Global vaccination strategies: similarities, differences and lessons

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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?

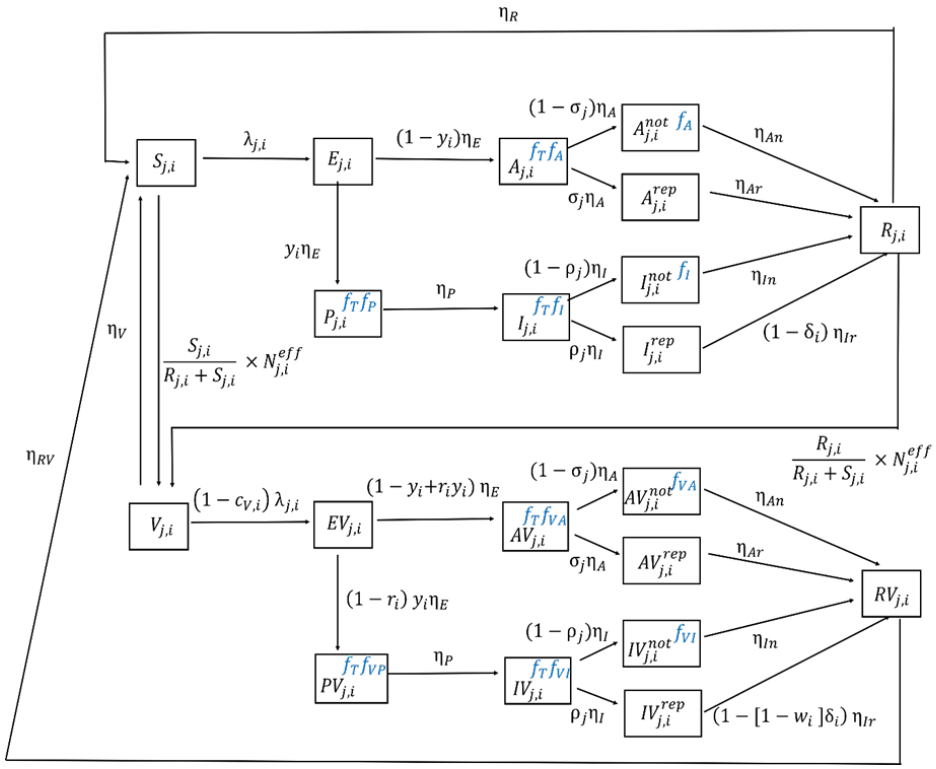
Healthcare system and Testing
- Capabilities
- Policies

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



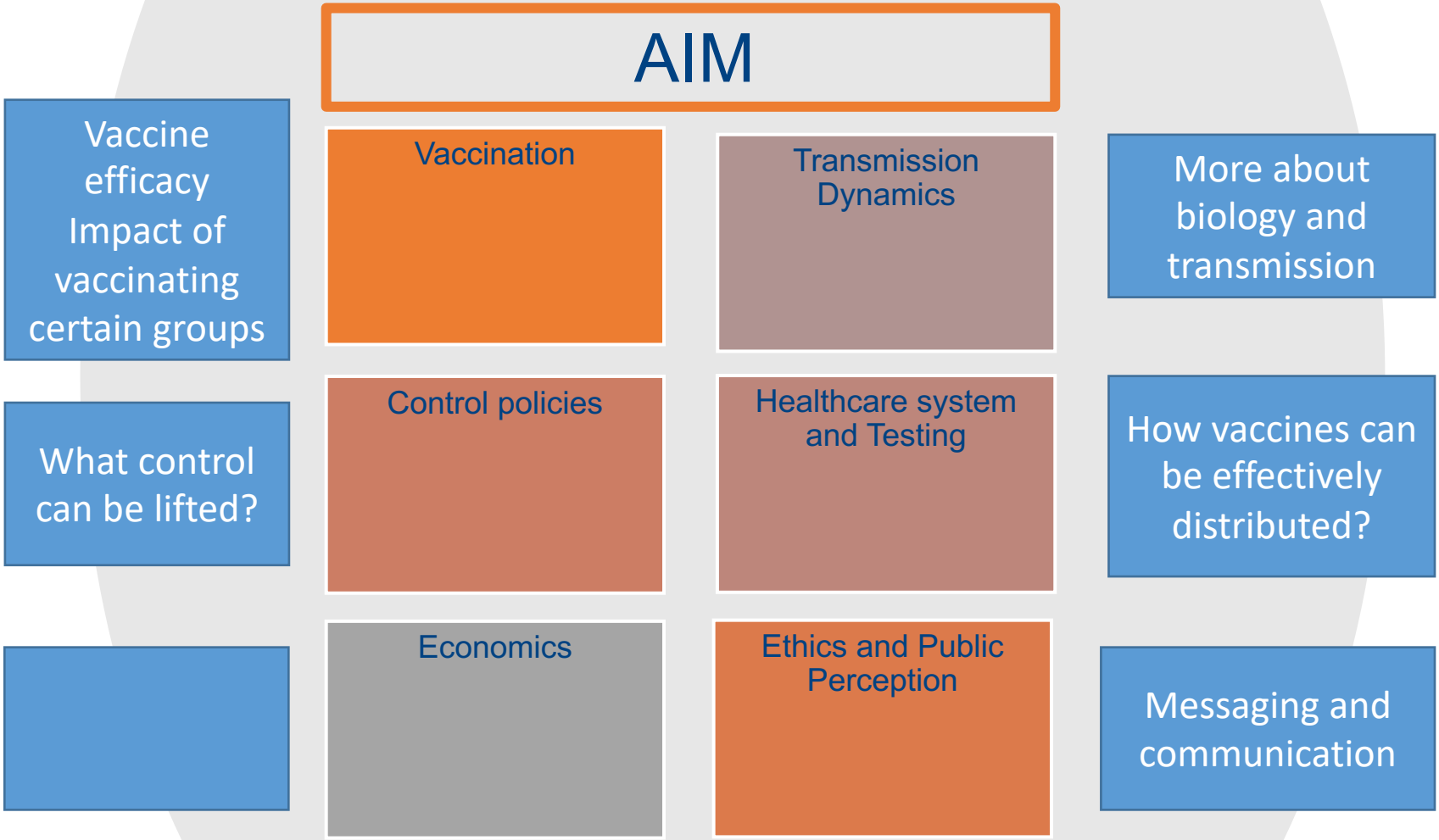
After first vaccinations

- 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).

