Overview of Current Vaccine Rollout Plans

Walter A. Orenstein, MD, DSc (Hon)

Professor of Medicine, Global Health, Epidemiology, and Pediatrics
Associate Director, Emory Vaccine Center
Emory University, Atlanta, GA

WSPID Webinar on COVID-19 Vaccines
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Dr. Orenstein is a member of the Scientific Advisory Board for Moderna Inc.

Vaccines Don’t Save Lives.
Vaccinations Save Lives.

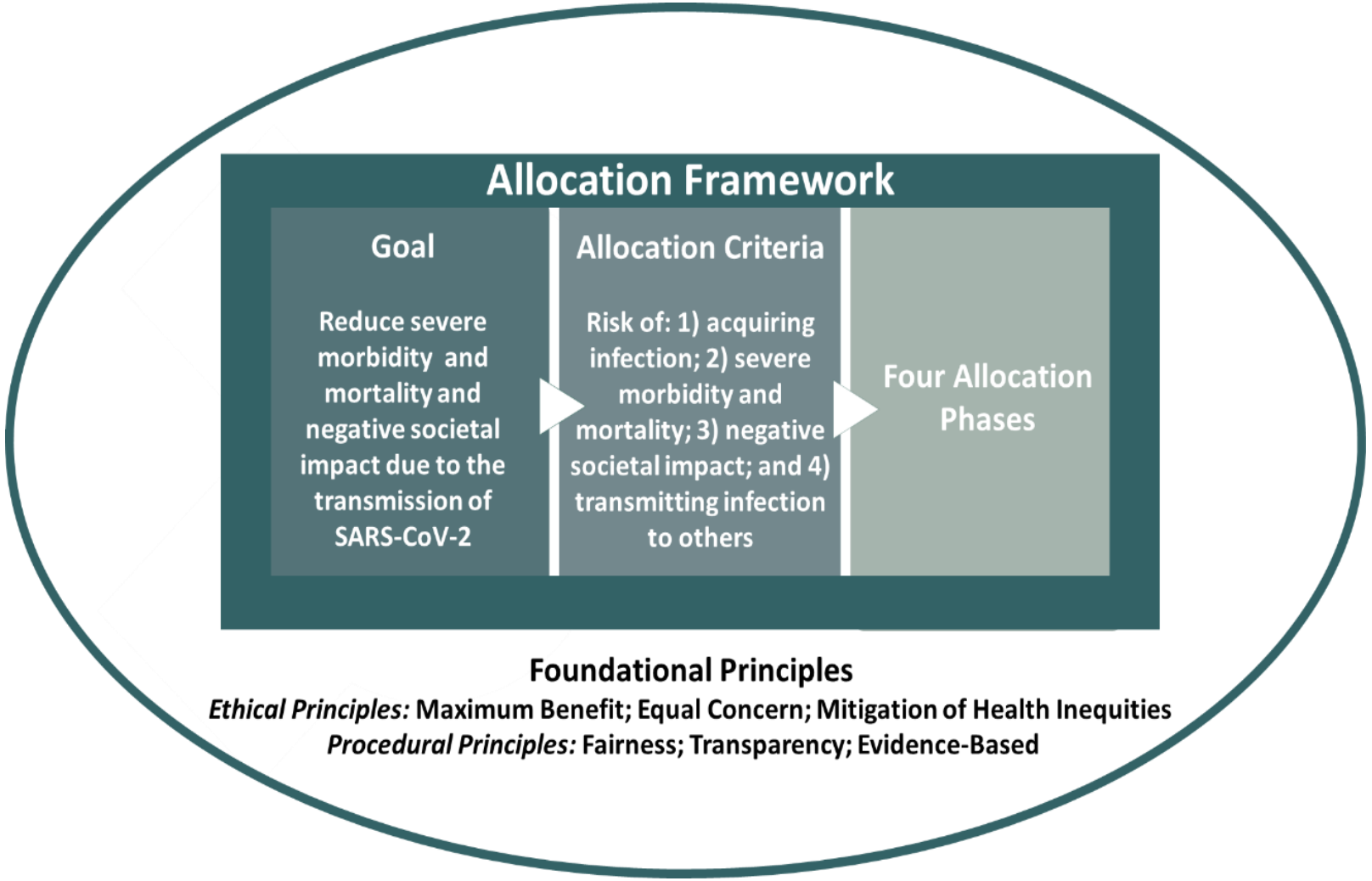
Topics to be covered

- What things will we not know through the trials & what will be needed in the post-licensure period?
- Insights into how vaccines will be allocated and used (emergency use, risk groups, general population)
- Methods for assessing vaccine effectiveness in observational studies
- Importance of continued vaccine safety monitoring
- How realistic is herd immunity & what will it take to get there?
- COVAX Initiative

Questions that may be unanswered at the time COVID-19 vaccines become available

- Priority Groups for Vaccines and how to determine them
- Duration of Immunity
- Risk factors for vaccine failure and waning immunity
- Potential rare causally related vaccine adverse events and risk factors for those events
- Impact of vaccine in reducing transmission
- Barriers to vaccine access and acceptance and how to overcome those barriers

Elements of the Framework



https://www.nationalacademies.org/event/10-02-2020/final-report-public-release-webinar-framework-for-equitable-allocation-of-covid-19-vaccine. Accessed 12/1/2020

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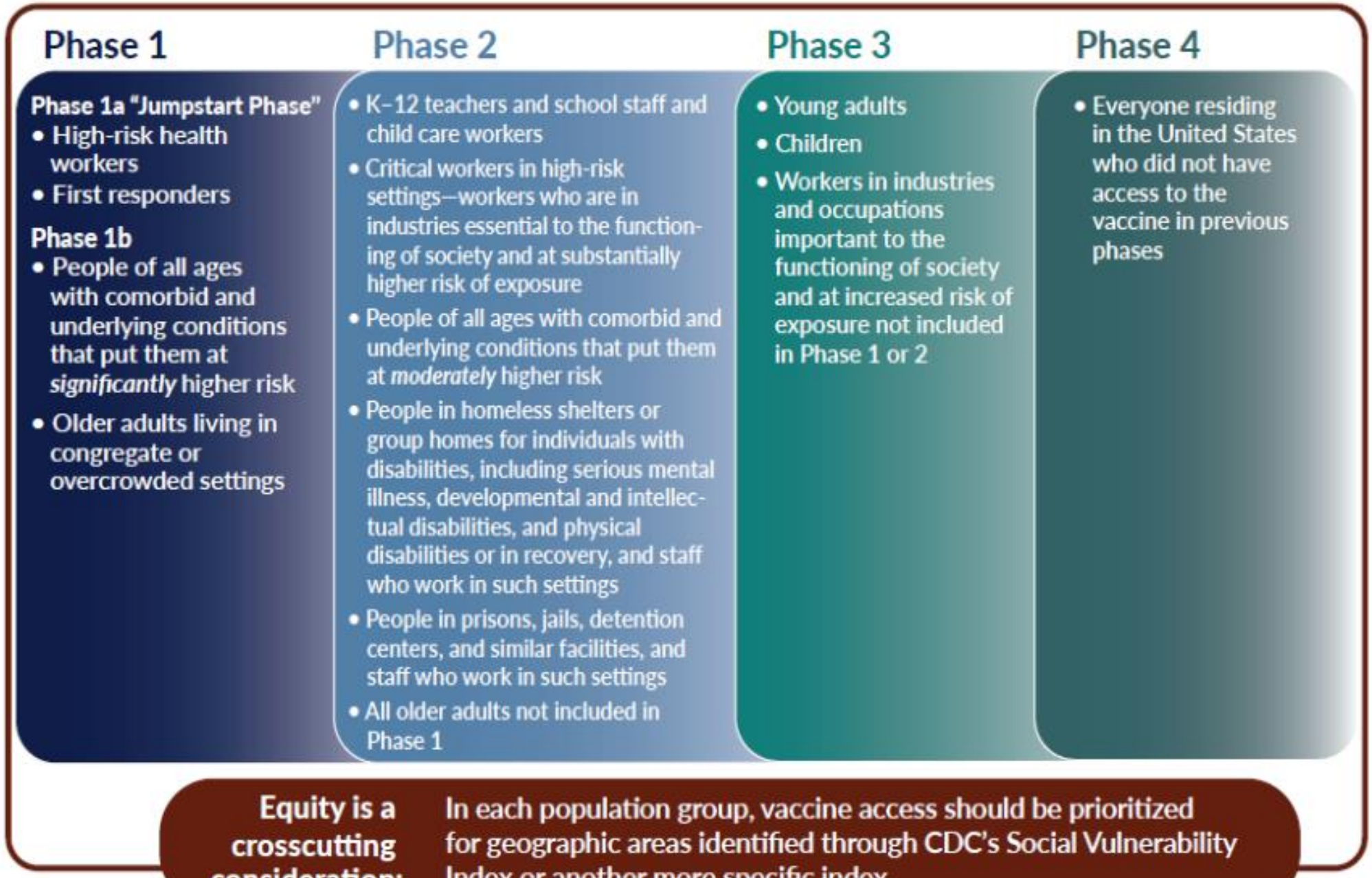
Rate Ratio of Hospitalization and Death By Age Group

