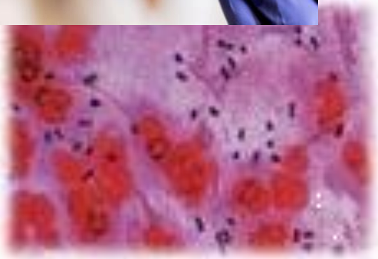






COVID-19 Vaccines

Paying for Vaccines and Vaccine Development




MSc IHTM

22 February 2023

Andrew Farlow

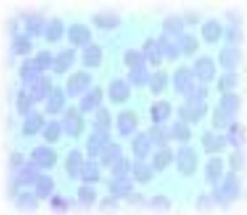
Global Health Policy Partnership

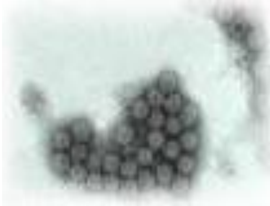
Senior Fellow, Oxford Martin School

Co-Chair, Supply &Market Dynamics and Medicine Quality Working Group of the COVID-19 Clinical Research Coalition

www.andrewfarlow.com

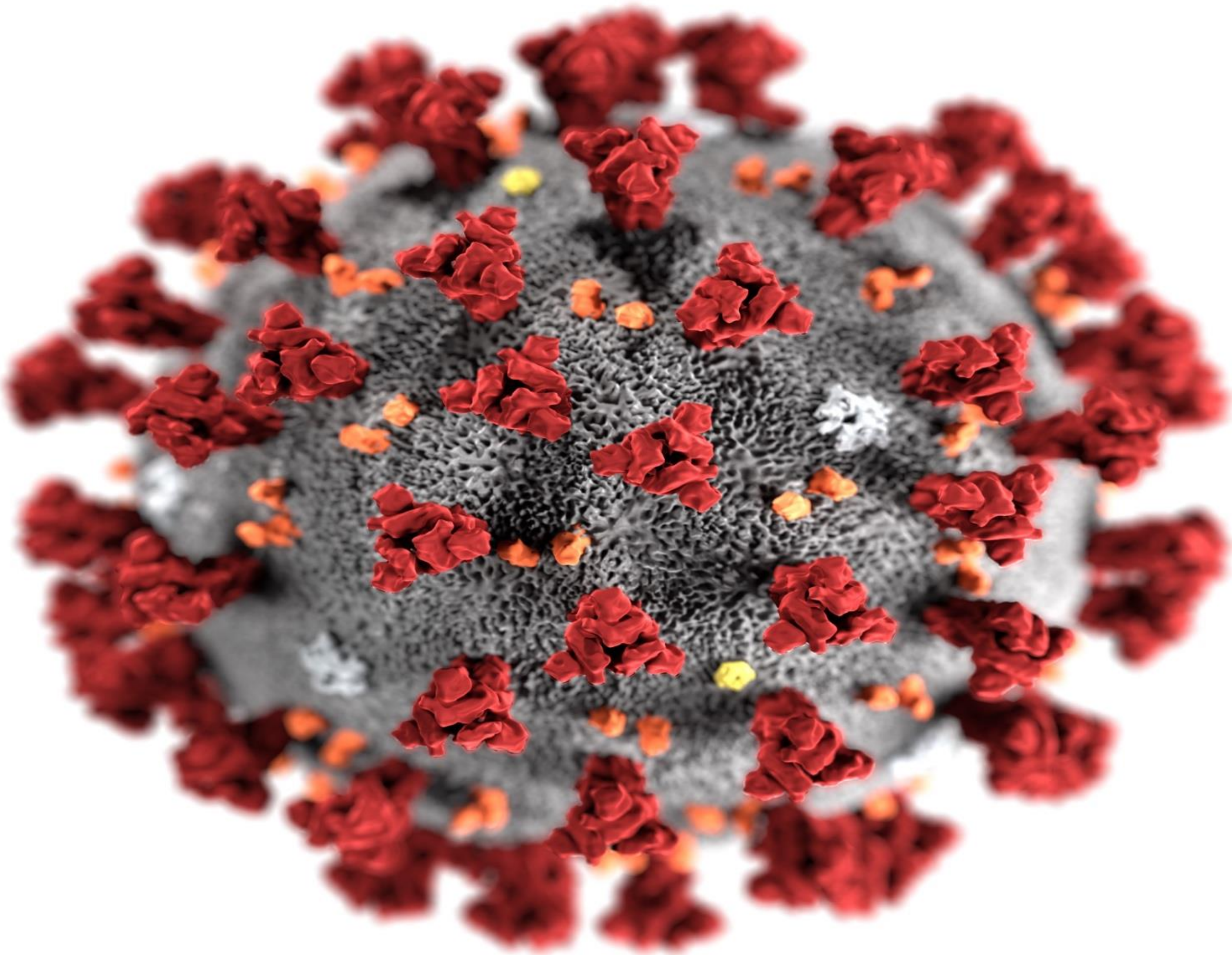




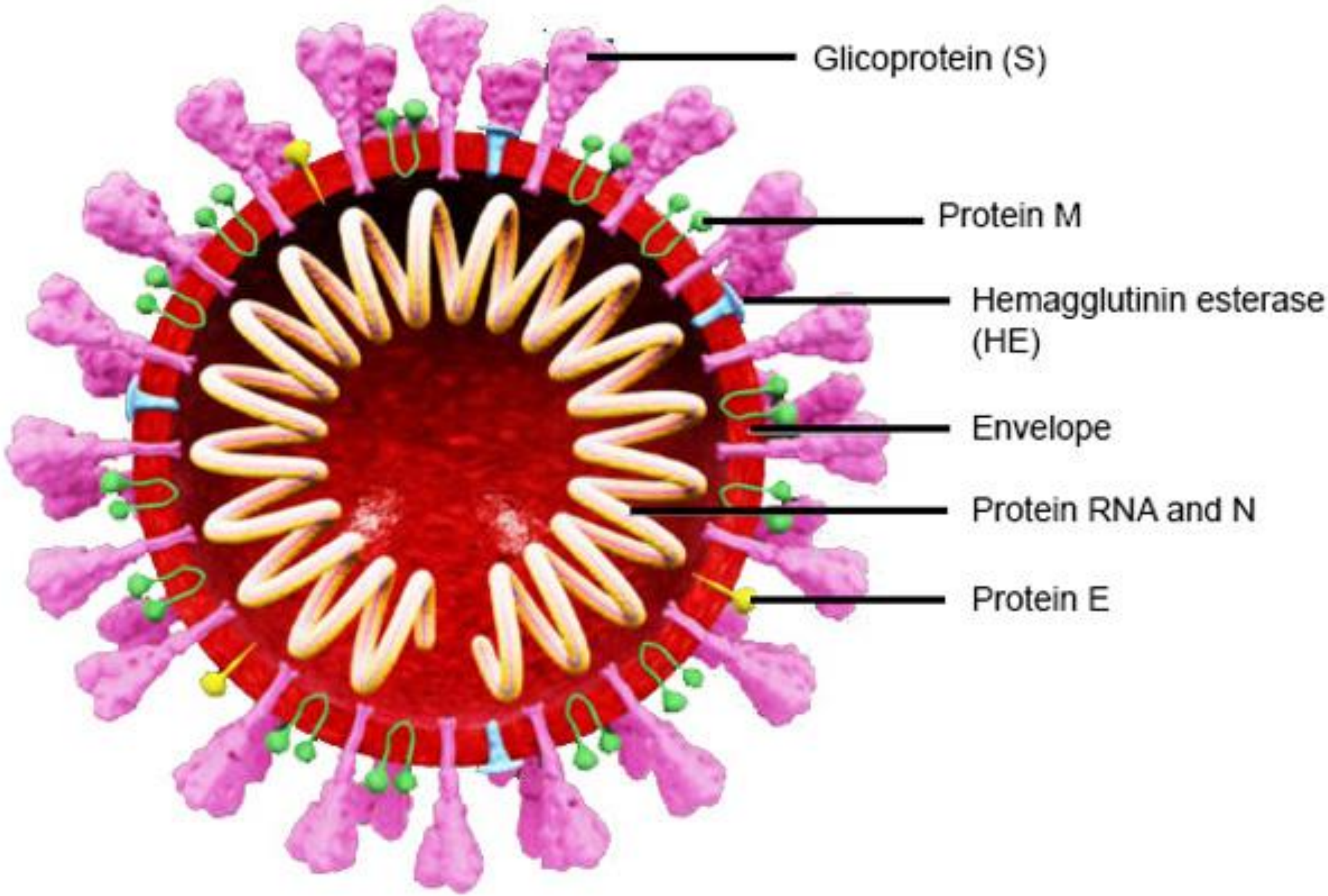



Where’s (insert name of your favorite Oxford vaccine scientist)?

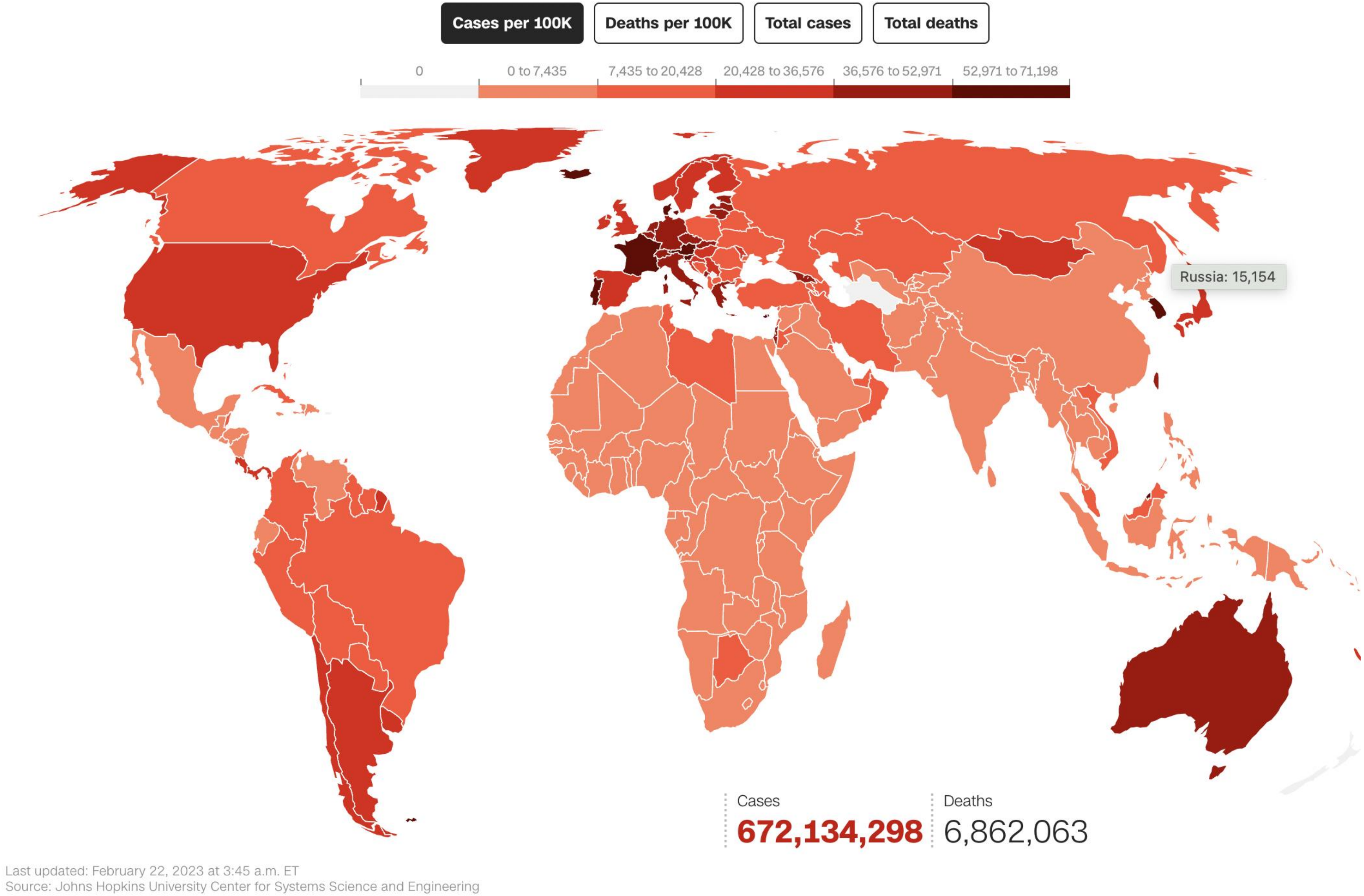
COVID-19: A pretty virus…but lethal



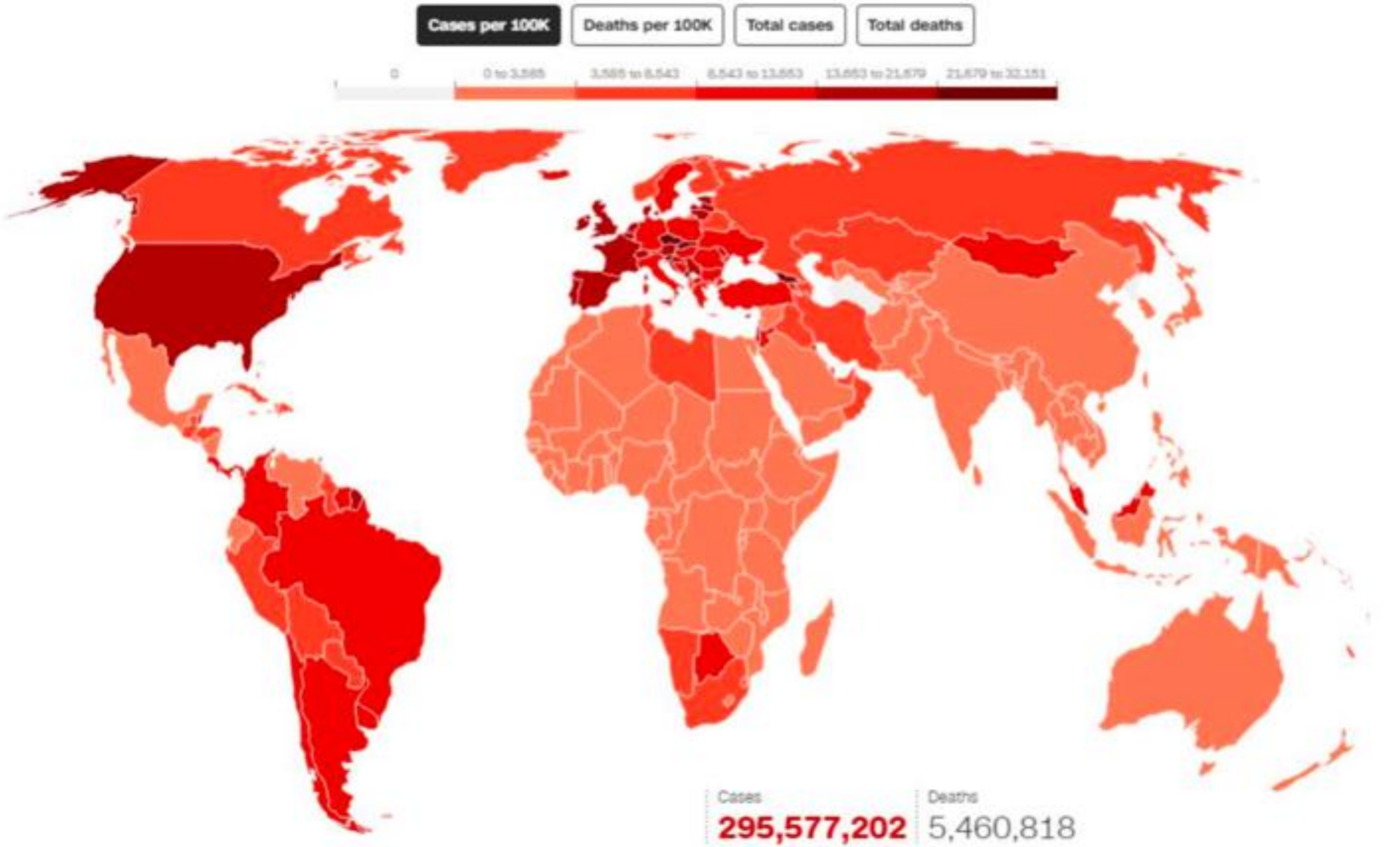
COVID-19: The virus



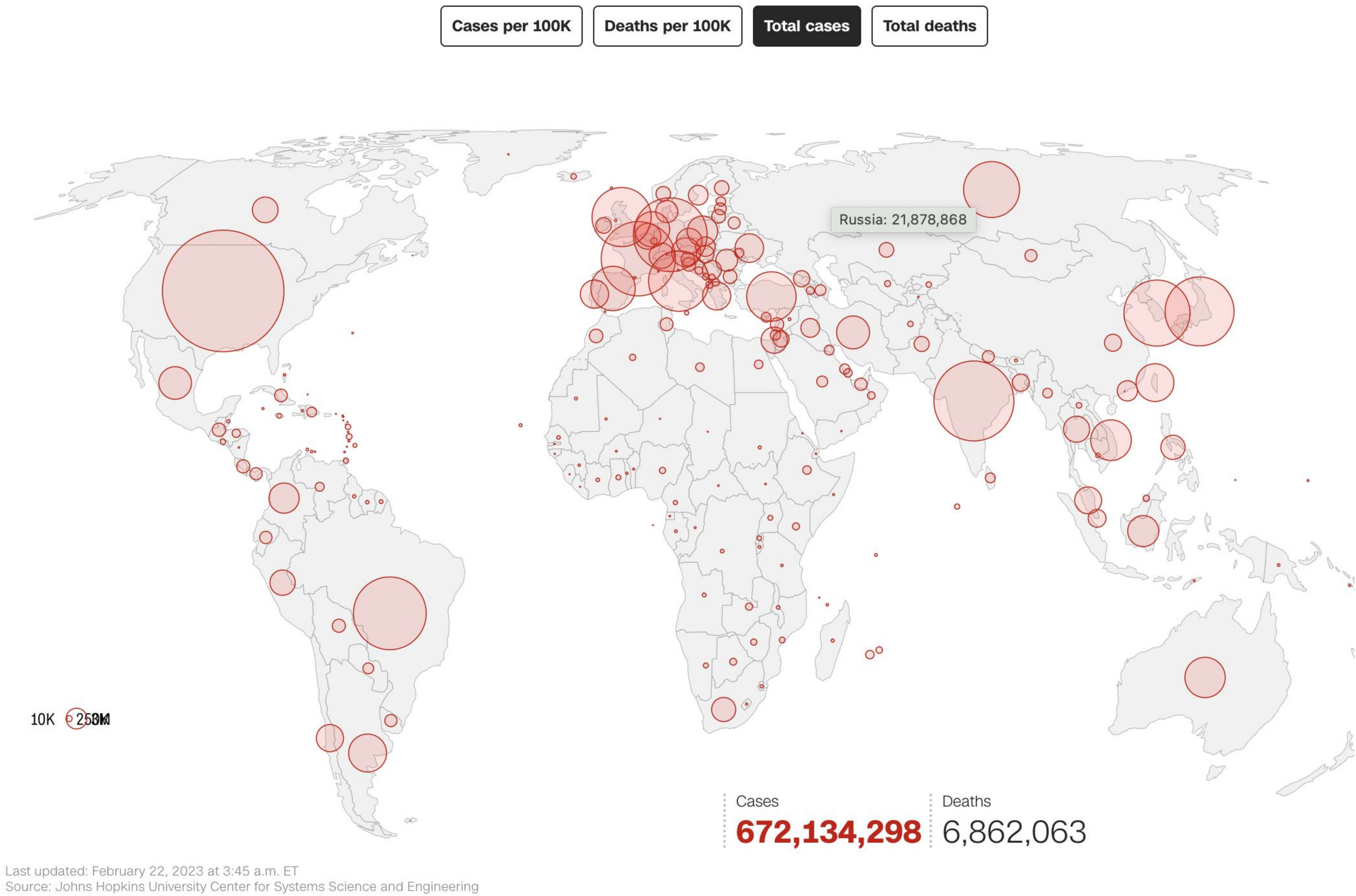
Cumulative confirmed COVID-19 cases per 100K, as of 22 February 2023



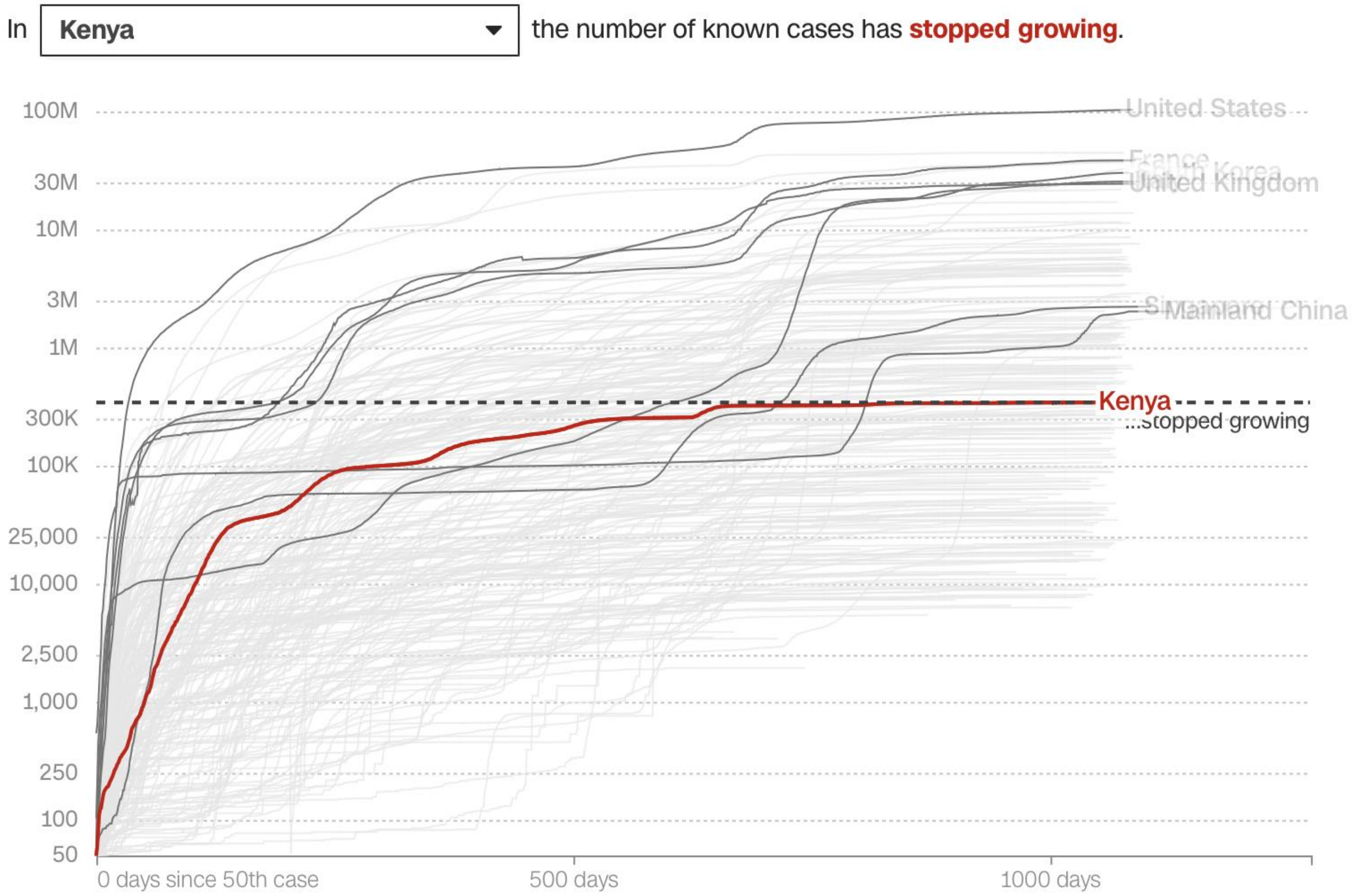
Cumulative confirmed COVID-19 cases per 100K, as of 5 January 2022 (for comparison)



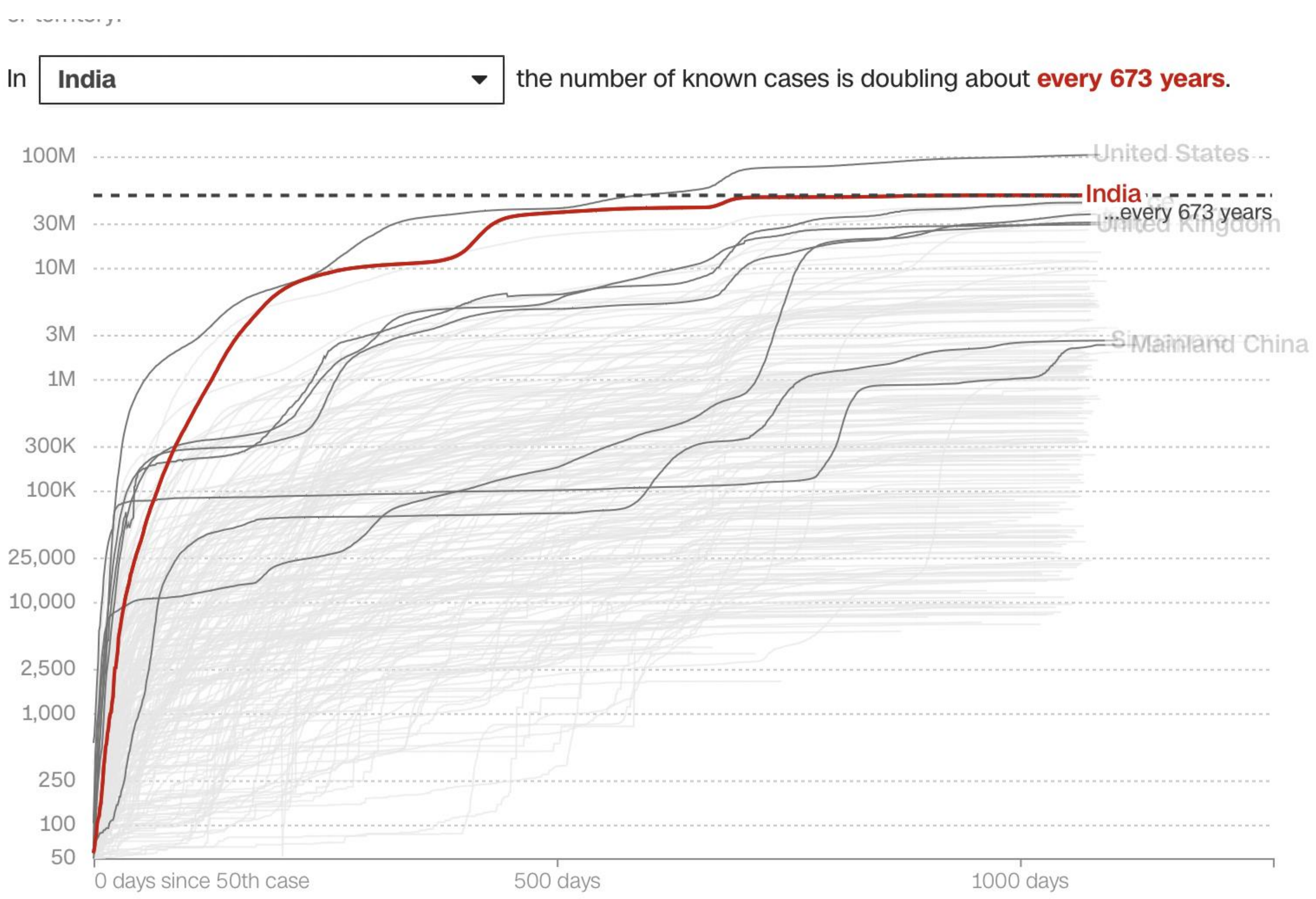
Total confirmed COVID-19 cases to 22 Feb 2023



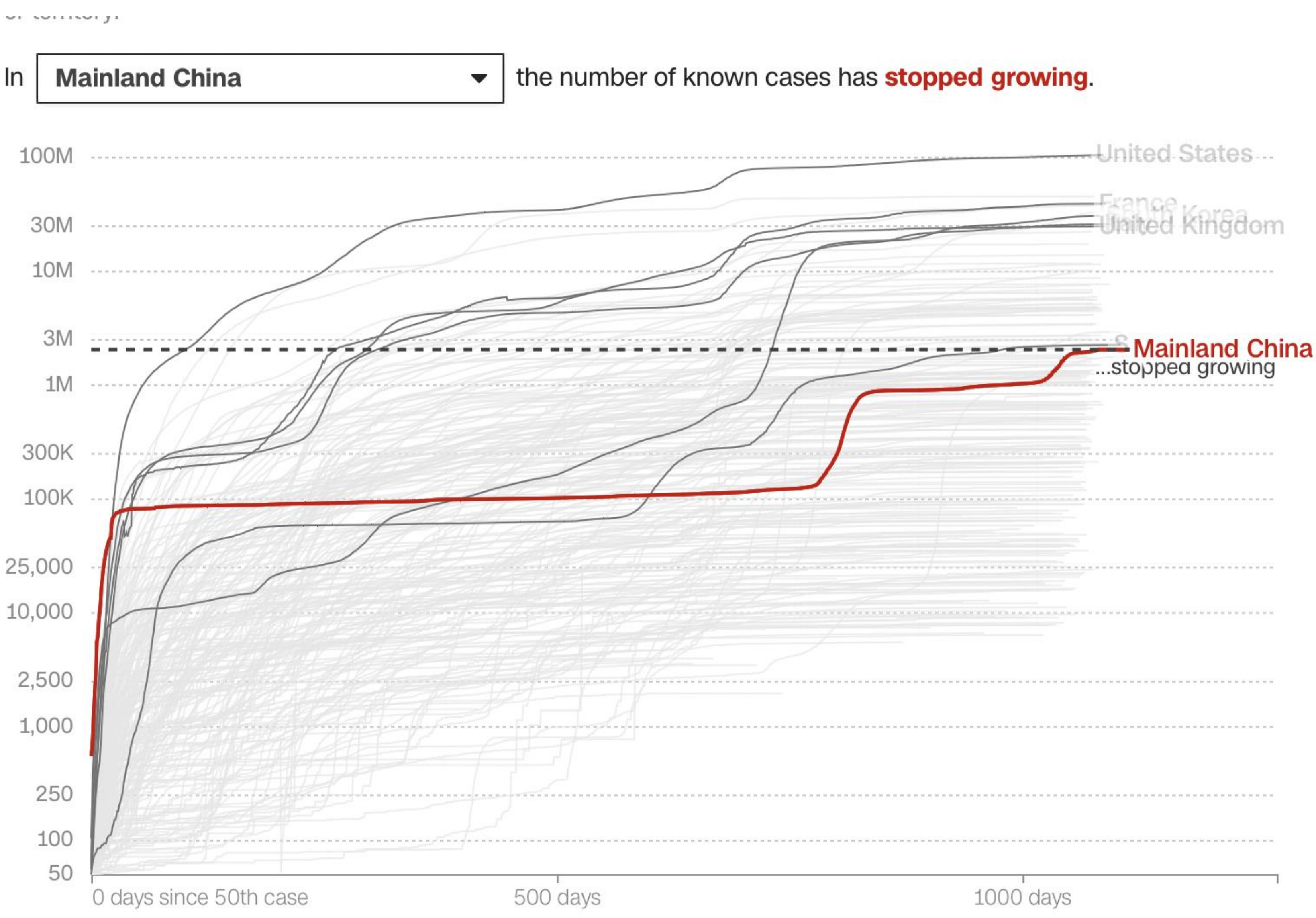
Growth rate of cases: Kenya



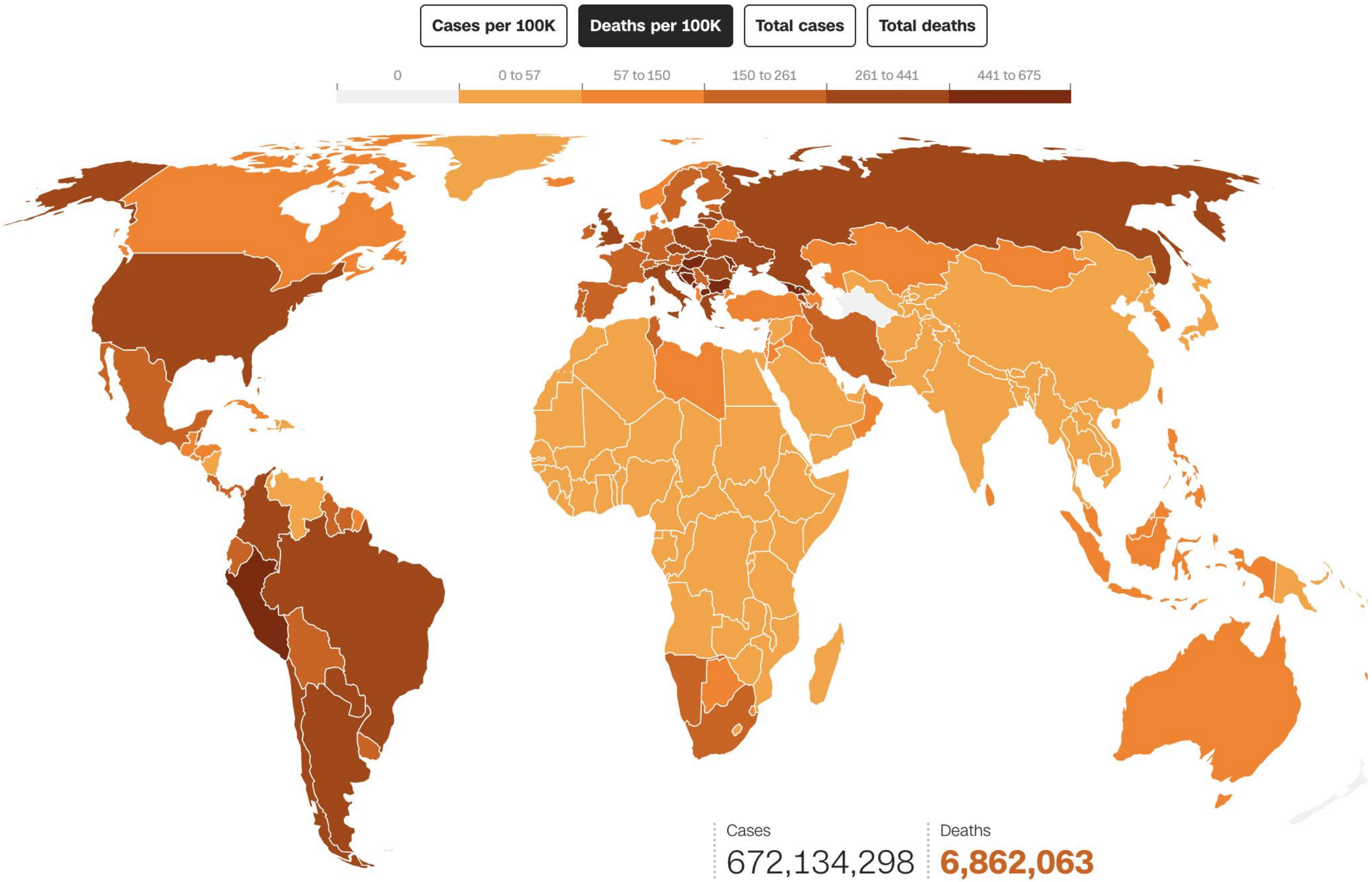
Growth rate of cases: India



Growth rate of cases: China

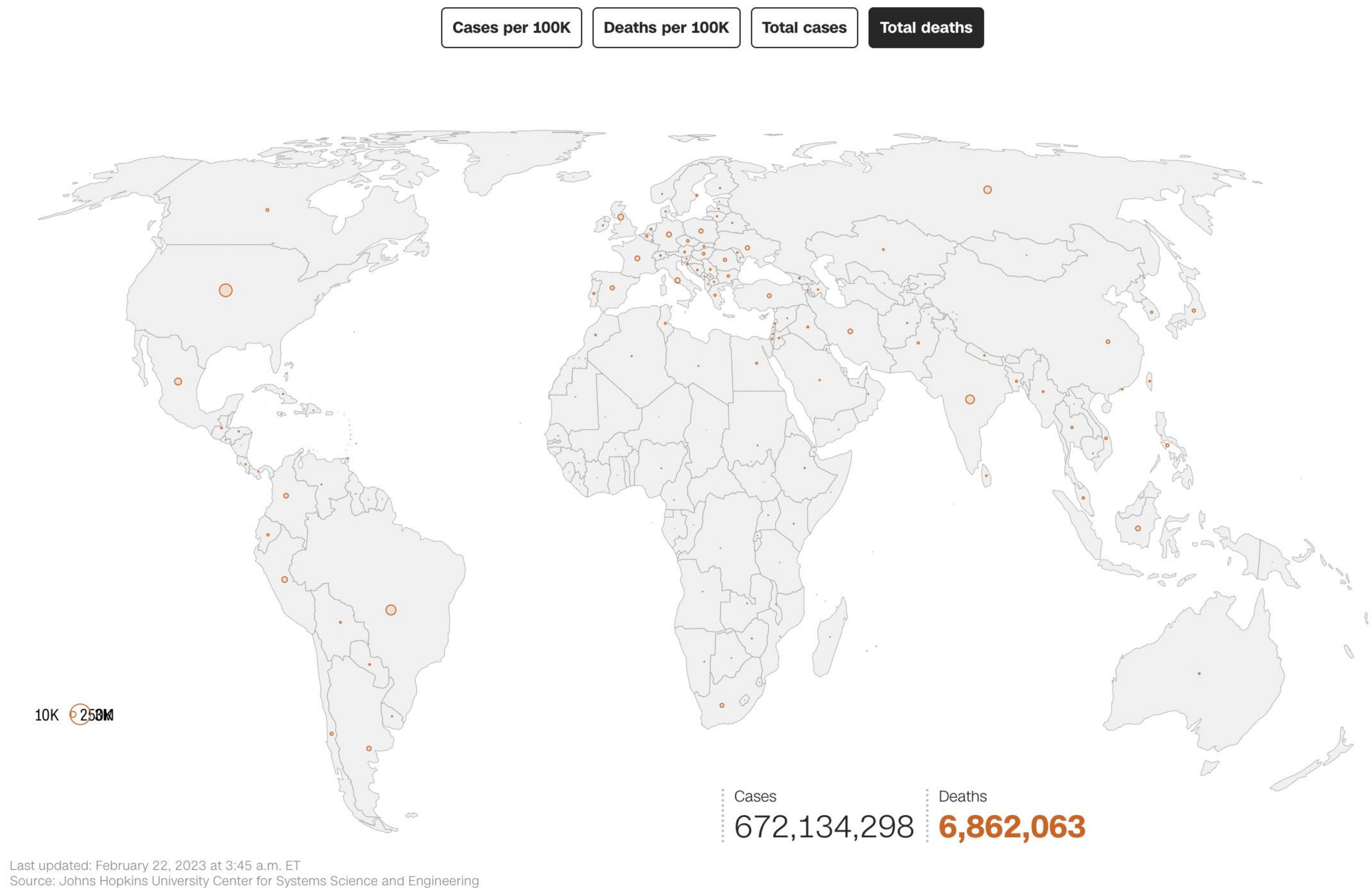


Deaths per 100K, 22 February 2023

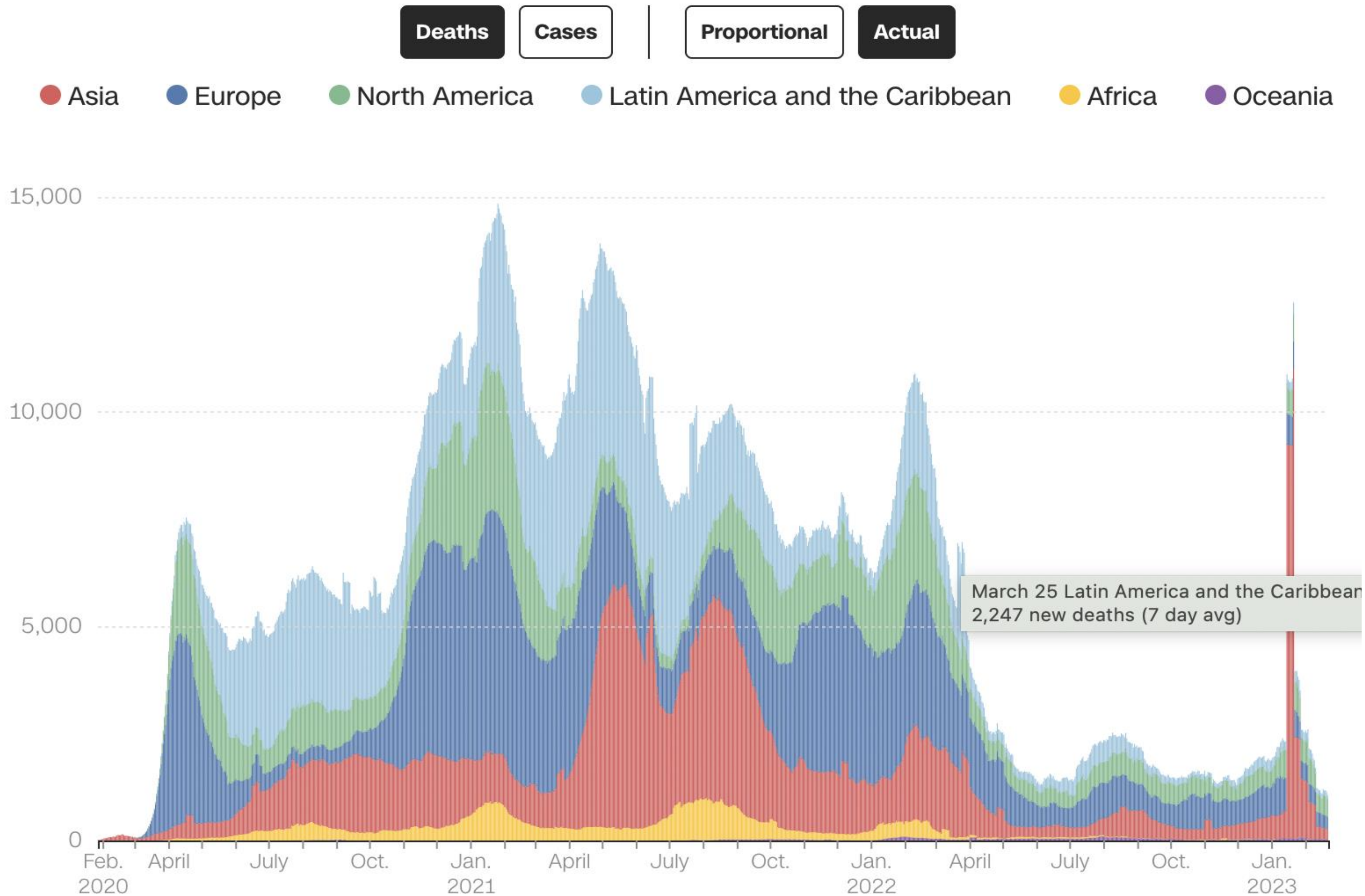


Last updated: February 22, 2023 at 3:45 a.m. ET
Source: Johns Hopkins University Center for Systems Science and Engineering

Total COVID-19 deaths to 22 Feb 2023



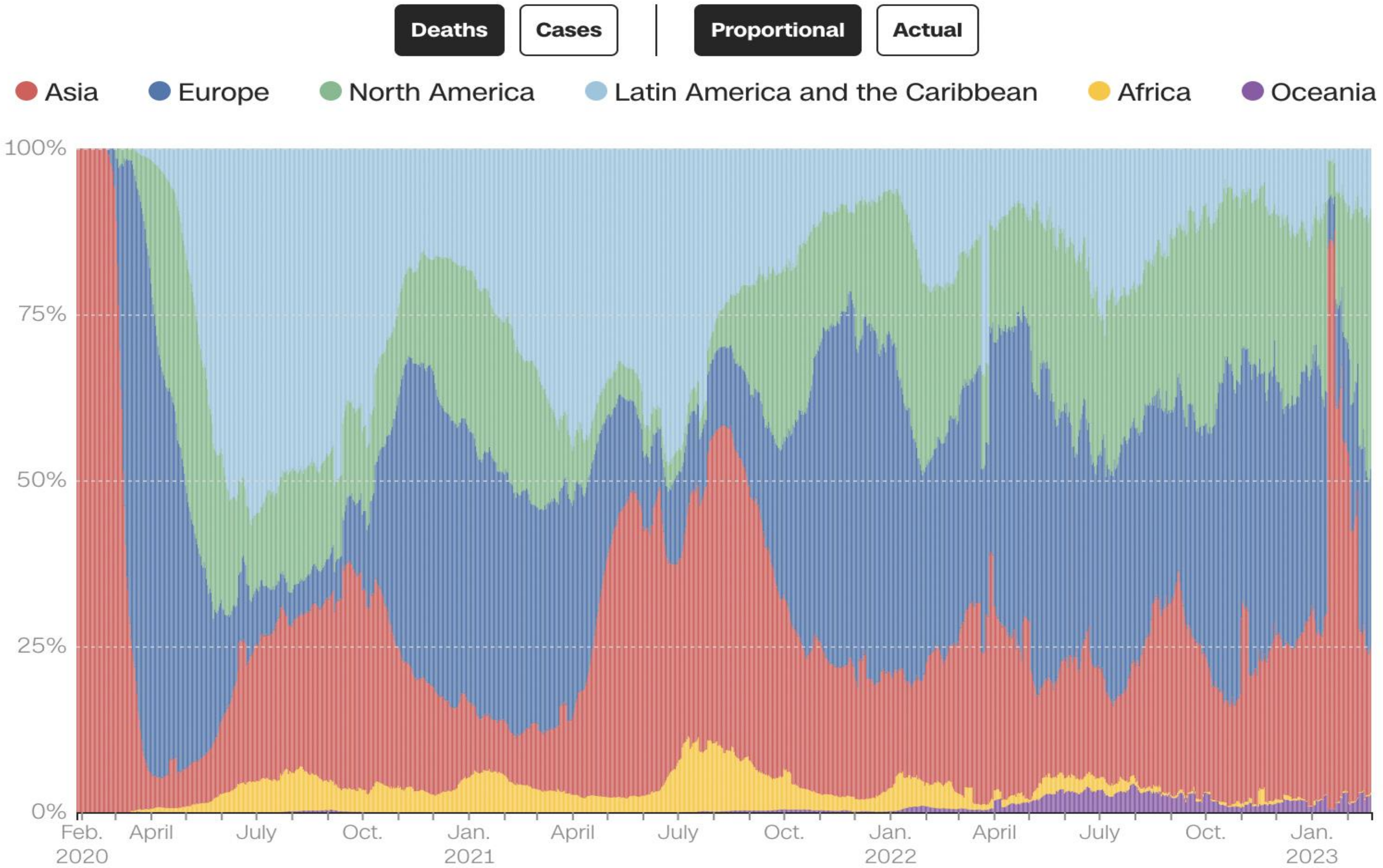
Deaths actual, to 22 Feb 2023



Regions are based on United Nations definitions. Americas have been broken down into subregions (Latin America and the Caribbean and North America).
Last updated: February 22, 2023 at 4:45 a.m. ET
Source: Johns Hopkins University Center for Systems Science and Engineering

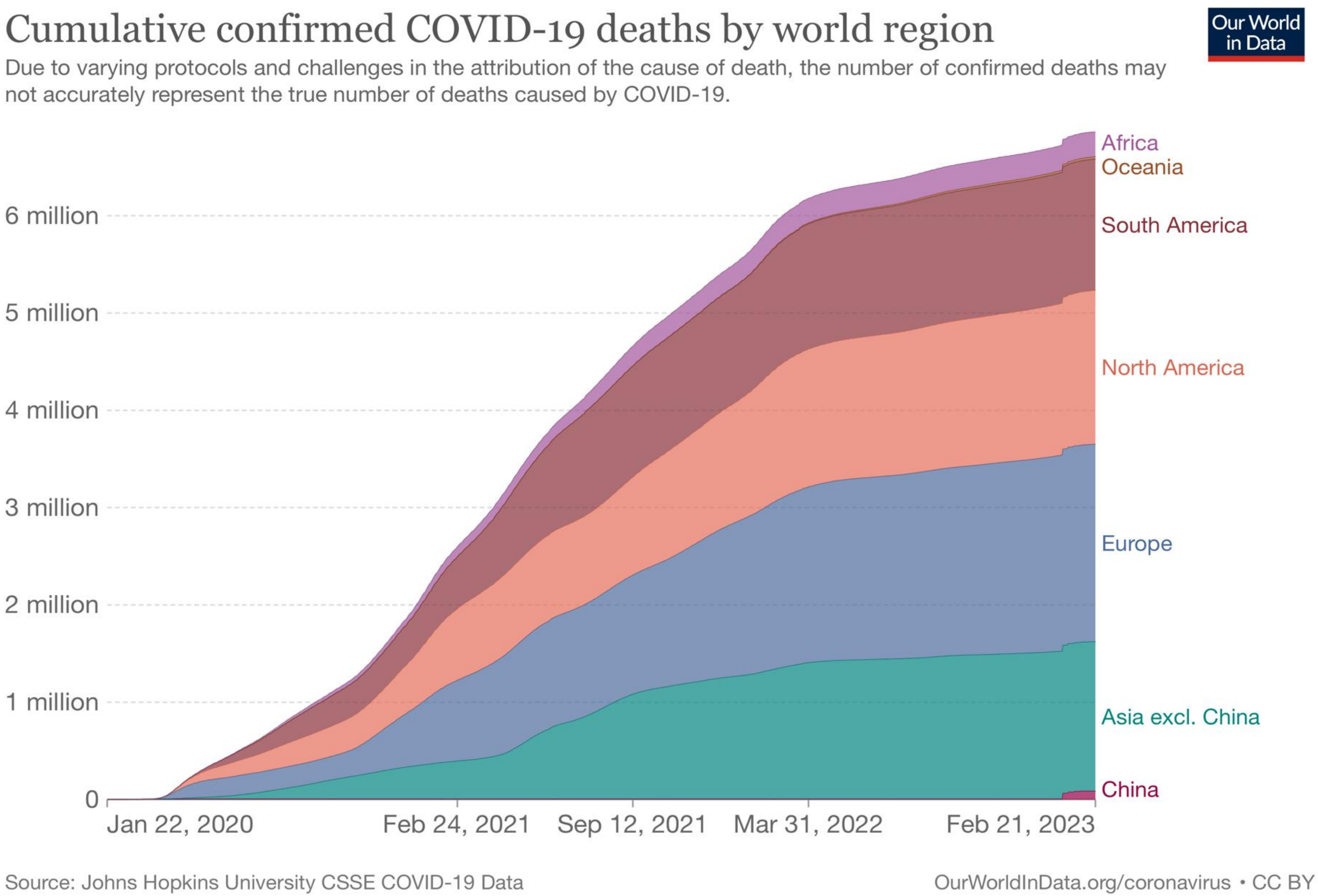
Deaths proportional, to 22 Feb 2023

This chart uses rolling, seven-day averages. This approach makes trends clearer and smooths out anomalies, such as the lack of reporting during the weekend.



