MMWR)". The main content area has a light blue background and features the title "Use of JYNNEOS (Smallpox and Monkeypox Vaccine, Live, Nonreplicating) for Preexposure Vaccination of Persons at Risk for Occupational Exposure to Orthopoxviruses: Recommendations of the Advisory Committee on Immunization Practices — United States, 2022". Below the title is the date "Weekly / June 3, 2022 / 71(22);734–742" and a note "On May 27, 2022, this report was posted online as an MMWR Early Release." A red "Please note:" section states "This report has been corrected. An [erratum](#) has been published." At the bottom, a list of authors is provided: "Agam K. Rao, MD¹; Brett W. Petersen, MD¹; Florence Whitehill, DVM^{1,2}; Jafar H. Razeq, PhD³; Stuart N. Isaacs, MD⁴; Michael J. Merchlinsky, PhD⁵; Doug Campos-Outcalt, MD⁶; Rebecca L. Morgan, PhD⁷; Inger Damon, MD, PhD¹; Pablo J. Sánchez, MD⁸; Beth P. Bell, MD⁹ ([VIEW AUTHOR AFFILIATIONS](#))".

*<https://www.cdc.gov/mmwr/volumes/71/wr/mm7122e1.htm>

Weekly mpox incidence,* by vaccination status among males aged 18–49 years eligible for vaccination§

July 31, 2022 – October 1, 2022 (43 U.S. jurisdictions**)



Mpox incidence among unvaccinated individuals was **7.4 (95% CI = 6.0–9.1)** times as high as **persons receiving 1 dose of JYNNEOS vaccine.**

Mpox incidence among unvaccinated individuals was **9.6 (95% CI = 6.9–13.2)** times as high as **persons receiving 2 doses of JYNNEOS vaccine.**

No difference observed in vaccine performance **between subcutaneous and intradermal administration.**

* Cases per 100,000 population. Rate in vaccinated persons = number of probable or confirmed cases reported to CDC with date of illness onset, specimen collection, lab test completion, admission, diagnosis, discharge, case investigation start date, or date first electronically submitted or reported to the county, state, or public health department (earliest available date) ≥14 days after receiving the first dose or second dose of JYNNEOS vaccine among total vaccinated population as of 2 weeks previously. Rate in unvaccinated persons = number of probable or confirmed cases reported to CDC without evidence of vaccination among total unvaccinated population.

§ Gay, bisexual, and other men who have sex with men who have HIV infection or who are eligible to receive HIV preexposure prophylaxis were considered eligible for vaccination.

¶ Alabama, Alaska, California, Colorado, Connecticut, District of Columbia, Florida, Georgia, Hawaii, Idaho, Illinois, Iowa, Kansas, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Michigan, Minnesota, Mississippi, Missouri, Montana, Nevada, New Hampshire, New Mexico, New York (excluding New York City), North Dakota, Ohio, Oklahoma, Oregon, Pennsylvania, Puerto Rico, Rhode Island, South Carolina, South Dakota, Tennessee, Utah, Vermont, Virginia, West Virginia, Wisconsin, and Wyoming.

** Jurisdictions were included if age and sex assigned at birth or gender identity was available for ≥70% of cases reported, vaccination status was available for ≥50% of cases in males (defined by either sex assigned at birth or gender identity) aged 18–49 years or the jurisdiction confirmed cases were linked to immunization registry entries, and de-identified vaccination administration data were submitted to CDC.

ACIP vote

ACIP recommends the 2-dose* JYNNEOS vaccine series for persons aged 18 years and older at risk of mpox during an mpox outbreak[§]

*Dose 2 administered one month after dose 1

[§] Public health authorities determine whether there is an mpox outbreak; a single case may be considered an mpox outbreak at the discretion of public health authorities. Other circumstances in which a public health response may be indicated include ongoing risk of introduction of mpox into a community due to disease activity in another geographic area.

Seasonal Influenza Vaccines

Summary as of the Week Ending February 11, 2023

- U.S. influenza activity rose early, peaking nationally during late November/early December
 - Percent of tests positive peaked at ~26%; currently ~1.7%
- Influenza A(H3N2) viruses have predominated, with co-circulation of influenza A(H1N1)pdm09 viruses.
- The cumulative influenza-associated hospitalization rate has leveled in recent weeks to ~59/100,000
- 111 influenza-associated pediatric deaths reported this far this season.
- Overall influenza activity is increased compared with the previous two seasons.
- U.S. influenza activity is currently low.

Summary of Vaccine Effectiveness from Three Flu VE Networks*

- Across three Flu VE platforms, we observed **consistent influenza vaccine effectiveness** during the 2022-2023 season.
- Influenza **vaccination provided substantial protection** against inpatient, emergency department, and outpatient illness **among all ages**.
- Influenza **vaccination provided substantial protection among important high-risk groups** (ages 65+ and immunocompromised).

*Data from the New Vaccine Surveillance Network (NVSN), Flu and Other Viruses in the Acutely Ill Network (IVY), & VISION Network

Vaccine effectiveness against laboratory confirmed influenza A* in hospital and ED settings, September 13, 2022–January 25, 2023**

	Vaccine Effectiveness							
	Influenza positive		Influenza negative ¹		Unadjusted		Adjusted ²	
	N vaccinated /Total	(%)	N vaccinated /Total	(%)	VE %	95% CI	VE %	95% CI
Influenza A								
All 6 mos – 17 years	123/640	19	750/2256	33	52	(41 to 62)	49	(36 to 60)
Inpatient	19/131	15	288/913	32	63	(39 to 78)	68	(46 to 81)
ED	104/507	21	461/1330	35	51	(38 to 62)	42	(25 to 56)
A/H3N2	98/478	21	750/2256	33	48	(34 to 59)	45	(29 to 58)
A/H1N1	23/139	17	750/2256	33	60	(37 to 75)	56	(28 to 72)

* Of 335 influenza-positive specimens sequenced, 250 were A(H3N2) clade 3C.2a1b.2a.2b and 32 were clade 3C.2a1b.2a.2a.1 and 38 were A(H1N1) clade 6B.1A.5a.2a.1. There were 16 coinfections with Influenza and SARS-CoV-2 that were excluded from the VE estimate.

