Global vaccination strategies: similarities, differences and lessons

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Assistant Professor,
Saw Swee Hock School of Public Health
Overview

- Vaccination impact modelling in Singapore
- What can we learn from vaccination strategies in different places?
- What is different about the strategies in different places?
Vaccination program

**AIM**

**Vaccination**
- Known and unknown characteristics
- Availability

**Transmission Dynamics**
- Biological
- Setting specific

**Control policies**
- What can be lifted?
- What do stakeholders want to be lifted?

**Healthcare system and Testing**
- Capabilities
- Policies

**Economics**
- Strategies cost-vaccination and NPIs
- Impact on wider economy

**Ethics and Public Perception**
- Of control and vaccination policies
Mathematical model

- Focus on vaccination in the transmission process for Singapore
- Standard age-structured SEIR transmission model
  - Included other NPIs
  - Dorms and not-dorms transmission
  - Singapore healthcare parameters
  - Importations

- Input of different numbers of vaccines and actions given to different groups
After first vaccinations

• Using modelling to look at patterns with different vaccinations and strategies and optimal testing strategies for continued control

• Given the vaccination and strategy
  • What are the NPIs that can be lifted?
  • What is the optimal testing strategy to detect and stop transmission chains?

• Understanding about the vaccine
  • Want to know what the impact of the vaccination on infectivity is.
  • Length of immunity (measuring Ab etc. as well disease outcomes).
In different settings?

- Lots of global modelling work on this both country specific and more general
- Can work from one country be transposed to another?
  - Current state of the epidemic
  - Demographics
  - Numbers and which vaccines
- What are the general characteristics that need to be considered?
What can we learn from other places?

AIM

- Vaccine efficacy
  - Impact of vaccinating certain groups
- Vaccination
- Control policies
- Transmission Dynamics
- Healthcare system and Testing
- Economics
- Ethics and Public Perception
- More about biology and transmission
- How vaccines can be effectively distributed?
- Messaging and communication
What is different in the decisions in different places?

**AIM**

**Vaccination**
- Vaccine availability, interpretation of evidence
- Desire to lift different controls
- Availability of vaccine, impact of virus and control

**Transmission Dynamics**
- Current transmission
  - Who is high incidence and high risk of severe disease?

**Control policies**
- Different rollout speed and plans

**Healthcare system and Testing**

**Economics**

**Ethics and Public Perception**
- Vaccine acceptance and uptake
  - Perceptions of other controls
  - Speed necessary
Summary

• Modelling can be part of evidence used for understanding the impact of different vaccine strategies
• Many factors important in a vaccination strategy
• As different countries take different strategies
  • Interesting to understand why
  • To learn what we can from different places
https://www.bloomberg.com/graphics/covid-vaccine-tracker-global-distribution/
COVID-19 Vaccines in the U.S. : State of the Science

Jesse Clark, MD, MSc
Associate Professor-in-Residence
Department of Medicine, Division of Infectious Diseases
Department of Family Medicine
UCLA David Geffen School of Medicine
Outline

• Where are we?
  • What is the current state of vaccine development and distribution in the U.S.?

• How did we get here?
  • What was the process for identifying and evaluating SARS CoV-2 vaccines in the U.S.?
  • What were some of the successes and limitations of vaccine clinical trials to date?

• What happens now?
  • Future plans for vaccine distribution
  • Development of new vaccine candidates
Where are we?

- Moderna and Pfizer BioNTech mRNA vaccines both shown >90% effective and in distribution across U.S.
  - Distribution prioritizing: 1) Healthcare workers and residents/staff of nursing homes/LTC facilities; 2) People over 75 years old; 3) People over 65 years old or with high-risk medical conditions; 4) Everyone else
- 4 other vaccine candidates (Novavax, Janssen, AstraZeneca, Sanofi) in trials, with preliminary evidence of effectiveness for A-Z product (62.1% vs. 90.0%?)
- Additional vaccine candidates in varying stages of development
How did we get here?

• **Operation Warp Speed (OWS)**

  • Created in May, 2020 OWS sought to “deliver tens of millions of doses of a SARS-CoV-2 vaccine — with demonstrated safety and efficacy, and approved or authorized by the FDA for use in the U.S. population — beginning at the end of 2020 and to have as many as 300 million doses of such vaccines available and deployed by mid-2021.”