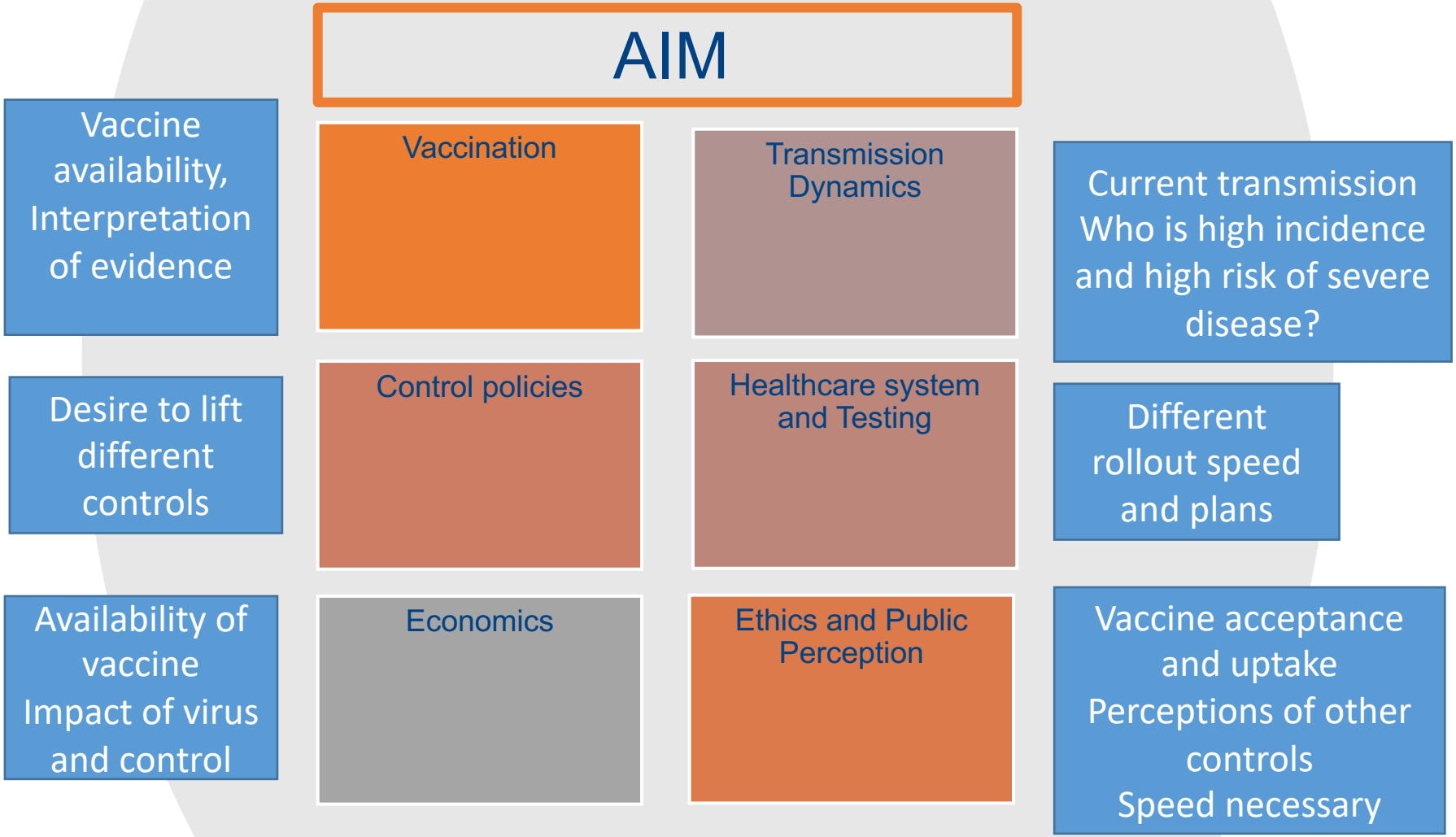
In different settings?

- 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?

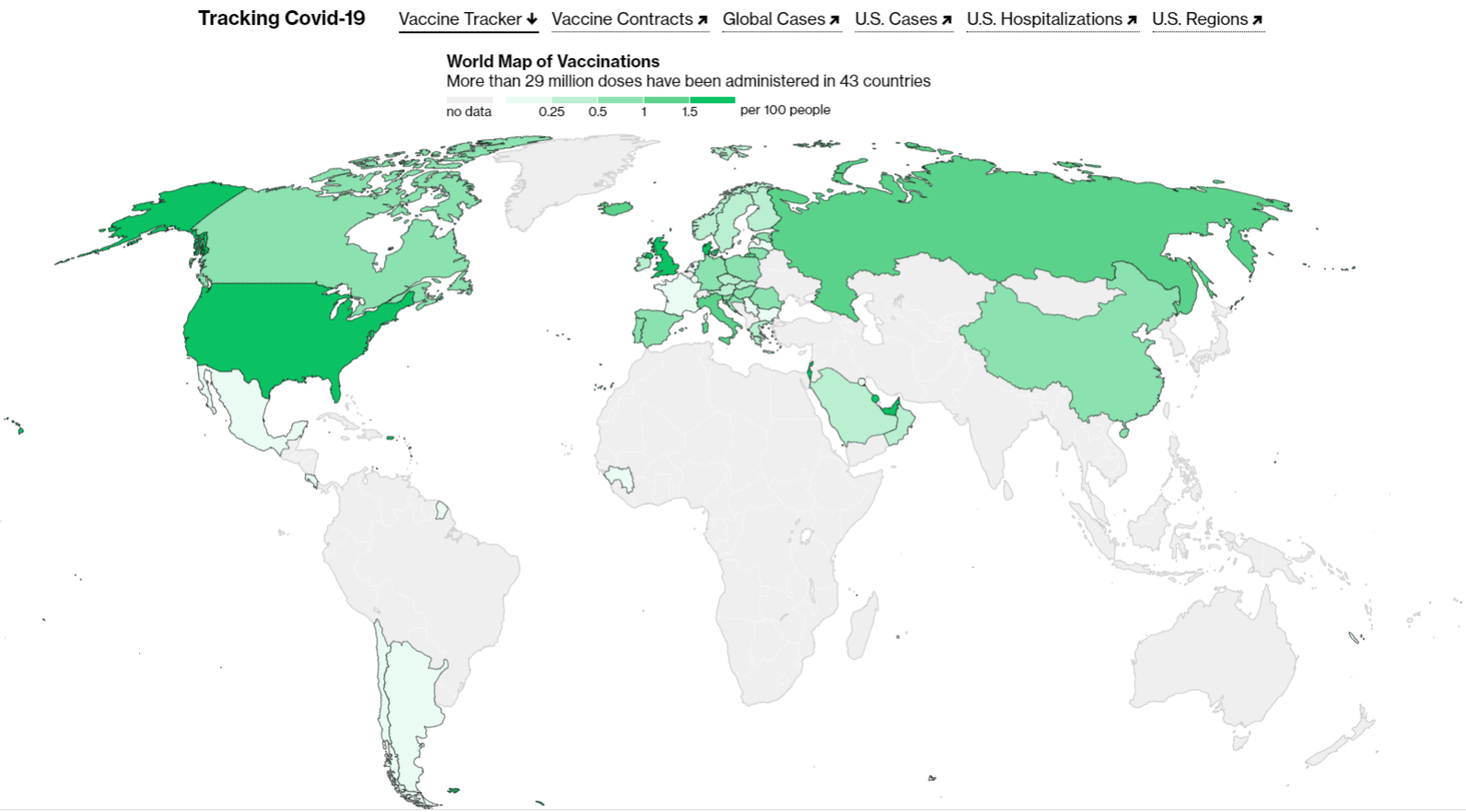


What is different in the decisions in different places?