Rate ratios compared to 18-29 year olds		
	Hospitalization	Death
0-4 years	4x lower	9x lower
5-17 years	9x lower	16x lower
18-29 years	Comparison Group	Comparison Group
30-39 years	2x higher	4x higher
40-49 years	3x higher	10x higher
50-64 years	4x higher	30x higher
65-74 years	5x higher	90x higher
75-84 years	8x higher	220x higher
85+ years	13x higher	630x higher

https://www.cdc.gov/coronavirus/2019-ncov/covid-data/investigations-discovery/hospitalization-death-by-age.html - accessed 12-1-20



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Recommendations - I

1. Leverage and expand the use of existing systems, structures, and partnerships across all levels of government and provide the necessary resources.
2. Provide and administer COVID-19 vaccine with no out-of-pocket costs for those being vaccinated.
3. Create and appropriately fund a COVID-19 vaccine risk communication and community engagement program.
4. Develop and launch a COVID-19 vaccine promotion campaign.
5. Build an evidence base for effective strategies for COVID-19 vaccine promotion and acceptance.

Adapted from: https://www.nationalacademies.org/event/10-02-2020/final-report-public-release-webinar-framework-for-equitable-allocation-of-covid-19-vaccine. Accessed 12/1/2020

Recommendations - II

Support equitable allocation of COVID-19 vaccine globally

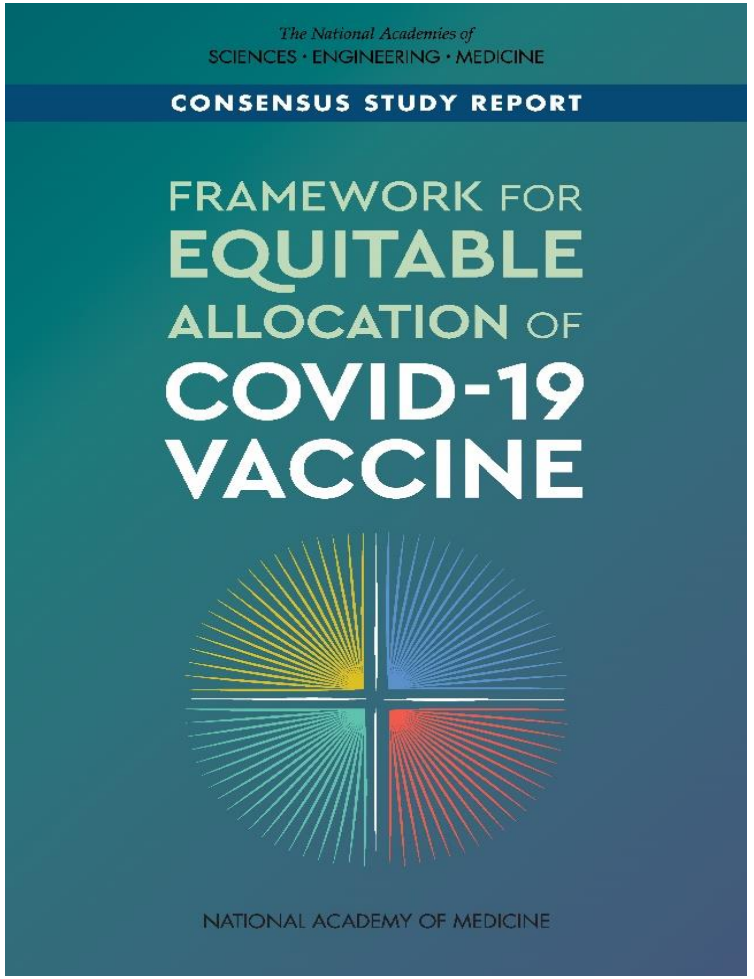
The U.S. government should commit to a leadership role in the equitable allocation of COVID-19 vaccine globally, including:

- Opt in to the COVAX Facility
- Deploy a proportion (e.g., 10 percent) of the U.S. vaccine supply for global allocation.
- This deployment should be implemented through the COVAX Facility led by GAVI.
- Engage with and support the World Health Organization and its member states to optimize the fair and equitable allocation of COVID-19 vaccines both between and within all nations, regardless of their income level.

Adapted from: https://www.nationalacademies.org/event/10-02-2020/final-report-public-release-webinar-framework-for-equitable-allocation-of-covid-19-vaccine. Accessed 12/1/2020

Public Release

Free PDF of the report and related materials are available at: https://www.nationalacademies.org/our-work/a-framework-for-equitable-allocation-of-vaccine-for-the-novel-coronavirus



Accessed 12/1/2020

Emergency Use Authorization (EUA)

Food Drug & Cosmetic Act, 21 USC 360bbb-3: access to unapproved drug, unlicensed vaccine, or uncleared device.

With each EUA decision, FDA weighs known and potential benefits of product against known and potential risks.

- EUAs helped speed access to COVID-19 diagnostic tests, N95 respirators, and remdesivir.

How Can There Be Enough Information to Grant an EUA But Not License a Vaccine? Examples:

- Results are positive, but sponsor has not yet manufactured three lots that consistently meet quality checks.
- Results are positive, but FDA staff have not finished reviewing hundreds of thousands of pages of primary data.

Is EUA Status a Low-Quality or Substandard Approval? No, when supported by sufficient objective evidence.

If COVID-19 Vaccine Released via EUA, How Would Clinicians Handle It Differently? Voluntary

Healthcare providers (HCPs) and potential patients must be informed:

- that HHS Secretary authorized EUA.
- of extent benefits and risks of vaccine are unknown, and
- of option to accept or decline administration,
- of known and potential benefits and risks of vaccine,
- of alternatives.
- of consequences of declining administration.