  • Public-Private partnership: Private companies responsible for product development and distribution aided by “the full capacity of the U.S. government to ensure that no technical, logistic, or financial hurdles hinder vaccine development or deployment.”

  • Identified 4 different platform technologies (1) mRNA 2) Replication-defective live-vector, 3) Recombinant-subunit-adjuvanted protein, 4) Attenuated replicating live-vector) and sought to develop 2 candidate vaccines for each technology.
COVID-19 Vaccine-Prevention Trials Network (CoVPN)

• **Structure**
  
  • Redeployment of NIH-funded HIV research networks: AIDS Clinical Trials Group (ACTG), HIV Vaccine Trials Network (HVTN), HIV Prevention Trials Network (HPTN)
  
  • Ready-made, consolidated national framework for the rapid implementation of clinical trials for both prevention and treatment research of SARS CoV-2

• **Activities**
  
  • Vaccine development (OWS)
  
  • Monoclonal antibodies (Post-Exposure Prophylaxis, Treatment of Infection)
  
  • Epidemiology of COVID-19 transmission in U.S.
OWS Vaccine Candidates

• mRNA
  • Pfizer/BioNTech and Moderna

• Replication-defective live-vector
  • Astra-Zeneca and Janssen

• Recombinant-subunit-adjuvanted protein
  • Novavax and Sanofi-GSK

• Attenuated replicating live-vector
  • TBA
Clinical Trial Experiences I

- Pfizer/BioNTech vaccine developed independently
  - BioNTech developed vaccine/Pfizer responsible for clinical trial
  - 152 sites in US (n=130), Europe, South America, South Africa
  - 2 doses of BNT162b2 (30 ug per dose, 21 days apart)
  - Goal of enrolling 60,000 participants at sites across U.S. in order to meet pre-specified outcome-based endpoints as quickly as possible
- 43,548 enrolled and 37,706 included in initial analysis
  - 83% white, 28% Hispanic/Latinx, 9% African-American
  - 42% older than 55 years
- 162 cases in placebo arm and 8 cases in vaccine arm occurring >7 days after second injection
### Table 2. Vaccine Efficacy against Covid-19 at Least 7 days after the Second Dose.*

<table>
<thead>
<tr>
<th>Efficacy End Point</th>
<th>BNT162b2</th>
<th>Placebo</th>
<th>Vaccine Efficacy, % (95% Credible Interval)‡</th>
<th>Posterior Probability (Vaccine Efficacy &gt;30%)§</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of Cases</td>
<td>Surveillance Time (n)†</td>
<td>No. of Cases</td>
<td>Surveillance Time (n)†</td>
</tr>
<tr>
<td></td>
<td>(N=18,198)</td>
<td>8</td>
<td>2.214 (17,411)</td>
<td>162</td>
</tr>
<tr>
<td>Covid-19 occurrence at least 7 days after the second dose in participants without evidence of infection</td>
<td>(N=19,965)</td>
<td>9</td>
<td>2.332 (18,559)</td>
<td>169</td>
</tr>
</tbody>
</table>

*禁忌症和未报告不良反应。
†观察时间（n）。
‡95%置信区间。
§后验概率（疫苗有效性>30%）。

Polack et al., NEJM 2020
Figure 3. Efficacy of BNT162b2 against Covid-19 after the First Dose.

Shown is the cumulative incidence of Covid-19 after the first dose (modified intention-to-treat population). Each symbol represents Covid-19 cases starting on a given day. Filled symbols represent severe Covid-19 cases. Some symbols represent more than one case, owing to overlapping dates. The inset shows the same data on an enlarged y axis, through 21 days. Surveillance time is the total time in 1000 person-years for the given end point across all participants within each group at risk for the end point. The time period for Covid-19 case accrual is from the first dose to the end of the surveillance period. The confidence interval (CI) for vaccine efficacy (VE) is derived according to the Clopper–Pearson method.
Clinical Trial Experiences II

