Lessons from the COVID-19 pandemic and response to future pandemics

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INSTITUT PASTEUR

le cnam

COVID-19 : « the perfect storm »

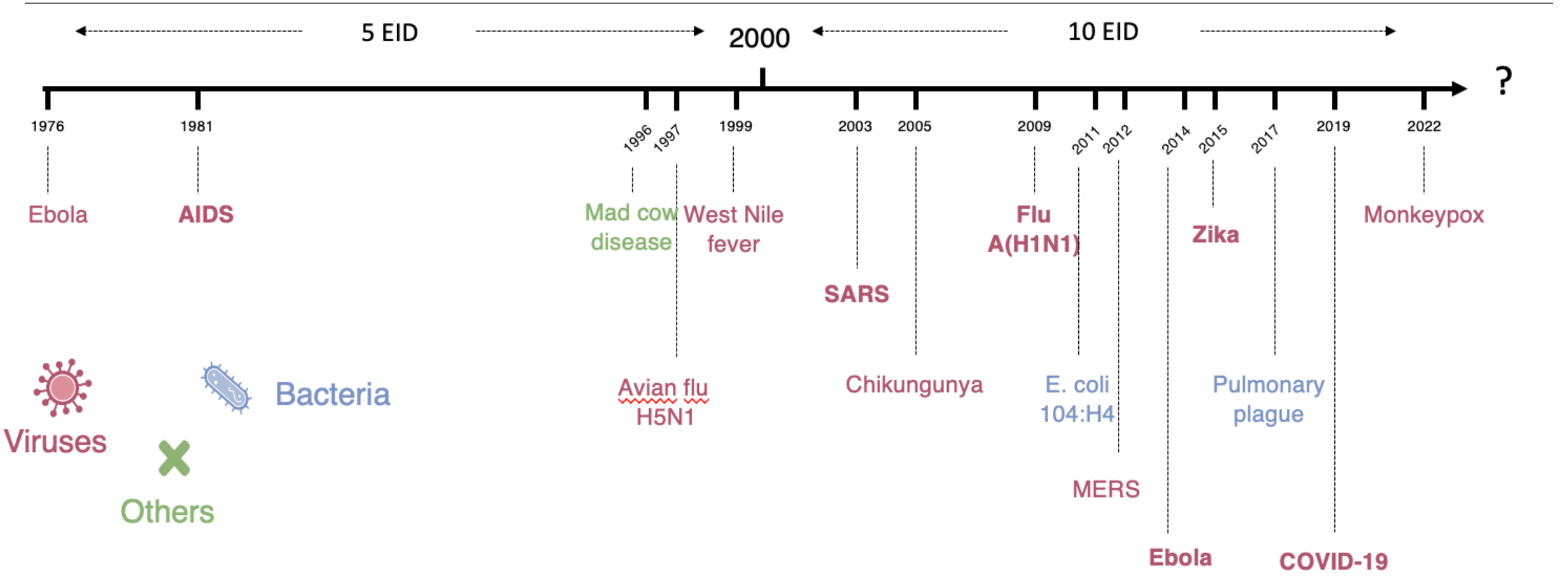
⇨ COVID-19 mortality by the end of 2022 :
- 25 million excess deaths worldwide (The Economist)
- 170,000 COVID-19 deaths in France (SpF, DREES, Inserm)

⇨ Post intensive care unit sequellae, long COVID

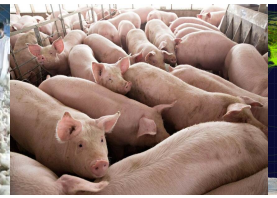
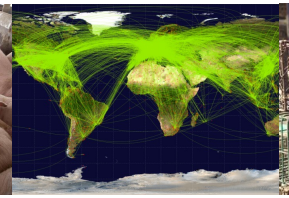
⇨ Mental health, children education

⇨ Lost output: 12,500 billion dollars (IMF) (2020-2024)
Global cost: 424 billion euros in France (2020-2022)

Increase in emerging infectious diseases incidence over time








Which strategy worked best for COVID-19 pandemic control ?

Strategies for epidemic control

Herd Immunity

Let Covid-19 spread without collective control measures

Objective: reach herd immunity through natural infections

Zero Covid

Implement strict lockdown-like measures for a prolonged time period

Objective: virus suppression (on a national or regional level)

Softer version: « aggressive » tracking & tracing

Stop and Go

Alternate between tightening and easing of restrictive measures, based on hospital saturation level

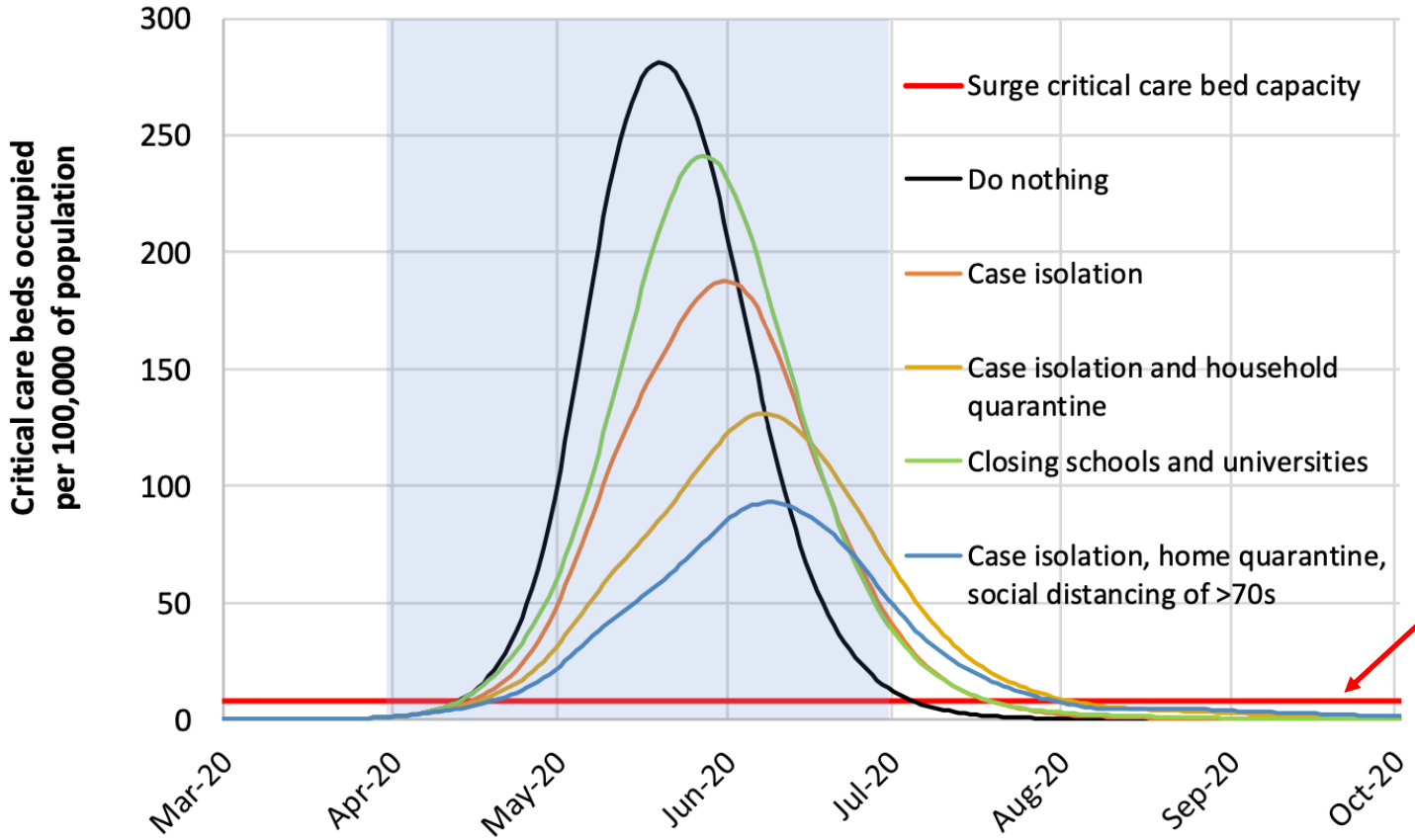
Objective: improved short-term acceptability

Act Early and Hard

Anticipate epidemic upturns and apply early, preventive ‘‘braking’’ measures

Objective: preserve health system, maintain morbi-mortality at low level, limit restrictions intensity and duration