These facts will appear in succinct **fact sheets** that must be given to each potential recipient.

No obligation to collect signatures attesting to understanding.

HHS establishes conditions for distribution.

From: www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization

Slide provided by John Grabenstein

The Need to Overcome Vaccine Hesitancy

- Multiple surveys have shown public concerns about the rushing of vaccines to availability
- Concerns particularly focused on whether the vaccines will be safe
- Conspiracy theories of collusion of government with drug companies, provider organizations to promote unsafe and/or ineffective vaccines
- Lack of understanding what Emergency Use Authorization (EUA) or Emergency Use Listing (EUL) means

Critical Issues to Overcome Vaccine Hesitancy

- Need to understand the reasons for vaccine hesitancy. In essence, need to fund research to determine those reasons
- Also need to fund research into how to overcome hesitancy
- In essence, need the right message, delivered by the right messenger, through the right communications channels
- At least some of the hesitancy appears to be due to perception the vaccines are not being adequately tested for safety. In essence, speed is leading to cutting corners in assuring vaccines are safe

Types of Potential Studies for Observational Studies of COVID-19 Vaccine Effectiveness

- Cohort Studies
- Traditional Case-Control Studies
- Test-Negative Case-Control Studies
- Screening Method
- Regression Discontinuity Design

- For accurate determination of vaccine effectiveness it is critical to determine vaccination status accurately

Cohort Studies – Prospective and/or Retrospective

- Can there be prospective randomized allocation to groups targeted for vaccine in settings where supply is limited?
- Strengths:
  - Results easily communicated to policy makers and stakeholders
  - Can estimate the burden of COVID-19 in a population and help in determining the impact of vaccination
- Weaknesses:
  - Need to be able to enumerate cohorts of vaccinees and non-vaccinees, prospectively or retrospectively, which are comparable
  - For retrospective studies, need to enumerate vaccination status independent of COVID-19 status
  - Need to assure cohorts have equal access to diagnostic tests. How can this be done?
    - For example, active surveillance and testing based on meeting a case definition
  - Potential for confounding in healthcare seeking behaviors and other variables
  - Expense

Traditional Case-Control Studies

- Strengths:
  - More efficient than cohort studies, smaller numbers, less cost
  - Can focus efforts on finding cases instead of following large populations
  - Fewer non-cases needed compared to cohort studies
- Weaknesses:
  - Misclassification of vaccination status greater compared to cohort studies, especially prospective cohort studies
  - Selection bias. HCWs may be more likely to test cases who are unvaccinated then cases of illness among COVID-19 vaccinees
  - Choosing controls comparable to characteristics of cases (e.g., minimizing bias in control access to vaccination versus cases) – How can bias be minimized?

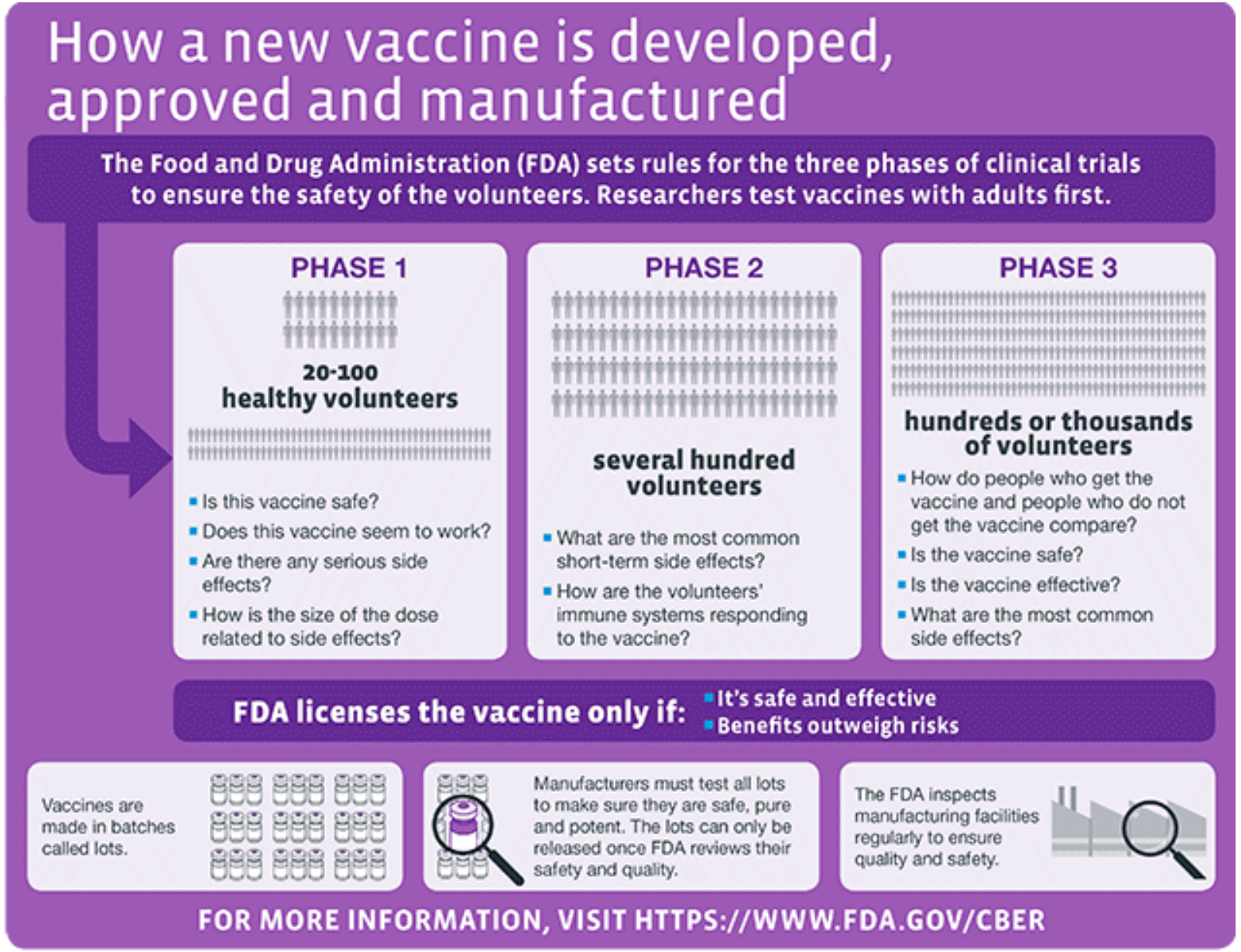
Test-Negative Design

- Strengths
  - Minimize bias of differences in healthcare seeking behavior of vaccinees and non-vaccinees. Also all cases and controls seek care for comparable illnesses
  - All cases and controls seek care at same facilities potentially decreasing differences in access to vaccines in different communities
  - Vaccination status usually obtained before results of laboratory tests available
  - Test sensitivity and specificity if high should minimize misclassification
- Weaknesses
  - HCWs may be less likely to test vaccinees
  - Will vaccination status ascertainment be accurate?
  - Will tests used be sensitive and specific? Should specific tests be recommended?
  - If tests are done early in illness, test positive patients may be more likely to seek care later as clinical illness intensifies (e.g., should cases in hospital be limited to those tested after hospitalization?)
  - Will vaccinees be more likely to have underlying illnesses which are exacerbated with respiratory illness of different causes leading to increase in vaccination of non-COVID cases?

