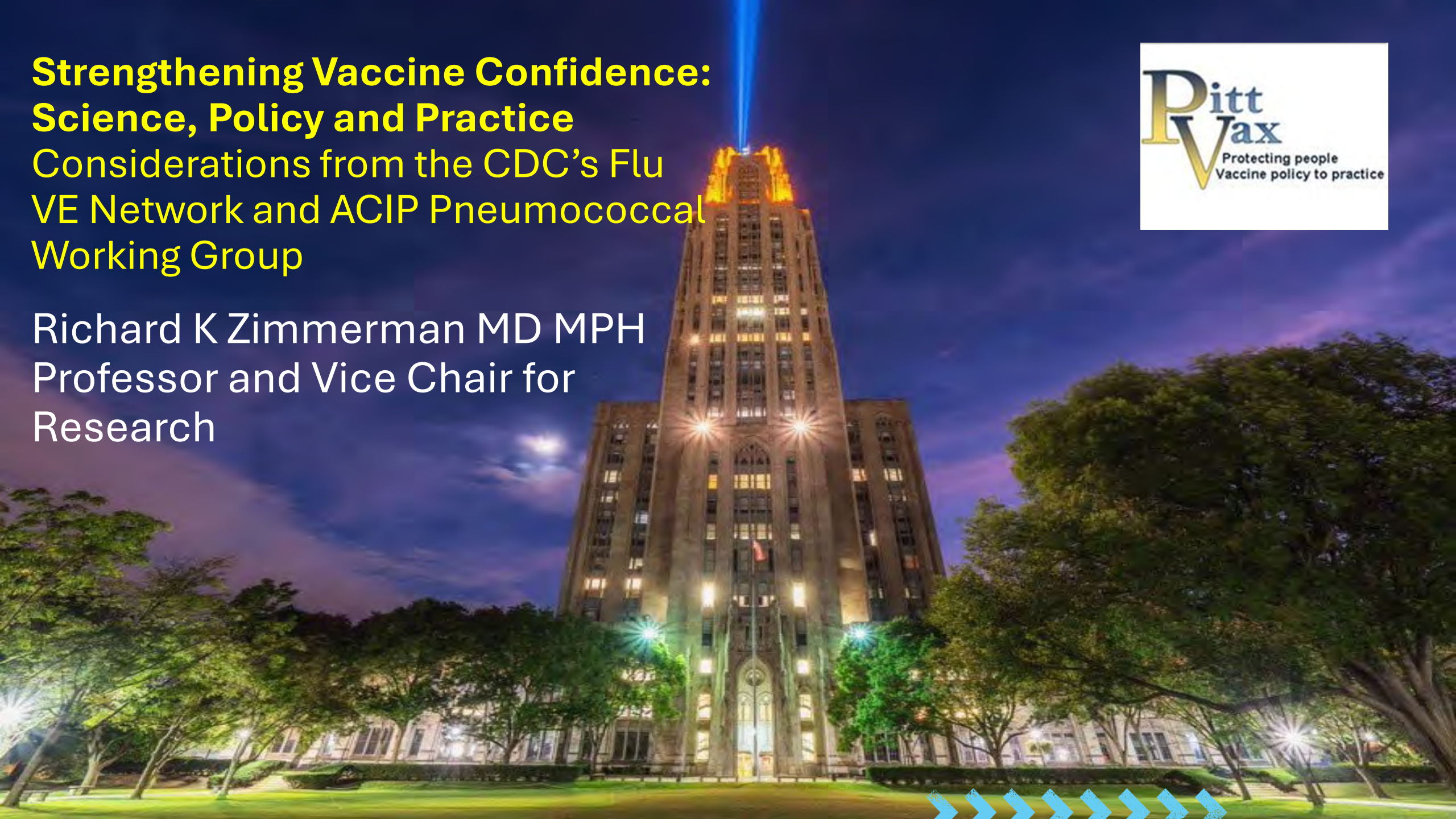
Strengthening Vaccine Confidence: Science, Policy and Practice

Considerations from the CDC's Flu VE Network and ACIP Pneumococcal Working Group

Richard K Zimmerman MD MPH
Professor and Vice Chair for Research

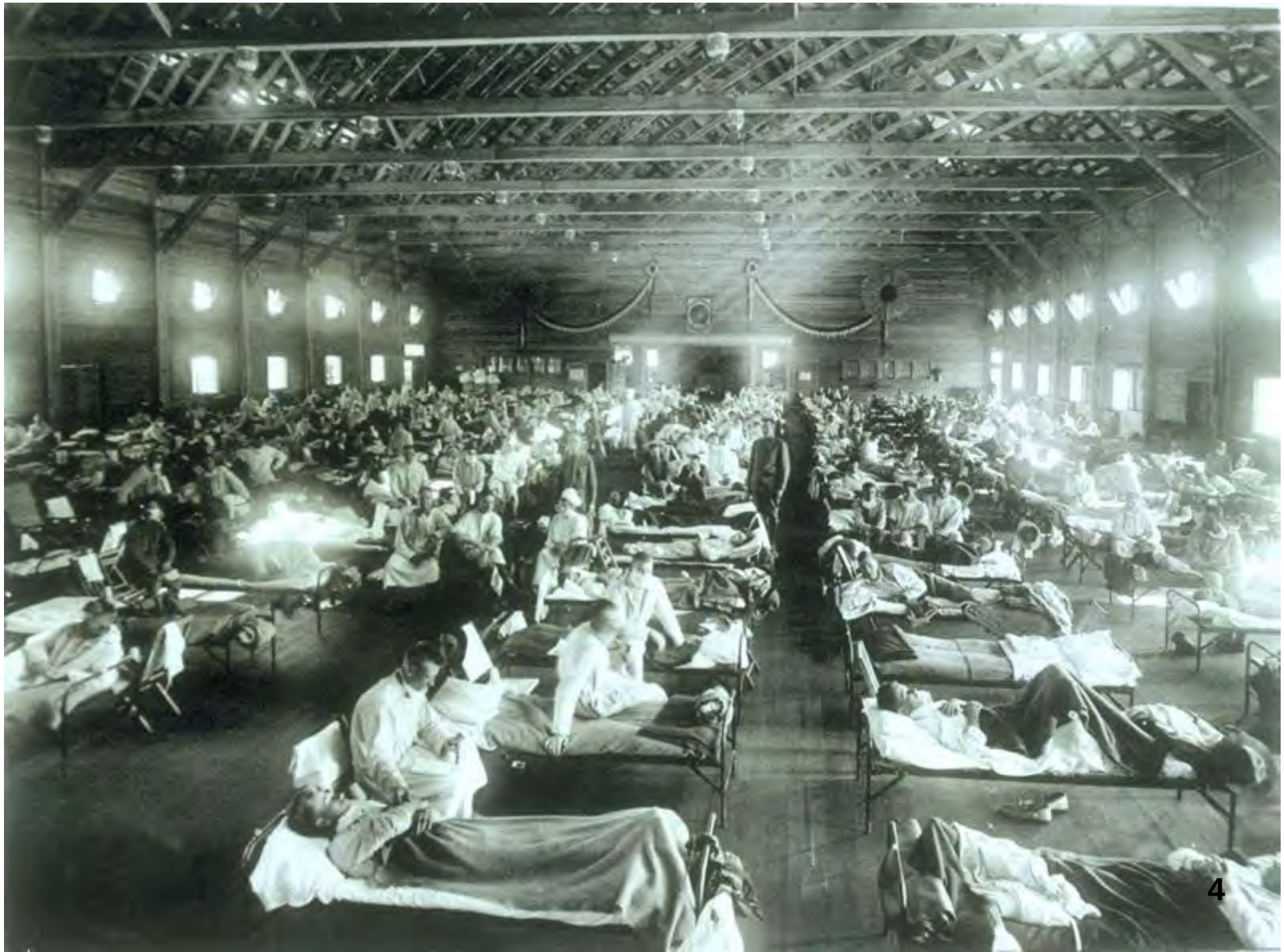


Conflicts of Interest

- Dr. Zimmerman: Research grants from Sanofi Pasteur, NIH, and CDC
- Primarily federally funded

1918 Influenza Pandemic

- At Fort Riley, an army private reports to the camp hospital just before breakfast on March 11 complaining of fever, sore throat, and headache. By noon, the camp's hospital had dealt with over 100 ill soldiers. By week's end that number jumped to 500.



1918 Influenza Pandemic

- Dr. Victor Vaughn, acting surgeon general of the army, receives urgent orders to proceed to Camp Devens. Once there, what Vaughn sees changes his life forever:
  - "I saw hundreds of young stalwart men in uniform coming into the wards of the hospital. Every bed was full, yet others crowded in. The faces wore a bluish cast; a cough brought up the blood-stained sputum. In the morning, the dead bodies are stacked about the morgue like cordwood."
- On that day at Camp Devens, 63 men died from influenza.

- www.pbs.org/wgbh/amex/influenza/sfeature

1918 Pandemic

- 25% attack rate in US
- Lowered US life expectancy by 12 years
- 10%-20% fatality rate among infected
- Killed 50 million worldwide
  - More than any other pandemic in known history

Global Influenza Pandemic: Estimated Impact in United States

- • In the absence of any control measures (vaccination or drugs), expert estimates of a “medium–level” pandemic:
  - 15% and 35% of the U.S. population could be affected
  - 18 million to 42 million require outpatient visits, with another 20 million to 47 million sick people
  - 314,000 to 734,000 hospitalized
  - 89,000-207,000 deaths
  - Overall economic impact: $71.3 billion to $166.5 billion

- • Due to antigenic shift

- Source: http://www.cdc.gov/flu/avian/gen-info/pandemics.htm

When Will the Next Pandemic Occur?

- New strain with little experience or resistance among humans
- Highly communicable
- Reassortment between animals and humans
  - Communicability from human strain; high pathogenicity from animal strain
- Reassortment could occur in a human infected with a human and an animal strain
  - Or, in an animal infected with both human and animal strains
  - Or, as a mutation in an animal strain that allows transmission among humans

Avian Flu

- H7N9 infections in people and poultry in China
- Sporadic infections in people; most with poultry exposure
- Rare limited person-to-person spread
- No sustained or community transmission
- High mortality: 359 of 918 known infections
- 2023-24 H5N1 occurring in birds, cows, cats

Republished from CRIENGLISH.com at:
http://en.chinabroadcast.cn/2239/2005-1-28/88@201395.htm

3 transmission Modes: Large Droplet, small droplet, Hand/Fomite

Vaccine Types

- Inactivated inactivated influenza vaccine (IIV): subvirion or purified surface antigen preparations
  - Older whole-inactivated product off the market; higher reaction rates
  - One brand (afluria) by jet injector (needle-free)
- Live attenuated influenza vaccine (LAIV)
  - Online in Fall of 2025 without going to a provider
- Recombinant Vaccine (Flublok) – can use if severe egg allergy as no egg -- ≥18
  - 40% higher VE in mismatch year
- Cell culture derived – egg-free - Flucelvax
- Adjuvanted IIV for elderly (MF59 adjuvant)
- High dose IIV for the elderly
- Coming: mRNA and combo mRNA Flu-COVID

Influenza vaccine options by age - children

Age group years	IIV: Fluzone* FluLaval* Fluarix Afluria	Cell-culture Flucelvax*	LAIV
6mo-2 years	X	X	
2-3 yrs	X	X	X
4 years	X	X	X
5-18 yrs	X	X	X
Egg-free		X	

- *Multidose vials of these products contain thimerosal (mercury derivative) as perservative
- Single dose vials or syringes do not contain thimerosal.

Influenza vaccine options by age

Age group years	IIV	Recombinant (RIV)	Cell-culture IIV	LAIV	IIV High Dose	IIV adjuvanted
18-49	X	X	X	X		
50-64	X	X	X			
≥65	X	X	X		X	X
Egg-free		X	X			
Prefer for seniors		X			X	X

- RIV = FluBlok
- Cell-culture = Flucelvax
- IIV adjuvanted = Fluad
- IIV High Dose= Fluzone HD

Inactivated Influenza Vaccine: Adverse Effects

- Placebo-controlled trial
- 20% of vaccinees compared with 5% of placebo recipients had sore arm ($P < .001$)
- No other significant differences

- Source: *JAMA*. 1990;264:1140.