Modeling impact of interventions
Critical care beds occupancy - UK



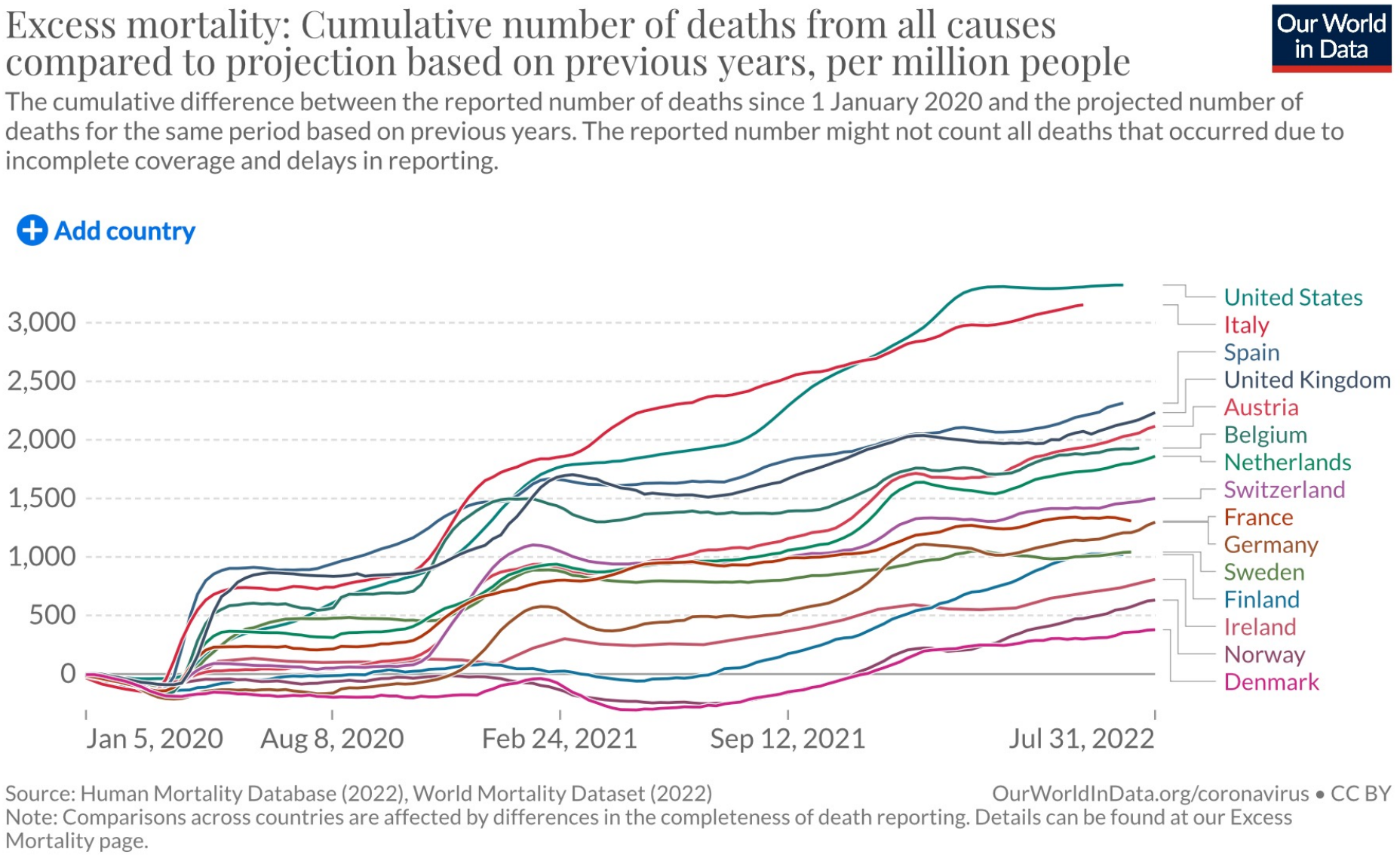
« We therefore conclude that epidemic suppression is the only viable strategy at the current time »

Maximum ICU bed capacity

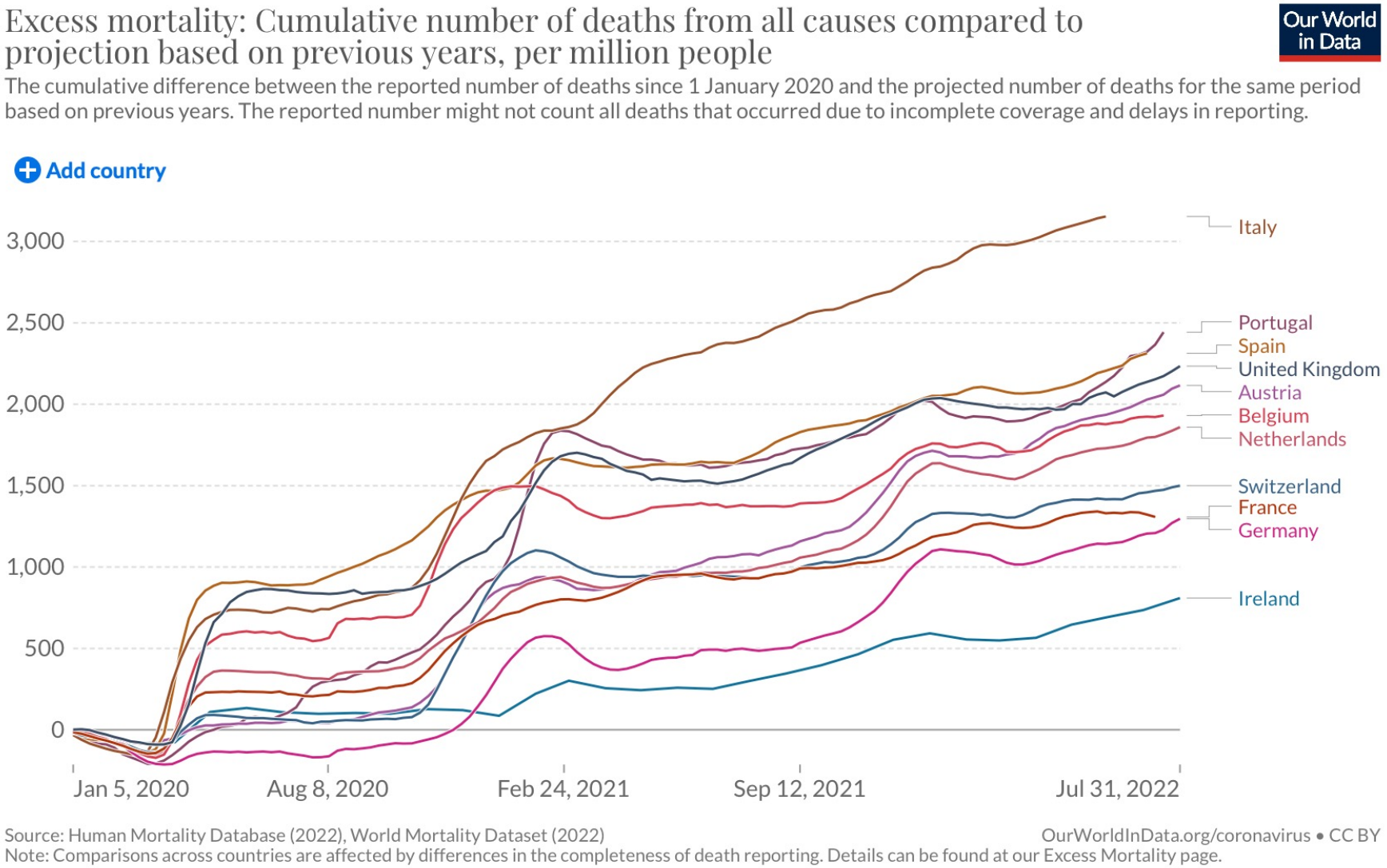
(Ferguson et al., Imperial College Response Team, 16 March 2020)

And the unthinkable happened… 17 March 2020

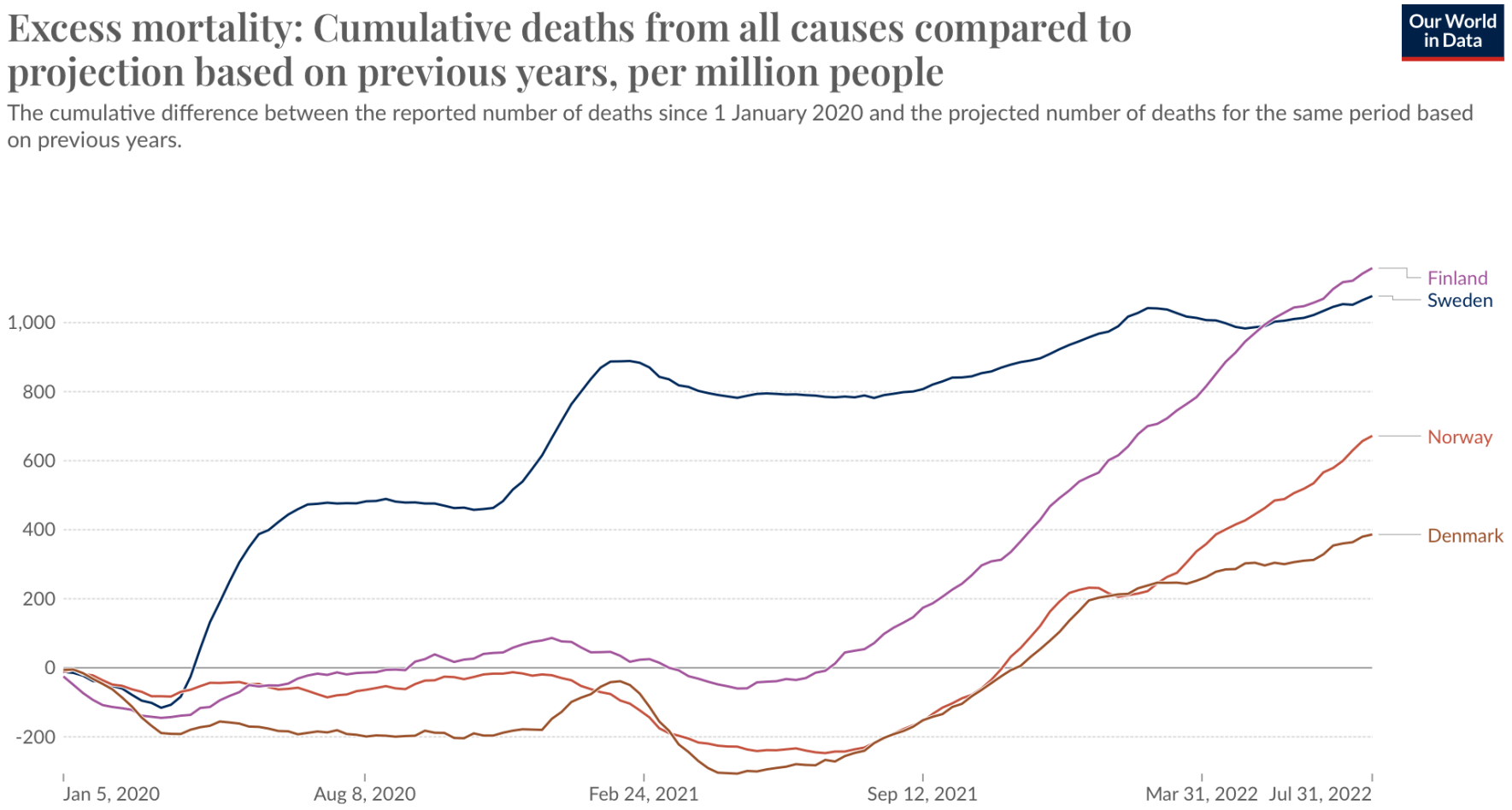
Western Europe and the U.S.