The Screening Method

- Strengths:
  - Markedly reduced expenses since vaccination status of the community is available from other measures such as surveys
  - Do not have to collect data since the surveys presumable are existing
- Weaknesses:
  - Survey data may not be representative of the population from which cases are being collected
    - For example, differences in healthcare access and healthcare seeking behavior
  - Vaccination status data may come from administrative data rather than surveys

Pre-licensure activities form the foundation of vaccine safety *



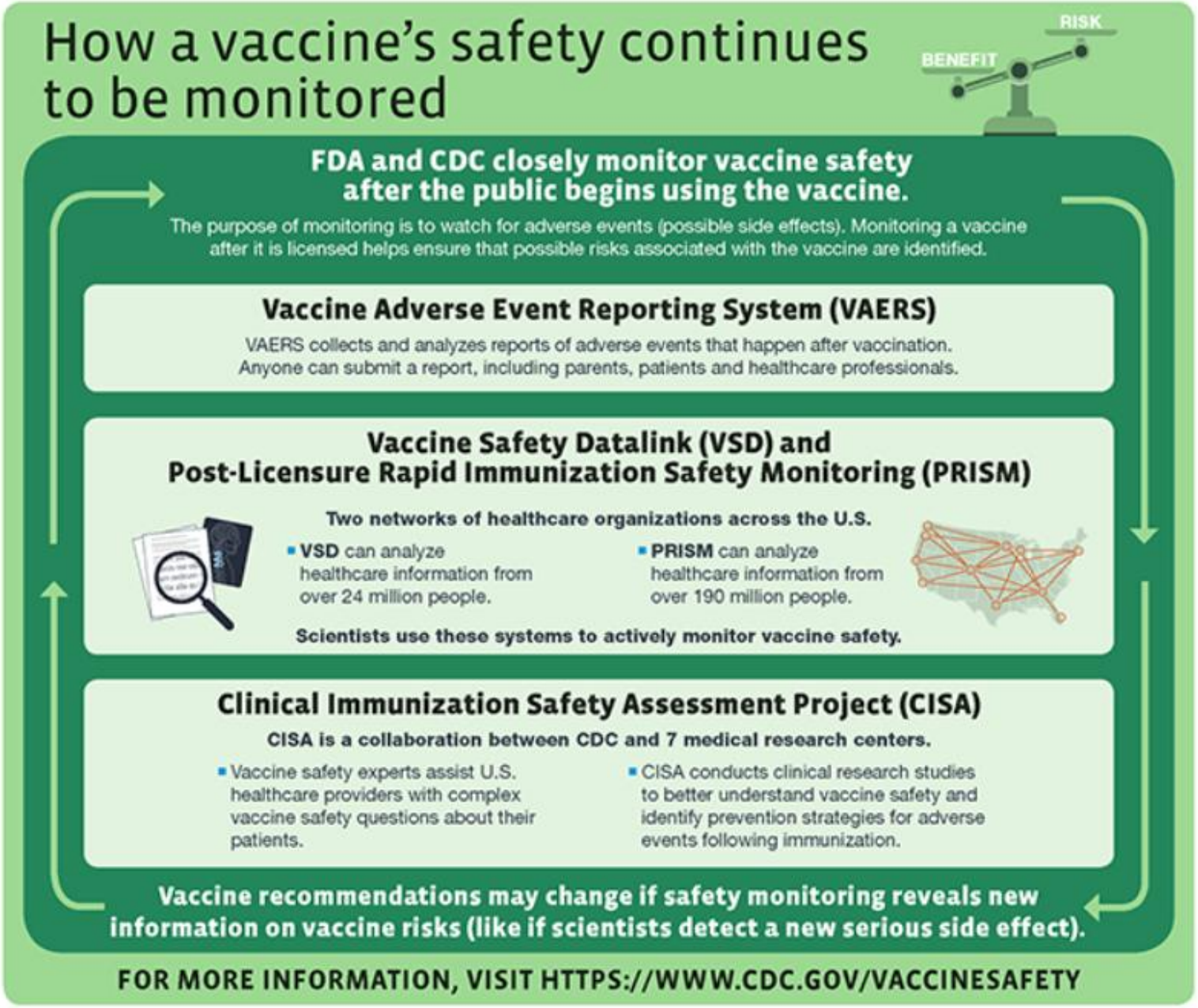
*source: https://www.cdc.gov/vaccines/parents/infographics/journey-of-child-vaccine.html

Provided by Frank DeStefano, Director, Vaccine Safety Office, CDC

Critical Needs for Assessing Vaccine Safety Post Rollout of COVID-19 Vaccines

- Collect background rates of various clinical syndromes to potentially be compared with rates following vaccination
- Work with vaccine providers and healthcare providers to report adverse events following vaccines
- Have systems to be able to assess rates of clinical syndromes post-vaccination to compare with background rates
- Have committees of experts to evaluate whether events following vaccination are likely to be causally or only coincidentally related to vaccines

Vaccine Safety Continues to be Monitored



Work Group Considerations: Objectives of the COVID-19 Vaccine Program

- Ensure safety and effectiveness of COVID-19 vaccines
- Reduce transmission, morbidity, and mortality in the population
- Help minimize disruption to society and economy, including maintaining healthcare capacity
- Ensure equity in vaccine allocation and distribution

Identifying vaccine priority groups: Current challenges and preliminary Work Group assumptions

