SIR MODELS & HERD IMMUNITY

Micaela Martinez, PhD

WE ACT for Environmental Justice

Susceptible-Infected-Recovered Models

(1) Population size

$$N = S + I + R$$

(2) Change in susceptible over time

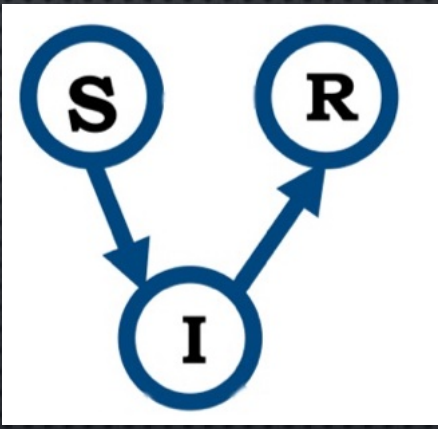
$$\frac{dS}{dt} = \mu N - \beta IS - \delta S$$

(3) Change in infected over time

$$\frac{dI}{dt} = \beta IS - \gamma I - \alpha I - \delta I$$

(4) Change in recovered over time

$$\frac{dR}{dt} = \gamma I - \delta R$$

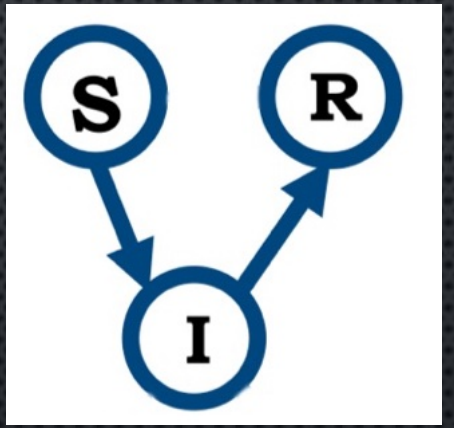


Susceptible-Infected-Recovered Models

+ individuals added to the class
- individuals leaving the class

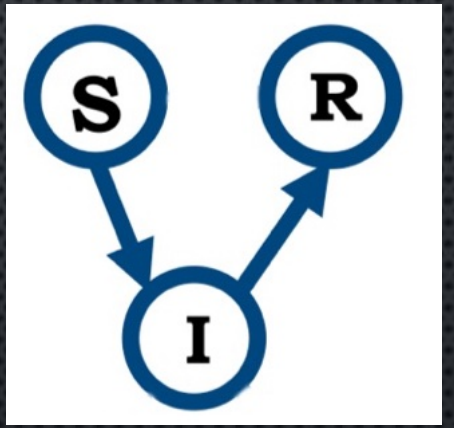
(2) Change in susceptible over time

$$\frac{dS}{dt} = \underbrace{\mu N}_{\text{New births}} - \underbrace{\beta I S}_{\text{New infections}} - \underbrace{\delta S}_{\text{Natural death}}$$



Susceptible-Infected-Recovered Models

+ individuals added to the class
- individuals leaving the class



(3) Change in infected over time

$$\frac{dI}{dt} = \beta IS - \gamma I - \alpha I - \delta I$$

New infections

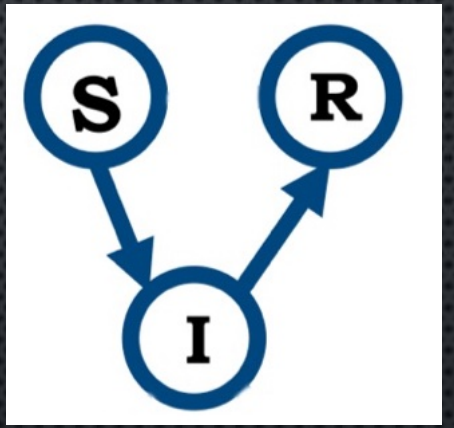
Infection-induced mortality

recovery

Natural death

Susceptible-Infected-Recovered Models

+ individuals added to the class
- individuals leaving the class



(4) Change in recovered over time

$$\frac{dR}{dt} = \gamma I - \delta R$$

recovery

Natural death

Growth of the Infected Class

$$\frac{dI}{dt} = \beta I S - \gamma I - \alpha I - \delta I$$

$$\frac{dI}{dt} = \underbrace{\beta S I}_{\text{Rate in}} - \underbrace{(\gamma + \alpha + \delta) I}_{\text{Rate out}}$$

Growth of the Infected Class

$\beta S = (\gamma + \alpha + \delta)$ Size of infected class remains constant

$\beta S > (\gamma + \alpha + \delta)$ Infected class grows (rate in > rate out)

$\beta S < (\gamma + \alpha + \delta)$ Infected class shrinks

Calculating the Reproductive Ratio

$$\frac{\beta S}{(\gamma + \alpha + \delta)}$$

If greater than 1, the infectious agent is successfully spreading and the infected class grows in size

Called the reproductive ratio because it tells us how many new infections "reproduced" by each infected individual before they leave the infected class

The Basic Reproductive Number

• **basic reproduction number, R_0**: average number of infections caused by a typical infected individual in a population consisting only of susceptibles; if $R_0 > 1$, the infectious agent can start to spread.

$$\frac{\beta S}{(\gamma + \alpha + \delta)}$$

For R0 assume S = N = 1

In this example, we are representing S, I, and R are fractions of the population in each state; thus, N = 1

The Basic Reproductive Number

• **basic reproduction number, R_0**: average number of infections caused by a typical infected individual in a population consisting only of susceptibles; if $R_0 > 1$, the infectious agent can start to spread.

$$R_0 = \frac{\beta}{\gamma + \alpha + \delta}$$

For R0 assume S = N = 1

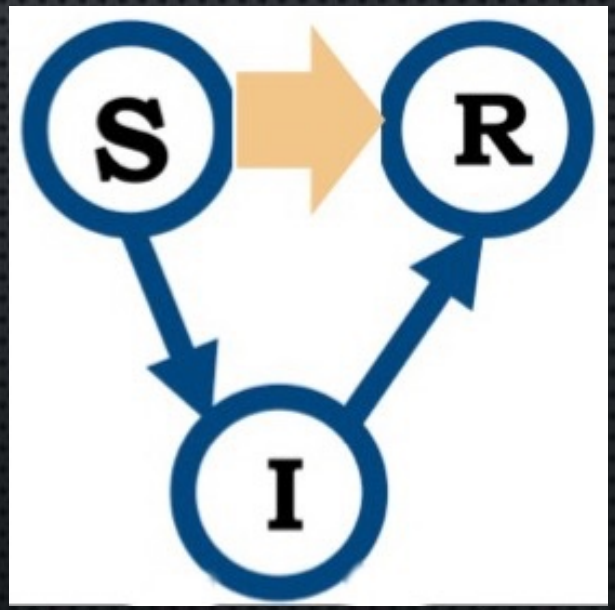
In this example, we are representing S, I, and R are fractions of the population in each state; thus, N = 1

- Anthrax
- Cervical Cancer (Human Papillomavirus)
- Diphtheria
- Hepatitis A
- Hepatitis B
- *Haemophilus influenzae* type b (Hib)
- Human Papillomavirus (HPV)
- Influenza (Flu)
- Japanese encephalitis (JE)
- Measles
- Meningococcal
- Mumps
- Pertussis
- Pneumococcal
- Polio
- Rabies
- Rotavirus
- Rubella
- Shingles (Herpes Zoster)
- Smallpox
- Tetanus
- Typhoid
- Tuberculosis (TB)
- Varicella (Chickenpox)
- Yellow Fever

Vaccination

To keep the infected class from growing, S can be reduced via vaccination

$$\frac{\beta S}{(\gamma + \alpha + \delta)}$$

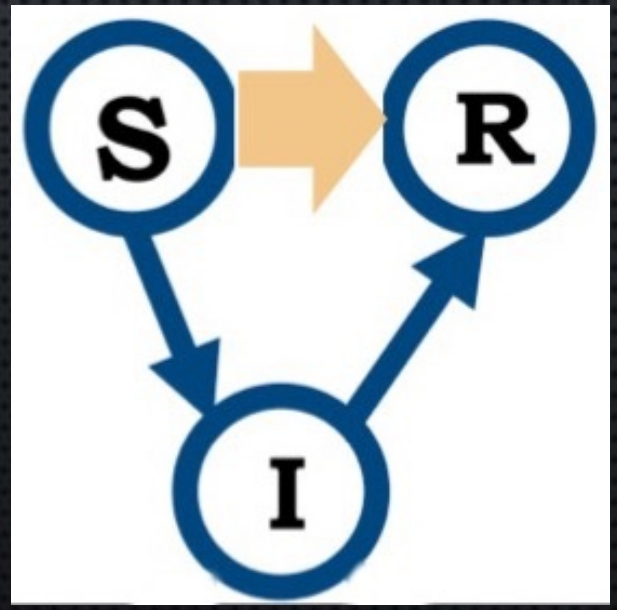


http://www.cdc.gov/vaccines/vpd-vac/vpd-list.htm

Herd Immunity

$$\frac{\beta S}{(\gamma + \alpha + \delta)} < 1$$

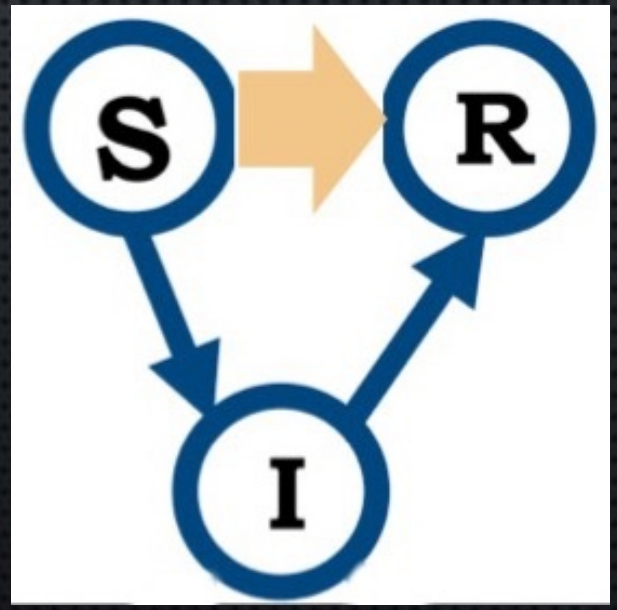
To keep the infected class from growing (prevent epidemics), not everyone needs to be vaccinated



Vaccinate enough such that infected class shrinks

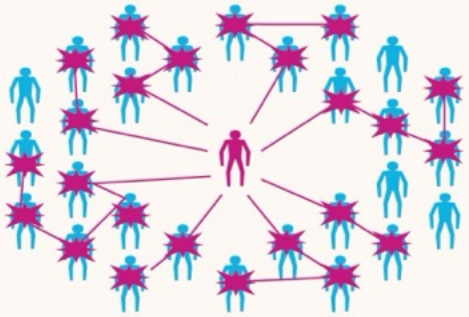
Herd Immunity

Herd Immunity occurs when **a sufficient proportion of a population is immune** (via vaccination and/or prior infection) to make transmission unlikely. Even individuals not vaccinated (such as newborns and those with chronic illnesses) are offered some protection because the disease has little opportunity to spread within the population.

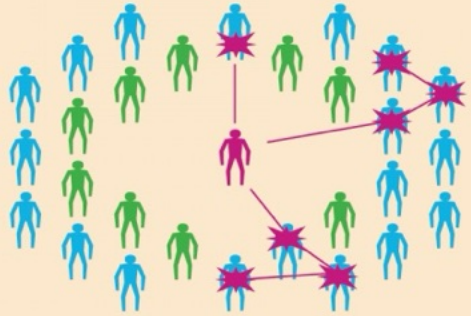


http://www.cdc.gov/vaccines/about/terms/glossary.htm

HOW HERD IMMUNITY WORKS



When no one has immunity, contagion has many opportunities to spread quickly.



The more immunity we have in the system, the less often contagion comes into contact with the susceptible.

Spread of contagious disease is contained.

Herd Immunity

Credit: UC Davis

Disease Eradication

Disease eradication: driving the infectious agent to extinction (local vs. global)

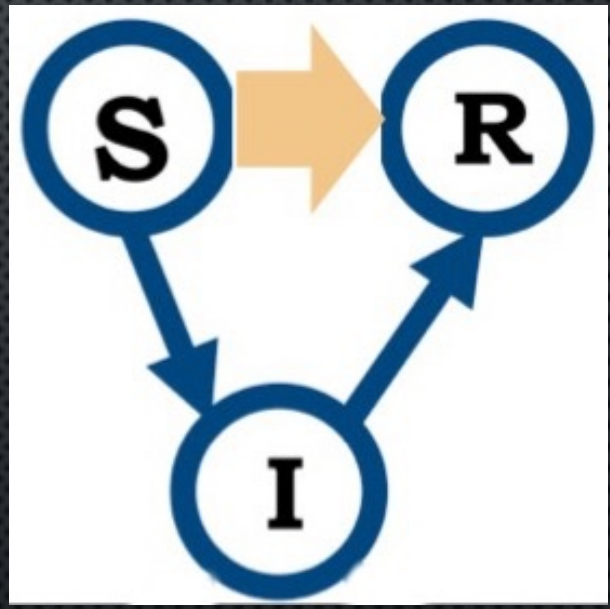
$$\frac{\beta S}{(\gamma + \alpha + \delta)} < 1$$

Local eradication happens if *S* is small-enough that the number of infected individuals declines to zero

Eradication Criterion

Calculating the critical vaccination fraction

$$\frac{\beta S}{(\gamma + \alpha + \delta)} < 1$$



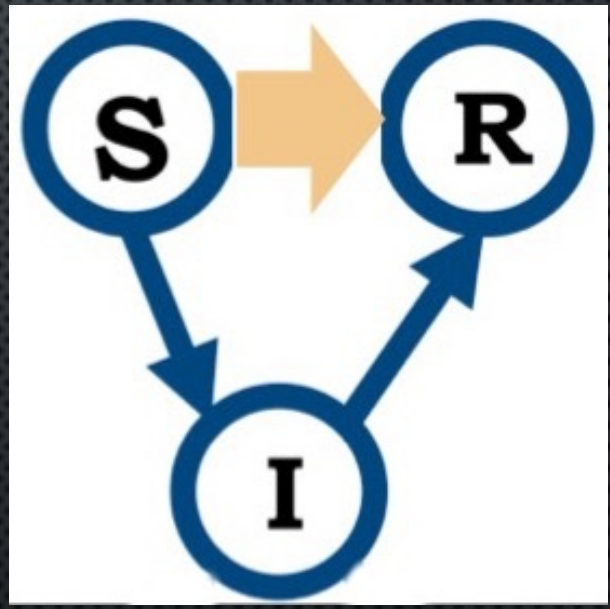
Eradication Criterion

Calculating the critical vaccination fraction

$$S < \frac{\gamma + \alpha + \delta}{\beta}$$

$$S_{\text{critical}} = \frac{\gamma + \alpha + \delta}{\beta} = \frac{1}{R_0}$$

$$V_{\text{critical}} = 1 - \frac{1}{R_0}$$



R0 and Eradication

infection	Geographic location	R0	$V_{critical}$ (%)
measles	England & Wales	16-18	94%
measles	Kansas, USA	5-6	83%
pertussis	Maryland, USA	16-17	94%
chicken pox	New Jersey, USA	7-8	88%
mumps	Netherlands	11-14	93%
rubella	West Germany	6-7	86%
polio	USA	5-6	83%

Eradication vs. Elimination

Global Eradication:
driving the infectious agent to **extinction globally**

Disease Elimination:
interruption of endemic transmission or maintaining the disease below a defined threshold

What have we eradicated or eliminated?