CDC Influenza Vaccine Effectiveness Networks

- **Four networks to evaluate vaccine effectiveness (VE) against laboratory- confirmed influenza for children, adolescents, and adults in the outpatient and inpatient settings**

Acknowledgement: Most slides from

Aaron M. Frutos, PhD, MPH

On behalf of CDC Influenza Vaccine Effectiveness Collaborators

Advisory Committee on Immunization Practices

February 28, 2024

US Flu VE Network sites, 2021-22 season

2023-2024 Influenza VE Methods

- **Enrollees:** Ambulatory patients aged >6 months attending medical facility
- Acute respiratory illness with cough <7 days duration

- **Design:** Test-negative case-control design
  - Cases: Influenza PCR-positive
  - Control patients testing negative for influenza and for SARS-
  - Comparing vaccination odds among case patients with influenza confirmed by molecular assay versus control patients testing negative for influenza and SARS-CoV-2

Pediatric VE against any influenza

	Influenza test result by influenza vaccination status, no. vaccinated/Total (%)		
	Influenza-positive	**Influenza-negative**	**VE (95% CI)**
US Flu VE (Outpatient)	29/283 (10)	182/736 (25)	67 (48, 80)

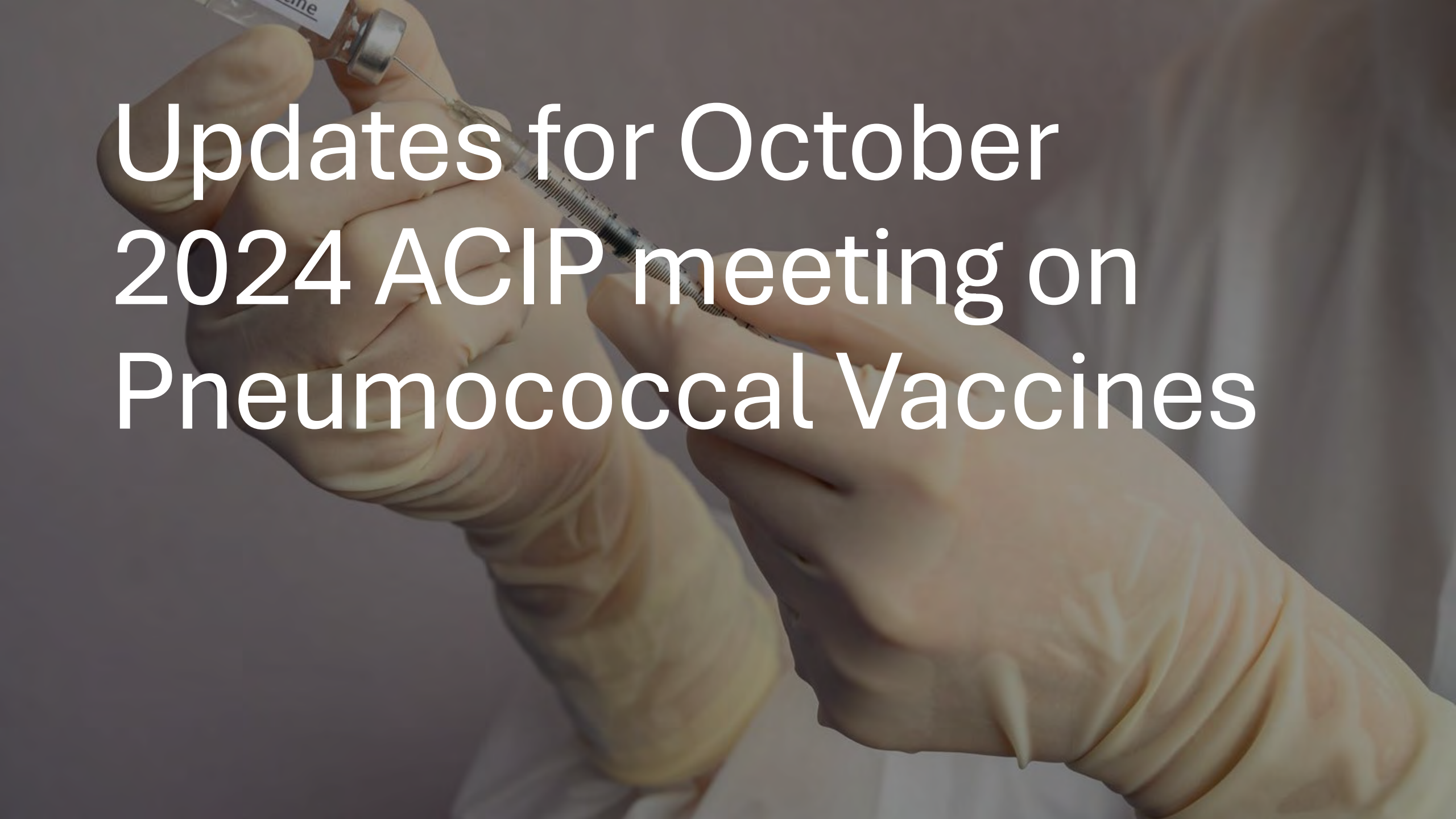
Adult VE against any influenza adults and those ≥65

	Influenza test result by influenza vaccination status, no. vaccinated/Total (%)		
	Influenza-positive	**Influenza-negative**	**VE (95% CI)**
US Flu VE (Outpatient)	177/568 (31)	803/1,807 (44)	33 (16, 47)

VE= 48% (24%-64%) in Pittsburgh

	Influenza test result by influenza vaccination status, no. vaccinated/Total (%) ≥65		
	Influenza-positive	**Influenza-negative**	**VE (95% CI)**
US Flu VE (Outpatient)	41/79 (52)	300/439 (68)	51 (14, 72)

Wild to Mild Public Info Campaign



Updates for October 2024 ACIP meeting on Pneumococcal Vaccines

Currently Recommended Adult Pneumococcal Vaccines

	1	3	4	5	6A	6B	7F	9V	14	18C	19A	19F	23F	22F	33F	8	10A	11A	12F	15B	2	9N	17F	20	15A	15C	16F	23A	23B	24F	31	35B
PCV15																																
PCV20																																
PPSV23																																
PCV21																																

21-valent pneumococcal conjugate vaccine (CAPVAXIVE™, Merck):

- **Approved by the FDA for adults aged ≥18 years on June 17, 2024[1]**

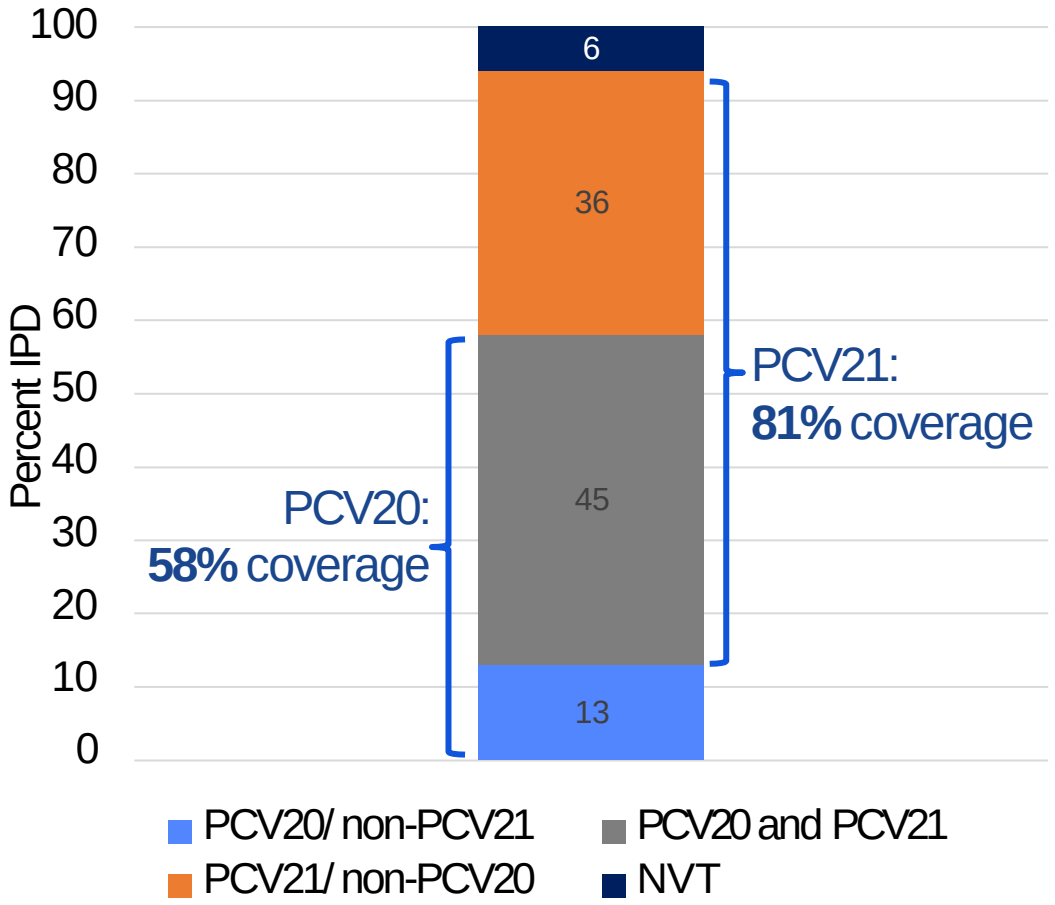
First vaccine oriented to adult serotypes

PCV15=15-valent pneumococcal conjugate vaccine
PCV20=20-valent pneumococcal conjugate vaccine
PCV21=21-valent pneumococcal conjugate vaccine
PPSV23=23-valent pneumococcal polysaccharide vaccine

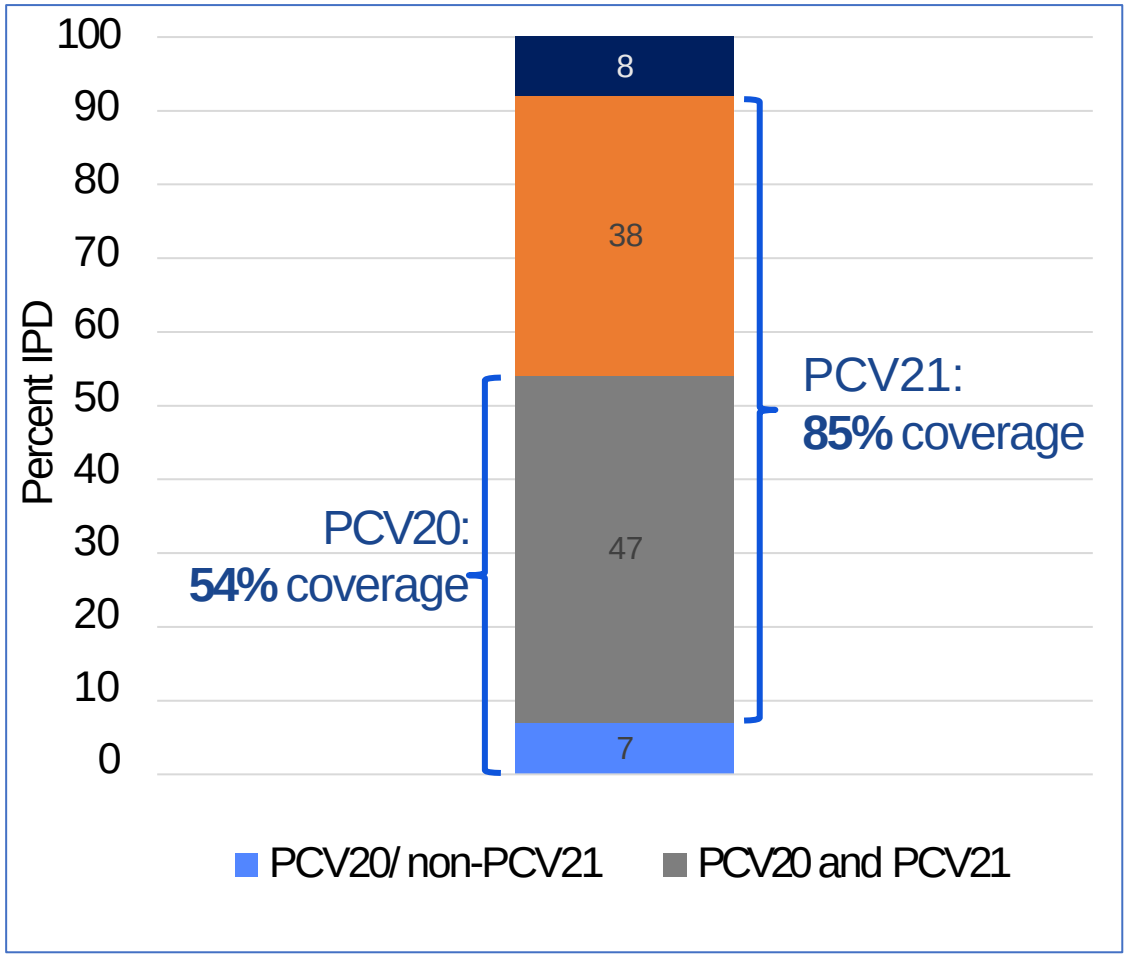
1. U.S. FDA Approves CAPVAXIVE™ (Pneumococcal 21-valent Conjugate Vaccine) for Prevention of Invasive Pneumococcal Disease and Pneumococcal Pneumonia in Adults - Merck.com