- **Moderna vaccine developed through OWS program**
  - 2 doses of mRNA-1273 delivered 28 days apart
    - Goal of enrolling 30,000 participants at clinical trial sites across the United States with goal of determining effectiveness over 6-month period
    - 25-40% of participants over 65 years old and/or from high-risk groups (cardiovascular or pulmonary disease, obesity, DM, HIV)
    - Racial and ethnic diversity encouraged but no pre-established parameters for representation
  - 30,420 participants enrolled
    - 24.8% over 65; 16.7% under 65 “High-risk” category
    - 20.5% Hispanic or Latino; 10.2% African-American
A Per-Protocol Analysis

Vaccine Efficacy (95% CI)

- Placebo: 94.1% (89.3 – 96.8%
- mRNA-1273:

Incidence Rate (95% CI)

- Placebo: 56.5 (48.7 – 65.3) per 1000 person-yr
- mRNA-1273: 3.3 (1.7 – 6.0)

Cumulative Event Rate (%)

Days since Randomization

No. at Risk

Placebo: 14,073 14,073 14,073 14,072 13,416 12,992 12,361 11,147 9474 6563 3971 1172 0
mRNA-1273: 14,134 14,134 14,134 14,133 13,483 13,073 12,508 11,315 9684 6721 4094 1209 0
**B Modified Intention-to-Treat Analysis**

<table>
<thead>
<tr>
<th>Vaccine Efficacy (95% CI)</th>
<th>Incidence Rate (95% CI) per 1000 person-yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>93.0 (88.9–95.6)</td>
</tr>
<tr>
<td>mRNA-1273</td>
<td>79.8 (70.5–89.9)</td>
</tr>
<tr>
<td></td>
<td>5.6 (3.4–8.8)</td>
</tr>
</tbody>
</table>

**Cumulative Event Rate (%)**

![Graph showing cumulative event rates over days since randomization.]

**No. at Risk**

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>mRNA-1273</th>
</tr>
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<tbody>
<tr>
<td>0</td>
<td>14,598</td>
<td>14,550</td>
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<tr>
<td>10</td>
<td>14,590</td>
<td>14,543</td>
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<td>20</td>
<td>14,567</td>
<td>14,532</td>
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<tr>
<td>120</td>
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</table>

**Covid-19 Onset**

<table>
<thead>
<tr>
<th></th>
<th>Placebo (N=14,598)</th>
<th>mRNA-1273 (N=14,550)</th>
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<tbody>
<tr>
<td>Randomization to 14 days after dose 1</td>
<td>11</td>
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<td>14 Days after dose 1 to dose 2</td>
<td>35</td>
<td>2</td>
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<td>Dose 2 to 14 days after dose 2</td>
<td>19</td>
<td>0</td>
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<tr>
<td>Starting 14 days after dose 2</td>
<td>204</td>
<td>12</td>
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<tr>
<td>Total (any time after randomization)</td>
<td>269</td>
<td>19</td>
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</table>
Figure B: Systemic Events

- Any Adverse Event
- Fever
- Headache
- Fatigue
- Myalgia
- Arthralgia
- Nausea or Vomiting
- Chills

Percentage of Participants

Baden et al., NEJM 2020
Where do we go from here? (Scientific Issues)

• Production and distribution of approved vaccines
  • Cold Chain: mRNA vaccines require -80C freezer storage (Pfizer vaccine viable for 5 days; Moderna viable for 30 days)
  • Scale-up of production for mRNA vaccines unprecedented

• Evaluating new vaccine candidates
  • Other vaccines in pipeline may have advantages (cost, production and storage requirements, side effects, efficacy)
  • How to enroll and follow participants in trials of experimental vaccines when they have access to an effective one?
Where do we go from here? (Social Issues)

• Ensuring access to all individuals
  • No OWS for vaccine allocation and distribution
    • Early rollout in U.S. has been problematic
    • Absence of a national plan for distribution with local regulations developed on an improvisational basis
  • Acceptability of vaccines/mistrust in minority communities
  • Logistics of distributing vaccine to underserved areas
  • What is an effective level of population coverage?
Imposing Risk: Public Health Ethics & Covid-19

Dr. Diego S. Silva
Sydney Health Ethics
APRU - January 13, 2021
**As Rollout Falters, Scientists Debate New Vaccinations**

Should second doses be delayed? Should most adults receive half-doses? Scientists disagree.