Regions are based on United Nations definitions. Americas have been broken down into subregions (Latin America and the Caribbean and North America).
Last updated: February 22, 2023 at 3:45 a.m. ET
Source: Johns Hopkins University Center for Systems Science and Engineering

Cumulative confirmed COVID-19 deaths by region to Feb 2023



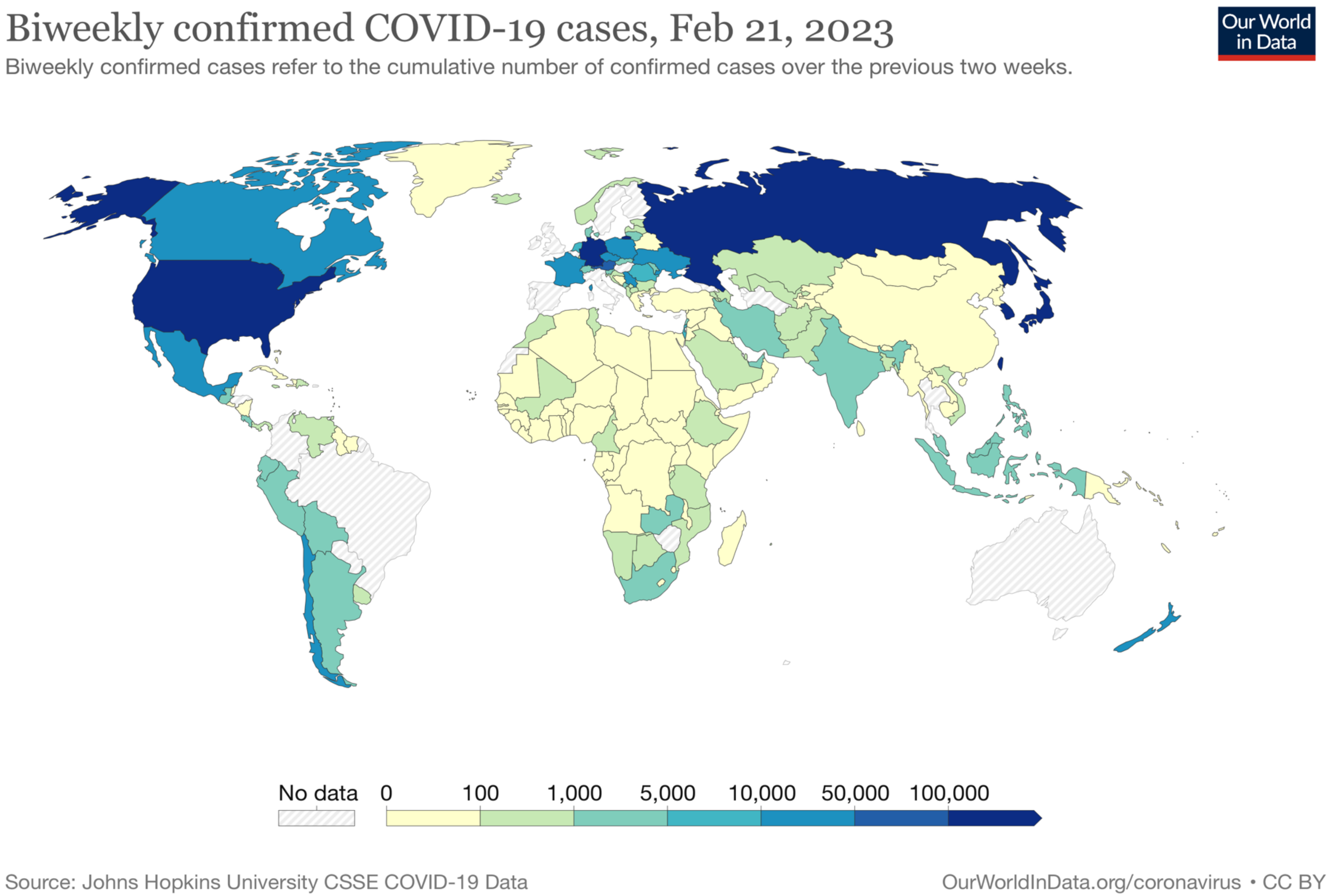
Total cases and deaths, selection countries Feb 2023

Location	Cases	...per 100K people	Deaths	...per 100K people
United States	103,170,118	31,431	1,117,838	341
India	44,686,483	3,270	530,762	39
France	38,553,269	57,491	161,169	240
Germany	38,043,874	45,763	167,491	201
Brazil	36,987,682	17,526	698,050	331
Japan	33,158,158	26,261	71,931	57
South Korea	30,458,857	58,904	33,887	66
Italy	25,547,414	42,369	187,850	312
United Kingdom	24,445,039	36,576	218,632	327
Russia	21,892,777	15,164	387,932	269
Turkey	17,042,722	20,428	101,492	122
Spain	13,755,956	29,220	119,186	253
Vietnam	11,526,834	11,950	43,186	45
Australia	11,347,698	44,739	19,265	76
Argentina	10,043,308	22,349	130,458	290
Taiwan	9,970,937	41,865	17,672	74
Netherlands	8,591,582	49,568	22,992	133
Iran	7,567,161	9,127	144,817	175
Mexico	7,430,816	5,825	332,850	261
Indonesia	6,734,606	2,489	160,892	59

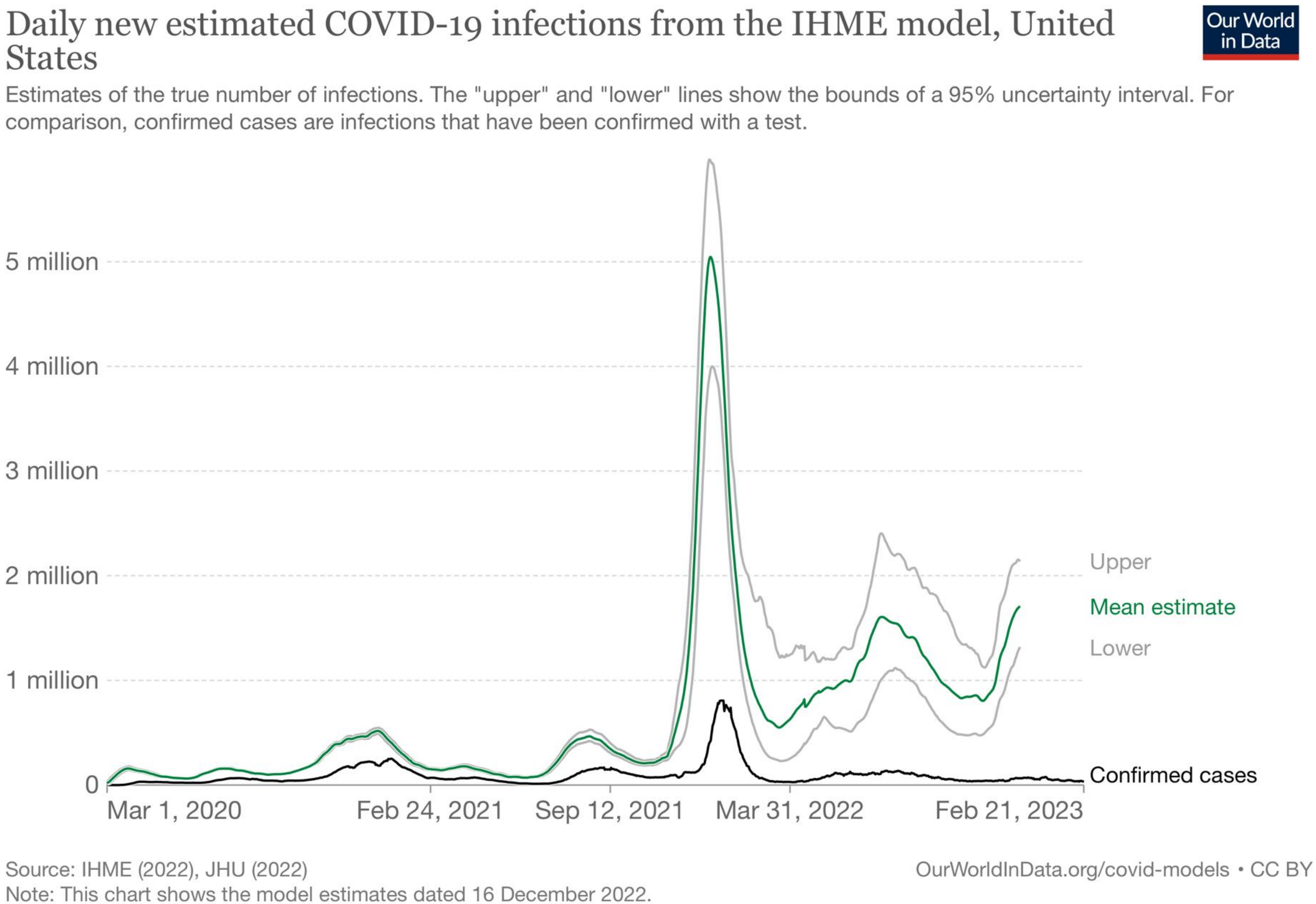
Total cases, selection countries Jan 2022 (left in since interesting comparisons)

Location	Cases	...per 100K people	Deaths	...per 100K people
United States	48,202,506	14,685	776,537	237
India	34,572,523	2,530	468,554	34
Brazil	22,076,863	10,461	614,186	291
United Kingdom	10,110,412	15,128	144,724	217
Russia	9,403,480	6,513	267,527	185
Turkey	8,726,370	10,460	76,233	91
France	7,364,380	10,982	116,416	174
Iran	6,105,101	7,363	129,549	156
Germany	5,782,482	6,956	100,890	121
Argentina	5,325,560	11,851	116,517	259
Spain	5,131,012	10,899	87,955	187
Colombia	5,063,177	10,058	128,394	255
Italy	4,994,891	8,284	133,627	222
Indonesia	4,255,936	1,573	143,808	53
Mexico	3,882,792	3,044	293,859	230
Ukraine	3,588,916	8,086	90,345	204
Poland	3,507,828	9,238	83,037	219
South Africa	2,958,548	5,052	89,791	153
Philippines	2,831,177	2,619	48,205	45
Malaysia	2,619,577	8,199	30,280	95

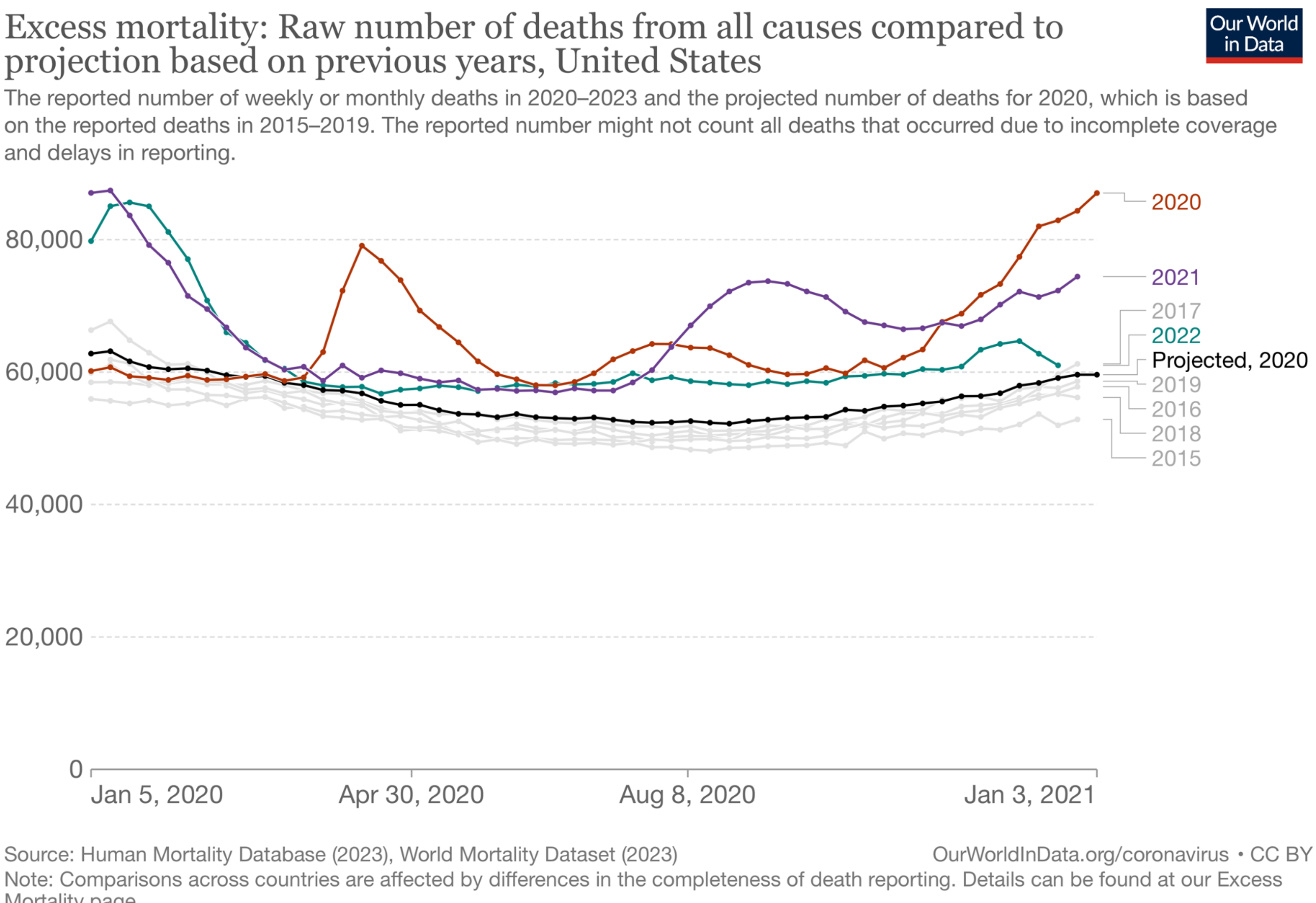
Where are we now: Recent (biweekly) confirmed case situation



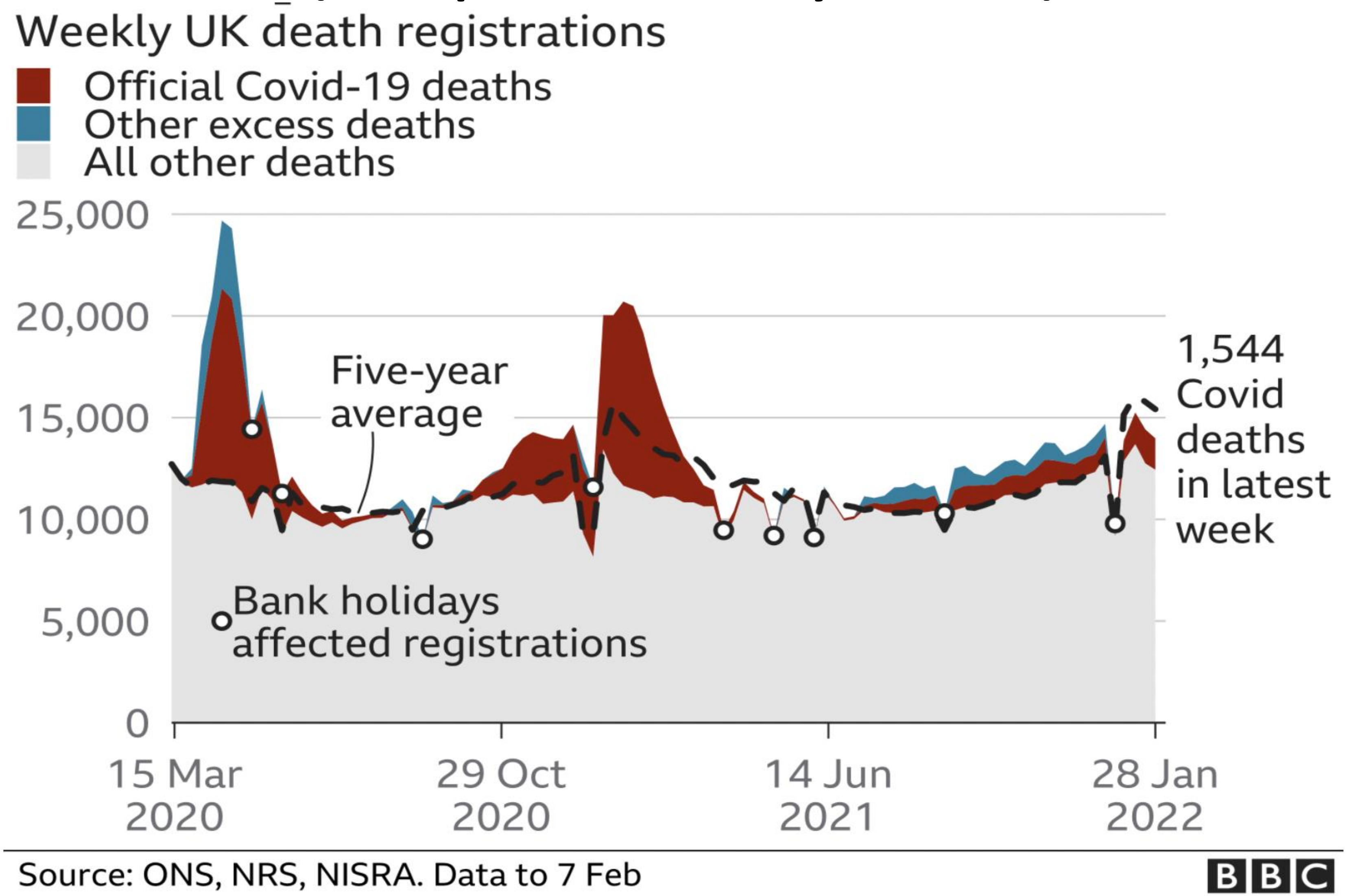
Now we estimate (since no longer routinely test)



Excess mortality (weekly) world



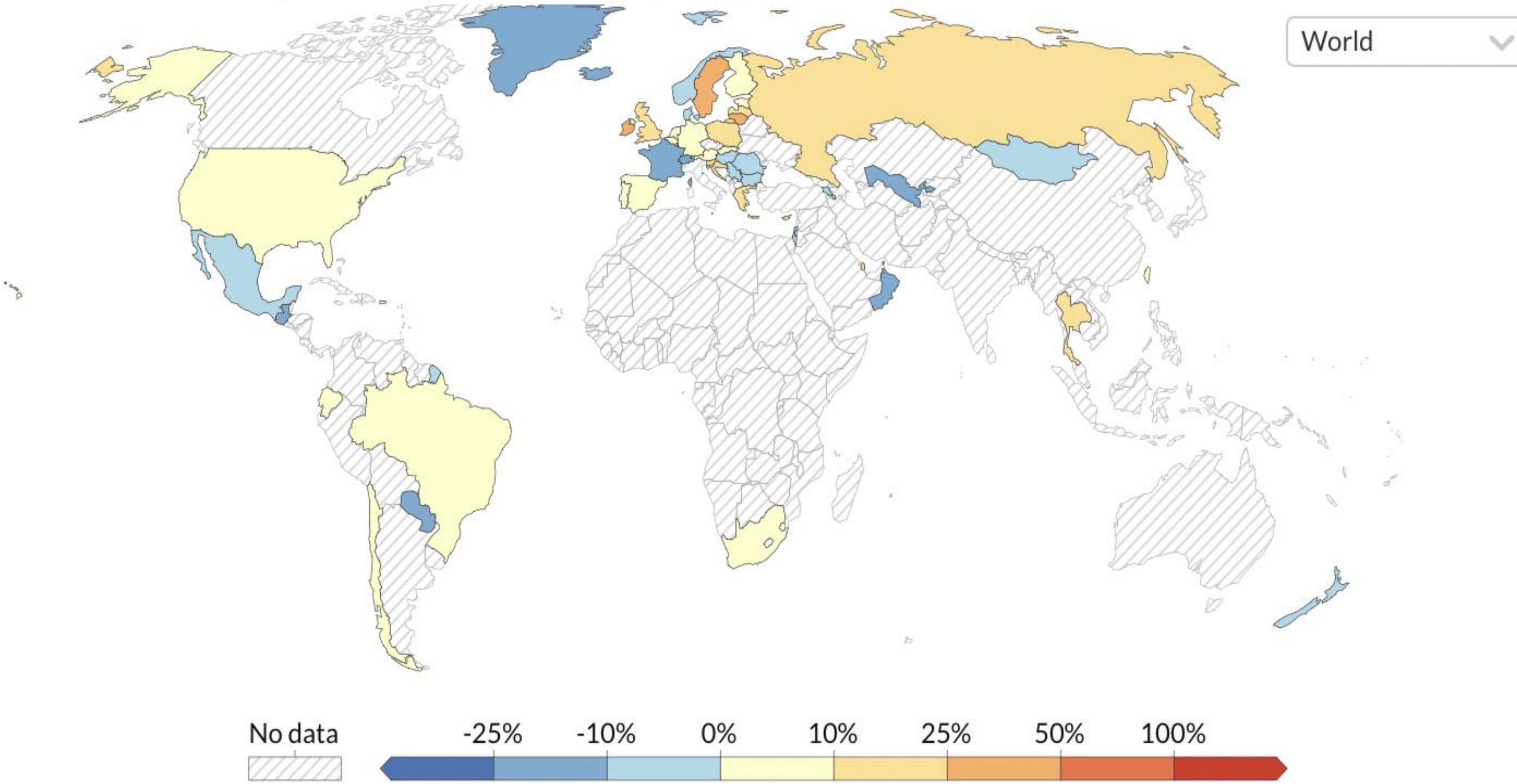
UK: COVID-19 Excess mortality (snapshot early 2022)



Excess mortality: world

Excess mortality: Deaths from all causes compared to projection, Jan 31, 2023

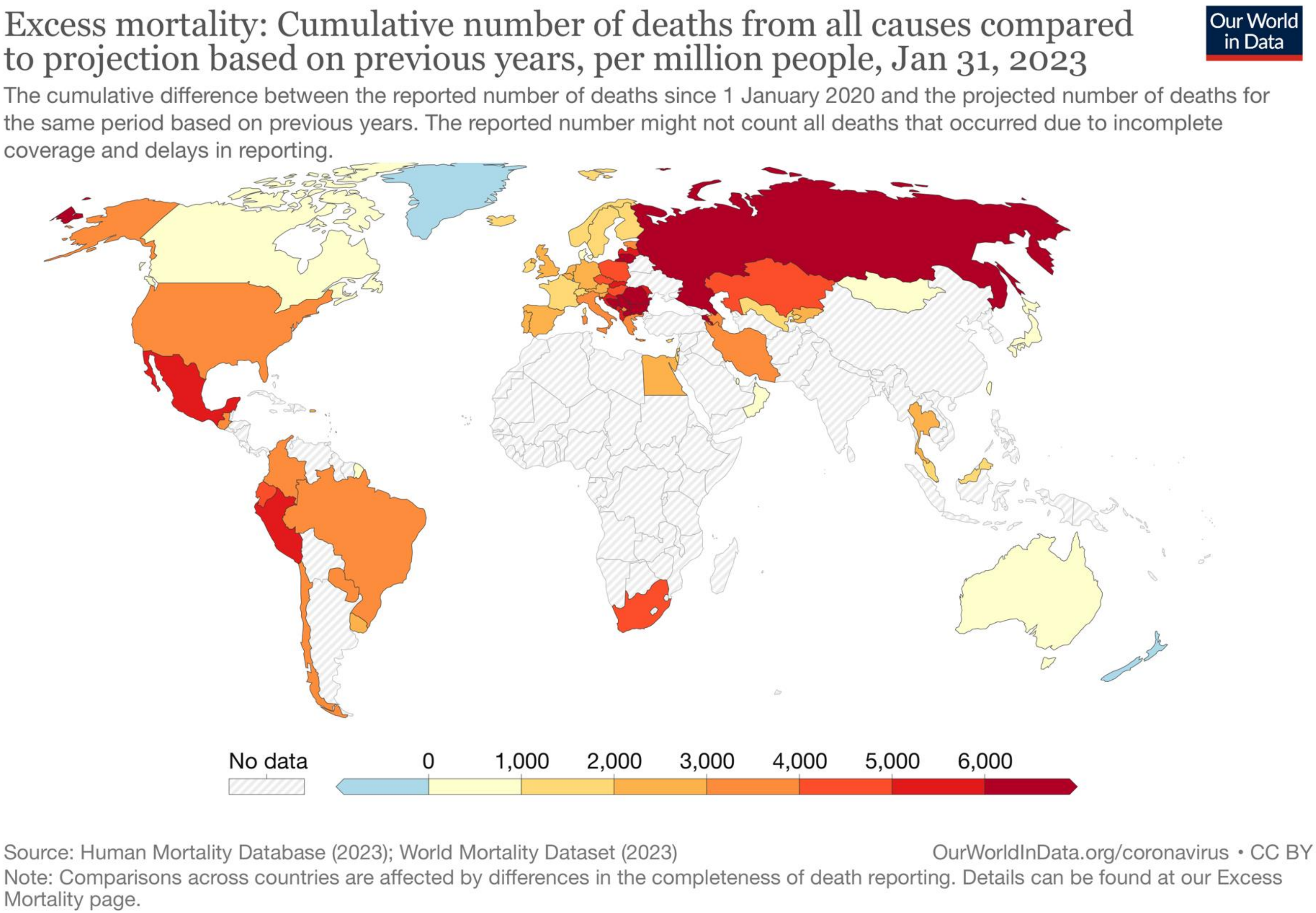
The percentage difference between the reported number of weekly or monthly deaths in 2020–2023 and the projected number of deaths for the same period based on previous years. The reported number might not count all deaths that occurred due to incomplete coverage and delays in reporting.



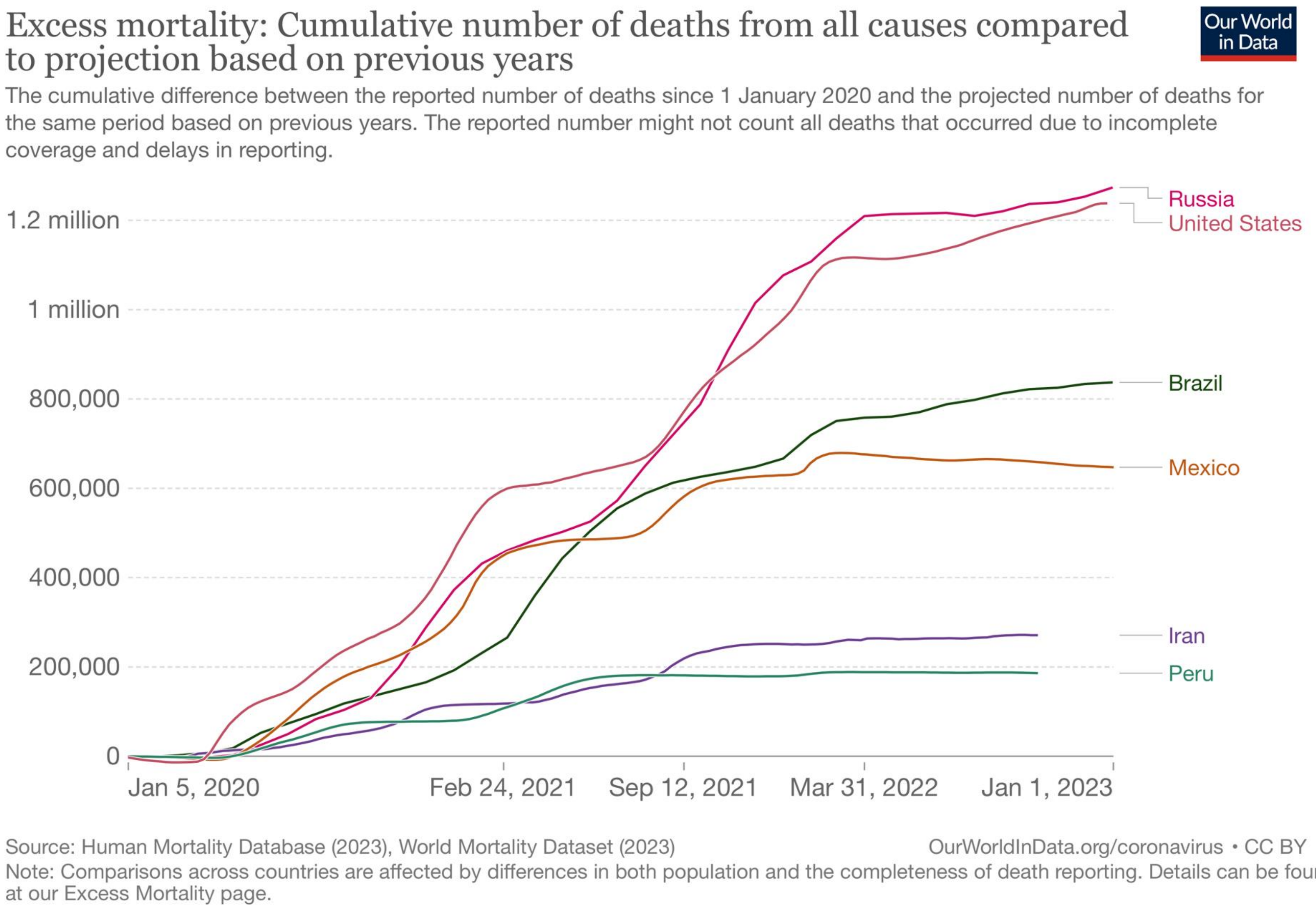
Source: Human Mortality Database (2023); World Mortality Dataset (2023)

Note: Comparisons across countries are affected by differences in the completeness of death reporting. Details can be found at our Excess Mortality page.

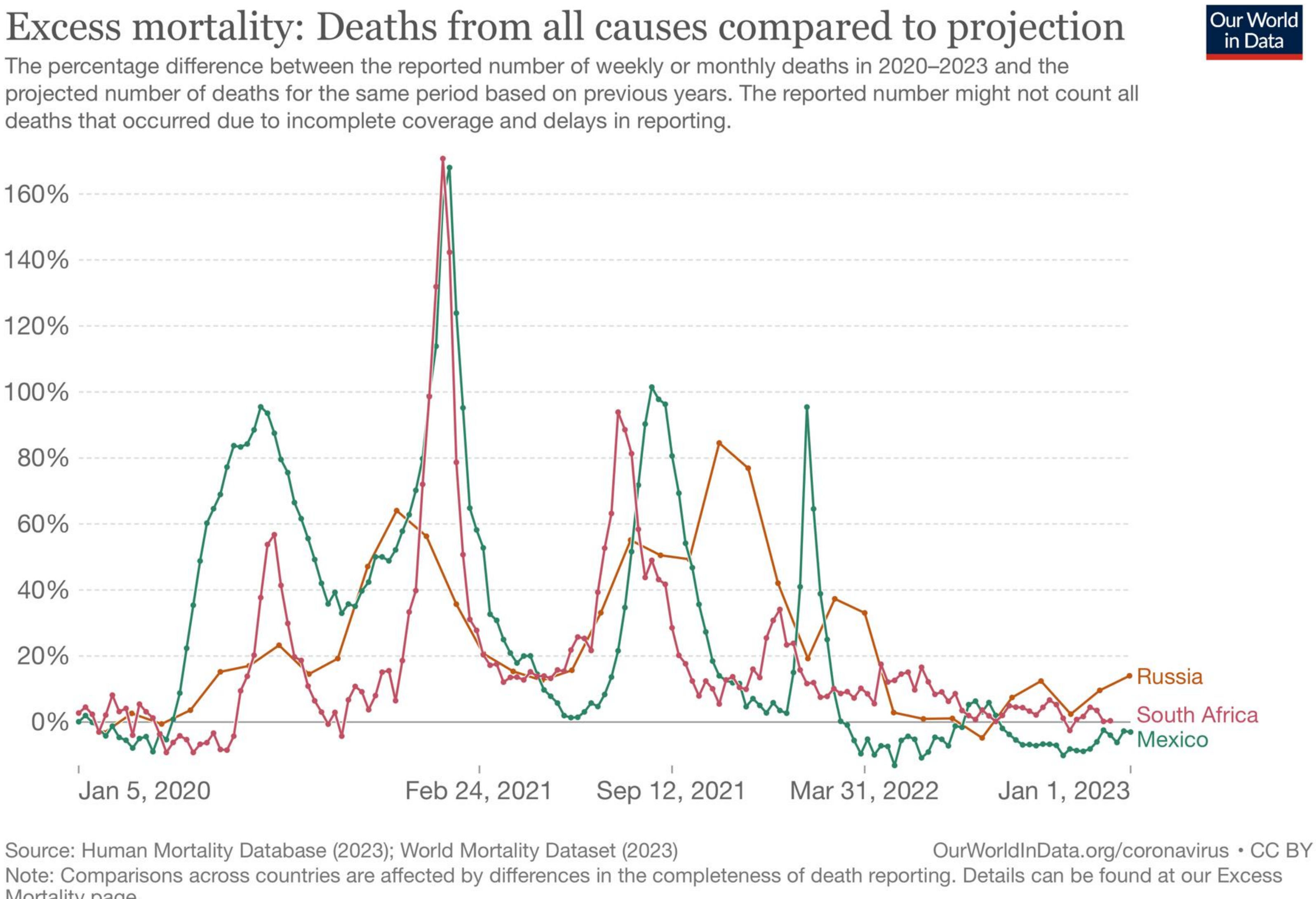
Excess mortality per capita to Jan 2023



Excess all cause mortality, cumulative select countries



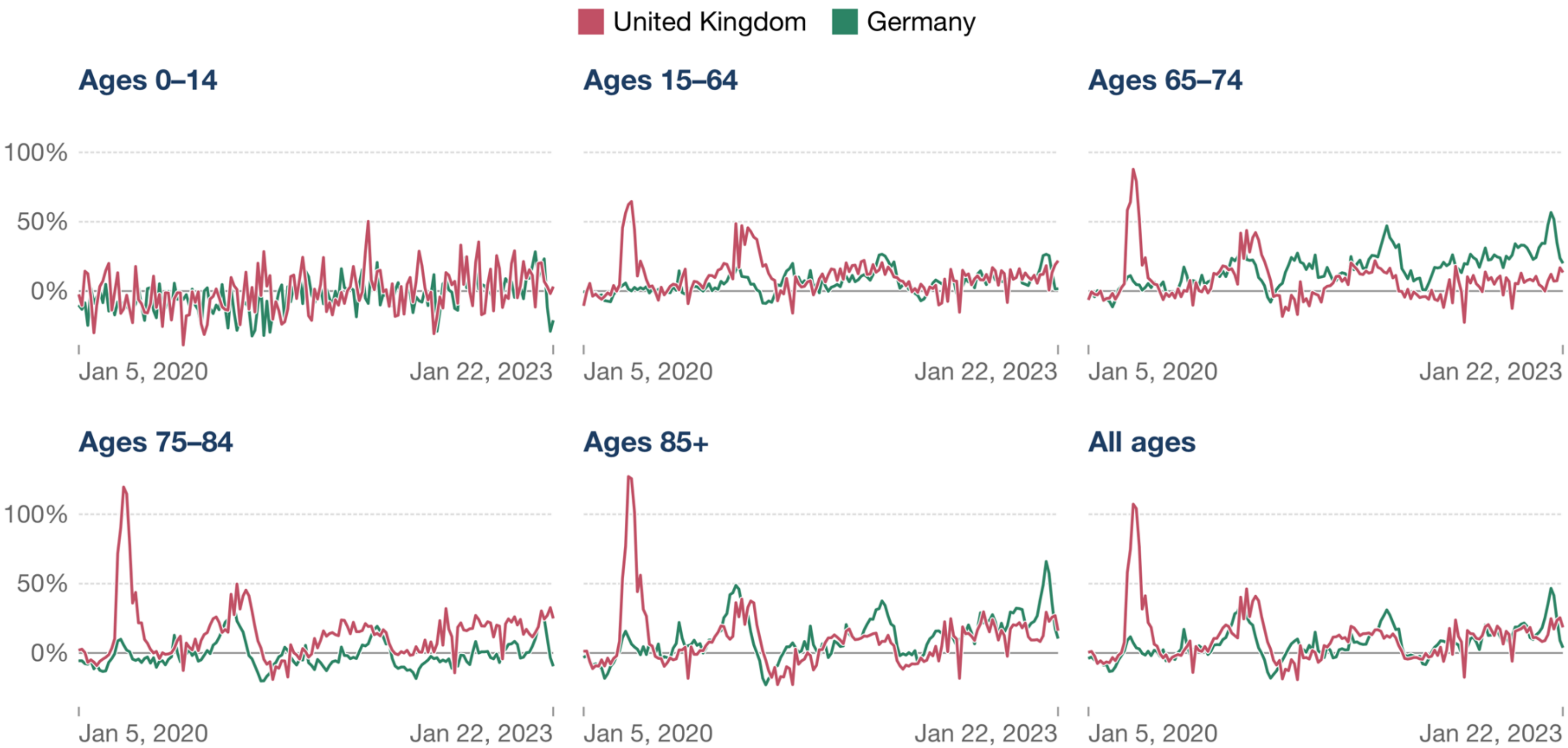
Excess mortality, select countries



Excess mortality UK and Germany

Excess mortality: Deaths from all causes compared to projection based on previous years, by age

The percentage difference between the reported number of weekly or monthly deaths in 2020–2023 — broken down by age group — and the projected number of deaths for the same period based on previous years. The reported number might not count all deaths that occurred due to incomplete coverage and delays in reporting.