Proportion of IPD by vaccine-type among adults with a pneumococcal vaccine indication, 2018–2022

19-64 years old (*with a risk-based indication*)



≥65 years old



PCV20/ non-PCV21 serotype: 1, 4, 5, 6B, 9V, 14, 18C, 19F, 23F, 15B
PCV20/ in-PCV21 serotypes: 3, 6A, 7F, 19A, 22F, 33F, 8, 10A, 11A, 12F, +6C
PCV21/ non-PCV20 serotypes: 9N, 17F ,20, 15A, 15C, 16F, 23A, 23B, 24F, 31, 35B

Gierke February 2024 ACIP meeting presentation

Requests from the Committee to the Pneumococcal WG at the June ACIP meeting

- **Present summary of data on whether age-based recommendation for pneumococcal vaccines should be lowered to age ≥50 years for all PCVs (not just PCV21) at the October ACIP meeting**
  - Voting members felt that there were not enough data to make a decision on PCVs other than PCV21
  - Anticipating implementation challenges by having different age-based recommendations by vaccine
- **Request to also consider discontinuing the recommendation for PPSV23**

Summary of Work Group Interpretation of EtR and Policy Options

PCV Use in Adults aged ≥50 years

October 23, 2024

Miwako Kobayashi, MD, MPH

PICO for WG discussion through October 2024

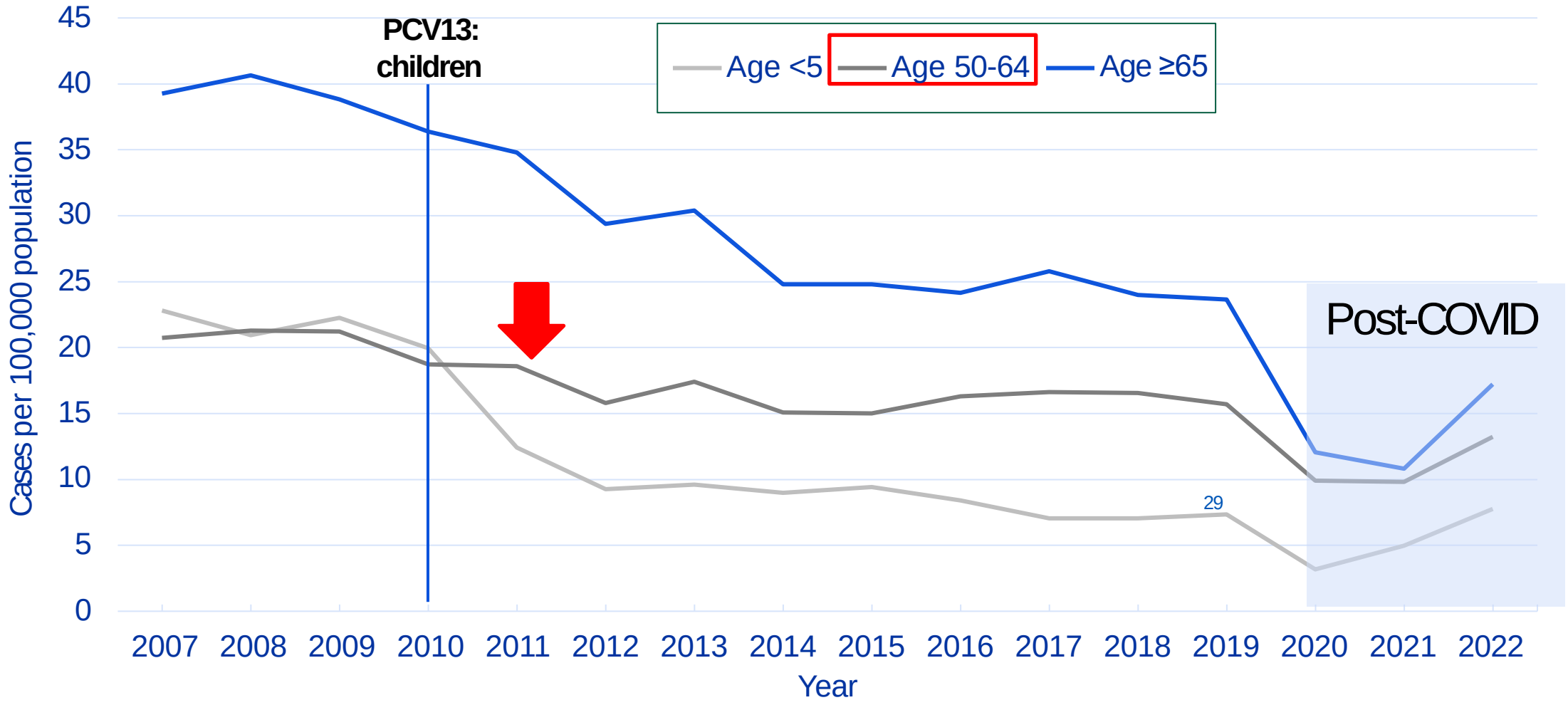
Policy question:	Should a single dose of pneumococcal conjugate vaccine (PCV) be recommended for all PCV-naïve adults aged 50–64 years?
Population	PCV-naïve adults aged 50–64 years in the United States
Intervention	One dose of PCV15*, PCV20, or PCV21 *In series with PPSV23
Comparison	Current risk-based vaccine recommendation (CMC or IC)
Outcomes	Vaccine type (VT)-IPD, VT-non-bacteremic pneumococcal pneumonia, VT-pneumococcal mortality, serious adverse events

CMC=chronic medical conditions (i.e., alcoholism; chronic heart disease, including congestive heart failure and cardiomyopathies; chronic liver disease; chronic lung disease, including chronic obstructive pulmonary disease, emphysema, and asthma; cigarette smoking; or diabetes mellitus); IC=immunocompromising condition(i.e., chronic renal failure, nephrotic syndrome, immunodeficiency, iatrogenic immunosuppression, generalized malignancy, HIV infection, Hodgkin disease, leukemia, lymphoma, multiple myeloma, solid organ transplant, congenital or acquired asplenia, or sickle cell disease or other hemoglobinopathies). Those with a cerebrospinal fluid leak and a cochlear implant are also included among those with a risk-based vaccine indication.

Evidence to Recommendations (EtR) framework

EtR Domain	Question
Public Health Problem	• Is the problem of public health importance?
Benefits and Harms	• How substantial are the desirable anticipated effects? • How substantial are the undesirable anticipated effects? • Do the desirable effects outweigh the undesirable effects? • What is the overall certainty of this evidence for the critical outcomes?
Values	• Does the target population feel the desirable effects are large relative to the undesirable effects? • Is there important variability in how patients value the outcomes?
Acceptability	• Is the intervention acceptable to key stakeholders?
Resource Use	• Is the intervention a reasonable and efficient allocation of resources?
Feasibility	• Is the intervention feasible to implement?
Equity	• What would be the impact of the intervention on health equity?

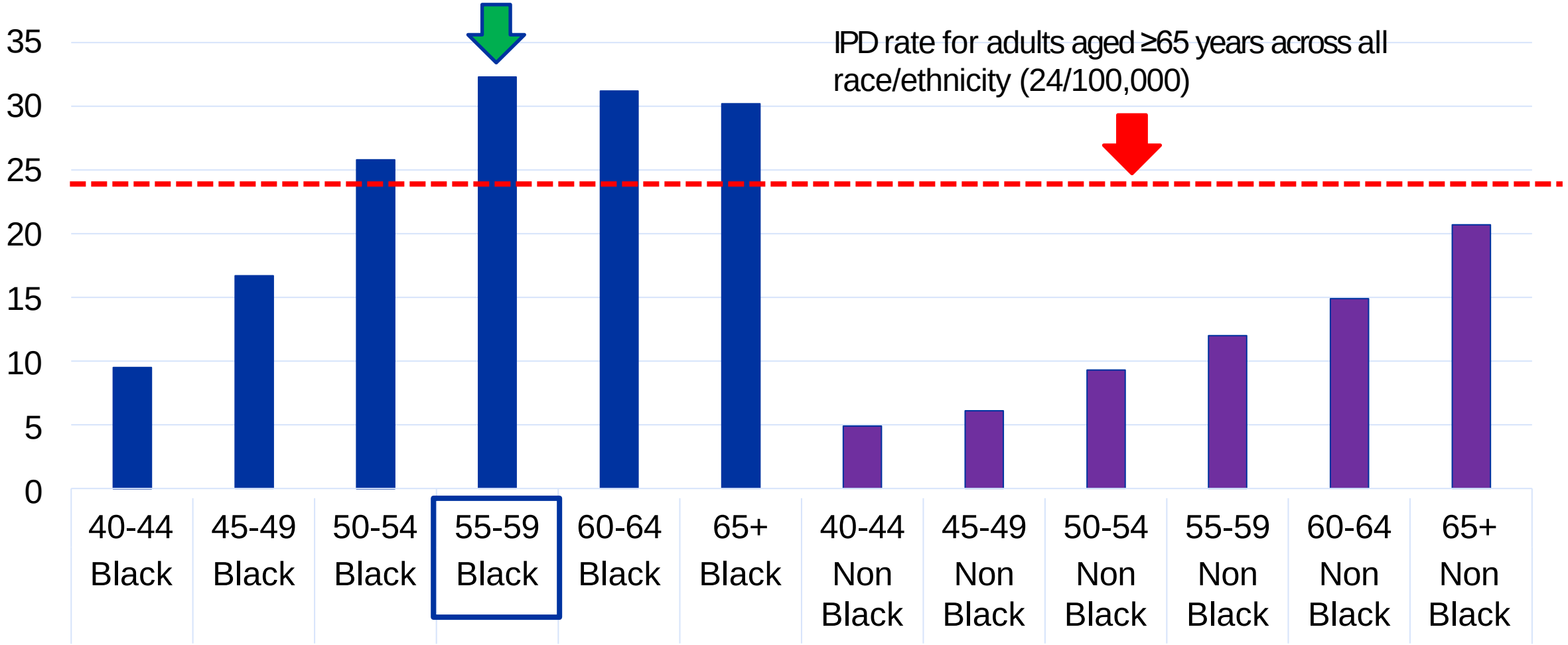
Invasive pneumococcal disease (IPD) incidence rates, by age group, 2007–2022



Source: CDC's Active Bacterial Core surveillance

Adapted from Gierke Feb 2024 ACIP meeting presentation

IPD rates (any pneumococcal serotype) in Black adults peak at a younger age compared with Non-Black adults



ABCs 2018 –2019 unpublished data

Updated targeted literature search

- Previously conducted systematic review of literature and presented summary of findings and GRADE for PCV15[1], PCV20[2], PCV21[3]
- Updated literature search (August and September, 2024) based on current PICO question
- 6 PCV15 trials, 3 PCV20 trials, and 7 PCV21 trials included in the updated review (list of studies available in supplemental slides)

1. Presented summary of literature search through February 18, 2021
2. Presented summary of literature search through March 31, 2022
3. Presented summary of literature search through October 17, 2023