By Katherine J. Wu and Rebecca Robbins

Published Jan. 3, 2021 | Updated Jan. 8, 2021

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**Cuomo Widens Eligibility After Vaccine Delays**

Three million more people will be permitted to schedule vaccines, off to a dispiriting start.

By Joseph Goldstein

Jan. 8, 2021
Take home message & overview

Hh

1. What is ethics?
2. The context of COVID-19 and associated vaccines
3. Commonly discussed ethical issues
4. An underlying concern: risk and risk imposition
5. A heuristic for risk imposition
6. Moving forward: fostering virtue in students and ourselves
What is ethics?

- About how we *ought* to live
- The rules and principles that *should* guide our actions
- Determining who we *should* be

- Different from law
- Different from human rights

- Why ethics?
  - Underpins law and human rights
  - Much of life falls outside purview of law and human rights
'Living in limbo': Australians stranded overseas set back by latest travel restrictions

London: Australians trying to get home from overseas are urging the government to establish a reliable quarantine system after a wave of flight cancellations were triggered by new caps on arrivals due to the mutant strain of COVID-19.

Stuart Kemp, 31, and his English wife had booked flights, quit their jobs and shipped their belongings home to Melbourne at the end of six years of living and working in Britain.
Commonly discussed ethical issues

- Vaccine allocation and distribution
- Who gets a ventilator, who doesn’t
- Border restrictions and the IHR
- Communicating uncertainty in ‘post-truth’ world
- Addressing stigma, discrimination
- Etc.
An underlying concern: risk and risk imposition

- Risk = description of hazard + probability of hazard
- Uncertainty abounds
- Balancing the risks and benefits of proposed public health measures
- Some risks of PH measures are done unto free persons without their consent
An underlying concern: risk and risk imposition

Ethics interested in:

1. **Risk**= description of hazard + probability of hazard + cause of hazard
2. Just distribution of risk
A heuristic for risk imposition (policy makers)

1. $x$ acts in light of reasonably discoverable facts regarding risk $y$,
2. there are some benefits related to risk $y$ that can be shared with $z$ either directly or indirectly,
3. imposing risk $y$ should be justifiable to $z$ given $z$ is in the greatest position of risk,
4. steps should be taken by $x$ to minimize potential harms associated with risk $y$, and
5. $z$ should be compensated should a harm come about from the actualization of the risk through carelessness or recklessness

NB no. 1: Necessary but not sufficient conditions, e.g., no discussion of procedural fairness
NB no. 2: Much conceptual work underpinning heuristic
Case one

Action: disregarding COVID-19 vaccine schedules

Risk: reducing chance and amount (how much?) of immunization
Case two
Action: mandatory vaccination
Risk: violation of bodily integrity, autonomy
Developing virtuous persons
Thank you!

Twitter: @DiegoSilvaPhD

Email: diego.silva@sydney.edu.au
The latest development of Covid-19 vaccines

Fuqiang Cui
Peking University School of Public Health
13 January 2021
Strategies to control communicable diseases

• Manage the source of infection
  • Tracing contact
  • Isolating
  • Quarantine

• Interrupt the route of transmission
  • Wearing mask
  • Keeping physical distance
  • Washing hands

• Protect the susceptible population
  • Vaccination
  • Health education
Value of Vaccines

• Disease control benefits
  • Eradication
  • Elimination

• Control of mortality, morbidity and complications
  • For the individual
  • For society

• Protection of the unvaccinated population
  • Herd protection
  • Source drying

• Prevention of related diseases and cancer
  • Protection against related diseases
  • Cancer prevention

• Societal and other benefits
  • Health-care and other savings for society
  • Preventing development of antibiotic resistance
  • Extending life expectancy
  • Safe travel and mobility
  • Other public health benefits
    • Empowerment of women
    • Protection against bioterrorism
    • Promoting economic growth
    • Enhancing equity
    • Promoting peace

https://www.who.int/bulletin/volumes/86/2/07-040089/en/
Landscape of COVID-19 Candidate Vaccines Globally