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/

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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

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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, Astra-Zeneca, 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.*

Efficacy End Point	BNT162b2		Placebo		Vaccine Efficacy, % (95% Credible Interval)‡	Posterior Probability (Vaccine Efficacy >30%)§
	No. of Cases	Surveillance Time (n)†	No. of Cases	Surveillance Time (n)†		
		(N=18,198)		(N=18,325)		
Covid-19 occurrence at least 7 days after the second dose in participants without evidence of infection	8	2.214 (17,411)	162	2.222 (17,511)	95.0 (90.3–97.6)	>0.9999
		(N=19,965)		(N=20,172)		
Covid-19 occurrence at least 7 days after the second dose in participants with and those without evidence of infection	9	2.332 (18,559)	169	2.345 (18,708)	94.6 (89.9–97.3)	>0.9999

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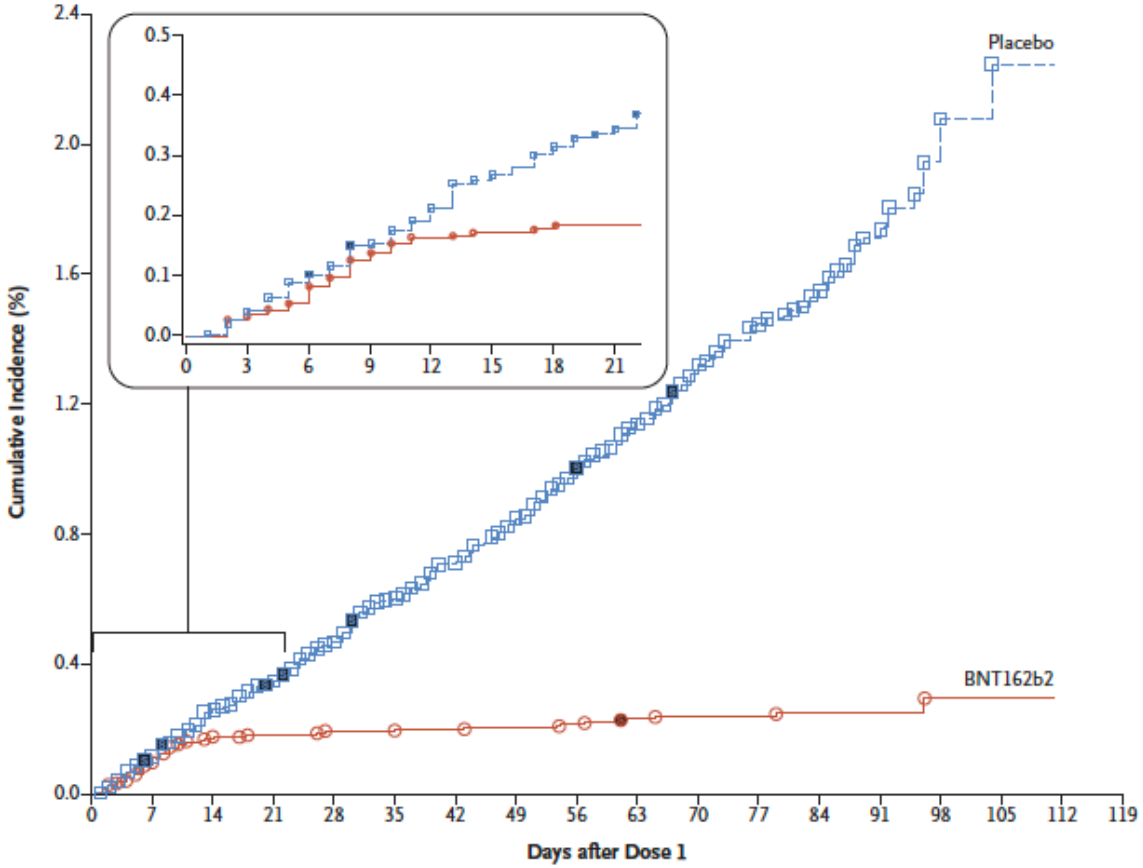
Polack et al., NEJM 2020



Efficacy End-Point Subgroup	BNT162b2, 30 μg (N=21,669)		Placebo (N=21,686)		VE (95% CI)
	No. of participants	Surveillance time *person-yr (no. at risk)*	No. of participants	Surveillance time *person-yr (no. at risk)*	*percent*
Covid-19 occurrence					
After dose 1	50	4.015 (21,314)	275	3.982 (21,258)	82.0 (75.6–86.9)
After dose 1 to before dose 2	39		82		52.4 (29.5–68.4)
Dose 2 to 7 days after dose 2	2		21		90.5 (61.0–98.9)
≥7 Days after dose 2	9		172		94.8 (89.8–97.6)

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.