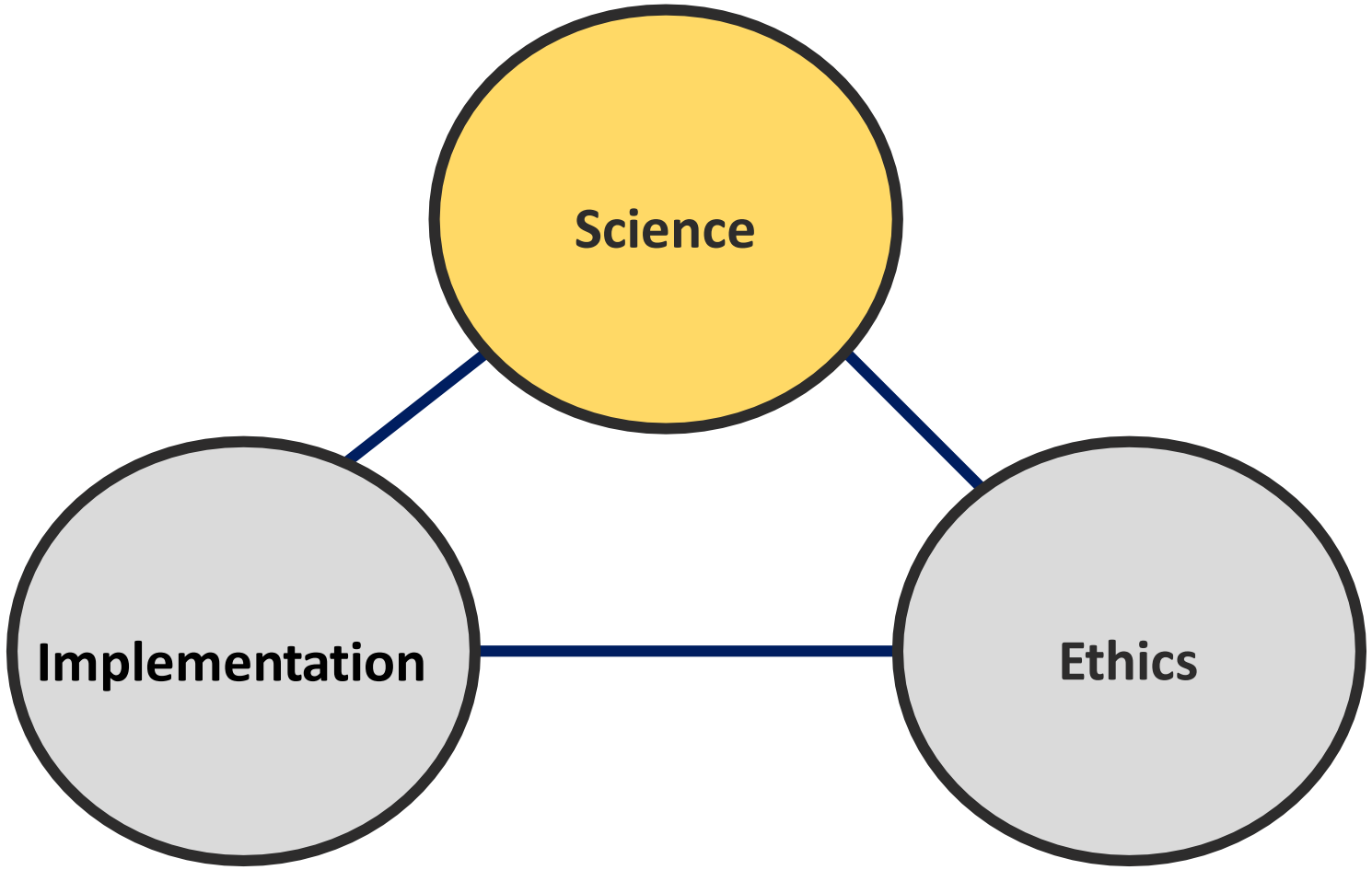
Challenges	Work Group assumptions for prioritization
Evolving understanding of COVID-19 epidemiology and immunology	• Prioritization should occur based on the information available to date and be continually refined based on data • A substantial proportion of the U.S. population, regardless of age, location, or occupation, remains susceptible to COVID-19.
Current absence of data on safety and efficacy of COVID-19 vaccines	• Vaccines will not be administered until safety and efficacy have been demonstrated. • Concerns for reduced efficacy in certain populations (e.g., older adults, immunocompromised individuals) should not preclude their inclusion as priority groups while data are pending.
Unknown timing and number of vaccine doses	• Number of initial doses may not be sufficient to vaccinate everyone in the priority groups, necessitating sub-prioritization. • Vaccine doses will become available in incremental quantities over several months.

Additional data to inform prioritization

- Remaining information gaps in certain population subgroups:
  - Risk of disease and severe outcomes
  - Vaccine safety and efficacy
  - Transmission dynamics and level of population immunity

- Additional data to inform prioritization will be helpful, though may need to make decisions in the setting of unknowns for vaccine implementation planning

Allocation of initial COVID-19 vaccine: Phase 1

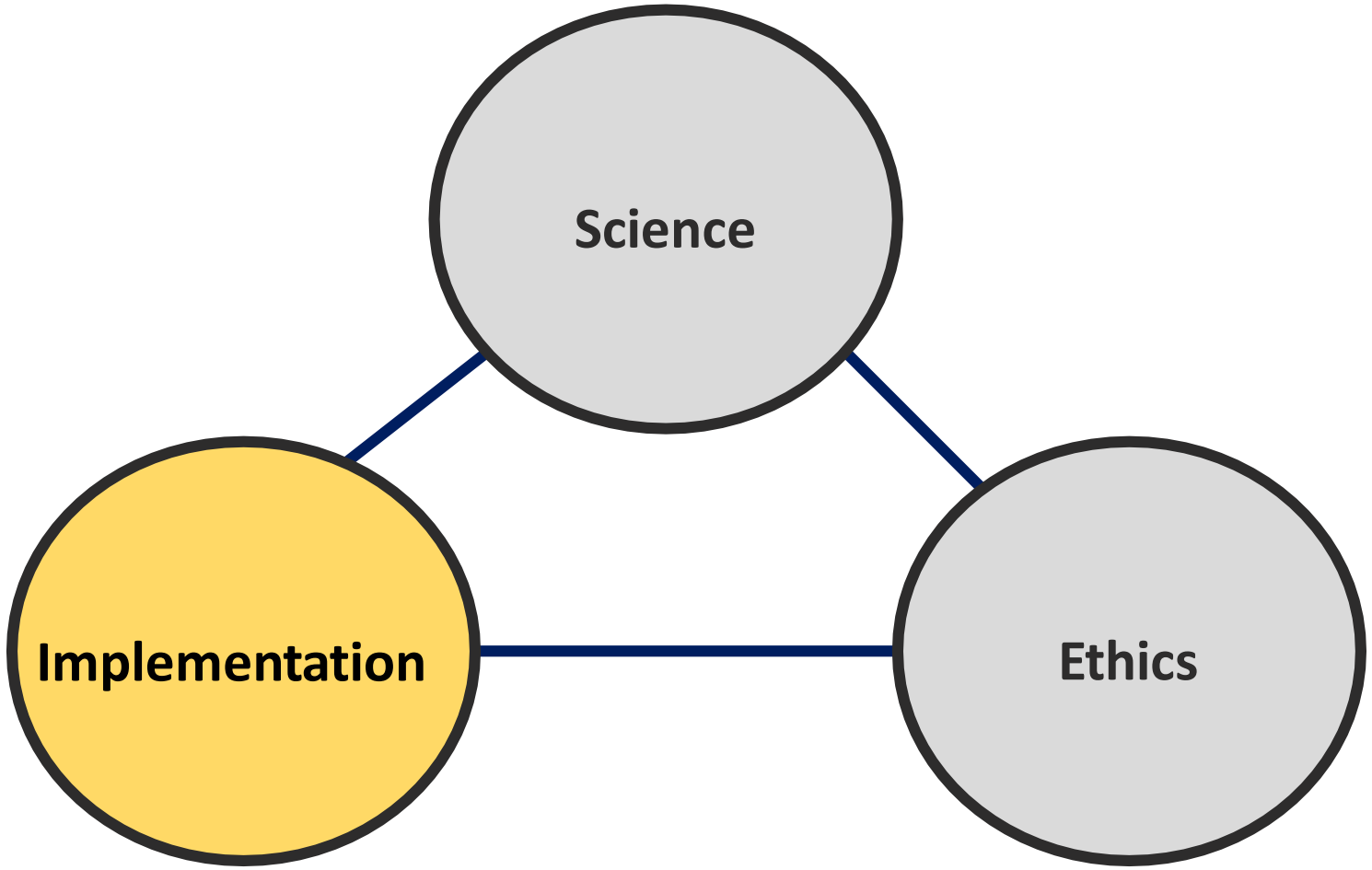


Science:

- COVID-19 disease burden
- Balance of benefits & harms of vaccine

From Kathleen Dooling: Phased Allocation of COVID-19 Vaccines, ACIP 11-23-20

Allocation of initial COVID-19 vaccine: Phase 1



Implementation:

- Values of target group
- Feasibility

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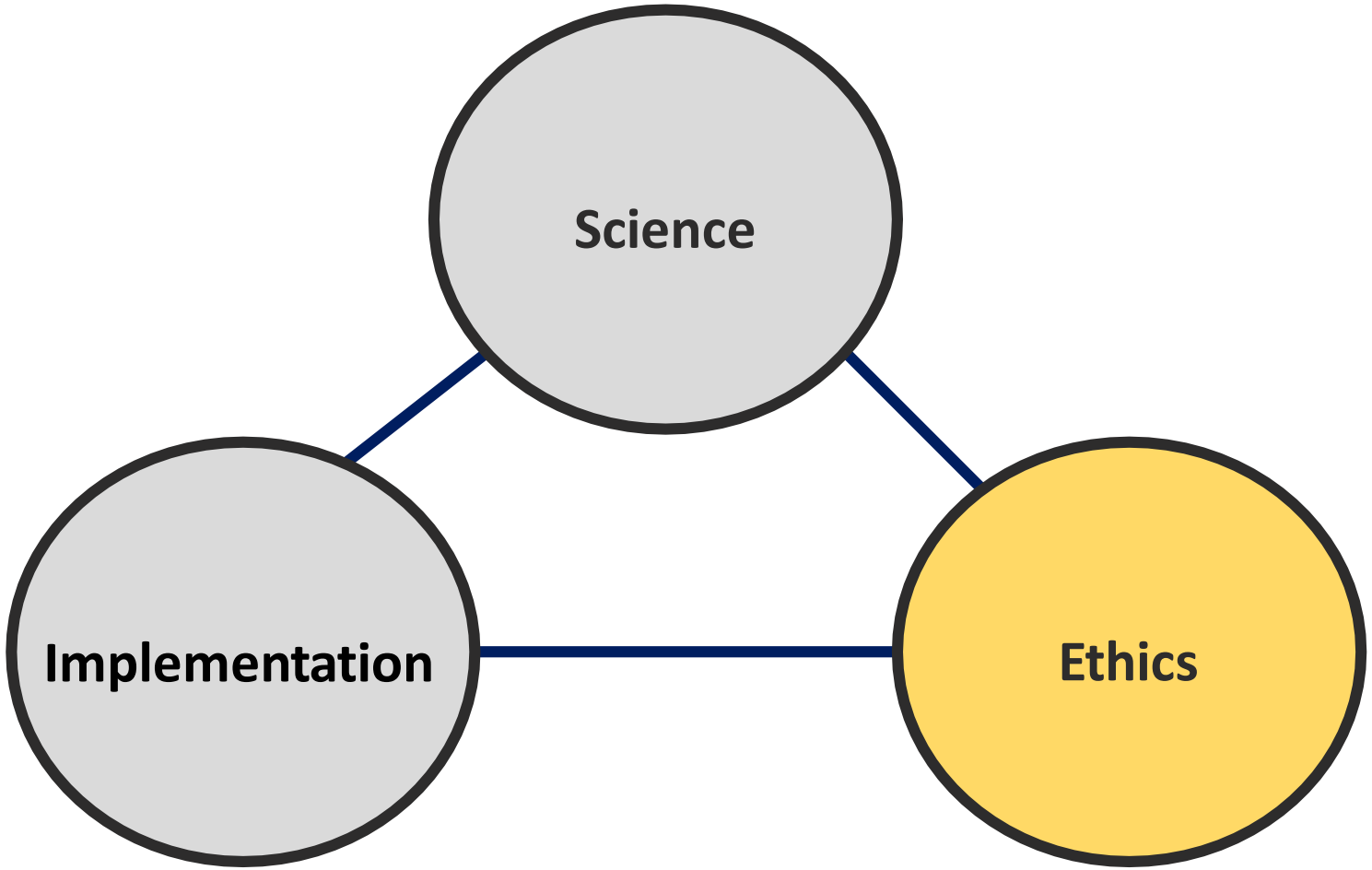
Allocation of initial COVID-19 vaccine: Phase 1



Ethical Principles:

- Maximize benefits & minimize harms
- Promote justice
- Mitigate health inequities
- Promote transparency

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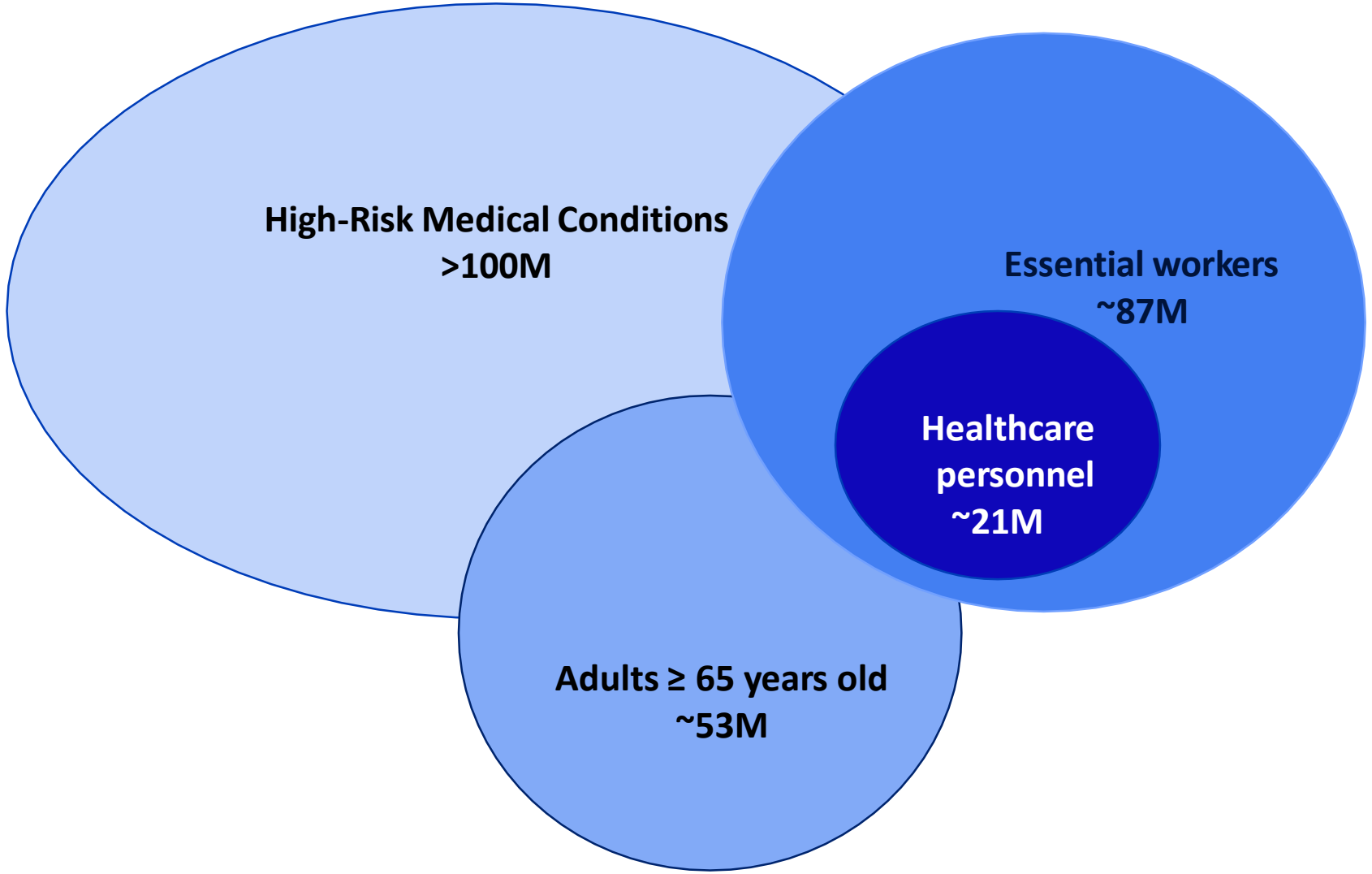
Proposed Groups for Phase 1 vaccination