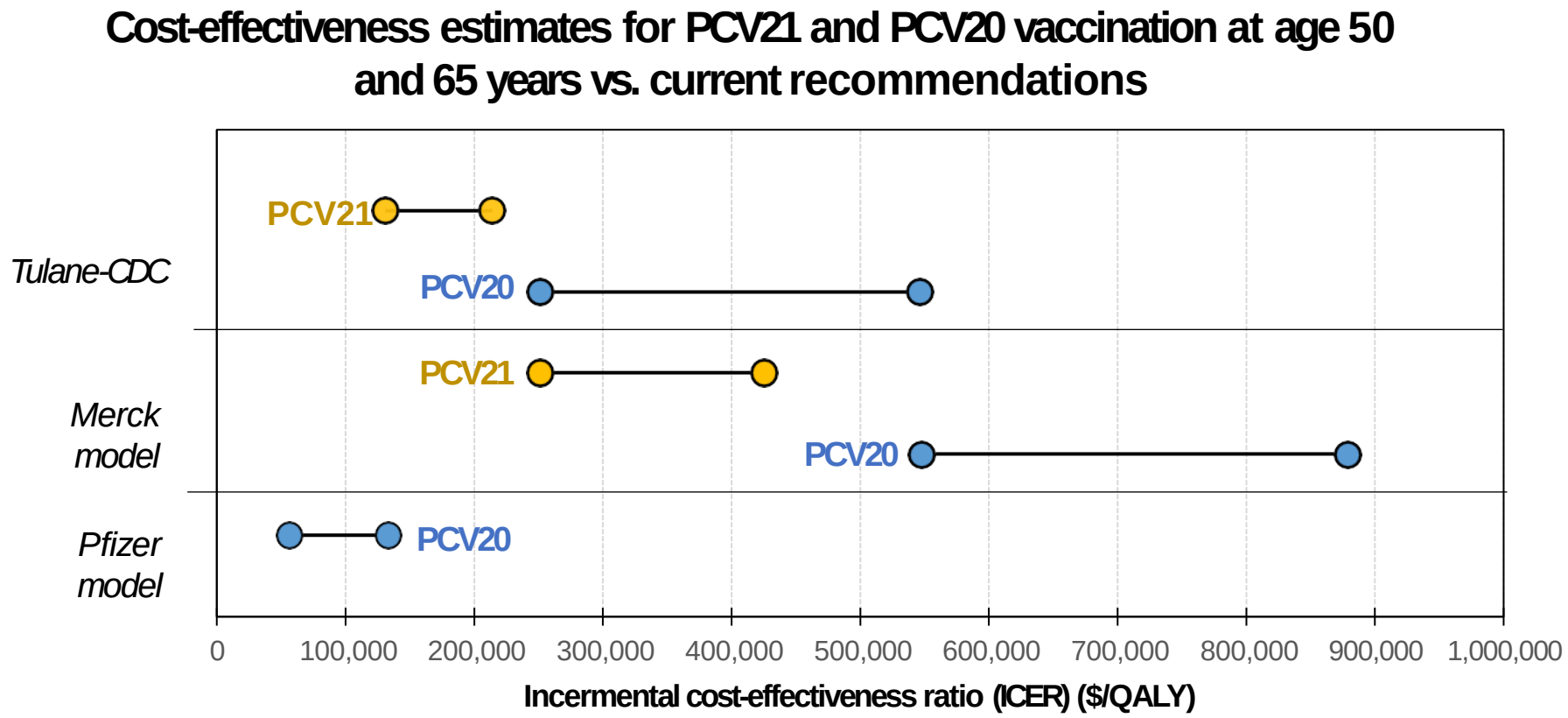
PCV clinical trial data (immunogenicity)

Conclusions remain unchanged

- PCV15: **Noninferior**[1] to PCV13 for all shared serotypes; had statistically significantly greater response[2] for non-PCV13 serotypes 22F and 33F vs. PCV13
- PCV20: **Noninferior**[3] to PCV13 for all shared serotypes; **noninferior**[3] to PPSV23 for 6/7 non-PCV13 serotypes (not met for serotype 8)
- PCV21: **Noninferior**[4] to PCV20 for 10/10 shared serotypes; had statistically significantly greater response[5] for 10/11 PCV21-unique serotypes (except serotype 15C)

1. Noninferiority defined as the lower bound of the 2-sided 95% CI of the OPA GMT ratio (PCV15/PCV13) to be >0.5.
2. Statistically significantly greater response for unique serotypes (22F and 33F) defined as the lower bound of the 2-sided 95% CI of the OPA GMT ratio (PCV15/PCV13) to be >2.0 and the lower bound of the 2-sided 95% CI of the differences (PCV15-PCV13) between the proportions of participants with a ≥4-fold rise to be >0.1 (or 10 percentage points)
3. Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the OPA GMT ratio (PCV20/comparator vaccine) for that serotype was greater than 0.5 (2-fold criterion).
4. Noninferiority for GMT ratio was defined as the lower bound of the 2-sided 95% CI of the OPA GMT ratio [PCV21 / (Comparator Vaccine)] to be >0.5.
5. Statistically significantly greater response for GMT ratio was defined as the lower bound of the 2-sided 95% CI of the OPA GMT ratio [PCV21 / (Comparator Vaccine)] to be >2.0. Statistically significantly greater response for difference in proportions of participants with a ≥4-fold rise in serotype-specific OPA responses from baseline to 30 days postvaccination was defined as the lower bound of the 2-sided 95% CI of the differences [PCV21 – (Comparator Vaccine)] between the proportions of participants with a ≥4-fold rise from baseline to 30 days postvaccination to be >0.1.

Summary of model findings, “adding” strategies



- From the “adding” comparisons, all strategies improved health, but none were cost-saving
- Cost per QALY gained estimates for PCV20 had a wider range, more uncertainty than PCV21
- In two of three models, PCV21 had lower costs per QALY gained than PCV20

Summary of Work Group Interpretations of EtR Domains

EtR Domains	Work Group Interpretation
Public Health Problem	Yes
Equity	Probably increased
Benefits and Harms	
a. Benefits	Moderate
b. Harms	Minimal
c. Benefit>Harm?	Favors intervention
Values and Preferences	
a. Desirable>Undesirable?	Probably yes/yes
b. Uncertainty?	Probably not important uncertainty or variability
Acceptability	Yes
Resource Use	Probably yes/Yes
Feasibility	Probably yes/Yes

Key factors in the WG recommendations

1. Health equity: Higher pneumococcal disease rates in Black/African American adults, with earlier peak
2. Risk prevalence: 33–54% of adults aged 50–64 years already with indication for risk-based pneumococcal vaccination*
3. Vaccine coverage: Age-based recommendation likely to improve uptake vs. risk-based recommendation
4. Simplicity: Easier to implement uniform recommendation across all PCVs
5. Economic consideration: PCV21 at age 50 (and 65 years) had lower cost/QALY gained than PCV20, while both PCV21 and PCV20 improved health outcomes
6. Serotype coverage: the serotype compositions of PCV20 and PCV21 are quite different

*Data is for adults with any of the following condition and is not an exhaustive list of conditions: chronic heart disease, chronic lung disease, chronic liver disease, diabetes, smoking, alcoholism, weakened immune system due to prescriptions, weakened immune system due to health condition, solid cancer (not including non-melanoma skin cancer or unknown type of skin cancer) and blood cancer. Source NHIS 2020.

†Except for In certain adult populations in the western United States where high percentages (i.e., ≥30%) of IPD caused by serotype 4 have occurred

PCV-naïve adults* (or adults with unknown history)

- **A single dose of PCV (PCV15, PCV20, or PCV21) is recommended for all adults aged ≥50 years and for adults aged 19–49 years with certain underlying conditions or risk factors† who have not received a PCV or whose vaccination history is unknown.**
- **If PCV15 is administered, a single dose of PPSV23§ should be administered ≥1 year after the PCV15 dose. A minimum interval of 8 weeks can be considered if PCV15 is used in adults with an immunocompromising condition¶, cochlear implant, or CSF leak.**

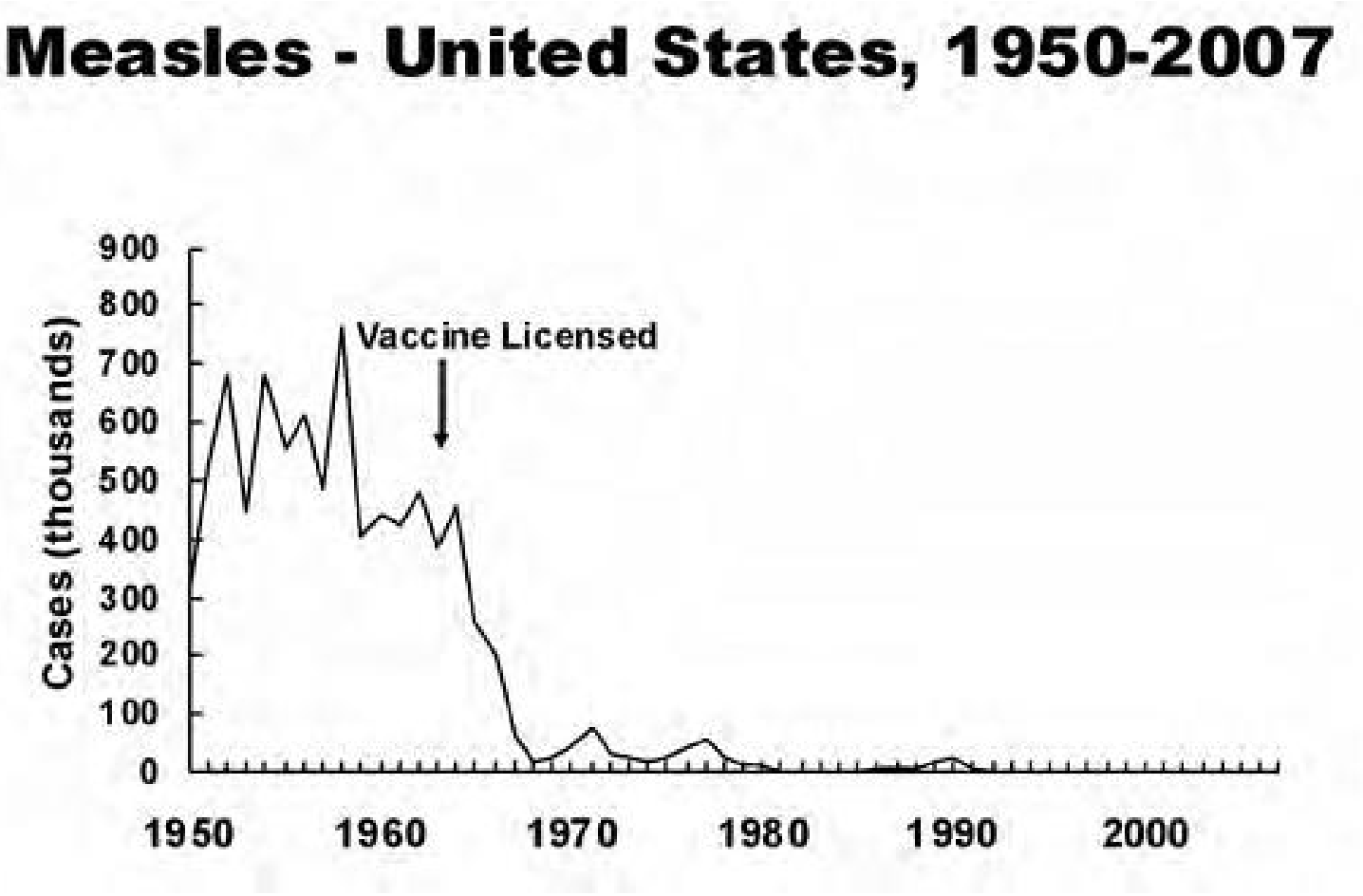
*Includes adults who received PCV7 only

† Alcoholism; chronic heart, liver, or lung disease; chronic renal failure; cigarette smoking; cochlear implant; congenital or acquired asplenia; cerebrospinal fluid leak; diabetes mellitus; generalized malignancy; HIV; Hodgkin disease; immunodeficiency; iatrogenic immunosuppression; leukemia, lymphoma, or multiple myeloma; nephrotic syndrome; solid organ transplant; sickle cell disease; or other hemoglobinopathies.

§For adults who have received PCV15 but have not completed their recommended pneumococcal vaccine series with PPSV23, 1 dose of PCV21 or PCV20 may be used if PPSV23 is not available.

¶Chronic renal failure, nephrotic syndrome, immunodeficiency, iatrogenic immunosuppression, generalized malignancy, HIV infection, Hodgkin disease, leukemia, lymphoma, multiple myeloma, solid organ transplant, congenital or acquired asplenia, or sickle cell disease or other hemoglobinopathies.