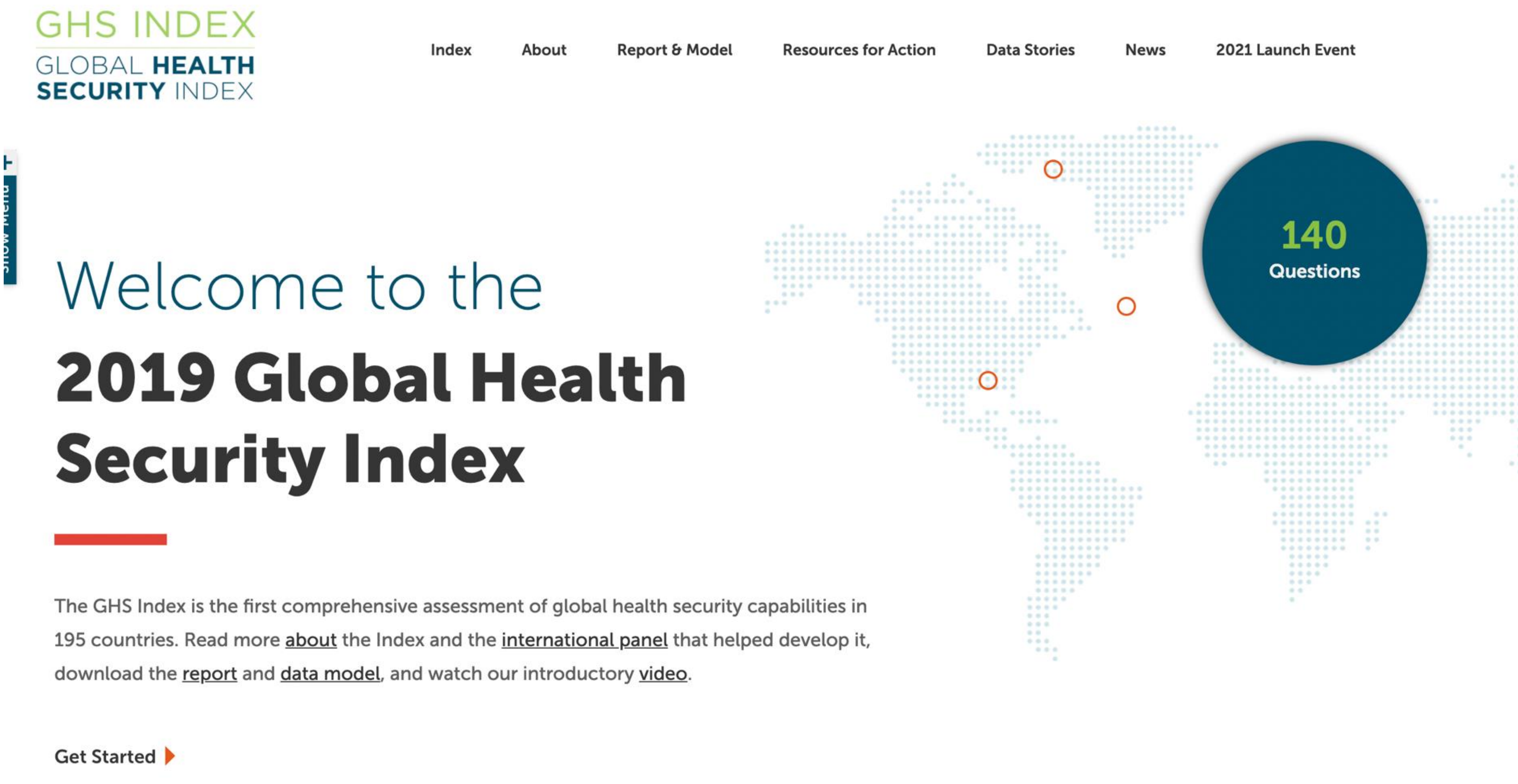


Source: Human Mortality Database (2023); World Mortality Dataset (2023)

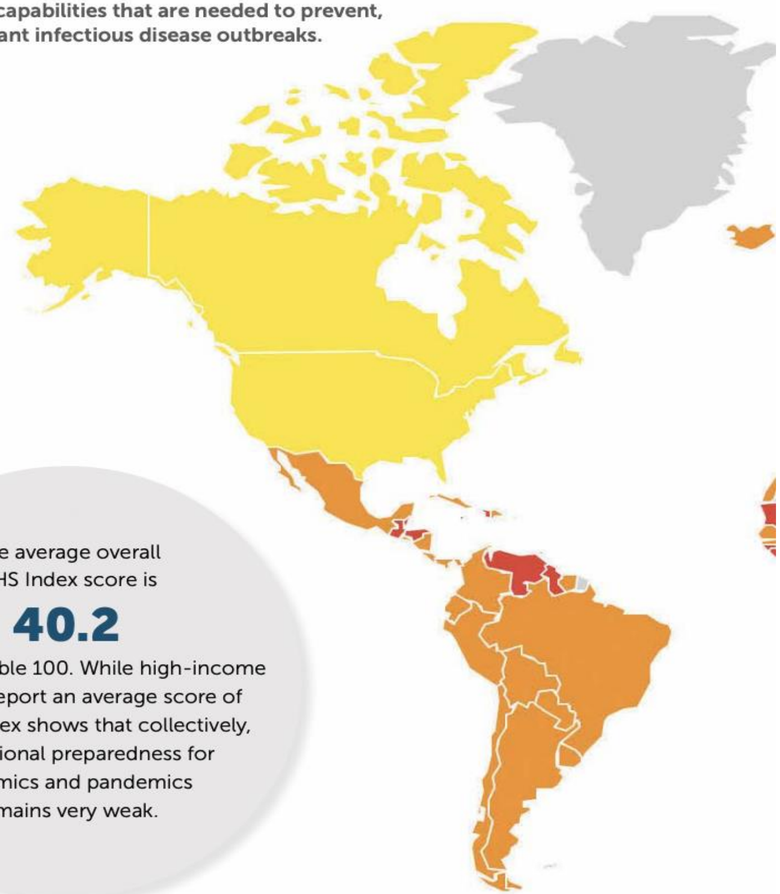
OurWorldInData.org/coronavirus • CC BY

Note: Comparisons across countries are affected by differences in the completeness of death reporting. Details can be found at our Excess Mortality page.

How well were we prepared?



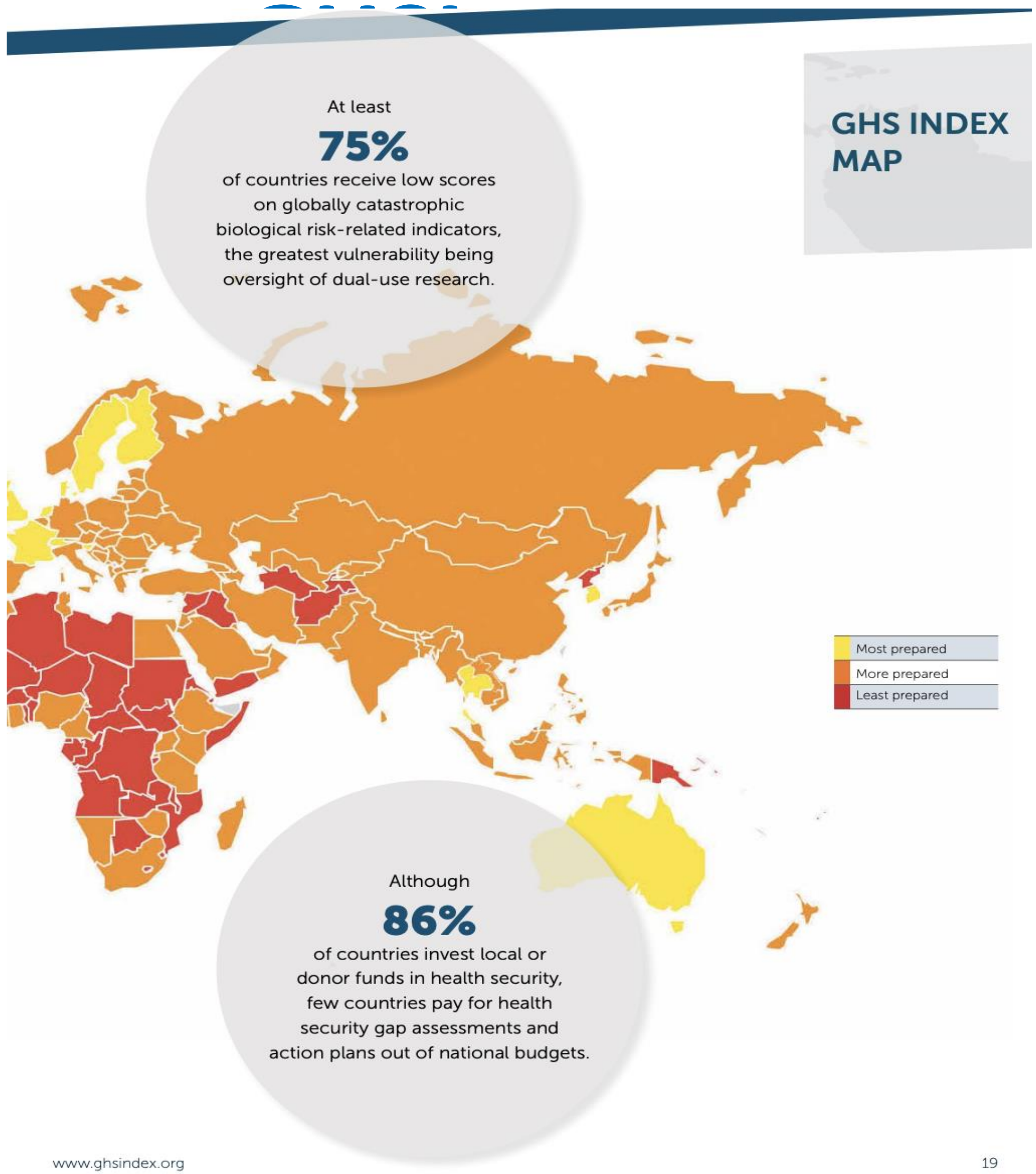
The Global Health Security (GHS) Index analysis finds no country is fully prepared for epidemics or pandemics. Collectively, international preparedness is weak. Many countries do not show evidence of the health security capacities and capabilities that are needed to prevent, detect, and respond to significant infectious disease outbreaks.



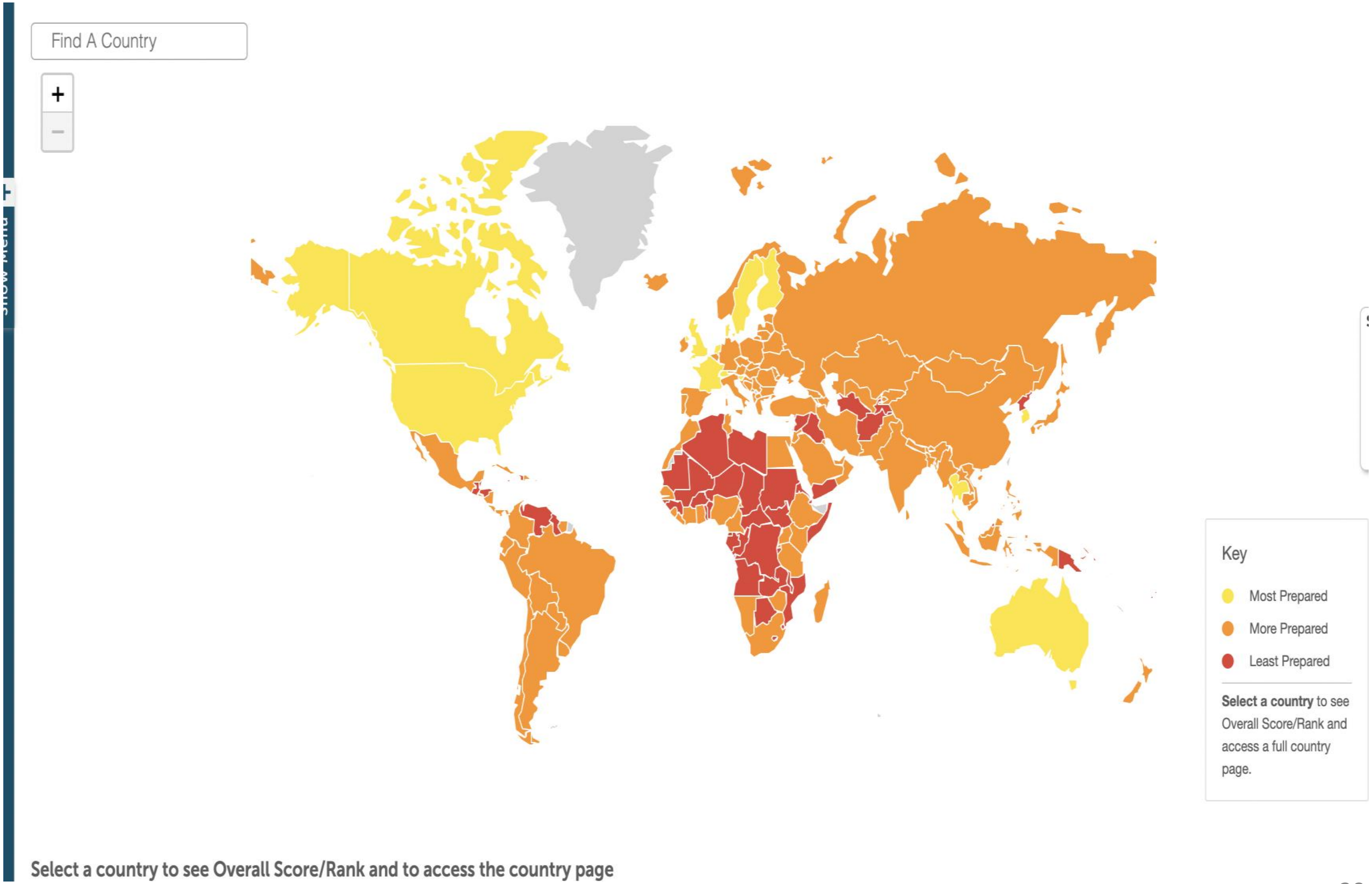
The average overall GHS Index score is

40.2

out of a possible 100. While high-income countries report an average score of 51.9, the Index shows that collectively, international preparedness for epidemics and pandemics remains very weak.


GHS INDEX MAP
At least
75%
of countries receive low scores on globally catastrophic biological risk-related indicators, the greatest vulnerability being oversight of dual-use research.
Although
86%
of countries invest local or donor funds in health security, few countries pay for health security gap assessments and action plans out of national budgets.
Most prepared
More prepared
Least prepared
www.ghsindex.org
19

GHSI


Find A Country
Key
Most Prepared
More Prepared
Least Prepared
Select a country to see Overall Score/Rank and access a full country page.
Select a country to see Overall Score/Rank and to access the country page

OVERALL SCORE		
Rank		Score
1	United States	83.5
2	United Kingdom	77.9
3	Netherlands	75.6
4	Australia	75.5
5	Canada	75.3
6	Thailand	73.2
7	Sweden	72.1
8	Denmark	70.4
9	South Korea	70.2
10	Finland	68.7
11	France	68.2
12	Slovenia	67.2
13	Switzerland	67.0
14	Germany	66.0
15	Spain	65.9
16	Norway	64.6
17	Latvia	62.9
18	Malaysia	62.2
19	Belgium	61.0
20	Portugal	60.3
21	Japan	59.8
22	Brazil	59.7
23	Ireland	59.0
24	Singapore	58.7
25	Argentina	58.6
26	Austria	58.5
27	Chile	58.3
28	Mexico	57.6
29	Estonia	57.0
30	Indonesia	56.6
31	Italy	56.2
32	Poland	55.4
33	Lithuania	55.0
34	South Africa	54.8
35	Hungary	54.0
35	New Zealand	54.0
37	Greece	53.8
38	Croatia	53.3
39	Albania	52.9
40	Turkey	52.4

1. PREVENTION OF THE EMERGENCE OR RELEASE OF PATHOGENS		
Rank		Score
1	United States	83.1
2	Sweden	81.1
3	Thailand	75.7
4	Netherlands	73.7
5	Denmark	72.9
6	France	71.2
7	Canada	70.0
8	Australia	68.9
9	Finland	68.5
10	United Kingdom	68.3
11	Norway	68.2
12	Slovenia	67.0
13	Germany	66.5
14	Ireland	63.9
15	Belgium	63.5
16	Brazil	59.2
17	Kazakhstan	58.8
18	Austria	57.4
19	South Korea	57.3
20	Turkey	56.9
21	Armenia	56.7
22	Hungary	56.4
23	Chile	56.2
23	Singapore	56.2
25	Latvia	56.0
26	Croatia	55.2
27	New Zealand	55.0
28	Greece	54.2
29	Ecuador	53.9
30	Slovakia	53.5
31	Georgia	53.2
32	Spain	52.9
33	Portugal	52.8
34	Switzerland	52.7
35	Malaysia	51.4
36	Czech Republic	51.1
37	Poland	50.9
38	Indonesia	50.2
39	Vietnam	49.5
40	Japan	49.3

2. EARLY DETECTION & REPORTING FOR EPIDEMICS OF POTENTIAL INTERNATIONAL CONCERN		
Rank		Score
1	United States	98.2
2	Australia	97.3
2	Latvia	97.3
4	Canada	96.4
5	South Korea	92.1
6	United Kingdom	87.3
7	Denmark	86.0
7	Netherlands	86.0
7	Sweden	86.0
10	Germany	84.6
11	Spain	83.0
12	Brazil	82.4
13	Lithuania	81.5
13	South Africa	81.5
15	Thailand	81.0
16	Italy	78.5
17	Greece	78.4
18	Ireland	78.0
19	Estonia	77.6
20	Mongolia	77.3
21	France	75.3
22	Georgia	75.0
23	Argentina	74.9
24	Saudi Arabia	74.4
25	Albania	74.3
26	El Salvador	73.9
27	Slovenia	73.7
28	Austria	73.2
28	Malaysia	73.2
30	Chile	72.7
31	Croatia	72.3
32	Ecuador	71.2
32	Mexico	71.2
34	Laos	70.4
35	Japan	70.1
36	Kenya	68.6
37	Indonesia	68.1
38	Zimbabwe	65.6
39	Kyrgyz Republic	64.7
40	Singapore	64.5

3. RAPID RESPONSE TO AND MITIGATION OF THE SPREAD OF AN EPIDEMIC		
Rank		Score
1	United Kingdom	91.9
2	United States	79.7
3	Switzerland	79.3
4	Netherlands	79.1
5	Thailand	78.6
6	South Korea	71.5
7	Finland	69.2
8	Portugal	67.7
9	Brazil	67.1
10	Australia	65.9
11	Singapore	64.6
12	Slovenia	63.3
13	France	62.9
14	Sweden	62.8
15	Spain	61.9
16	Malaysia	61.3
17	Canada	60.7
18	Chile	60.2
19	Denmark	58.4
20	Norway	58.2
21	New Zealand	58.1
22	Madagascar	57.8
23	South Africa	57.7
24	Micronesia	56.9
25	Uganda	56.5
26	Armenia	55.5
27	Serbia	55.1
28	Germany	54.8
29	Latvia	54.7
30	Indonesia	54.3
31	Japan	53.6
32	India	52.4
33	Hungary	52.2
34	Albania	52.0
34	Laos	52.0
36	Bosnia and Herzegovina	51.8
37	Peru	51.7
38	Morocco	51.5
39	Mexico	50.8
40	Argentina	50.6

GHS INDEX RESULTS

All data are normalized to a scale of 0 to 100, where 100 = best health security conditions.

- Most prepared
- More prepared
- Least prepared

4. SUFFICIENT & ROBUST HEALTH SYSTEM TO TREAT THE SICK & PROTECT HEALTH WORKERS

Rank		Score
1	United States	73.8
2	Thailand	70.5
3	Netherlands	70.2
4	Canada	67.7
5	Denmark	63.8
6	Australia	63.5
7	Switzerland	62.5
8	France	60.9
9	Finland	60.8
10	Belgium	60.5
11	United Kingdom	59.8
12	Spain	59.6
13	South Korea	58.7
14	Norway	58.5
15	Malaysia	57.1
16	Serbia	56.6
17	Portugal	55.0
18	Argentina	54.9
18	Slovenia	54.9
20	Sweden	49.3
21	Poland	48.9
22	Germany	48.2
23	Latvia	47.3
24	Mexico	46.9
25	Austria	46.6
25	Japan	46.6
27	Croatia	46.5
28	Iceland	46.4
29	Nicaragua	45.9
30	China	45.7
30	Turkey	45.7
32	New Zealand	45.2
33	Brazil	45.0
33	Peru	45.0
35	Saudi Arabia	44.8
36	India	42.7
37	Israel	42.2
38	Singapore	41.4
39	Bulgaria	41.0
40	Belarus	40.6

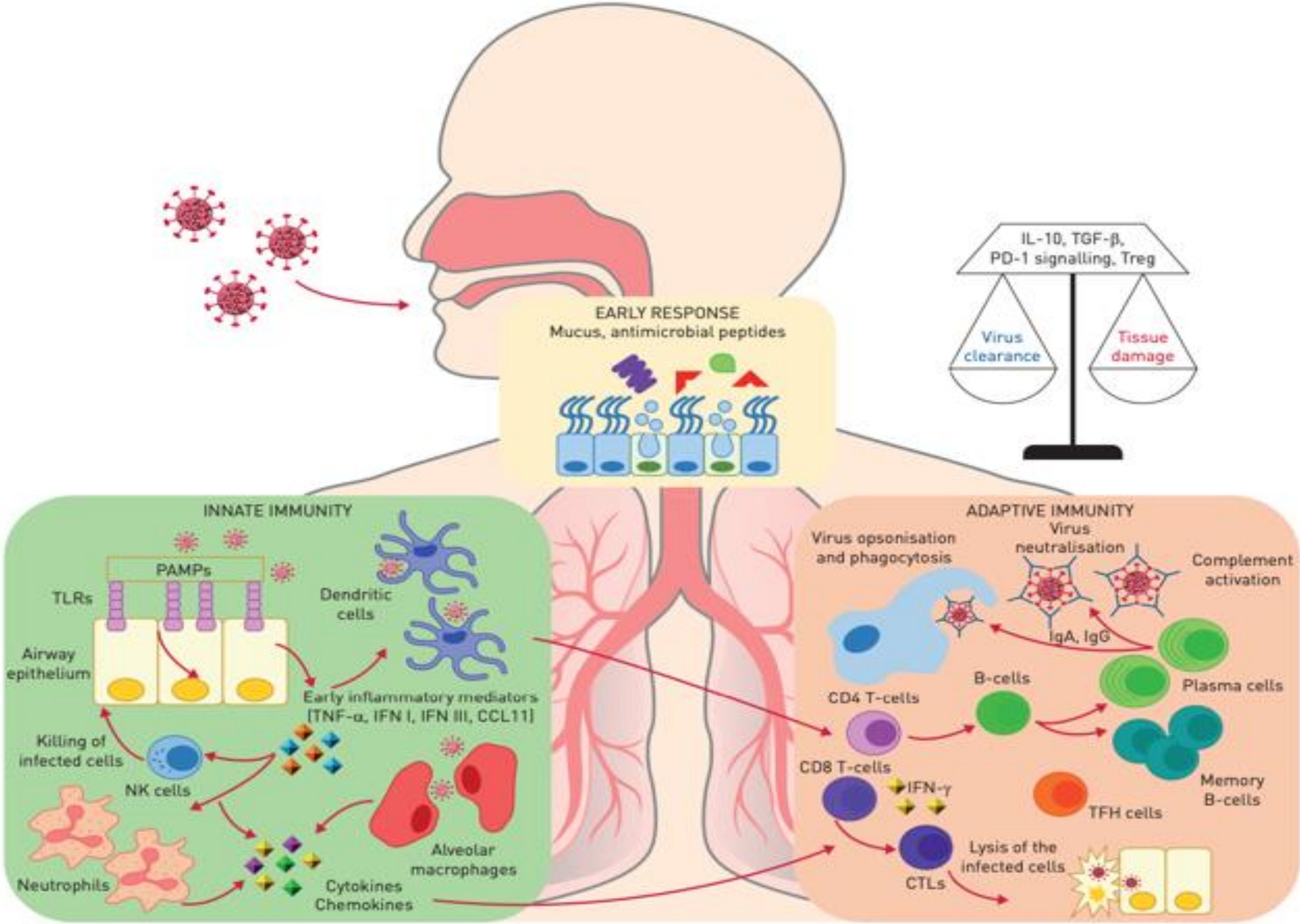
5. COMMITMENTS TO IMPROVING NATIONAL CAPACITY, FINANCING AND ADHERENCE TO NORMS

Rank		Score
1	United States	85.3
2	United Kingdom	81.2
3	Australia	77.0
4	Finland	75.4
5	Canada	74.7
6	Mexico	73.9
7	Indonesia	72.5
8	Lithuania	72.1
8	Slovenia	72.1
10	Liberia	71.5
11	Sweden	71.3
12	Thailand	70.9
13	Japan	70.0
14	Argentina	68.8
15	Estonia	67.6
16	Kenya	67.1
17	Ethiopia	65.8
18	Switzerland	65.6
19	Uganda	65.4
20	Kyrgyz Republic	64.8
21	Vietnam	64.6
22	Norway	64.4
23	South Korea	64.3
23	Turkey	64.3
25	United Arab Emirates	63.4
26	Peru	63.0
26	Portugal	63.0
28	Denmark	62.6
29	Germany	61.9
29	Italy	61.9
31	Bulgaria	61.5
32	Netherlands	61.1
32	Spain	61.1
34	Uzbekistan	60.5
35	Colombia	60.1
36	Cambodia	60.0
37	Cameroon	59.9
38	Belgium	59.7
39	New Zealand	59.4
40	Myanmar	59.1

6. OVERALL RISK ENVIRONMENT AND COUNTRY VULNERABILITY TO BIOLOGICAL THREATS

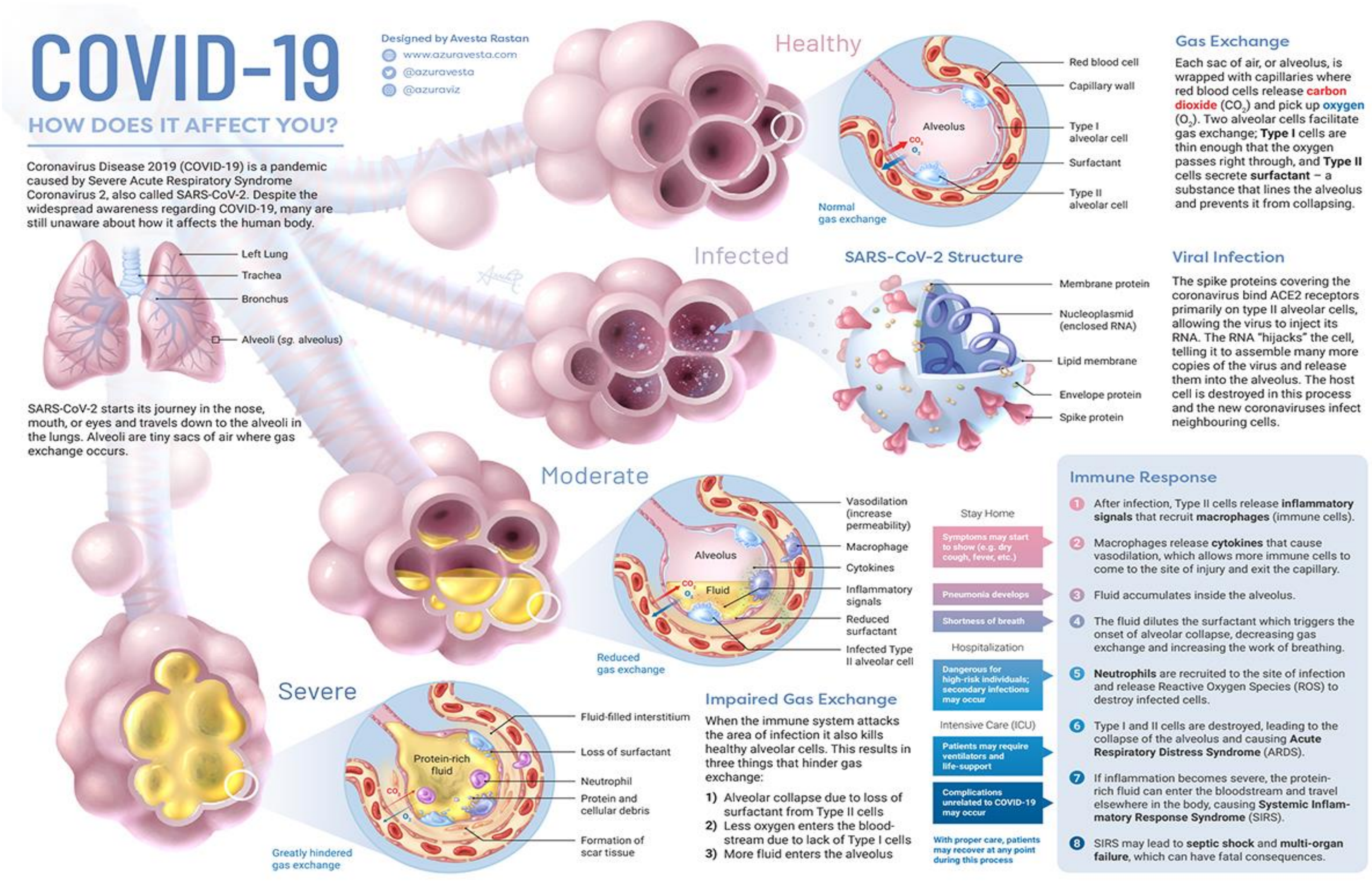
Rank		Score
1	Liechtenstein	87.9
2	Norway	87.1
3	Switzerland	86.2
4	Luxembourg	84.7
5	Austria	84.6
6	Sweden	84.5
7	Andorra	83.5
8	Monaco	83.1
9	France	83.0
10	Canada	82.7
11	Germany	82.3
12	Netherlands	81.7
13	Iceland	81.2
14	Finland	81.1
15	Singapore	80.9
16	San Marino	80.5
17	Denmark	80.3
18	Australia	79.4
19	Belgium	78.2
19	United States	78.2
21	Ireland	77.4
22	Portugal	77.3
23	New Zealand	77.2
24	Spain	77.1
25	Uruguay	74.8
26	United Kingdom	74.7
27	South Korea	74.1
28	Czech Republic	74.0
29	Slovenia	73.7
30	Estonia	73.3
31	United Arab Emirates	72.4
32	Malta	72.3
33	Malaysia	72.0
34	Costa Rica	71.7
34	Japan	71.7
36	Slovakia	71.5
37	Seychelles	71.1
38	Chile	70.1
39	Barbados	69.9
40	Cyprus	69.6

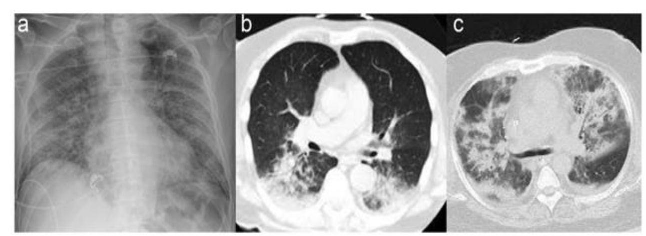
Early emphasis on respiratory system



After-lecture notes of use for the last slide

- The **lungs and gut are exposed to environmental substances and pathogens.**
- The **early protection response to respiratory viruses includes mucus, surfactants and antiviral peptides** that can **prevent initial attachment and viral entry.**
- Respiratory viruses enter via the respiratory epithelium. **Epithelial cells have a key role in initiating the immune response by recognising viral components** (pathogen-associated molecular patterns (PAMPs)) via Toll-like receptors (TLRs) and intracellular receptors. in particular neutrophils and natural killer (NK) cells. **NK cells have the ability to kill virus-infected cells via perforin–granzyme-dependent mechanisms** or by the Fas–Fas ligand pathway. Moreover, alveolar macrophages, recruited monocytes and macrophages as well as **dendritic cells pick pathogen components** and **contribute to the immune response**. **All of these cells produce cytokines and chemokines that are important for the establishment of the adaptive responses and of the antiviral state.**
- The **adaptive response to respiratory viruses is mediated by both T- and B-cell compartments**. T-cells contribute to the generation of the B-cell response. B-cells produce antibodies that may neutralise the respiratory viruses directly by binding to viral surface proteins that are essential for entry of the virus into host cells or through the ligation of Fc receptors to trigger the complement cascade and antibody-dependent cell-mediated cytotoxicity.
- **Antibodies are in the form of IgA, mainly in the upper respiratory tract, or IgG, in the lower respiratory tract. Viral clearance is also mediated by CD8+-specific T-cells with cytolytic activity.** The protective antiviral T-cell response is mainly mediated by IFN-γ production and is therefore biased toward a T-helper cell (Th) 1 response, whereas other T-cell subsets such as Th2 cells and Th17 cells play a minor role and they may be responsible for lung tissue damage. Moreover, regulatory mechanisms adopted by T-cells such as interleukin (IL)-10 secretion, or upregulation of inhibitory receptors such as programmed cell death protein 1 (PD-1) or expansion of the T-regulatory (Treg) cell subsets, work to balance tissue damage and viral clearance. TNF: tumour necrosis factor; CTL: cytotoxic T-lymphocyte; TFH: T-follicular helper; TGF: transforming growth factor. (Your body is a rather remarkable machine with its own protection squad!)


COVID-19
HOW DOES IT AFFECT YOU?
Designed by Avesta Rastan
www.azuravesta.com
@azuravesta
@azuraviz
Coronavirus Disease 2019 (COVID-19) is a pandemic caused by Severe Acute Respiratory Syndrome Coronavirus 2, also called SARS-CoV-2. Despite the widespread awareness regarding COVID-19, many are still unaware about how it affects the human body.
Left Lung
Trachea
Bronchus
Alveoli (sg. alveolus)
SARS-CoV-2 starts its journey in the nose, mouth, or eyes and travels down to the alveoli in the lungs. Alveoli are tiny sacs of air where gas exchange occurs.
Healthy
Alveolus
CO_2
O_2
Red blood cell
Capillary wall
Type I alveolar cell
Surfactant
Type II alveolar cell
Normal gas exchange
Gas Exchange
Each sac of air, or alveolus, is wrapped with capillaries where red blood cells release carbon dioxide (CO_2) and pick up oxygen (O_2). Two alveolar cells facilitate gas exchange; Type I cells are thin enough that the oxygen passes right through, and Type II cells secrete surfactant – a substance that lines the alveolus and prevents it from collapsing.
Infected
SARS-CoV-2 Structure
Membrane protein
Nucleoplasmid (enclosed RNA)
Lipid membrane
Envelope protein
Spike protein
Viral Infection
The spike proteins covering the coronavirus bind ACE2 receptors primarily on type II alveolar cells, allowing the virus to inject its RNA. The RNA "hijacks" the cell, telling it to assemble many more copies of the virus and release them into the alveolus. The host cell is destroyed in this process and the new coronaviruses infect neighbouring cells.
Moderate
Alveolus
Fluid
CO_2
O_2
Vasodilation (increase permeability)
Macrophage
Cytokines
Inflammatory signals
Reduced surfactant
Infected Type II alveolar cell
Reduced gas exchange
Severe
Protein-rich fluid
CO_2
O_2
Fluid-filled interstitium
Loss of surfactant
Neutrophil
Protein and cellular debris
Formation of scar tissue
Greatly hindered gas exchange
Impaired Gas Exchange
When the immune system attacks the area of infection it also kills healthy alveolar cells. This results in three things that hinder gas exchange:
1) Alveolar collapse due to loss of surfactant from Type II cells
2) Less oxygen enters the blood-stream due to lack of Type I cells
3) More fluid enters the alveolus
Stay Home
Symptoms may start to show (e.g. dry cough, fever, etc.)
Pneumonia develops
Shortness of breath
Hospitalization
Dangerous for high-risk individuals; secondary infections may occur
Intensive Care (ICU)
Patients may require ventilators and life-support
Complications unrelated to COVID-19 may occur
With proper care, patients may recover at any point during this process
Immune Response
1 After infection, Type II cells release inflammatory signals that recruit macrophages (immune cells).
2 Macrophages release cytokines that cause vasodilation, which allows more immune cells to come to the site of injury and exit the capillary.
3 Fluid accumulates inside the alveolus.
4 The fluid dilutes the surfactant which triggers the onset of alveolar collapse, decreasing gas exchange and increasing the work of breathing.
5 Neutrophils are recruited to the site of infection and release Reactive Oxygen Species (ROS) to destroy infected cells.
6 Type I and II cells are destroyed, leading to the collapse of the alveolus and causing Acute Respiratory Distress Syndrome (ARDS).
7 If inflammation becomes severe, the protein-rich fluid can enter the bloodstream and travel elsewhere in the body, causing Systemic Inflammatory Response Syndrome (SIRS).
8 SIRS may lead to septic shock and multi-organ failure, which can have fatal consequences.

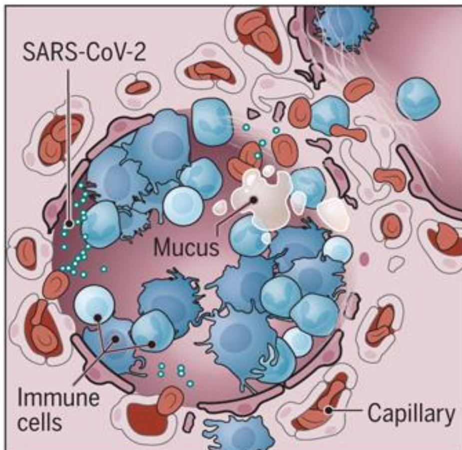

a
b
c

COVID-19: How the virus harms you

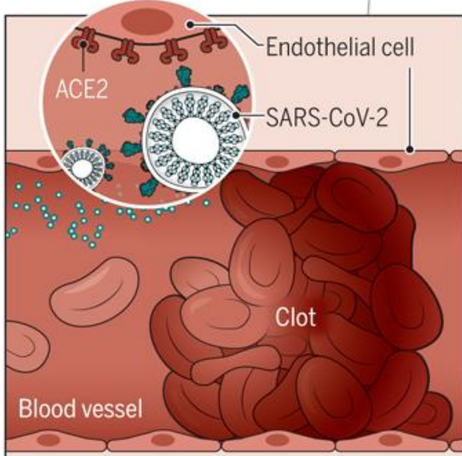
An invader's impact

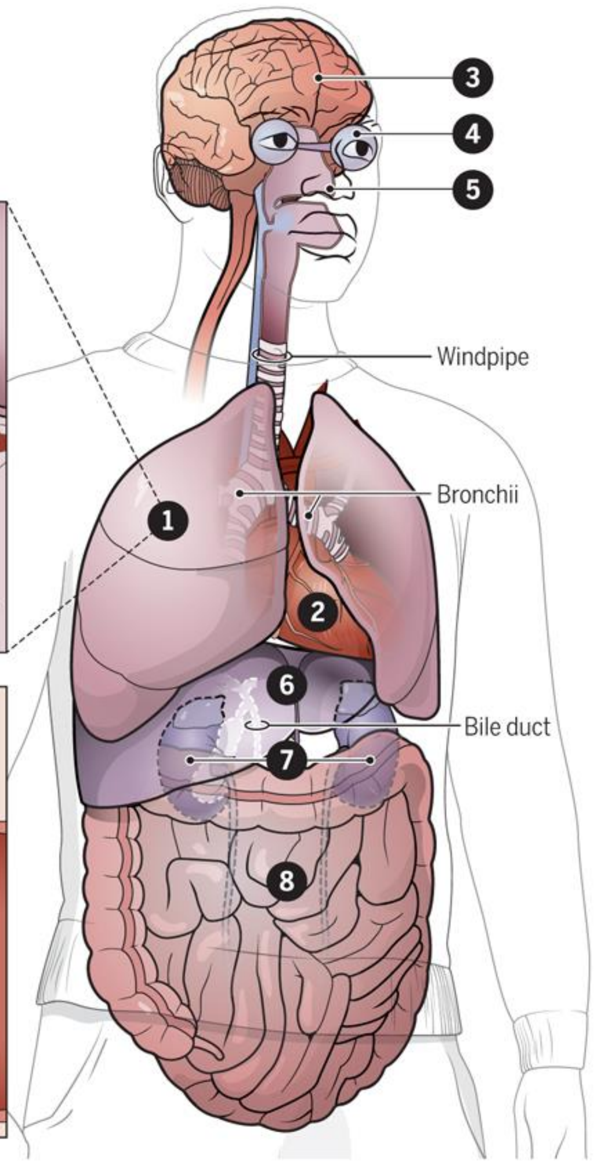
In serious cases, SARS-CoV-2 lands in the lungs and can do deep damage there. But the virus, or the body's response to it, can injure many other organs. Scientists are just beginning to probe the scope and nature of that harm.

1 Lungs
A cross section shows immune cells crowding an inflamed alveolus, or air sac, whose walls break down during attack by the virus, diminishing oxygen uptake. Patients cough, fevers rise, and breathing becomes labored.



2 Heart and blood vessels
The virus (teal) enters cells, likely including those lining blood vessels, by binding to angiotensin-converting enzyme 2 (ACE2) receptors on the cell surface. Infection can also promote blood clots, heart attacks, and cardiac inflammation.





3 Brain
Some COVID-19 patients have strokes, seizures, confusion, and brain inflammation. Doctors are trying to understand which are directly caused by the virus.

4 Eyes
Conjunctivitis, inflammation of the membrane that lines the front of the eye and inner eyelid, is more common in the sickest patients.

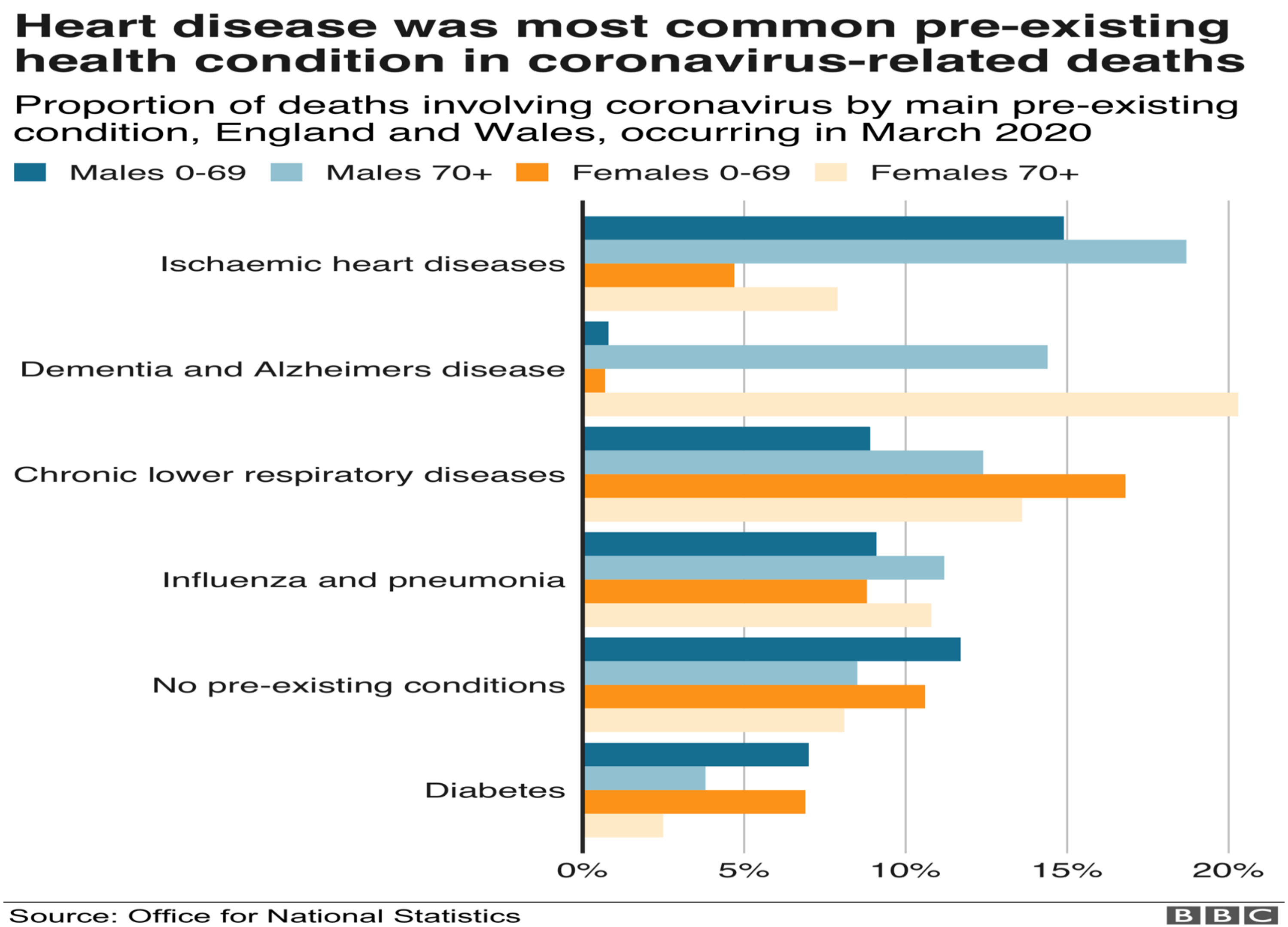
5 Nose
Some patients lose their sense of smell. Scientists speculate that the virus may move up the nose's nerve endings and damage cells.

6 Liver
Up to half of hospitalized patients have enzyme levels that signal a struggling liver. An immune system in overdrive and drugs given to fight the virus may be causing the damage.