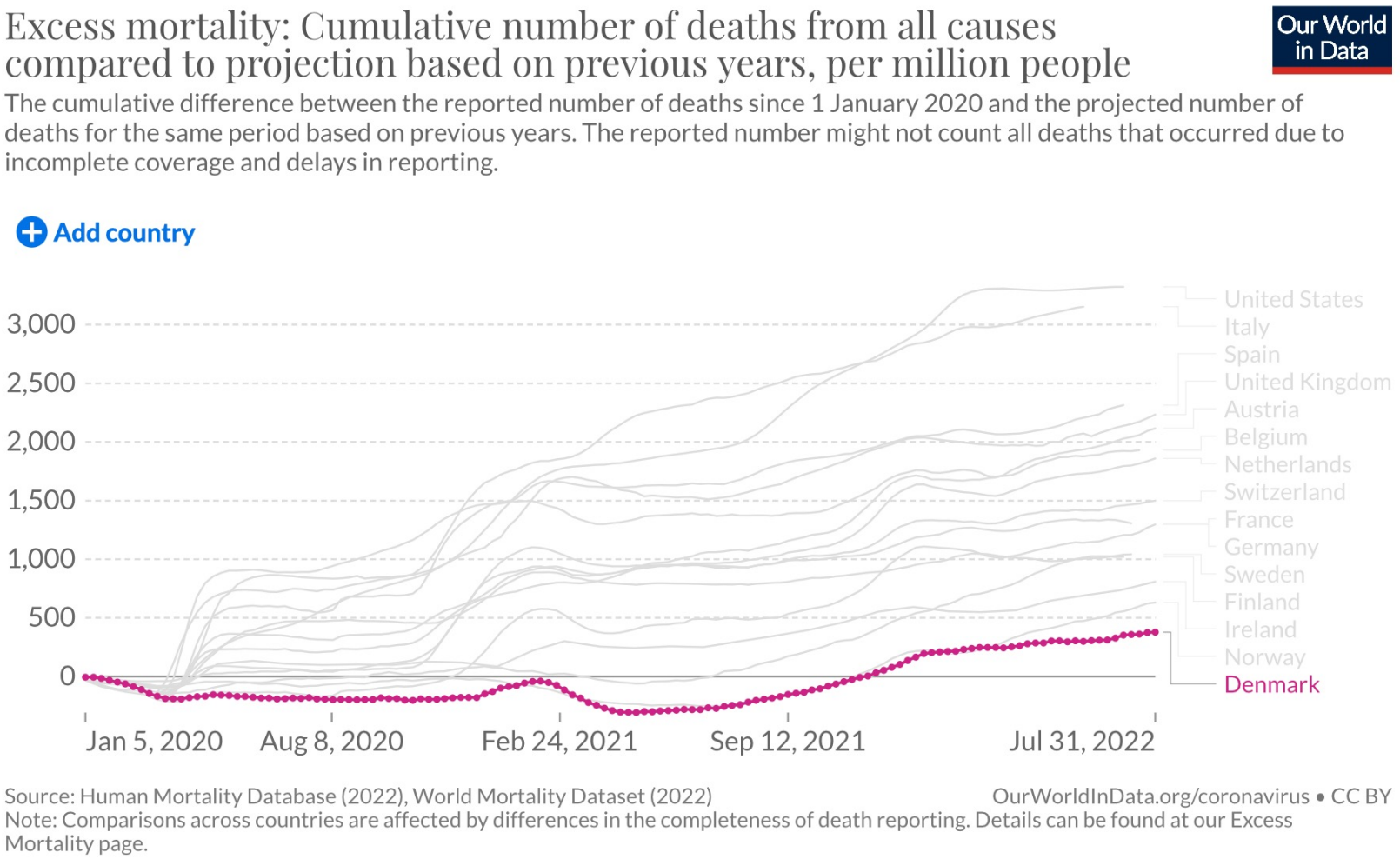
Stop and Go: the case of most Western Europe



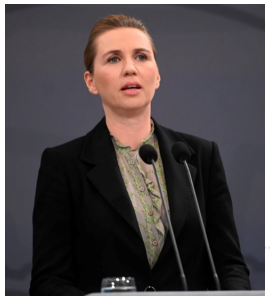
Herd immunity policy: The case of Sweden



Anticipate: The case of Denmark



Weekly hospital admissions for COVID-19 per million, Denmark, 2020-2022



Mette Frederiksen
March 11, 2020

Immunization

Hospital admission levels reached by European countries in « crisis » times

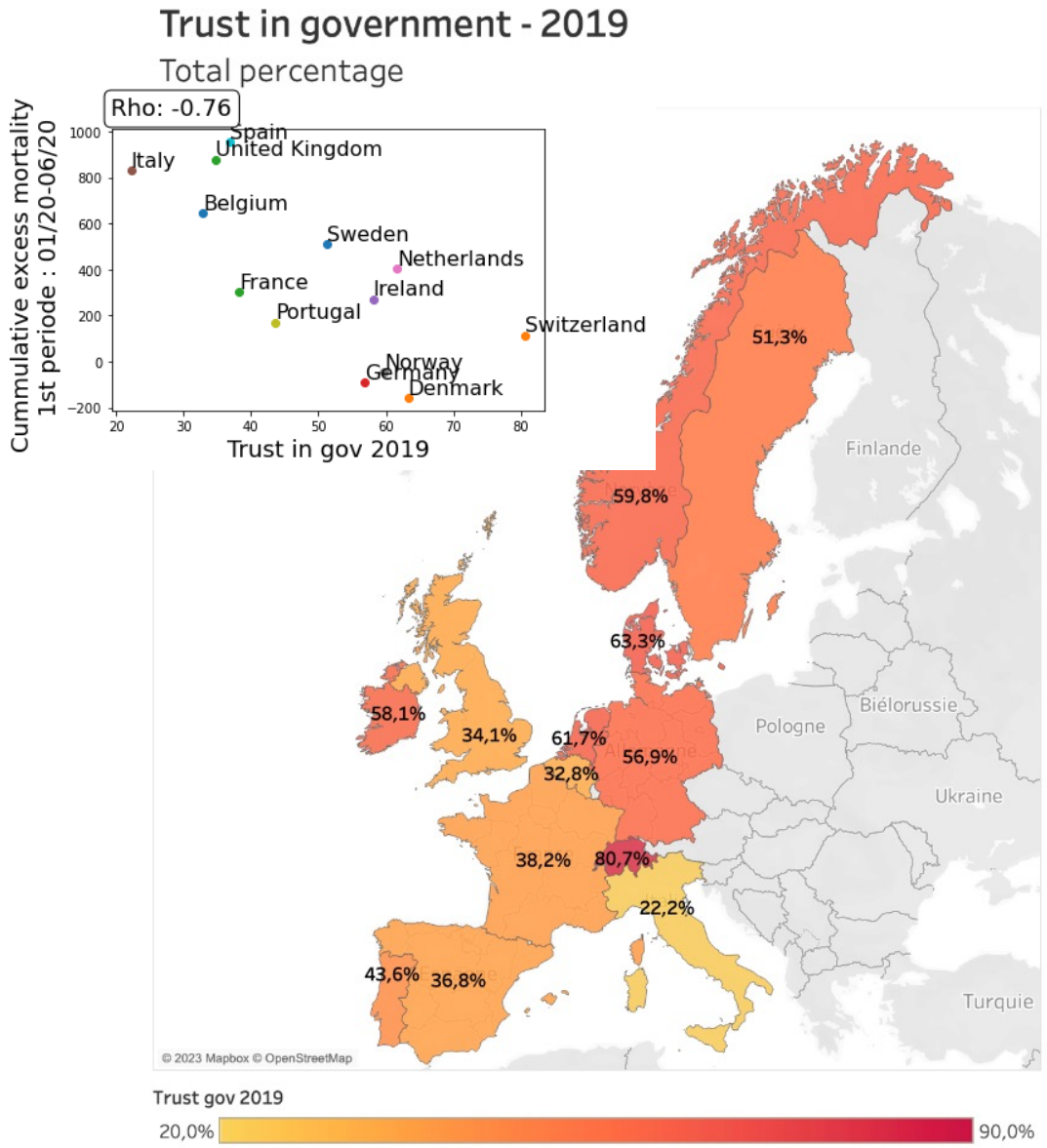
Data source: Official data collated by Our World in Data – Last updated 22 February 2024 – Learn more about this data