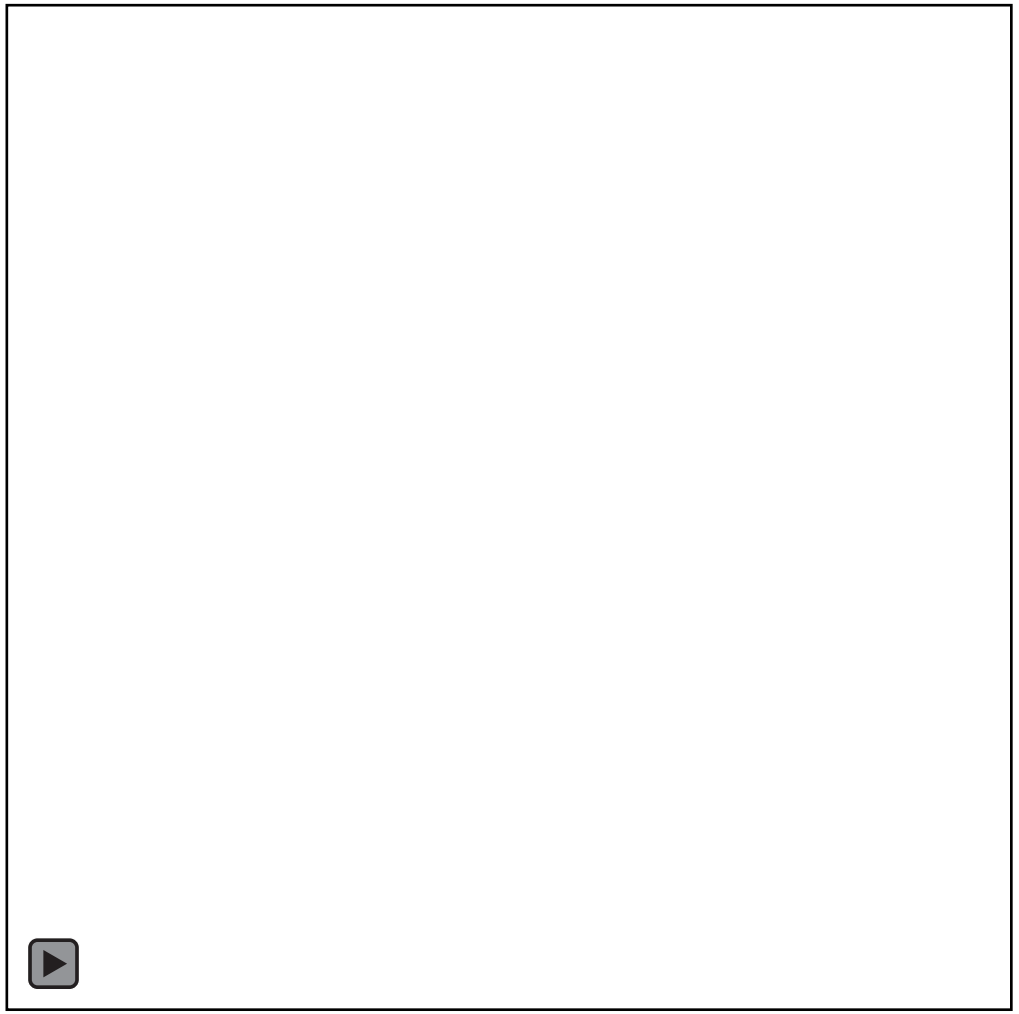
Overcoming vaccine hesitancy



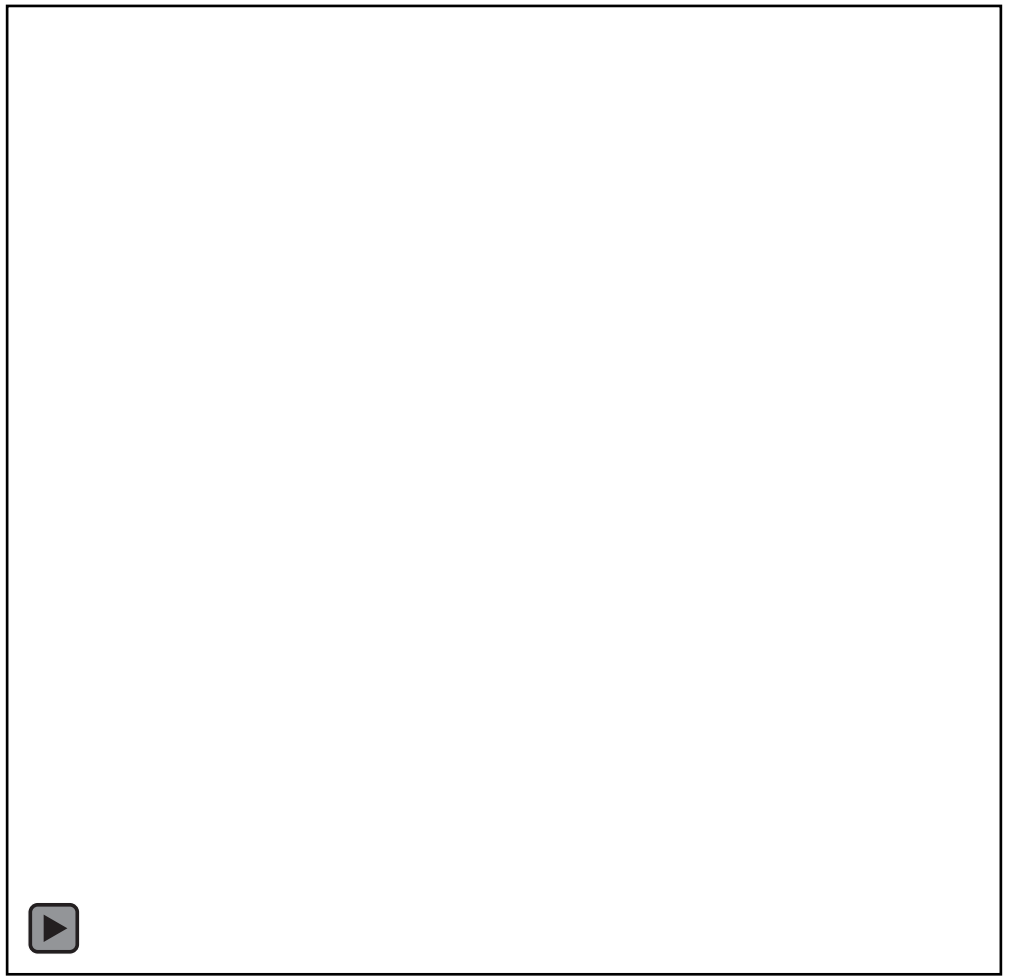
Measles Simulation in Allegheny

FRED Web (pitt.edu)

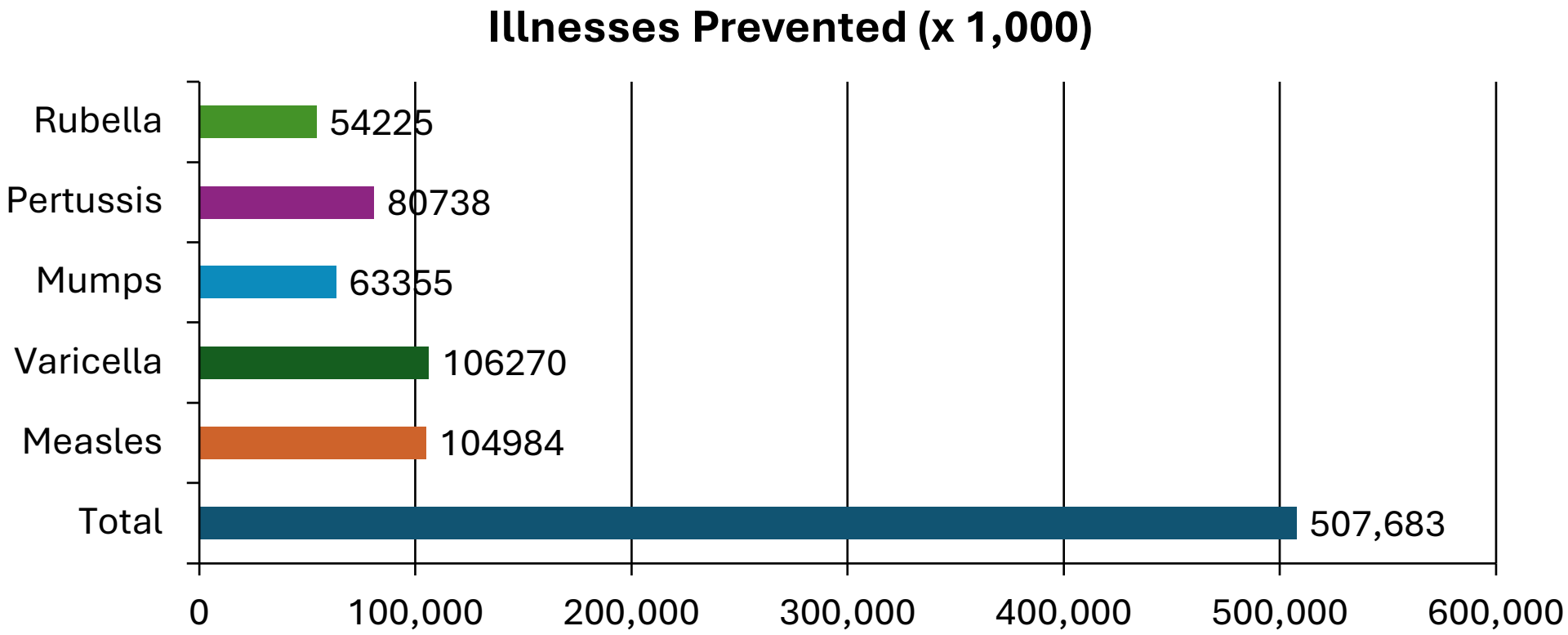
Coverage 80%



Coverage 95%

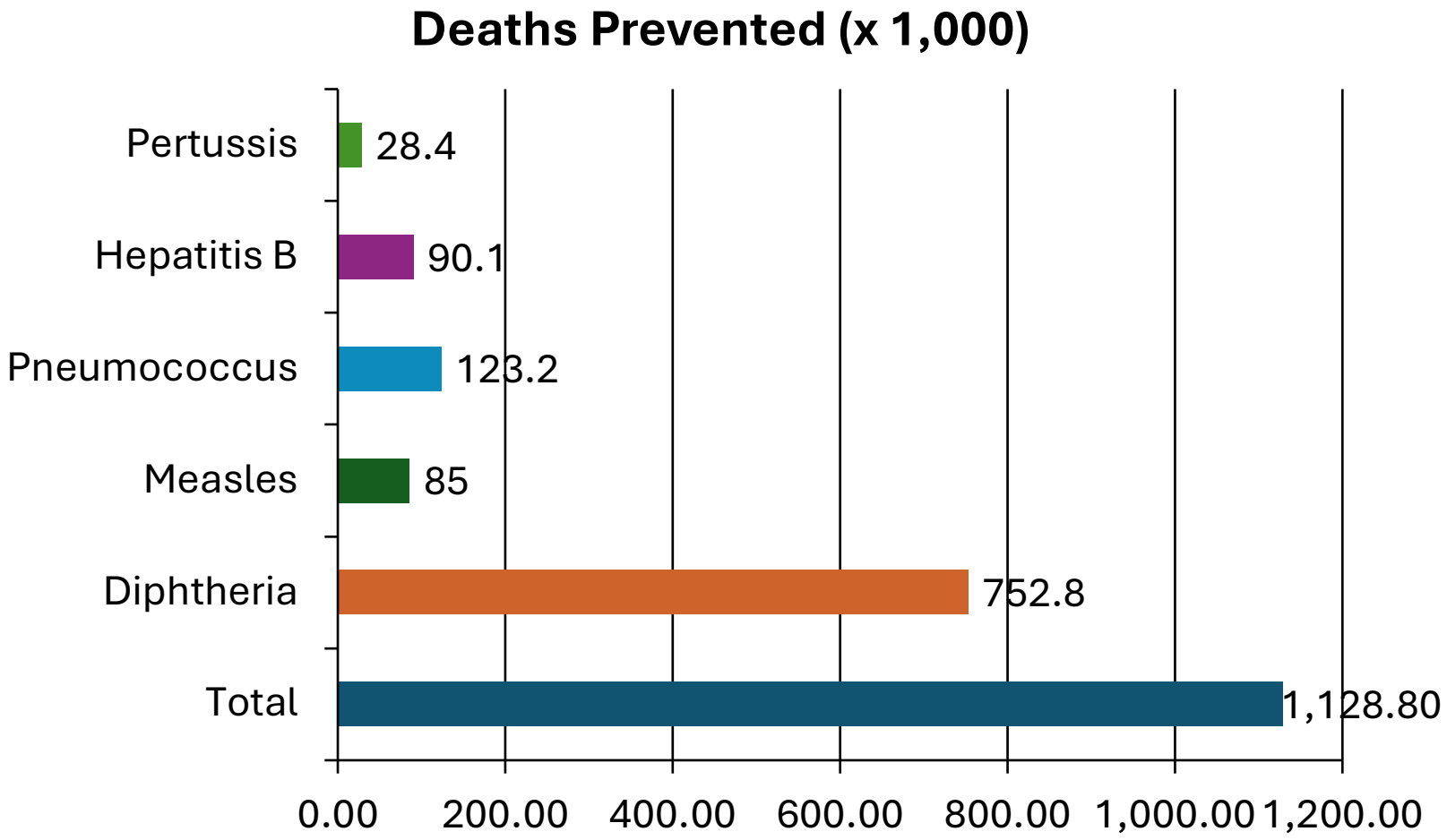


Top 5 Vaccine-preventable Diseases by Illnesses and Total Prevented by Childhood Vaccination, US, 1994-2023