By 11 Jan, 2021

✓ 289 vaccine candidates

✓ 220 candidate vaccines in preclinical evaluation

✓ 69 candidate vaccines in clinical evaluation

✓ 5 licensed (EUL+EUA)

Ref: https://vac-ishtm.shinyapps.io/ncov_vaccine_landscape/
https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines
# Progress of Covid-19 vaccines by different R&D Routes

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<thead>
<tr>
<th>Type</th>
<th>Pre-clinical</th>
<th>Phase 1</th>
<th>Phase 1/2</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Used/Licensed</th>
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<td>RNA</td>
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<td>1</td>
<td>3</td>
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<td>DNA</td>
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<td>4</td>
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<td>6</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>3</td>
<td>35</td>
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<tr>
<td>Replicating viral vector</td>
<td>18</td>
<td>2</td>
<td>2</td>
<td>1</td>
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<td>1</td>
<td>1</td>
<td>6</td>
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<td>Virus-like particle</td>
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<td>0</td>
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<td>19</td>
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<td>3</td>
<td>0</td>
<td>0</td>
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<td>38</td>
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<td><strong>Total</strong></td>
<td><strong>220</strong></td>
<td><strong>19</strong></td>
<td><strong>23</strong></td>
<td><strong>6</strong></td>
<td><strong>20</strong></td>
<td><strong>10</strong></td>
<td><strong>289</strong></td>
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</table>

Ref: [https://vac-lshtm.shinyapps.io/ncov_vaccine_landscape/](https://vac-lshtm.shinyapps.io/ncov_vaccine_landscape/)  11 Jan 2021
Covid-19 vaccines in phase 3 clinic trial (15+5)

- **RNA platform**
  - US-Moderna/NIAID (mRNA-1273)
  - Germany-China-US-BioNTech/Fosun Pharma/Pfizer (BNT162)
  - Germany-CureVac (CVnCov)

- **DNA platform**
  - US/Korea-Inovio/IVI (INO-4800)
  - Japan-Osaka University/AnGes/Takara (AG0302-COVID19)

- **Non-Replicating Viral Vector platform**
  - Oxford/AstraZeneca
  - China-CanSino/Beijing Institute of Biotechnology (Ad5-nCoV)
  - Russia-Gamaleya Research Institute (Gam-COVID-Vac/Sputnik V)

- **Virus-like Particle platform**
  - Canada-Medicago Inc (CoVLP)

- **Inactivated Virus platform**
  - India-Bharat Biotech/ICMR/NIV (COVAXIN)
  - China-Institute of Medical Biology (Inactivated vaccine)
  - Kazakhstan-NISKhi (QAZCOVID-IN)
  - China-Beijing institute(CNBG)
  - China-Wuhan Institute of CNBG
  - China-Sinovac (CoronaVac)

- **Protein Subunit platform**
  - China-Anhui Zhifei (ZF2001)
  - China/the U.K./the U.S.-Clover/GSK/Dynavax (SCB-2019)
  - US-Covaxx/UNMC (UB-612)
  - US- Novavax (NVX-CoV2373)

Ref: https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines
# Clinical trial design of phase 3 vaccines

<table>
<thead>
<tr>
<th>Manufacturer (Vaccine)</th>
<th>Number of doses</th>
<th>Timing of doses</th>
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<tbody>
<tr>
<td><strong>RNA vaccine</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>US-Moderna/NIAID (mRNA-1273)</td>
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<td></td>
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<tr>
<td>Germany-China-US-BioNTech/Fosun Pharma/Pfizer (BNT162)</td>
<td>2</td>
<td>0, 28d</td>
</tr>
<tr>
<td>Germany-CureVac (CVnCov)</td>
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<tr>
<td><strong>DNA vaccine</strong></td>
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<td>Oxford/AstraZeneca</td>
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<tr>
<td>China-CanSino/Beijing Institute of Biotechnology (Ad5-nCoV)</td>
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<tr>
<td>Russia-Gamaleya Research Institute (Gam-COVID-Vac/Sputnik V)</td>
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<td><strong>Virus-like particle</strong></td>
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<tr>
<td>Canada-Medicago Inc (CoVLP)</td>
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<tr>
<td><strong>Inactivated</strong></td>
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<td>China-Beijing institute(CNBG)</td>
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<td>China-Sinovac (CoronaVac)</td>
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<tr>
<td>China-Wuhan Institute of CNBG (WIBP vaccines)</td>
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<td><strong>Protein subunit</strong></td>
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<tr>
<td>China-Anhui Zhifei (ZF2001)</td>
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<td></td>
</tr>
<tr>
<td>US-Novavax (NVX-CoV2373)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The requirements for vaccine development