OurWorldInData.org/coronavirus | CC BY

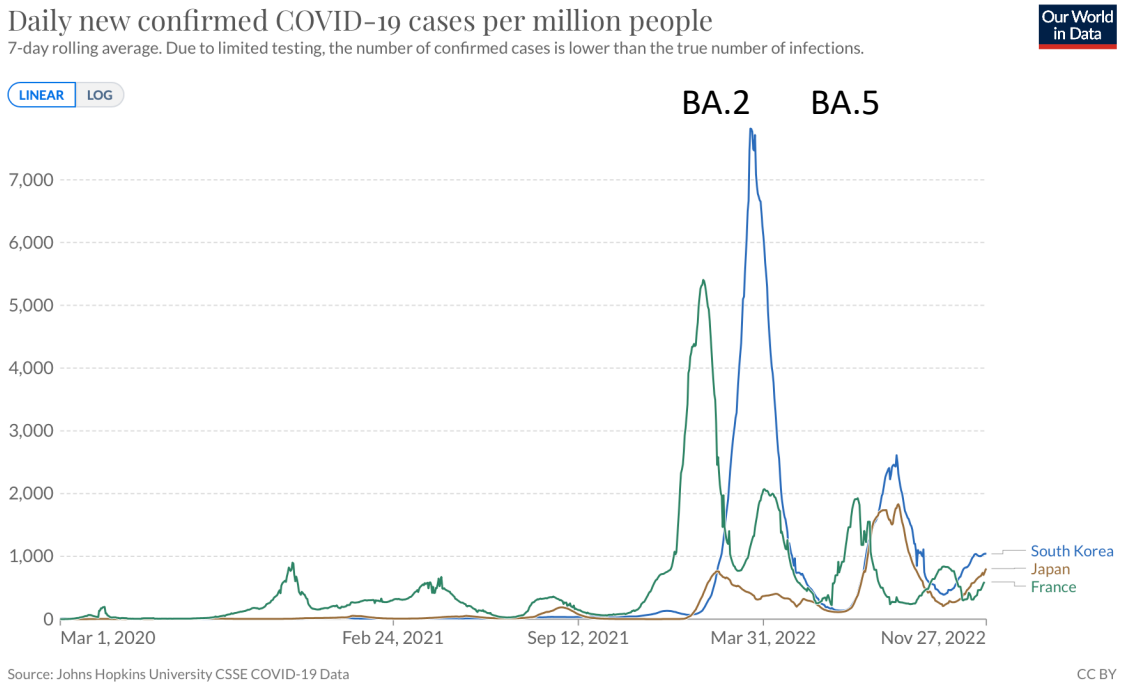
Trust in government

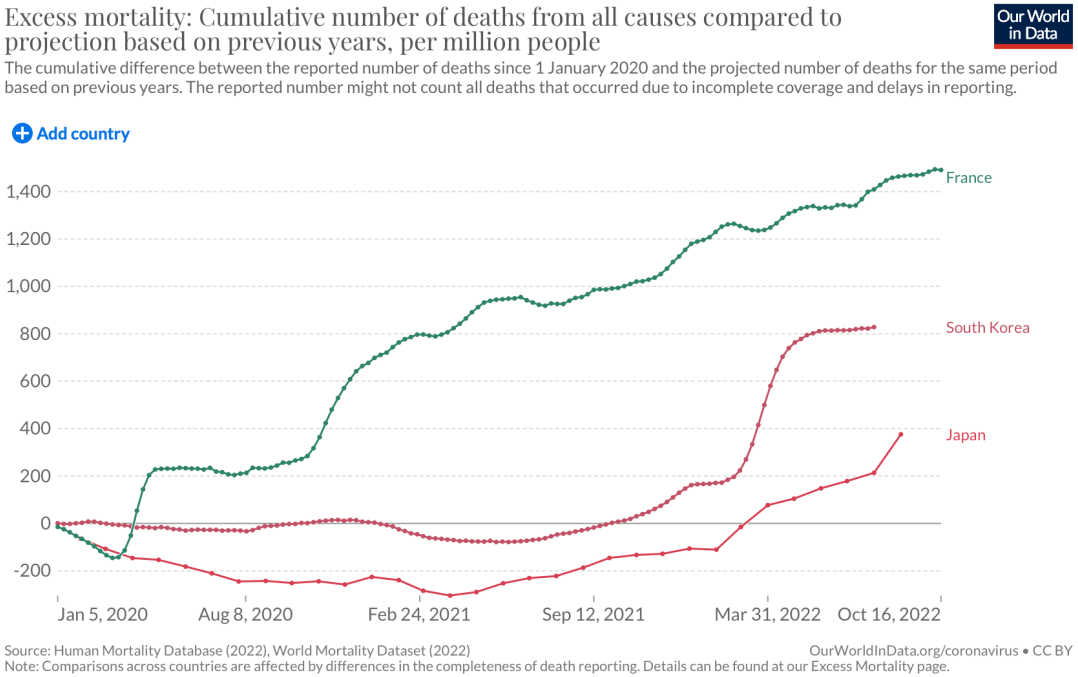
Source OECD

Trust in government :
Refers to the share of people who report having confidence in the national government. The data shown reflect the share of respondents answering “yes” to the survey question: “In this country, do you have confidence in… national government? The sample is ex ante designed to be nationally representative of the population aged 15 and over.

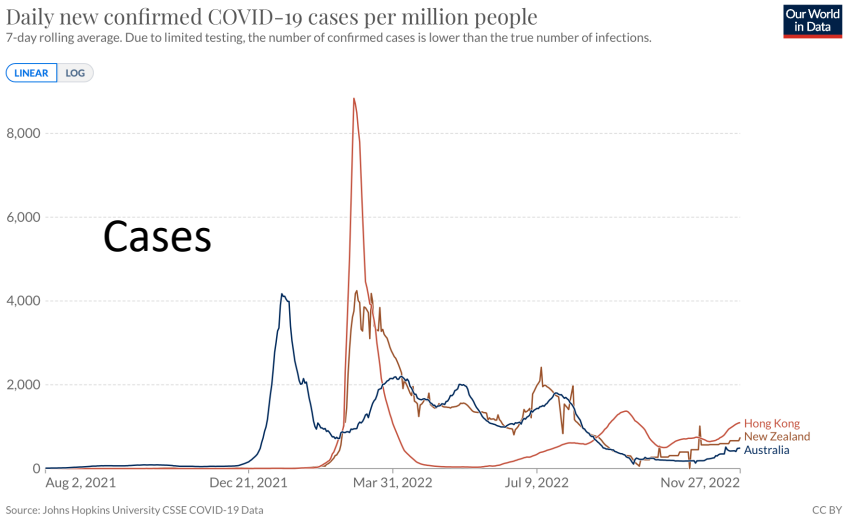


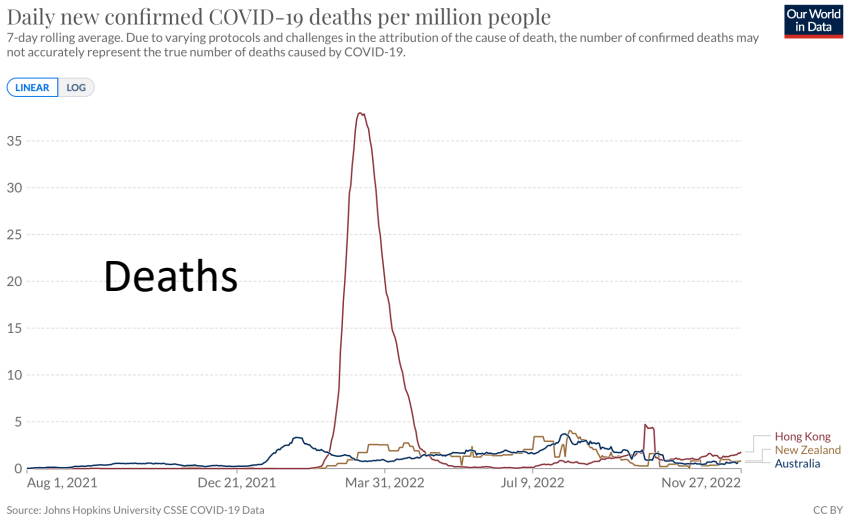
« Aggressive » contact tracing, isolation & quarantine + masking South Korea and Japan

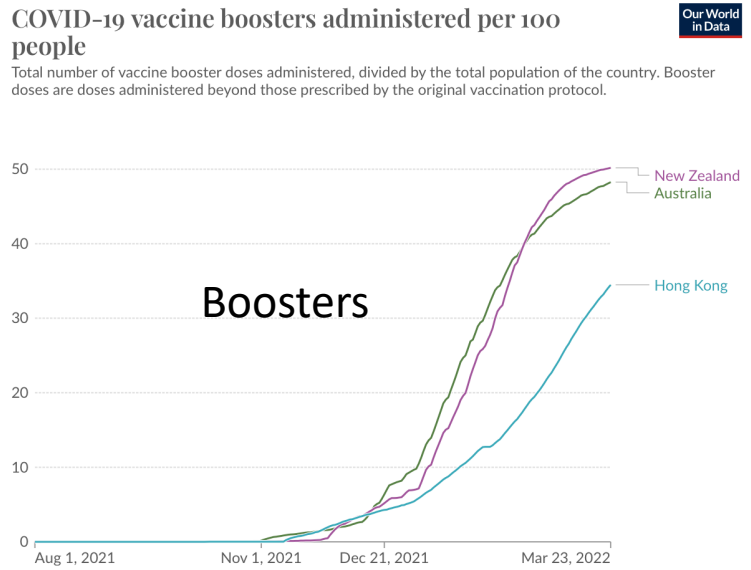


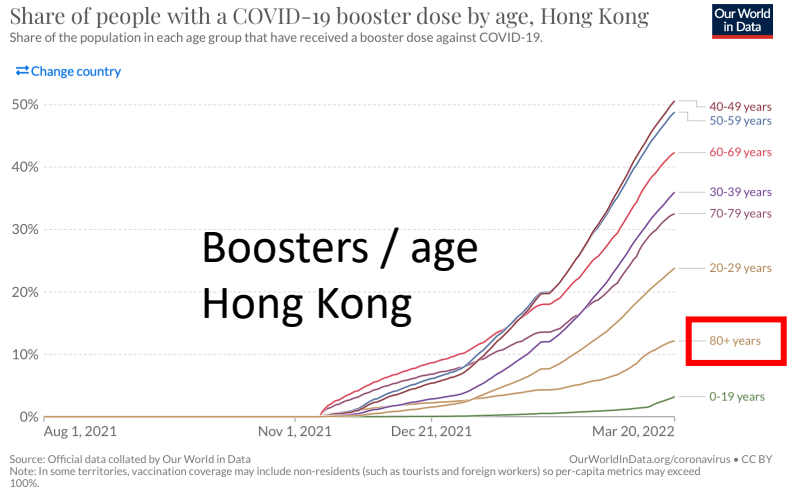


Zero Covid policy: needs coupling with vaccination of elderly Australia, New Zealand and Hong Kong