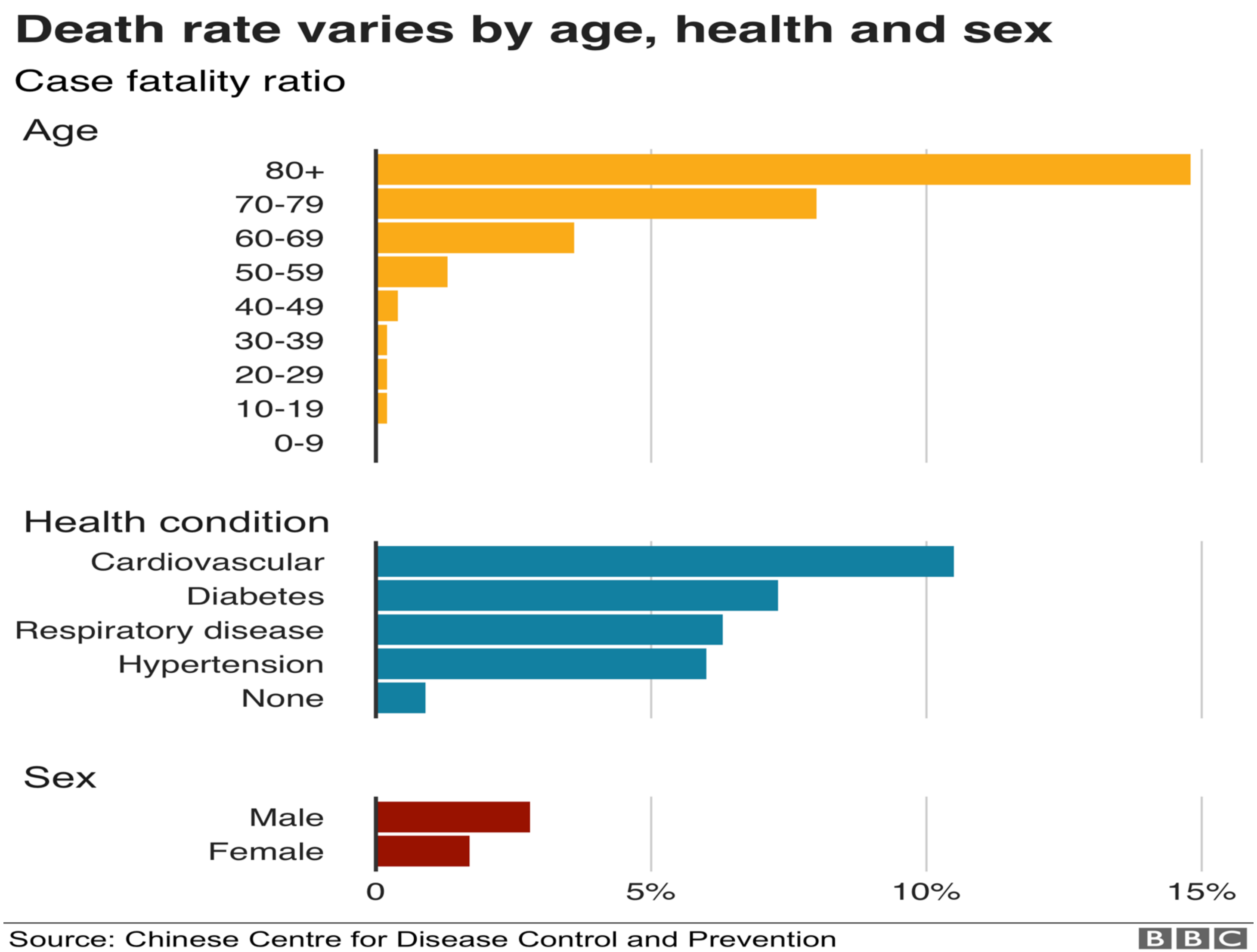
7 Kidneys
Kidney damage is common in severe cases and makes death more likely. The virus may attack the kidneys directly, or kidney failure may be part of whole-body events like plummeting blood pressure.

8 Intestines
Patient reports and biopsy data suggest the virus can infect the lower gastrointestinal tract, which is rich in ACE2 receptors. Some 20% or more of patients have diarrhea.

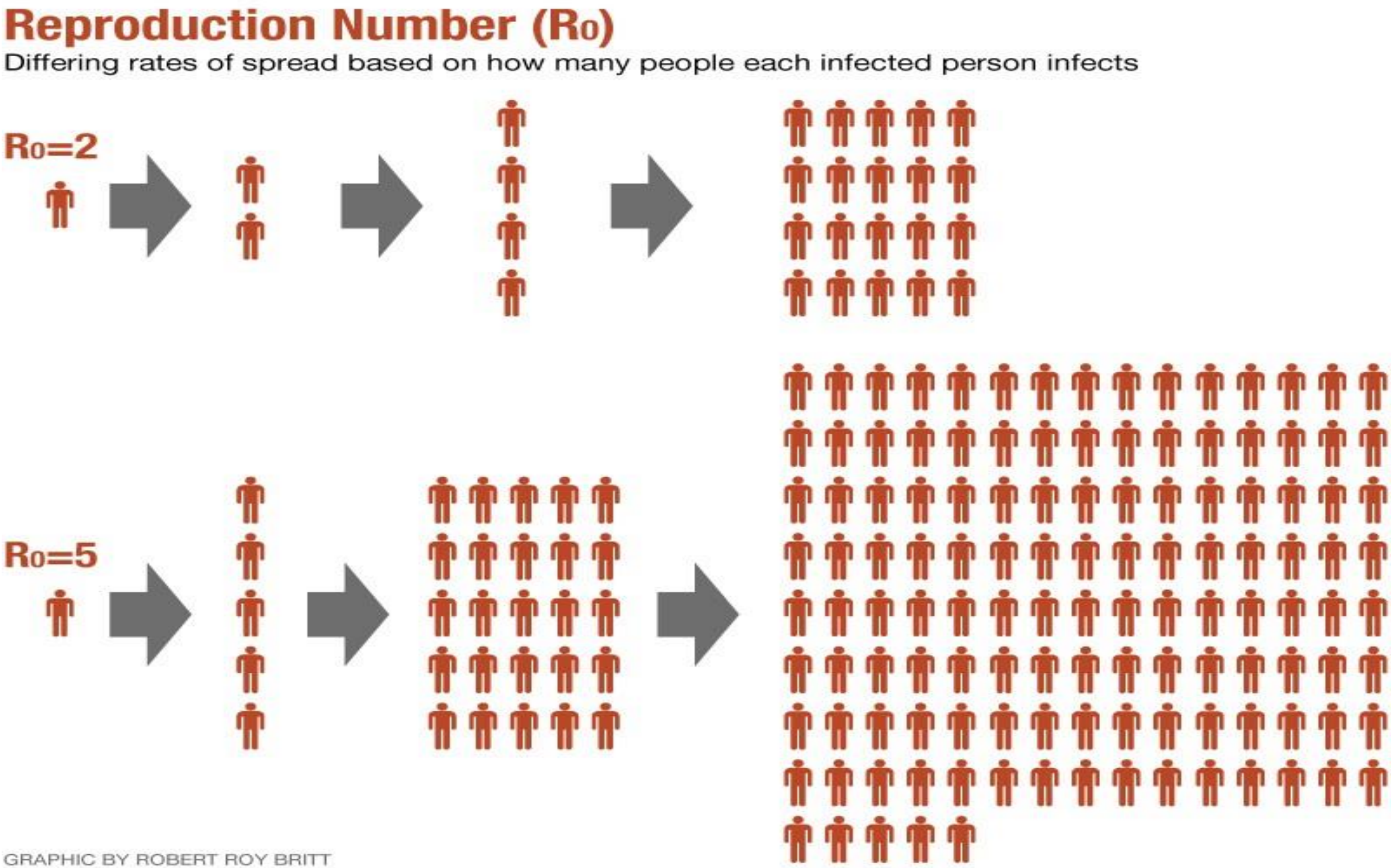
COVID-19: Risk factors



COVID-19: Risk factors = age

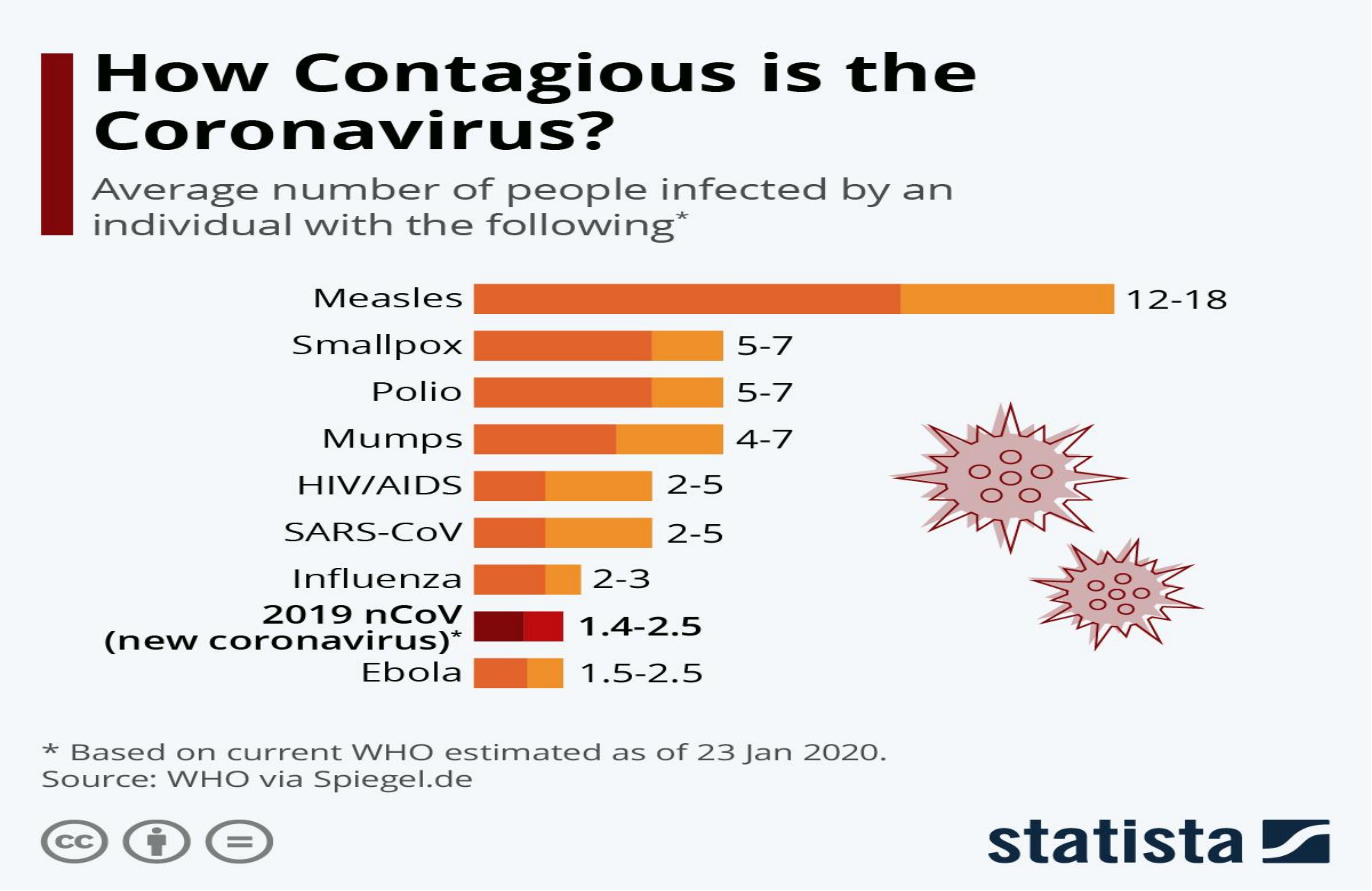


COVID-19: R is exponential

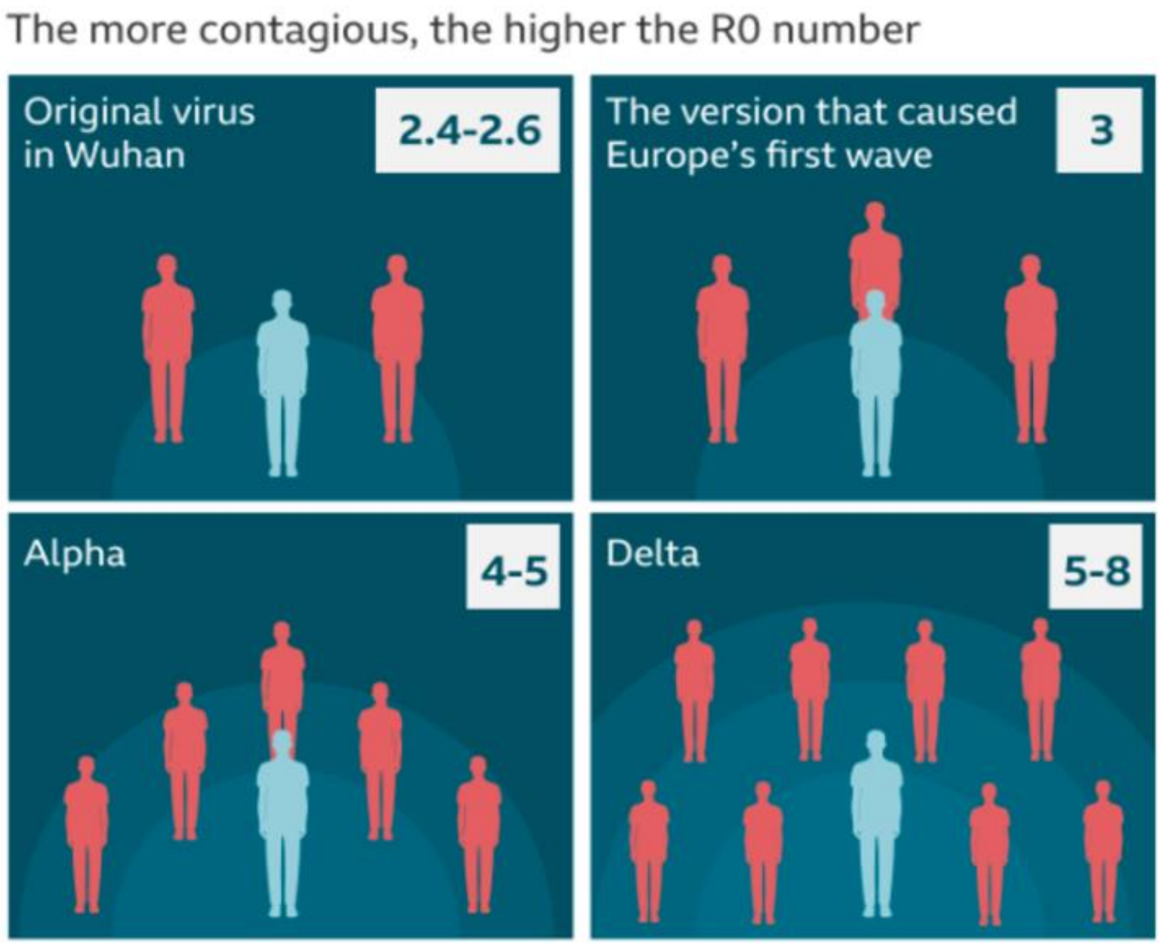


COVID-19: How contagious is it?…

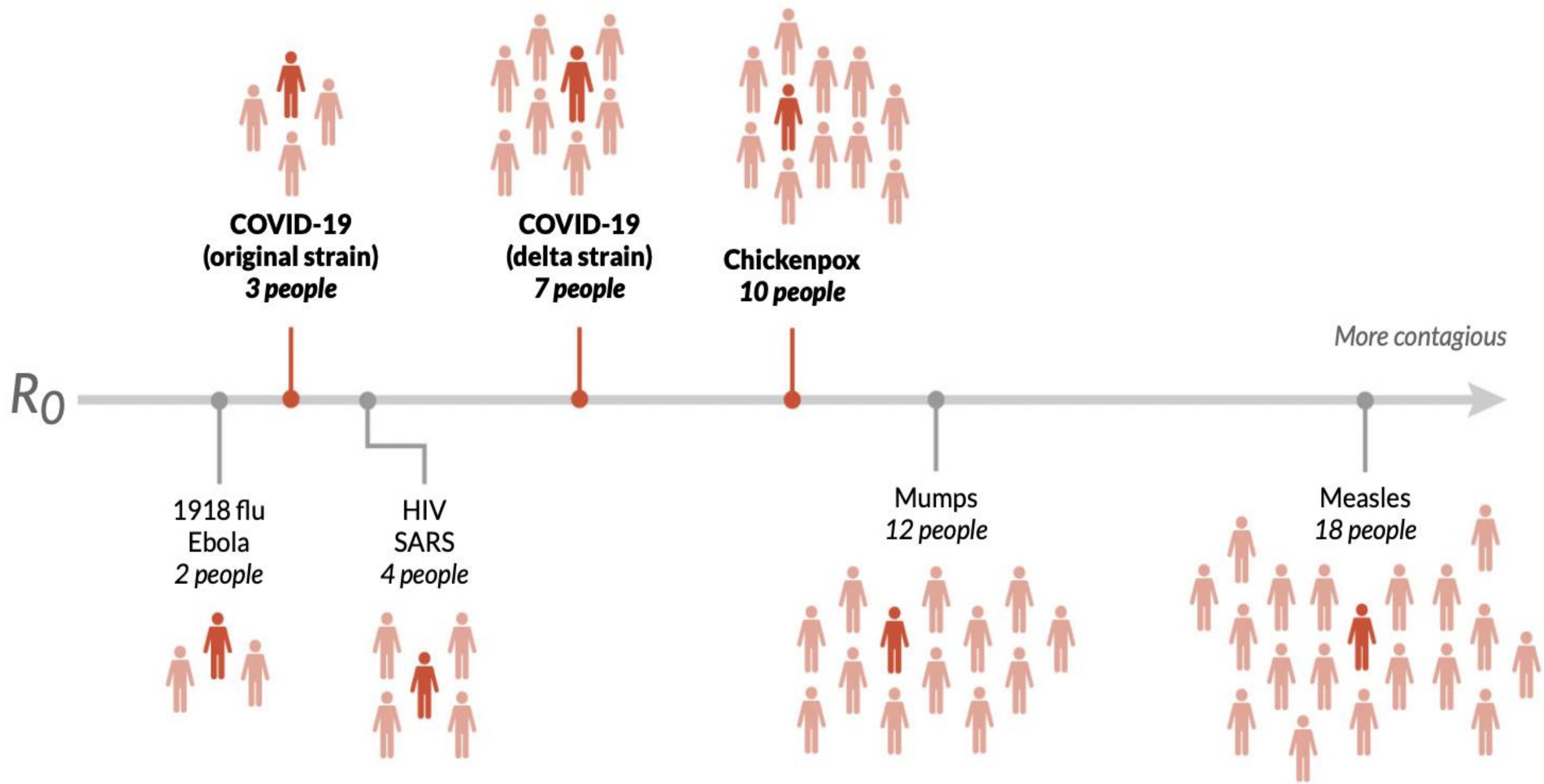
COVID-19: How Contagious is it? Jan 2020



How the R0 numbers of COVID-19 variants compare



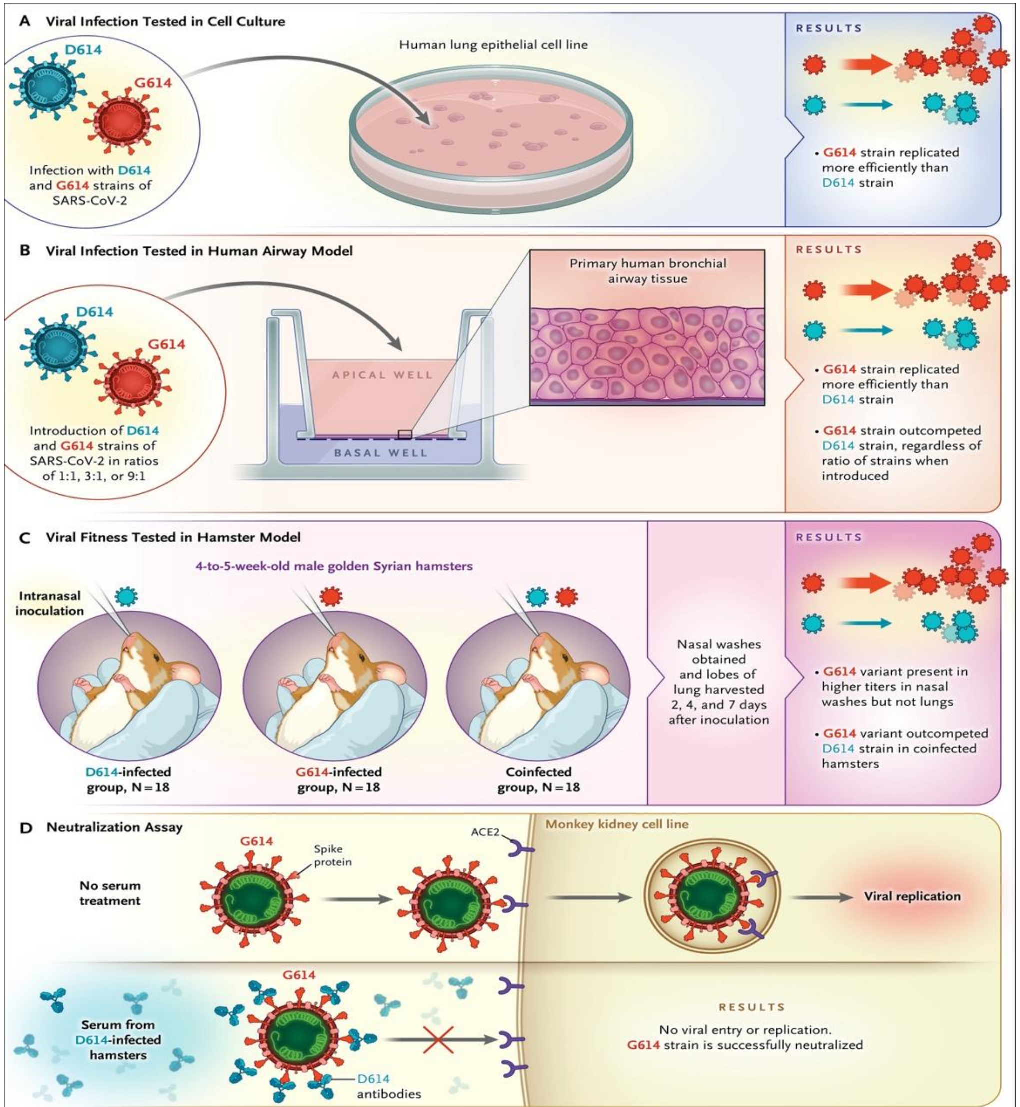
COVID-19: How Contagious is it? Aug 2021



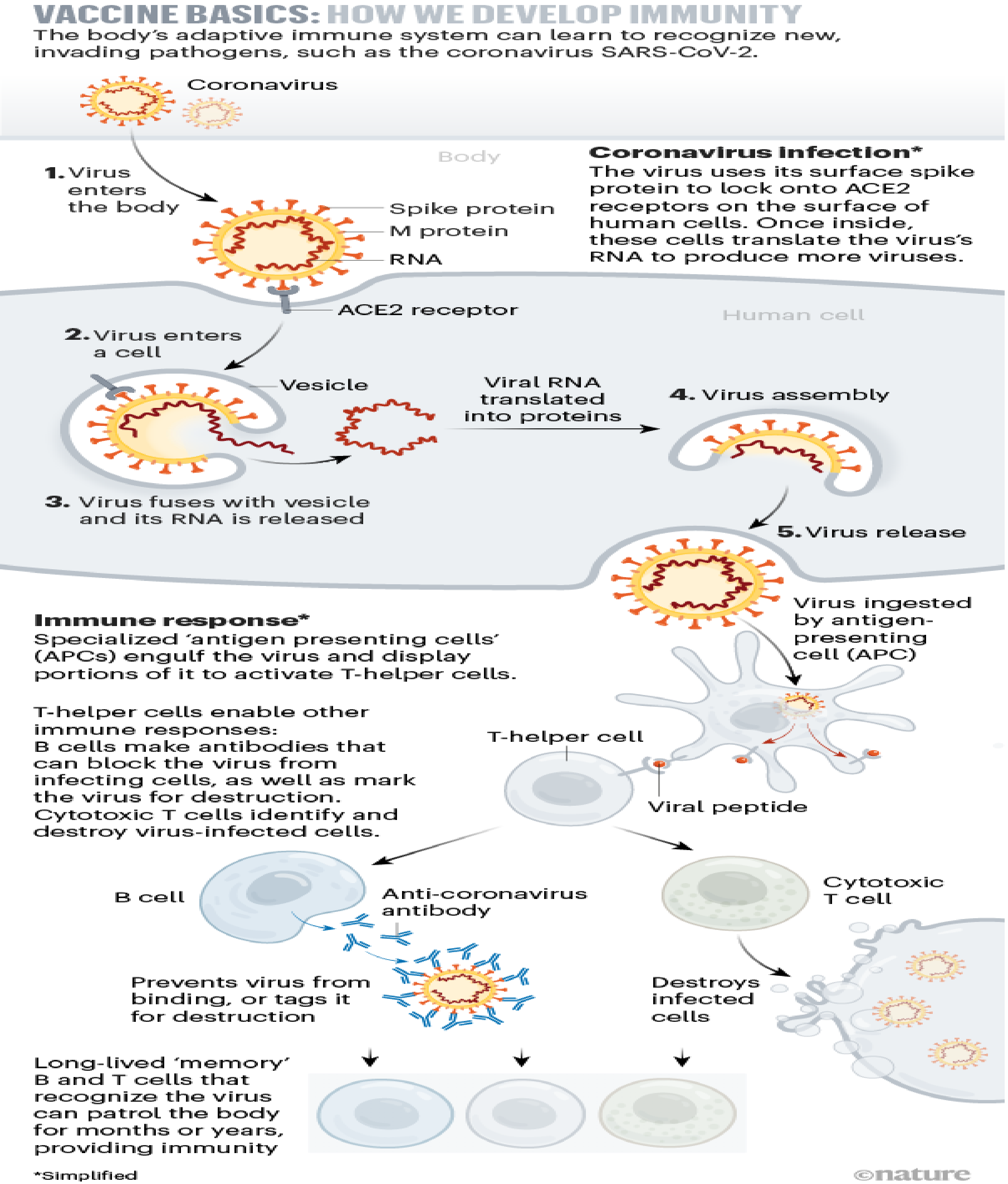
Source: The Lancet (1918 flu, SARS), University of Michigan School of Public Health (COVID-19, ebola, measles), Johns Hopkins University School of Public Health (chickenpox), Proceedings of the National Academy of Sciences (HIV), Tom Wenseleers at the University of Leuven (COVID-19 delta variant), Australian Government Department of Health (mumps)

Credit: Michaeleen Doucleff, Alyson Hurt and Adam Cole/NPR. Icon by Gerard Higgins/The Noun Project.

Testing transmissibility

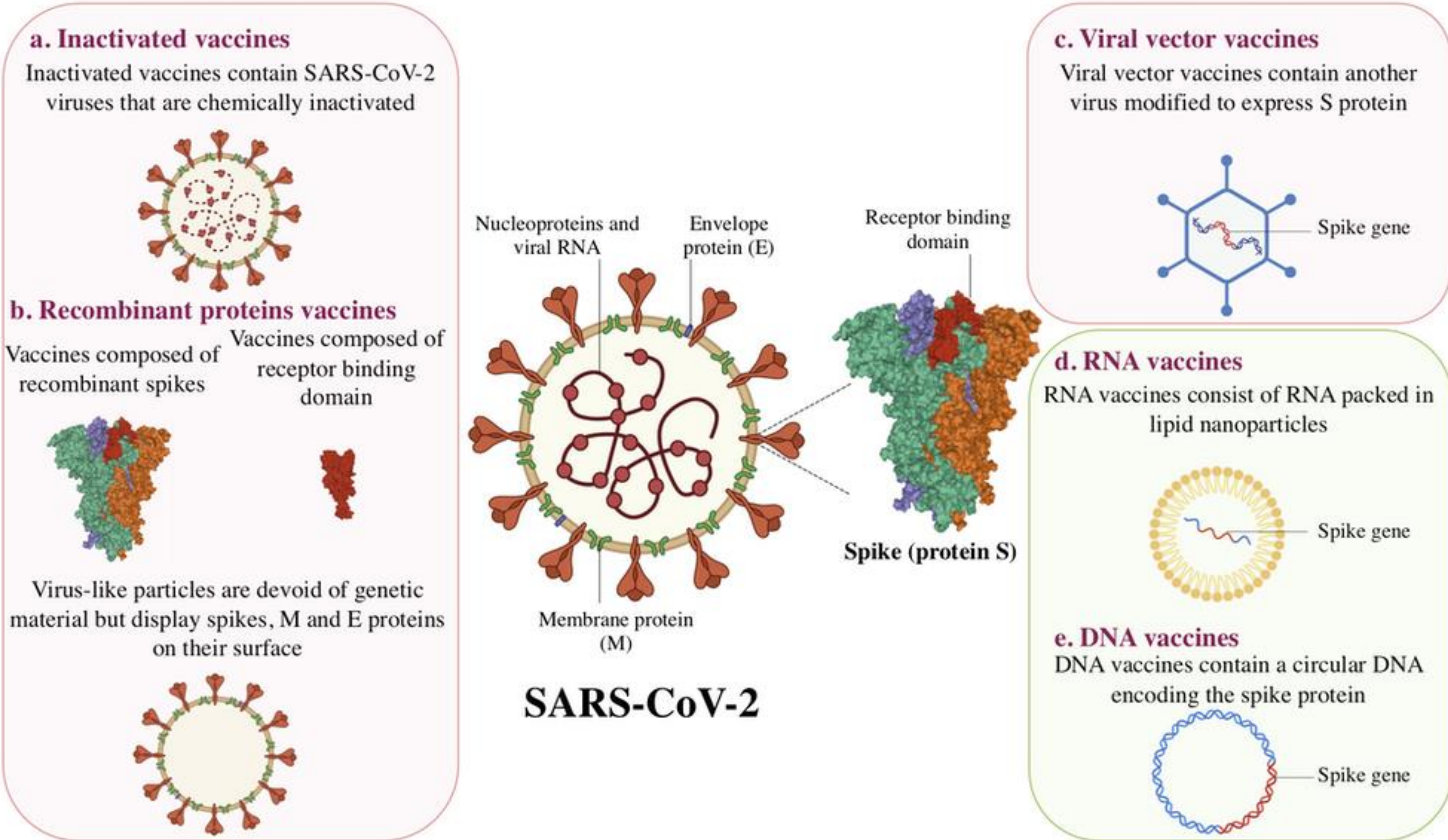


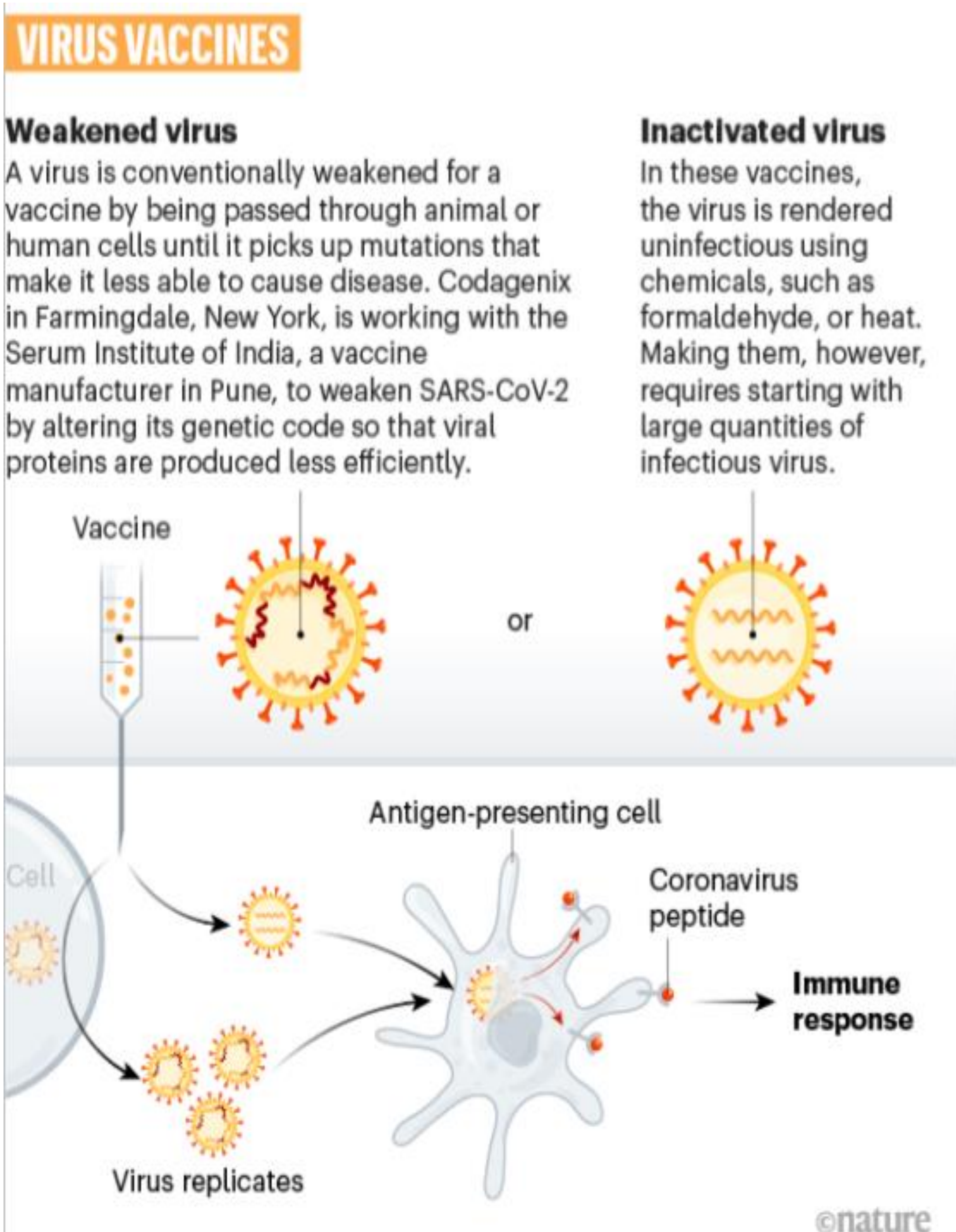
A study recently reported by Plante et al.[5] showed that a variant of SARS-CoV-2 carrying the spike protein D614G substitution results in increased virus infectivity and yield in human lung epithelial cells (Panel A), in primary human airway tissue (Panel B), and in the upper airway of hamsters (Panel C). These data suggest that the D614G mutation results in enhanced transmissibility. In addition, serum samples from D614-virus–infected hamsters can efficiently neutralize the G614 virus from infecting cells (Panel D), which suggests that SARS-CoV-2 vaccines, all of which are based on the D614 variant of the spike protein, will protect against G614 variants of the virus.



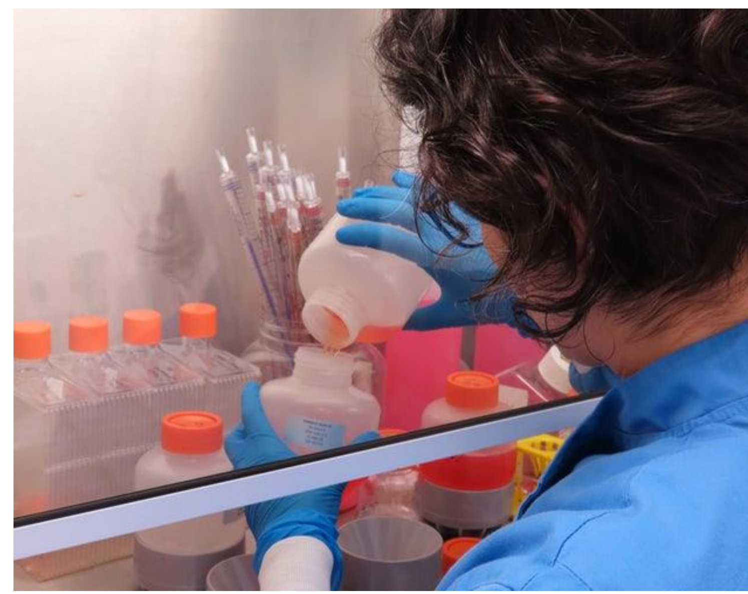
How to develop immunity to COVID-19

Types of vaccine





Different types of vaccines….

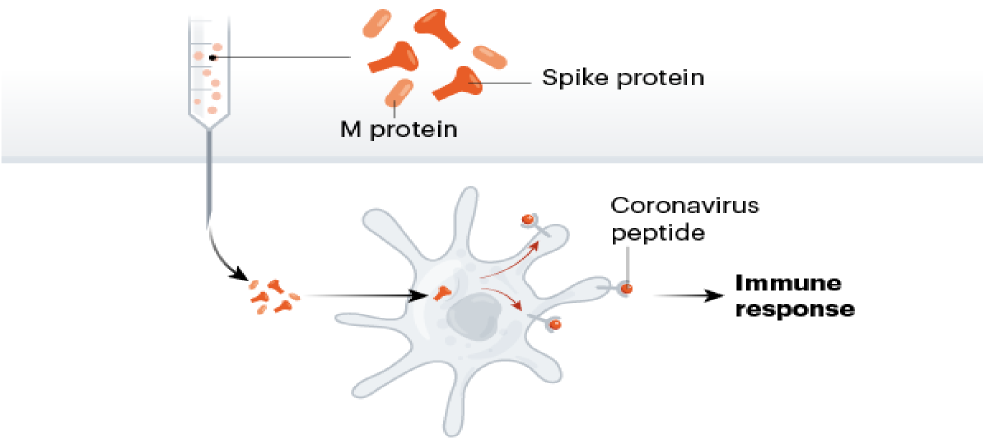


Different types of vaccines….

PROTEIN-BASED VACCINES

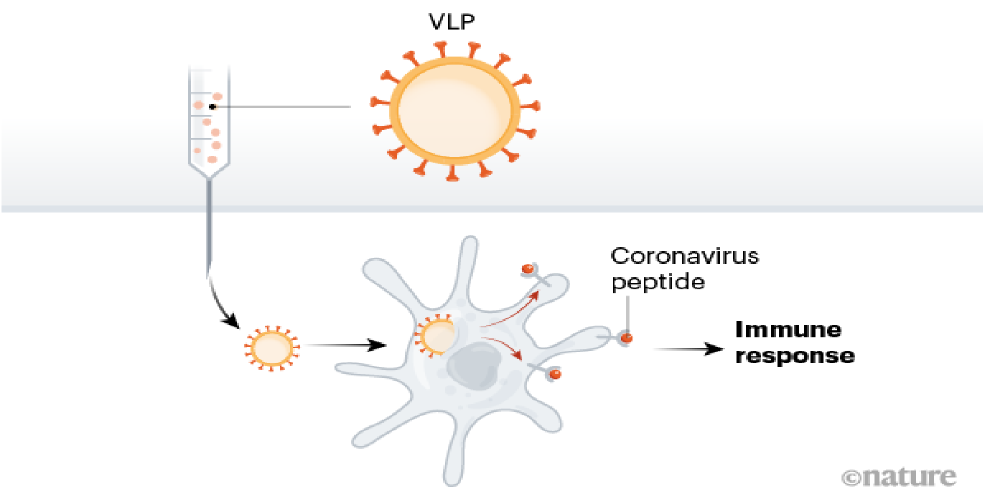
Protein subunits

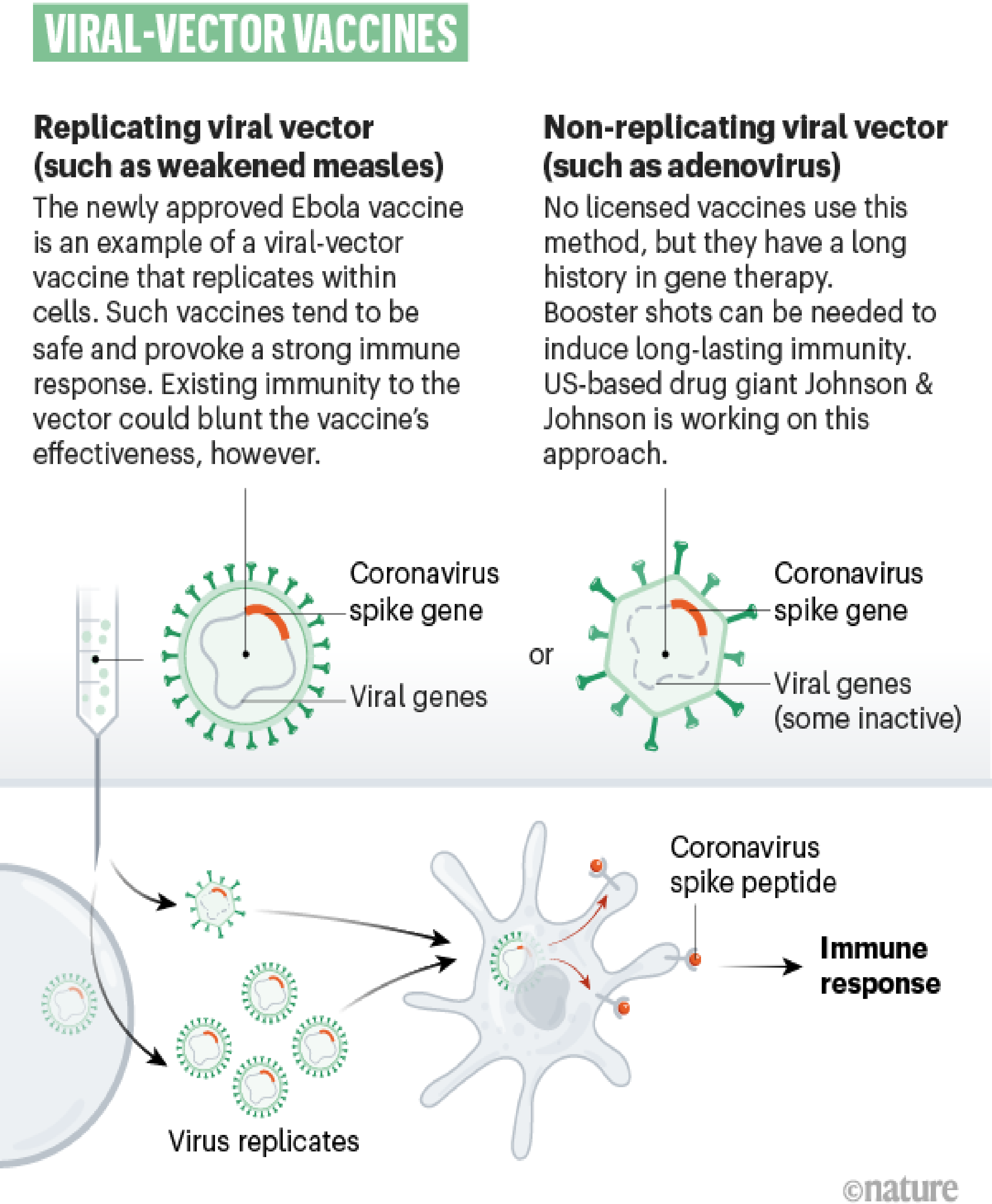
Twenty-eight teams are working on vaccines with viral protein subunits — most are focusing on the virus's spike protein or a key part of it called the receptor binding domain. Similar vaccines against the SARS virus protected monkeys against infection but haven't been tested in people. To work, these vaccines might require adjuvants — immune-stimulating molecules delivered alongside the vaccine — as well as multiple doses.



Virus-like particles

Empty virus shells mimic the coronavirus structure, but aren't infectious because they lack genetic material. Five teams are working on 'virus-like particle' (VLP) vaccines, which can trigger a strong immune response, but can be difficult to manufacture.