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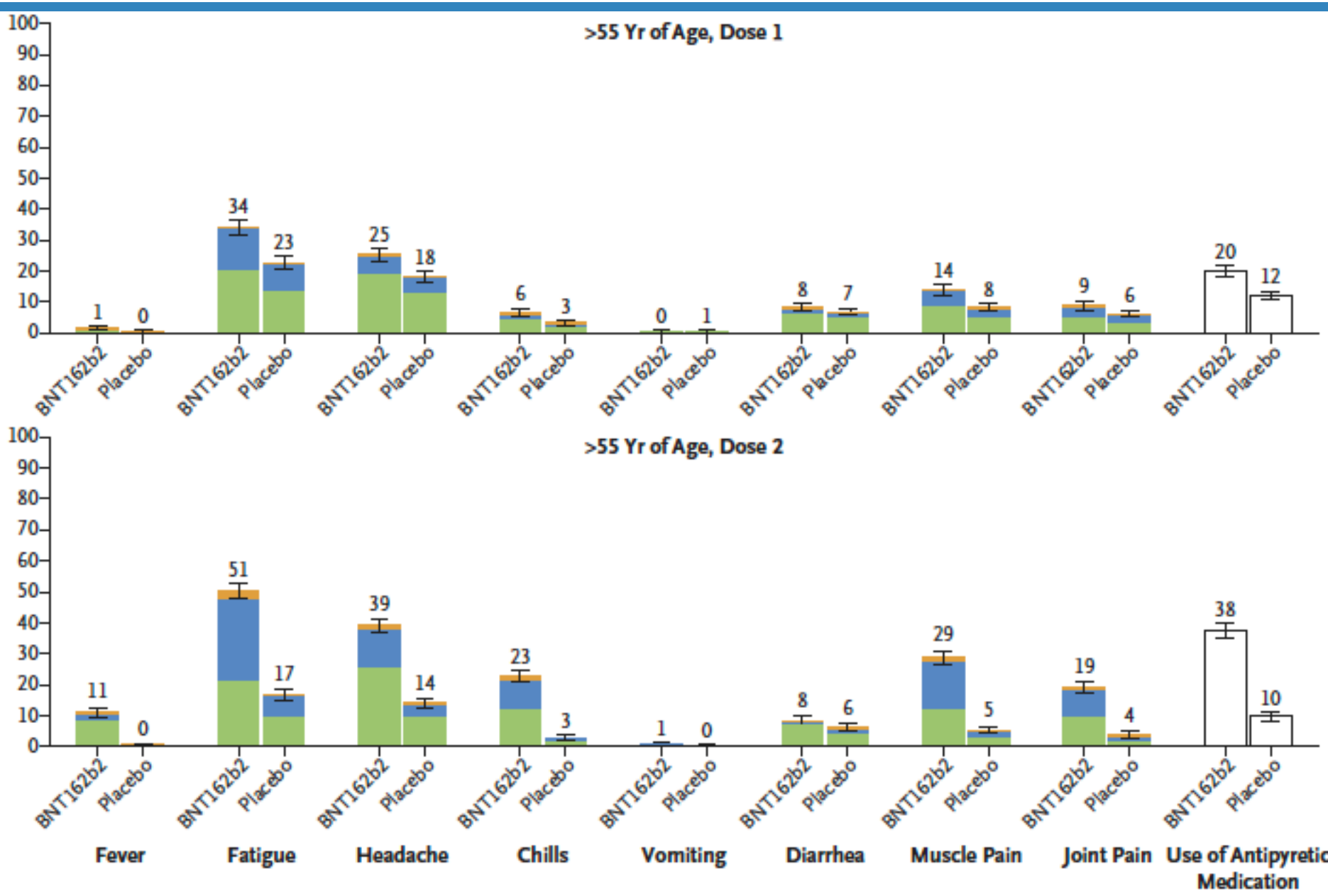
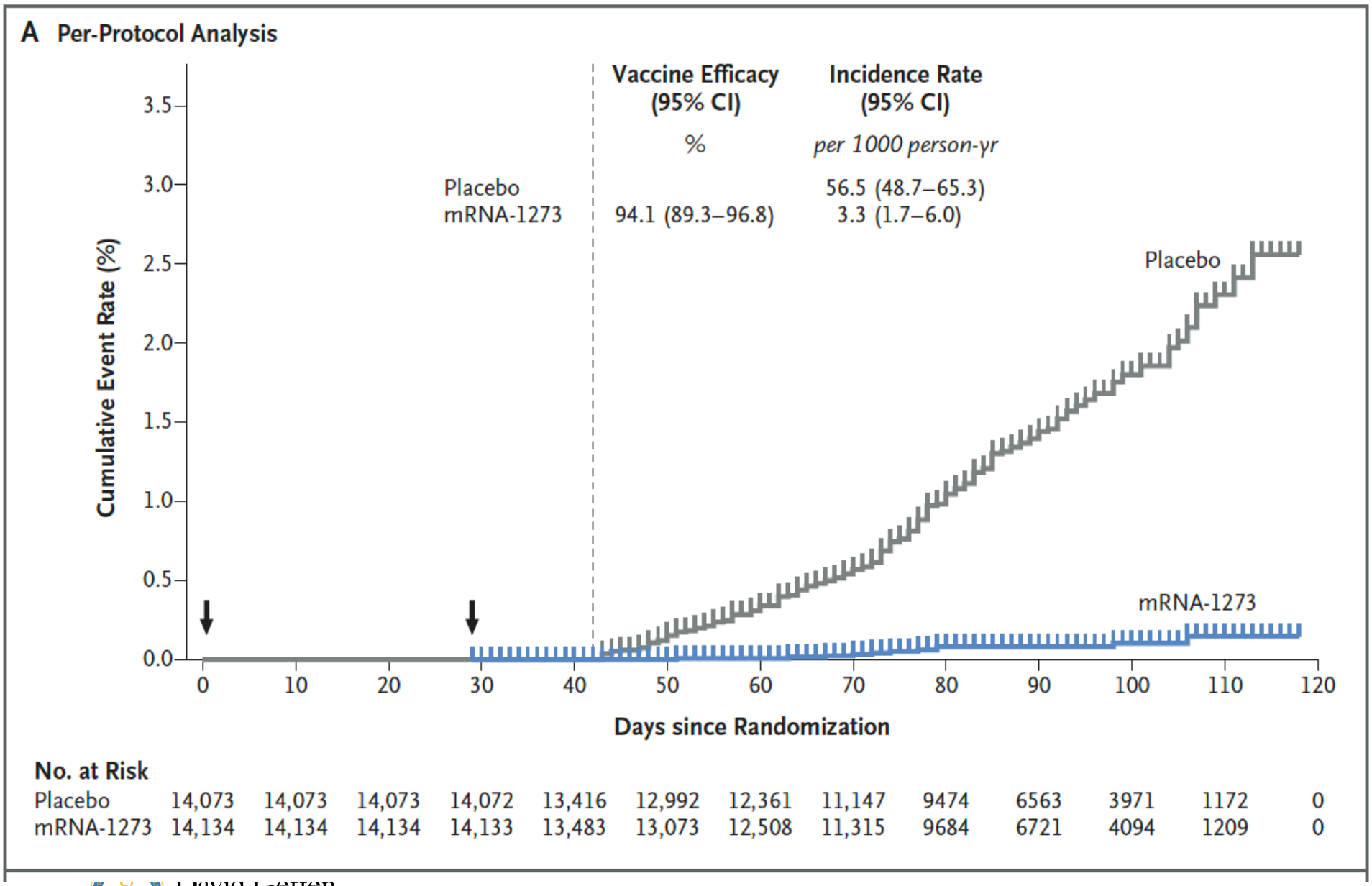
NEJM 2020