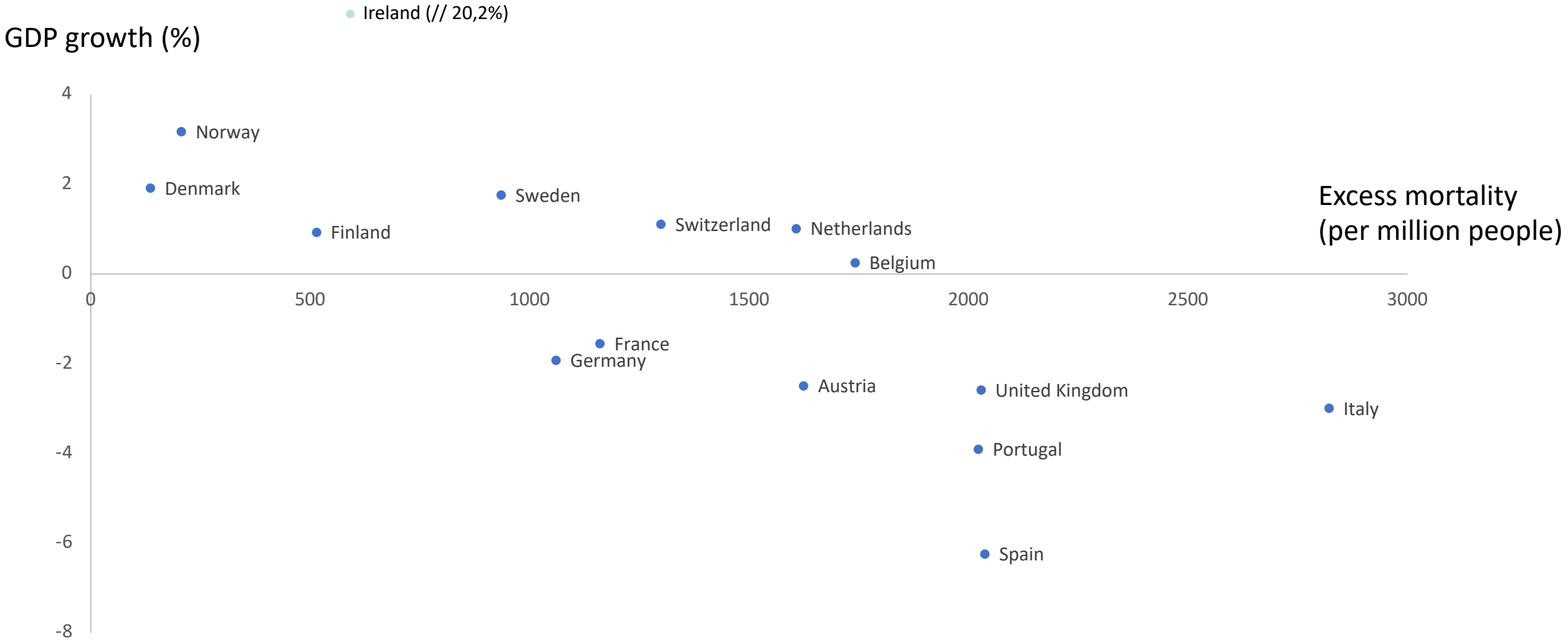






It is not health against the economy. It is health with the economy !

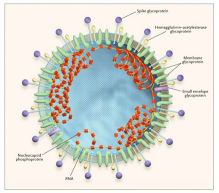
Excess mortality per million people versus GDP growth, Europe, 2020-1

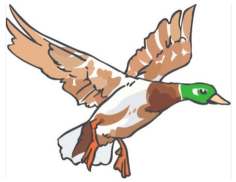


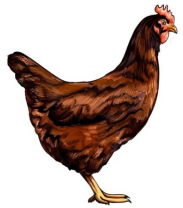
(Source: Our World in Data & IMF)

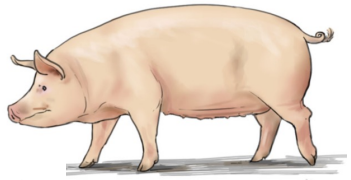
What are the main threats and what should be done to mitigate the risk of future pandemics?

How do viruses « emerge »?









Insect vector

Virus

Animal reservoir

Intermediate host

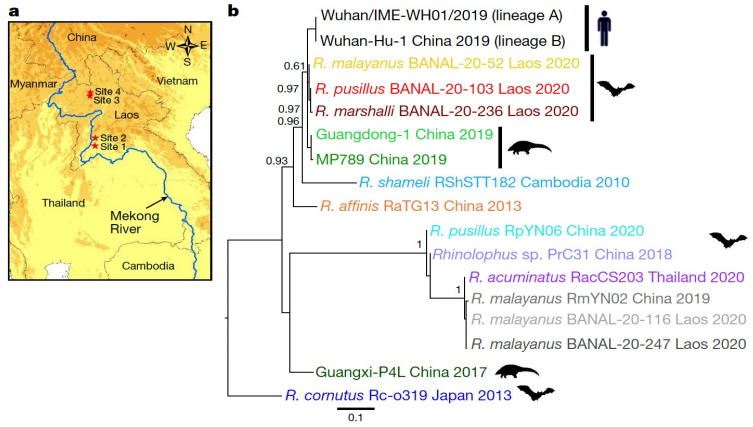
Transmission to humans

Transmission among humans and spread

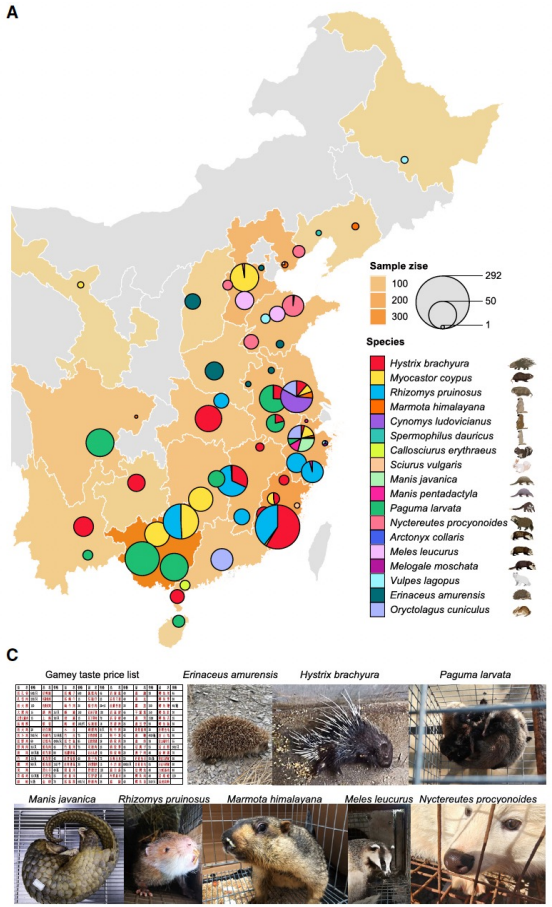
Bats and beta-coronaviruses: SARS-CoV, MERS-CoV, SARS-CoV-2

nature
https://doi.org/10.1038/s41586-022-04532-4
Accelerated Article Preview

Bat coronaviruses related to SARS-CoV-2 and infectious for human cells



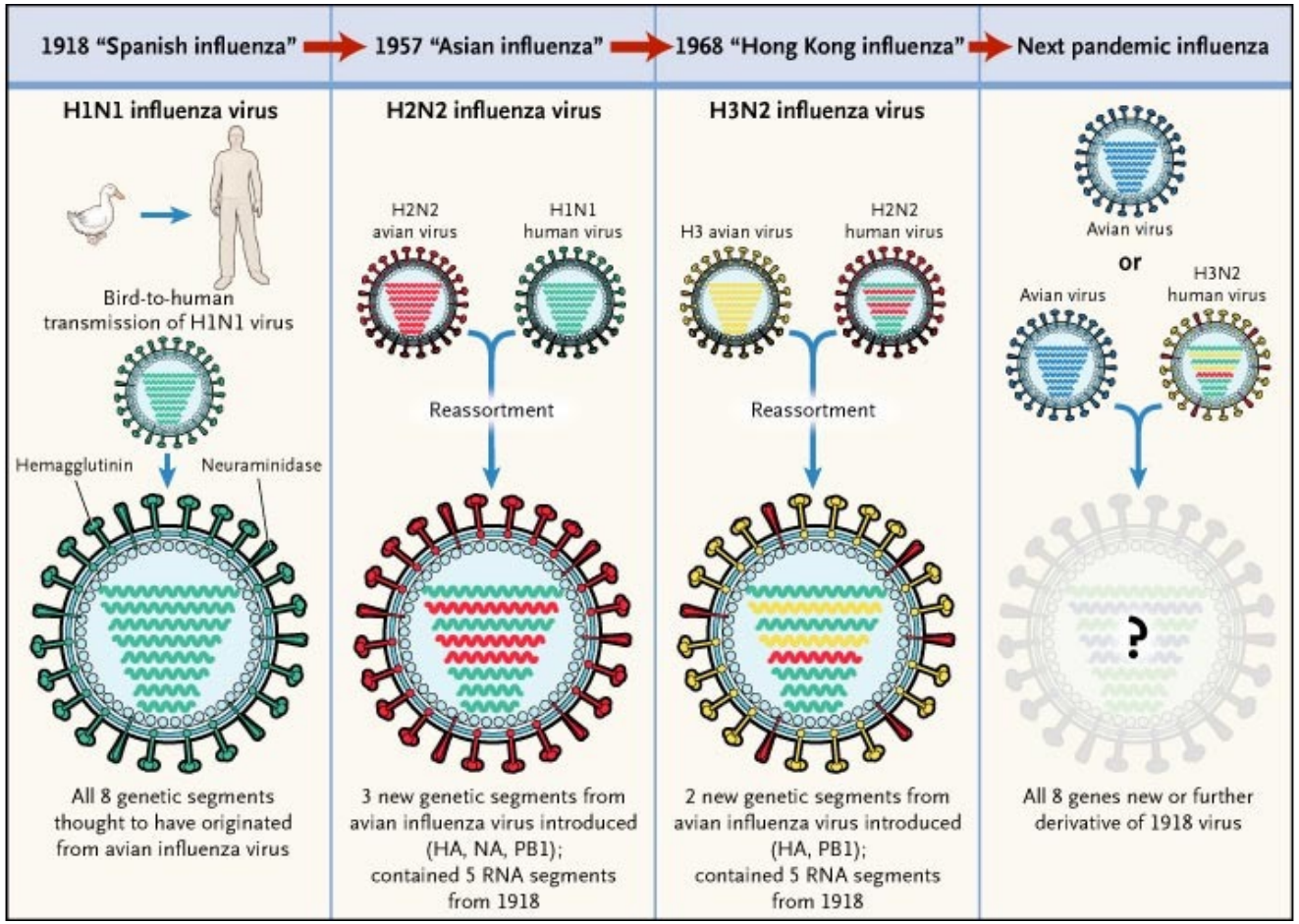
(Temmam, Nature, 2022)