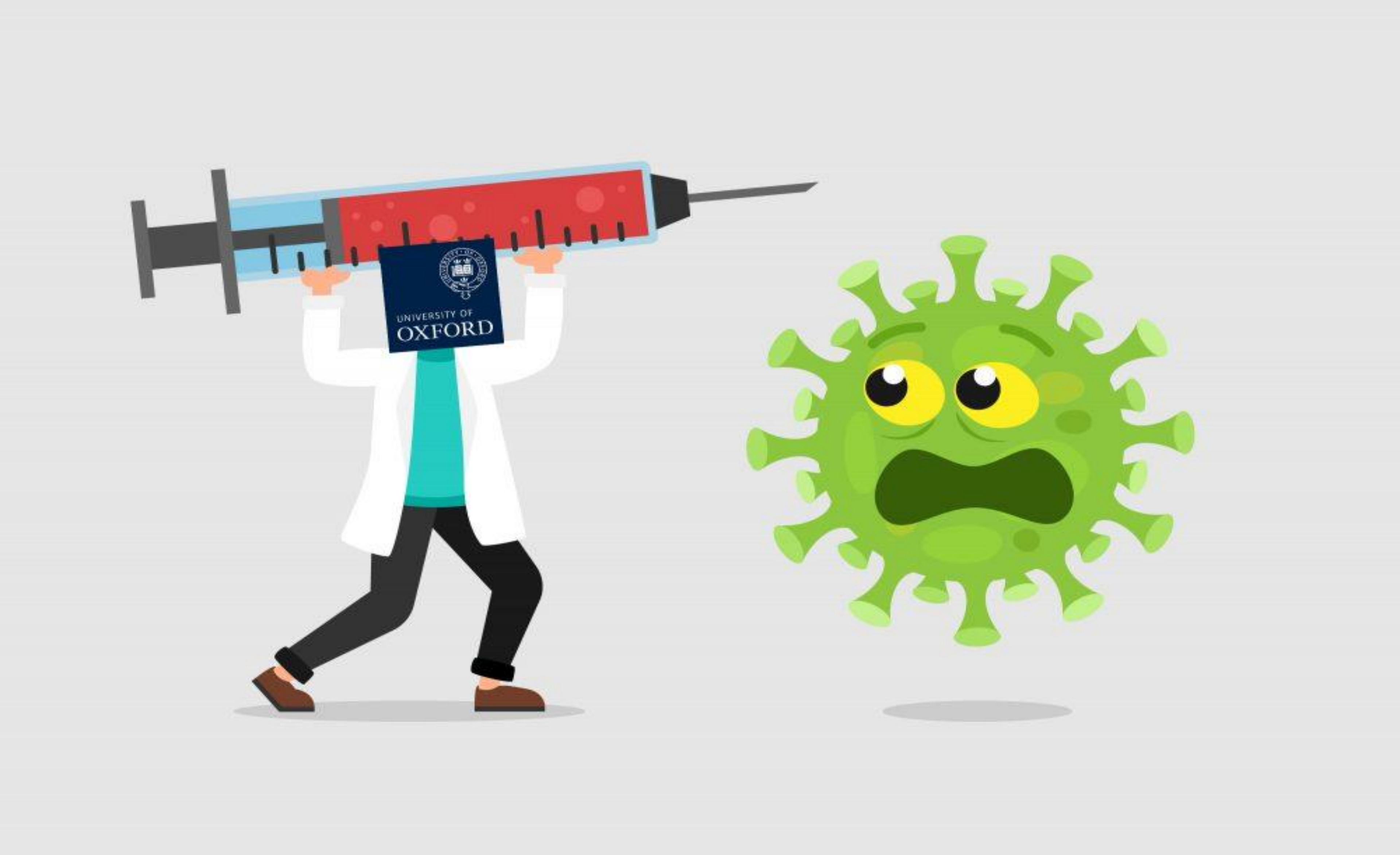


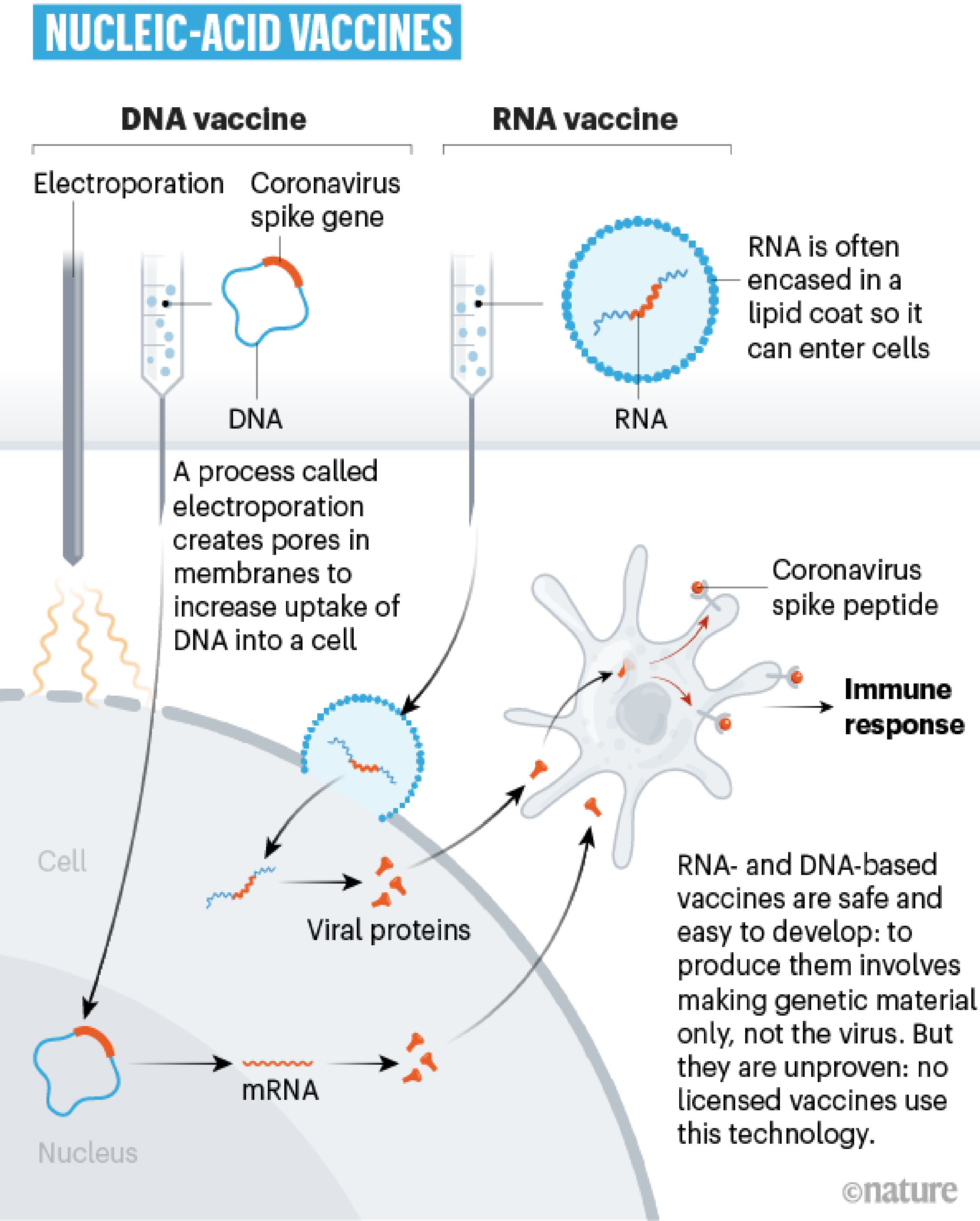


Different types of vaccines....

Since these appeared in The journal Nature…we now have vaccines using this approach. I use the diagrams for nice illustrations.

Oxford/AZ is an example of the last





Different types of vaccines....

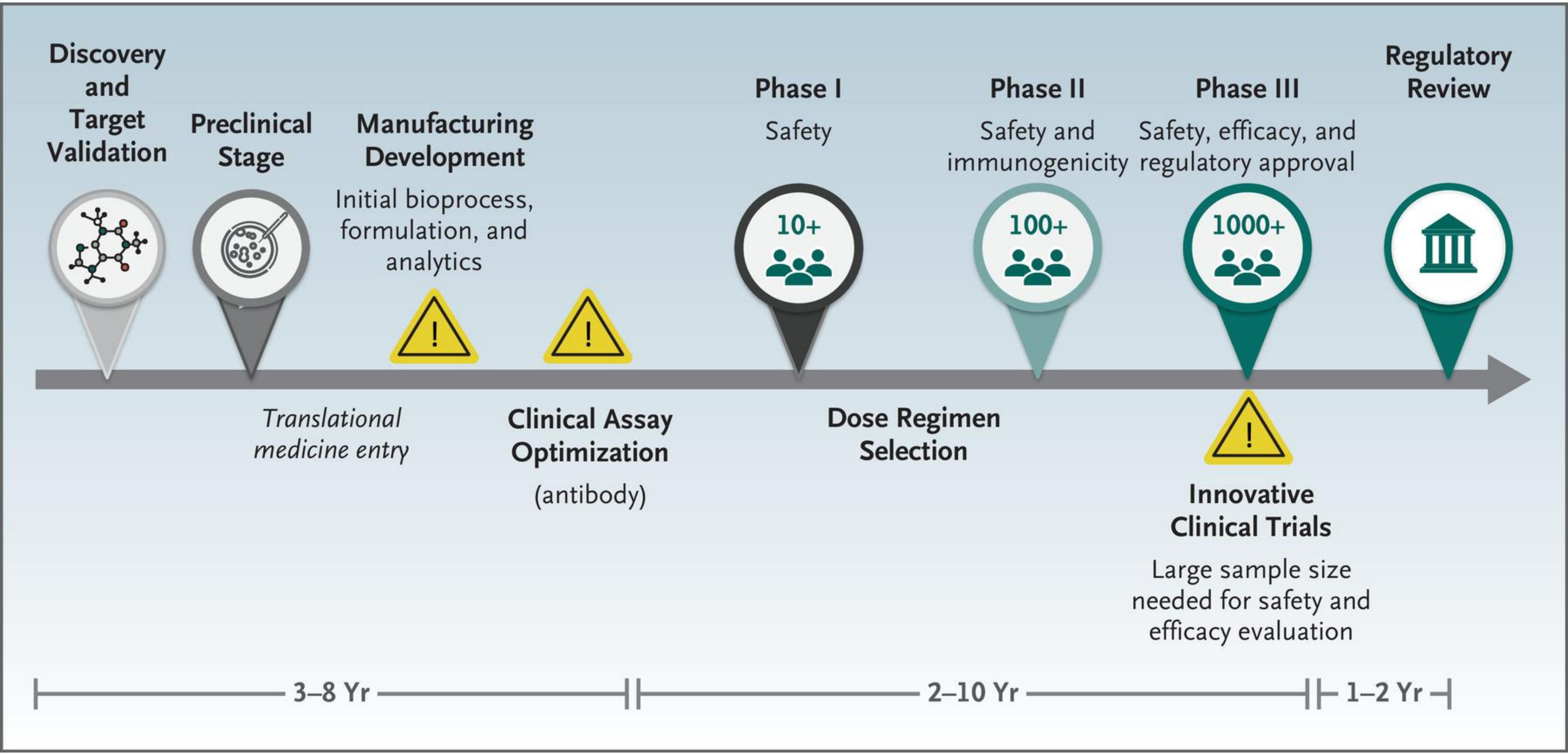
mRNA: Cells own protein-making machinery, ribosomes, make parts of the virus (in most cases, the spike protein)

...How life changed since these figures appeared in Nature!

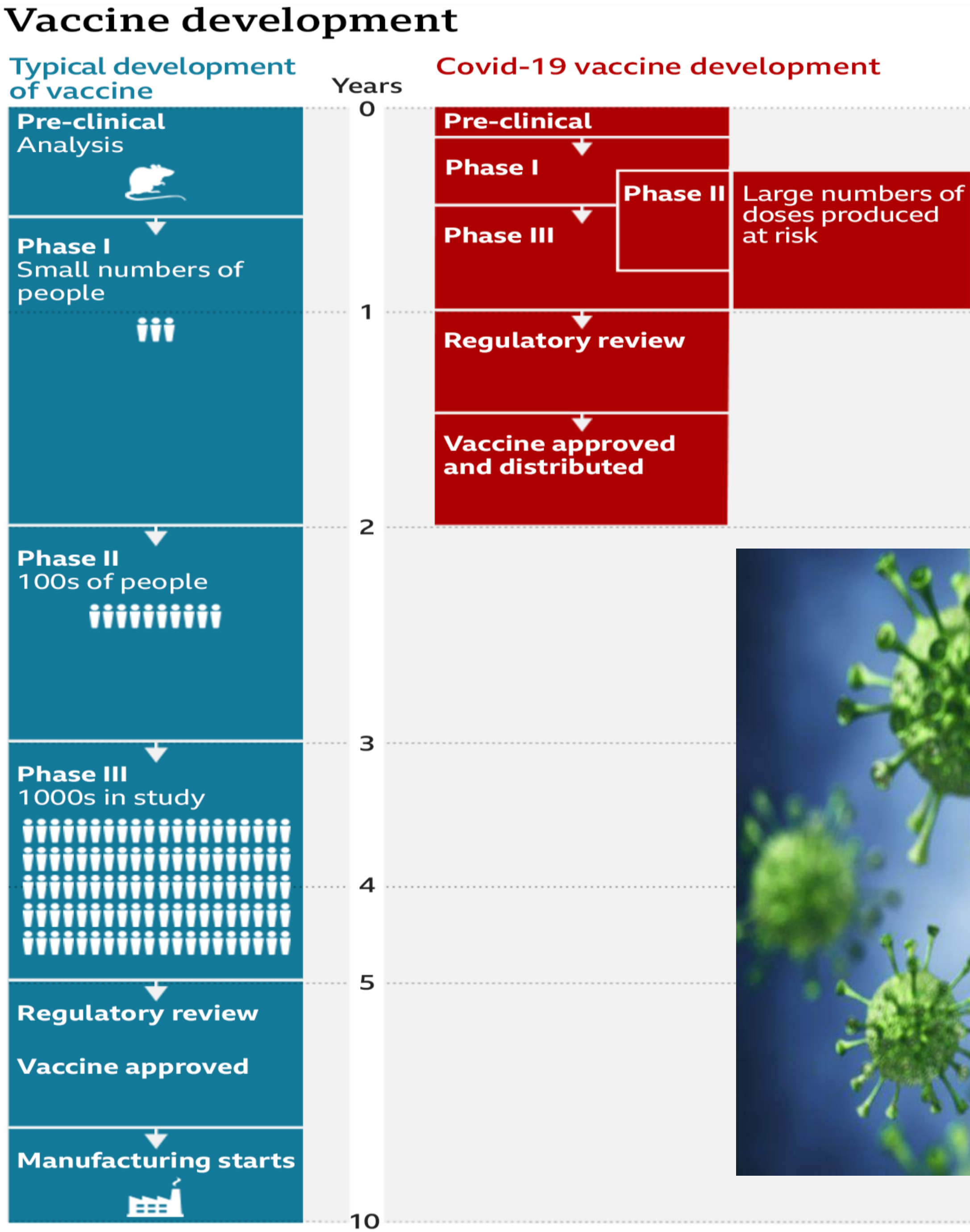
Quick breakout discussion

- Which technologies are likely to generate ‘better vaccines’, likely to be “easier” to use, likely to be good against variants, safer, may work better in some populations than others, etc.?
- Which are likely to be easier to scale?
- Do competing technologies help or hinder?
- Or should we exploit the many technologies and manufacturing and delivery capacities?
- Are some technologies more for the long-term and others of short duration value?
- How do you interpret vaccine efficacy (VE) data?
- What about vaccine safety data?

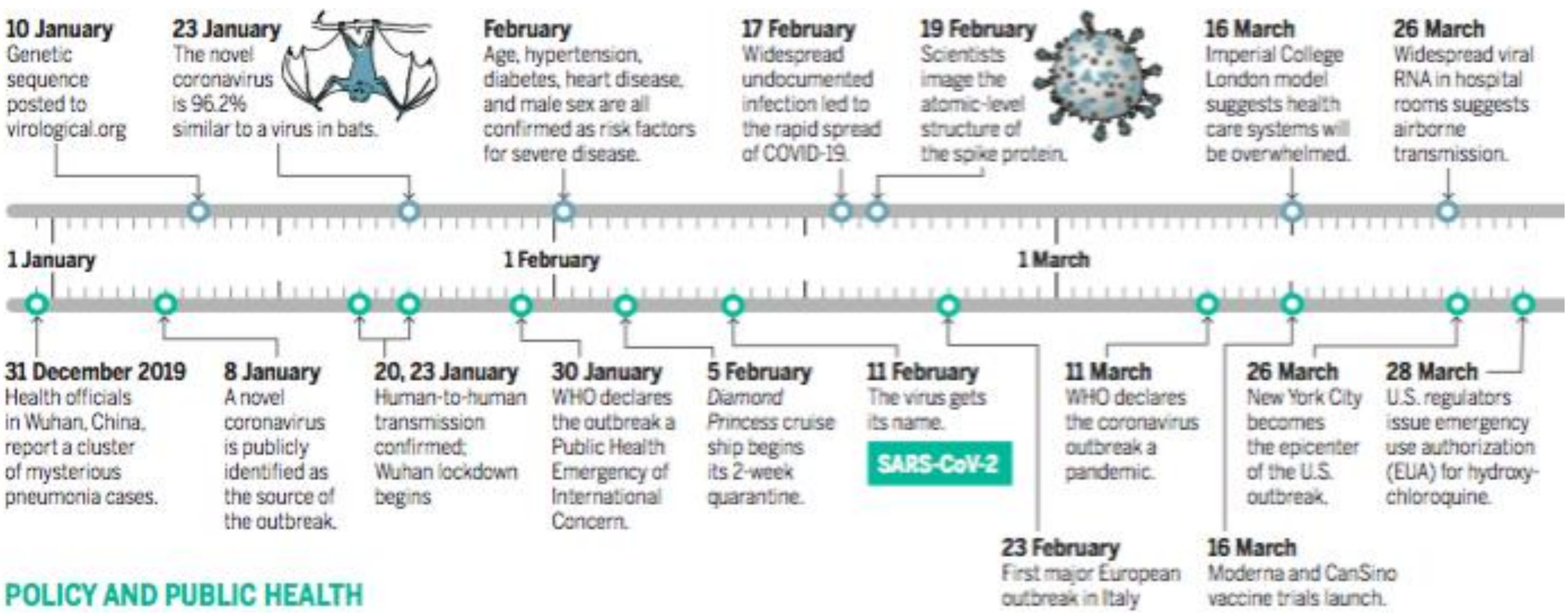
The normal stages of development…too long in a pandemic



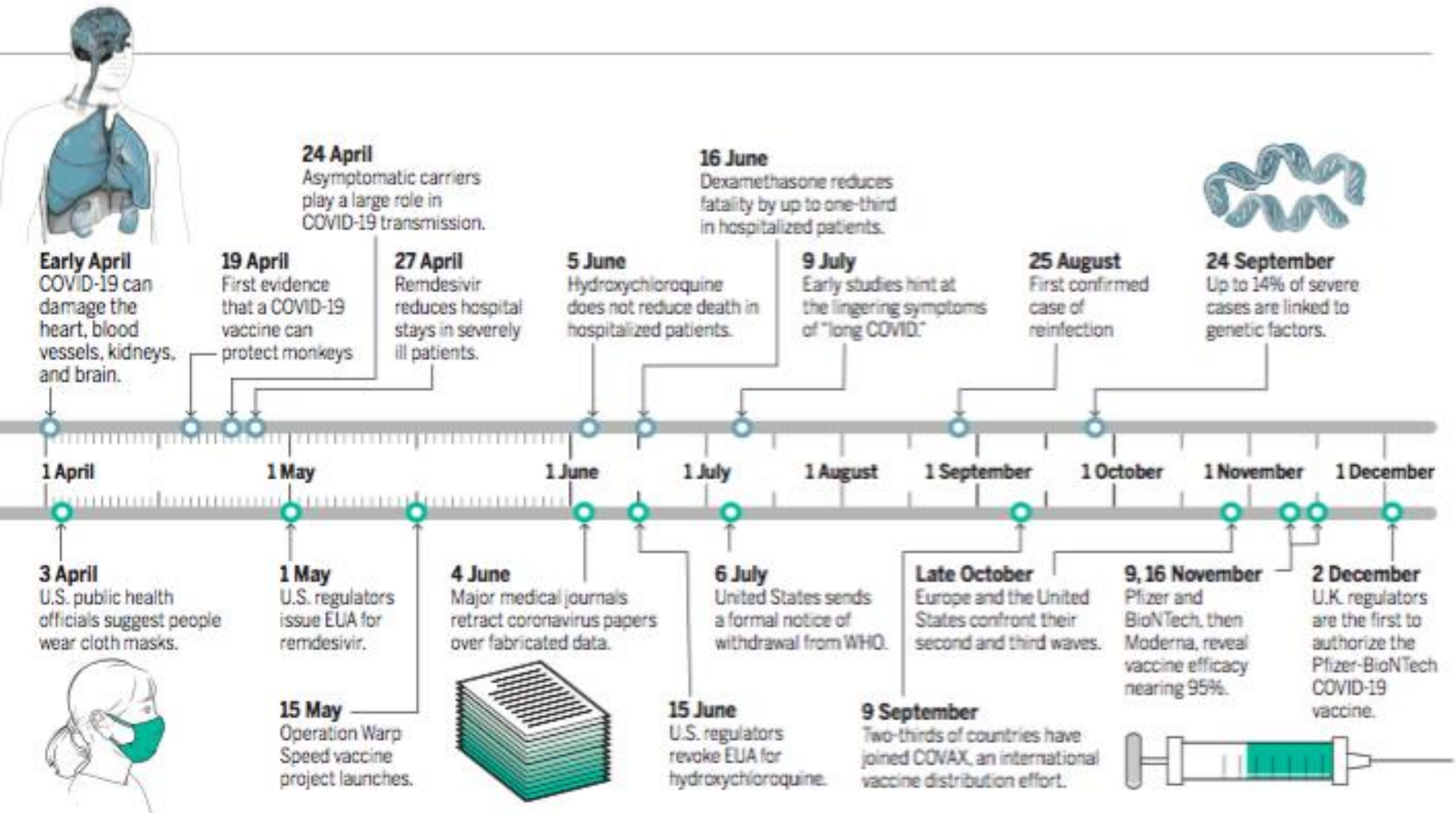
Shrinking time-lines in a global emergency is critical



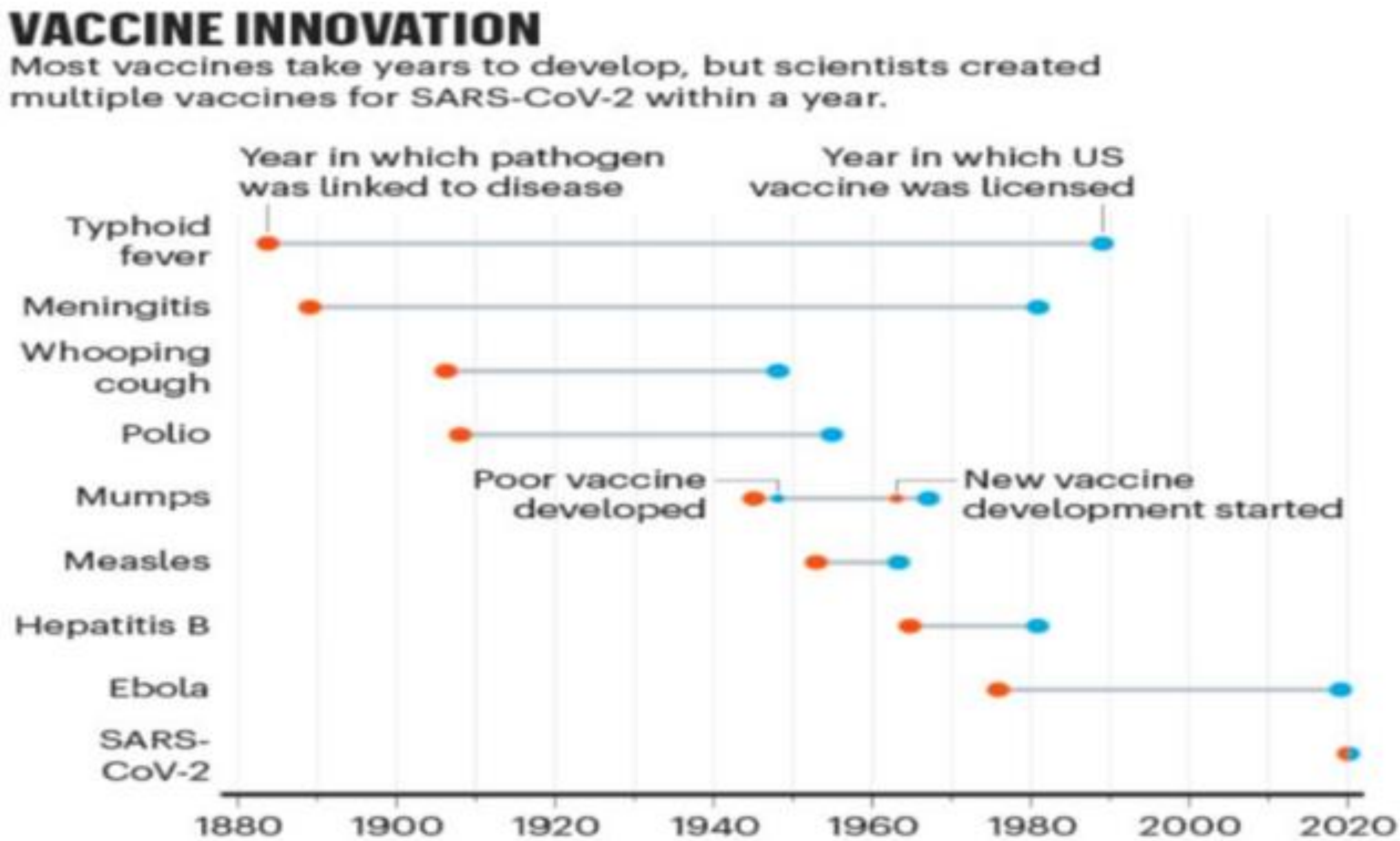
A remarkable time-line (or, what you can do if you put your mind to it… and back that up with resources!)

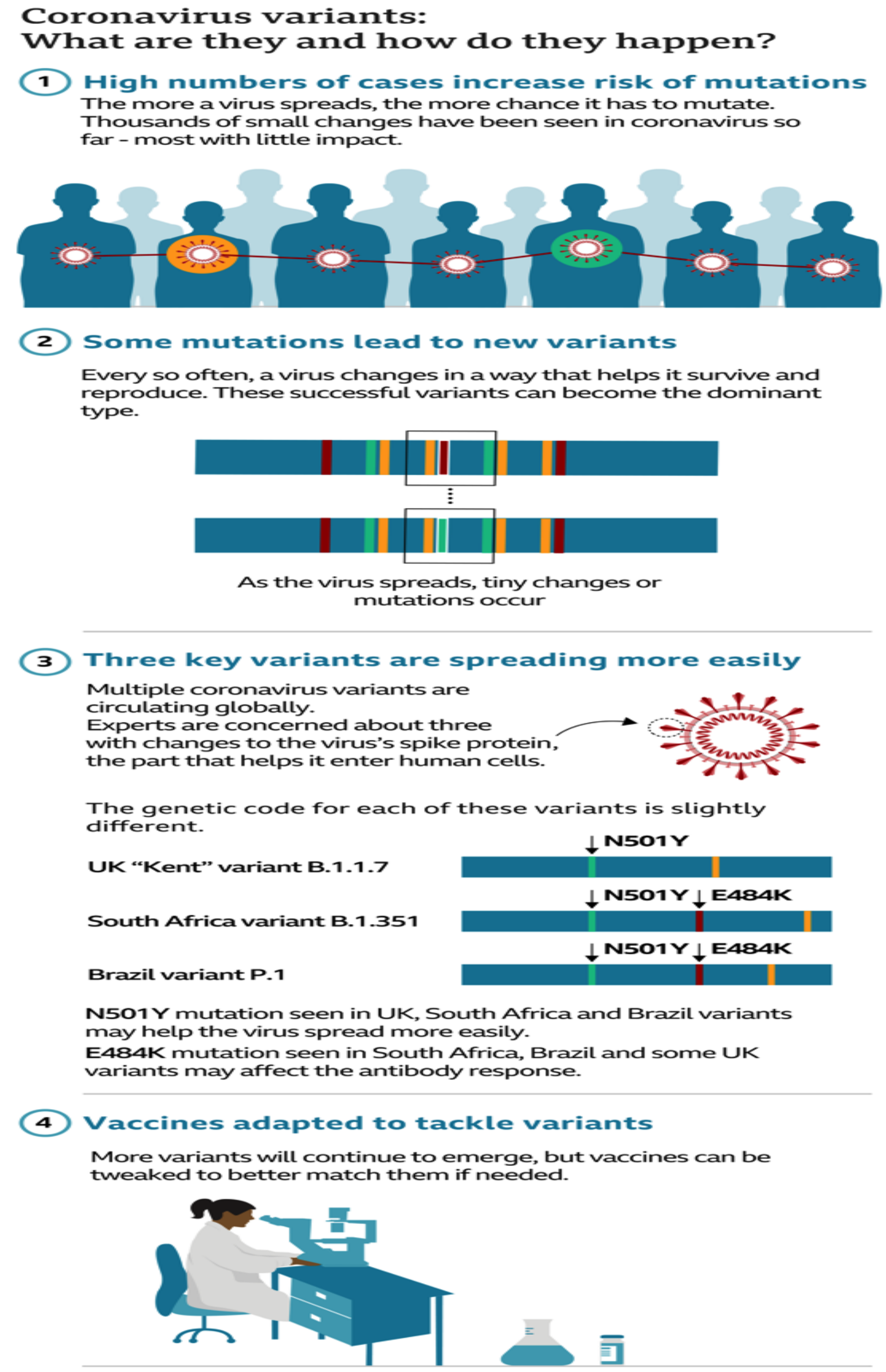


Remarkable time-line…



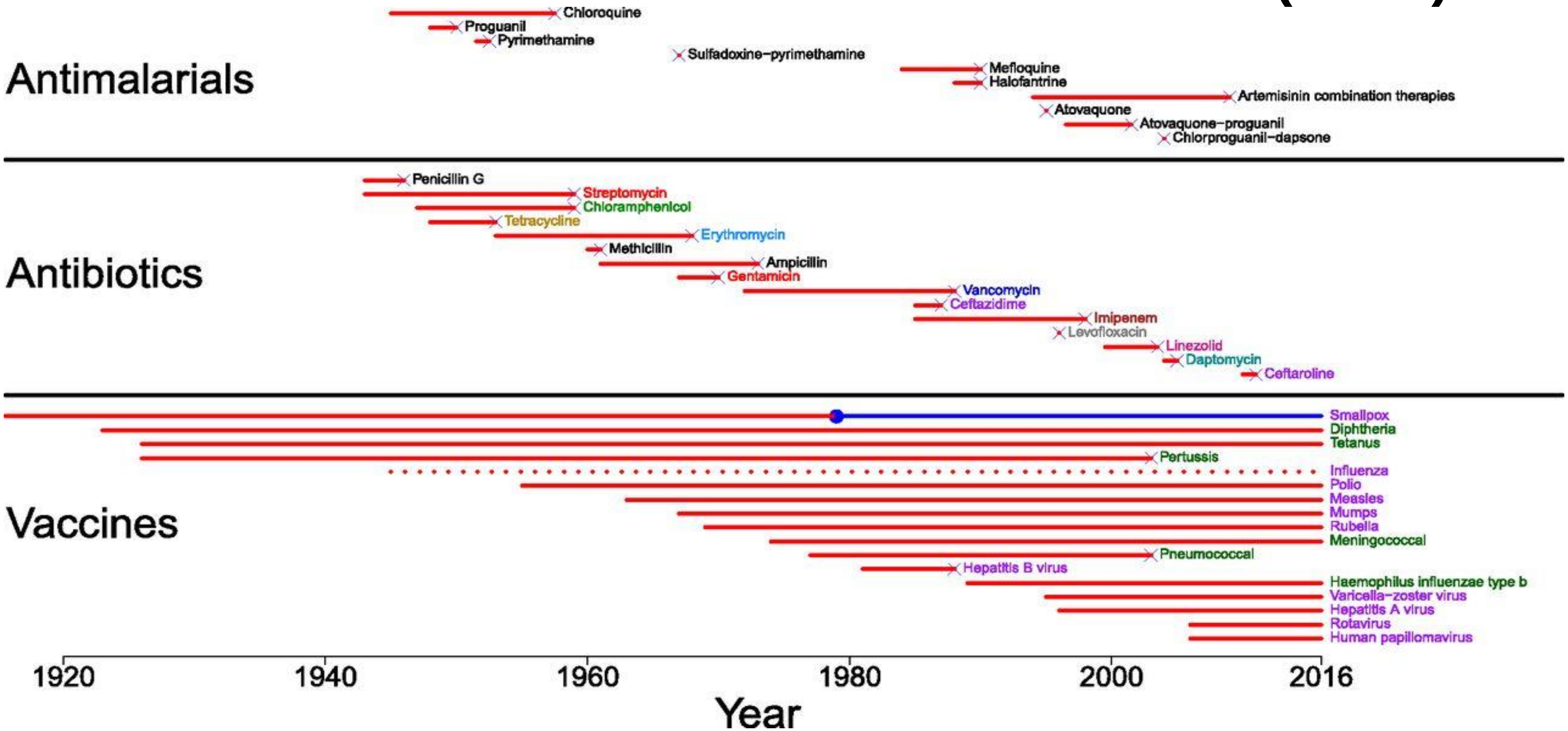
Vaccine development timelines for different diseases





What about variants?

Time to first documented failure in humans due to resistance (“x”)



David A. Kennedy, and Andrew F. Read PNAS 2018;115:51:12878-12886

Different classes of antibiotic drugs = different colors.

Viral vaccines =purple

bacterial vaccines = green

= small pox eradication (no more chance to evolve resistance)

Dotted = Influenza routinely changed to try to match circulating virus strains

Three key features of most vaccines prevent resistance evolving

All documented cases of vaccine resistance = **at least one of the following missing**:

- Vaccine induces an immune response that protects hosts by targeting **multiple non-overlapping virus epitopes** (= parts of an antigen that are recognized by the immune system, i.e., by antibodies, B cells, or T cells) **simultaneously**, thereby generating **redundant and evolutionarily-robust protection**
  - Resistance likely **requires multiple mutations**, not just one, on the same genetic background
  - Redundant immune protection delays the evolution of vaccine resistance, a bit like combination drug therapies delaying the evolution of antibiotic resistance, or combination antimalarial drugs that delay antimalarial resistance
  - Resistance evolves quickly against SARS-CoV-2 monoclonal neutralizing antibodies relative to combinations of antibodies
  - (yet to be demonstrated?) for SARS-CoV2 diverse T-cell responses can similarly delay resistance evolution
- Vaccine **suppresses pathogen growth within hosts** and **stops transmission from vaccine-protected hosts**
  - little pathogen diversity generated during pathogen growth within vaccinated hosts, and effects of selection on any resistance mutations are minimal
- Vaccine-induced immune response protects against **all circulating serotypes of the target pathogen**
  - new virus variants would need to be generated before resistance could be a problem, since vaccine resistance does not pre-exist

Combined together, these three features would make the probability of **resistance emergence vanishingly small. There lack makes it much more probable.**

Other things to keep in mind

- Antimicrobial drugs can be tailored to individual patients at time of treatment (if good diagnostics)
- But choice of a vaccine is done a long time before pathogen exposure and can’t be adapted
- As soon as vaccine resistance emerges, all vaccinated individuals could be unprotected
- Widespread resistance might render entire vaccination campaigns retroactively ineffective
- Because pre-existing antibodies frequently interfere with vaccine efficacy, we cannot assume a new vaccine would restore protection
- Large fraction of COVID-19 candidate vaccines target the spike protein of the virus or the receptor binding domain of the spike protein, such that evolution of vaccine resistance against one vaccine could simultaneously undermine others (= ‘collateral’ or ‘cross’ resistance in the language of antimicrobial drug resistance)

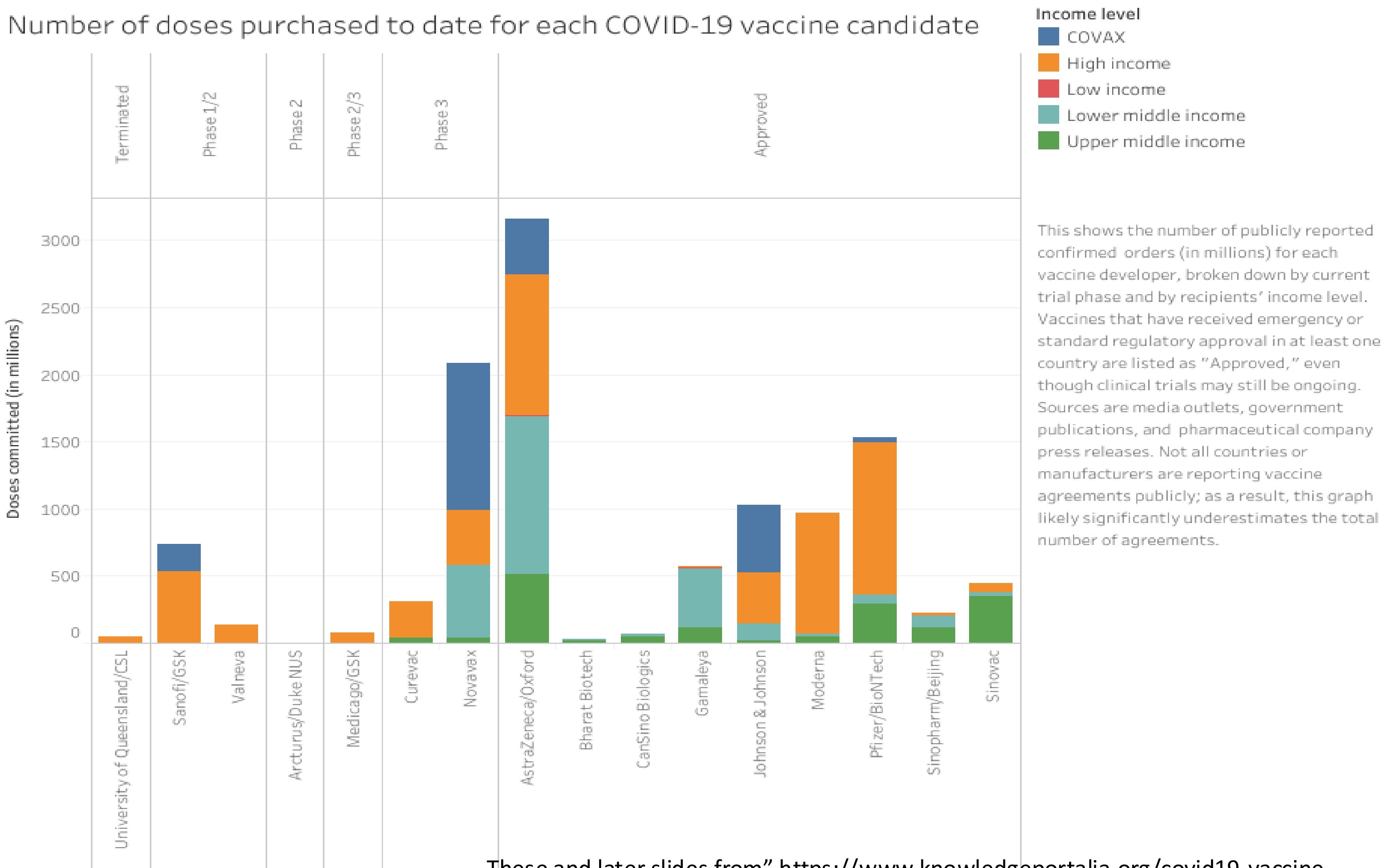
Breakout group discussion

- What are the likely future pathways for resistance?
- How might vaccine deployment strategies be used to prevent resistance?
- (Remember that many cases of resistant COVID-19 evolved from very sick patients fighting the virus over a long stretch of time… i.e., within-host evolution)
- What about tweaking vaccines? What are the logistics of that? Is it now worthwhile?
- Are new variants bound to be less virulent (c.f. recent Jan/Feb NERVTAG analysis)?
- As countries come off lockdown, what are the risks and how should they be mitigated?

Did anyone spot the trial issue?

- Quantifying redundancy of immune protection generated by vaccination is key for determining the likelihood of resistance evolution
- So, all vaccines should be assessed as early as possible for the likelihood they will drive resistance evolution
- This assessment can be in a controlled manner during clinical trials, and not waiting for promising efficacy results to evaporate after vaccine is licensed
- Is this being done…?

What vaccines have sold well?

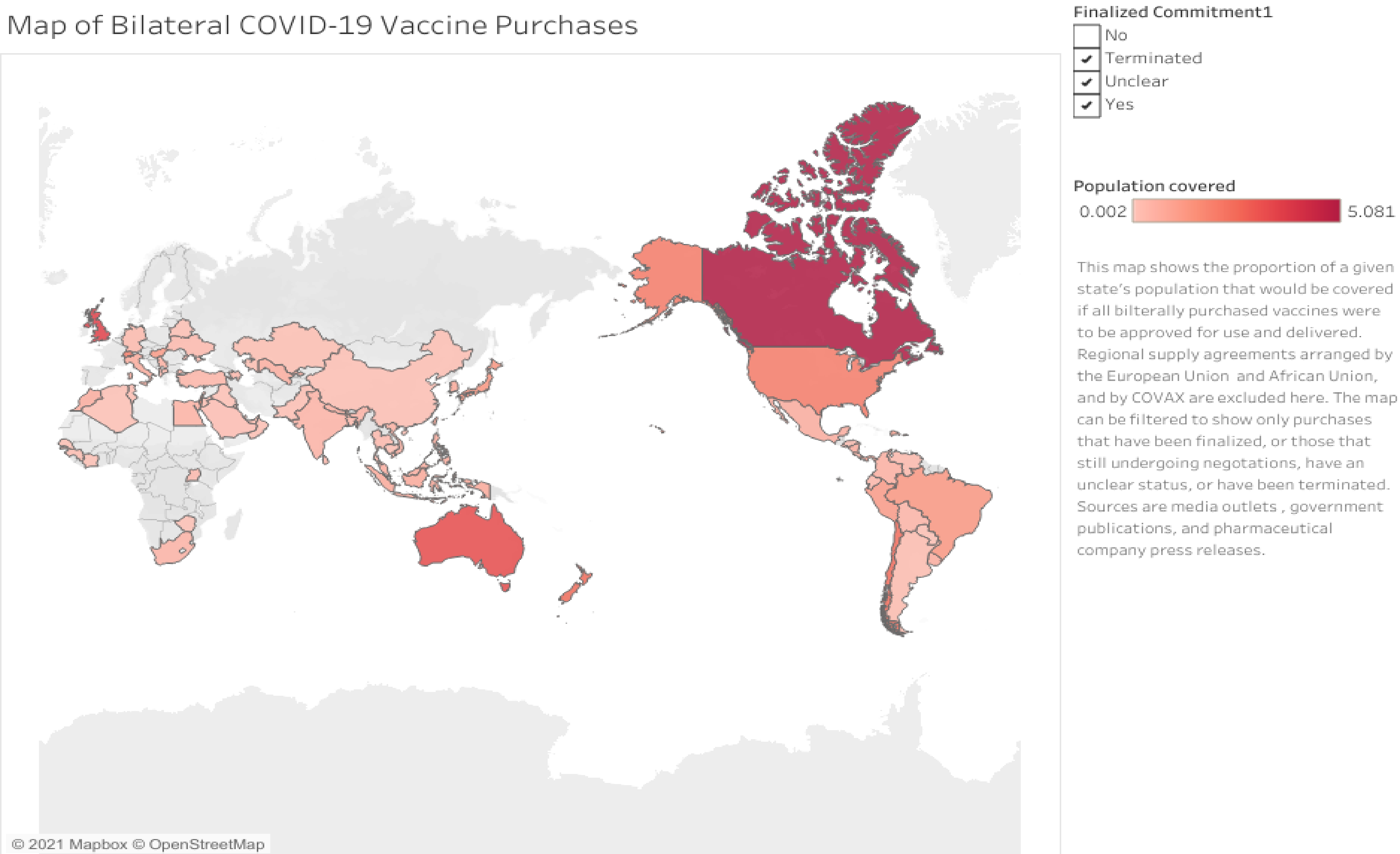


These and later slides from" https://www.knowledgeportalia.org/covid19-vaccine-arrangements

A year ago… 16 vaccine candidates with sales…but...

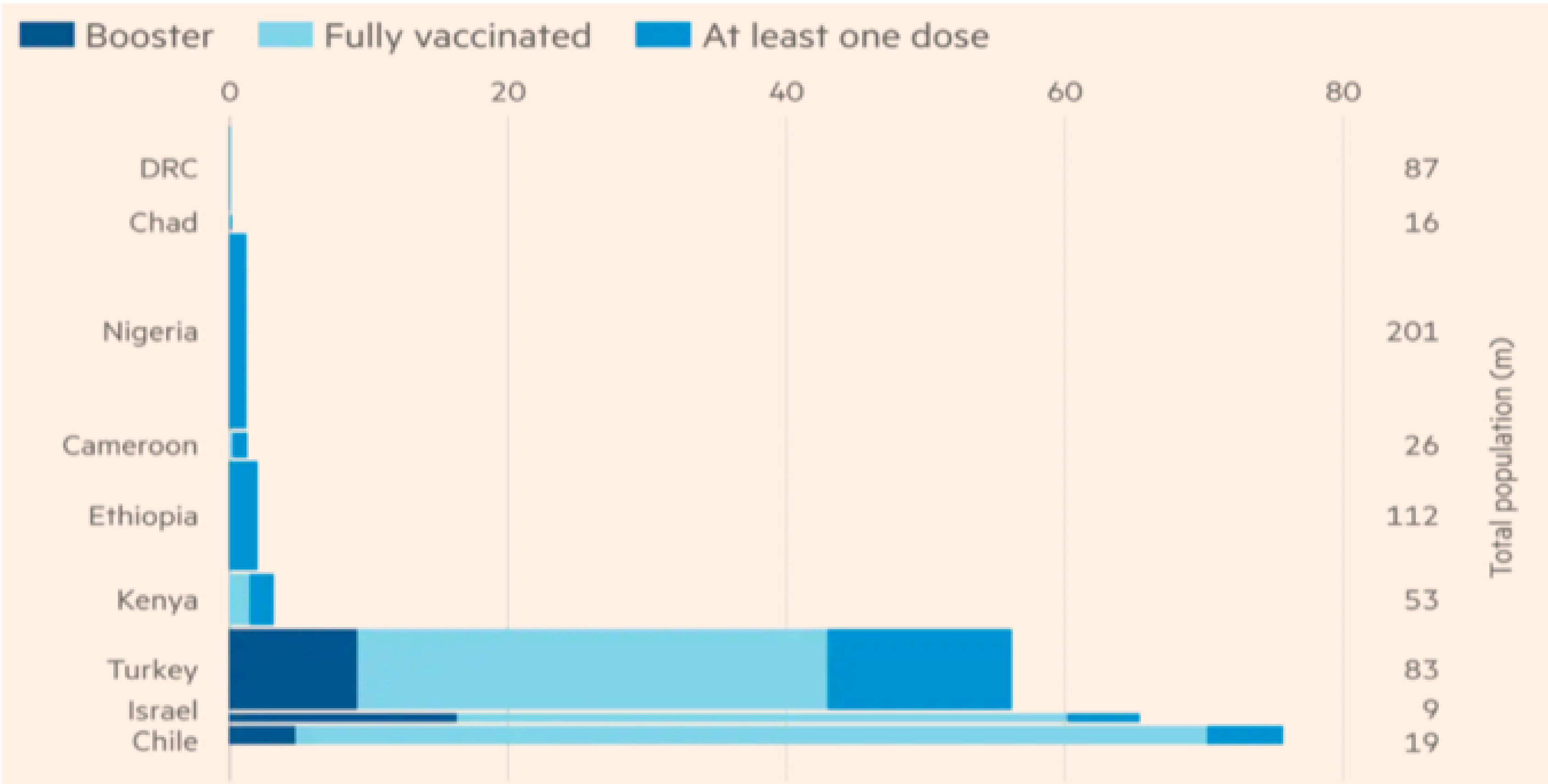
- 27 in late-stage (Phase 2 or 3) development or post-registration
- Publicly-reported purchase agreements for 16
- AstraZeneca publicly committed to supply the greatest number of doses – at approximately 3 billion doses
- Pfizer/BioNTech about 1.5 billion

Who has bought COVID-19 vaccines?