Eradicated:
Smallpox
Rinderpest (veterinary)

Eradication Attempts:
Yellow fever
Yaws
Malaria

Eradication "in progress":
Polio
Guinea Worm

Eliminated:
Leprosy
Measles (regions)
Rubella (Americas)

Imperfect Vaccine Efficacy

$$V_{\text{critical}} = 1 - \frac{1}{R_0}$$

$V_{critical}$ are those effectively immunized. We must account for vaccine failure

Imperfect Vaccine Efficacy

$$V_{\text{critical}} = 1 - \frac{1}{R_0}$$

$$V_{\text{critical}} = V_{\text{administered}} * \text{efficacy}$$

$$V_{\text{administered}} = \frac{1}{\text{efficacy}}\left(1 - \frac{1}{R_0}\right)$$

$V_{critical}$ are those effectively immunized. We must account for vaccine failure

THE LANCET
Respiratory Medicine

NEWS | ONLINE FIRST

Omicron variant and booster COVID-19 vaccines

Talha Khan Burki

Published: December 17, 2021 • DOI: https://doi.org/10.1016/S2213-2600(21)00559-2 •

The original strain of SARS-CoV-2 has an R0 of 2·5, while the delta variant (B.1.617.2) has an R0 of just under 7. Martin Hibberd, professor of emerging infectious diseases at London School of Hygiene & Tropical Medicine (London, UK), reckons omicron's R0 could be as high as 10. In the UK, cases of omicron are doubling

Exercises

$$V_{\text{critical}} = 1 - \frac{1}{R_0}$$

$$V_{\text{critical}} = V_{\text{administered}} * \text{efficacy}$$

$$V_{\text{administered}} = \frac{1}{\text{efficacy}}\left(1 - \frac{1}{R_0}\right)$$

(ex) Assume R0:

OG SARS-CoV-2 R0 = 2.5

Delta variant is R0 = 7

Omicron variant is R0 = 10

What fraction of the population needs to be vaccinated if we have a vaccine that is 100%, 90%, 70% of 50% effective in blocking transmission? I.e., efficacy 1, 0.9, 0.7, and 0.5

Exercises

(ex) Assume R0:

OG SARS-CoV-2 R0 = 2.5: 60%, 67%, 86%, 120%

Delta is R0 = 7: 86%, 95%, 122%,170%

Omicron is R0 = 10: 90%, 100%, 129%, 180%

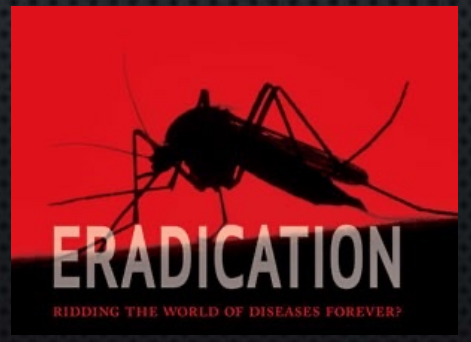
What fraction of the population needs to be vaccinated if we have a vaccine that is 100%, 90%, 70% of 50% effective in blocking transmission?

Initiatives

Disease Elimination and Eradication Efforts:

Malaria
Rubella
Rabies
Measles

Which programs will be set back due to COVID-19 pandemic?



break

Lecture 3: Vaccination

Micaela E. Martinez
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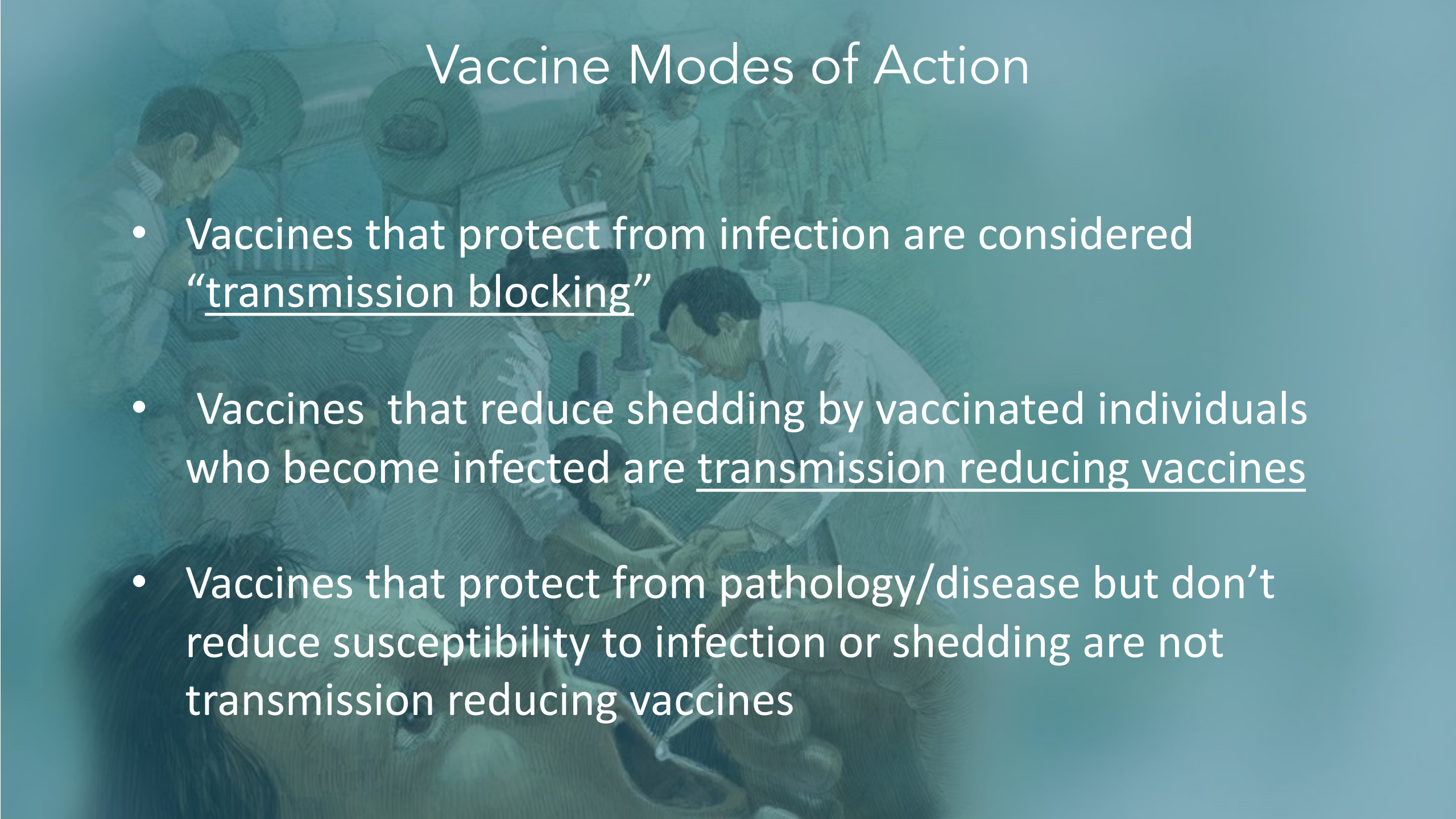
Vaccine Modes of Action

Vaccines have several modes of action, i.e., the way(s) by which they confer protection.

These can include any of the following alone or in combination:

- protection from infection
- reduction of shedding
- protection from disease/pathology

Vaccine Modes of Action



- Vaccines that protect from infection are considered "transmission blocking"
- Vaccines that reduce shedding by vaccinated individuals who become infected are transmission reducing vaccines
- Vaccines that protect from pathology/disease but don't reduce susceptibility to infection or shedding are not transmission reducing vaccines

- Anthrax
- Cervical Cancer (Human Papillomavirus)
- Diphtheria
- Hepatitis A
- Hepatitis B
- *Haemophilus influenzae* type b (Hib)
- Human Papillomavirus (HPV)
- Influenza (Flu)
- Japanese encephalitis (JE)
- Measles
- Meningococcal
- Mumps
- Pertussis
- Pneumococcal
- Polio
- Rabies
- Rotavirus
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- Tetanus
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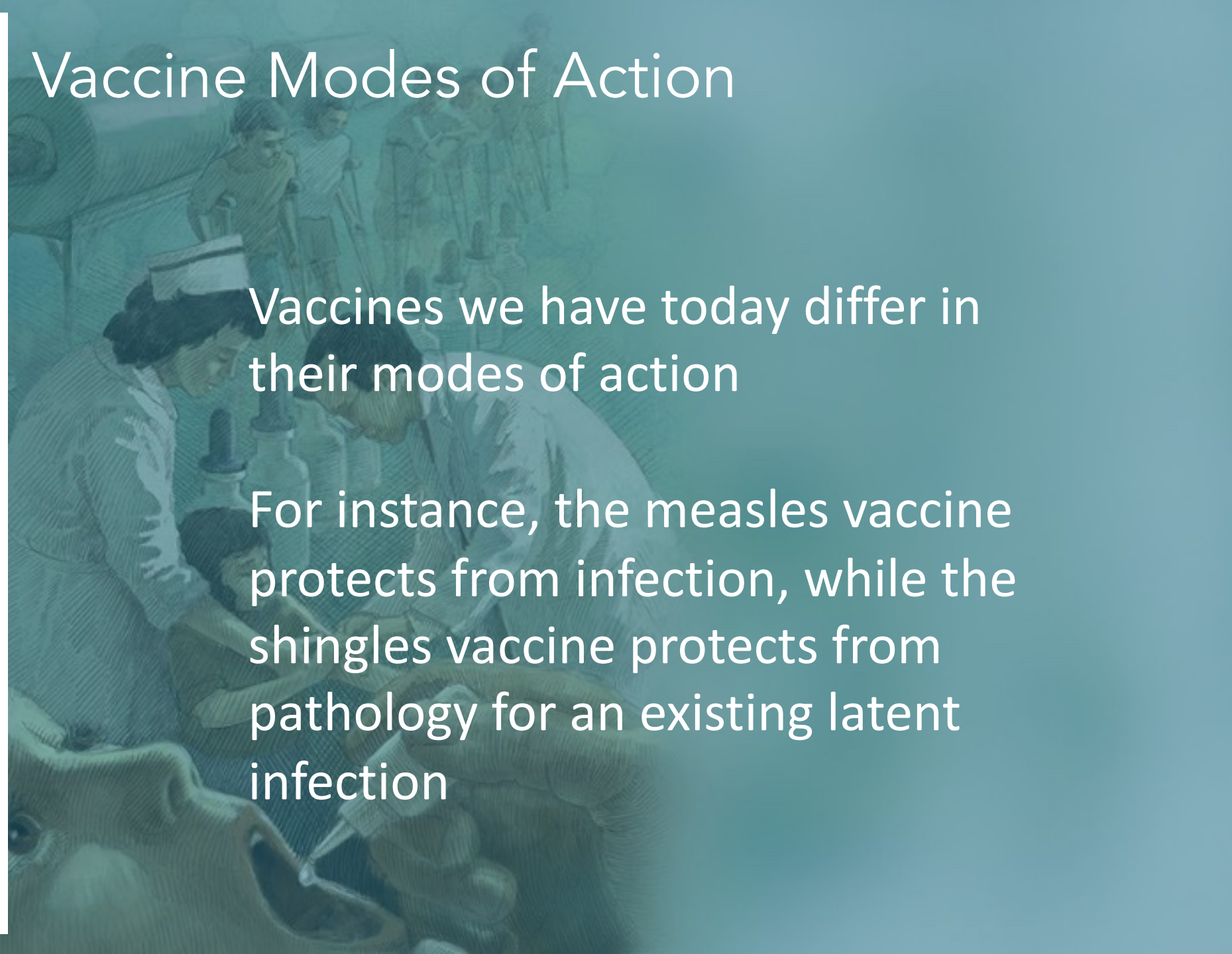
- Yellow Fever