** Site specific influenza seasons were determined from local influenza activity at each site.

¹ Persons testing negative for both influenza and SARS-CoV-2 using molecular assays.

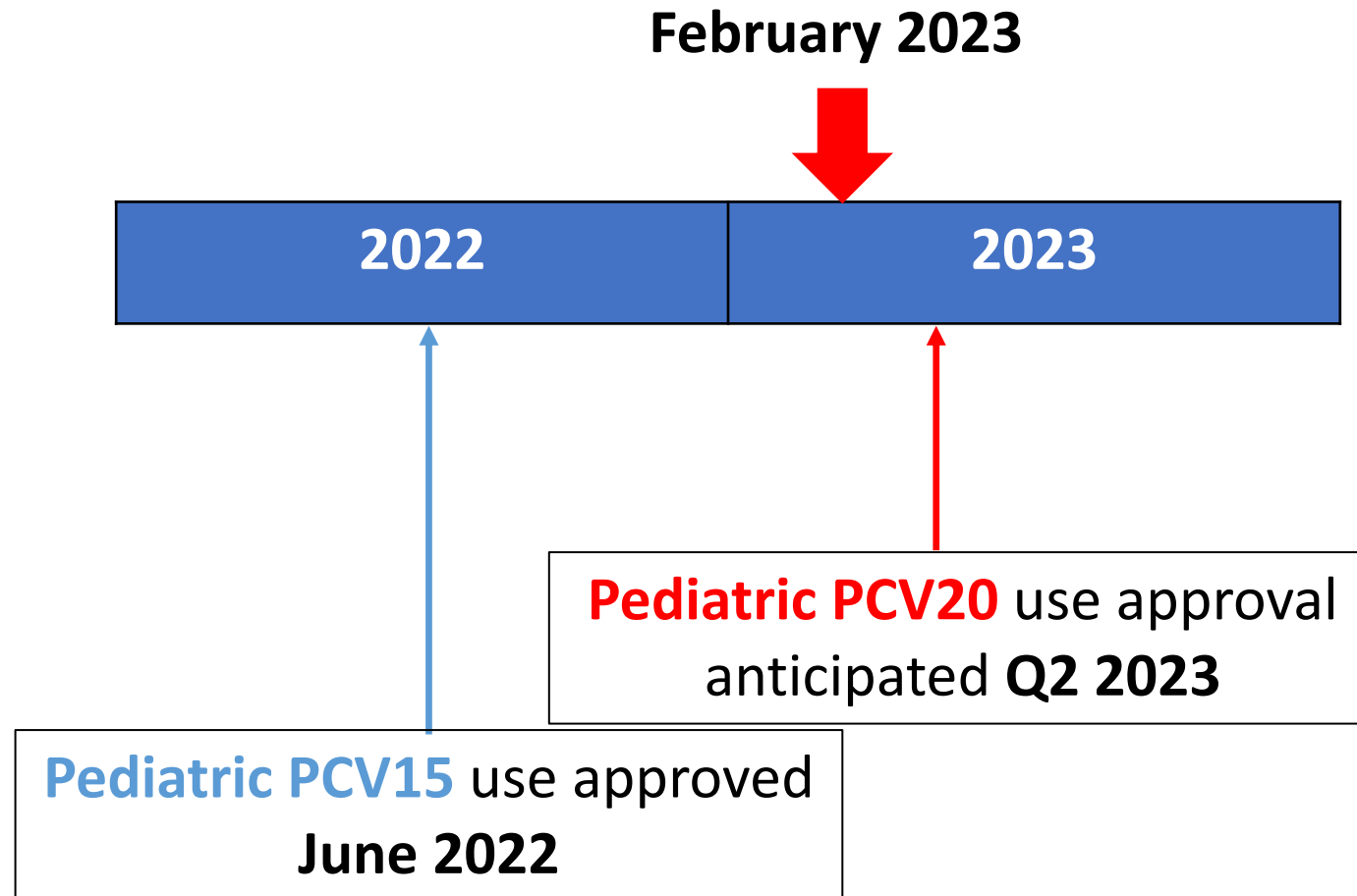
² Multivariable logistic regression models adjusted for site, age, and calendar time.

Pneumococcal Vaccines

Pneumococcal vaccines currently recommended for use in the United States

	Recommended for children	Recommended for adults
Pneumococcal conjugate vaccines		
PCV13	✓	
PCV15	✓	✓
PCV20		✓
Pneumococcal polysaccharide vaccine		
PPSV23	Risk-based recommendations	If previously received PCV13 or PCV15

Approval of PCV20 use among Children Anticipated in 2023



Policy questions considered by the Work Group

- Should **PCV20** be recommended as an option for pneumococcal conjugate vaccination **according to currently recommended dosing and schedules, for U.S. children aged <2 years?**
- Should **PCV20 without PPSV23** be recommended as an option for pneumococcal vaccination **for U.S. children aged 2–18 years with underlying medical conditions that increase the risk of pneumococcal disease?**

Benefits and Harms

Do the desirable effects outweigh the undesirable effects?

- Routine PCV20 use for children aged <2 years

Favors Intervention (PCV20):

- PCV20 is expected to prevent more disease compared with current PCVs (PCV13, PCV15)

Favors Both (PCV20 or PCV13/PCV15):

- Clinical implications of the **lower** immunogenicity PCV20 compared with PCV13 unknown
- Clinical implications of **improved** immunogenicity of PCV15 against serotype 3* unknown

Meningococcal Vaccines

ACIP is discussing two MenABCWY vaccines

	MenACWY component	MenB component	Status
Pfizer	Nimenrix™*	Trumemba®§	Could be licensed October 2023
GSK	Menveo§	Bexero§	Regulatory submission expected 2 nd half 2023

*not licensed in the United States

§ licensed in the United States

Vaccine	Birth	1 mo	2 mos	4 mos	6 mos	9 mos	12 mos	15 mos	18 mos	19–23 mos	2–3 yrs	4–6 yrs	7–10 yrs	11–12 yrs	13–15 yrs	16 yrs	17–18 yrs
Meningococcal (MenACWY-D ≥9 mos, MenACWY-CRM ≥2 mos, MenACWY-TT ≥2years)			See Notes											1 st dose		2 nd dose	
Meningococcal B (MenB-4C, MenB-FHbp)														See Notes			