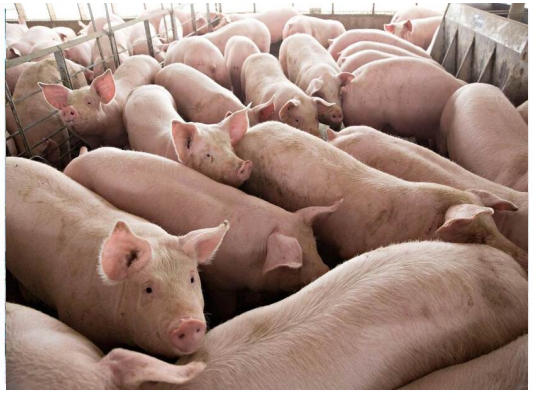
(He, Cell, 2022)

Fight deforestation
&
control market

Influenza viruses



(Belshe, NEJM, 2005)



Birds
& Animal farming
surveillance
-
+/- vaccination

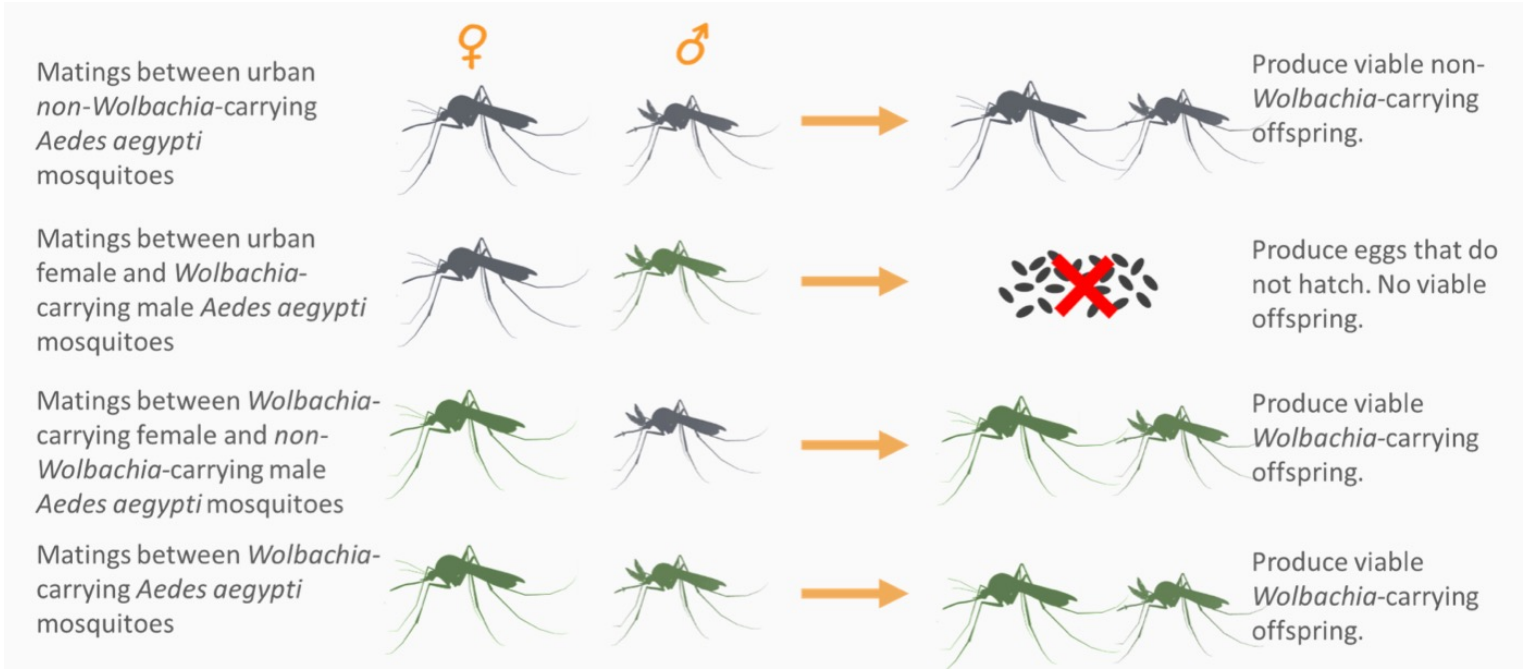
Economics for pandemic prevention

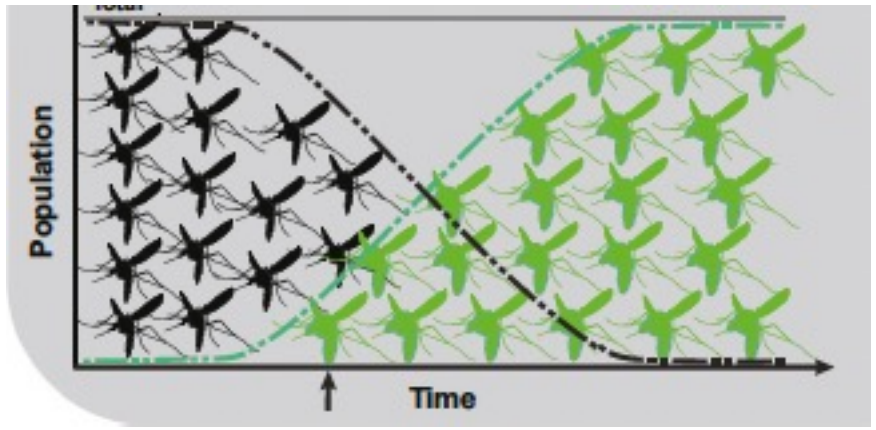
ITEM	VALUES (2020 $)
Expenditures on preventive measures	
Annual funding for monitoring wildlife trade (CITES+)	$250–$750 M
Annual cost of programs to reduce spillovers	$120–$340 M
Annual cost of programs for early detection and control	$217–$279 M
Annual cost of programs to reduce spillover via livestock	$476–$852 M
Annual cost of reducing deforestation by half	$1.53–$9.59 B
Annual cost of ending wild meat trade in China	$19.4 B
TOTAL GROSS PREVENTION COSTS (*C*)	**$22.0–$31.2 B**
Ancillary benefit of prevention	
Social cost of carbon	$36.5/tonne
Annual CO_2 emissions reduced from 50% less deforestation	118 Mt
Ancillary benefits from reduction in CO_2 emissions	$4.31 B
TOTAL PREVENTION COSTS NET OF CARBON BENEFITS (*C*)	**$17.7–$26.9 B**

Damages from COVID-19	
Lost GDP in world from COVID-19	$5.6 T
Value of a statistical life (*V*) adjusted for COVID-19 mortality structure	$5.34 M or $10.0 M
Total COVID-19 world mortality (Q_D) forecast by 28 July 2020, 50th percentile with 95% error bounds	590,643 [473,209, 1,019,078]
Value of deaths in world from COVID-19 = $Q_D \times V$	
Lowest ($5.34 M × 2.5th percentile mortality forecast)	$2.5 T
Middle ($10 M × 50th percentile mortality forecast)	$5.9 T
Highest ($10 M × 97.5th percentile mortality forecast)	$10.2 T
TOTAL DISEASE DAMAGES (*D*):	
Lowest ($5.34 M × 2.5th percentile mortality forecast)	**$8.1 T**
Middle ($10 M × 50th percentile mortality forecast)	**$11.5 T**
Highest ($10 M × 97.5th percentile mortality forecast)	**$15.8 T**

(Dobson, Science, 2020)