Health and Economic Benefits of Routine Childhood Immunizations in the Era of the Vaccines for Children Program — United States, 1994–2023 (cdc.gov)

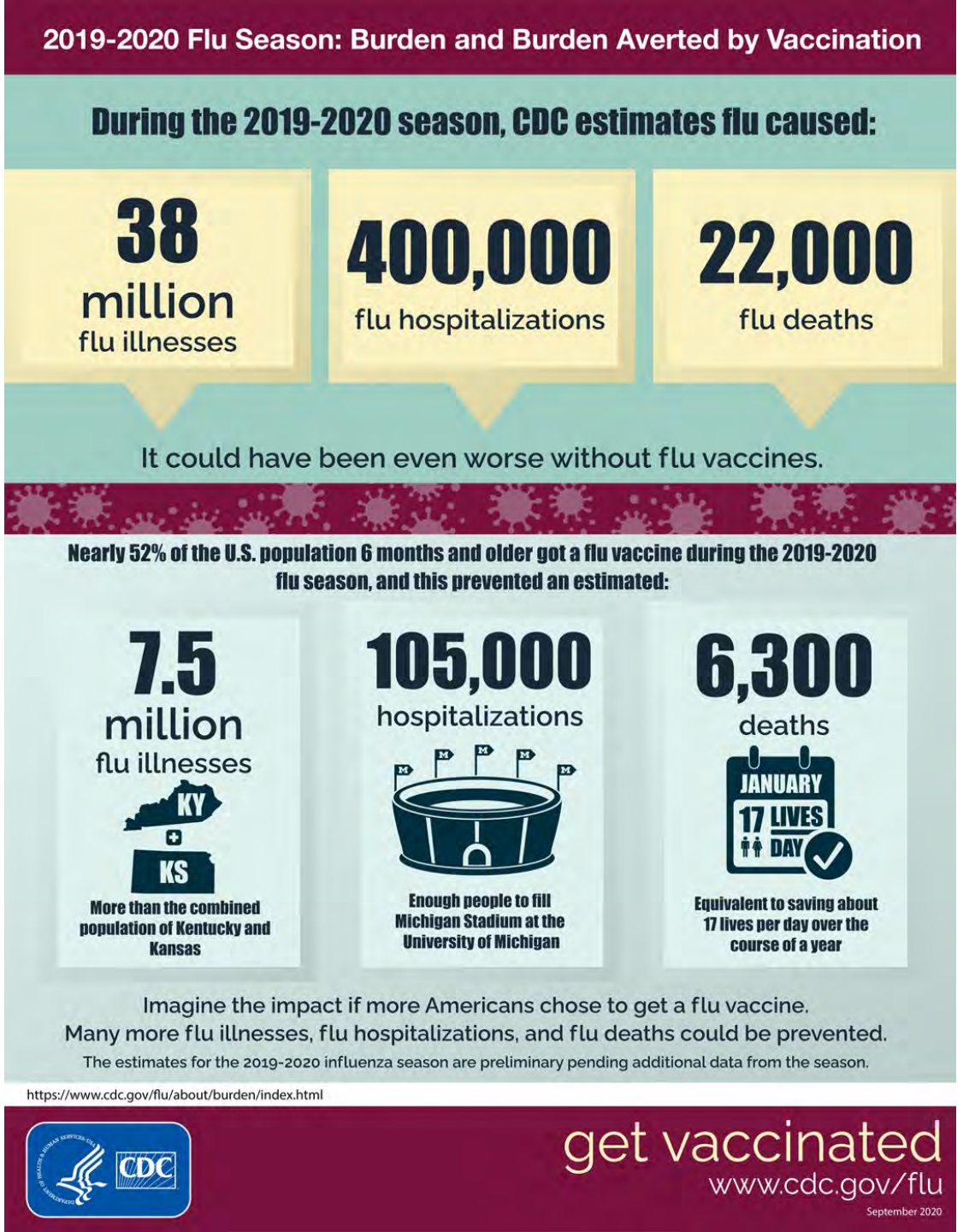
Top 5 Vaccine-preventable Diseases by Deaths Prevented by Childhood Vaccination, US, 1994-2023



Health and Economic Benefits of Routine Childhood Immunizations in the Era of the Vaccines for Children Program — United States, 1994–2023 (cdc.gov)

Flu Burden & Averted Burden

- **2017-2018**
  - 808,129 hospitalizations
  - 61,099 flu deaths



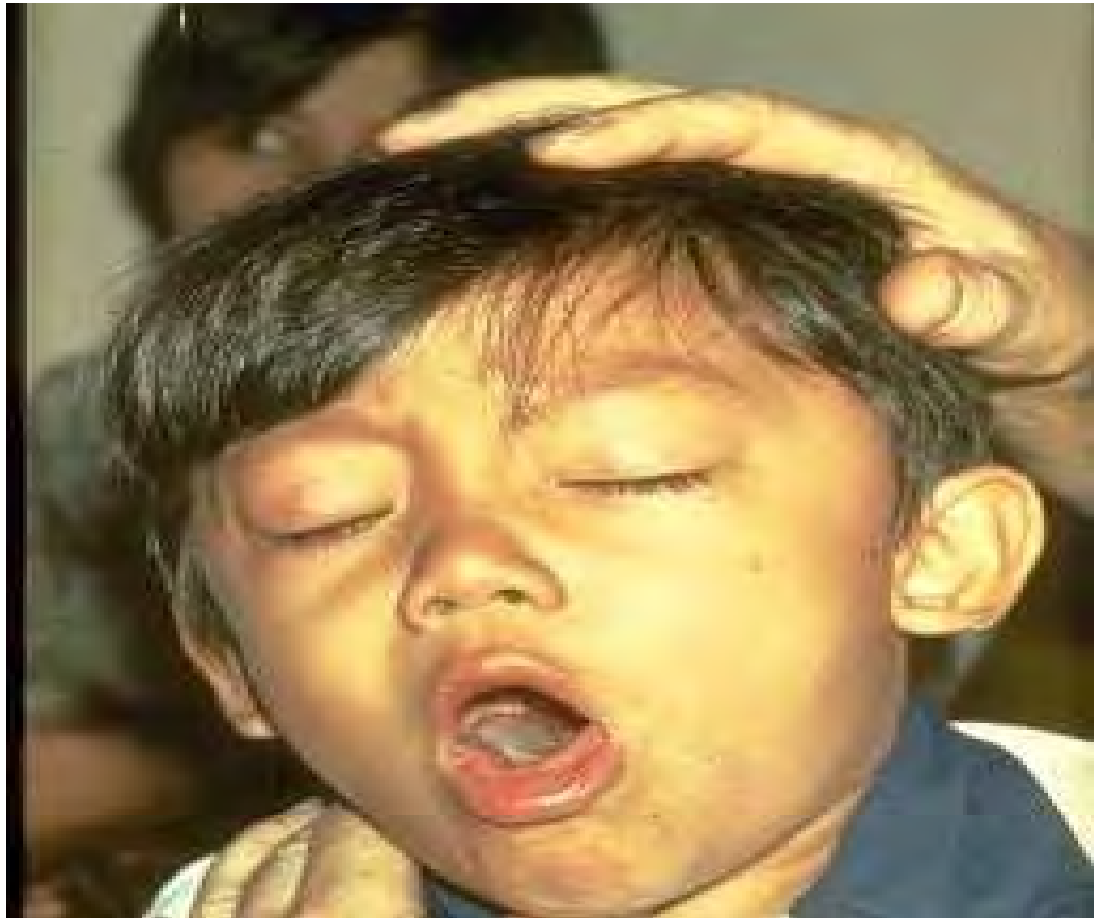
Faith and Science – epistemology from the perspective of faith

- Original source of truth is God
- Because God is all-knowing, there can be no new truth that God has not already known
- So scientists are finding God's truth in created world, whether they know it or not
  - "Thinking God's thoughts after Him (Her)"
- God is not afraid of science
- God created the regularities that permit science to occur
- Faith and science do not have to be opposed to each other
  - Unfortunately, starting points often differ

Biblically, Why Vaccinate?

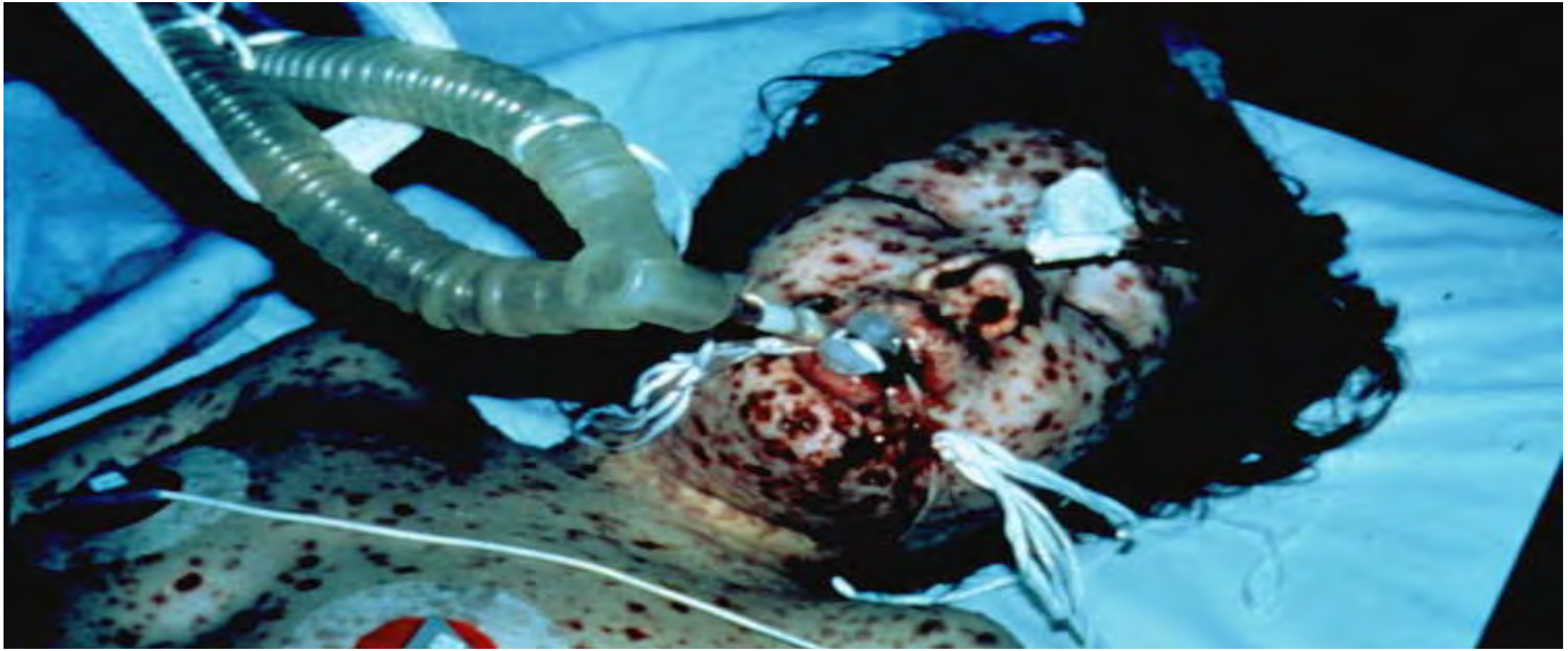
- When you build a new house, be sure to put a railing around the edge of the roof. Then you will not be responsible if someone falls off and is killed." (Deuteronomy 22:8, Good News Translation (GNT))
- Physical protection, even with human-made instruments, is seen as a blessing: "May his towns be protected with iron gates." (Deuteronomy 33:25, GNT)
- Animals who might gore others were to be penned, at penalty of death (Exodus 21:29)
- The "Love one another" passages in the New Testament support caring for another, with direct attention to caring for physical needs: "…our love should not be just words … shows itself in action." (1 John 3:18 GNT). Being vaccinated dramatically reduces the risk that one will transmit virus to others.
- Promote justice and avoid freeriding on herd immunity