>55 Yr of Age, Dose 1
100
90
80
70
60
50
40
30
20
10
0
1
0
34
23
25
18
6
3
0
1
8
7
14
8
9
6
20
12
BNT162b2
Placebo
>55 Yr of Age, Dose 2
11
0
51
17
39
14
23
3
1
0
8
6
29
5
19
4
38
10
Fever
Fatigue
Headache
Chills
Vomiting
Diarrhea
Muscle Pain
Joint Pain
Use of Antipyretic Medication

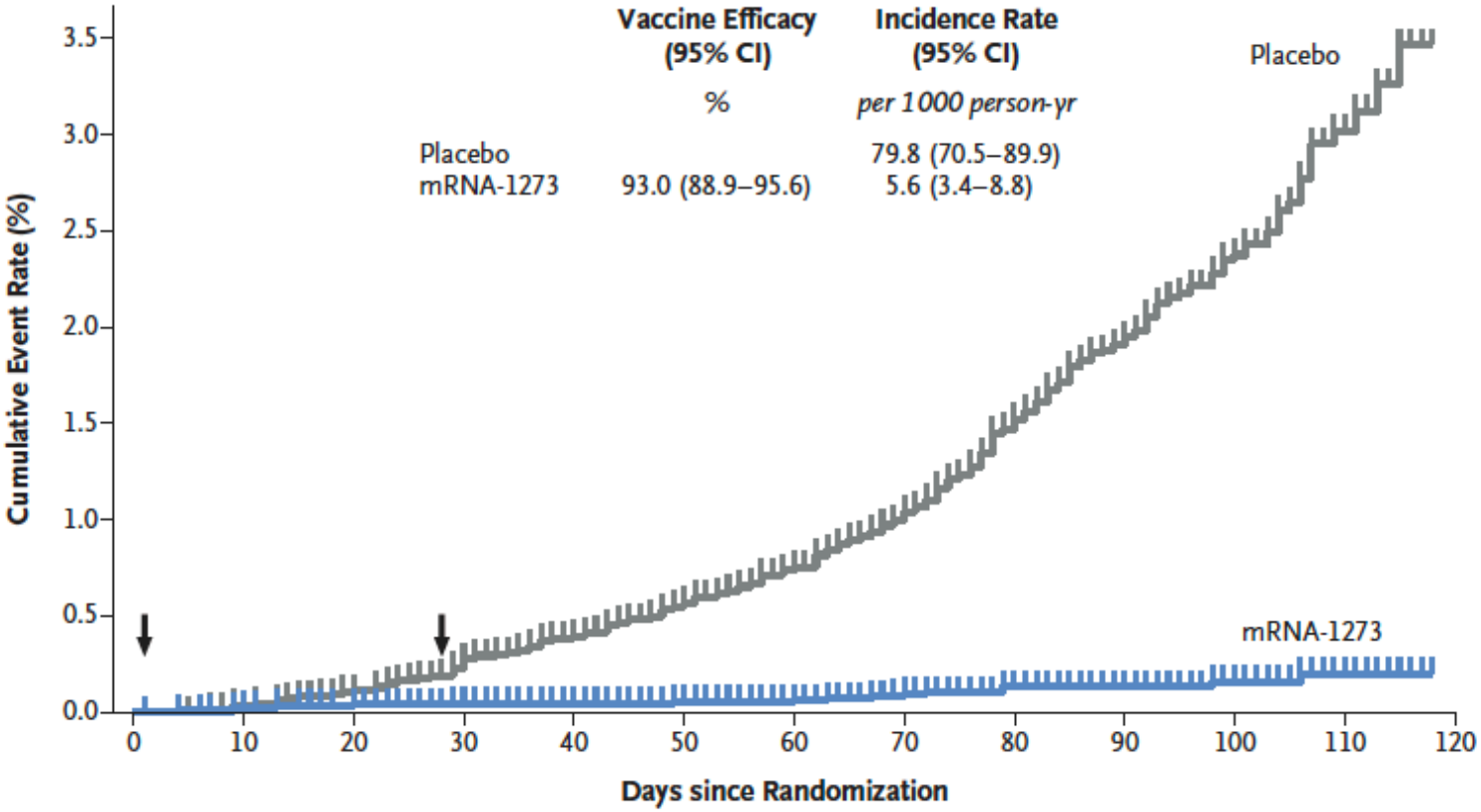
Clinical Trial Experiences II

- 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



Baden et al., NEJM 2020

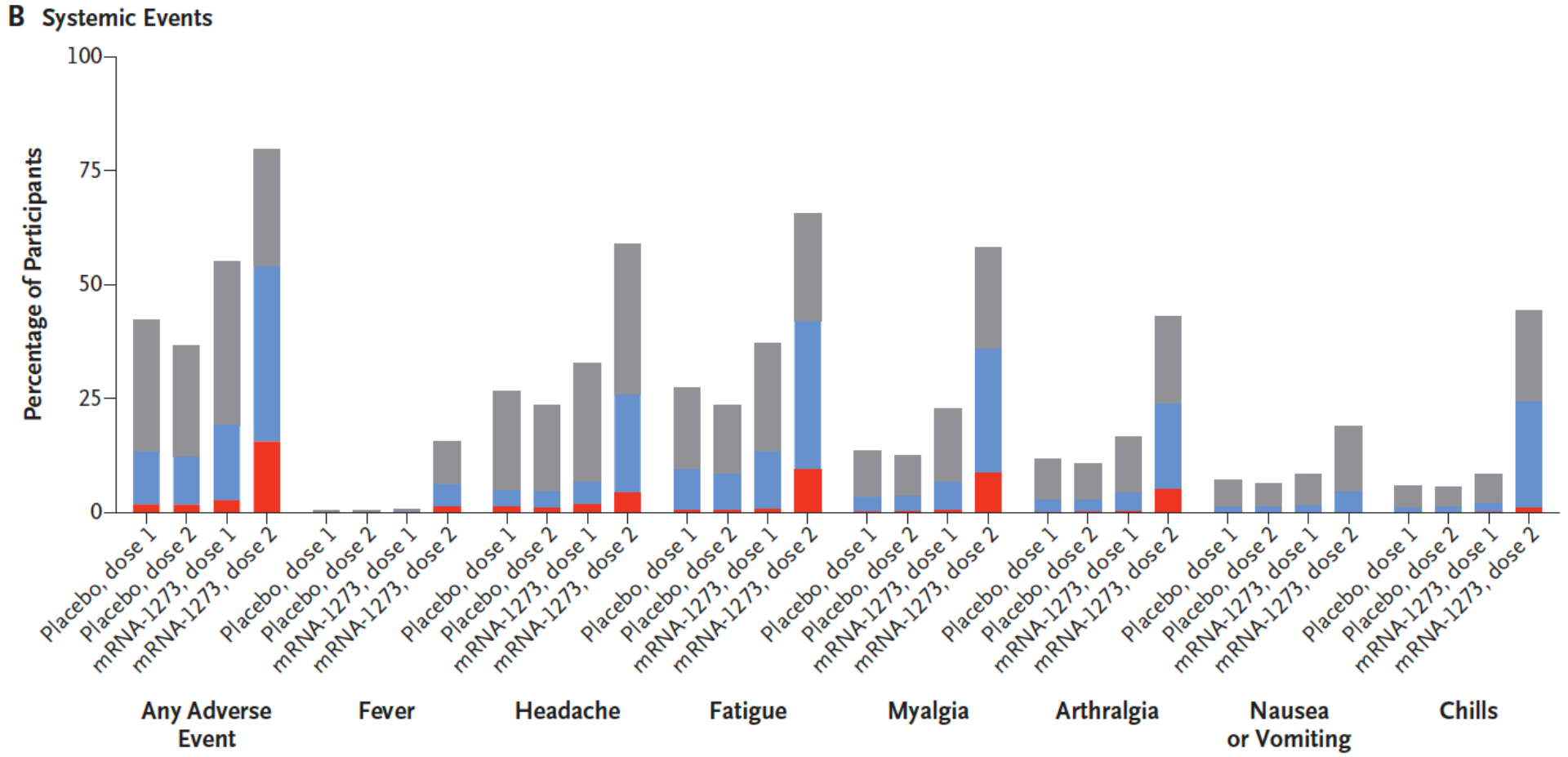
B Modified Intention-to-Treat Analysis



No. at Risk

Placebo	14,598	14,590	14,567	14,515	13,806	12,352	12,694	11,450	9736	6729	4067	1200	0
mRNA-1273	14,550	14,543	14,532	14,504	13,825	13,398	12,791	11,573	9911	6871	4179	1238	0

Covid-19 Onset	Placebo (N=14,598)	mRNA-1273 (N=14,550)
Randomization to 14 days after dose 1	11	5
14 Days after dose 1 to dose 2	35	2
Dose 2 to 14 days after dose 2	19	0
Starting 14 days after dose 2	204	12
Total (any time after randomization)	269	19



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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?

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Imposing Risk: Public Health Ethics & Covid-19

Dr. Diego S. Silva
Sydney Health Ethics
APRU - January 13, 2021

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The New York Times | https://nyti.ms/354aFlu

As Rollout Falters, Scientists Debate New Vaccinat

Should second doses be delayed? Should most adults receive half-doses? So

By Katherine J. Wu and Rebecca Robbins

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

The New York Times | https://nyti.ms/38oAXBe