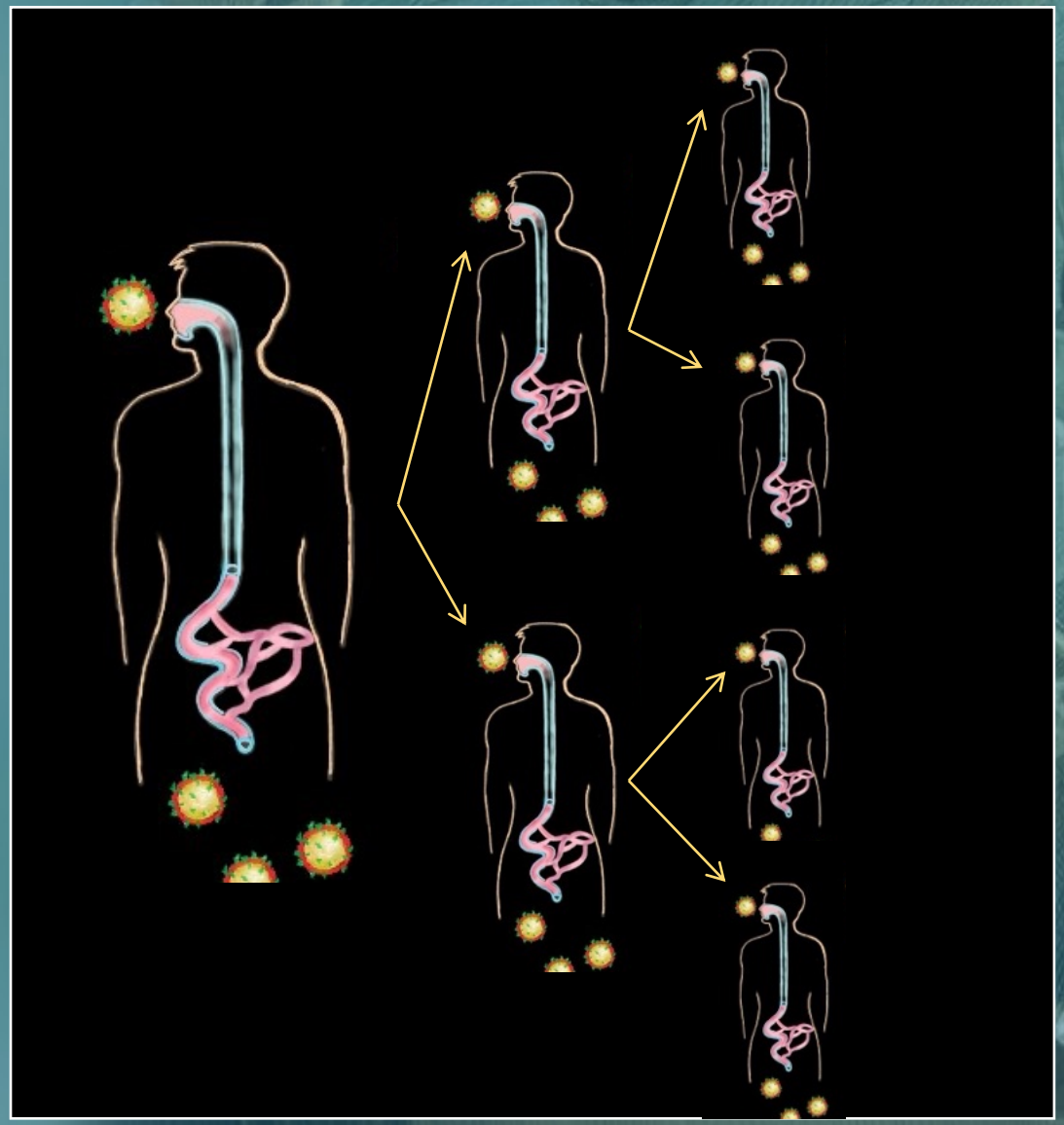
Vaccine Modes of Action



Vaccines we have today differ in their modes of action

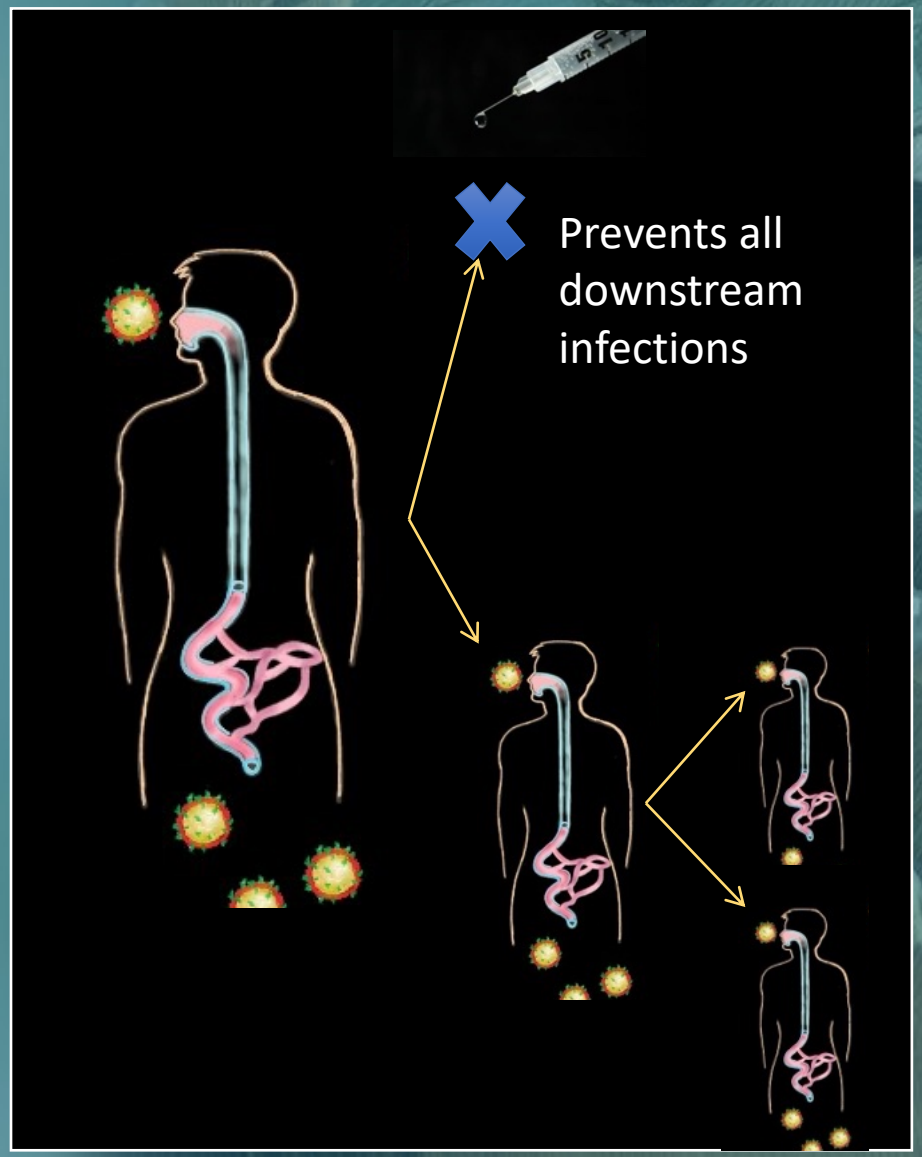
For instance, the measles vaccine protects from infection, while the shingles vaccine protects from pathology for an existing latent infection

How do vaccines work? [Mode of action]



Consider a fecal-oral transmission enteric pathogen where each infected individual infects 2 others

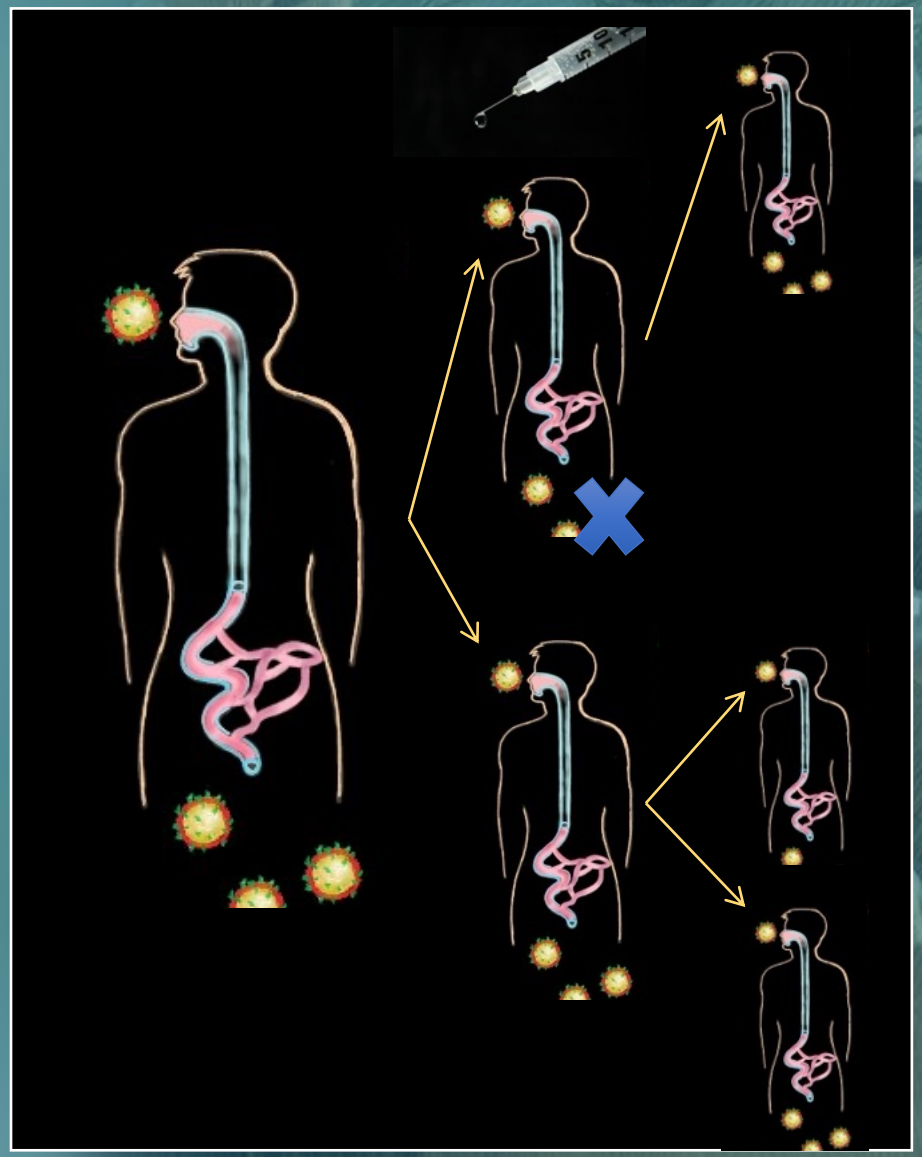
How do vaccines work? [Mode of action]



(1) Reduces susceptibility to infection

Protects vaccinated individual & others in the population (ripple effect)

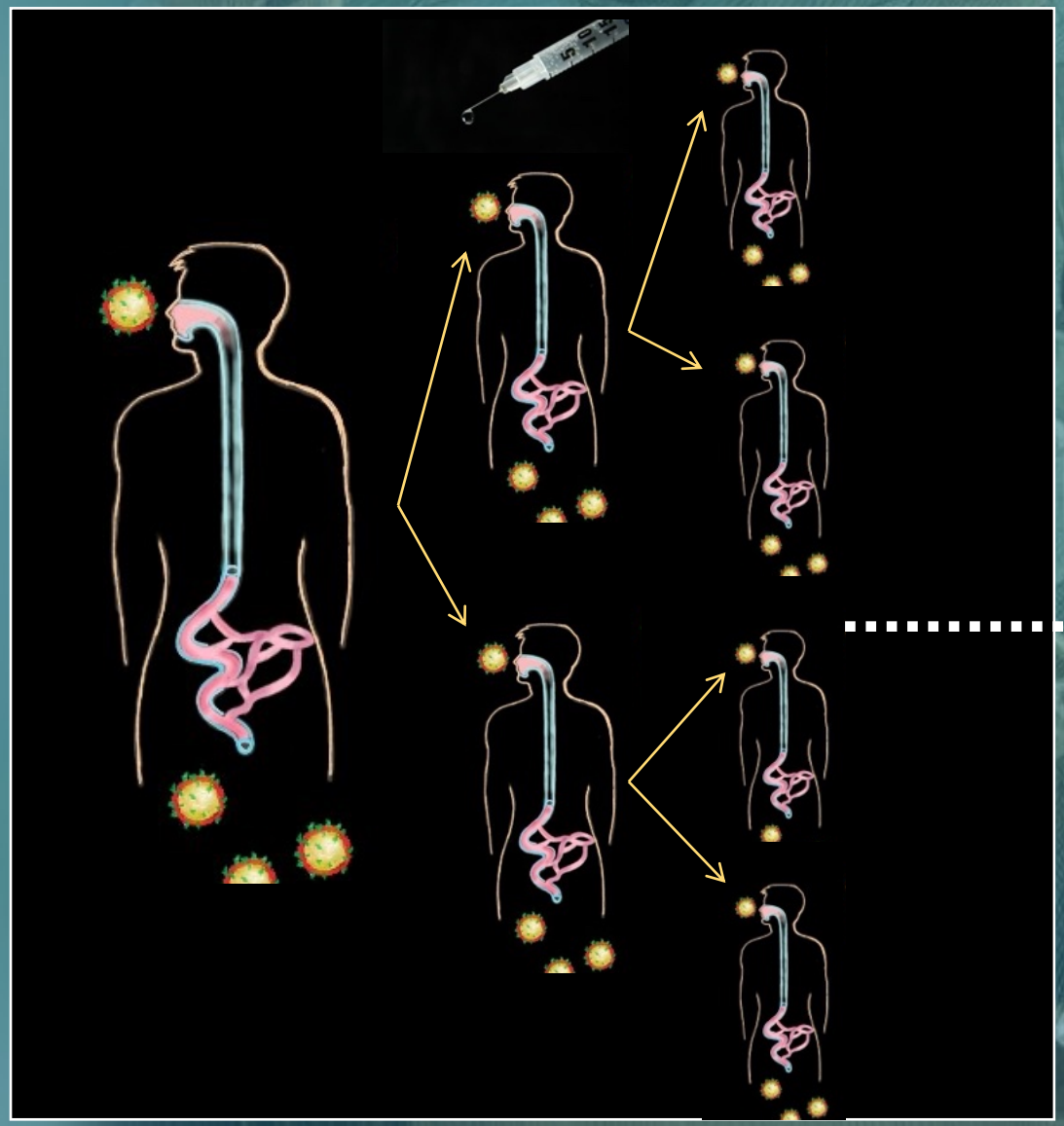
How do vaccines work? [Mode of action]



(2) Reduces infectiousness

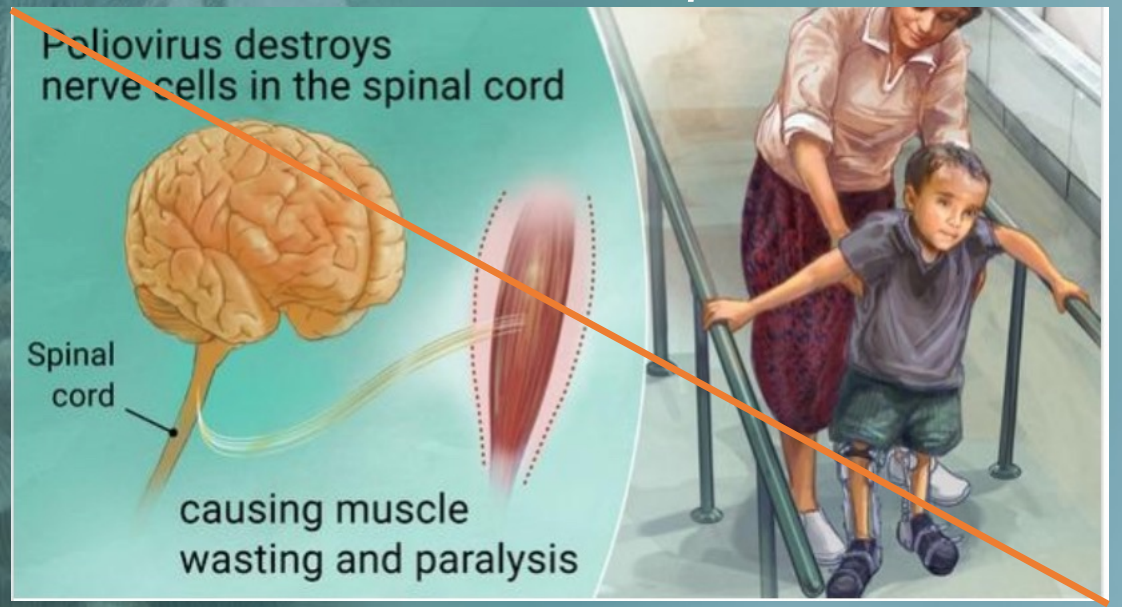
Protects others in the population (downstream effect)

How are the vaccines working?