Policy Questions for Each Pentavalent Vaccine

- Should the pentavalent vaccine be included as an option for MenACWY/MenB vaccination in people currently recommended to receive both vaccines?
 - For example, 16 year olds¹
- Should the pentavalent vaccine be included as an option for people currently recommended to receive MenACWY only?
 - For example, 11–12 year olds
- Should the pentavalent vaccine be included as an option for people currently recommended to receive MenB only?
 - For example, during a serogroup B outbreak

¹ 16 year olds who decide to receive the MenB vaccine based on shared clinical decision-making

Work Group Reflections and Next Steps

- Pfizer's MenABCWY vaccine appears to be noninferior to MenACWY+MenB based on clinical trial data presented
- Data gaps
 - 3-dose schedule for high-risk populations
 - Adults older than 25 years
- Next steps
 - Reviewing additional immunologic persistence data for a single dose
 - GRADE and EtR — will focus on pentavalent vaccine studies
 - Cost effectiveness study will be conducted

Proposed Timeline of ACIP Presentations



*if licensed by FDA

Polio Vaccines

Proposed Language for Unvaccinated and Incompletely Vaccinated Adults

- Majority of work group believe pros of uniform recommendation outweigh cons; approximately 1/3 favor maintaining the current risk-based recommendation

Majority Recommendation:

Adults who are known or suspected to be unvaccinated or incompletely vaccinated against polio should complete a primary vaccination series with IPV.

Clinical Considerations:

In general, unless there are specific reasons to believe they were not vaccinated, most adults who were born and raised in the United States can assume they were vaccinated against polio as children.

Strong Majority of Work Group Agree with Current Recommendation for Adult IPV Booster

- Risk-based
- Shared clinical decision-making

Proposed Language:

- Adults who have received a primary series of tOPV or IPV in any combination and who are at increased risk of poliovirus exposure may receive another dose of IPV. Available data do not indicate the need for more than a single lifetime booster dose with IPV for adults.

Respiratory Syncytial Virus Vaccines

RSV is the leading cause of hospitalization in U.S. infants

- Most (68%) infants are infected in the first year of life and nearly all (97%) by age 2¹
- Premature infants born at <30 weeks gestation had hospitalization rates ~3x higher than term infants²
 - Preterm infants have higher rates of ICU admission, mechanical ventilation³
 - Average cost of hospitalization in infant <29 weeks ~4x higher than for term infant³
- 79% of children hospitalized with RSV aged <2 years had no underlying medical conditions²
- 2-3% of all infants will be hospitalized for RSV^{2,4}



Image: Goncalves et al. Critical Care Research and Practice 2012

¹Glezen et al, Arch Dis Child, 1986; ²Hall et al, Pediatrics, 2013; ³McLaurin et al, J Perinatol, 2016; ⁴Langley & Anderson, PIDJ, 2011

RSV is a major cause of severe illness in older adults

- Frequent, often unrecognized, cause of severe respiratory illnesses
- Lower awareness of RSV in adults among healthcare providers and the public
- Likely under-detected, with RSV testing often not performed
- Burden of severe disease may be comparable to influenza, with variability across seasons
- Adults with co-morbidities, immunocompromised adults, and long-term care facility residents may be particularly at risk for severe illness
- High proportion of those hospitalized with RSV have severe outcomes, including ICU admission and death
- Long-term health consequences

Products ACIP is discussing for prevention of RSV

- Recombinant protein subunit vaccines using the prefusion conformation of the RSV F protein
 - Pfizer: RSV bivalent prefusion F vaccine (RSVpreF)
 - GSK: RSV prefusion F vaccine with AS01_E adjuvant (RSV-PreF3)
- Long acting monoclonal antibody against the prefusion RSV F protein
 - Sanofi/AstraZeneca: nirsevimab

Product	Infant	Maternal	Older adult
Nirsevimab	✓		
RSVpreF		✓	✓
RSV-PreF3			✓

Policy Questions - Nirsevimab

- Should one dose of nirsevimab be recommended a) at birth for all infants born during October to March and b) when entering first RSV season and <8 months of age for all infants born during April through September?
- Should one dose of nirsevimab be recommended for children <20 months of age with increased risk of severe disease entering their second RSV season?

Work Group Considerations - 1st RSV season

- The Work Group supports recommending nirsevimab a) at birth for all infants born during October to March and b) when entering first RSV season and <8 months of age for all infants born during April through September
- Many expressed concerns about feasibility and equity, particularly because inclusion in the Vaccines for Children program is unknown
- Some members of the Work Group expressed concern that at higher prices, nirsevimab may not be a reasonable and efficient allocation of resources
 - The price of the product (which is not yet licensed) is unknown

Work Group Considerations - 2nd RSV season

- WG would like more time to consider which infants and children would be sufficiently high risk to warrant nirsevimab in their 2nd RSV season
 - Limited efficacy and safety data
 - Limited data to measure the risk of severe disease in the 2nd RSV season
 - At this time, WG recommended nirsevimab for those who are eligible for palivizumab in their 2nd RSV season, since assumed to be cost effective
 - WG will continue to evaluate other conditions

Policy Question – Pfizer RSV Vaccine in Pregnancy

- Should the Pfizer RSV bivalent prefusion F vaccine be recommended for all pregnant people as a single dose given at 24–36 weeks gestation?
- This recommendation would be considered in the context of the current standard of care for prevention of RSV disease in infants at the time of ACIP vote.