Cuomo Widens Eligibility After Vaccine

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

By Joseph Goldstein

Jan. 8, 2021

The University of Sydney

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Coronavirus

'I'm not an anti-vaxxer, but...' US health workers' vaccine hesitancy raises alarm

Amanda Holpuch in New York

@holpuch

Sun 10 Jan 2021 19.00 AEDT

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Registered nurse Valerie Massaro administers the second dose of the Pfizer/BioNTech vaccine to health care workers at the Hartford Convention Center in Hartford, Connecticut, this week. Photograph: Joseph Prezioso/AFP/Getty Images

With up to 40% of frontline workers in LA county refusing Covid-19 inoculation experts warn that understanding and persuasion are needed

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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

The context of COVID-19 and associated vaccines

The Sydney Morning Herald

World Europe Coronavirus pandemic

'Living in limbo': Australians stranded overseas set back by latest travel restrictions

For our free coronavirus pandemic coverage, learn more here.

By Latika Bourke
January 10, 2021 — 12.00am

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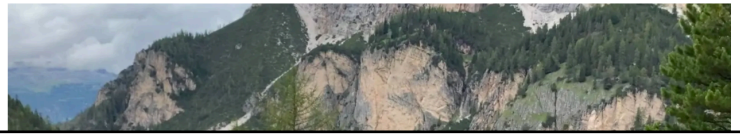
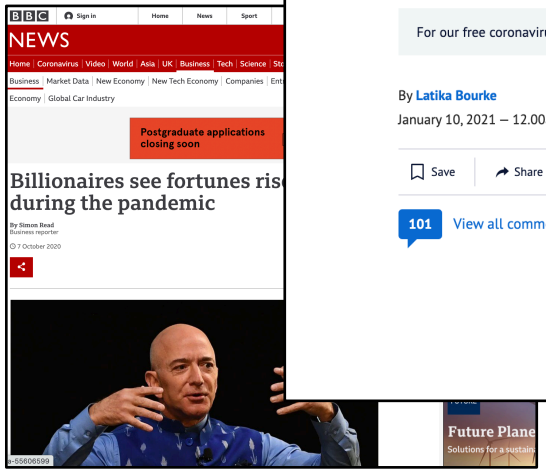
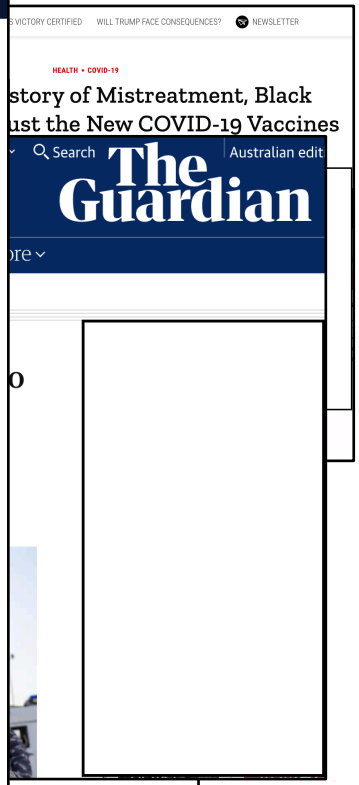
London: Australians trying to get home from overseas are urging the government to establish a reliable quarantine system after a wave of flight cancellations were triggered by new caps on arrivals due to the mutant strain of COVID-19.