Wolbachia-infected mosquitoes



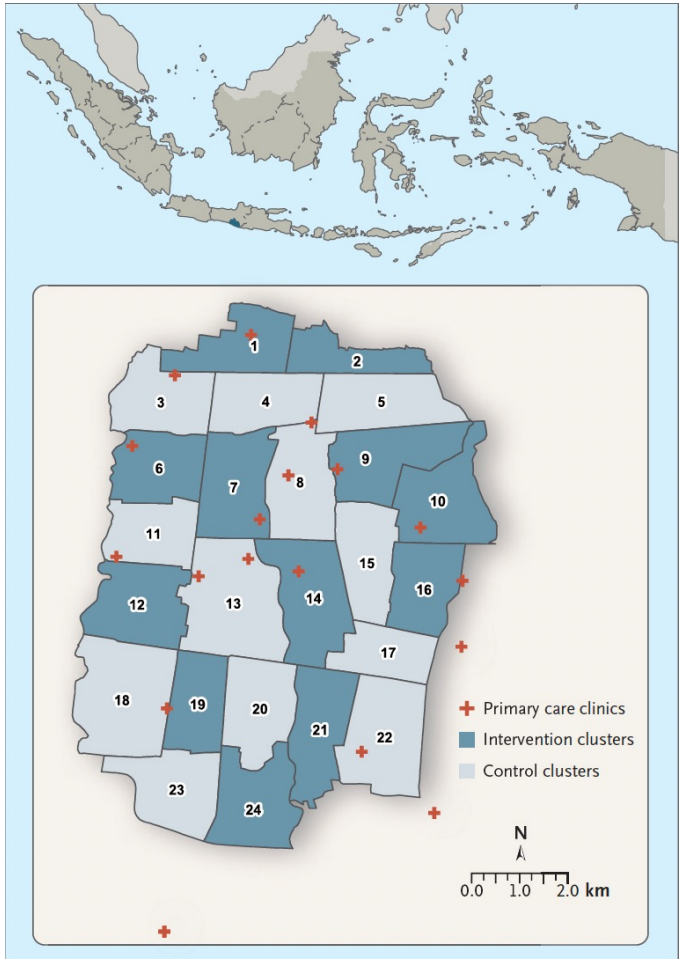


Resistant to pathogens


(Credit: Kevin Frayer/Getty Images)

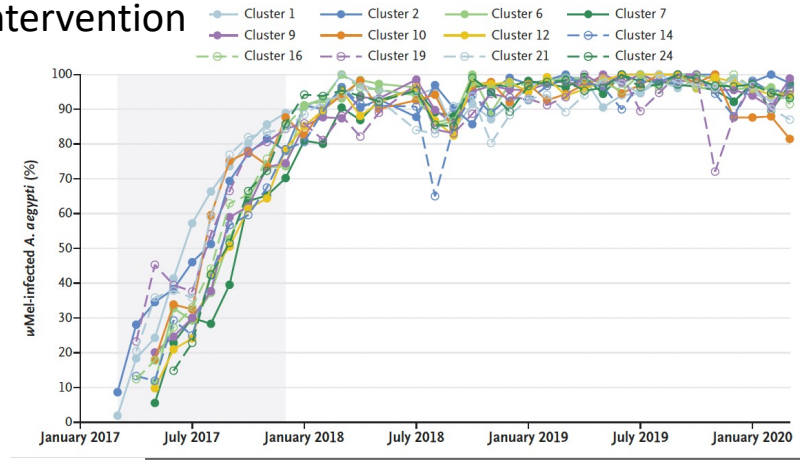

(Credit: WMP Brasil)

Efficacy of Wolbachia-Infected Mosquito Deployments for the Control of Dengue, Indonesia, 2017-2020

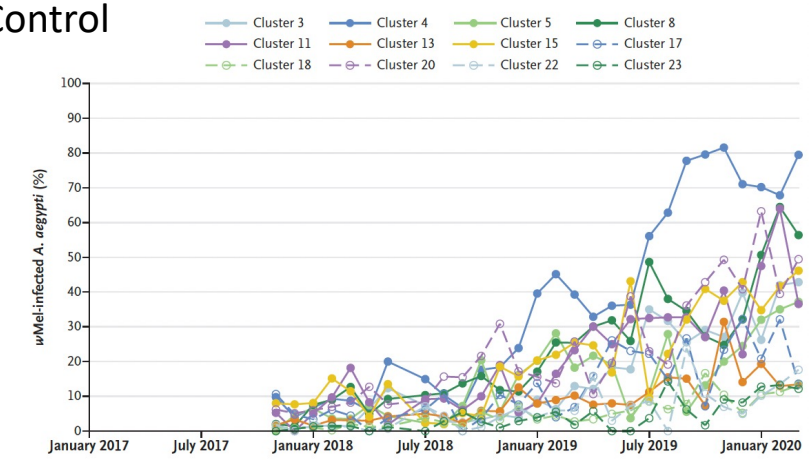


Proportion of *A. aegypti* infected with *w*Mel

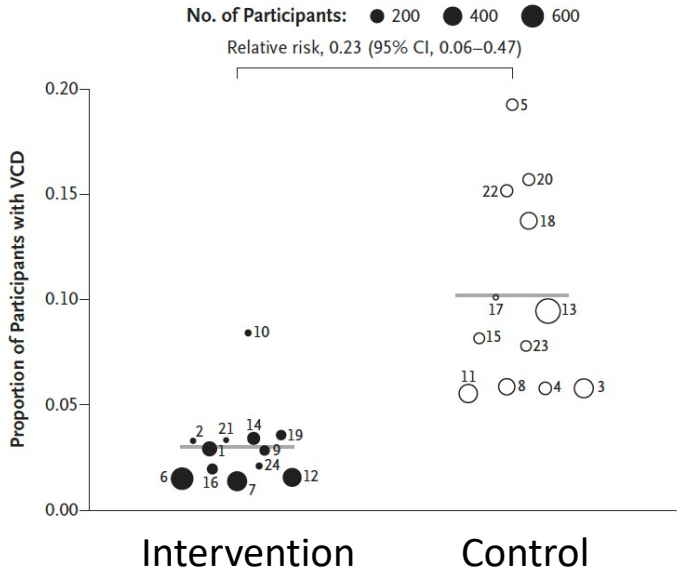
Intervention



Control



Proportion with dengue

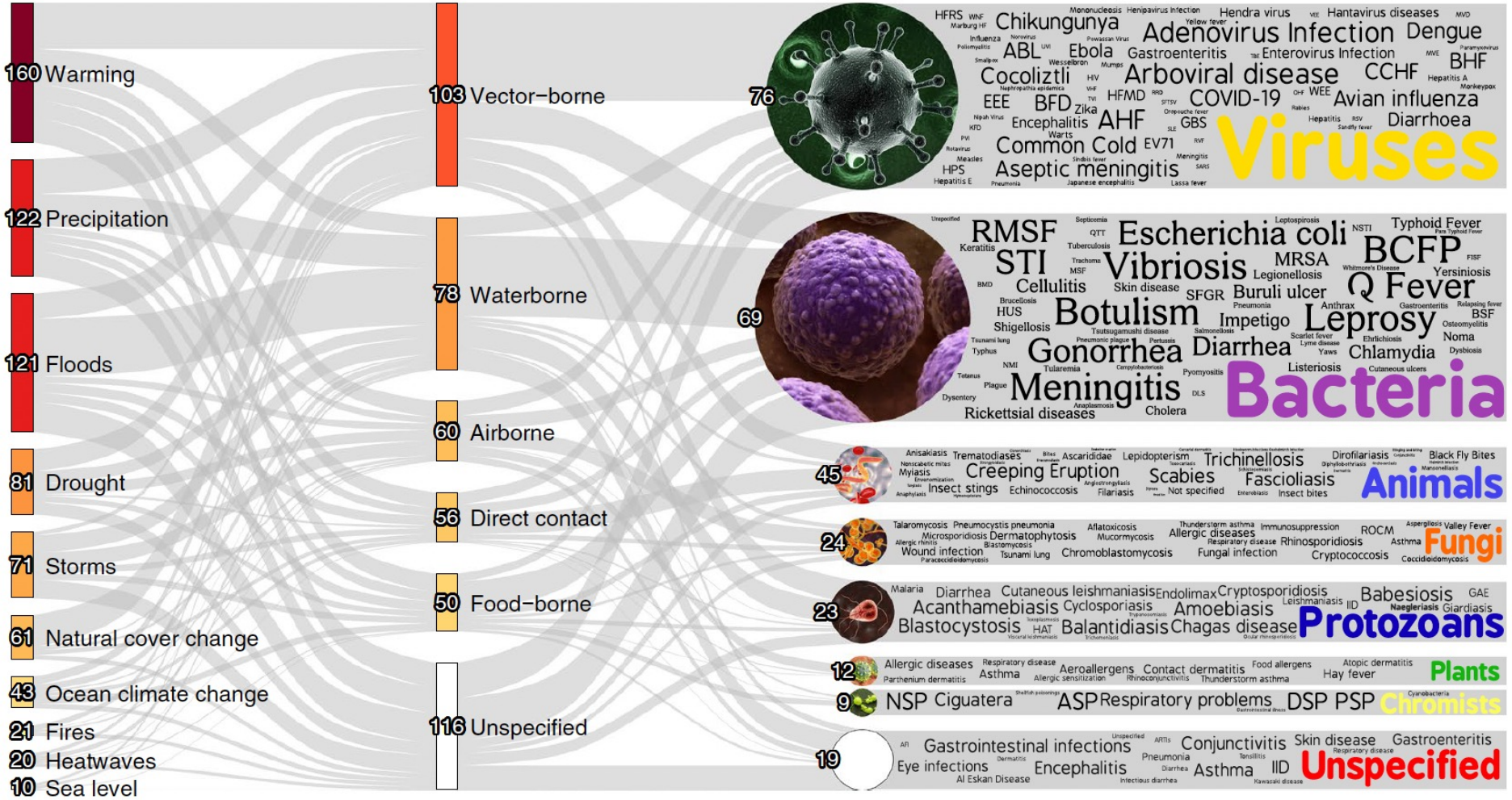


Intervention efficacy:
77.1% (65.3%-84.9%)

(Utarini, NEJM, 2021)