Key considerations regarding RSV bivalent prefusion F vaccine: timing of dose within pregnancy

- Dosing window in the trial was 24 through 36 weeks gestation
- Currently there are no data available on efficacy stratified by gestational age at time of administration
- Majority of infants in phase 3 trial were born ≥ 37 weeks gestation (94% in RSV bivalent preF arm and 95% in placebo arm)
- Most doses in the phase 3 trial were given at ≥ 28 weeks gestation
 - 25% doses given at ≥ 24 to < 28 weeks
 - 30% doses given at ≥ 28 to < 32 weeks
 - 45% doses given at ≥ 32 to < 37 weeks
 - 0.1% doses given at ≥ 37 weeks

Key considerations for RSV bivalent prefusion F vaccine: number of total lifetime doses

- All pregnant people in the trial received their first and only dose of RSV vaccine
- Currently there are no data available on
 - Efficacy of the first lifetime dose during subsequent pregnancies
 - Safety of additional doses given in subsequent pregnancies

Policy Questions – RSV Vaccines for Older Adults

- Possible policy recommendations* for RSV vaccination of U.S. older adults
 - Should RSV vaccines be recommended for U.S. adults aged ≥ 65 years?
 - Should RSV vaccines be recommended for U.S. adults aged ≥ 60 years?

*FDA has not yet completed review of safety and efficacy data for the GSK adjuvanted RSVpreF3 vaccine and the Pfizer bivalent RSVpreF vaccine. ACIP recommendations would be made only if the vaccines are approved and licensed by FDA.

Work Group interpretation

- GSK's adjuvanted RSVpreF3 and Pfizer's bivalent RSVpreF vaccines both have demonstrated significant efficacy against lower respiratory tract illness caused by RSV among older adults
 - Trials underpowered to show efficacy against RSV hospitalization
 - Groups at highest risk of severe RSV disease were under-represented in clinical trials
- At least one case of inflammatory neuropathy has been observed among recipients of each investigational vaccine
- If licensed, post licensure surveillance for both safety and vaccine effectiveness will be critical

Chikungunya Vaccine

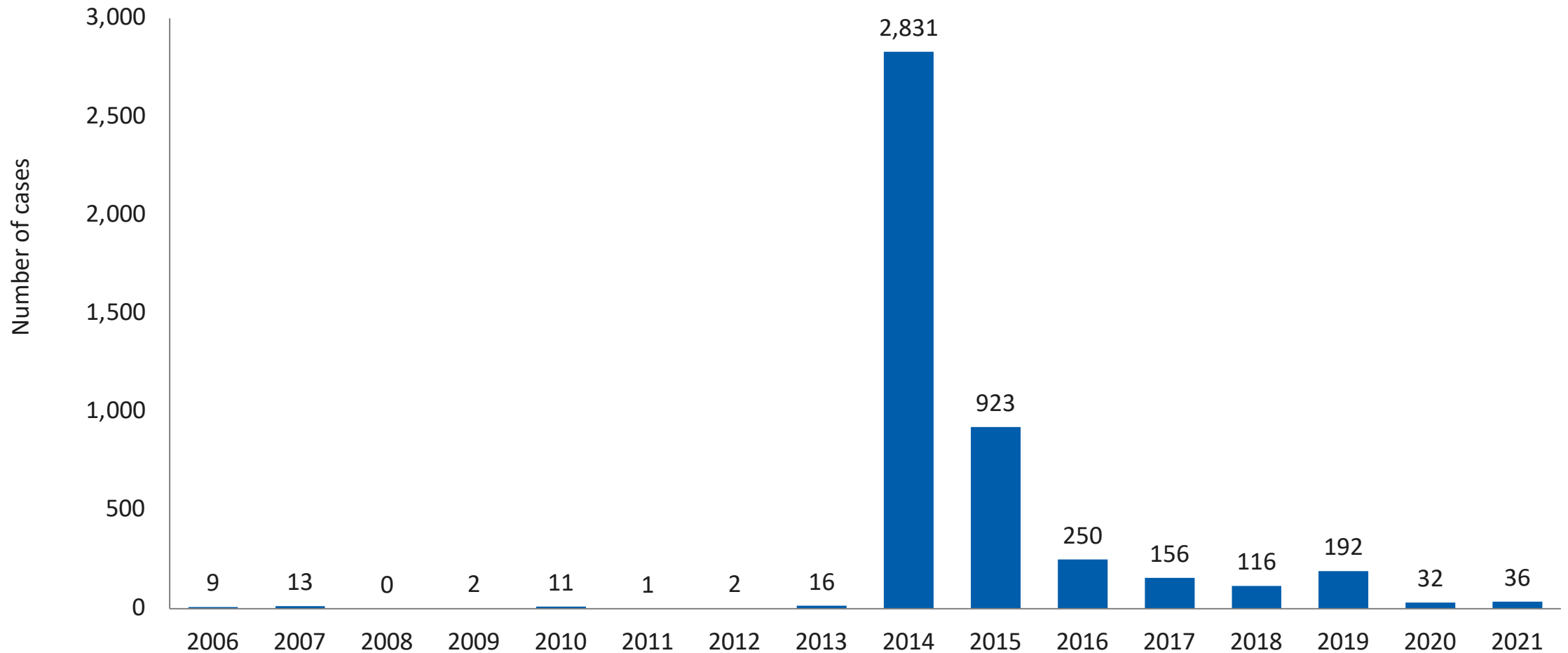
Chikungunya

- Mosquito-borne viral disease
 - Primarily human-mosquito-human transmission
 - Main vectors are *Aedes aegypti* and *Aedes albopictus*
- Clinically characterized by acute onset of fever and often severe polyarthralgia
- Acute symptoms typically resolve in 7-10 days; mortality is very rare
- Significant proportion of patients have continued or recurrent arthralgia in months and years following acute illness
- Risk factors for severe disease
 - Age >65 years
 - Underlying medical conditions
 - Neonate infected through intrapartum transmission