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

@kylejglenn

- 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

@claybanks

A heuristic for risk imposition (policy makers)

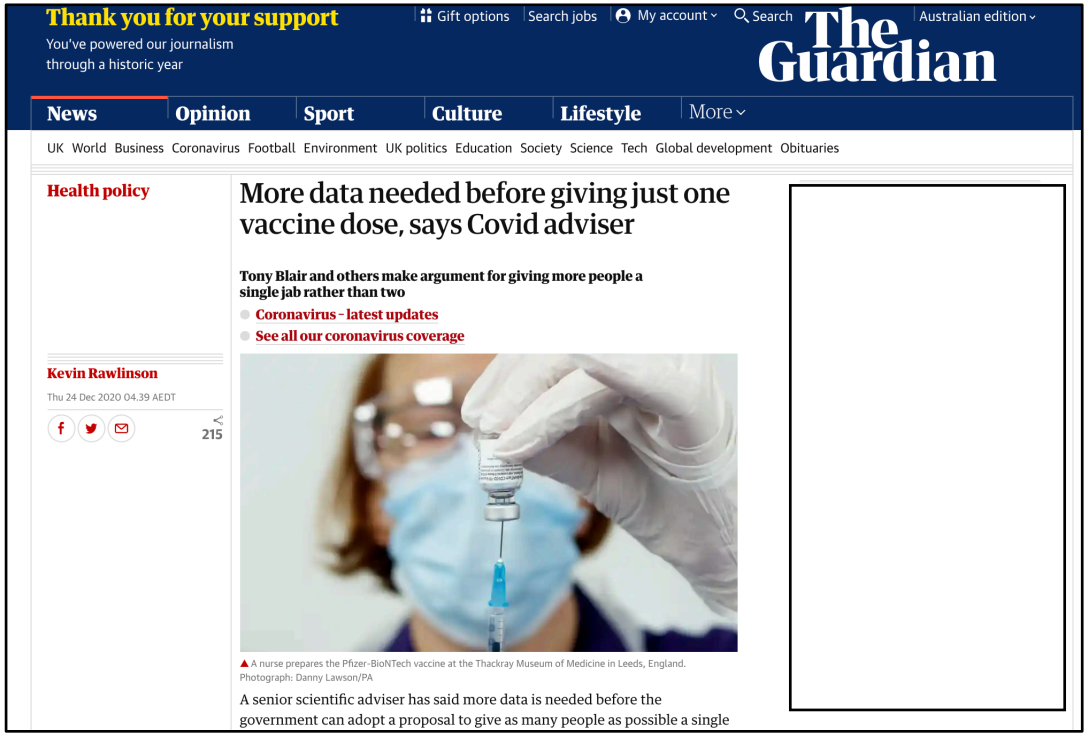
1. x acts in light of reasonably discoverable facts regarding risk y,
2. there are some benefits related to risk y that can be shared with z either directly or indirectly,
3. imposing risk y should be justifiable to z given z is in the greatest position of risk,
4. steps should be taken by x to minimize 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



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Health policy

More data needed before giving just one vaccine dose, says Covid adviser

Tony Blair and others make argument for giving more people a single jab rather than two

Coronavirus - latest updates

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Kevin Rawlinson

Thu 24 Dec 2020 04.39 AEDT

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▲ A nurse prepares the Pfizer-BioNTech vaccine at the Thackray Museum of Medicine in Leeds, England. Photograph: Danny Lawson/PA

A senior scientific adviser has said more data is needed before the government can adopt a proposal to give as many people as possible a single

Case two

Action: mandatory vaccination

Risk: violation of bodily integrity, autonomy

Developing virtuous persons

Thank you!

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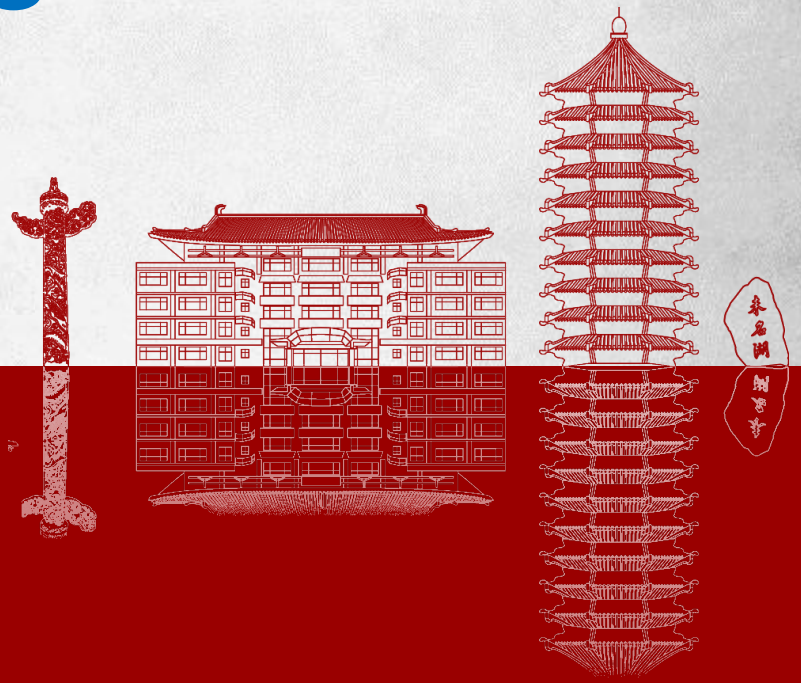
The latest development of Covid-19 vaccines



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-lshtm.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

	Pre-clinical	Phase 1	Phase 1/2	Phase 2	Phase 3	Used/Licensed	Total
RNA	29	2	1	1	3	2	36
DNA	18	2	4	0	2	0	26
Non-replicating viral vector	25	6	0	0	4	3	35
Replicating viral vector	18	2	2	1	0	0	23
Inactivated	10	1	1	1	6	4	19
Live-attenuated	3	1	0	0	0	0	4
Protein subunit	67	3	11	3	4	1	89
Virus-like particle	17	0	1	0	1	0	19
Other/Unknown	33	2	3	0	0	0	38
Total	220	19	23	6	20	10	289

Ref: https://vac-lshtm.shinyapps.io/ncov_vaccine_landscape/ 11 Jan 2021

Covid-19 vaccines in phrase 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);
  - US-Janssen (Ad26.COV2.S)
- 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

	Manufacturer (Vaccine)	Number of doses	Timing of doses
RNA vaccine	US-Moderna/NIAID (mRNA-1273)	2	0, 28d
	Germany-China-US-BioNTech/Fosun Pharma/Pfizer (BNT162)		0, 21d
	Germany-CureVac (CVnCov)		0, 28d
DNA vaccine	US/Korea-Inovio/IVI (INO-4800)		0, 28d
	Japan-Osaka University/AnGes/Takara (AG0302-COVID19)		0, 14d
Non-replicating viral vector	Oxford/AstraZeneca		0, 28d
	China-CanSino/Beijing Institute of Biotechnology (Ad5-nCoV)	1	0d
	Russia-Gamaleya Research Institute (Gam-COVID-Vac/Sputnik V)	2	0, 21d
	US-Janssen (Ad26.COV2.S)		0, 56d
Virus-like particle	Canada-Medicago Inc (CoVLP)		0, 21d
Inactivated	India-Bharat Biotech/ICMR/NIV (COVAXIN)		0,21d
	China-Institute of Medical Biology (Inactivated vaccine)		0, 14d
	Kazakhstan-NISKhI (QAZCOVID-IN)		0, 21d
	China-Beijing institute(CNBG)		0, 21d
	China-Sinovac (CoronaVac)		0, 14d
	China-Wuhan Institute of CNBG (WIBP vaccines)		0, 21d
Protein subunit	China-Anhui Zhifei (ZF2001)	3	0, 30d, 60d
	China/UK/US-Clover/GSK/Dynavax (SCB-2019)	2	0, 21d
	US-Covaxx (UB-612)		0, 28d
	US-Novavax (NVX-CoV2373)		1, 21d

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.