<u>August ACIP meeting</u>

Phase 1a:

-Healthcare Personnel

Phase 1b:

-Essential Workers

-High-Risk Med Conditions

-Adults ≥ 65 years old

From Kathleen Dooling: Phased Allocation of COVID-19 Vaccines, ACIP 11-23-20

Proposed groups for Phase 1 vaccination

Healthcare Personnel [1] (~21million)	Essential Workers (non-healthcare) [1] (~87 million)	Adults with high-risk medical conditions [2] (>100 Million)	Adults age ≥65 years [3] (53 Million)
		Examples	
• Hospitals • Long-term care facilities • Outpatient • Home health care • Pharmacies • EMS • Public health	• Food & Agriculture • Food Service • Transportation • Education • Energy • Police • Firefighters • Manufacturing • IT & Communication • Water & Wastewater	• Obesity • Severe Obesity • Diabetes • COP • Heart Condition • Chronic kidney • Cancer • Smoking • Solid Organ Transplant • Sickle cell disease	• Community Dwelling • Congregate ~3M [4] • Skilled Nursing Facility (~1.3 M) • Assisted living • Facilities (~0.8 M) • Residential care communities (~0.6 M) • HUD Senior Housing (~0.3M)

1. https://www.cisa.gov/publication/guidance-essential-critical-infrastructure-workforce
2. https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical conditions.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019ncov%2Fneed-extra-precautions%2Fgroupsat-higher-risk.html
3. United States Census Bureau https://www.census.gov/topics/population/older-ging.html
4. Vital and Health Statistics, Series 3, Number 43 (cdc.gov)

From Kathleen Dooling: Phased Allocation of COVID-19 Vaccines, ACIP 11-23-20

Summary of Work Group Considerations supporting vaccinating healthcare personnel in Phase 1a

Science

- As of Nov 21, at least 228,503 confirmed COVID-19 cases among HCP, with 822 deaths[1]
- COVID-19 exposure (inside and outside the healthcare setting) results in absenteeism due to quarantine, infection and illness. Vaccination has the potential to reduce HCP absenteeism
- LTCF modeling demonstrates more cases and death averted at the facility by vaccinating staff compared to vaccinating residents[2]

Implementation

- Acute care HCPs have high uptake of influenza vaccine[3]– high vaccine acceptance
- Many acute healthcare facilities have the equipment and expertise to carry out large scale vaccination with a vaccine that requires ultra-cold storage

Ethics

- Preserves health care services essential to the COVID-19 response and the overall health care system
- HCP group is inclusive of all job types in healthcare settings and is racially and ethnically diverse

1. https://covid.cdc.gov/covid-data-tracker/#health-care-personnel
2. Slayton, Modeling Allocation Strategies for the initial SARS-CoV-2 Vaccine Supply, ACIP Aug 21, 2020, https://www.cdc.gov/vaccines/acip/meetings/slides-2020-08.html
3. Influenza Vaccination Coverage Among Health Care Personnel- United States, 2018-2019 Influenza Season, https://www.cdc.gov/vaccines/acip/meetings/slides-2020-08.html

One world, protected.

Together we are stronger than we are apart

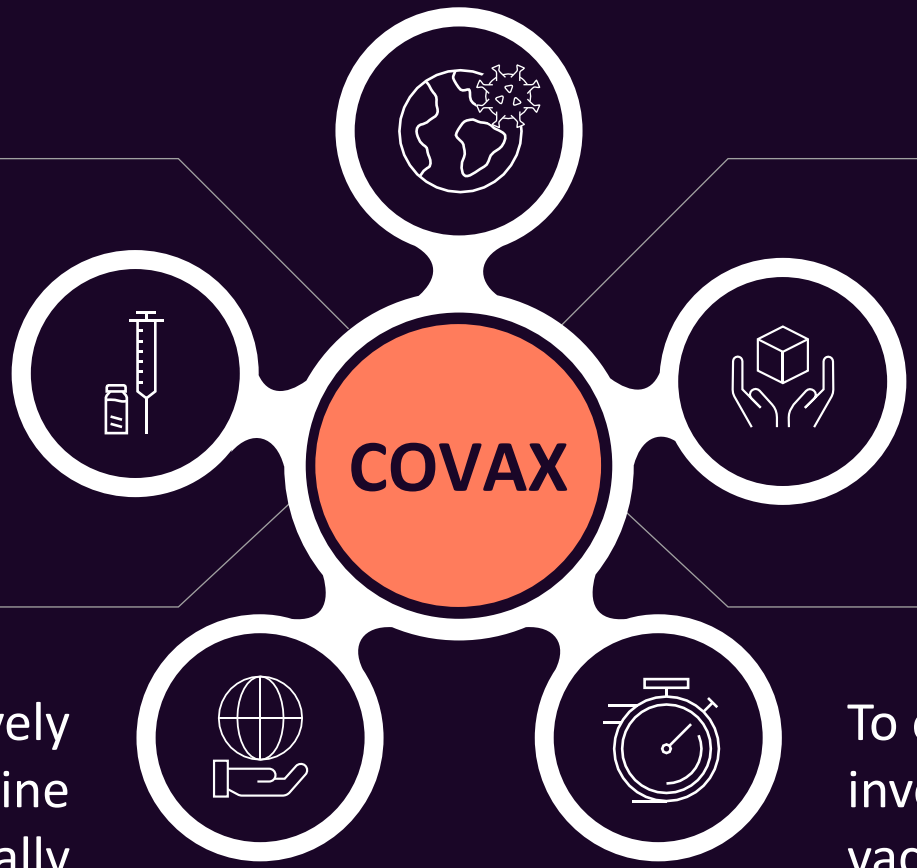
CEPI	Supporting vaccine research, development and manufacturing scale-up from the lab to the production facility	unicef	Coordinating procurement and distribution across COVAX participants
Gavi The Vaccine Alliance	Pooling procurement and incentivizing manufacturing expansion to secure supply of safe and efficacious vaccines	Pan American Health Organization	Supporting procurement and distribution for COVAX participants in the Americas
World Health Organization	Providing normative guidance on vaccine policies, safety, regulation, and allocation	**Multilateral Development Banks**	Offering critical financing support including directly to participants

Provided by Ann Lindstrom, WHO, December 2020

Objectives of COVAX

To end the acute phase of the pandemic by end 2021

To deliver 2 billion doses by end 2021



To guarantee fair and equitable access to COVID19 vaccines for all participants

To support the largest actively managed portfolio of vaccine candidates globally

To offer a compelling return on investment by delivering COVID19 vaccines as quickly as possible

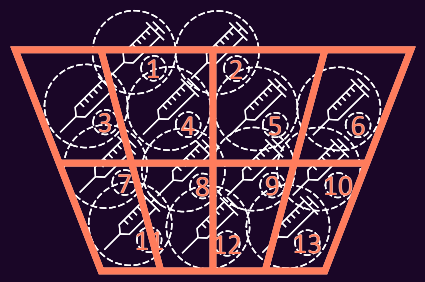
Provided by Ann Lindstrom, WHO, December 2020

The Facility aspires to a robust diversified portfolio of around 10 or more vaccine candidates

Selection of vaccines diversified across different technology platforms, manufacturing locations/ capacities, and other factors; volumes tailored accordingly