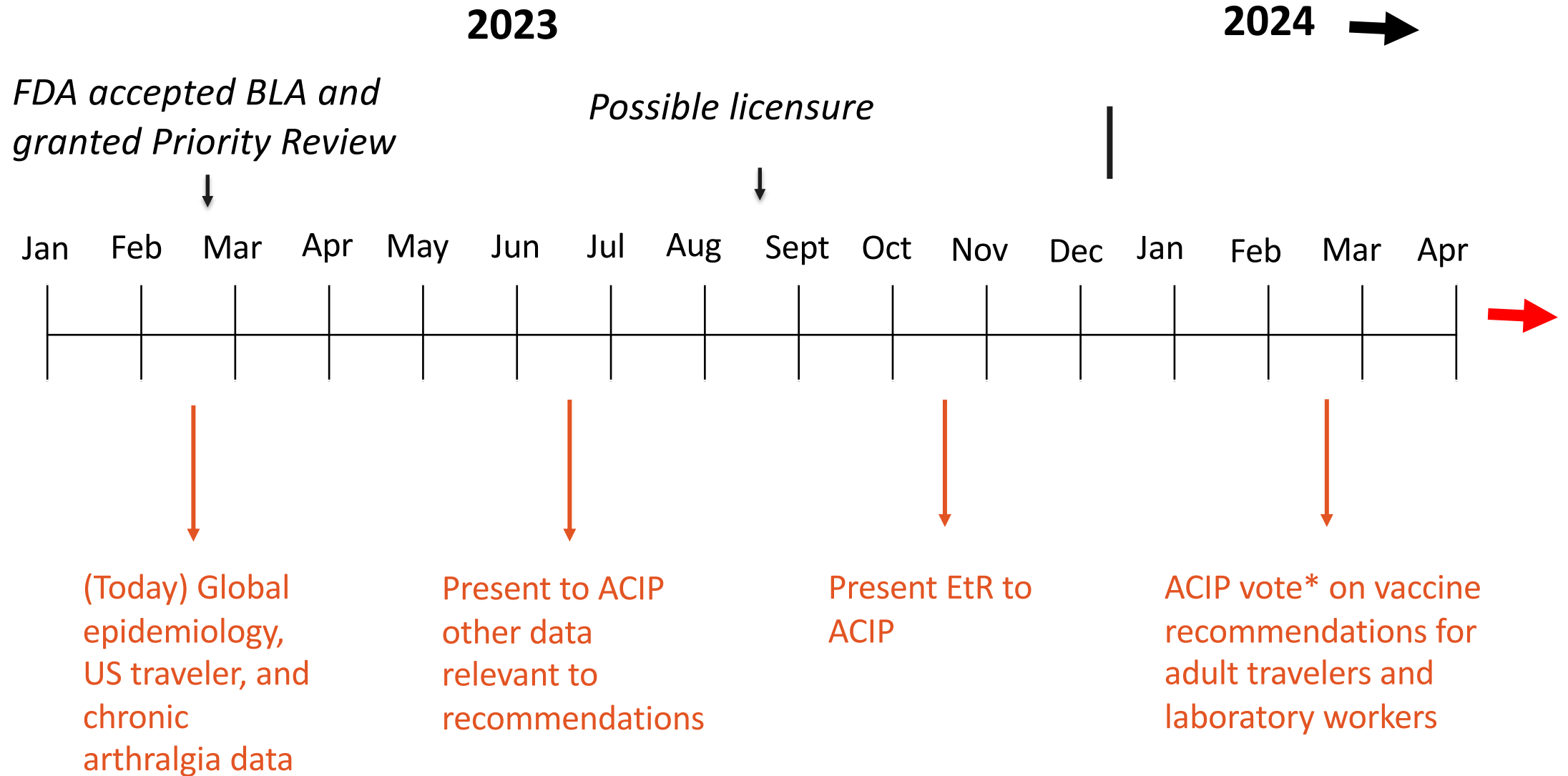
Chikungunya vaccine

- Live attenuated vaccine administered as a single dose (Valneva)
 - Based on La Reunion strain of East Central South African genotype
 - Attenuation by reverse genetics resulting in 60aa deletion within the nsP3 protein
- FDA has accepted Valneva's Biologics License Application (BLA) and granted priority review, with licensure possible in August 2023
- No chikungunya vaccine ever licensed in United States or globally
- Chikungunya Vaccines Work Group formed in May 2022 to develop policy options for ACIP's consideration for use of chikungunya vaccine among U.S. persons at risk of chikungunya, including
 - Travelers
 - Residents of U.S. territories and states with, or at risk of, transmission
 - Laboratory workers

Chikungunya virus disease cases in US travelers, 2006–2021 (N=4,590)



Work Group timeline (tentative)



*if licensed by FDA

Dengue Vaccines

Dengvaxia™ ACIP Recommendation June 2021



Three doses of Dengvaxia are indicated for the prevention of dengue disease caused by dengue virus serotypes 1, 2, 3, and 4 in people 9–16 years old with:

- laboratory confirmation of previous dengue virus infection

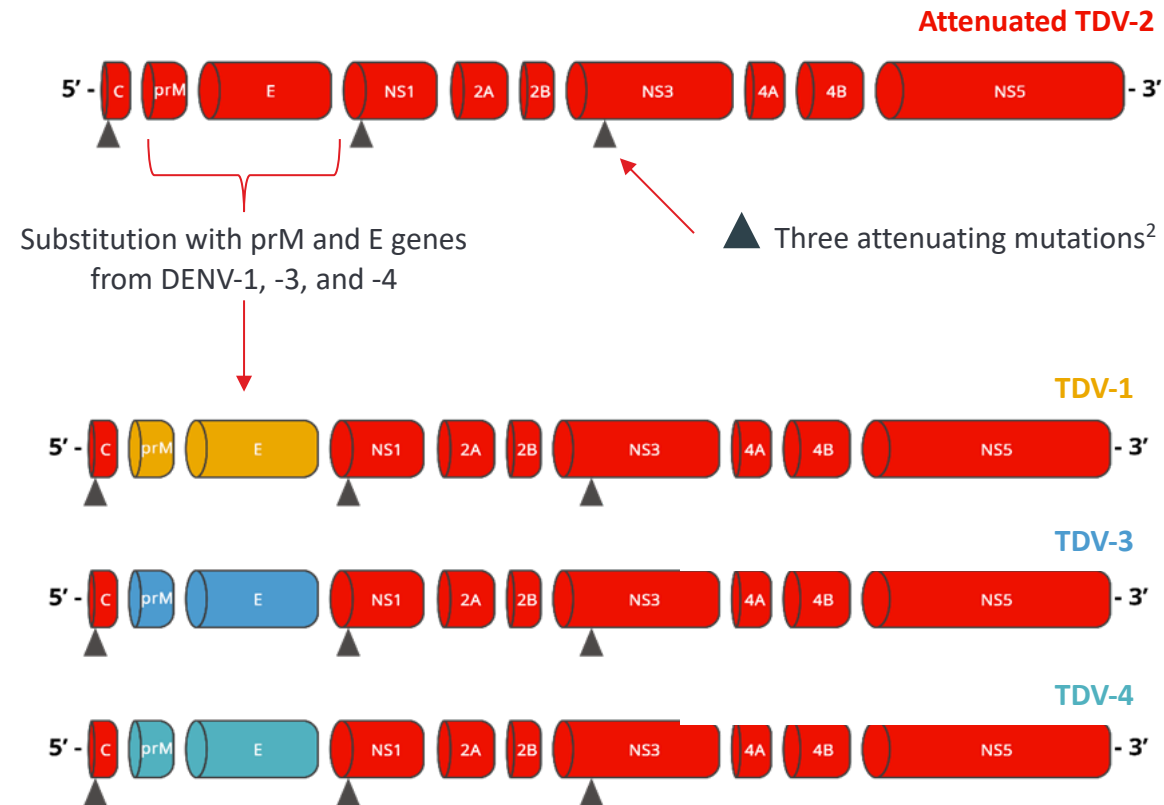
AND

- living in endemic areas.

TAK-003 is based on a live, attenuated DENV-2 virus backbone expressing E and prM proteins of all four DENV serotypes



Genetic structure and design of TAK-003¹⁻³



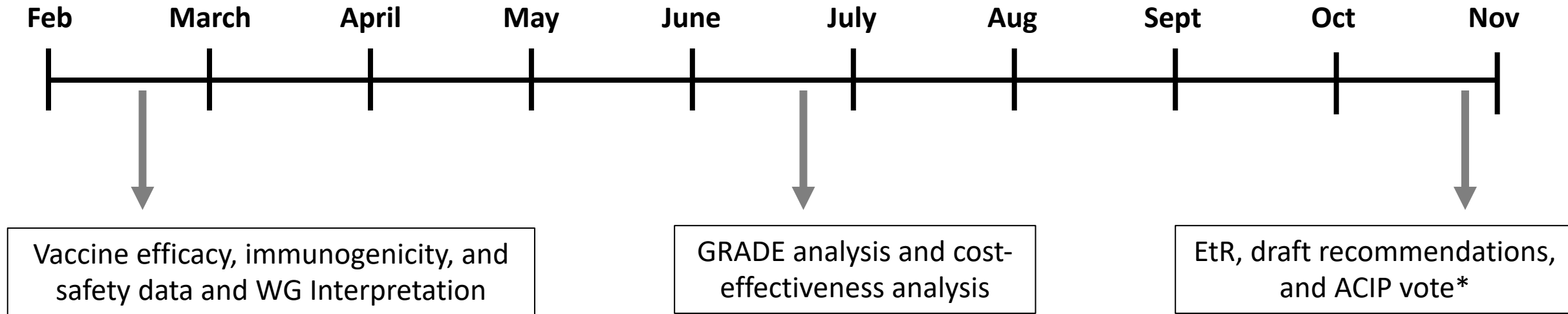
C, capsid; DENV, dengue virus; E, envelope; NS, non-structural; prM, pre-membrane; TDV, tetravalent dengue vaccine.

1. Osorio JE, et al. *Expert Rev Vaccines* 2016;15:497–508; 2. Osorio JE, et al. *Vaccine* 2015;33:7112–7120; 3. Patel SS, et al. *Clin Infect Dis* 2022. doi:10.1093/cid/ciac418 [Epub ahead of print].

Summary of Work Group Interpretation – TAK-003

- Protects **seropositive** recipients against VCD and hospitalization due to any serotype
- Protects **seronegative** recipients against VCD and hospitalization for DENV-1 or DENV-2
- Does **NOT** protect **seronegative** recipients against VCD for DENV-3 and DENV-4
- Vaccine efficacy against hospitalization for DENV-4 among **seronegative** recipients is unknown.
 - Only 1 DENV-4 hospitalization, limiting efficacy assessment
- No efficacy against hospitalization for DENV-3 among **seronegative** vaccine recipients compared to placebo (-87.9%; 95% CI: -573.4–47.6%)
 - Data insufficient to rule out an increased risk among vaccine recipients

Anticipated Timeline for TAK-003 Presentations to ACIP



*if licensed by FDA

COVID-19 Vaccines

Considerations for future planning

COVID-19 vaccines

Where we are now:

Current recommendations
Vaccination rates
Hospitalization rates

COVID-19 vaccines:
Where we are now

COVID-19 vaccines:
Where we are going

Goal:
Simple
recommendations

How we get there:

How frequently should people get a COVID-19 vaccine?
Are there groups/populations who should have >1 vaccine per year?

Considerations for future planning

COVID-19 vaccines

- COVID-19 vaccines continue to be the **most effective tool** we have to prevent **serious illness, hospitalization and death from COVID-19**
- **Goal** of COVID-19 vaccine program continues to be **prevention of severe disease**
 - Prevention of post-COVID conditions, increased confidence in social interactions important as well
- Benefits of additional COVID-19 vaccine booster doses vary by **age, time since last dose**, and **COVID-19 incidence**
- A simplified, annual recommendation could help reduce vaccine and message fatigue
- A COVID-19 vaccine framework that is similar to a well understood influenza vaccine framework could be easy for COVID-19 vaccine providers to implement, and for the public to understand

Work Group interpretation

Considerations for future planning

- **Simple recommendations** are easier to communicate, which may improve uptake
 - The Work Group was very supportive of simplified recommendations and planning for future COVID-19 vaccines, which could include updated COVID-19 vaccines
- **Uncertainties remain** for ideal timing and populations for future boosters, especially if new immune escape variants develop
- The Work Group was **supportive** of a fall/annual COVID-19 vaccine program, with flexibility to adjust based on new data, especially for populations at high risk
- The Work Group will continue to **review data** to inform future deliberations:
 - Vaccine effectiveness of bivalent COVID-19 vaccines over time
 - Safety data of bivalent COVID-19 vaccines
 - Cost effectiveness analyses
 - COVID-19 epidemiology, including hospitalization rates among vaccinated and boosted persons
 - SARS-CoV-2 genomic surveillance and virus evolution
 - Data from vaccine manufacturers

Questions for ACIP

- Discussions about future COVID-19 vaccine recommendations are pre-decisional and intended to inform planning and additional analyses.
- What are ACIP's thoughts on a **simplified framework** for future COVID-19 vaccine recommendations?
 - What does ACIP think about **children** who may still need a **primary series**?
 - What does ACIP think about future recommendations for **older adults**?
 - What does ACIP think about future recommendations for **people with immunocompromising conditions**?