Bartsch S M , O&Sheafs K J , Msph M C F , et al. Vaccine Efficacy Needed for a COVID-19 Coronavirus Vaccine to Prevent or Stop an Epidemic as the Sole Intervention[J]. American Journal of Preventive Medicine, 2020.

Safety of Covid-19 Vaccines in Phase 2/3

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

Ref: https://www.medrxiv.org/content/10.1101/2020.12.21.20248643v1.full-text
https://jamanetwork.com/journals/jama/fullarticle/2769612
https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1703/5962856

Efficacy of Covid-19 Vaccines in Phase 2/3

Platform	Developer (vaccine name)	Seroconversion rate (%)	GMTs of Antibody
mRNA	US-Moderna/NIAID (mRNA-1273)	100	344
	Germany-China-US-BioNTech/Fosun Pharma/Pfizer (BNT162)	-	312
Protein subunit	China-Anhui Zhifei (ZF2001)	99	103
	US-Novavax (NVX-CoV2373)	-	195
Non-replicating viral vector	UK-Oxford/AstraZeneca	99	193
	Russia-Gamaleya Research Institute (COVID-Vac/Sputnik V)	100	49
	China-CanSino/Beijing Institute of Biotechnology (Ad5-nCoV)	96	18
	US-Janssen (Ad26.COV2.S)	92	214
Inactivated	China-Beijing institute(CNBG)	100	156
	India-Bharat Biotech/ICMR/NIV (COVAXIN)	98	197
	China-Institute of Medical Biology (Inactivated vaccine)	96	30
	China-Sinovac (CoronaVac)	94	28

Ref: https://www.medrxiv.org/content/10.1101/2020.12.20.20248602v1
https://www.nejm.org/doi/full/10.1056/NEJMoa2026920
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/Pflizer (BNT162 (b2)):

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

Ref: https://www.nejm.org/doi/full/10.1056/NEJMoa2034577

Safety and efficacy of Covid-19 Vaccines have been licensed

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

Ref: https://www.nejm.org/doi/full/10.1056/NEJMoa2034577
https://www.nejm.org/doi/full/10.1056/NEJMoa2035389
https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32661-1/fulltext

Five vaccines have been licensed (EUA/EUL)

- BioNTech/Pflizer (BNT162 (b2)) Emergency approval, UK 2 Dec; US 12 Dec 2020)
- Moderna/NIAID (mRNA-1273) Granted emergency use authorization, US 18 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

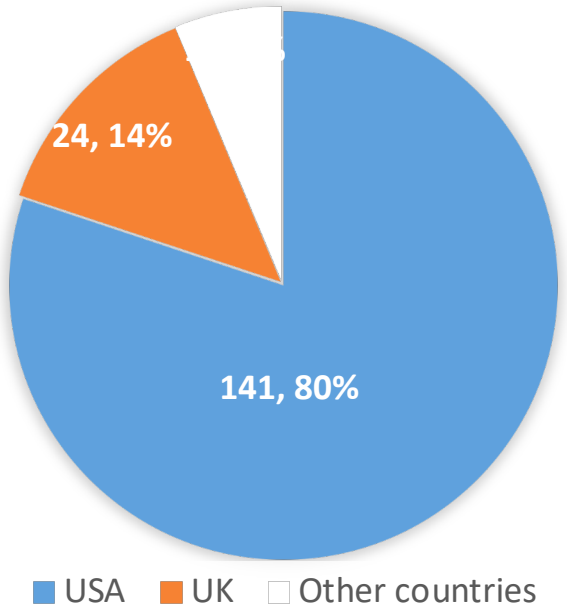
COVID-19 Vaccines R&D Routes in China

- 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)

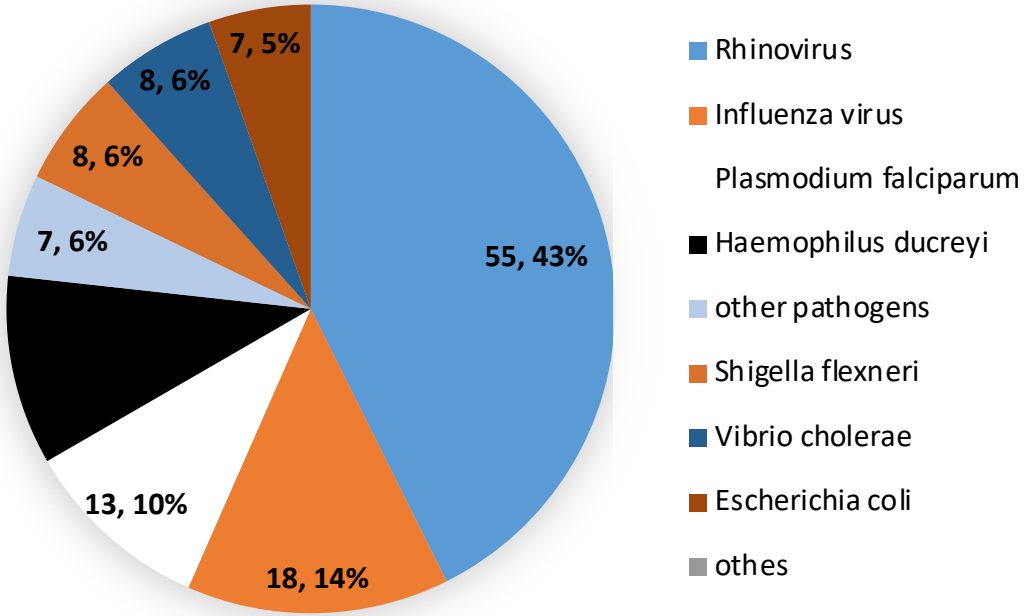
Ref: https://vac-lshtm.shinyapps.io/ncov_vaccine_landscape/

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



HCS in countries



Pathogens in HCS

Ref: Kalil Jennifer A, Halperin Scott A, Langley Joanne M. Human challenge studies: a review of adequacy of reporting methods and results [J]. Future microbiology, 2012, 7(4):481-95

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

Ref: https://www.gov.uk/government/news/expert-partnership-to-explore-and-establish-human-challenge-studies-of-covid-19-in-the-uk

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

Thanks