Locations where each vaccine is being used

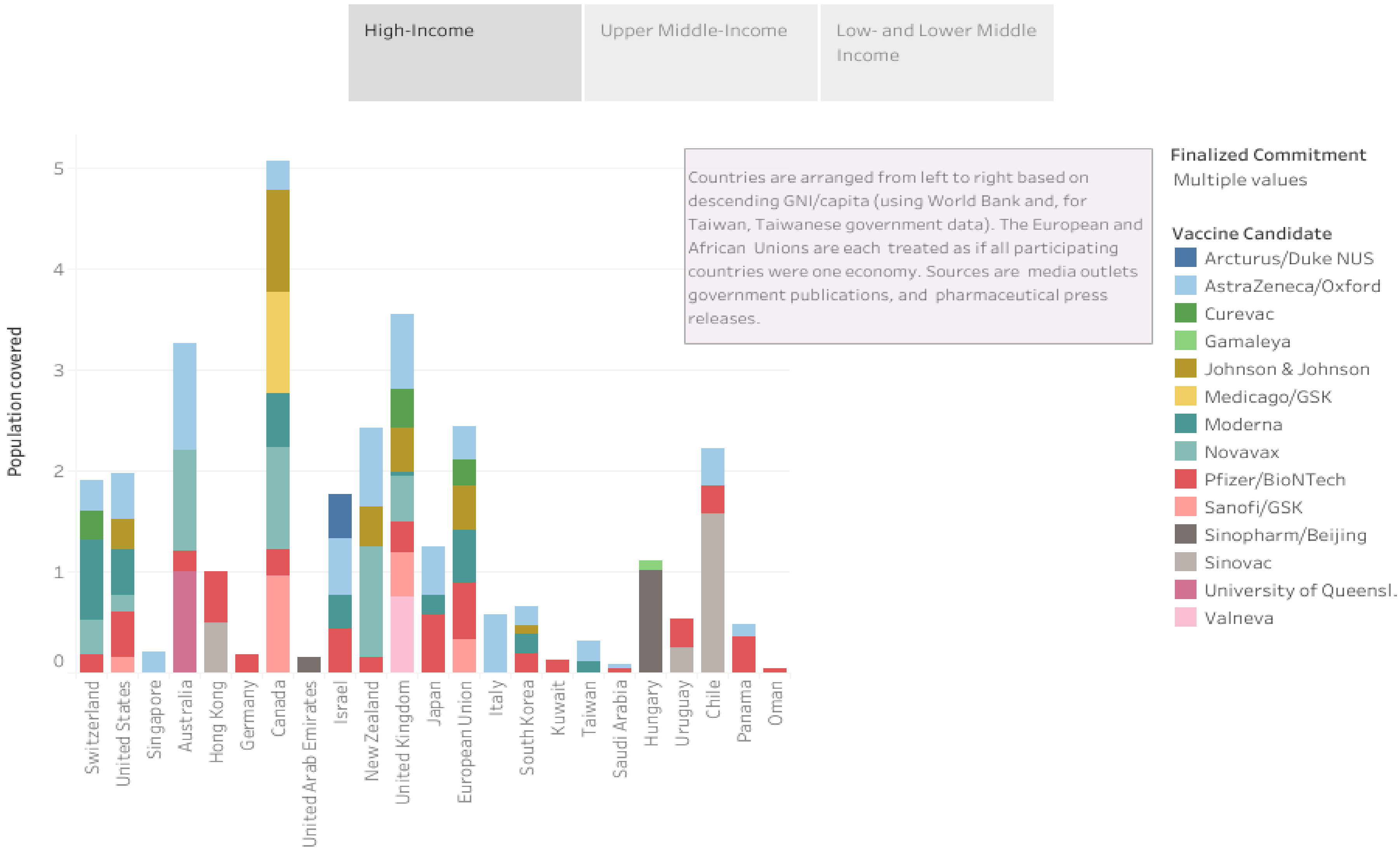
Booster shots



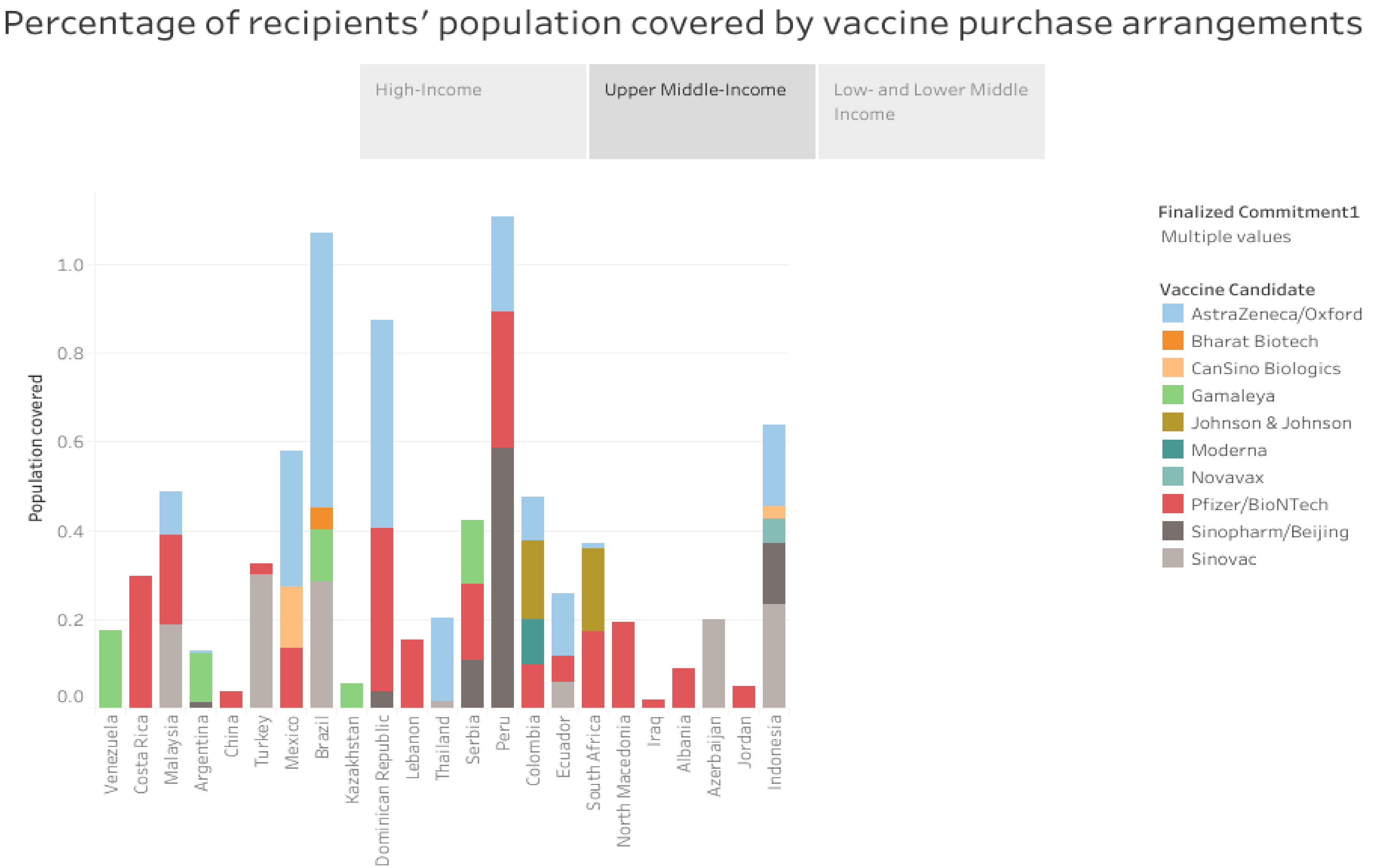
As of **early September 2021**, Turkey, Israel, and Chile had given more booster doses than all doses that had been given in half a dozen African countries put together including Nigeria, Ethiopia and the DRC which collectively make up 6% of the world's population

Some countries have rather a lot

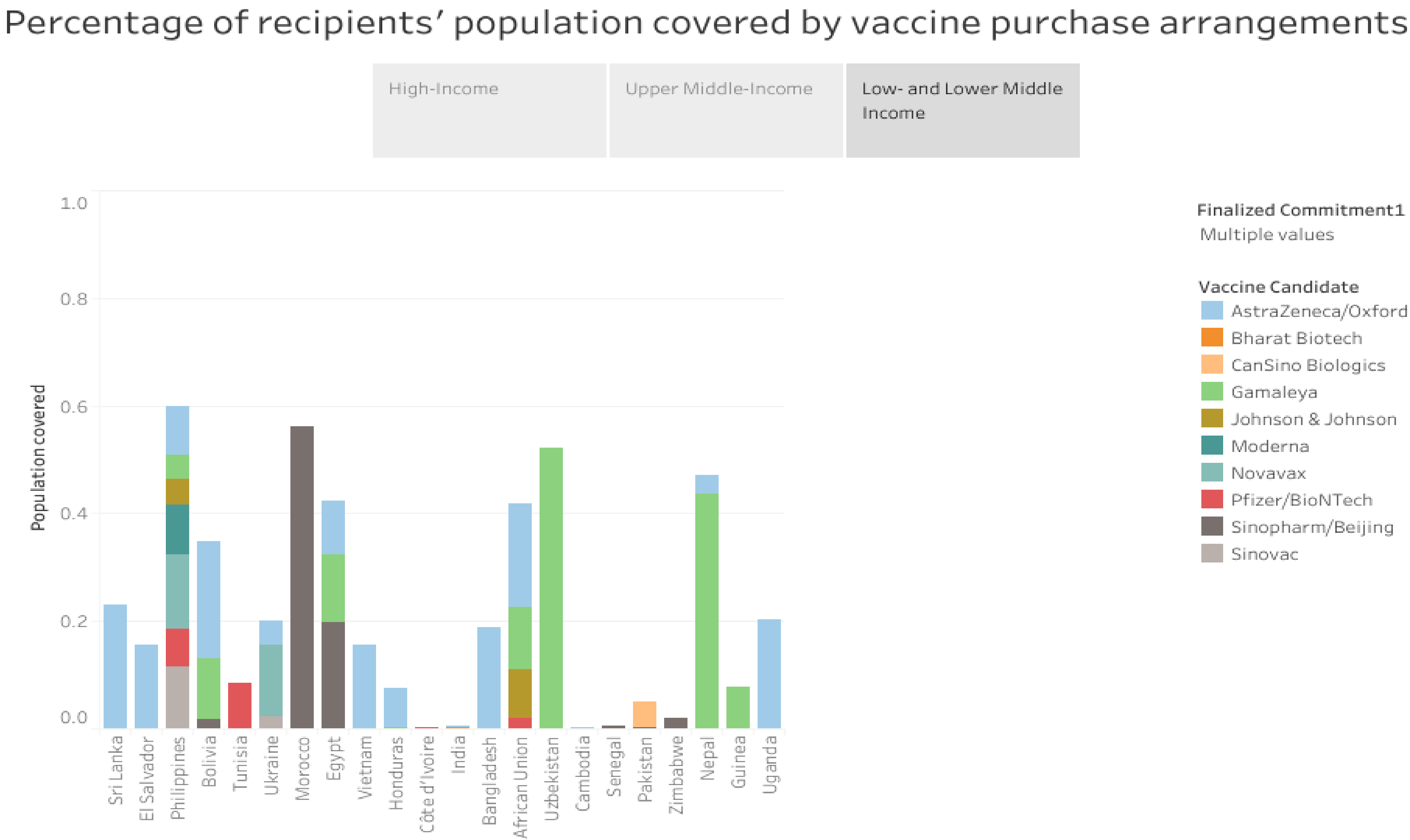
Percentage of recipients' population covered by vaccine purchase arrangements



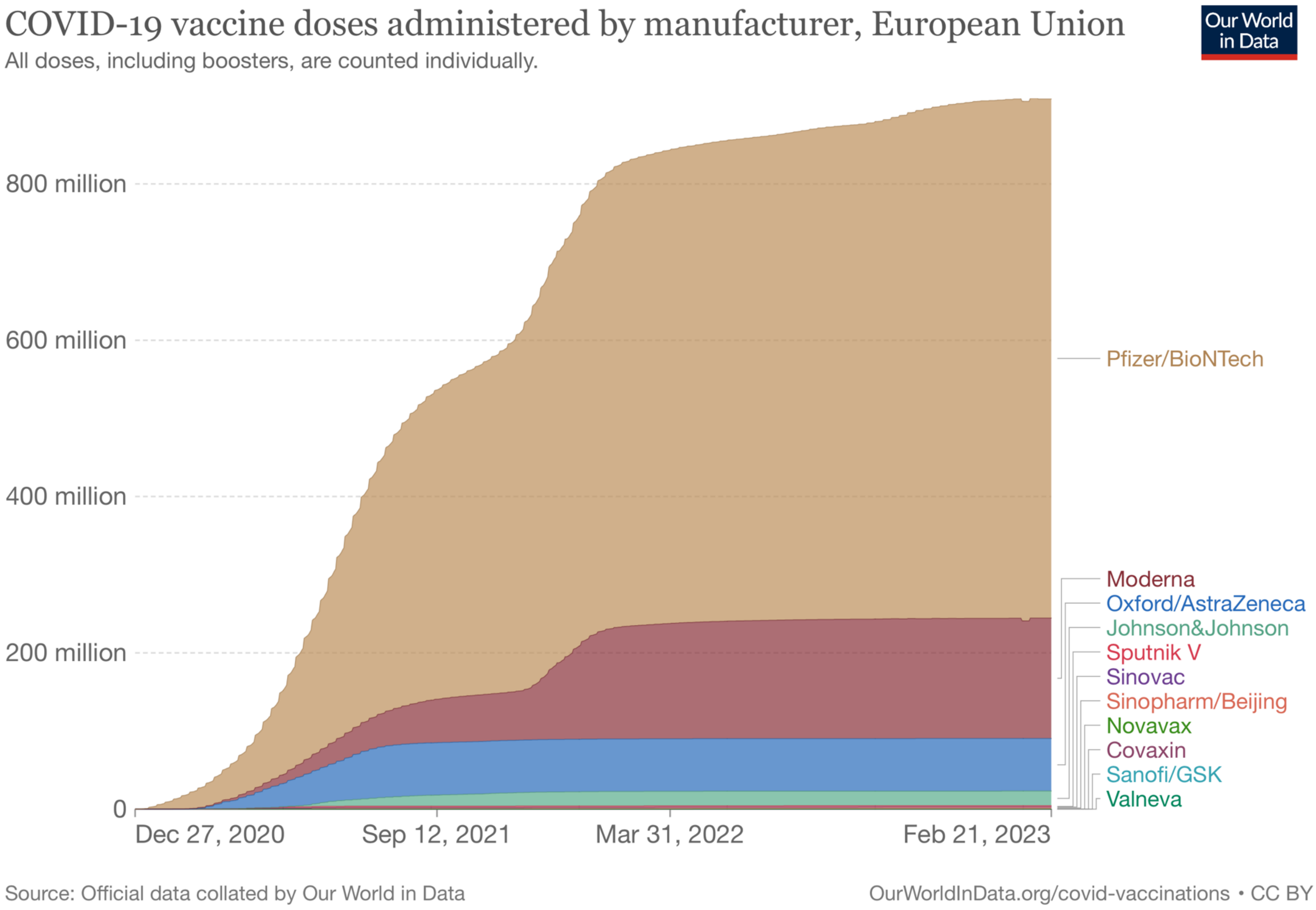
Others less so



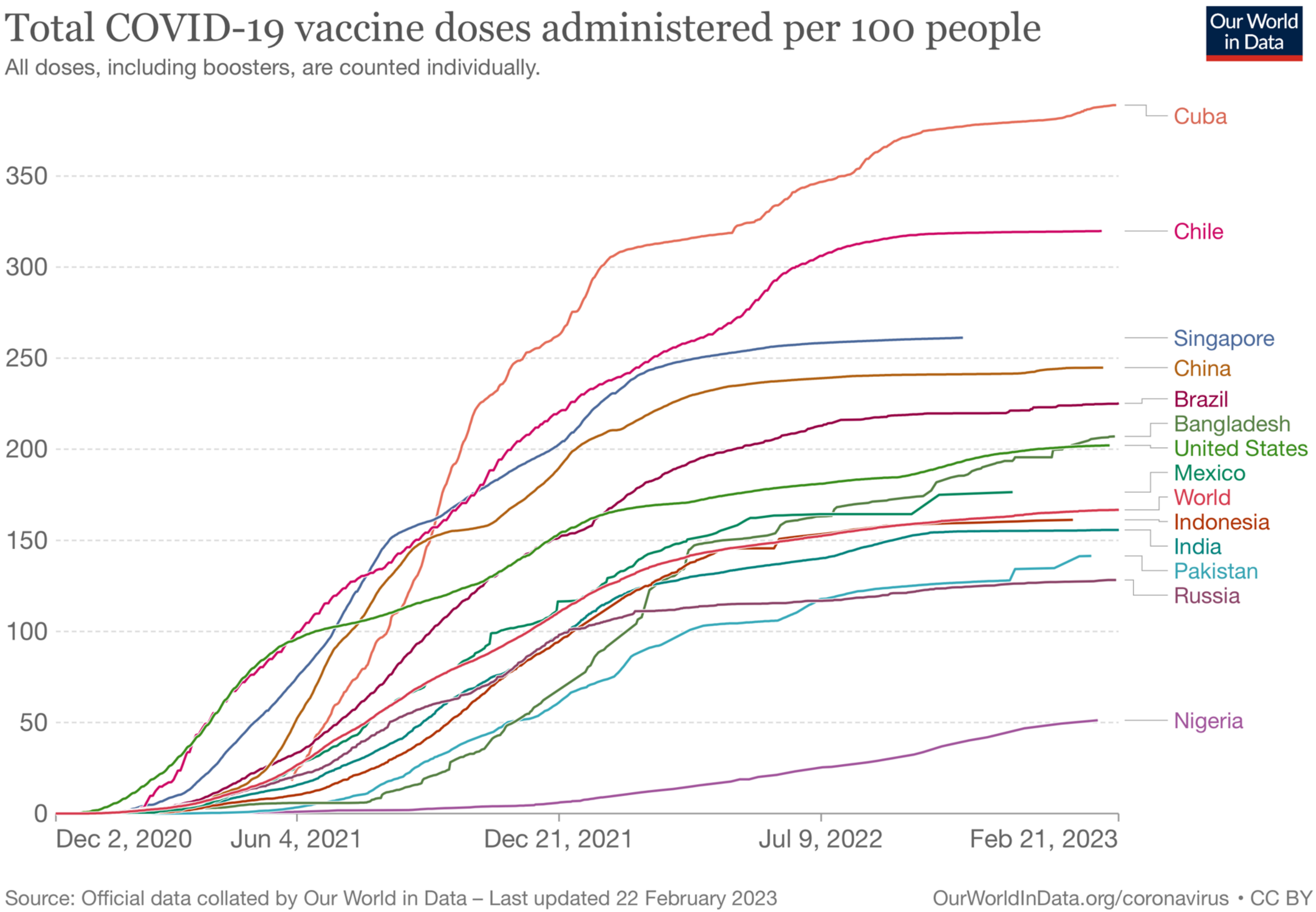
Others little (or none…not on diagram)



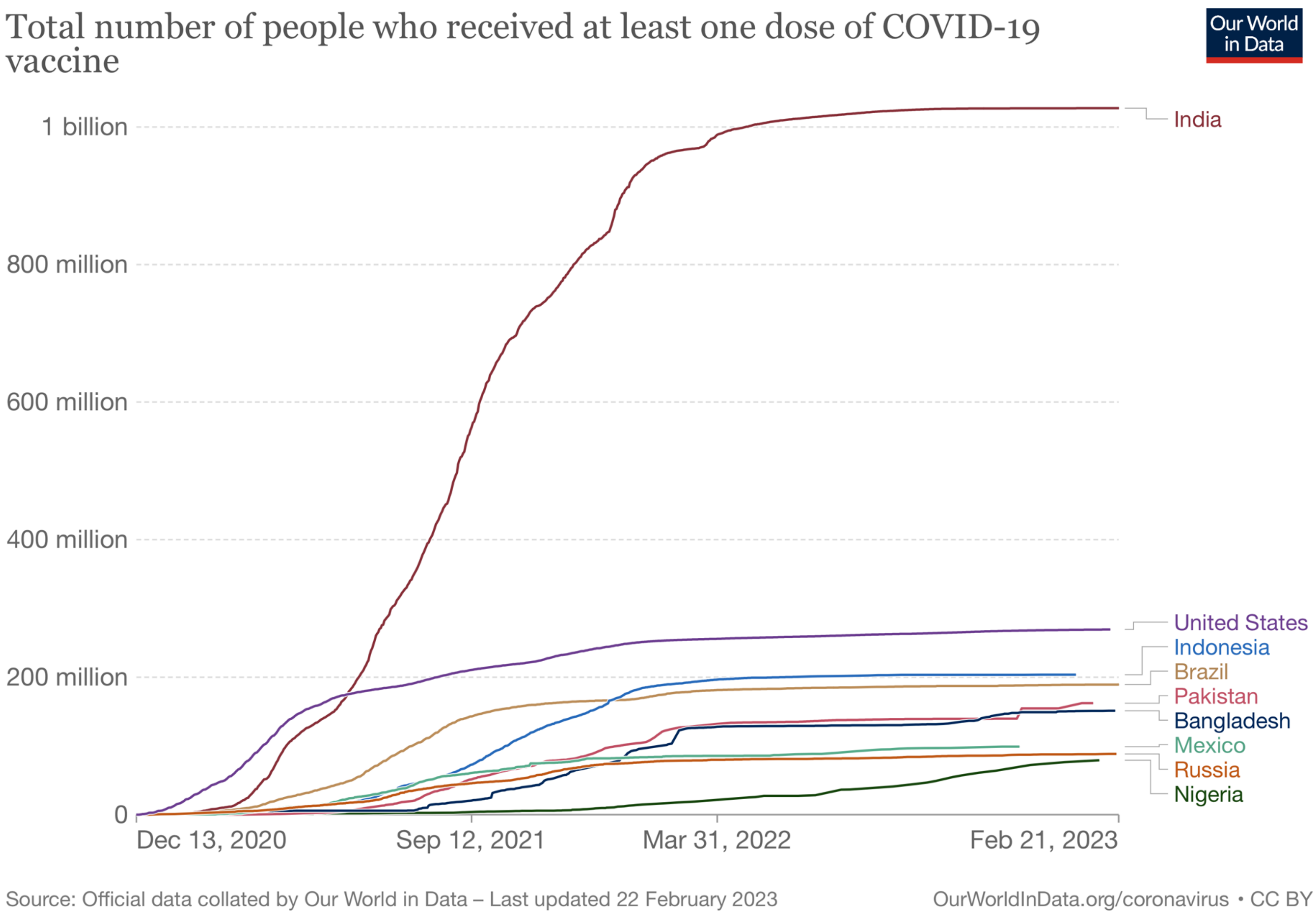
Vaccine doses by manufacturer, EU



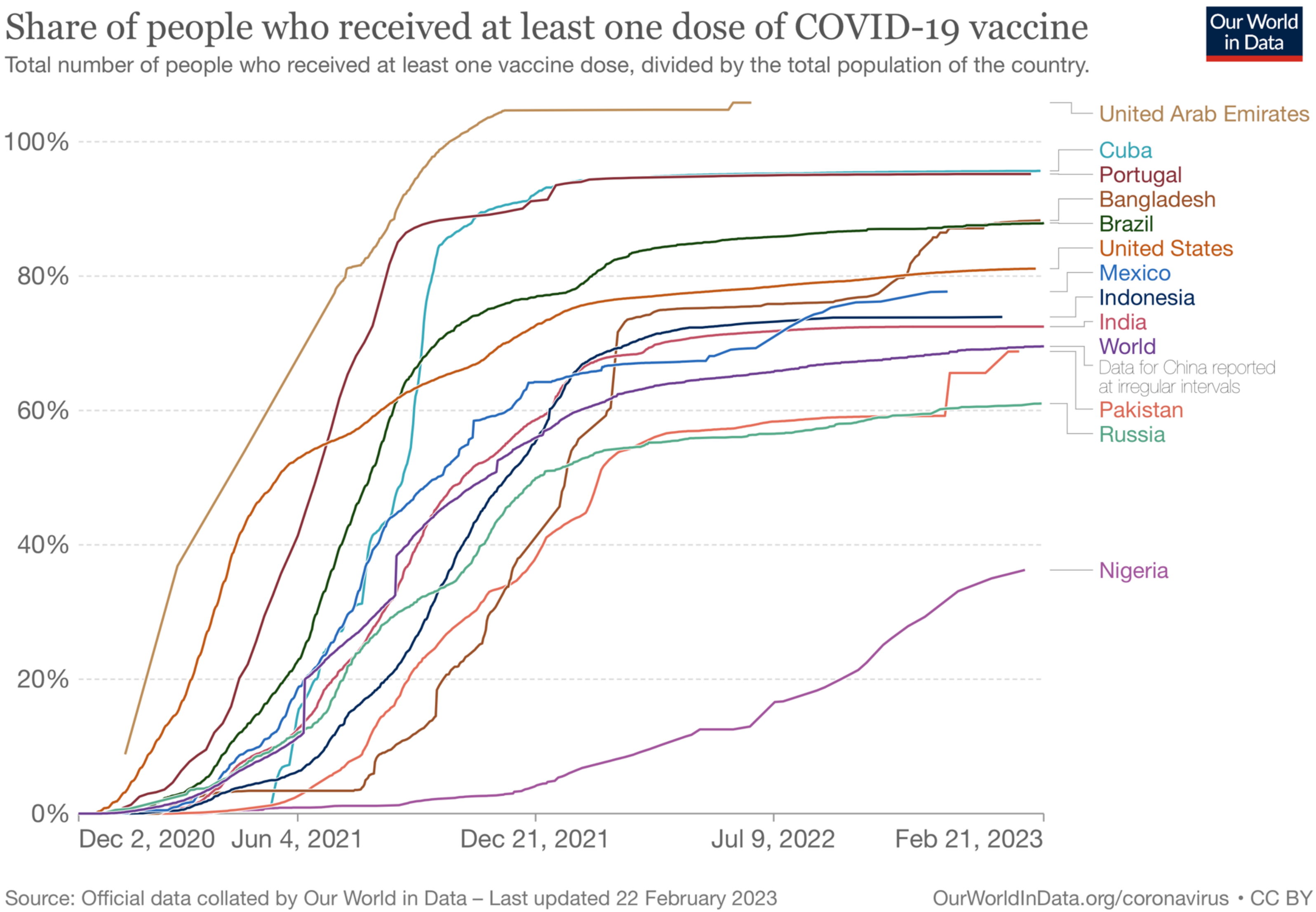
Total COVID-19 doses per capita



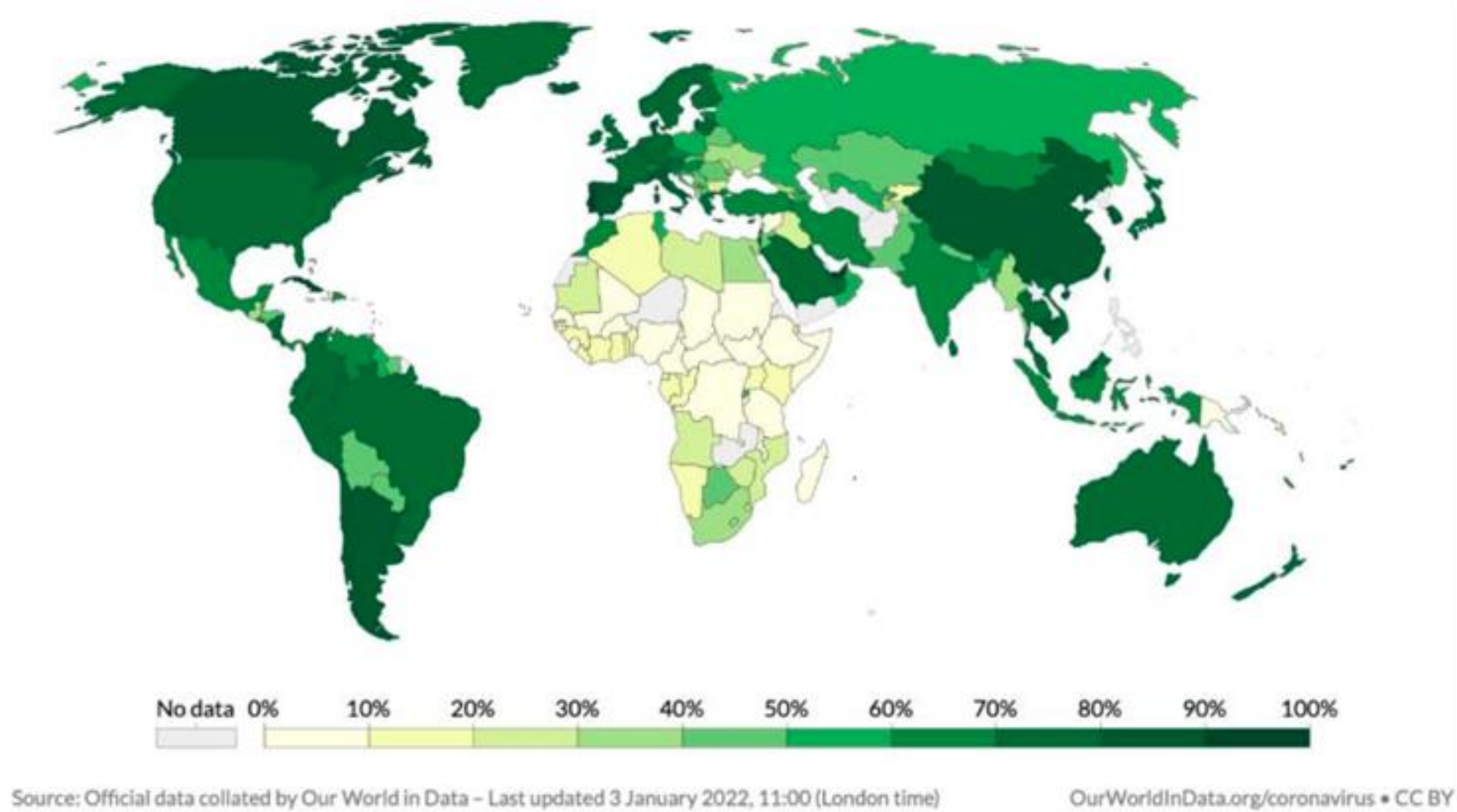
Number who received at least one dose



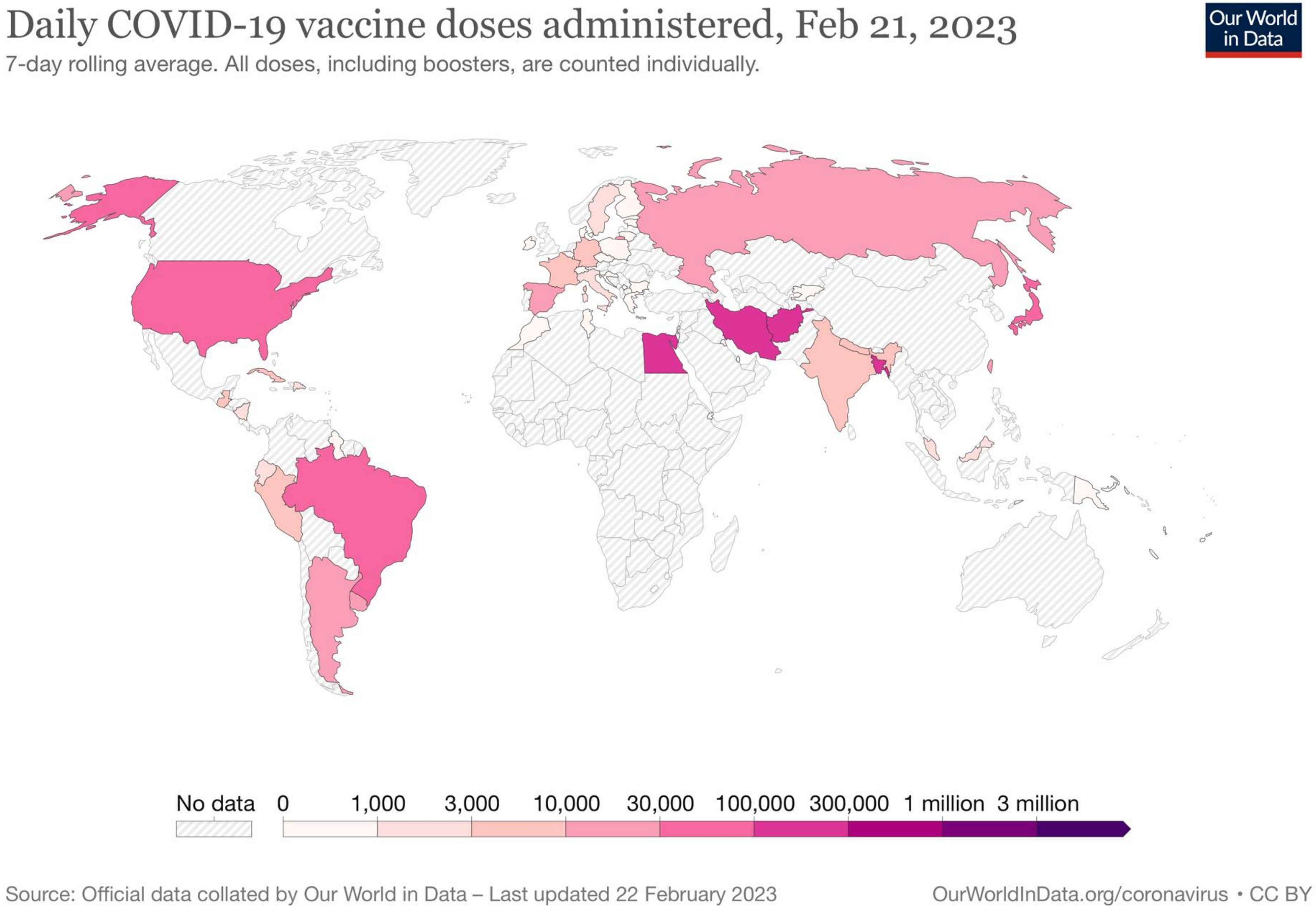
Share of those who received at least one dose



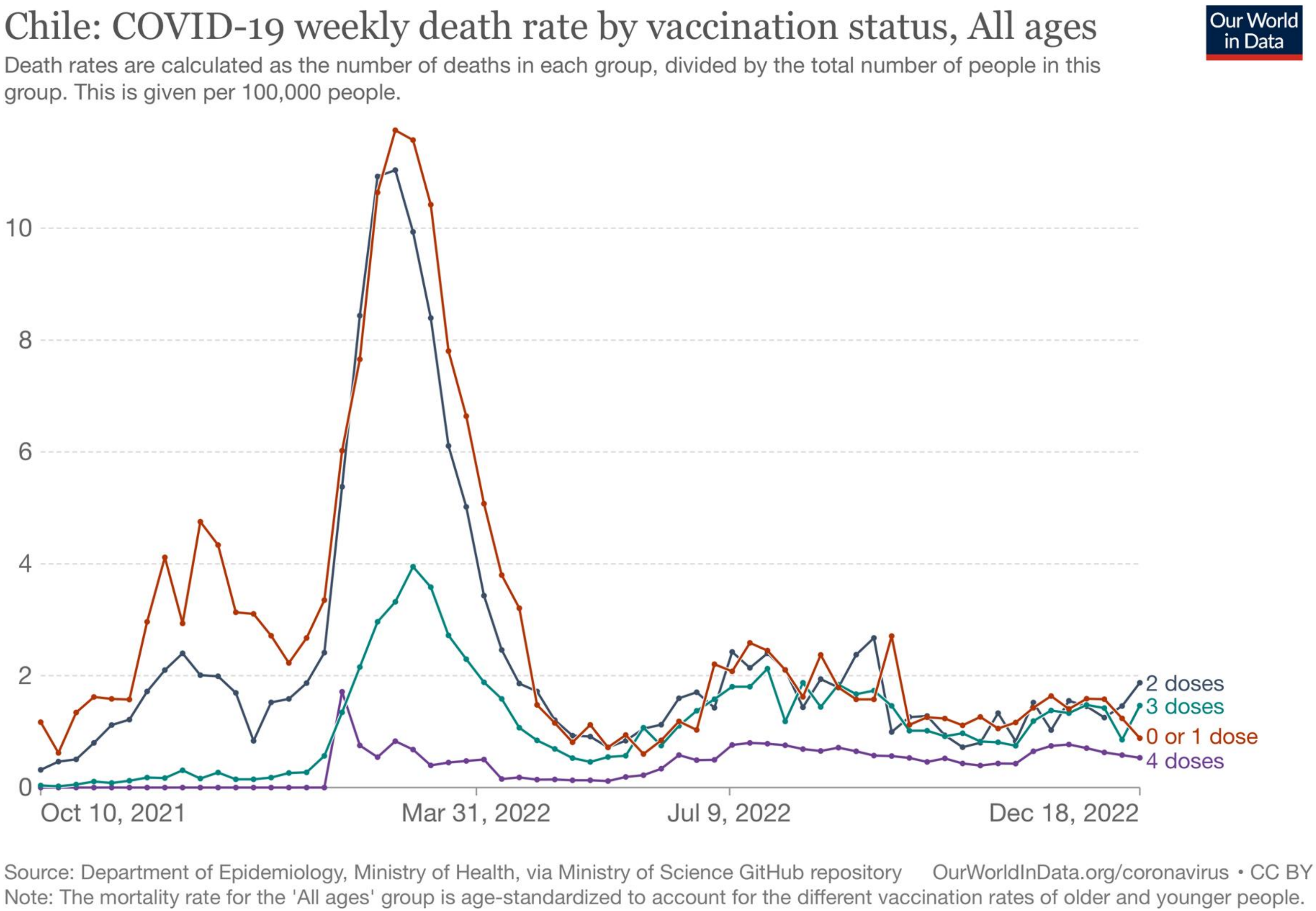
Percent received at least one dose of COVID-19 vaccine, as of 2 January 2022



Daily vaccine doses



COVID-19 death rate by vaccine status



But….

- Not all agreements publicly reported in a timely fashion
- Those reported, often lack basic information (total number of vaccines, prices, never mind timelines for delivery, liability arrangements, flexibility to re-sell)
- Lack of transparency makes it hard to model and track global access to COVID-19 vaccines
- Increases information asymmetry between sellers and buyers, and makes it difficult to assess the situation.
- Fairness of prices per does of AstraZeneca vaccine
  - Uganda 7 USD
  - South Africa 5.25 USD
  - EU 3.5 USD

Nature of contracts

- **Most contracts are between vaccine developers and governments** or intergovernmental organizations (i.e., African Union, European Union, and the COVAX facility).
- But many other more complicated arrangements,
  - e.g., a purchase agreement between a vaccine developer and government that includes an agreement to manufacture and/or distribute the vaccine via a local company
  - a private entity purchase vaccine doses from a vaccine developer to sell on the private market in a given country
- Great **disparities in vaccine access**
- Wealthy countries began making advance purchase agreements in the second and third quarter of 2020, well before any data available on which, if any, of the vaccines would prove to be safe and effective.
- 32 countries – Canada, the United Kingdom, Australia, Chile, New Zealand, and the 27 EU Member States, have publicly announced agreements that, if all vaccine candidates were to be approved by regulatory bodies, would provide enough doses to cover their entire populations at least twice over.
- Most of the countries announced agreements publicly secured enough doses to cover < 50% of their populations.

Vaccine purchases

Table of Vaccine Purchases

Buyer/recipient	Vaccine Candidate	Total Price (in USD million)	
COVAX	AstraZeneca/Oxford	Not Available	170
		600	240
	Johnson & Johnson	Not Available	500
	Novavax	Not Available	1,100
	Pfizer/BioNTech	Not Available	40
	Sanofi/GSK	Not Available	200
European Union	AstraZeneca/Oxford	1060	300
	Curevac	2767.5	225
	Johnson & Johnson	1700	200
	Moderna	8280	460
	Pfizer/BioNTech	9450	500
	Sanofi/GSK	2790	300
United States	AstraZeneca/Oxford	1200	300
	Johnson & Johnson	1000	100
	Moderna	4500	300
	Novavax	1600	100
	Pfizer/BioNTech	5972.48	300
	Sanofi/GSK	1050	100
African Union	AstraZeneca/Oxford	Not Available	500
	Gamaleya	Not Available	300
	Johnson & Johnson	1200	120
	Pfizer/BioNTech	337.5	50
Brazil	AstraZeneca/Oxford	Not Available	2
		942.65	260
	Bharat Biotech	286	20
	Gamaleya	Not Available	50
	Sinovac	Not Available	20
		195.65	100
United Kingdom	AstraZeneca/Oxford	Not Available	100
	Curevac	Not Available	50
	Johnson & Johnson	Not Available	[illegible]

Finalized Commitment1
Yes

Doses committed (in millions)
0 – 1,100

This table shows the number of vaccine doses committed (in millions) for each state and multilateral organization. Data can be filtered based on whether the commitment has been finalized. Sources are media outlets, government publications, and pharmaceutical company press releases.