Varicella Vaccine

25 Years of Varicella Vaccination Program in the United States: Health and Economic Impact during 1995–2019

Mona Marin, MD
Centers for Disease Control and Prevention, Atlanta, GA

Advisory Committee on Immunization Practices
Atlanta, GA
February 23, 2023

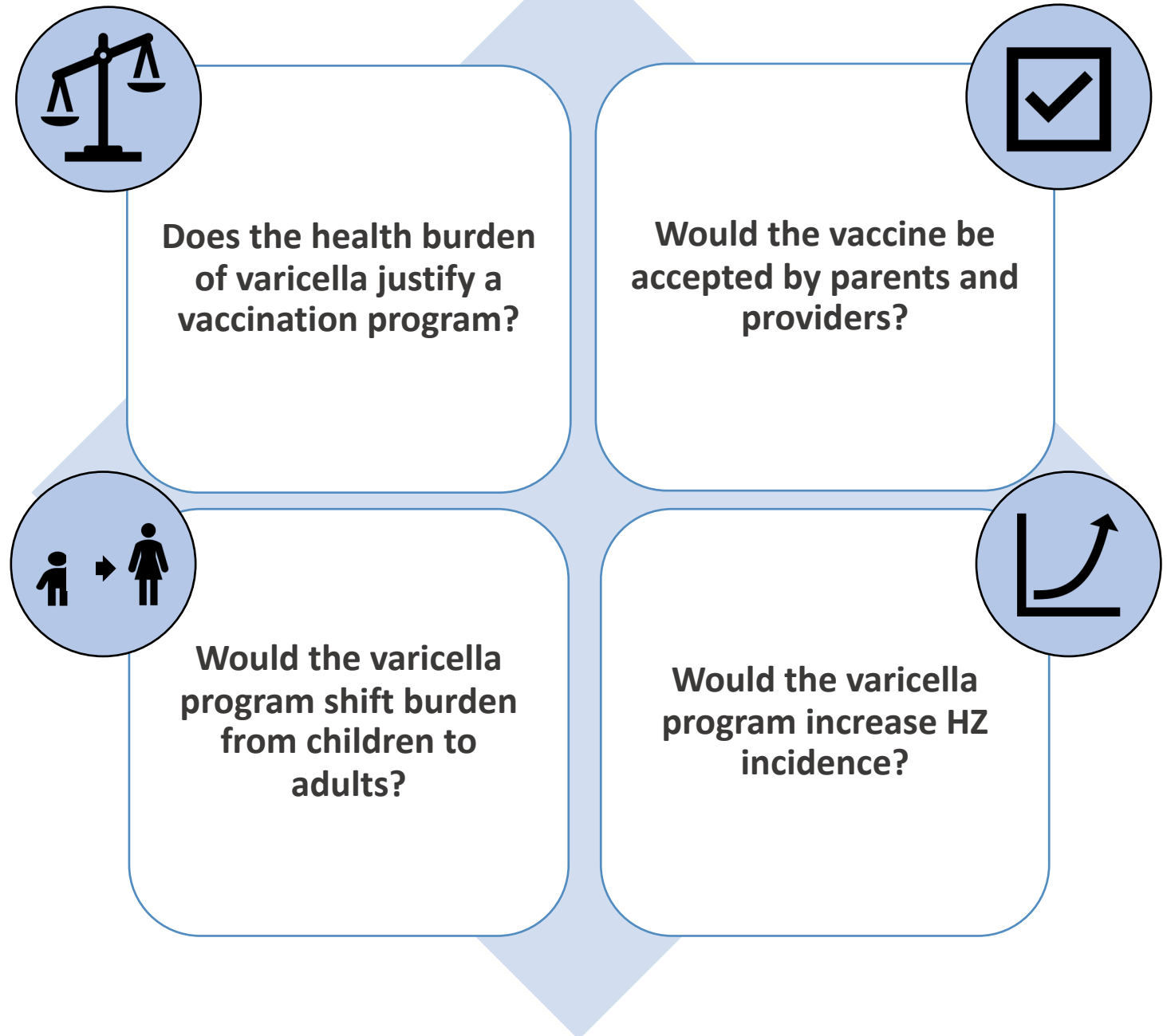
Before vaccine, varicella represented a significant health burden (medical and societal) in the United States.

Annual average, pre-vaccine

- Cases ~4 million
- Hospitalizations ~10,500–13,500
- Deaths ~100–150
- Congenital varicella syndrome ~44
- Greatest disease burden in children
 - >90% cases, 70% hospitalizations, 50% deaths