Pertussis



Polio

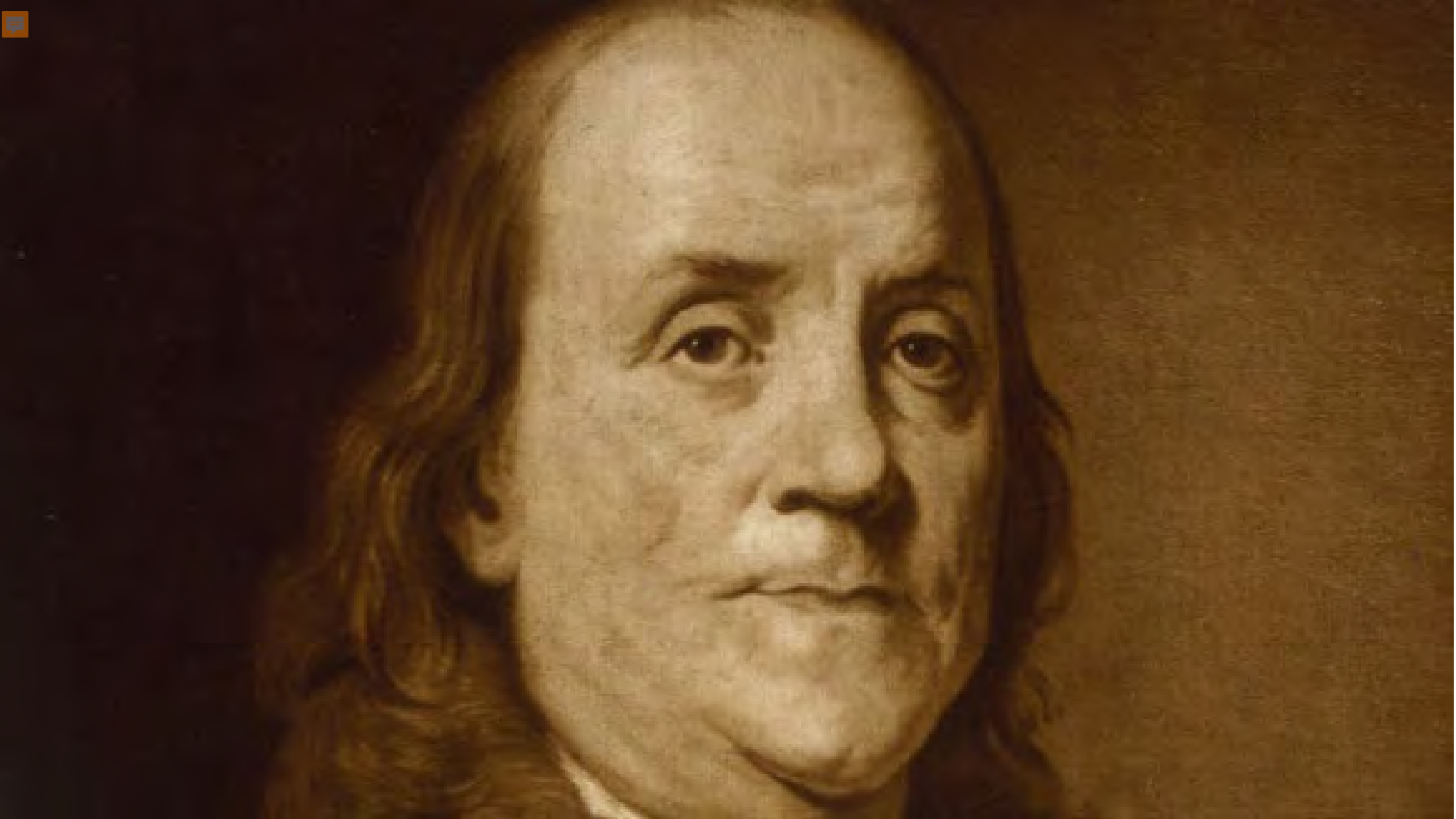
Varicella – secondary complications

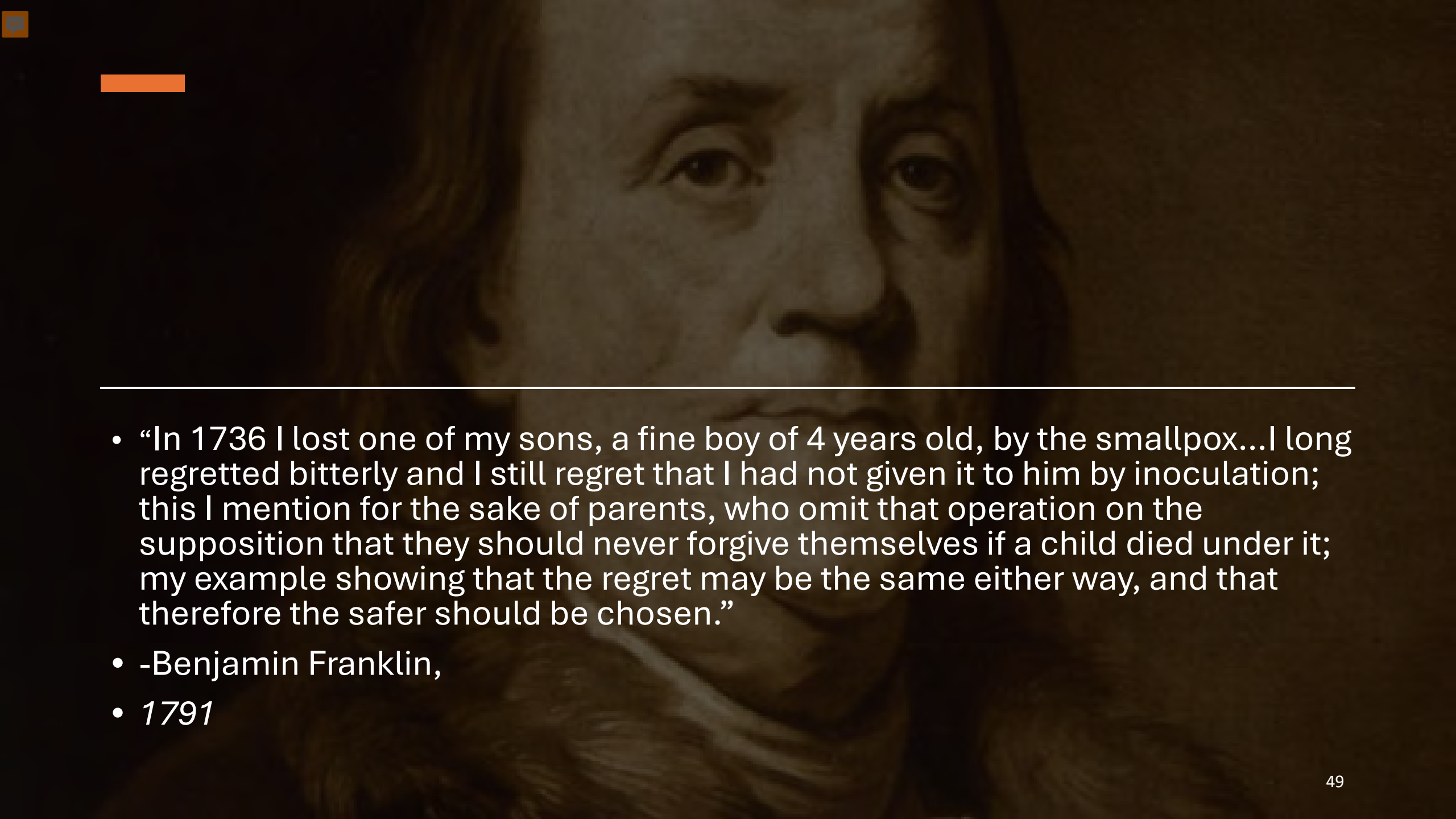


Discuss suffering from vaccine preventable diseases

Families Fighting Flu

www.familiesfightingflu.org



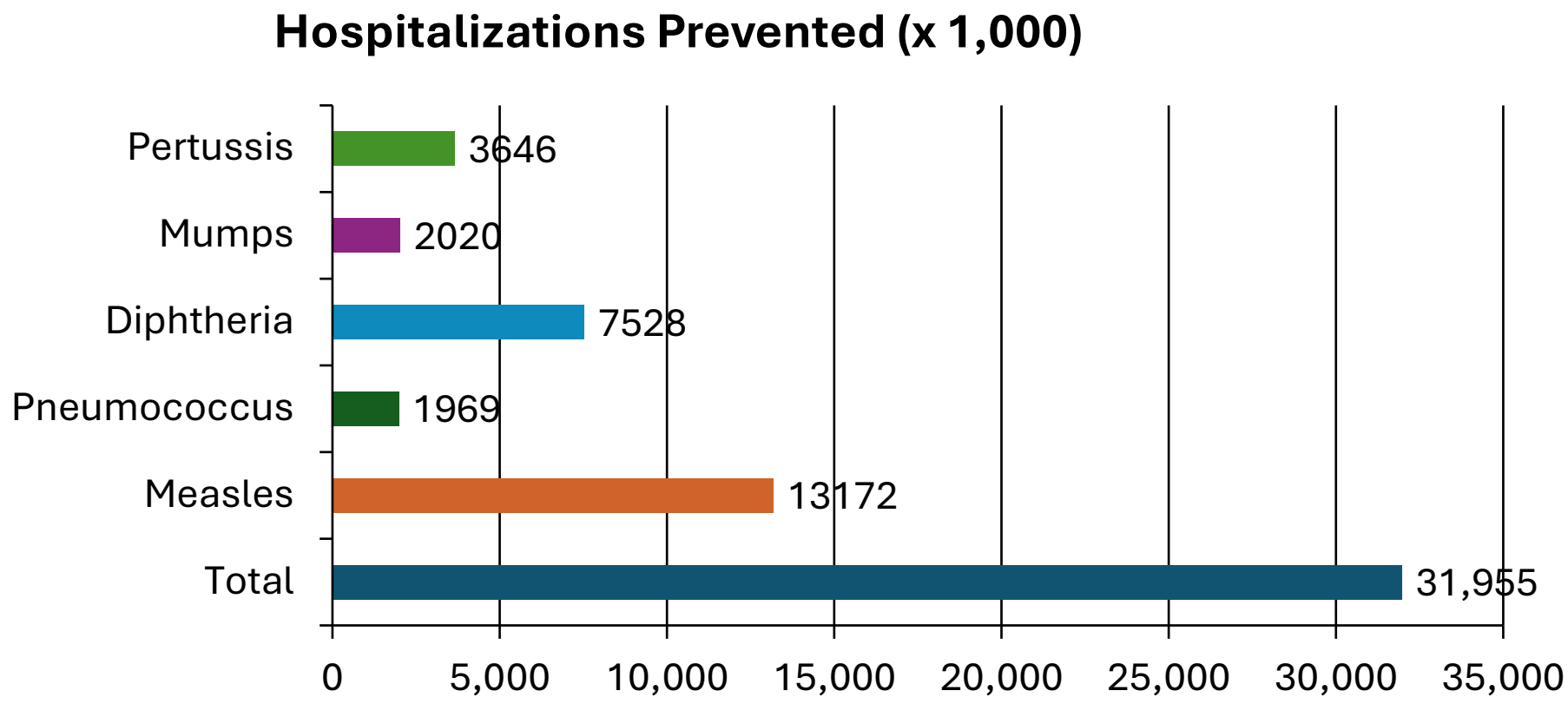


- “In 1736 I lost one of my sons, a fine boy of 4 years old, by the smallpox…I long regretted bitterly and I still regret that I had not given it to him by inoculation; this I mention for the sake of parents, who omit that operation on the supposition that they should never forgive themselves if a child died under it; my example showing that the regret may be the same either way, and that therefore the safer should be chosen.”
- -Benjamin Franklin,
- *1791*


Questions and Comments

Extras

Top 5 Vaccine-preventable Diseases by Hospitalizations Prevented by Childhood Vaccination, US, 1994-2023



Health and Economic Benefits of Routine Childhood Immunizations in the Era of the Vaccines for Children Program — United States, 1994–2023 (cdc.gov)

Orr Criteria for Moral Complicity

(1) timing
(2) proximity
(3) certitude,
(4) knowledge and
(5) intent

- Cell lines 1970s/1980s
  - Can you drive in South of US on road made with slave labor? Remote
- Distant
  - Chemistry class used in bomb making
  - Cell lines used many purposes & multiply
- Vaccines work well, history known
- Are vaccinees aware of history?
  - Drivers on roads in South aware? Cobalt in phones from child slave labor?
- Prevention of disease, protection of others

Orr RD. Addressing Issues of Moral Complicity: When? Where? Why? and Other Questions. Dignity. 2003; 9(2): The Center for BioEthics & Human Dignity, Trinity International University; 2003. Acccessed 5/5/2021
Addressing Issues of Moral Complicity: When? Where? Why? and Other Questions | The Center for Bioethics & Human Dignity (cbhd.org).