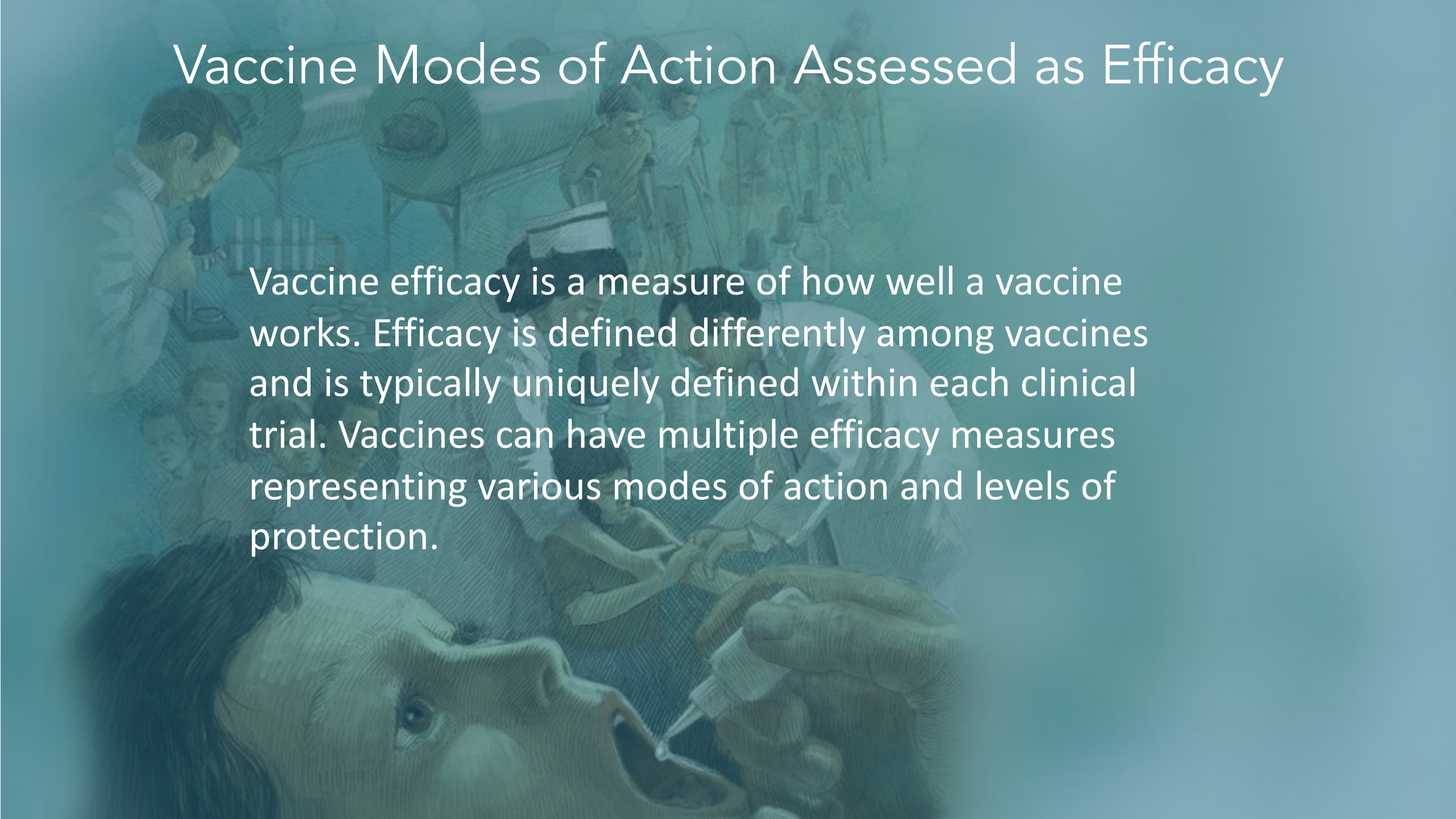
(3) Reduces symptoms

Protects vaccinated individuals from pathology



Martinez et al. (in prep)

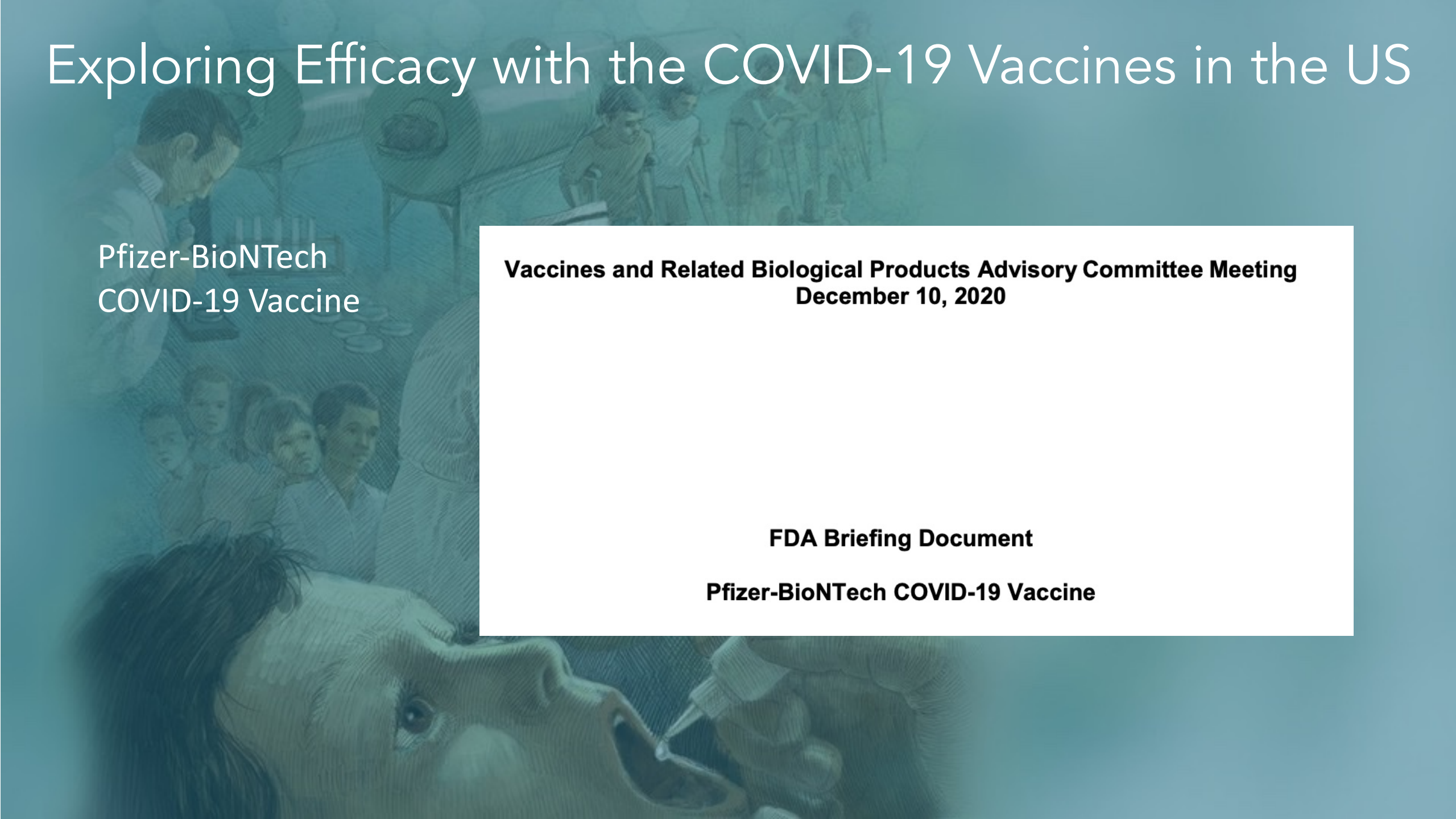
Vaccine Modes of Action Assessed as Efficacy



Vaccine efficacy is a measure of how well a vaccine works. Efficacy is defined differently among vaccines and is typically uniquely defined within each clinical trial. Vaccines can have multiple efficacy measures representing various modes of action and levels of protection.

Exploring Efficacy with the COVID-19 Vaccines in the US

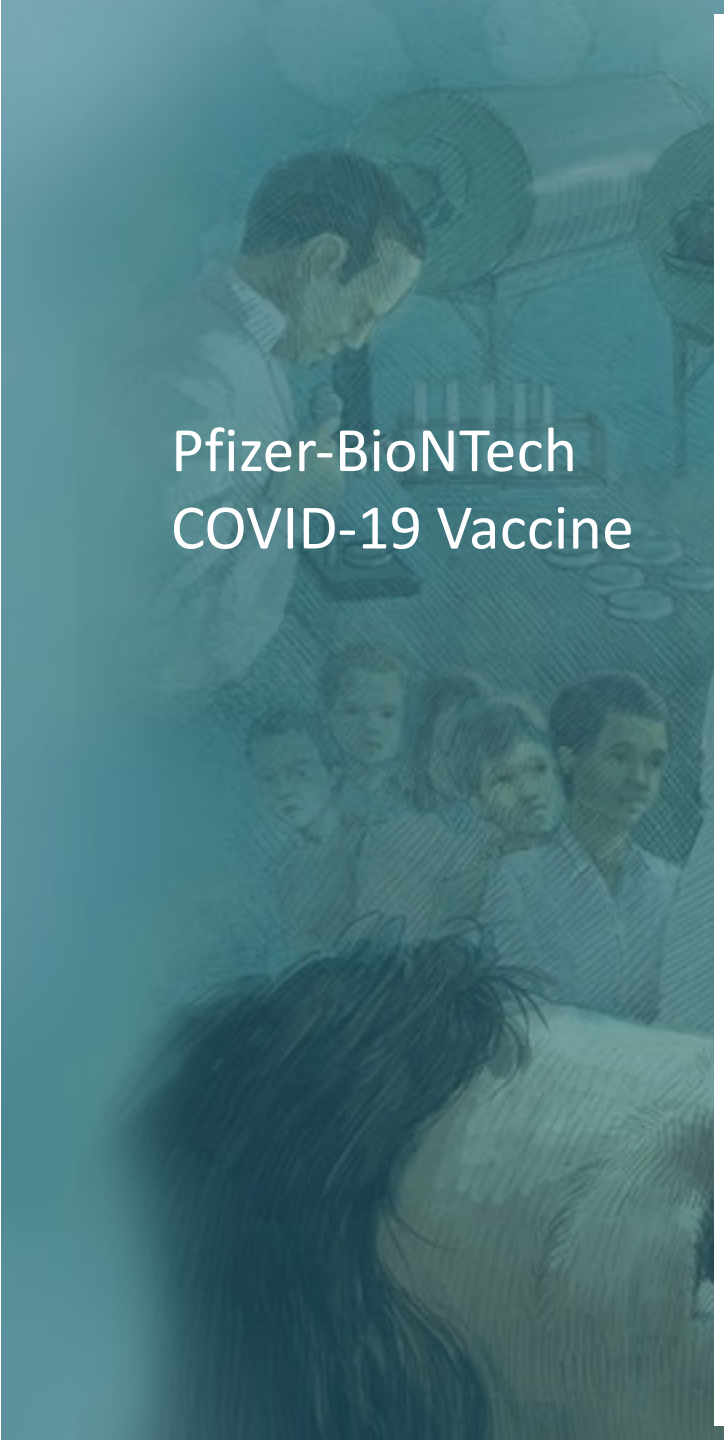
Pfizer-BioNTech
COVID-19 Vaccine



Vaccines and Related Biological Products Advisory Committee Meeting
December 10, 2020

FDA Briefing Document

Pfizer-BioNTech COVID-19 Vaccine



Pfizer-BioNTech COVID-19 Vaccine

Primary Efficacy Analyses

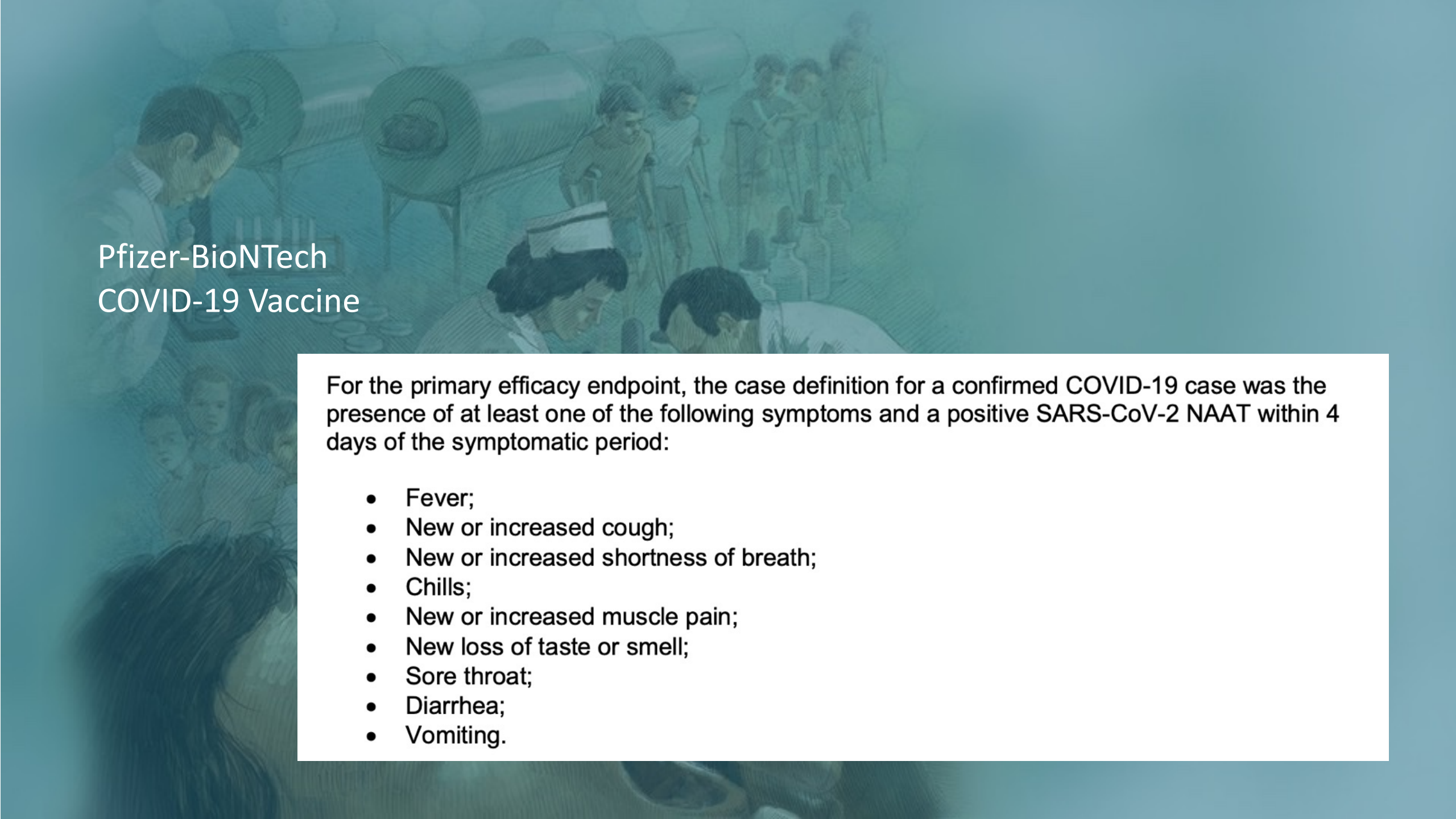
Efficacy Results – Primary Endpoint (Evaluable Efficacy Population)

For the first primary efficacy endpoint, vaccine efficacy (VE) for BNT162b2 against confirmed COVID-19 was evaluated in participants without evidence of prior SARS-CoV-2 infection prior to 7 days after Dose 2. For the second primary efficacy endpoint, VE for BNT162b2 against confirmed COVID-19 was evaluated in participants with and without evidence of prior SARS-CoV-2 infection prior to 7 days after Dose 2. Cases were counted from 7 days after Dose 2 for both endpoints. The criterion for success was met if the posterior probability that true vaccine efficacy >30% conditioning on the available data was >99.5% at the final analysis.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, VE against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0%. The case split was 8 COVID-19 cases in the BNT162b2 group compared to 162 COVID-19 cases in the placebo group (Table 6). The 95% credible interval for the vaccine efficacy was 90.3% to 97.6%, indicating that the true VE is at least 90.3% with a 97.5% probability, which met the pre-specified success criterion.