• The study found that the vaccine has to have an efficacy of at least 70% to prevent an epidemic and of at least 80% to largely extinguish an epidemic without any other measures (e.g., social distancing).

• WHO has set its own success benchmarks for COVID-19 vaccines, the higher benchmark calls for 70% efficacy and a duration of protection for one year, while the lower threshold calls for 50% efficacy for 6 months.

• Coronavirus vaccine developers now have some advice from the FDA: To win approval, any vaccine must be at least 50% more effective than placebo in preventing the disease.

## Safety of Covid-19 Vaccines in Phase 2/3

<table>
<thead>
<tr>
<th>Platform</th>
<th>Developer (vaccine name)</th>
<th>Any Local (%)</th>
<th>G3+AE (%)</th>
<th>Pain (%)</th>
<th>Fever (%)</th>
<th>Fatigue (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>mRNA</td>
<td>US-Moderna/NIAID (mRNA-1273)</td>
<td>92.2</td>
<td>15.8</td>
<td>88.2</td>
<td>15.5</td>
<td>63.3</td>
</tr>
<tr>
<td></td>
<td>Germany-China-US-BioNTech/Fosun Pharma/Pfizer (BNT162)</td>
<td>27</td>
<td>0.6</td>
<td>71</td>
<td>16</td>
<td>59</td>
</tr>
<tr>
<td>Protein subunit</td>
<td>China-Anhui Zhifei (ZF2001)</td>
<td>48</td>
<td>0</td>
<td>12</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>US-Novavax (NVX-CoV2373)</td>
<td>92.3</td>
<td>0</td>
<td>57.7</td>
<td>0</td>
<td>46.2</td>
</tr>
<tr>
<td>Non-replicating viral vector</td>
<td>UK-Oxford/AstraZeneca</td>
<td>88</td>
<td>0.7</td>
<td>51</td>
<td>0</td>
<td>45</td>
</tr>
<tr>
<td></td>
<td>Russia-Gamaleya Research Institute (Gam-COVID-Vac/Sputnik V)</td>
<td>-</td>
<td>0</td>
<td>58</td>
<td>50</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>China-CanSino/Beijing Institute of Biotechnology (Ad5-nCoV)</td>
<td>74</td>
<td>1</td>
<td>56</td>
<td>16</td>
<td>34</td>
</tr>
<tr>
<td></td>
<td>US-Janssen (Ad26.COV2.S)</td>
<td>71.4</td>
<td>10.9</td>
<td>-</td>
<td>19</td>
<td>-</td>
</tr>
<tr>
<td>Inactivated</td>
<td>China-Beijing institute(CNBG)</td>
<td>19.45</td>
<td>0.02</td>
<td>18</td>
<td>1.94</td>
<td>1.83</td>
</tr>
<tr>
<td></td>
<td>India-Bharat Biotech/ICMR/NIV (COVAXIN)</td>
<td>10.3</td>
<td>-</td>
<td>3.2</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>China-Institute of Medical Biology (Inactivated vaccine)</td>
<td>27.3</td>
<td>0</td>
<td>14.7</td>
<td>2.7</td>
<td>6.7</td>
</tr>
<tr>
<td></td>
<td>China-Sinovac (CoronaVac)</td>
<td>33</td>
<td>0</td>
<td>21</td>
<td>3.3</td>
<td>3.3</td>
</tr>
</tbody>
</table>

[https://jamanetwork.com/journals/jama/fullarticle/2769612](https://jamanetwork.com/journals/jama/fullarticle/2769612)
# Efficacy of Covid-19 Vaccines in Phase 2/3