Concern for Moral Complicity with Evil & fetal cell lines used in some but not all COVID vaccines

- Formal ethical analyses using Christian ethical principles shows vaccination is ethical
  - Orr Criteria
  - Rule of Double Effect – Aquinas (intention is key)
- Altruism and protecting others from a virus that is often transmitted while asymptomatic or pre-symptomatic
  - Pastor and wife who hurt their congregation – guard the flock?
  - Herd immunity protects the least of these
- Religious texts and many religious leaders support prevention and vaccination
- Most COVID-19 vaccines not developed in fetal cell lines
  - J&J developed in PER.C6 cell line from abortion about 1985
- If there is a concern, administer vaccines not developed in fetal cell lines – mRNA not developed but tested with cell lines; vaccines totally free of cell lines coming

The Vatican's Congregation for the Doctrine of the Faith

"It is morally acceptable to receive Covid-19 vaccines that have used cell lines from aborted fetuses in their research and production process." Due to the situation of the ongoing pandemic, "all vaccinations recognized as clinically safe and effective can be used in good conscience with the certain knowledge that the use of such vaccines does not constitute formal cooperation with the abortion from which the cells used in production of the vaccines derive . . . The morality of vaccination depends not only on one's own health, but also on the duty to pursue the common good"

Excuse: “God is sovereign”

- “God is sovereign;” therefore, “vaccination is unneeded because God will determine whether or not I am infected and the outcome if I am infected.”
- Analogical rebuttal: God is sovereign:
  - Don’t need gas in the car
  - Can play in the middle of a busy expressway
- God’s sovereignty is unquestionable
- He has ordained both human responsibility and freewill..

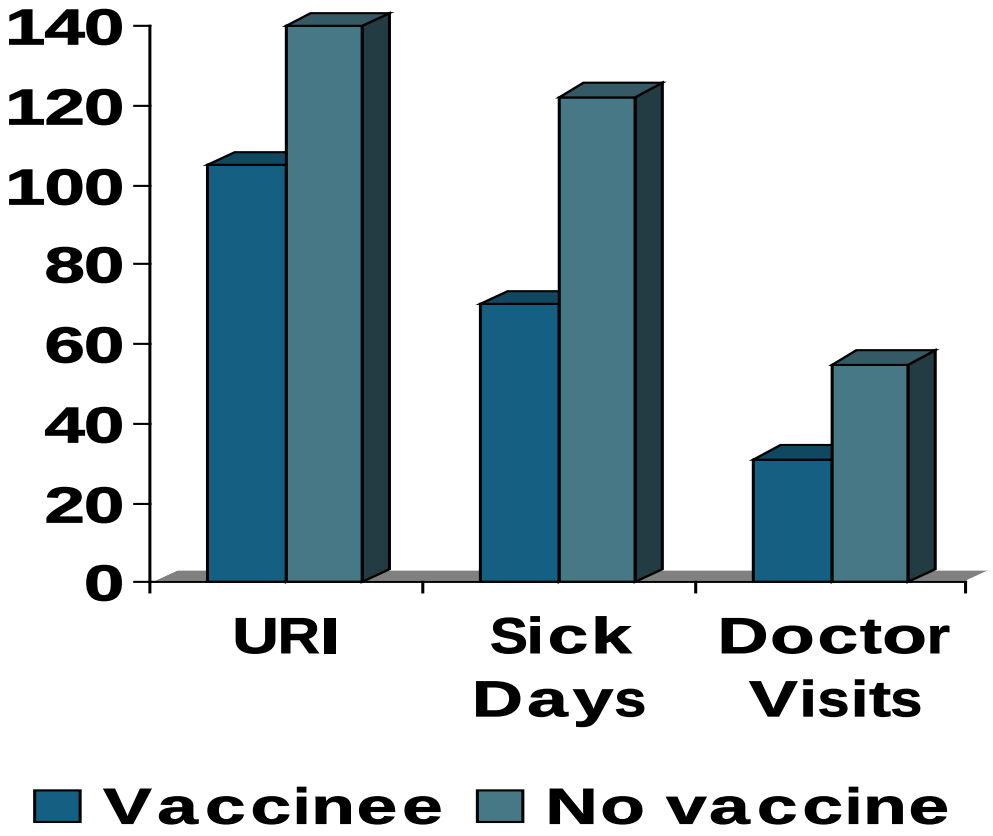
Excuse #1: “God is sovereign”

- God has ordained both human responsibility and freewill:
- Consider David’s sinful census against the advice of his general and the rebuke sent through Gad the prophet: “… ‘This is what the LORD says: “Take your choice: three years of famine, three months of being swept away before your enemies… or three days of the sword of the LORD…” Now then, decide how I should answer the one who sent me’” (1 Chronicles 21:11-12, NIV).
- The Westminster Confession of Faith: “From all eternity and by the completely wise and holy purpose of his own will, God has freely and unchangeably ordained whatever happens. This ordainment does not mean, however, that God is the author of sin (He is not), that he represses the will of his created beings, or that he takes away the freedom or contingency of secondary causes. Rather, the will of created beings and the freedom and contingency of secondary causes are established by Him.”[6]
- To resign all responsibility for contracting or transmitting COVID-19 suggests an underlying philosophy of determinism, leaving humans to dance on the strings of a grand puppet-master.

New ACIP recommendation in Solid Organ Transplant Recipients

- All persons should receive an age-appropriate influenza vaccine (i.e., one approved for their age), with the following exception: solid organ transplant recipients aged 18 through 64 years on immunosuppressive medication regimens may receive either HD-IIV3 or aIIV3 as an acceptable option (without a preference over other age-appropriate IIV3s or RIV3).

Benefit of IIV in Healthy Adults Aged 18-64



- Saved $46.85 per person vaccinated

Source: *N Engl J Med.* 1995;333:889-893.

New Adult Pneumococcal Vaccines in Advanced Stages of Development

	1	3	4	5	6A	6B	7F	9V	14	18C	19A	19F	23F	22F	33F	8	10A	11A	12F	15B	2	9N	17F	20	15A	15C	16F	23A	23B	24F	31	35B	7C
PCV15																																	
PCV20																																	
PPSV23																																	
PCV21																																	
Pn-MAPS24v																																	
VAX-24																																	
VAX-31																																	

24-valent pneumococcal vaccines:

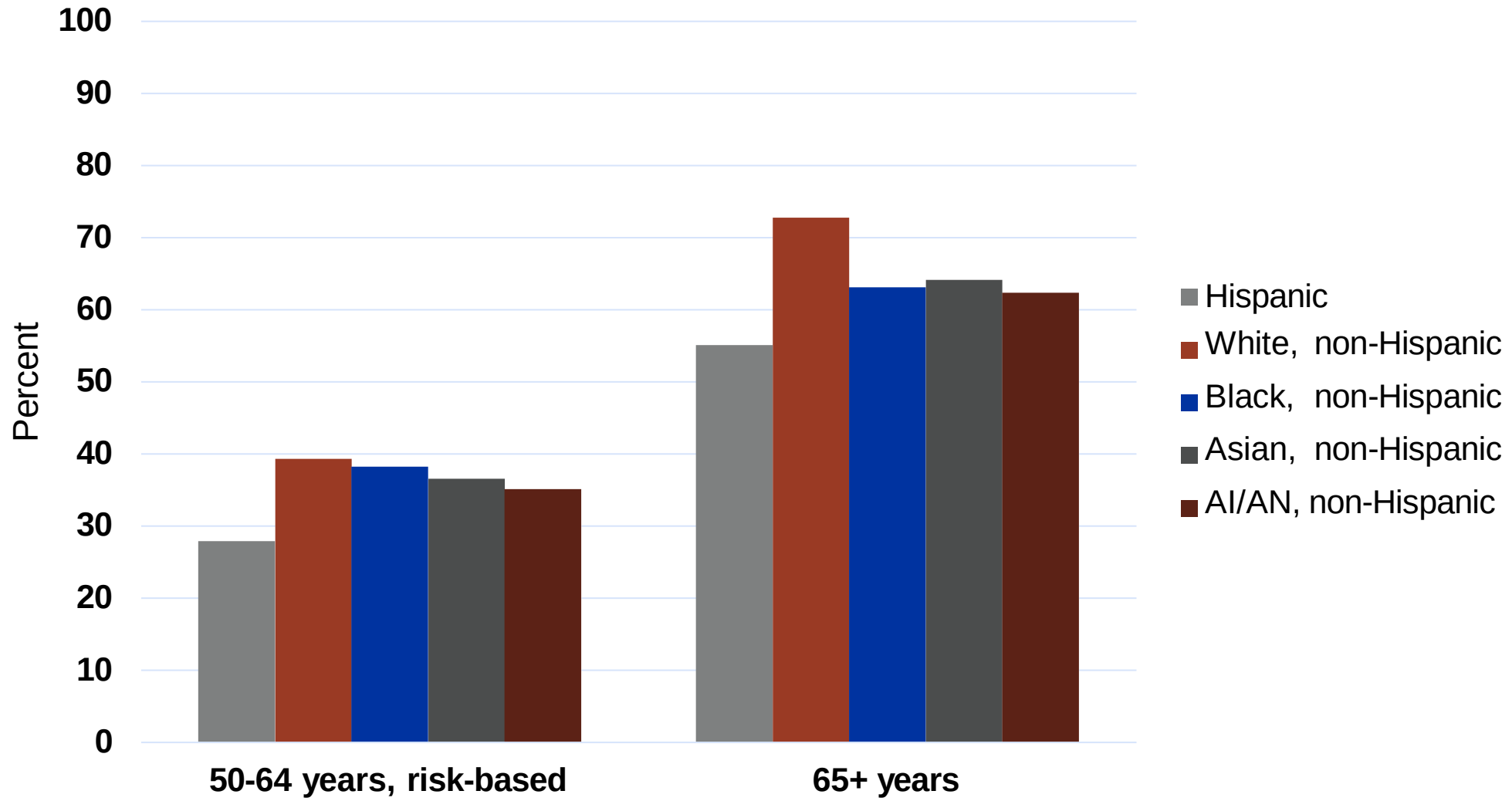
- **Pn-MAPS24v (GSK):** Completed phase 1/2 study for adults; Breakthrough Therapy Designation granted and next steps in preparation; undergoing phase 2 studies in infants[1]
- **VAX-24 (Vaxcyte):** Completed enrollment for phase 2 studies in infants[2]; topline results anticipated **in 2025**

31-valent pneumococcal vaccine (VAX-31, Vaxcyte):

- Reported topline results of phase 1/2 study in adults aged ≥50 years[3]; plan to initiate phase 3 pivotal non-inferiority study by **mid-2025**
- Plans to initiate VAX-31 Infant Phase 2 Study in **Q1 of 2025** following IND submission and clearance

1. Chichili et al. Vaccine 2022; 2. Vaxcyte Completes Enrollment of Phase 2 Study Evaluating VAX-24 for the Prevention of Invasive Pneumococcal Disease (IPD) in Infants - Vaxcyte, Inc.; 3. VAX-31 Phase ½ Study Topline Results in Adults Aged 50 and Older. September 3, 2024

Disparities in pneumococcal vaccine coverage by race/ethnicity exist for both age-based and risk-based indications



Source: BRFSS 2022; AI/AN=American Indian and Alaska Native

PCV13-experienced adults who have not completed the recommended vaccine series

- **A single dose of either PCV20 or PCV21 is recommended for adults aged ≥19 years who have started their pneumococcal vaccine series with PCV13 but have not received all recommended pneumococcal vaccine doses.**

Change:

- **Removed the option to complete vaccine series with PPSV23 for PCV13-experienced adults**

Rationale:

- **The potential need for repeated PPSV23 doses in adults who received PCV13 was one of the reasons for the complexity of the recommendation.**

PCV-naïve adults (or adults with unknown history)

Underlying conditions	Previous vaccination history	Age 19–49 years	Age ≥50 years
None	None	No vaccine recommendation	PCV21 OR PCV20 OR PCV15 → ≥1yr → PPSV23*
Chronic medical conditions	None	PCV21 OR PCV20 OR PCV15 → ≥8wks† → PPSV23* (PCV15 → ≥1yr → PPSV23*)	
CSF leak, cochlear implant	None		
Immuno-compromised	None		

*If adults previously received PPSV23 before receiving a dose of PCV15, it need not be followed by another dose of PPSV23
†A minimum interval of 8 weeks can be considered for adults with an immunocompromising condition, cochlear implant, or cerebrospinal fluid leak

Use of 21-Valent Pneumococcal Conjugate Vaccine Among U.S. Adults: Recommendations of the Advisory Committee on Immunization Practices — United States, 2024 | MMWR