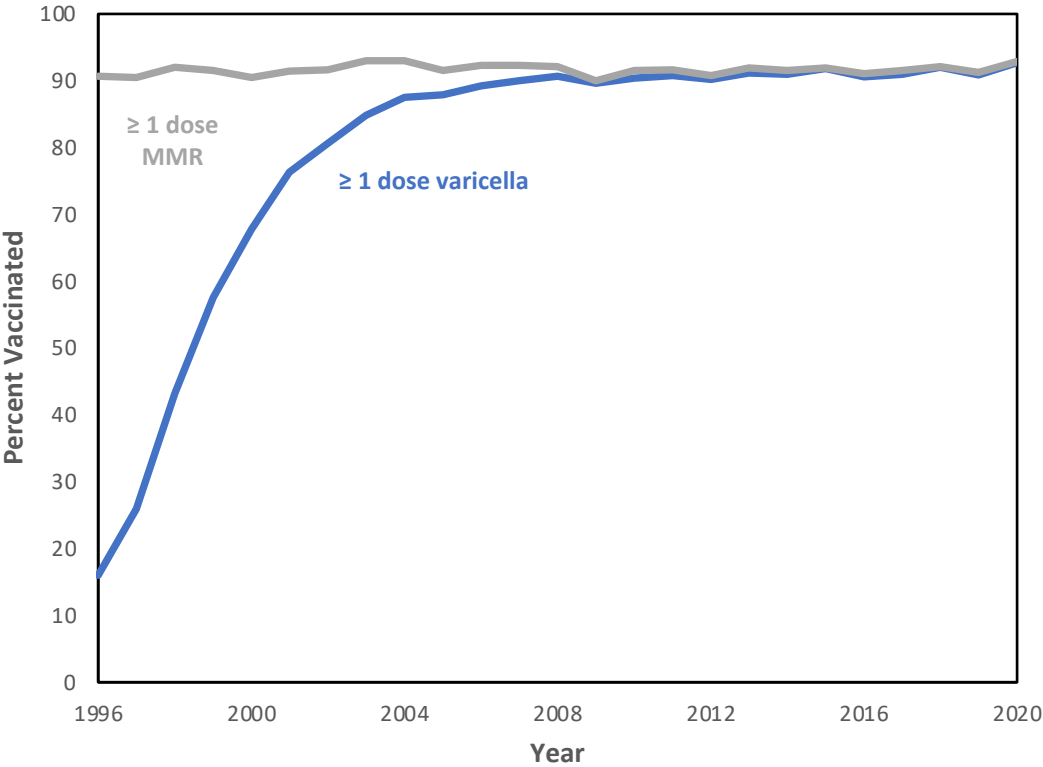
Debate around the time of varicella vaccine recommendations



Program implementation was highly successful.

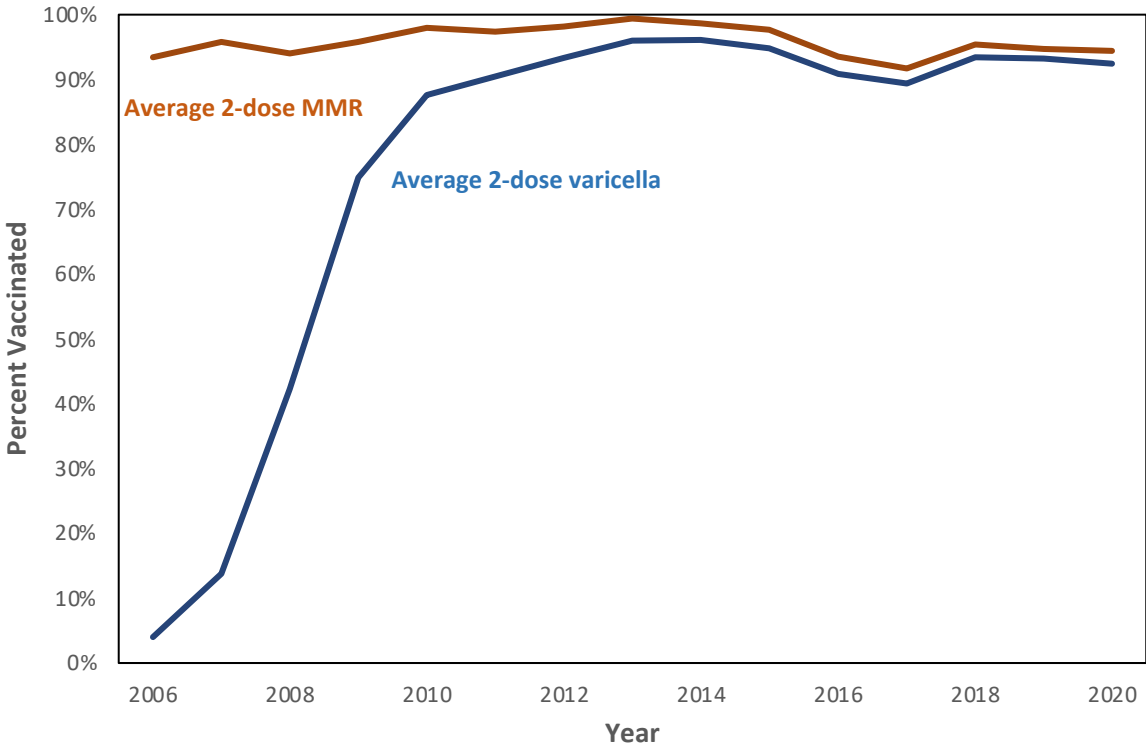
Vaccination coverage for ≥ 1 dose varicella and ≥ 1 dose MMR, children age 19–35 months, US 1996–2020

Data Source: National Immunization Survey



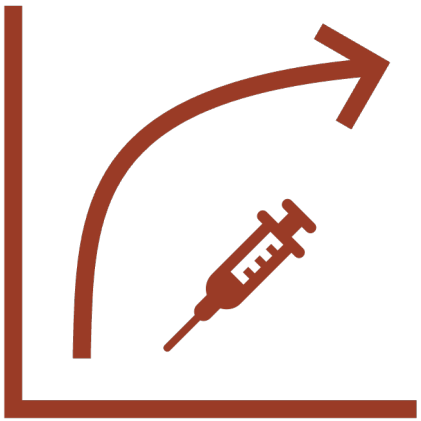
Vaccination coverage for ≥ 2 doses varicella and ≥ 2 doses MMR, children by age 7 years — 6 US states, 2006–2020

Data Source: Immunization Information System



US varicella vaccination resulted in substantial disease prevention and societal savings over 25 years of program implementation.

Effective, safe, and accepted vaccine



High vaccine coverage reached

Prevented morbidity & mortality



91 million cases



238,000 hospitalizations



1,933-2,446 deaths

Highly cost saving



\$23.4 billion

in net societal savings

No increase in HZ due to varicella program



Reduced HZ incidence in children/adolescents

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

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.

Photographs and images included in this presentation are licensed solely for CDC/NCIRD online and presentation use. No rights are implied or extended for use in printing or any use by other CDC CIOs or any external audiences.