<table>
<thead>
<tr>
<th>Platform</th>
<th>Developer (vaccine name)</th>
<th>Seroconversion rate (%)</th>
<th>GMTs of Antibody</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>mRNA</strong></td>
<td><strong>US-Moderna/NIAID (mRNA-1273)</strong></td>
<td>100</td>
<td>344</td>
</tr>
<tr>
<td></td>
<td><strong>Germany-China-US-BioNTech/Fosun Pharma/Pfizer (BNT162)</strong></td>
<td>-</td>
<td>312</td>
</tr>
<tr>
<td><strong>Protein subunit</strong></td>
<td><strong>China-Anhui Zhifei (ZF2001)</strong></td>
<td>99</td>
<td>103</td>
</tr>
<tr>
<td></td>
<td><strong>US-Novavax (NVX-CoV2373)</strong></td>
<td>-</td>
<td>195</td>
</tr>
<tr>
<td><strong>Non-replicating viral vector</strong></td>
<td><strong>UK-Oxford/AstraZeneca</strong></td>
<td>99</td>
<td>193</td>
</tr>
<tr>
<td></td>
<td><strong>Russia-Gamaleya Research Institute (COVID-Vac/Sputnik V)</strong></td>
<td>100</td>
<td>49</td>
</tr>
<tr>
<td></td>
<td><strong>China-CanSino/Beijing Institute of Biotechnology (Ad5-nCoV)</strong></td>
<td>96</td>
<td>18</td>
</tr>
<tr>
<td><strong>Inactivated</strong></td>
<td><strong>China-Beijing institute(CNBG)</strong></td>
<td>100</td>
<td>156</td>
</tr>
<tr>
<td></td>
<td><strong>India-Bharat Biotech/ICMR/NIV (COVAXIN)</strong></td>
<td>98</td>
<td>197</td>
</tr>
<tr>
<td></td>
<td><strong>China-Institute of Medical Biology (Inactivated vaccine)</strong></td>
<td>96</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td><strong>China-Sinovac (CoronaVac)</strong></td>
<td>94</td>
<td>28</td>
</tr>
</tbody>
</table>

Ref: [https://www.medrxiv.org/content/10.1101/2020.12.20.20248602v1](https://www.medrxiv.org/content/10.1101/2020.12.20.20248602v1)
[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31866-3/fulltext#supplementaryMaterial](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31866-3/fulltext#supplementaryMaterial)
Efficacy of Covid-19 Vaccines among high risk population in Phase 3

German/US BioNTech/Pfizer (BNT162 (b2)):

Participants with hypertension: Vaccine Efficacy 94.6%
Participants with obesity: Vaccine Efficacy 95.4%

## Safety and efficacy of Covid-19 Vaccines have been licensed

<table>
<thead>
<tr>
<th>Company</th>
<th>platform</th>
<th>Study population</th>
<th>AE</th>
<th>Total VE (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pfizer</td>
<td>mRNA</td>
<td>43,548</td>
<td>No SAE</td>
<td>95</td>
</tr>
<tr>
<td>Moderna</td>
<td>mRNA</td>
<td>30,420</td>
<td>No SAE</td>
<td>94.5</td>
</tr>
<tr>
<td>Oxford/AstraZeneca</td>
<td>Non-replicating viral vector</td>
<td>23,848</td>
<td>168 cases</td>
<td>70.4</td>
</tr>
<tr>
<td>Gamaleya Research Institute</td>
<td>Non-replicating viral vector</td>
<td>22,714</td>
<td>No SAE</td>
<td>92</td>
</tr>
<tr>
<td>Beijing Institute of Biological Products Sinopharm</td>
<td>Inactivated vaccine</td>
<td>45,000</td>
<td>No SAE</td>
<td>79.34</td>
</tr>
</tbody>
</table>

[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32661-1/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32661-1/fulltext)
Five vaccines have been licensed (EUA/EUL)

- BioNTech/Pfizer (BNT162 (b2)) Emergency approval, UK 2 Dec; US 12 Dec 2020
- University of Oxford/AstraZeneca (ChAdOx1-S) Approved for emergency use in the UK (30 Dec 2020) and India (03 Jan 2021).
- Gamaleya Research Institute, Russia’s approval of a COVID-19 vaccine (11 Aug 2020)
- Beijing Institute of Biological Products Sinopharm (BBIBP-CorV) Full or conditional approval, UAE. 09 Dec 2020, Bahrain (13 Dec 2020), and China (30 Dec 2020).