Table 6. Final Analysis of Efficacy of BNT162b2 Against Confirmed COVID-19 From 7 Days After Dose 2 in Participants Without Evidence of Prior SARS-CoV-2 Infection - Evaluable Efficacy Population

Pre-specified Age Group	BNT162b2 N[a] = 18198 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a] =18325 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)	Met Predefined Success Criterion*
All participants	8 2.214 (17411)	162 2.222 (17511)	95.0 (90.3, 97.6)[e]	Yes
16 to 55 years	5 1.234 (9897)	114 1.239 (9955)	95.6 (89.4, 98.6)[f]	NA
> 55 years and older	3 0.980 (7500)	48 0.983 (7543)	93.7 (80.6, 98.8)[f]	NA

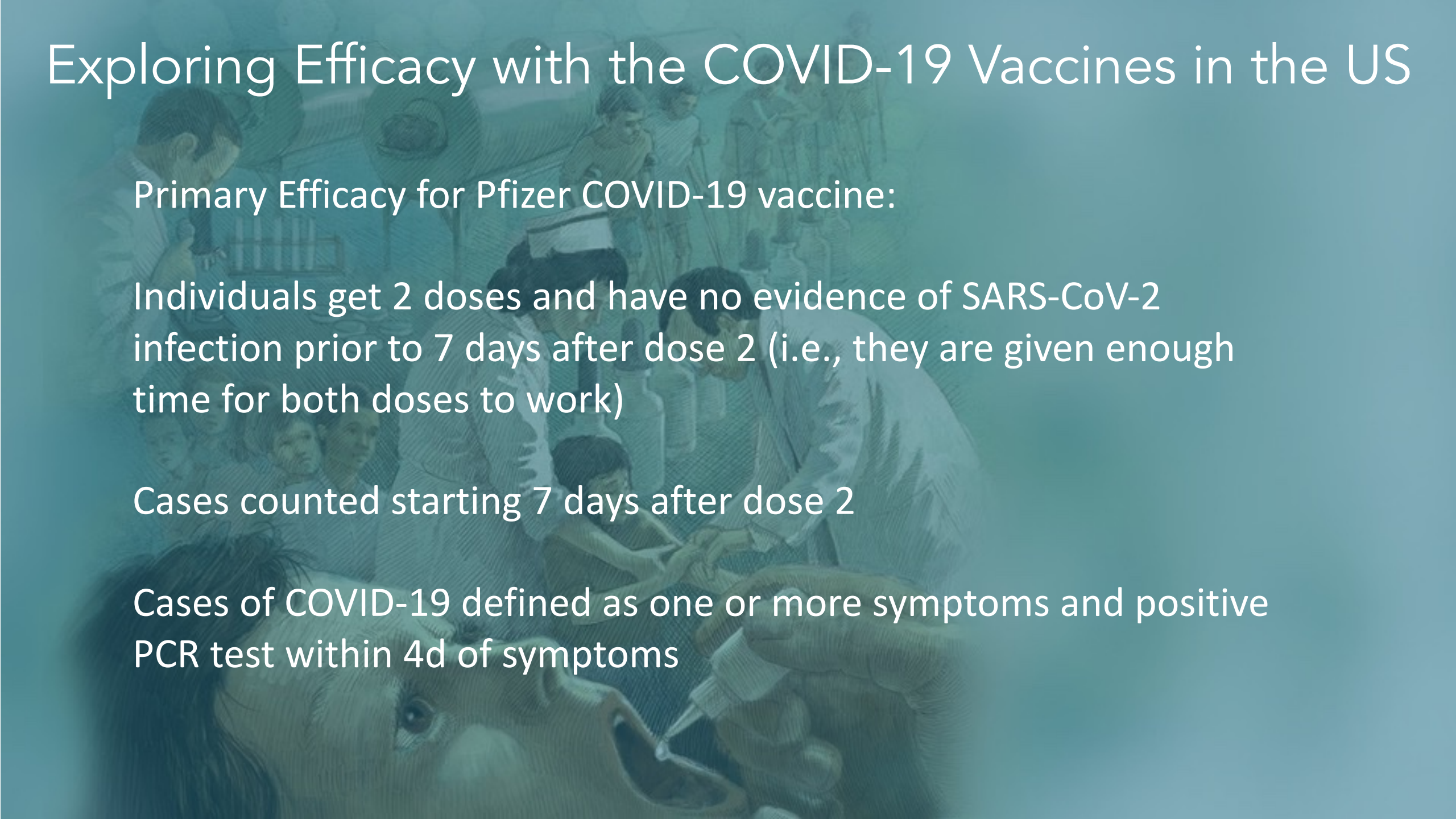


Pfizer-BioNTech COVID-19 Vaccine

For the primary efficacy endpoint, the case definition for a confirmed COVID-19 case was the presence of at least one of the following symptoms and a positive SARS-CoV-2 NAAT within 4 days of the symptomatic period:

- Fever;
- New or increased cough;
- New or increased shortness of breath;
- Chills;
- New or increased muscle pain;
- New loss of taste or smell;
- Sore throat;
- Diarrhea;
- Vomiting.

Exploring Efficacy with the COVID-19 Vaccines in the US



Primary Efficacy for Pfizer COVID-19 vaccine:

Individuals get 2 doses and have no evidence of SARS-CoV-2 infection prior to 7 days after dose 2 (i.e., they are given enough time for both doses to work)

Cases counted starting 7 days after dose 2

Cases of COVID-19 defined as one or more symptoms and positive PCR test within 4d of symptoms

Pfizer-BioNTech COVID-19 Vaccine used six efficacy metrics

Primary Efficacy Endpoints

Study C4591001 has two primary endpoints:

First primary endpoint: COVID-19 incidence per 1000 person-years of follow-up in participants without serological or virological evidence of past SARS-CoV-2 infection before and during vaccination regimen – cases confirmed ≥7 days after Dose 2

Second primary endpoint: COVID-19 incidence per 1000 person-years of follow-up in participants with and without evidence of past SARS-CoV-2 infection before and during vaccination regimen – cases confirmed ≥7 days after Dose 2

Secondary Efficacy Endpoints

Study C4591001 has secondary endpoints based on different approaches to COVID-19 case evaluation criteria as follows:

13

COVID-19 confirmed at least 14 days after Dose 2: COVID-19 incidence per 1000 person-years of follow up in participants either (1) without or (2) with and without serological or virological evidence of past SARS-CoV-2 infection before and during vaccination regimen – cases confirmed ≥14 days after Dose 2

Severe COVID-19: incidence per 1000 person-years of follow-up in participants either (1) without or (2) with and without evidence of past SARS-CoV-2 infection before and during vaccination regimen – cases confirmed either (1) ≥7 days after Dose 2 or (2) ≥14 days after Dose 2

CDC-defined COVID-19: incidence per 1000 person-years of follow-up in participants either (1) without or (2) with and without evidence of past SARS-CoV-2 infection before and during vaccination regimen – cases confirmed either (1) ≥7 days after Dose 2 or (2) ≥14 days after Dose 2.

Exploring Efficacy with the COVID-19 Vaccines in the US

Vaccines and Related Biological Products Advisory Committee Meeting
December 17, 2020

FDA Briefing Document

Moderna COVID-19 Vaccine

Exploring Efficacy with the COVID-19 Vaccines in the US

Other essential workers were also represented. The primary efficacy endpoint was efficacy of the vaccine to prevent protocol-defined COVID-19 occurring at least 14 days after the second dose in participants with negative SARS-CoV-2 status at baseline (i.e., negative RT-PCR and negative serology against SARS-CoV-2 nucleocapsid on Day 1).

Symptoms of COVID-19 experienced by participants during post-vaccination follow-up prompted an unscheduled illness visit and nasopharyngeal (NP) swab. NP samples were tested for SARS CoV-2 at a central laboratory using a reverse transcription-polymerase chain reaction (RT-PCR) test (Viracor; FDA authorized under EUA), or other sufficiently validated nucleic acid amplification-based test (NAAT). The central laboratory NAAT result is used for the case definition, unless it is not possible to test the sample at the central laboratory.

Moderna vaccine

. For the primary efficacy endpoint, the case definition for a confirmed COVID-19 case was defined as:

- At least TWO of the following systemic symptoms: Fever (≥38ºC), chills, myalgia, headache, sore throat, new olfactory and taste disorder(s), or
- At least ONE of the following respiratory signs/ symptoms: cough, shortness of breath or difficulty breathing, OR clinical or radiographical evidence of pneumonia; and
- NP swab, nasal swab, or saliva sample (or respiratory sample, if hospitalized) positive for SARS-CoV-2 by RT-PCR.

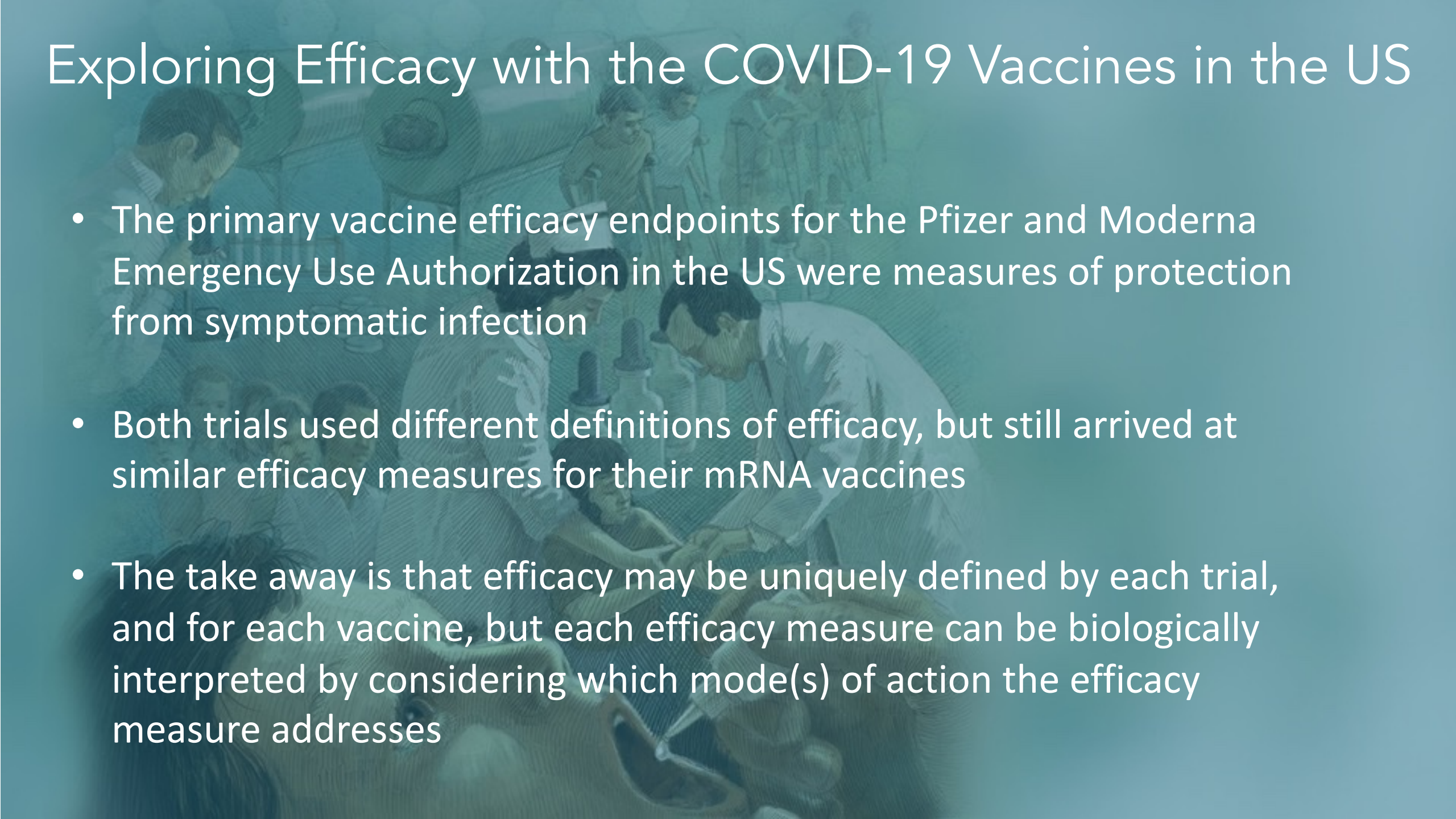
Exploring Efficacy with the COVID-19 Vaccines in the US

Table 9. Interim Analysis[a] for Primary Efficacy Endpoint, COVID-19 Starting 14 Days After the 2nd Dose, Per-Protocol Set

Primary Endpoint: COVID-19 (per adjudication committee assessment)	Vaccine Group N=13934 Cases n (%) (Incidence rate per 1,000 person-years)	Placebo Group N=13883 Cases n (%) (Incidence rate per 1,000 person-years)	Vaccine Efficacy (VE) % (95% CI)*	Met Predefined Success Criterion**
All participants	5 (<0.1) 1.840	90 (0.6) 33.365	94.5% (86.5%, 97.8%)	Yes
18 to <65	5 / 10407 (<0.1) 2.504	75 / 10384 (0.7) 37.788	93.4% (83.7%, 97.3%)	NA
65 and older	0 / 3527	15 / 3499 (0.4) 21.046	100%	NA

Moderna vaccine

Exploring Efficacy with the COVID-19 Vaccines in the US



- The primary vaccine efficacy endpoints for the Pfizer and Moderna Emergency Use Authorization in the US were measures of protection from symptomatic infection
- Both trials used different definitions of efficacy, but still arrived at similar efficacy measures for their mRNA vaccines
- The take away is that efficacy may be uniquely defined by each trial, and for each vaccine, but each efficacy measure can be biologically interpreted by considering which mode(s) of action the efficacy measure addresses

Exploring Efficacy with the COVID-19 Vaccines in the US

nature

Content Journal Info Publish

nature › news › article

NEWS · 19 FEBRUARY 2021

Can COVID vaccines stop transmission? Scientists race to find answers

Controlling the pandemic will require shots that prevent viral spread, but that feature is difficult to measure.

Smriti Mallapaty

Exploring Efficacy with the COVID-19 Vaccines in the US

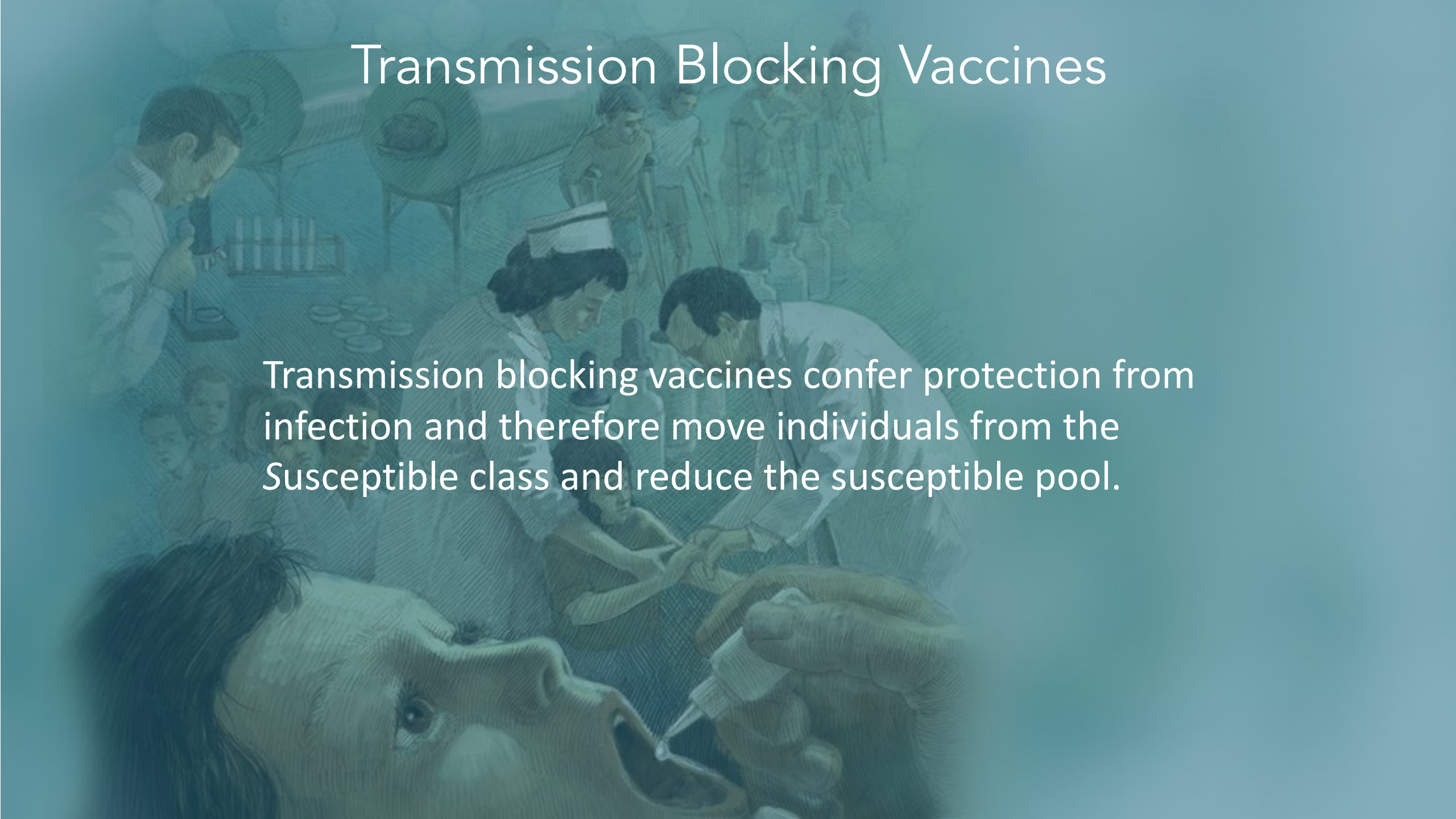
Impact and effectiveness of mRNA BNT162b2 vaccine against SARS-CoV-2 infections and COVID-19 cases, hospitalisations, and deaths following a nationwide vaccination campaign in Israel: an observational study using national surveillance data