Vaccine purchases

Table of Vaccine Purchases

Buyer/recipient	Vaccine Candidate	Total Price (in USD million)	
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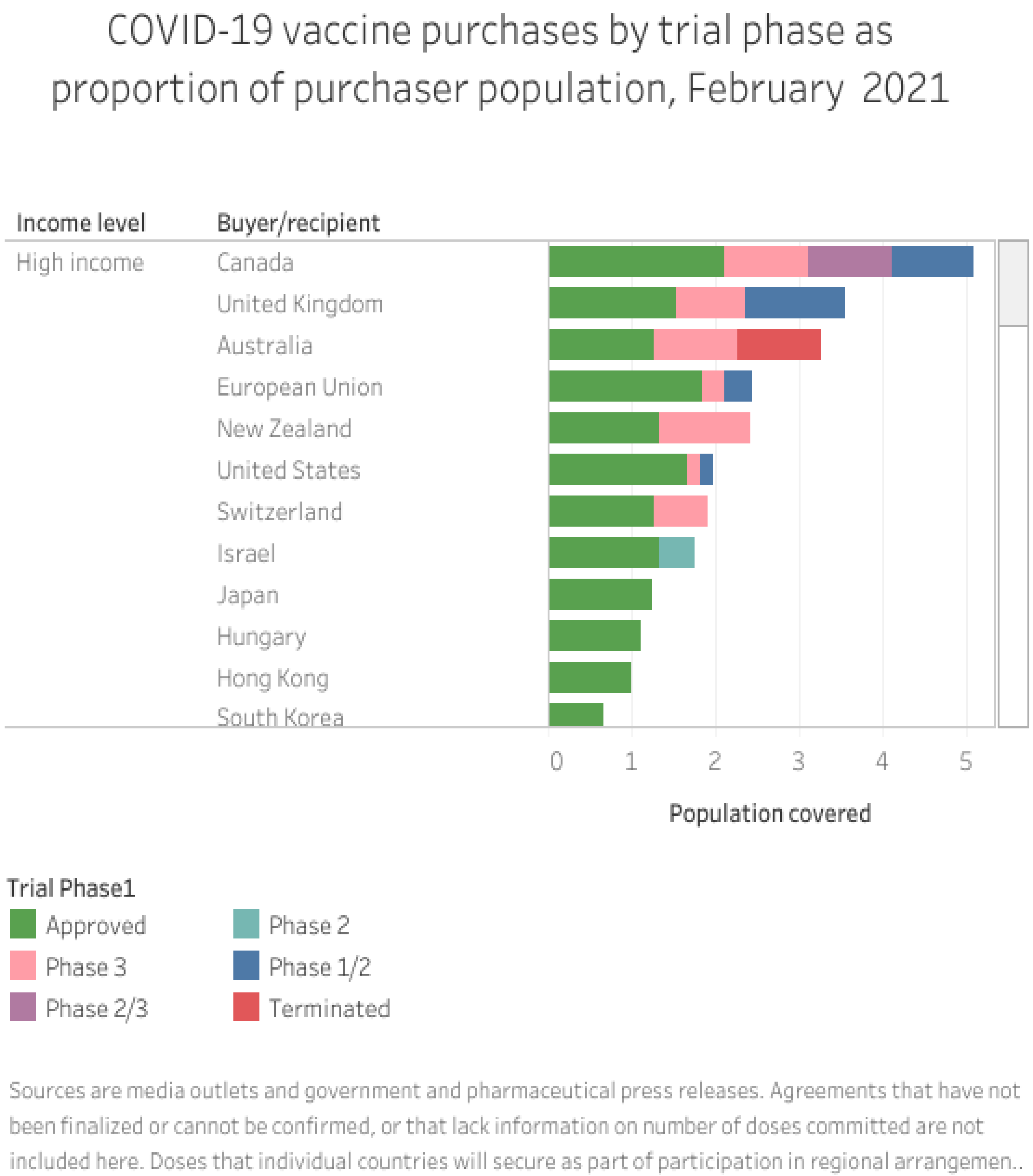
	Gamaleya	Not Available	50
	Sinovac	Not Available	20
		195.65	100
United Kingdom	AstraZeneca/Oxford	Not Available	100
	Curevac	Not Available	50
	Johnson & Johnson	Not Available	30
	Moderna	Not Available	5
	Novavax	Not Available	60
	Pfizer/BioNTech	Not Available	40
	Sanofi/GSK	Not Available	60
	Valneva	858	100
Indonesia	AstraZeneca/Oxford	500	100
	CanSino Biologics	Not Available	15
	Novavax	Not Available	30
	Sinopharm/Beijing	Not Available	75
	Sinovac	Not Available	126
Canada	AstraZeneca/Oxford	Not Available	22
	Johnson & Johnson	Not Available	38
	Medicago/GSK	Not Available	76
	Moderna	Not Available	40
	Novavax	Not Available	76
	Pfizer/BioNTech	Not Available	20
	Sanofi/GSK	Not Available	72
Japan	AstraZeneca/Oxford	Not Available	120
	Moderna	Not Available	50
	Pfizer/BioNTech	Not Available	144
Mexico	AstraZeneca/Oxford	Not Available	78
	CanSino Biologics	Not Available	35
	Pfizer/BioNTech	Not Available	34
Philippines	AstraZeneca/Oxford	Not Available	17

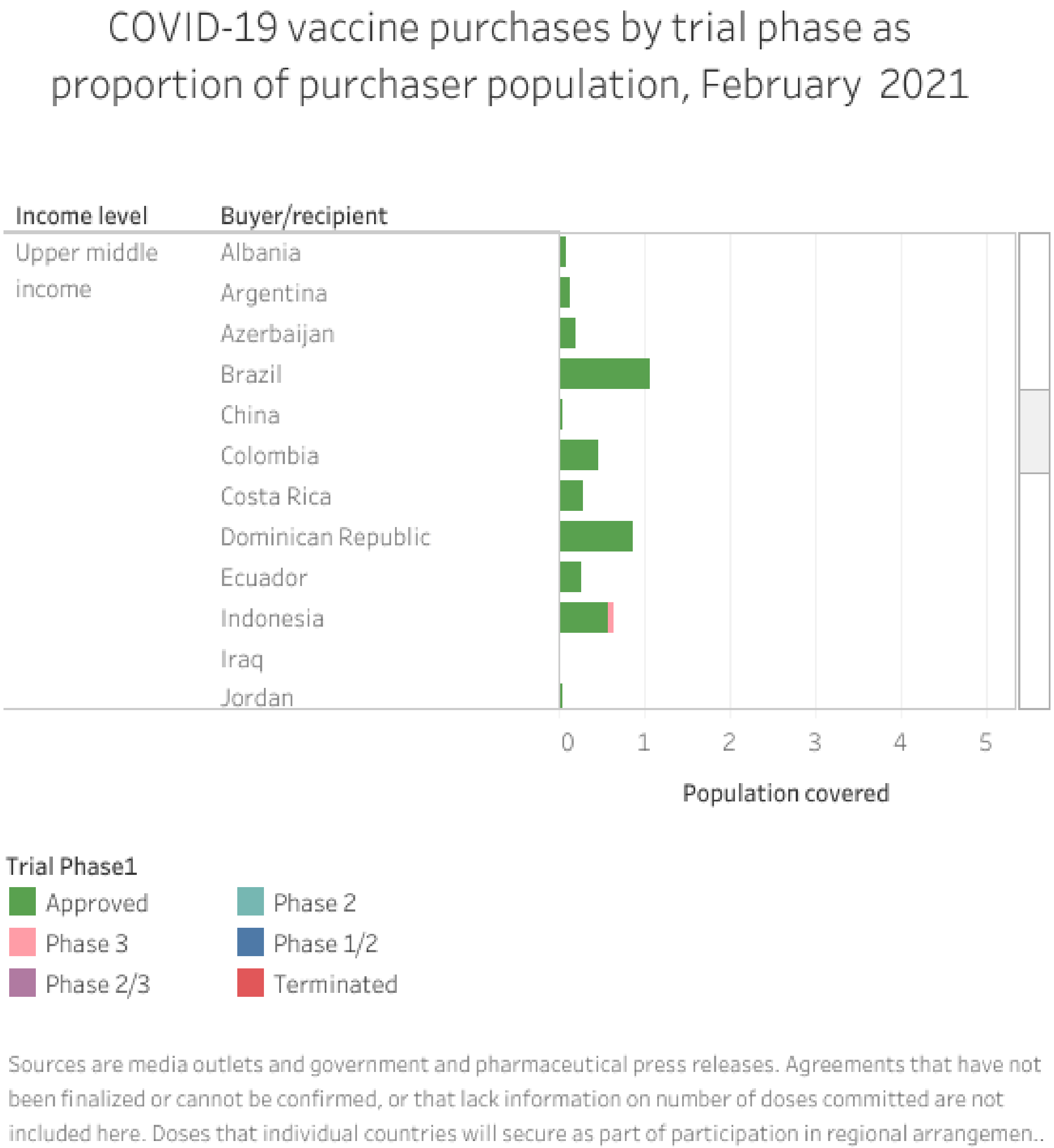
Finalized Commitment1
Yes

Doses committed (in millions)
0 — 1,100

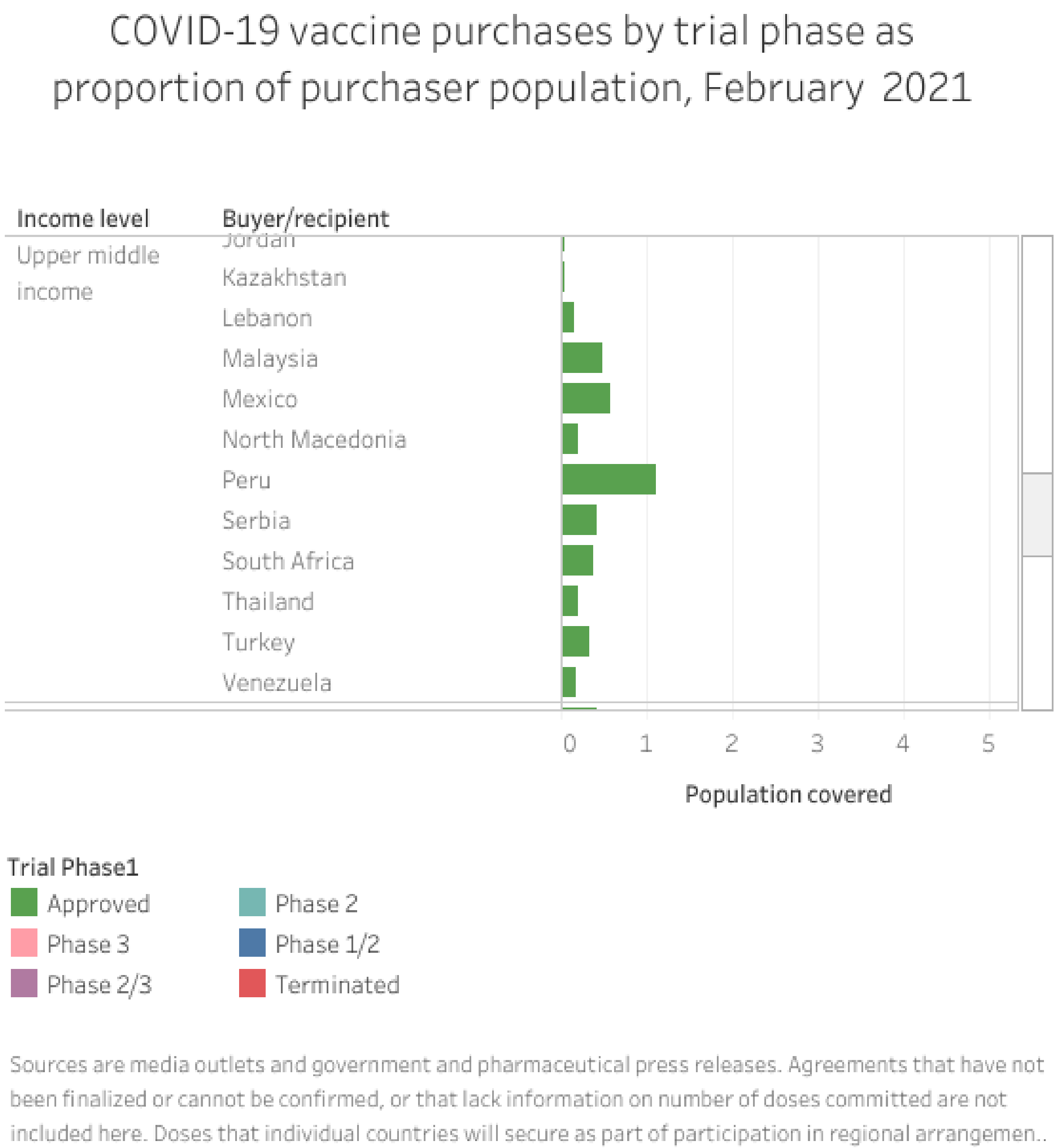
This table shows the number of vaccine doses committed (in millions) for each state and multilateral organization. Data can be filtered based on whether the commitment has been finalized. Sources are media outlets, government publications, and pharmaceutical company press releases.

Some purchased in advance well before licensed



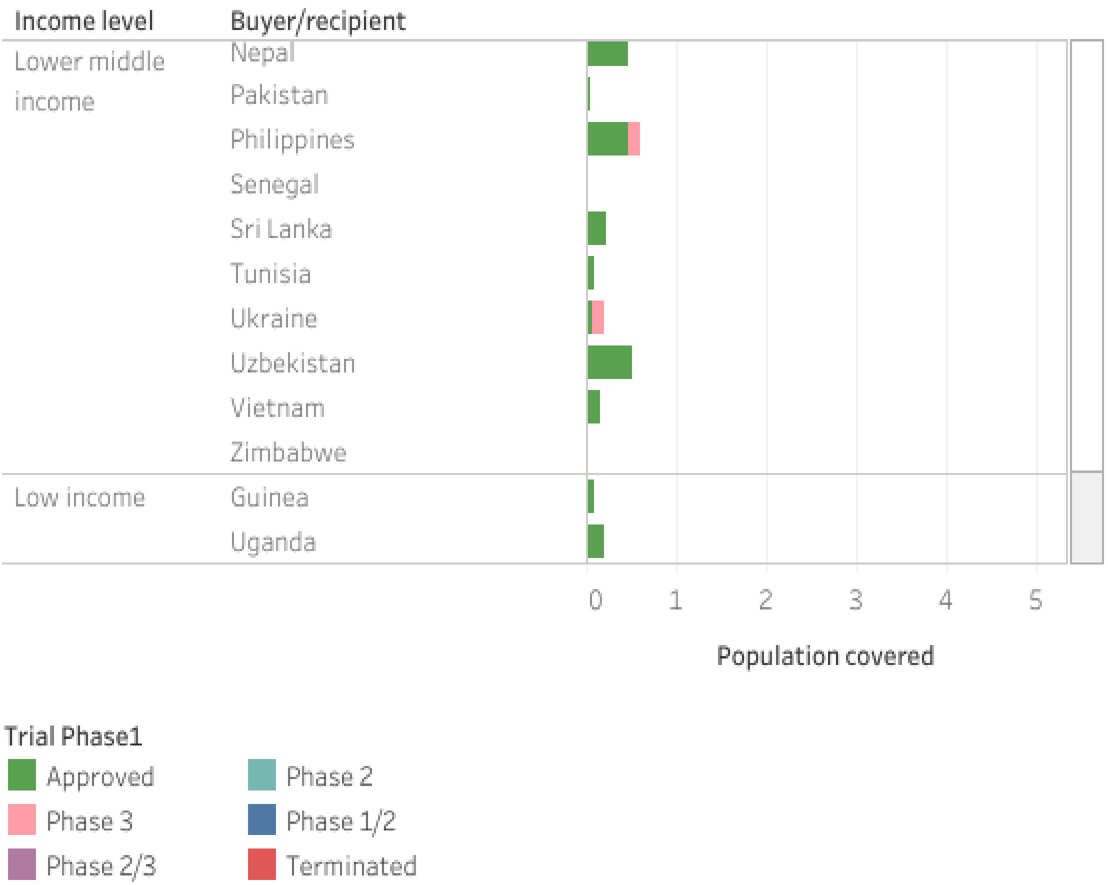


Most could not advance purchase before licensed



Many had to wait

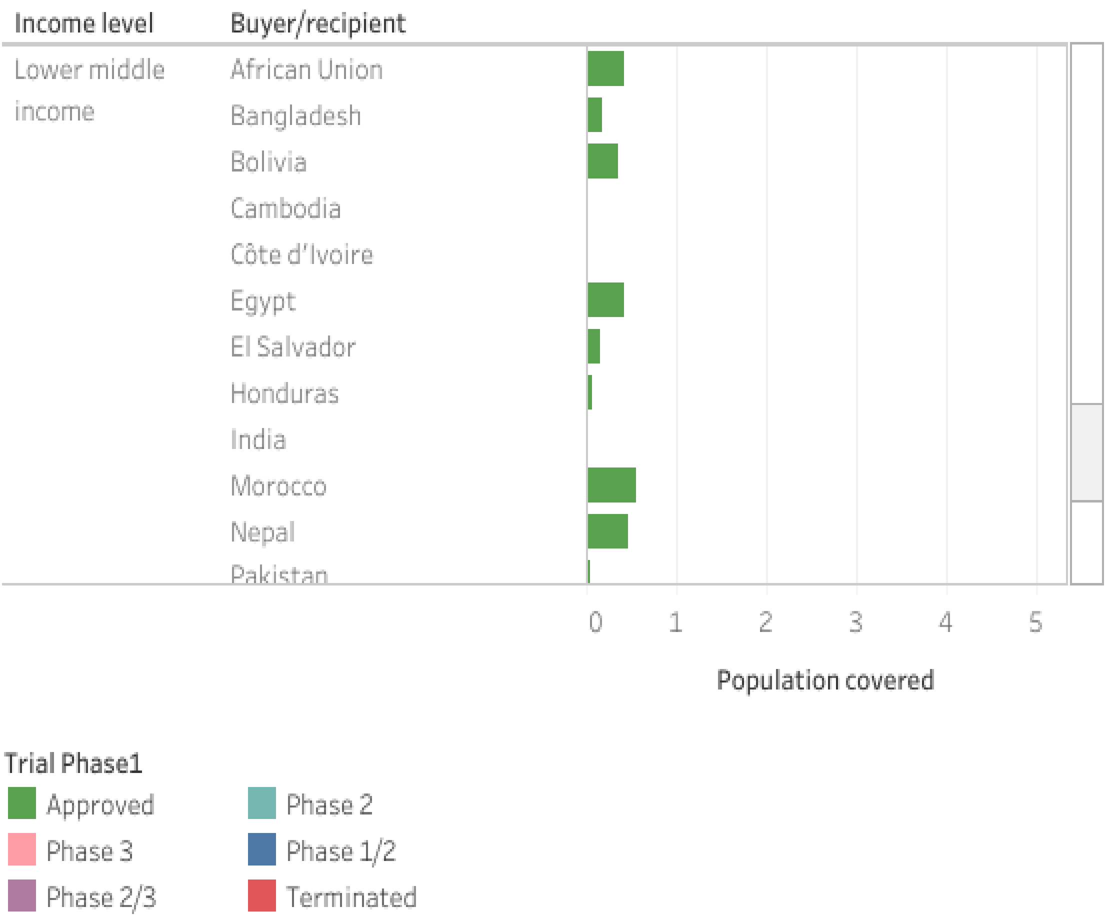
COVID-19 vaccine purchases by trial phase as proportion of purchaser population, February 2021



Sources are media outlets and government and pharmaceutical press releases. Agreements that have not been finalized or cannot be confirmed, or that lack information on number of doses committed are not included here. Doses that individual countries will secure as part of participation in regional arrangemen..

Many had to wait

COVID-19 vaccine purchases by trial phase as proportion of purchaser population, February 2021



Sources are media outlets and government and pharmaceutical press releases. Agreements that have not been finalized or cannot be confirmed, or that lack information on number of doses committed are not included here. Doses that individual countries will secure as part of participation in regional arrangemen..

Many had to wait

Vaccine donations…

Doses (in millions) of COVID-19 vaccines donated

Donor Country	Vaccine Candidate	Recipient Country	
India	AstraZeneca/Oxford	Afghanistan	0.500
		Antigua and Barbuda	0.040
		Bahrain	0.100
		Bangladesh	2.000
		Barbados	0.100
		Bhutan	0.150
		Cambodia	0.100
		Dominica	0.070
		Dominican Republic	0.030
		Maldives	0.100
		Mauritius	0.150
		Myanmar	1.500
		Nepal	1.000
		Nicaragua	0.500

Sum of Doses Committed (in millions)

0.001 – 3.000

Sources are media outlets, government publications, and pharmaceutical company press releases. Arrangements that have been reported but are lacking information on number of doses supplied are excluded.

Vaccine donations…

Doses (in millions) of COVID-19 vaccines donated

Donor Country	Vaccine Candidate	Recipient Country	
Dominica	AstraZeneca/Oxford	St. Kitts and Nevis	[illegible]
		St. Lucia	0.002
		St. Vincent and the Grenadi..	0.005
Russia	Gamaleya	Palestine	0.010
Senegal	Sinopharm/Beijing	Gambia, The	0.010
Serbia	Gamaleya	Montenegro	0.002
	Pfizer/BioNTech	North Macedonia	0.008
Barbados	AstraZeneca/Oxford	Belize	0.001
		Grenada	0.001
		Guyana	0.002
		St. Lucia	0.001
		Suriname	0.001
		Trinidad and Tobago	0.002
Undisclosed	Pfizer/BioNTech	Albania	0.001
Albania	Pfizer/BioNTech	Kosovo	

Sum of Doses Committed (in millions)

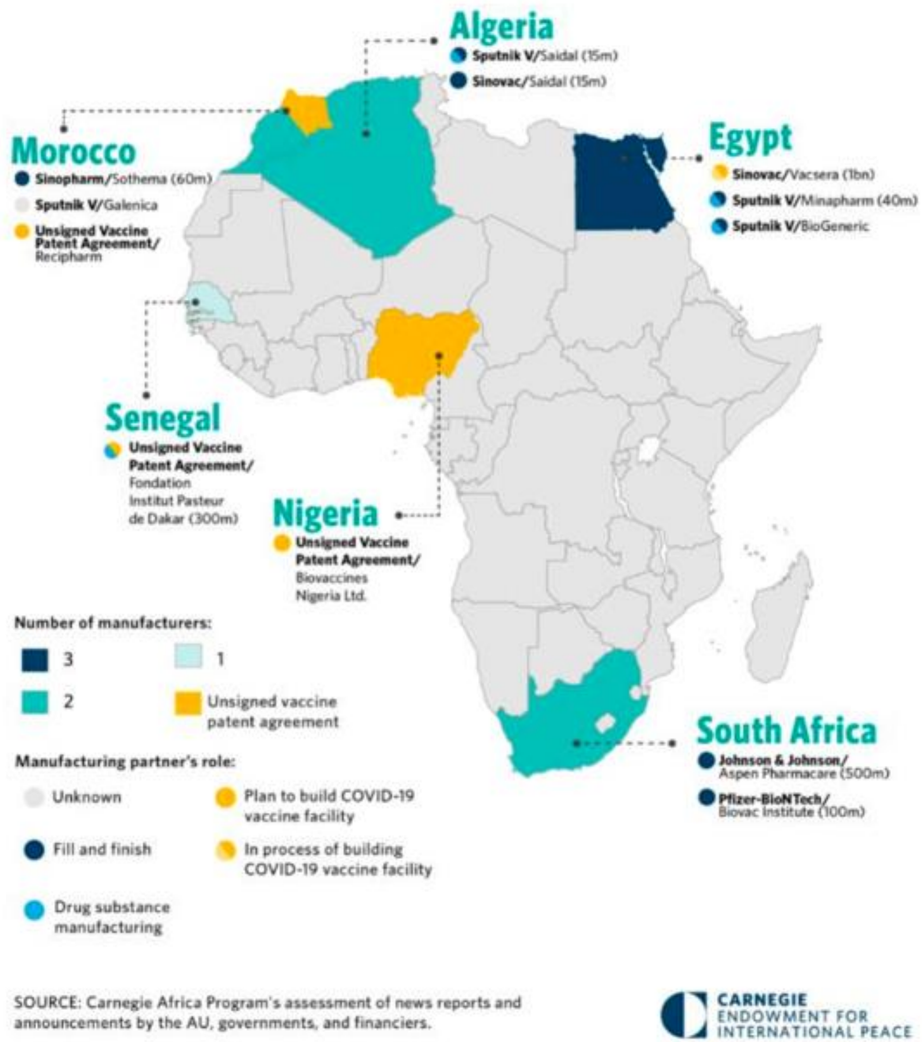
0.001 – 3.000

Sources are media outlets, government publications, and pharmaceutical company press releases. Arrangements that have been reported but are lacking information on number of doses supplied are excluded.

Rise of bilateral donations

- Just recently, some countries have started to donate (in some cases, to sell) vaccine doses to other countries, either from their purchased stocks or from domestically produced vaccines
- In the absence of adequate supply for COVAX, such donations may become an important way for countries without bilateral agreements with vaccine developers to obtain vaccines for their populations

African Vaccine Manufacturing Centres



Africa ideas…

- **Modular pandemic vaccine production system**, so that once a microbial threat is identified and sequenced, **sites in affected regions can manufacture vaccine with relative swiftness as part of a regional containment response**.
- Avoid technology that relies on bioreactors?
- Choose low-cost platforms like mRNA and protein and particle vaccines?
- Integrate **pathogen genomics into existing public health surveillance** systems in LMICs
- **Strengthen local base of scientific, technical, product-specific manufacturing and quality control expertise**
- **New technology transfer pathways.** LMICs seeded by sharing vaccine-specific knowledge and know-how through milestone-driven partnerships with vaccine centres of excellence (e.g. Sienna-based GSK global vaccines facility), **early transfer at proof-of-concept and at later stages of clinical development**. C.f. South Africa-based **Biovac.**

Africa ideas…

- Incentives and funding to support vaccine production at varying levels, such as land, tax incentives, infrastructure provision, and monetary support as a private public partnership. Of recent note: **Cuba, Brazil, and India**,
- **Integrate pharmaceutical manufacturing development into economic development planning**
- “small country solutions” to overcome pressure large nations face to first vaccinate the domestic population. E.g., **a select, distributed network of small nations could be formed to scale emergency vaccine quickly, supported by a humanitarian licensing scheme** similar to the UN-supported Medicines Patent Pool (MPP).

Breakout group discussion

- Can variants be stopped or are we just buying time?
- What challenges will new variants have for all of the above (supply, pandemic management, etc.)?
- Should all vaccine contract information be public? What would be the implications?
- In highly-vaccinated populations, how do you test/trial new vaccines?
- What principles of global public health would you use to design better contracts?
- Are donations the answer?
- What about IP and technology transfer and local manufacturing, etc.?
- How many vaccines do we need?

Some vaccine numbers…

- One dose per person = (presuming they all agree to take it) = 7.8 billion doses,
- Two dose per person = 16 billion
- If booster = 23 billion
- Typical wastage rate might add 10%-15% (guess-work though for the programs we envisage)
- If herd immunity can be achieved at 70%-80% coverage, lower numbers of doses, perhaps 5.5-6 billion, 11-12 billion, and 16-19 billion respectively (and if there is some background protection and if it can be measured in each settings, numbers might be lower still)
- But international travel from countries without herd immunity may mean countries want high coverage rates
- Increasing transmissibility will mean higher levels of coverage to get herd immunity
- This just one one cycle of immunization

What about reaching the world? A global response: COVAX

Allocation logic and algorithm to support allocation of vaccines secured through the COVAX Facility

Explainer based on commonly asked questions

15 February 2021

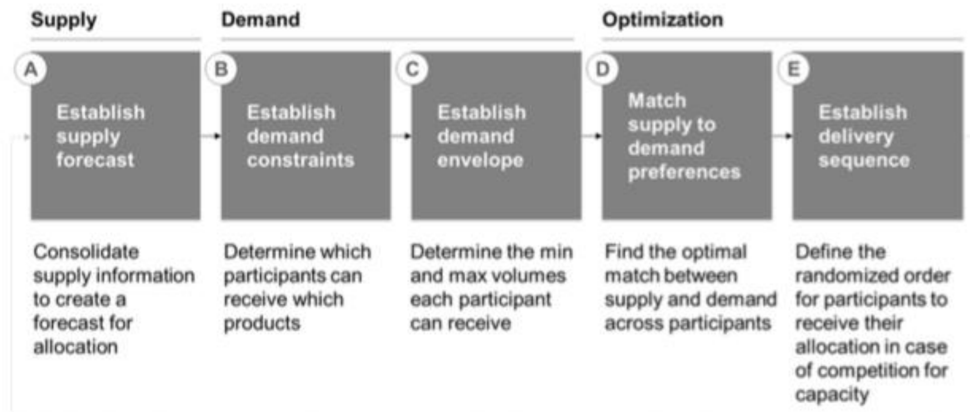


Exhibit 1: 5 key steps of the Allocation Algorithm logic

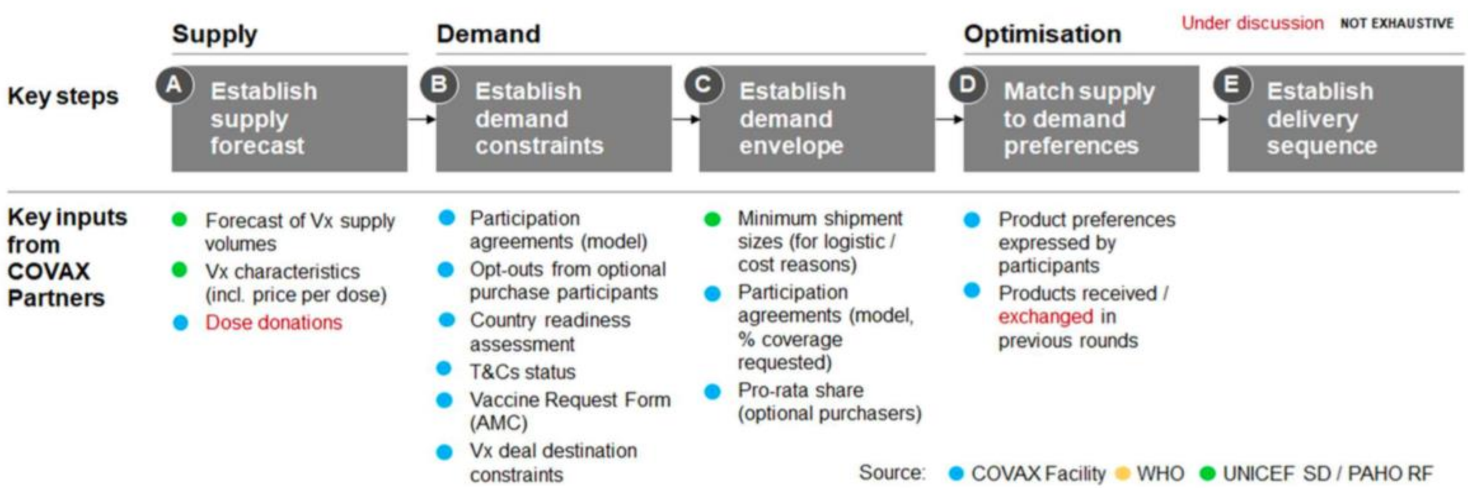
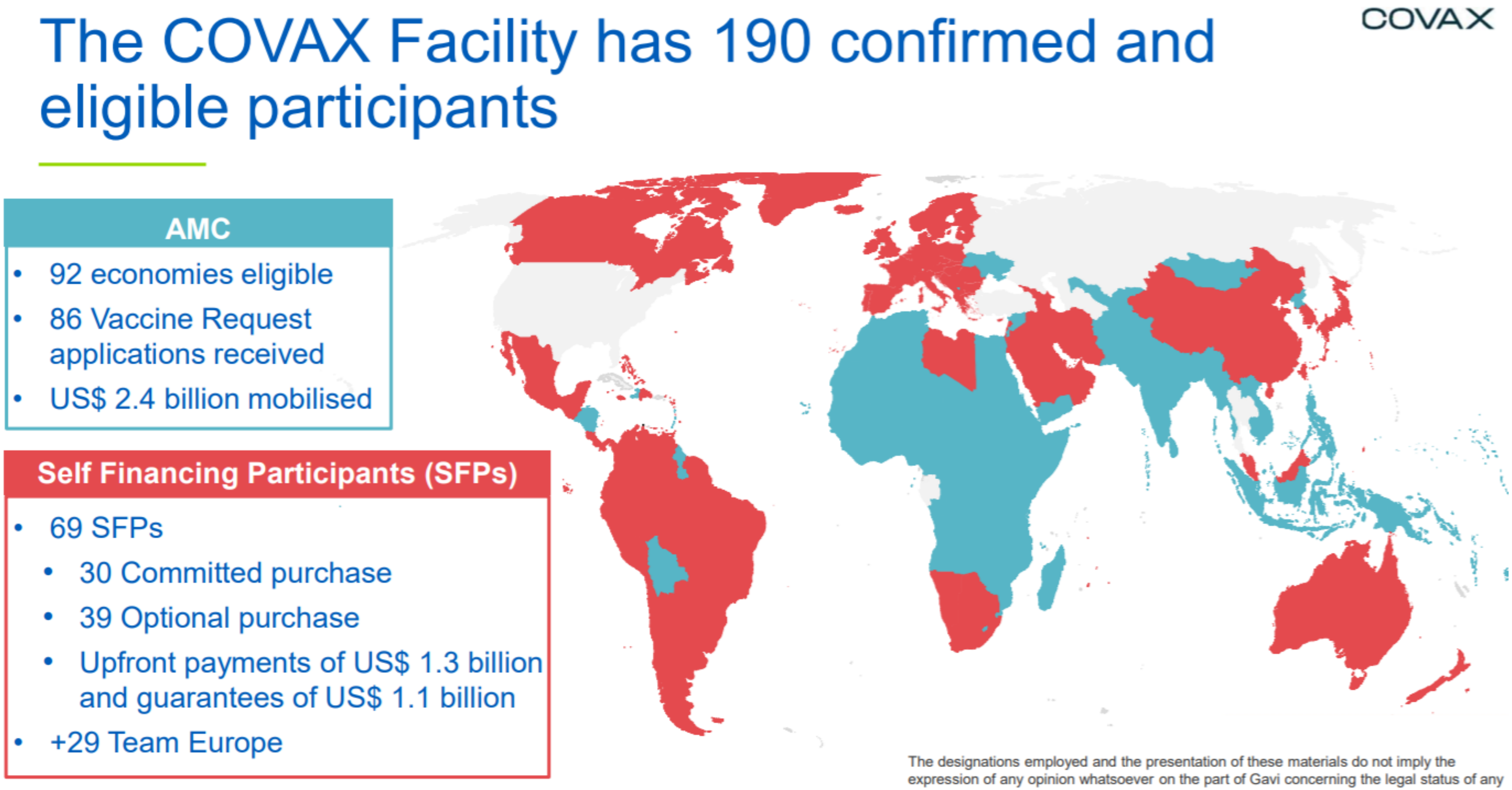


Exhibit 4: List of inputs into the Allocation logic and Algorithm

COVAX numbers



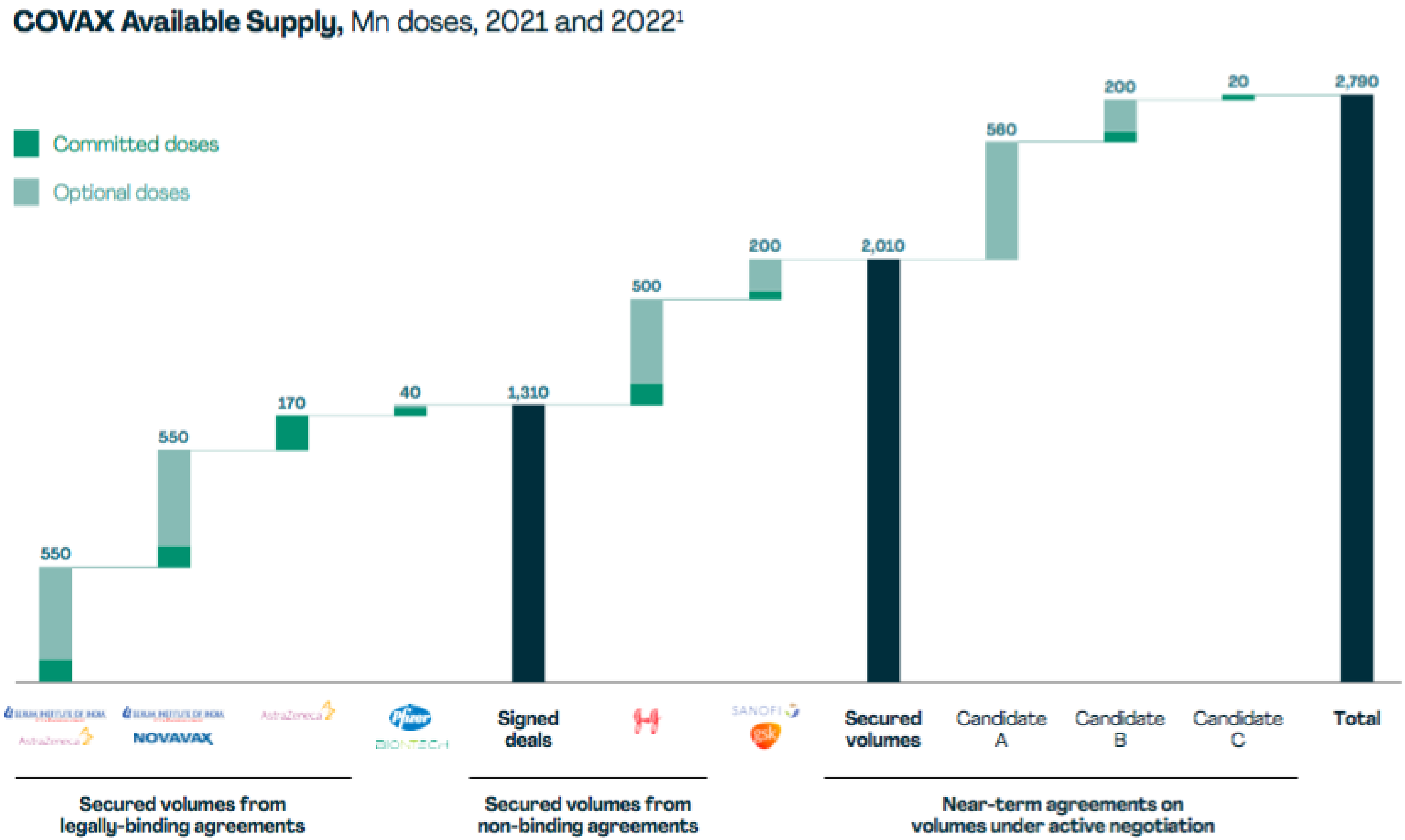
- As of February 3, 2021 COVAX was projecting coverage for 3.3% of the total population of participating countries in the first half of 2021
- Many countries, primarily low- and lower-middle income, relying entirely or largely on their participation in COVAX to secure access to vaccines

COVAX…

Objectives What are the goals for optimization?	Constraints What solutions are feasible?	Variables What values change to find solutions?
•Minimize population coverage inequality across participants •Maximize participant preference for products •Minimize unique products allocated to participants	•Maximum and minimum demand per participant •Optional participants must receive their *pro-rata* share over the course of a deal •Participants can only be assigned acceptable products •All supply must be allocated •Vaccine supply forecast for round •Minimum shipment size per product •Batch/shipping pallet size per product •Allocation capped at 20% •All participants must be allocated something •Unique products limit	•Number of batches/shipping pallets of assigned product to a participant •Product assignment to a participant •Achievable equity line

Exhibit 5: Objectives, Constraints, and Decision Variables used by the Allocation Algorithm

COVAX…



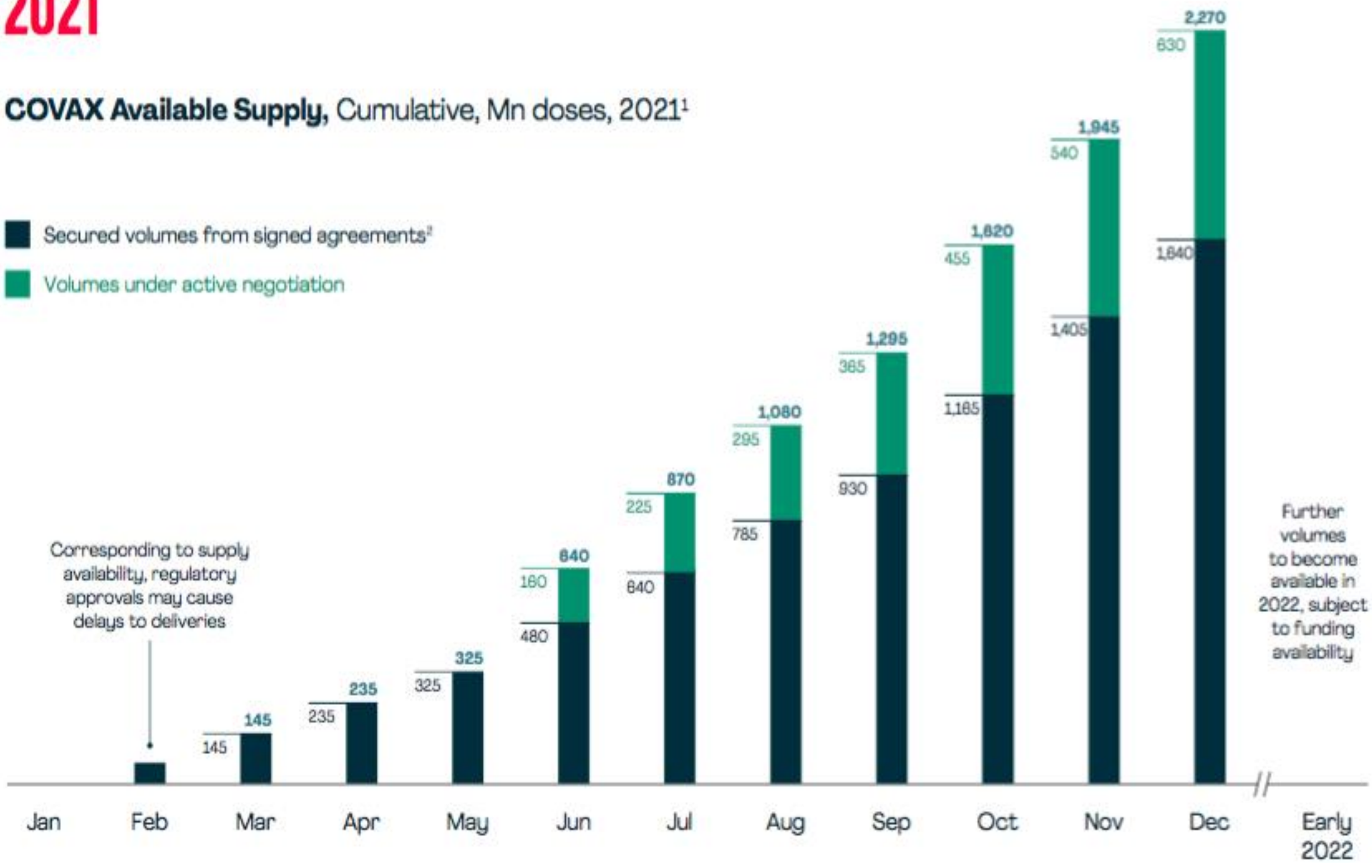
COVAX Available Supply, Mn doses, 2021 and 2022[1]
Committed doses
Optional doses
550
550
170
40
1,310
500
200
2,010
560
200
20
2,790
NOVAVAX
Signed deals
Secured volumes
Candidate A
Candidate B
Candidate C
Total
Secured volumes from legally-binding agreements
Secured volumes from non-binding agreements
Near-term agreements on volumes under active negotiation

COVAX…

COVAX FACILITY GLOBAL SUPPLY FORECAST 2021

PRELIMINARY AND SUBJECT TO ASSUMPTIONS
As per 2021-01-20

COVAX Available Supply, Cumulative, Mn doses, 2021[1]



[1] Supply refers to volumes of vaccine available from the manufacturer. Timing of forecasts is based on anticipated release of doses from manufacturers. Volumes for expected single-dose regimen vaccine candidates doubled to ensure comparability across vaccine candidates. Volumes have been rounded to the nearest 5M (except for those smaller than 5M), and so totals may not equal sum of segments.

[2] Signed agreements include legally-binding agreements, memoranda of understanding, and statements of intent.

CAVEATS

Contracts: Some of the supply included in the projections are linked to deals that are already concluded and some are currently being negotiated. Terms are subject to change.

Candidate attrition: Some candidates are still in clinical development. If they do not achieve positive clinical trial outcomes (safety and efficacy) and regulatory approval, these volumes will not be procured by COVAX.

Regulatory approval: Supply timing will depend on regulatory success and timelines, including reviews of individual batches ("batch release").

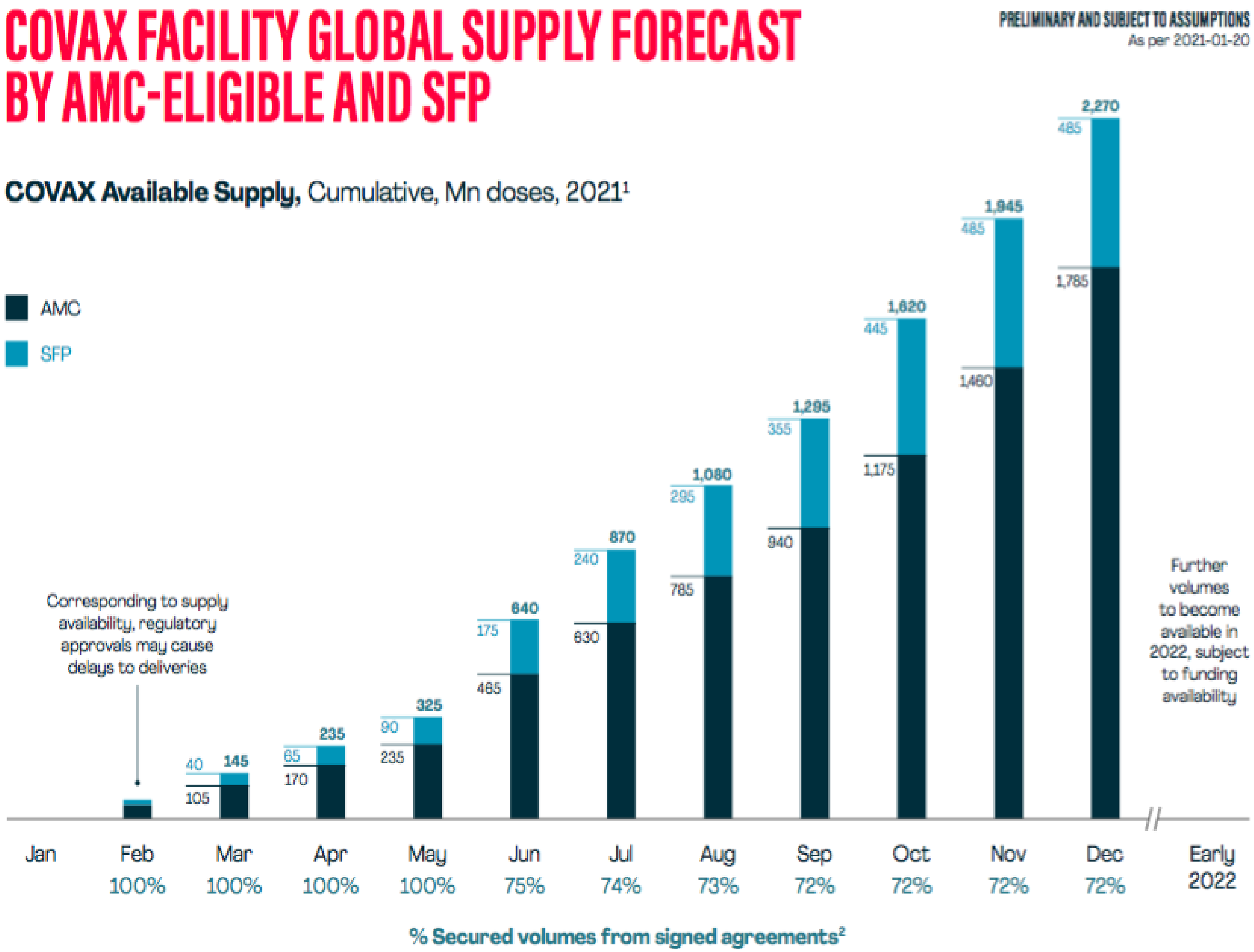
Manufacturing: In many cases, manufacturing is yet to reach full scale. Manufacturing productivity will be influenced by multiple factors, which will in turn influence volume and timing of supply.