Ref: https://vac.lshtm.shinyapps.io/ncov_vaccine_landscape/
Overview of Covid-19 Vaccines in Phase 3

- Six platforms, mostly 2 doses, intramuscular injection
- Intervals range from 14 days to 60 days
- The results of Phase II: safe, well tolerated and highly immunogenic
- Some of them has the potential to elicit protective humoral responses against COVID-19
- Neutralizing antibody responses may be higher than outpatients
COVID-19 Vaccines R&D Routes in China

• Six Parallel technical routes in development
  • mRNA vaccine
  • DNA vaccine
  • Adenovirus-5 vector vaccine
  • Attenuated influenza virus vector vaccine
  • Inactivated vaccine
  • Recombinant subunit vaccine

• 16 Vaccines in Clinical Trial

• Four Vaccines in Phase 3 clinical trial
  • Adenovirus vector vaccine: CanSino Biological Inc (Ad5-nCoV)
  • Inactivated vaccine: Wuhan Institute CNBP; Sinovac (CoronaVac)
  • mRNA vaccine: Anhui Zhifei Longcom Biopharmaceutical Chinese Academy of Sciences (ZF2001)

• One Vaccine have been licensed
  • Beijing Institute of CNBP (BBIBP-CorV)

Ref: https://vac-lshtm.shinyapps.io/ncov_vaccine_landscape/
History of Human Challenge Studies (HCS)

• Target:
  • Accelerating the development of treatments for diseases or vaccines

• From 1940s, human challenge studies have been performed safely
  • Malaria
  • Typhoid
  • Cholera
  • Norovirus
  • Flu
  • Zika

Human Challenge studies of COVID-19 in the UK

• Target:
  • To discover the smallest amount of virus to cause COVID-19

• Partnership
  • Imperial College London, hVIVO, the Royal Free London NHS Foundation Trust

• Duration (Approved by regulators and the ethics committee)
  • Jan-May 2021

• Design
  • Volunteers: healthy young adults in 18-30 years
  • Samples: up to 90
  • Strict control conditions
    • a controlled entrance to the facility
    • careful decontamination of waste
    • a dedicated laboratory for carrying out tests
    • air leaving the unit is cleaned
    • Medics and scientists closely monitor the effect on volunteers 24 hours per day

Priority population for vaccination in China

• Step 1, mainly for key population, including people work in imported cold chain port inspection and quarantine, the ship pilotage, aviation flight, the fresh market, public transportation, medical, CDC staff with high risk of infection, as well as to the high-risk countries or regions to work or study, try to alleviate the pressure of the type of disease prevention and control, reduce the risk of local cases and domestic outbreak.
  • Notably, the more vulnerable older groups are not among the priority groups for the first step.
  • Vaccine is free

• Step 2: With the approval of vaccine with conditions or the gradual increase of vaccine production, more vaccines will be put into use. Eligible people will be able to get the vaccine gradually.
What we have not known

WHO has set benchmarks for COVID-19 vaccines, the higher benchmark calls for 70% efficacy and a duration of protection for one year, while the lower threshold calls for 50% efficacy for 6 months. However, we have not known

• Efficacy among adolescents, children, and pregnant, etc
• Efficacy among people with cardiovascular disease, etc
• Safety among adolescents, children, and pregnant, people with cardiovascular and disease conditions, etc
• Duration of protection needs to be evaluated (6m-12m)
• ......
What we have to evaluate

• The trend of the pandemic
• The impact of the mutated virus on control strategy
• Effects of variation on vaccine efficacy
• Vaccine hesitancy
• The impact of vaccination on the epidemic
Concerns and Solutions

• The impact of pandemic is beyond the health
• No country is safe, until all countries are safe
• Vaccine alone is not enough, other measures matter
• Vaccine safety is a concern? Will people take the vaccine?
• Equity, affordability, accessibility?
• Vaccine Hesitancy?
• More solutions needed!!!
Thanks

“Knowing is not enough; we must apply. Willing is not enough; we must do.” —Goethe