Eric J Haas, Frederick J Angulo, John M McLaughlin, Emilia Anis, Shepherd R Singer, Farid Khan, Nati Brooks, Meir Smaja, Gabriel Mircus, Kaijie Pan, Jo Southern, David L Swerdlow, Luis Jodar, Yeheskel Levy, Sharon Alroy-Preis

Published May 15, 2021

Findings During the analysis period (Jan 24 to April 3, 2021), there were 232 268 SARS-CoV-2 infections, 7694 COVID-19 hospitalisations, 4481 severe or critical COVID-19 hospitalisations, and 1113 COVID-19 deaths in people aged 16 years or older. By April 3, 2021, 4 714 932 (72·1%) of 6 538 911 people aged 16 years and older were fully vaccinated with two doses of BNT162b2. Adjusted estimates of vaccine effectiveness at 7 days or longer after the second dose were 95·3% (95% CI 94·9–95·7; incidence rate 91·5 per 100 000 person-days in unvaccinated *vs* 3·1 per 100 000 person-days in fully vaccinated individuals) against SARS-CoV-2 infection, 91·5% (90·7–92·2; 40·9 *vs* 1·8 per 100 000 person-days) against asymptomatic SARS-CoV-2 infection, 97·0% (96·7–97·2; 32·5 *vs* 0·8 per 100 000 person-days) against symptomatic COVID-19, 97·2% (96·8–97·5; 4·6 *vs* 0·3 per 100 000 person-days) against COVID-19-related hospitalisation, 97·5% (97·1–97·8; 2·7 *vs* 0·2 per 100 000 person-days) against severe or critical COVID-19-related hospitalisation, and 96·7% (96·0–97·3; 0·6 *vs* 0·1 per 100 000 person-days) against COVID-19-related death. In all age groups, as vaccine coverage increased, the incidence of SARS-CoV-2 outcomes declined. 8006 of 8472 samples tested showed a spike gene target failure, giving an estimated prevalence of the B.1.1.7 variant of 94·5% among SARS-CoV-2 infections.

Transmission Blocking Vaccines



Transmission blocking vaccines confer protection from infection and therefore move individuals from the *S*usceptible class and reduce the susceptible pool.

Types of Vaccine Administration

- Routine immunization
- Pulsed vaccination/vaccination campaigns
- Catch-up campaigns
- Initial roll-out of new vaccine, often phased by risk and/or age group

2020 Recommended Immunizations for Children from Birth Through 6 Years Old

Vaccine	Birth	1 month	2 months	4 months	6 months	12 months	15 months	18 months	19–23 months	2–3 years	4–6 years
HepB	HepB	HepB			HepB						
RV			RV	RV	RV						
DTaP			DTaP	DTaP	DTaP		DTaP				DTaP
Hib			Hib	Hib	Hib	Hib					
PCV13			PCV13	PCV13	PCV13	PCV13					
IPV			IPV	IPV	IPV						IPV
Influenza (Yearly)*											
MMR											MMR
Varicella											Varicella
HepA§											

Is your family growing? To protect your new baby against whooping cough, get a Tdap vaccine. The recommended time is the 27th through 36th week of pregnancy. Talk to your doctor for more details.

Shaded boxes indicate the vaccine can be given during shown age range.

NOTE:
If your child misses a shot, you don't need to start over. Just go back to your child's doctor for the next shot. Talk with your child's doctor if you have questions about vaccines.

FOOTNOTES:

* Two doses given at least four weeks apart are recommended for children age 6 months through 8 years of age who are getting an influenza (flu) vaccine for the first time and for some other children in this age group.

§ Two doses of HepA vaccine are needed for lasting protection. The first dose of HepA vaccine should be given between 12 months and 23 months of age. The second dose should be given 6 months after the first dose. All children and adolescents over 24 months of age who have not been vaccinated should also receive 2 doses of HepA vaccine.

If your child has any medical conditions that put him at risk for infection or is traveling outside the United States, talk to your child's doctor about additional vaccines that he or she may need.

See back page for more information on vaccine-preventable diseases and the vaccines that prevent them.

For more information, call toll-free
1-800-CDC-INFO (1-800-232-4636)
or visit
www.cdc.gov/vaccines/parents

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

AAFP
AMERICAN ACADEMY OF FAMILY PHYSICIANS

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

Infant vaccination is the most common routine immunization

Indirect Protection via Cocooning

Surround Babies with Protection

CDC

Español (Spanish)

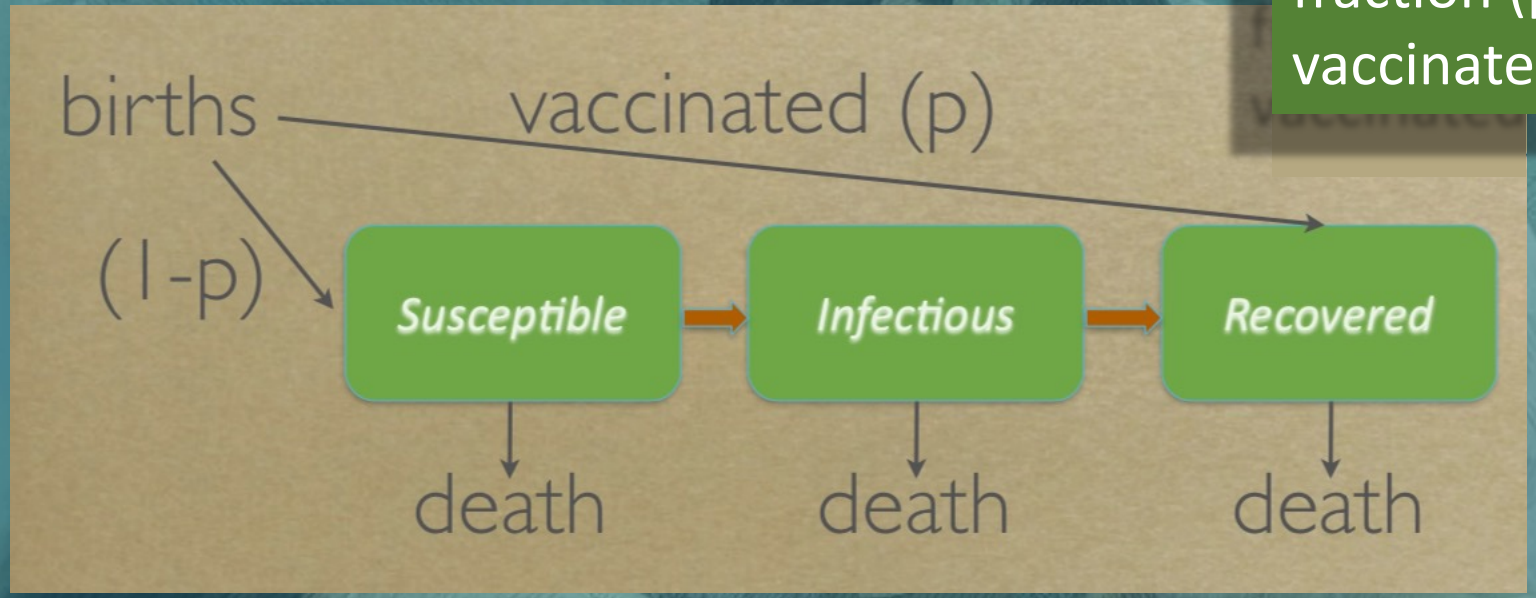
You can provide indirect protection to your baby by making sure everyone who is around him is up to date with their whooping cough vaccine. When your baby's family members and caregivers get a whooping cough vaccine they are not only protecting their own health, but also helping form a "cocoon" of disease protection around the baby during the first few months of life. Anyone who is around babies should be up-to-date with their whooping cough vaccine.

Your baby is most likely to catch whooping cough from someone at home

Infants too young to be vaccinated may be cocooned by vaccinated caretakers. This is one way in which vaccinated individuals may confer indirect protection to unvaccinated individuals

Infant Immunization – Routine Vaccination

Infant immunization generally treated in SIR models as a fraction (p) of newborns vaccinated



Slide from Rohani SISMID 2019

Infant Immunization – Routine Vaccination

$$\frac{dS}{dt} = \mu(1-p) - \beta SI - \mu S$$

$$\frac{dI}{dt} = \beta SI - (\mu + \gamma)I$$

$$\frac{dR}{dt} = \mu p + \gamma I - \mu R$$

If p is the critical vaccination threshold;
p = 1 - (1/R0)

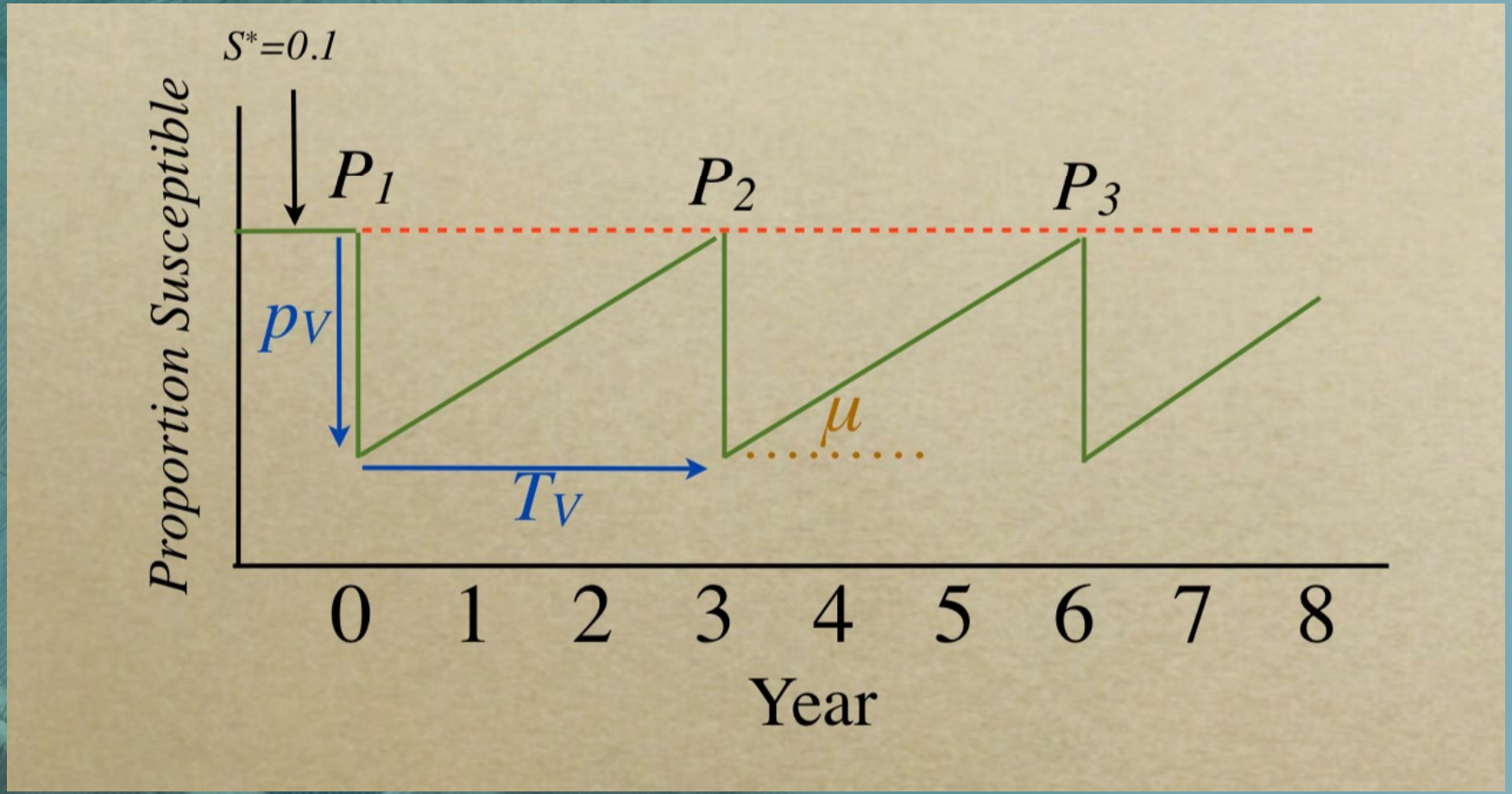
Vaccinate new birth cohorts at the critical vaccination level.

Catch-up campaigns can also be used to fill immunity gaps in older age groups

Slide from Rohani SISMID 2019

Pulsed Vaccination & Vaccination Campaigns

- pulse vaccinate to drop the susceptibility pool far below the critical threshold
- new births will build up the susceptible pool
- pulse again before the susceptible pool grows too much

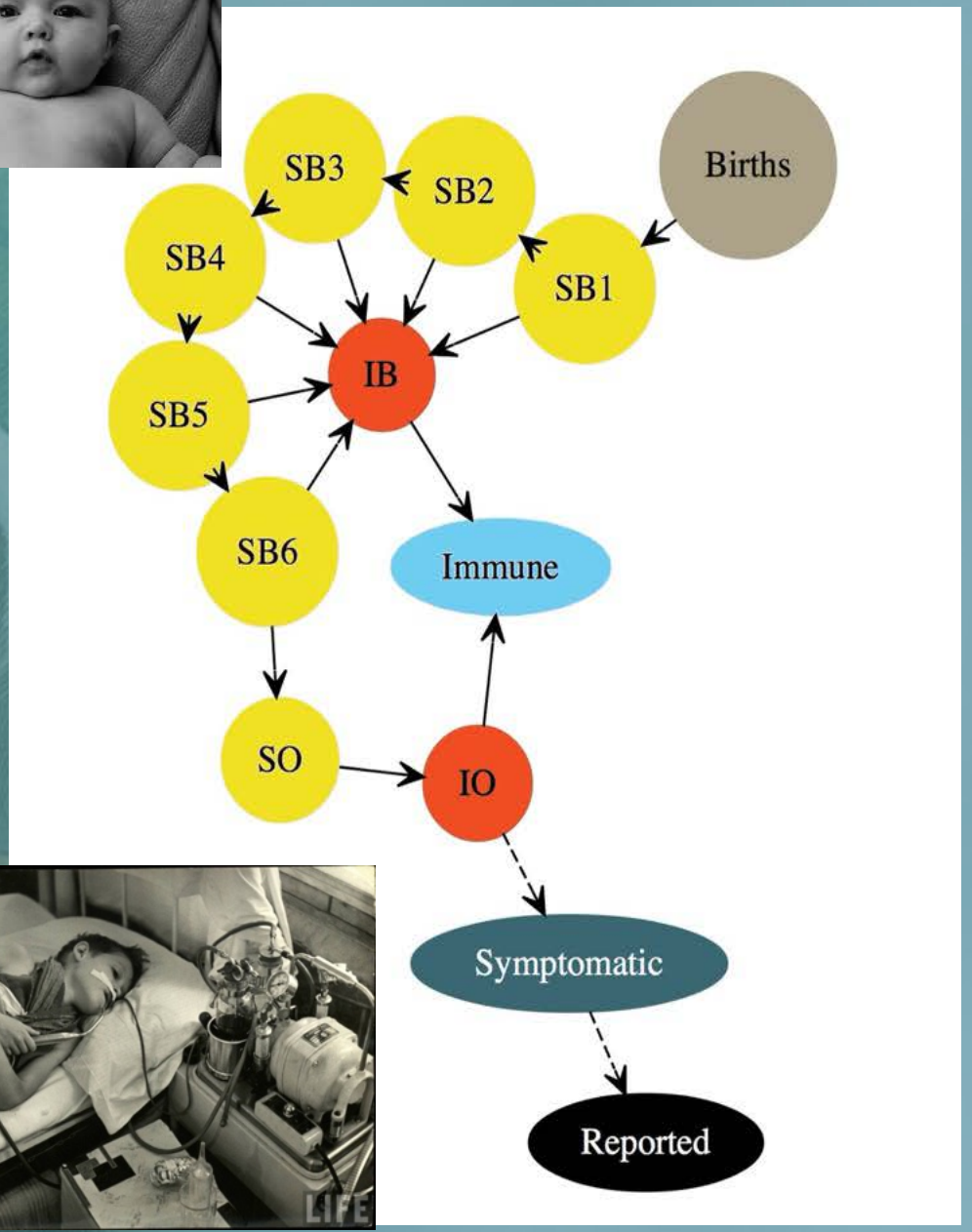


Slide from Rohani SISMID 2019

Polio Vaccination

IPV was initially studied and rolled-out in 2nd and 3rd graders before expanding across age groups and eventually becoming an infant vaccine