Delivery: Timing of delivery will depend on various factors, including local regulatory approval, country readiness, logistics, indemnification and liability in place, in-country distribution etc.

Funding availability: Total potential supply is shown; procurement of these doses will depend on COVAX AMC fundraising, AMC92 cost-sharing beyond donor-funded doses, and the final prices and volumes of doses allocated to AMC92.

Allocation: These supply forecasts reflect a preliminary distribution of doses based on each participant's share of available supply pro rata by demand and are to be treated as indicative. Final timing and volumes will be determined by the WHO Allocation Mechanism.

COVAX…



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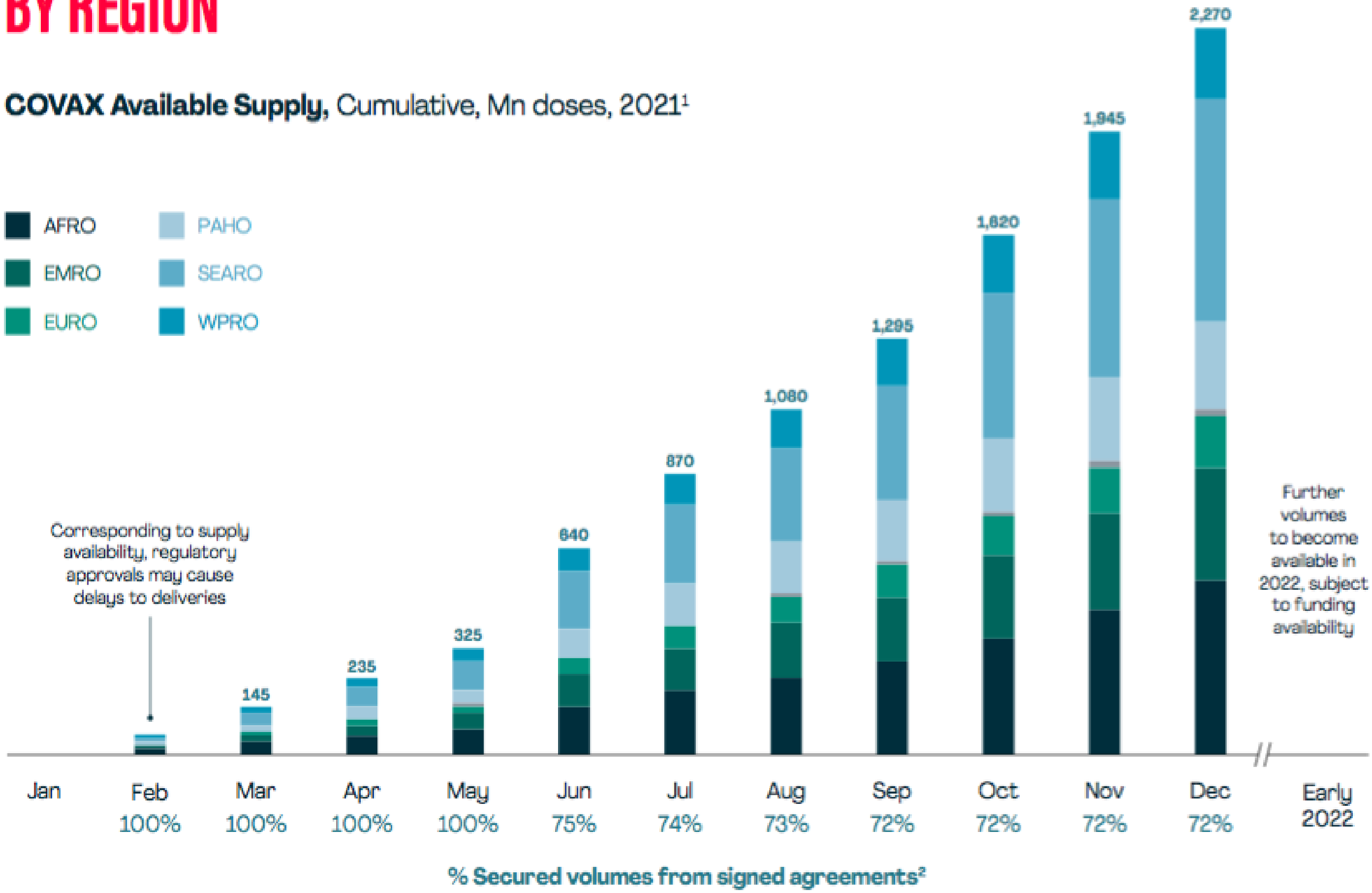
COVAX…

COVAX FACILITY GLOBAL SUPPLY FORECAST BY REGION

PRELIMINARY AND SUBJECT TO ASSUMPTIONS
As per 2021-01-20

COVAX Available Supply, Cumulative, Mn doses, 2021[1]



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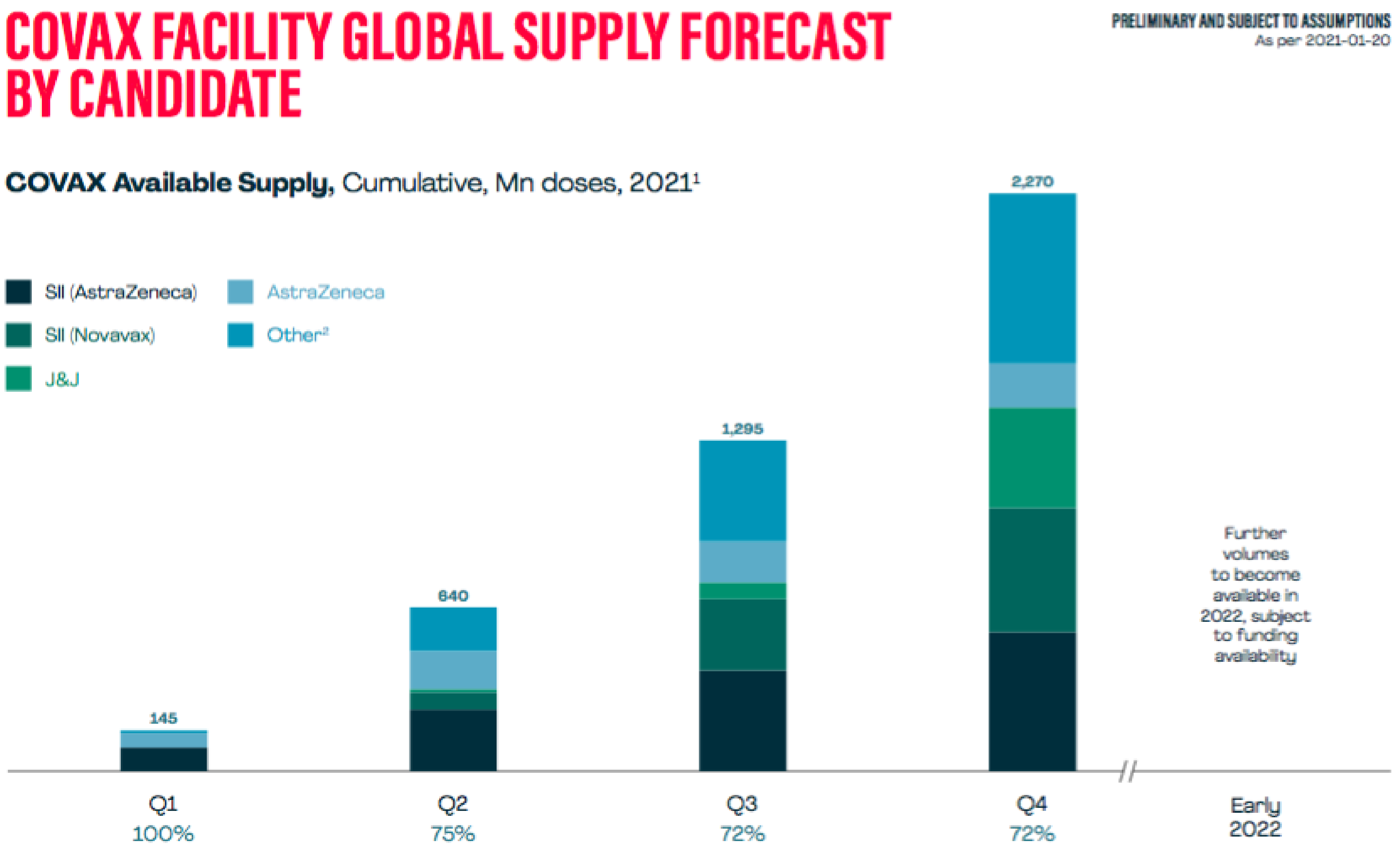
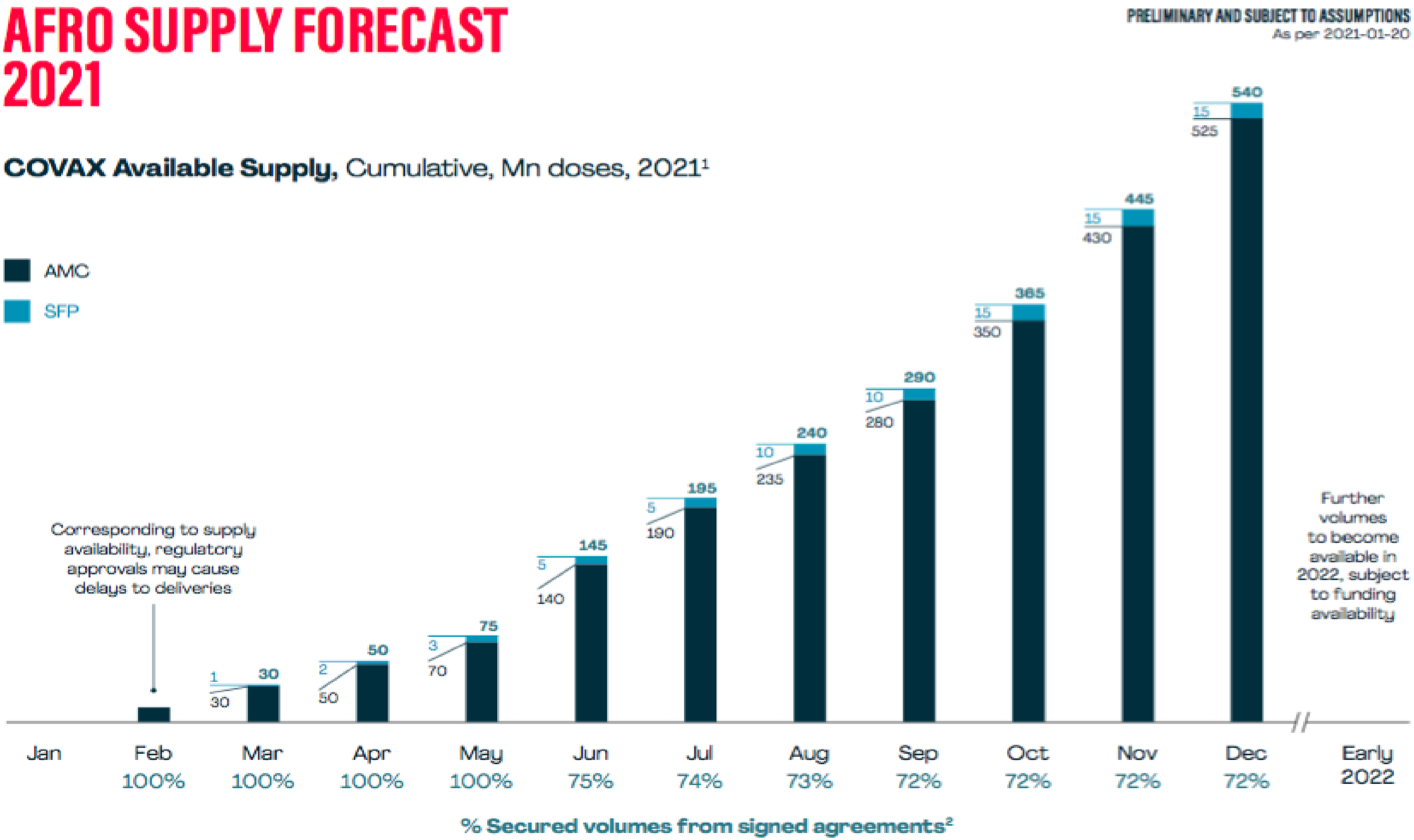
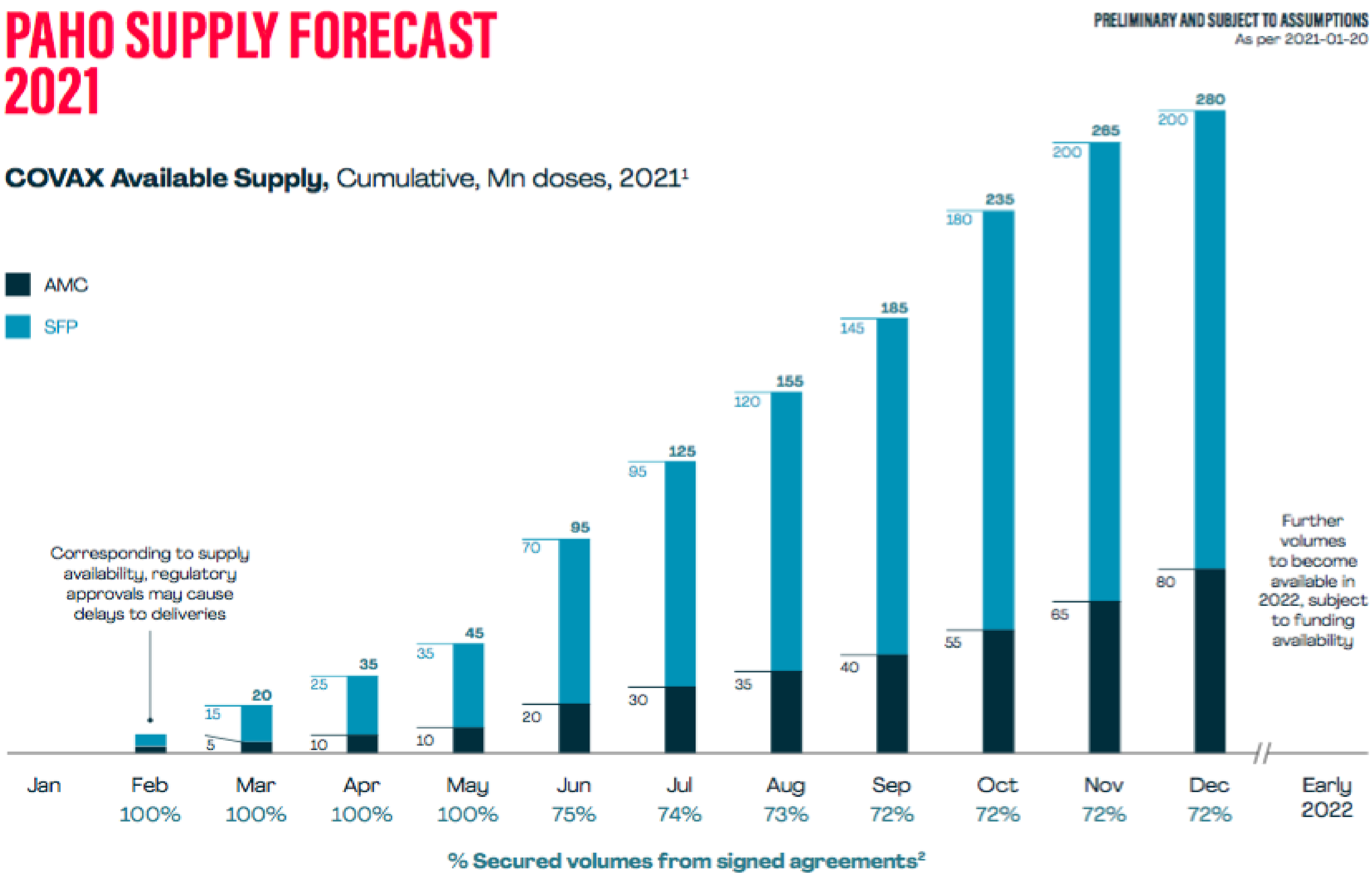
COVAX…


COVAX FACILITY GLOBAL SUPPLY FORECAST BY CANDIDATE
PRELIMINARY AND SUBJECT TO ASSUMPTIONS
As per 2021-01-20
COVAX Available Supply, Cumulative, Mn doses, 2021[1]
SII (AstraZeneca)
AstraZeneca
SII (Novavax)
Other[2]
J&J
145
640
1,295
2,270
Further volumes to become available in 2022, subject to funding availability
Q1
100%
Q2
75%
Q3
72%
Q4
72%
Early 2022

COVAX…


AFRO SUPPLY FORECAST
2021
PRELIMINARY AND SUBJECT TO ASSUMPTIONS
As per 2021-01-20
COVAX Available Supply, Cumulative, Mn doses, 2021[1]
AMC
SFP
Corresponding to supply availability, regulatory approvals may cause delays to deliveries
1
30
30
2
50
50
3
70
75
5
140
145
5
190
195
10
235
240
10
280
290
15
350
365
15
430
445
15
525
540
Further volumes to become available in 2022, subject to funding availability
Jan
Feb 100%
Mar 100%
Apr 100%
May 100%
Jun 75%
Jul 74%
Aug 73%
Sep 72%
Oct 72%
Nov 72%
Dec 72%
Early 2022
% Secured volumes from signed agreements[2]

COVAX…



PAHO SUPPLY FORECAST 2021
PRELIMINARY AND SUBJECT TO ASSUMPTIONS
As per 2021-01-20
COVAX Available Supply, Cumulative, Mn doses, 2021[1]
AMC
SFP
Corresponding to supply availability, regulatory approvals may cause delays to deliveries
15
20
5
25
35
10
35
45
10
70
95
20
95
125
30
120
155
35
145
185
40
180
235
55
200
265
65
200
280
80
Further volumes to become available in 2022, subject to funding availability
Jan
Feb 100%
Mar 100%
Apr 100%
May 100%
Jun 75%
Jul 74%
Aug 73%
Sep 72%
Oct 72%
Nov 72%
Dec 72%
Early 2022
% Secured volumes from signed agreements[2]

Breakout group discussion

- How should those being given vaccines be prioritized?
- Should healthy young people in the UK be allowed to donate their vaccine doses to those in greater need in poorer countries?
- Will herd immunity be reached and sustained? Where and when?
- What is the role of other non-vaccine interventions?
- How might behavioral change in the population impact short- and long-run vaccine efficacy?

What about FS (falsified and substandard) vaccines?

Figure 1. Countries with public reports on substandard or falsified COVID-19 vaccines. Countries with reports are indicated in orange. If a public report mentions a product name or a company, this detail is indicated on the map. Source of the information - see table 1.

What about vaccine confidence?

Next figures taken from ….

Mapping global trends in vaccine confidence and investigating barriers to vaccine uptake: a large-scale retrospective temporal modelling study

Alexandre de Figueiredo, Clarissa Simas*, Emilie Karafillakis, Pauline Paterson, Heidi J Larson*

Vaccine confidence

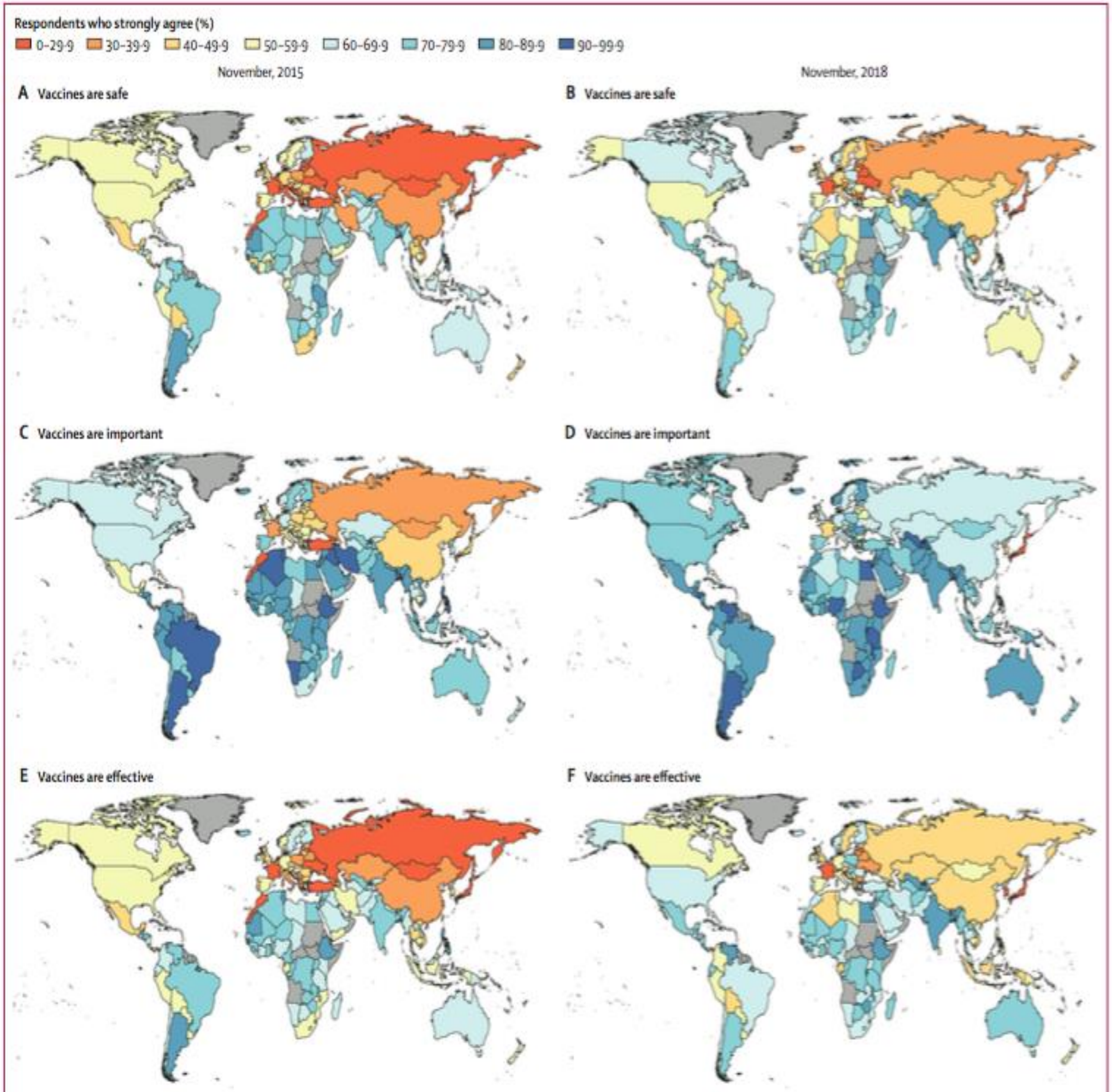


Figure 1: **Global trends in perceptions towards the safety of vaccines in November, 2015, and November, 2018**

Figure shows model-based estimates of the percentage of respondents strongly agreeing that vaccines are safe (panels A, B), important for children to have (panels C, D), and effective (panels E, F) in November, 2015, and November, 2018. No data were available for countries in grey.

Vaccine confidence

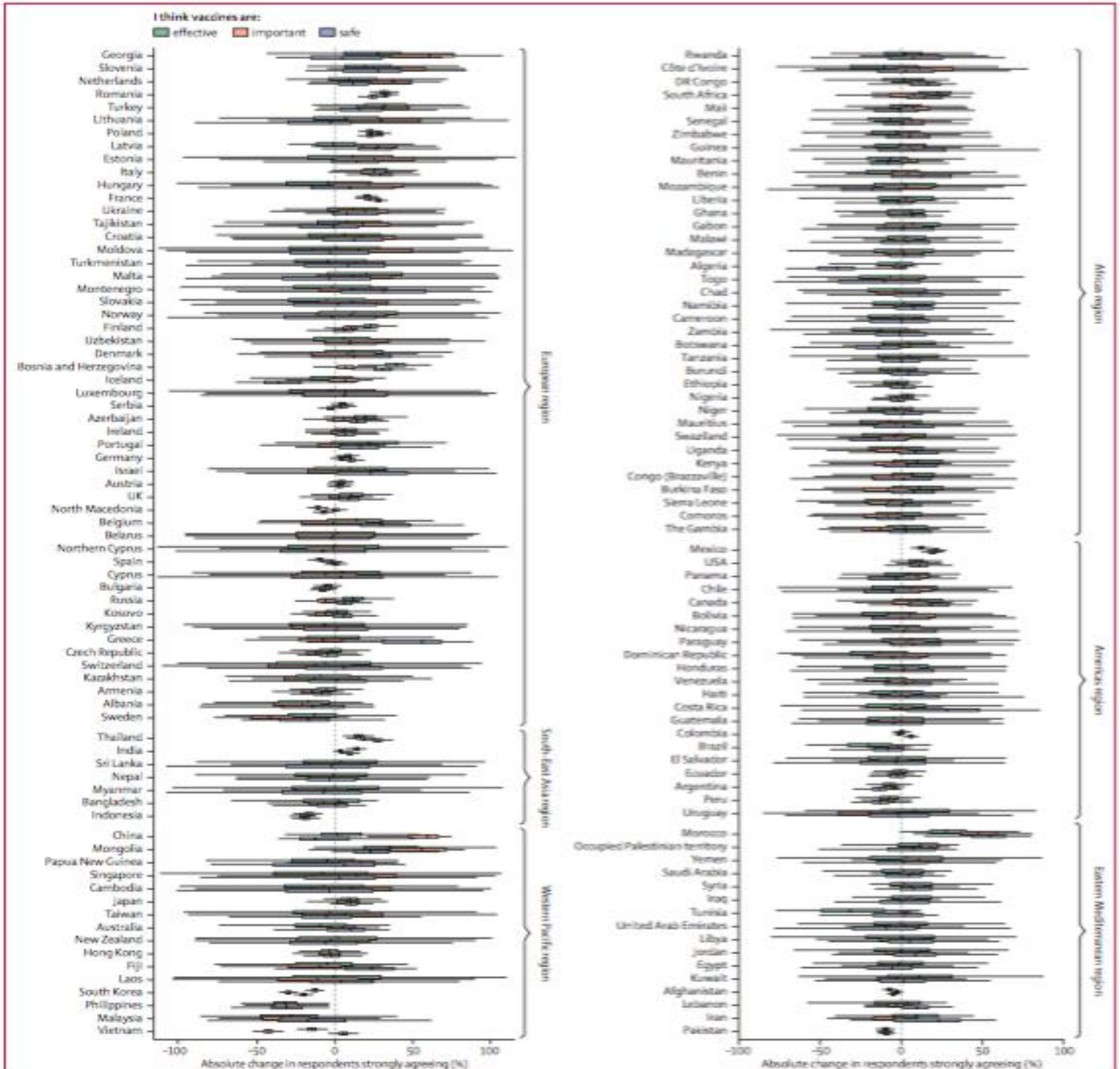


Figure 2: Distributions in absolute confidence changes between November, 2015, and December, 2019
Distributions of model-based estimates in the absolute differences in the proportions of respondents strongly agreeing that vaccines are safe, important, and effective. Positive values denote an increase in confidence between 2015 and 2019. Owing to increased uncertainty around estimates further away from survey dates, some significant changes in confidence over the study period are not captured by this figure.

Vaccine confidence

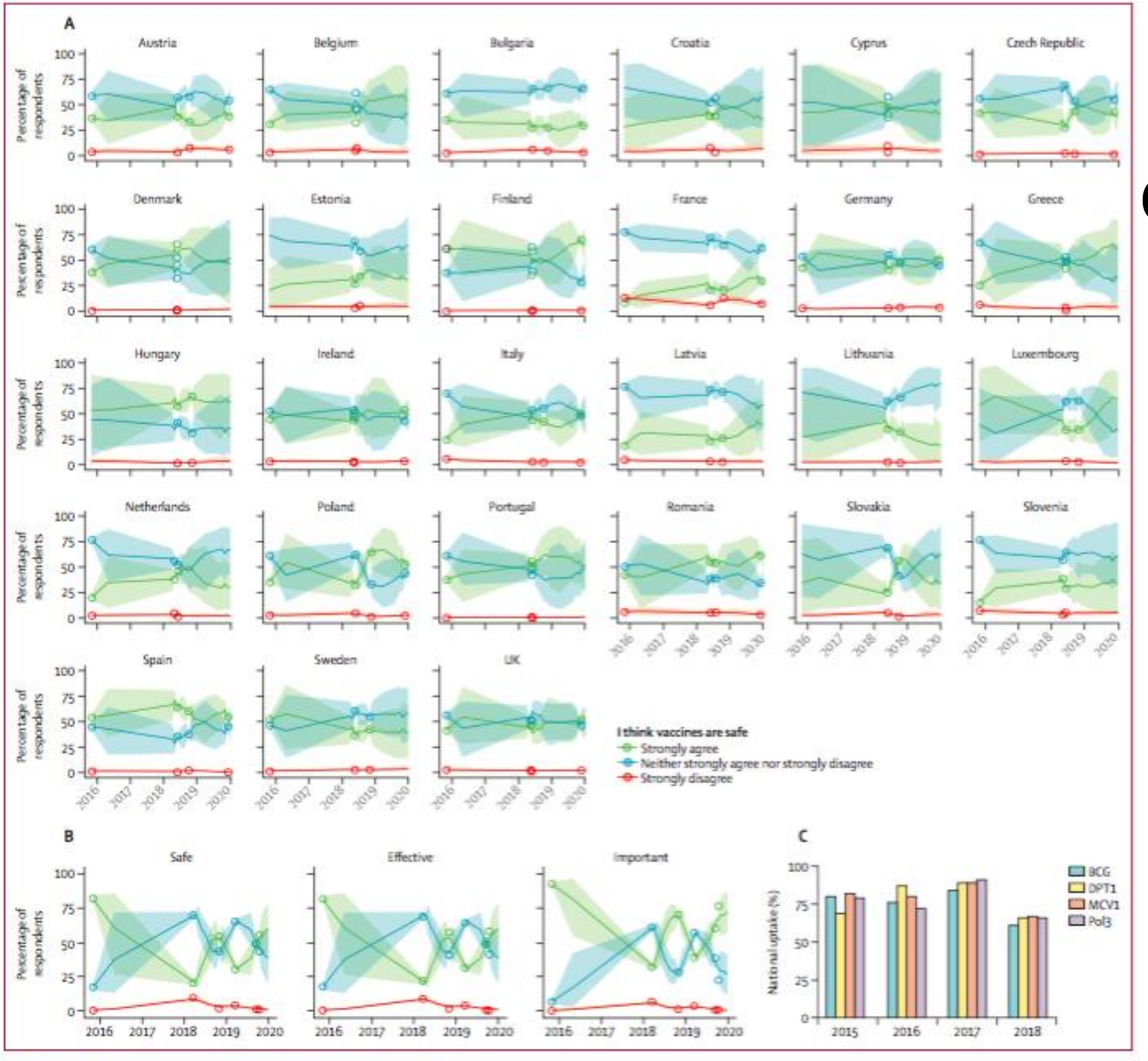


Figure 3: Trends in the perceived safety of vaccines in the EU and the Philippines

(A) Time series of estimated percentages of respondents in EU countries strongly agreeing, strongly disagreeing, or neither strongly agreeing nor strongly disagreeing that vaccines are safe. Lines are means and shaded regions are 95% HPD intervals. Circles show the observed percentage of respondents from raw data (appendix 2). Time series for all countries for all three confidence statements are shown in appendix 1 (pp 12–23). (B) Time series of survey responses across all three survey questions for the Philippines. (C) WHO-UNICEF national immunisation estimates for routine vaccination programmes in the Philippines against tuberculosis (BCG), diphtheria-pertussis-tetanus (DPT1), measles (MCV1), and polio (Pol3). HPD=highest posterior density.

Vaccine confidence

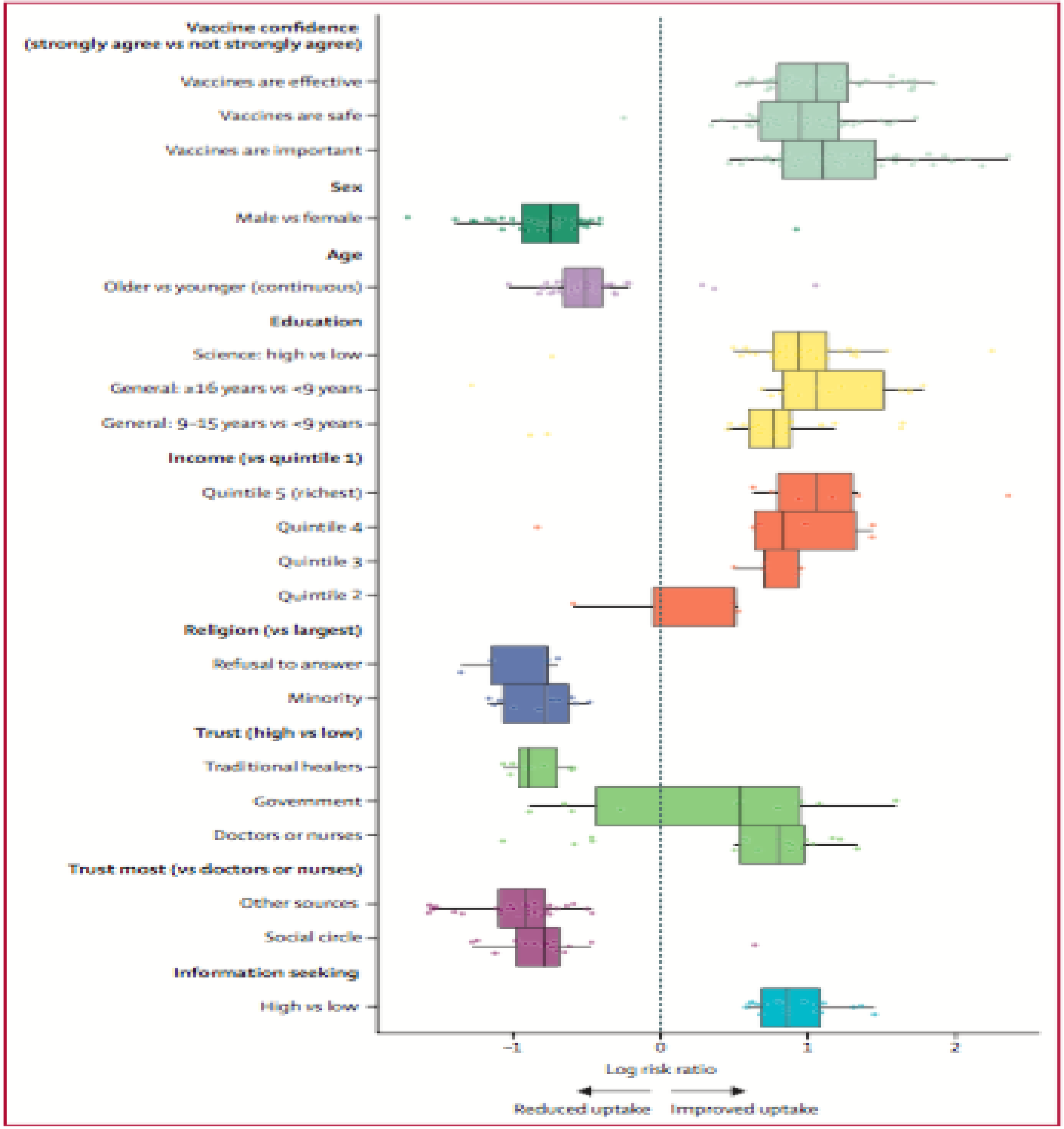


Figure 4: Univariate determinants of vaccine uptake within the Wellcome Global Monitor dataset
Global trends in univariate associations between vaccine uptake and confidence in vaccines, demographics and socioeconomic status, sources of trust, and information-seeking behaviours. Each point represents a significant association (95% HPD interval excludes zero) between a variable and uptake in a given country. Boxplots show the median log risk ratio and IQR. All variables (except age, which is continuous) are categorical and baseline groups are specified by each category (eg, high vs low denotes low as the baseline group; see the table for definitions). HPD=highest posterior density.

Vaccine confidence

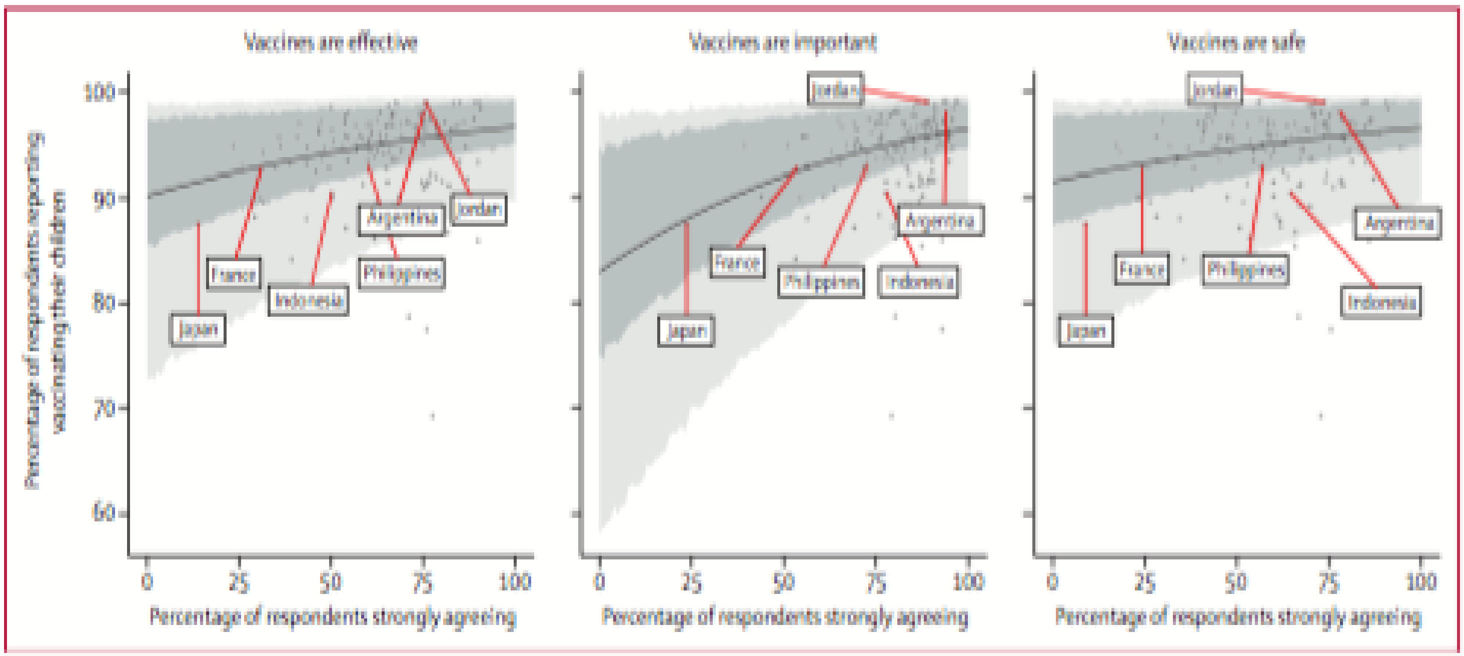
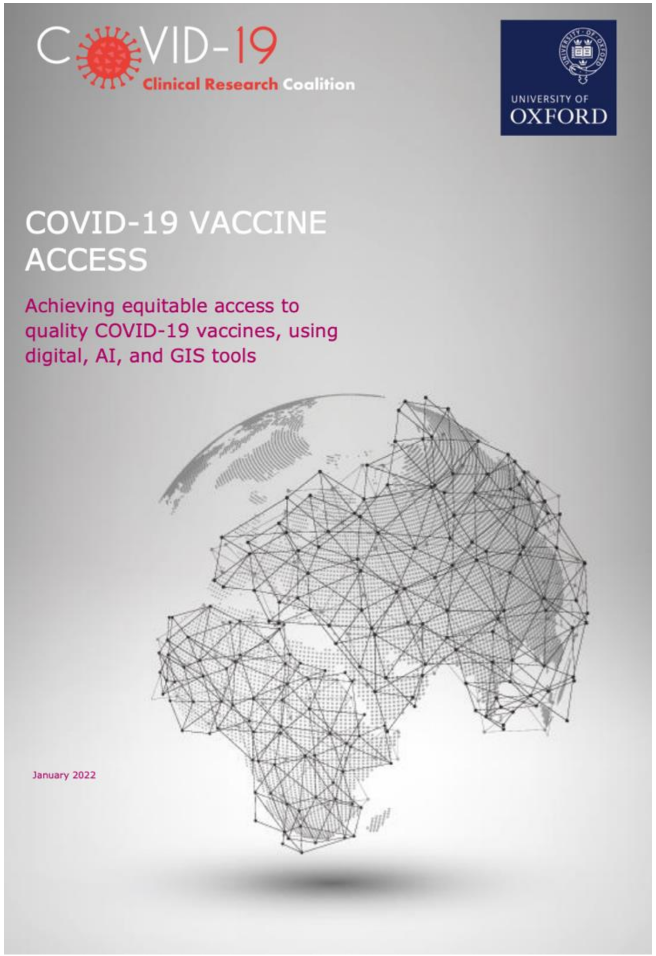


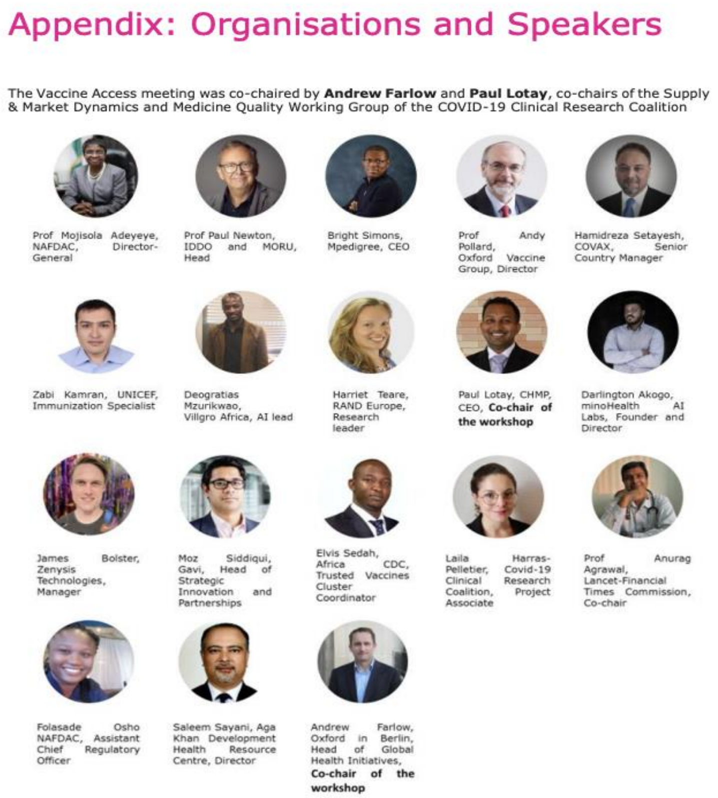
Figure 5: Association between national level vaccine uptake and vaccine confidence as reported in the Wellcome Global Monitor
The solid line represents the mean regression with 70% and 95% HPD intervals shaded in dark and light grey, respectively. Datapoints for (lowest confidence) and the Philippines (case study) are shown, alongside randomly selected countries. HPD=highest posterior density.

Last breakout discussion

- What are your own experiences and examples of lack of vaccine confidence (countries and health systems you worked in? personal experiences?)
- How is confidence created? And lost?
- Are scientists good at inspiring confidence? Politicians? Other?
- What is the role of social media?
- How will SF vaccines complicate all of this? What about vaccine 'donations'?
- How long will the pandemic last?
- What about the fact that SARS-CoV-2 has become endemic and we need to live with this reality?

Worth a read….





Appendix: Organisations and Speakers

The Vaccine Access meeting was co-chaired by **Andrew Farlow** and **Paul Lotay**, co-chairs of the Supply & Market Dynamics and Medicine Quality Working Group of the COVID-19 Clinical Research Coalition

Prof Mojisola Adeyeye, NAFDAC, Director-General

Prof Paul Newton, IDDO and MORU, Head

Bright Simons, Mpedigree, CEO

Prof Andy Pollard, Oxford Vaccine Group, Director

Hamidreza Setayesh, COVAX, Senior Country Manager

Zabi Kamran, UNICEF, Immunization Specialist

Deogratias Mzurikwao, Villgro Africa, AI lead

Harriet Teare, RAND Europe, Research leader

Paul Lotay, CHMP, CEO, **Co-chair of the workshop**

Darlington Akogo, minoHealth AI Labs, Founder and Director

James Bolster, Zenysis Technologies, Manager

Moz Siddiqui, Gavi, Head of Strategic Innovation and Partnerships

Elvis Sedah, Africa CDC, Trusted Vaccines Cluster Coordinator

Laila Harras-Pelletier, Covid-19 Clinical Research Coalition, Project Associate

Prof Anurag Agrawal, Lancet-Financial Times Commission, Co-chair

Folasade Osho NAFDAC, Assistant Chief Regulatory Officer

Saleem Sayani, Aga Khan Development Health Resource Centre, Director

Andrew Farlow, Oxford in Berlin, Head of Global Health Initiatives, **Co-chair of the workshop**

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