Illustrative portfolio

Candidate	Estimated # of doses by end 2021, M doses
AstraZeneca	300
Sanofi/GSK	200
SII (AZ and Novavax)	200 (+ options for more)
Selected candidate 4	300
Selected candidate 5	100
Selected candidate 6	500
Selected candidate 7	750
Selected candidate 8	150
Selected candidate 9	400
Selected candidate 10	200
Selected candidate 11	600
Selected candidate 12	300
TOTAL	**4,000**



To reach 2 B by end of 2021, the Facility is planning **for deals up to 4 B doses to account for an estimated 50% attrition rate**

The AMC is an innovative finance instrument which frontloads doses to achieve equitable access to COVID-19 vaccines

Objective

Accelerating the availability of effective vaccines

Securing at least 1 billion doses by the end of 2021 for AMC eligible economies

Making vaccines affordable

Impact

Protect health care workers and the most vulnerable populations

Help prevent the transmission of COVID-19 around the world

Help restart the world's economy by mitigating the impact of the pandemic

To achieve these we have raised $2.1bn and are launching a second round of funding for at least $5 billion

Provided by Ann Lindstrom, WHO, December 2020

Community Protection

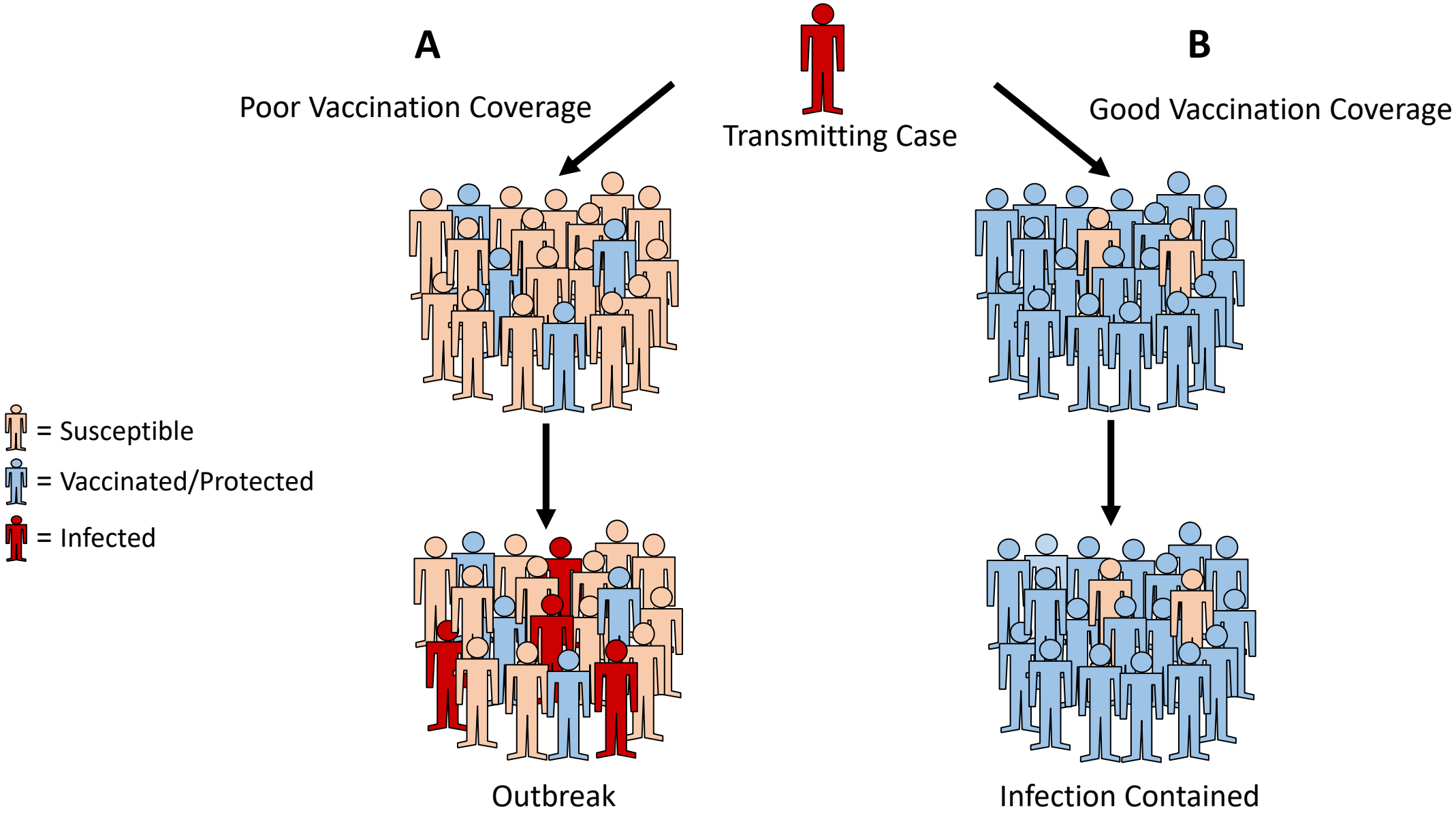


TABLE 77.2 Approximate Basic Reproduction Numbers (in Developed Countries) and Implied Crude Herd Immunity Thresholds[a] for Common Vaccine-Preventable Diseases[b]

Infection	Basic Reproduction Number (R_0)	Crude Herd Immunity Threshold, H (%)
Diphtheria	6–7	83–85
Influenza[c]	1.4–4	30–75
Measles	12–18	92–94
Mumps	4–7	75–86
Pertussis[d]	5–17	80–94
Polio[e]	2–20	50–95
Rubella	6–7	83–85
Smallpox	5–7	80–85
Tetanus	Not applicable	Not applicable
Tuberculosis[f]	?	?
Varicella[g]	8–10?	?

Fine PEM, et al. Chap 77 -Community Protection in Plotkin SA, Orenstein WA, Offit PA, Edwards KM, eds. *Plotkin's Vaccines,* 7th edition, Elsevier, 2018

[a]Herd immunity threshold (H), calculated as $1–1/R_0$.
[b]The values given in this table are approximate and crude; they do not properly reflect the tremendous range and diversity among populations, nor do they reflect the full immunologic complexity underlying the epidemiology and persistence of these infections. See text for further discussion.
[c]R_0 of influenza viruses probably varies greatly between subtypes.
[d]Note that immunity to *Bordetella pertussis* infection is not solid, and it wanes.
[e]Complicated by uncertainties over immunity to infection and variation related to hygiene standards.
[f]Protective immunity not defined.
[g]Immunity not sterile; herd immunity threshold not defined.
From Fine PEM. Herd immunity: history, theory, practice. Epidemiol Rev. *1993;15:265–302; and Anderson RM, May RM.* Infectious Diseases of Humans: Dynamics and Control. *Oxford, UK: Oxford University Press; 1991.*

Summary

- Critical factors to be considered in COVID-19 vaccine allocation include a focus on those most vulnerable to severe disease and critical infrastructures especially the healthcare infrastructure
- It is important to take advantage of existing infrastructure for vaccine delivery including cold chain and means of reaching populations not often covered in immunization programs, adults
- Older adults seem to be at greatest risk of severe COVID-19
- Likely priority groups include healthcare workers and adults in long term care facilities
- It is unclear at this stage, what priorities will be given to vaccinating children. Studies of COVID-19 vaccines are in early phases in children
- Critical to have ongoing strong systems to assess vaccine effectiveness and safety
- The COVAX Facility is critical to getting vaccines for low and middle income countries