Modeling Pre-Vaccine Transmission Dynamics

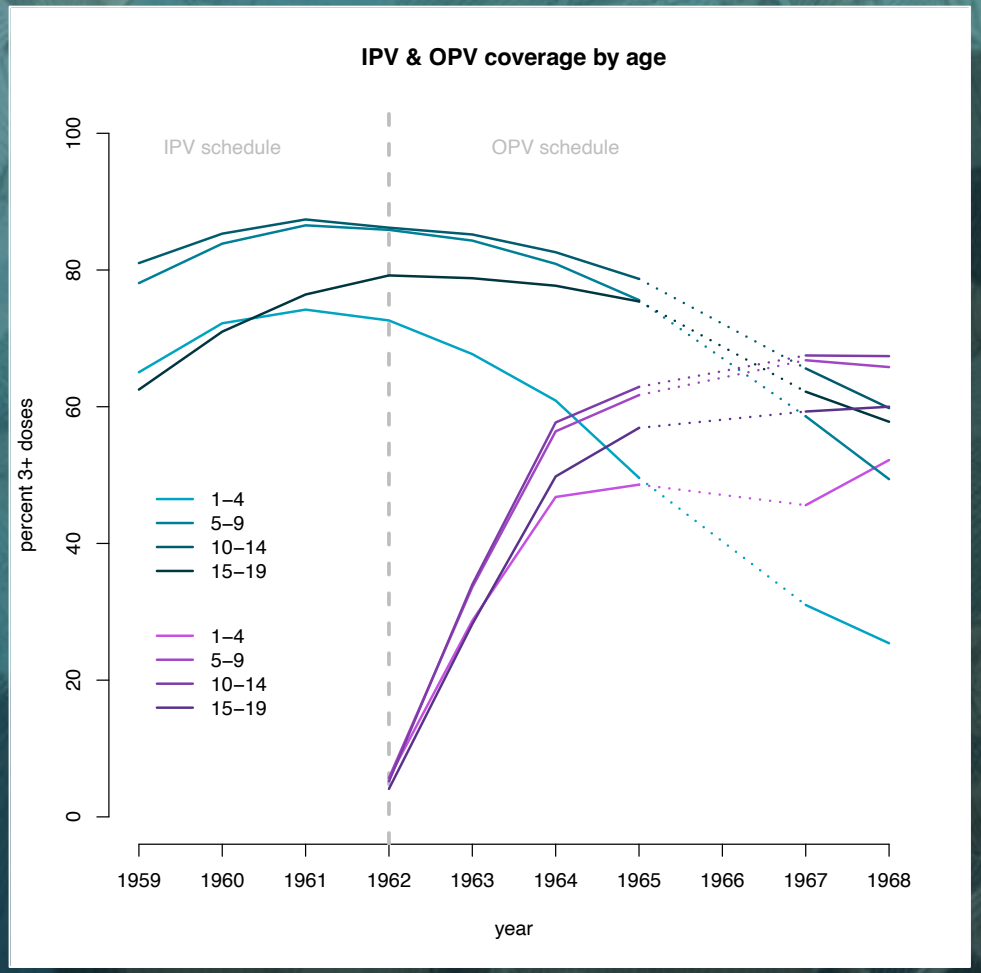


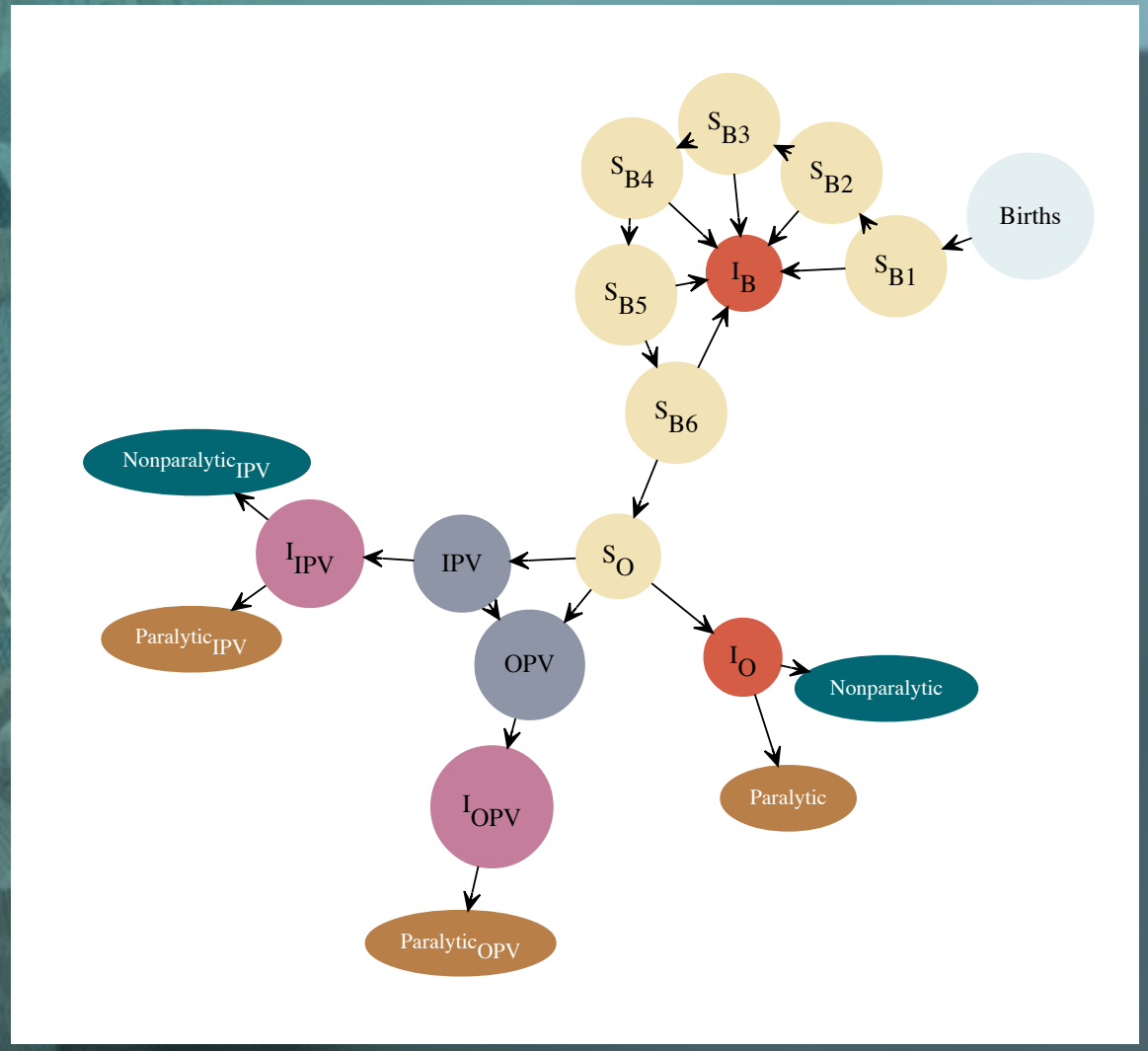
Types of data that can be used:

- Monthly, weekly, daily cases, hospitalizations, or deaths
- Monthly or annual births
- Annual population size

ME Martinez-Bakker, King, & Rohani 2015. PLoS Biology

Modeling Vaccine-Era Transmission Dynamics

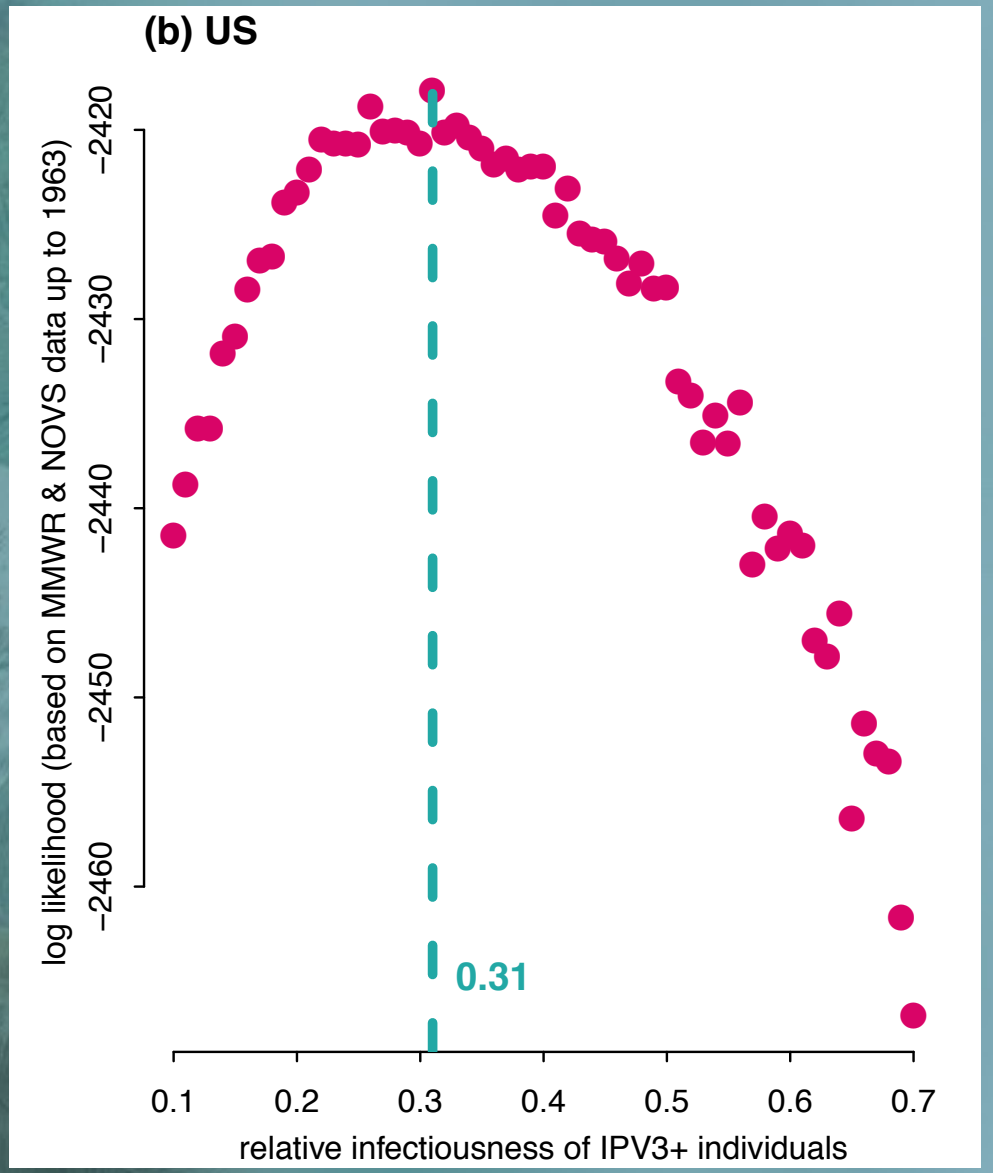




ME Martinez-Bakker, 2015. Dissertation

Salk Vaccine Efficacy

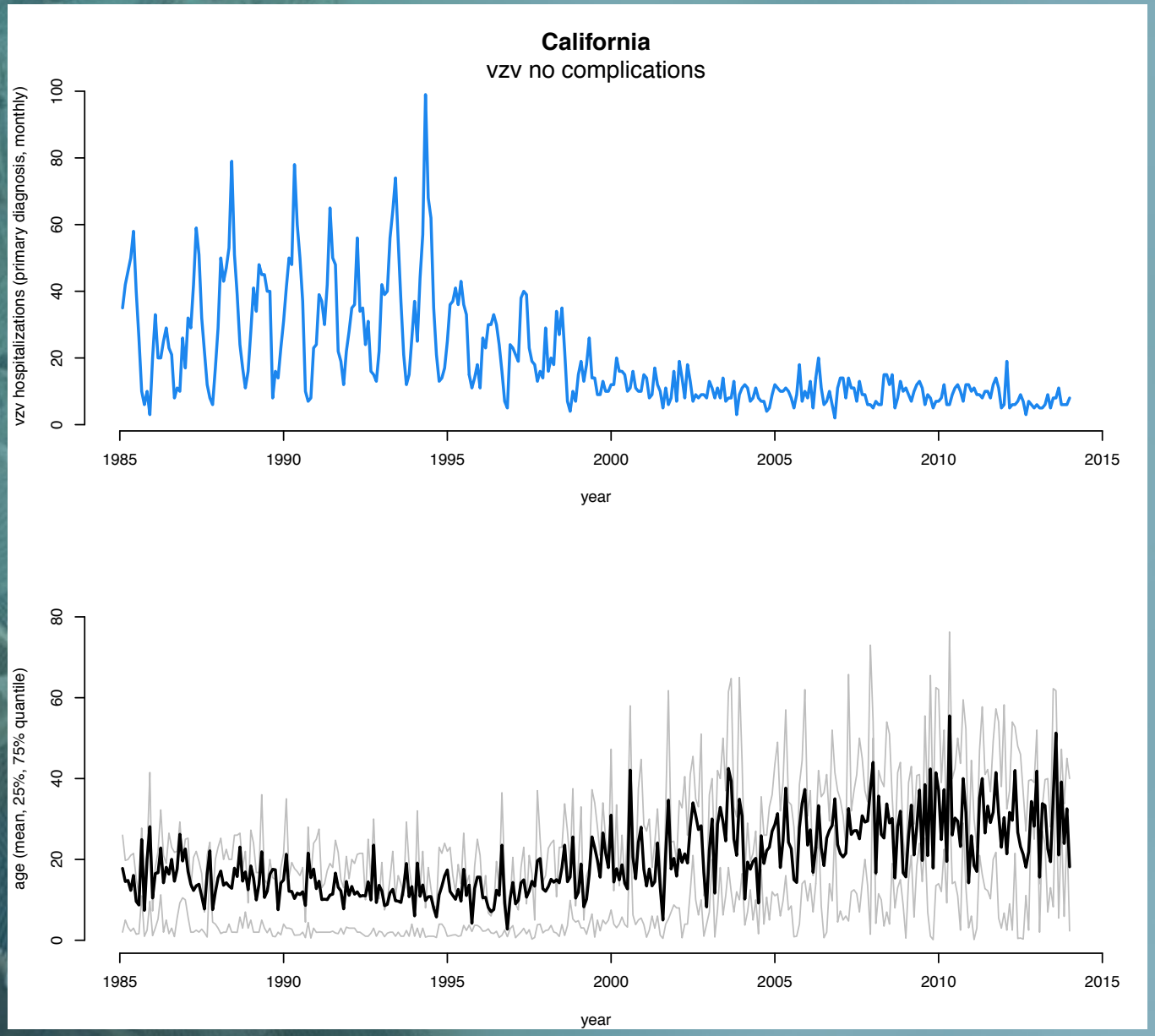
- Relative rates, compared to unvaccinated individuals
- Identifiability is an issue
- Integrate clinical trial data



Martinez et al. (in prep)

Considerations for New Vaccine Roll-Out

When transmission-reducing vaccines are rolled out, for childhood infectious diseases, there is often an increase in the mean age of infection as shown here by chickenpox hospitalizations in California



Jesus Cantu, Y Maldonado, Contopoulos-Ioannidis ME Martinez (in prep)

Measles Status

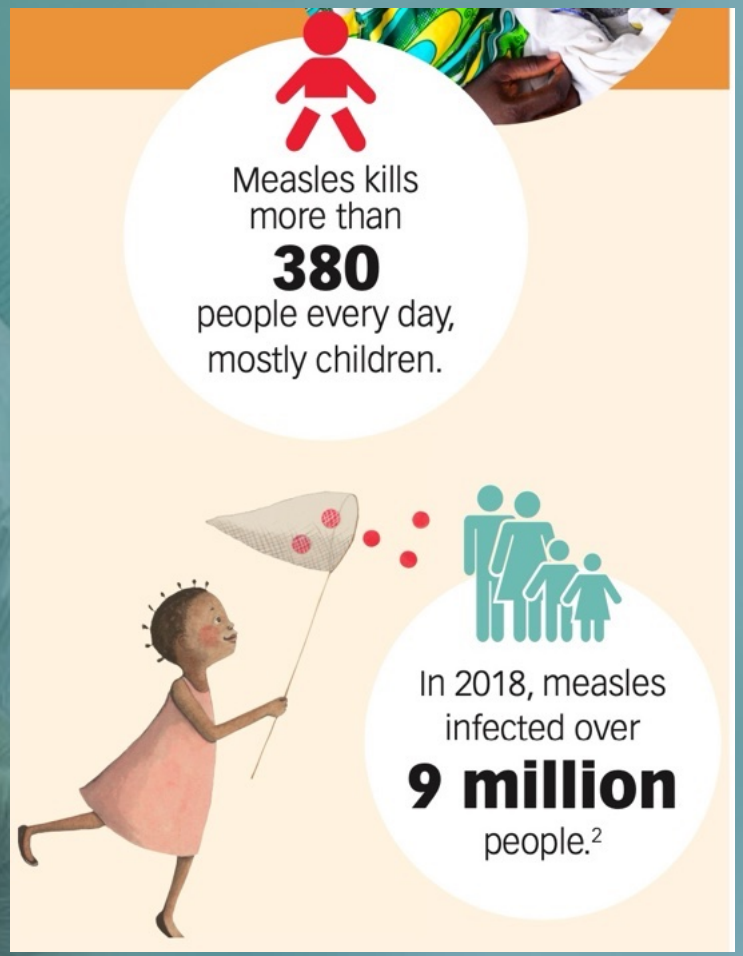
Health Topics | Countries | Newsroom | Emergencies

Home / News / UNICEF and WHO warn of perfect storm of conditions for measles outbreaks, affecting c

UNICEF and WHO warn of perfect storm of conditions for measles outbreaks, affecting children

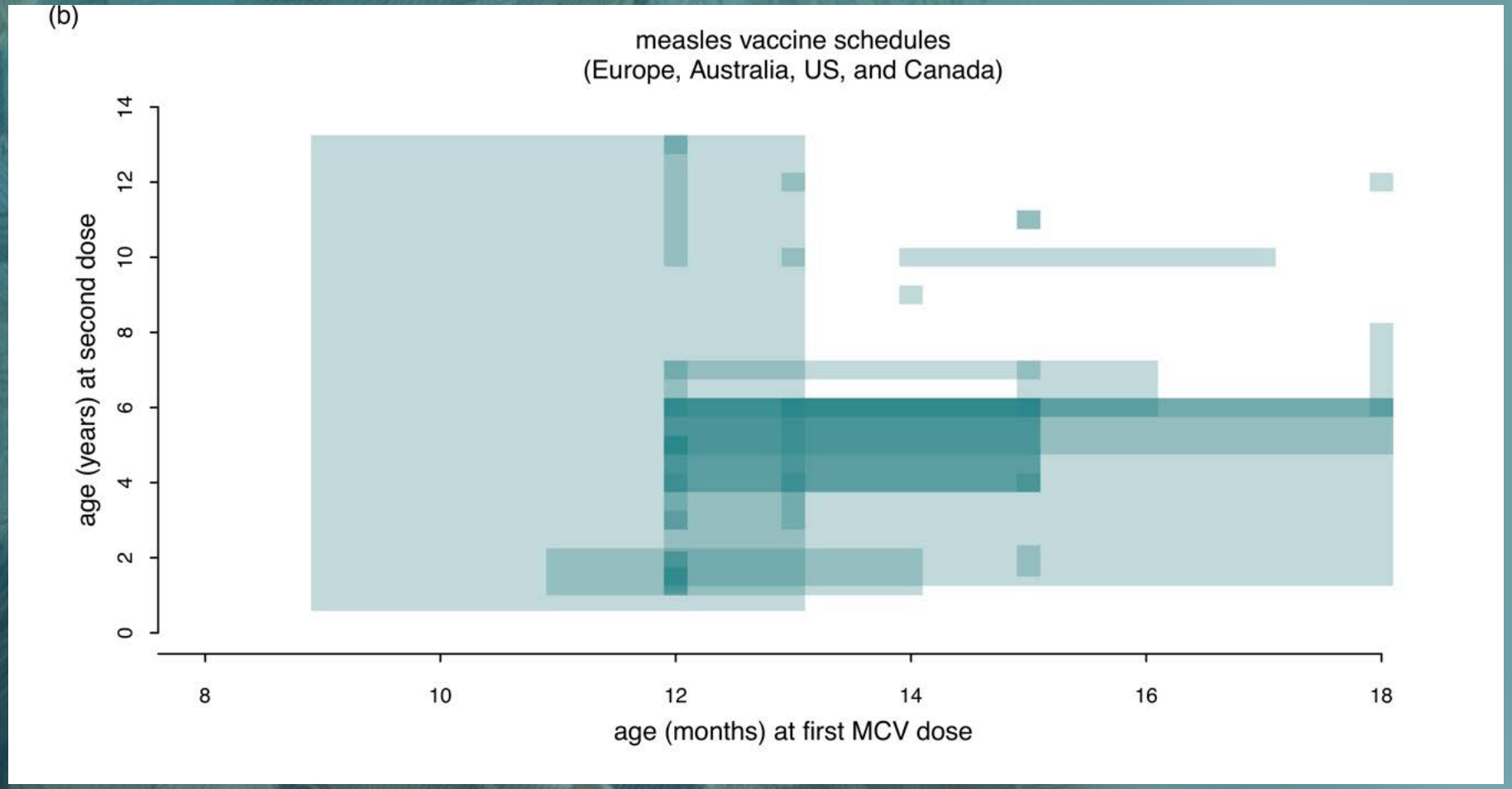
Reported worldwide measles cases increased by 79% in the first 2 months of 2022, compared to the same period in 2021, as WHO and UNICEF warn conditions ripe for serious outbreaks of vaccine-preventable illnesses

27 April 2022 | Joint News Release | New York/Geneva | Reading time: 4 min (1136 words)



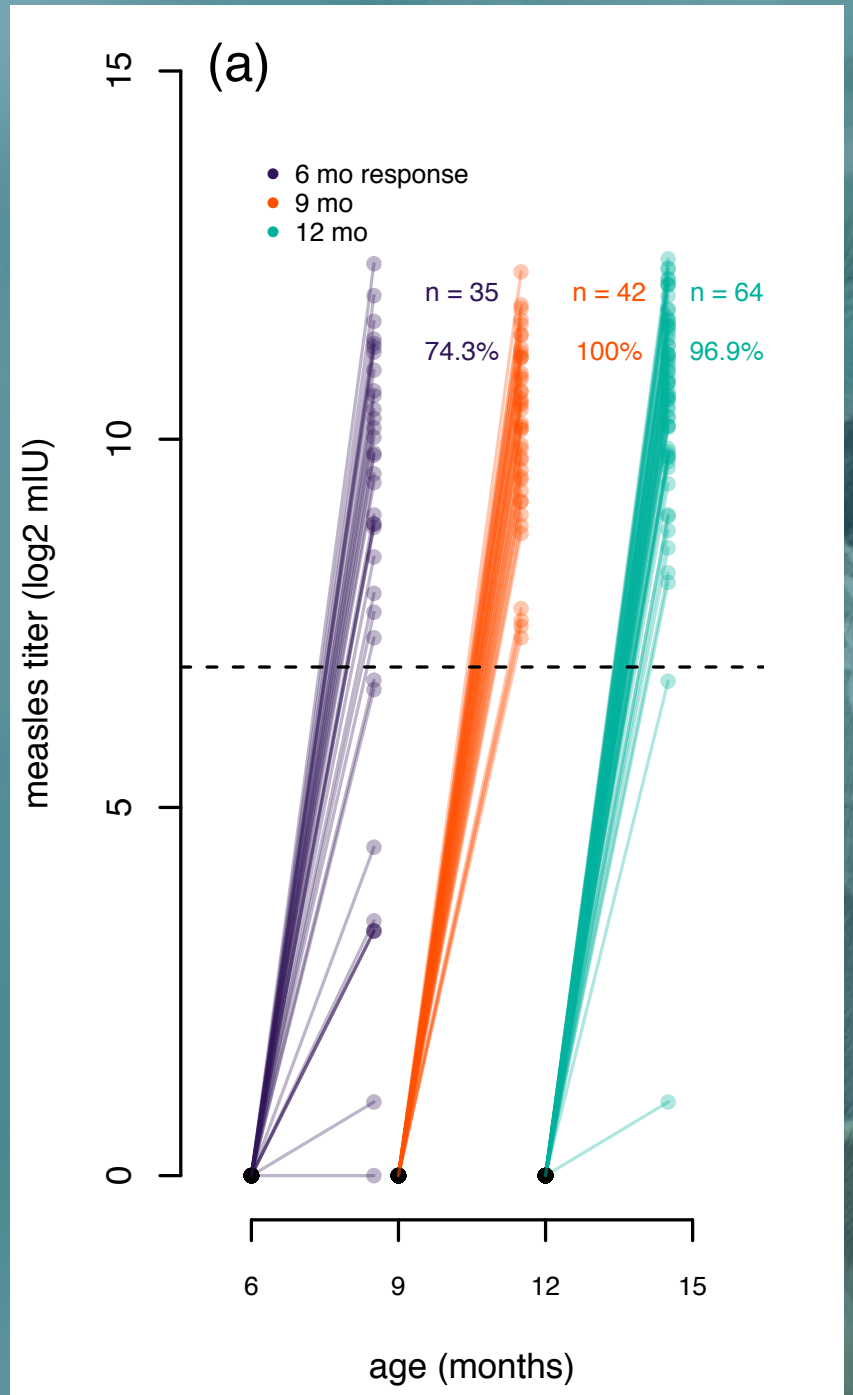
Stats from Measles & Rubella Initiative 2020 fact sheet.

Measles Routine Vaccination Schedule Differs Among Countries



Martinez, Wallinga, Gans, et al (in prep)

Variation in Vaccine Response



Young infants are less likely to have a robust antibody response to their first dose of measles vaccine

Martinez, Wallinga, Gans, et al (in prep)

Childhood Diseases as a Global Problem

5.3M under-5 deaths in 2018

50% from sepsis, tetanus, pneumonia, diarrhea, malaria, AIDS, measles, and meningitis

70-80% are infant deaths

Data from: https://data.unicef.org/topic/child-survival/under-five-mortality/

Childhood Diseases as a Global Problem

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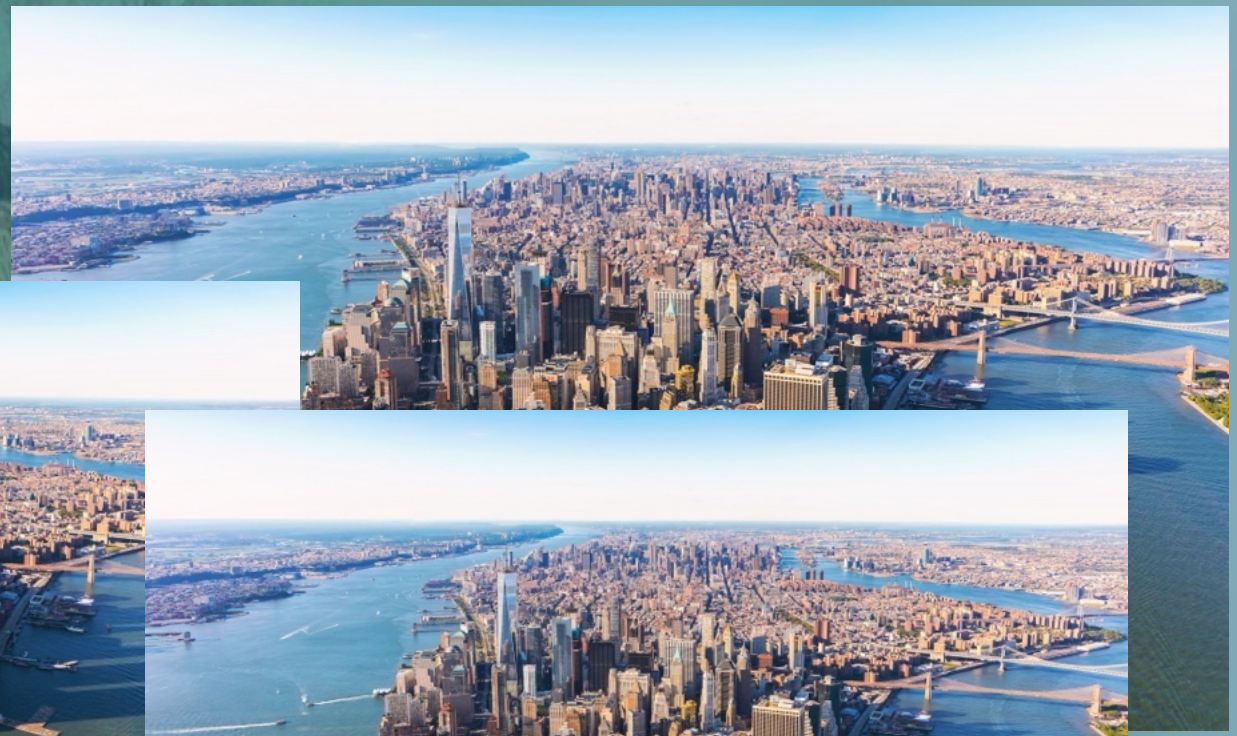

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