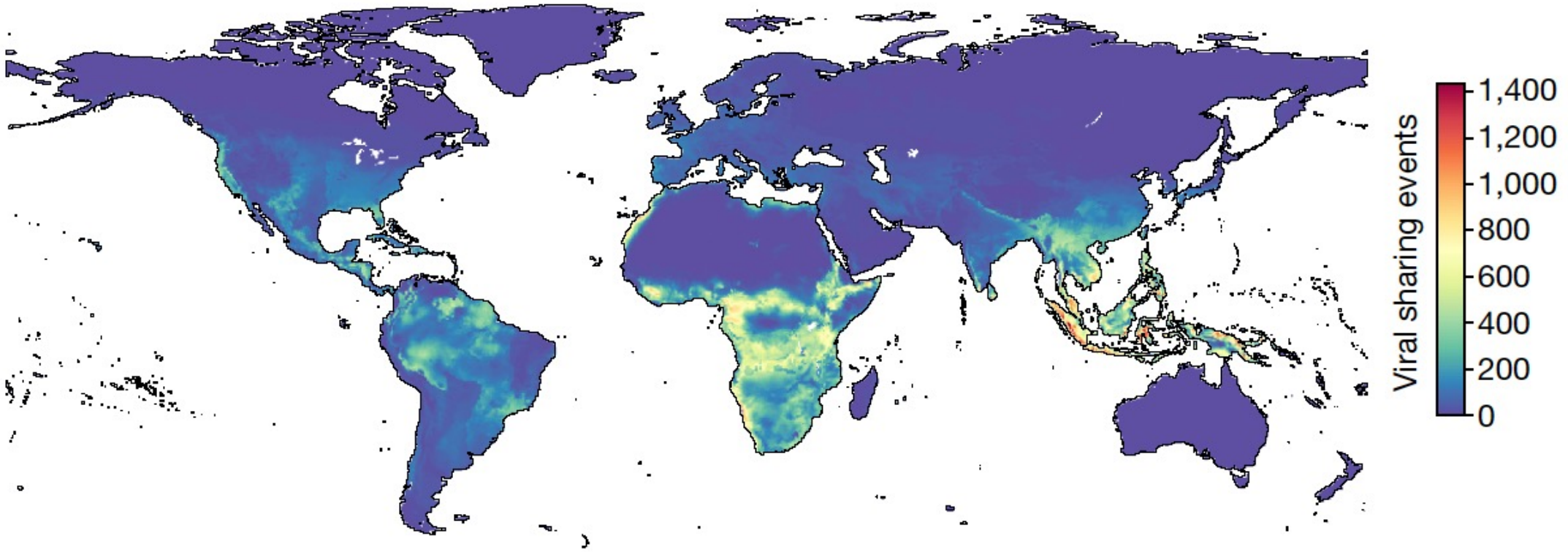
How may climate and environmental change affect future pandemics emergence ?

Climatic hazards and transmission pathways for diseases



(Mora et al, Nature Climate Change, 2022)

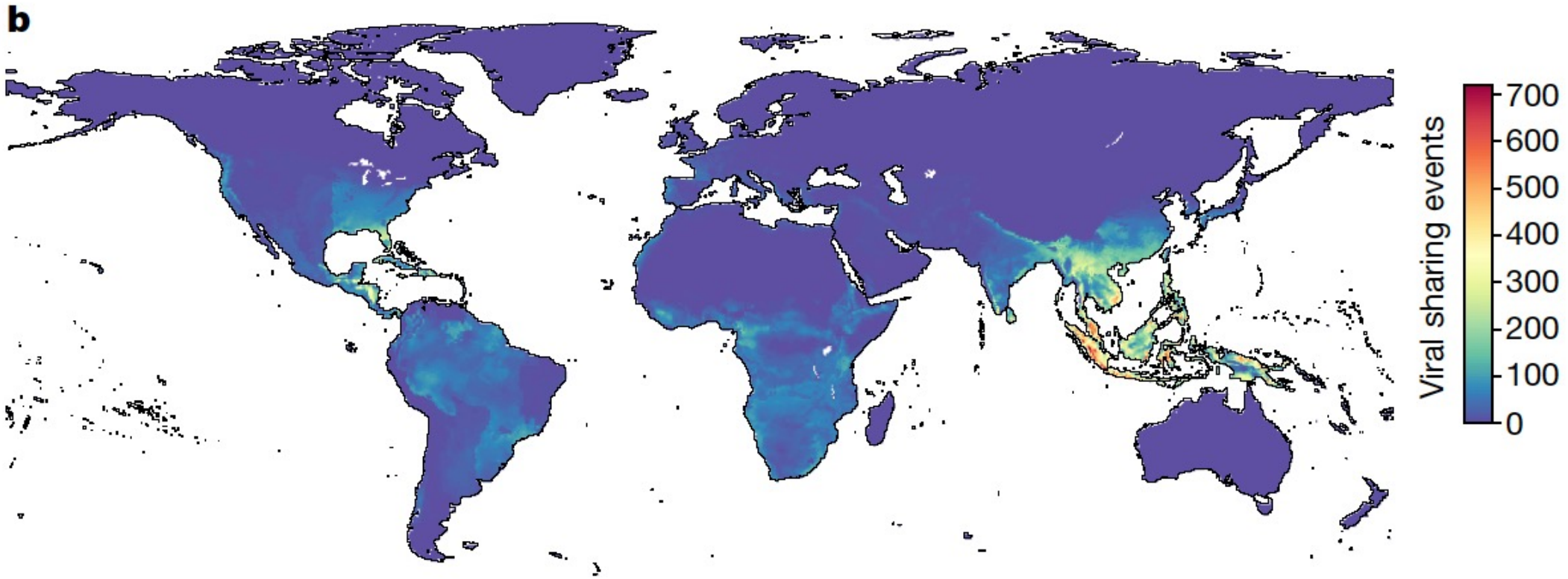
Projected number of novel viral sharing among mammal species in 2070 (no dispersal limits) - (SSP 1– RCP 2.6)



Change in climate and land use → >15,000 viral sharing events among mammals in high elevation and species-rich ecosystems

(Carlson, Nature, 2022)

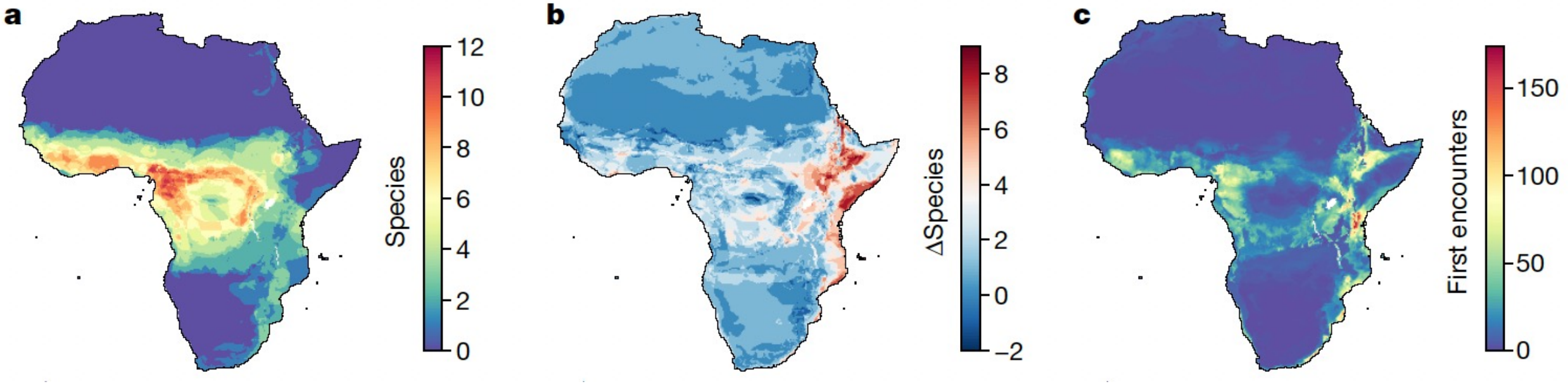
Projected number of novel viral sharing among mammal species in 2070 (with dispersal limits) - (SSP 1–RCP 2.6)



Bats will account for 90% of new encounters after constraining dispersal

(Carlson, Nature, 2022)

Range expansions of Zaire ebolavirus (ZEBOV) hosts - (SSP 1–RCP 2.6)



Predicted distribution of ZEBOV hosts

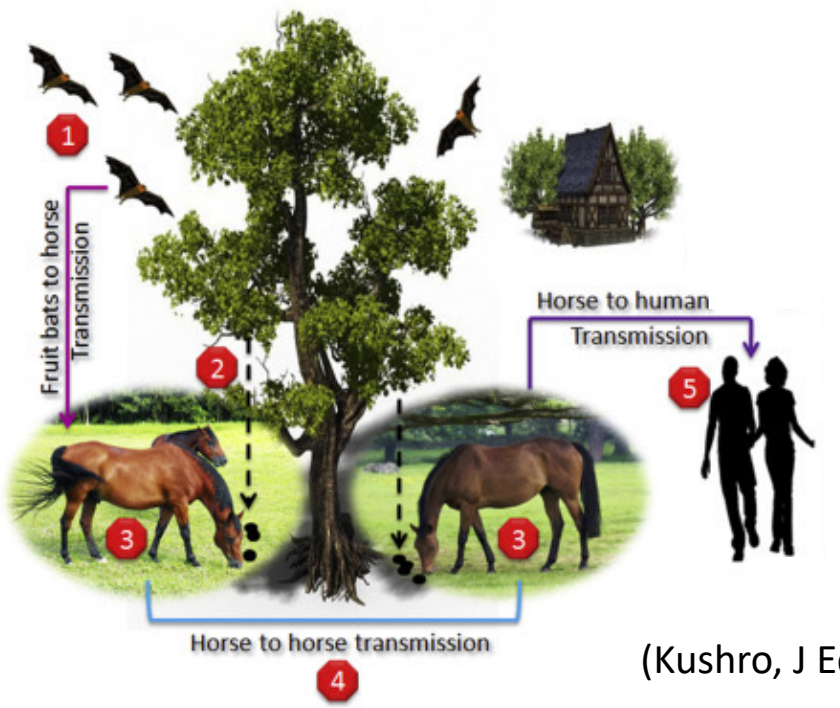
Change in richness of ZEBOV hosts

First encounters with non-Ebola hosts

13 possible hosts of ZEBOV and future first encounters → ~ 100 new viral sharing

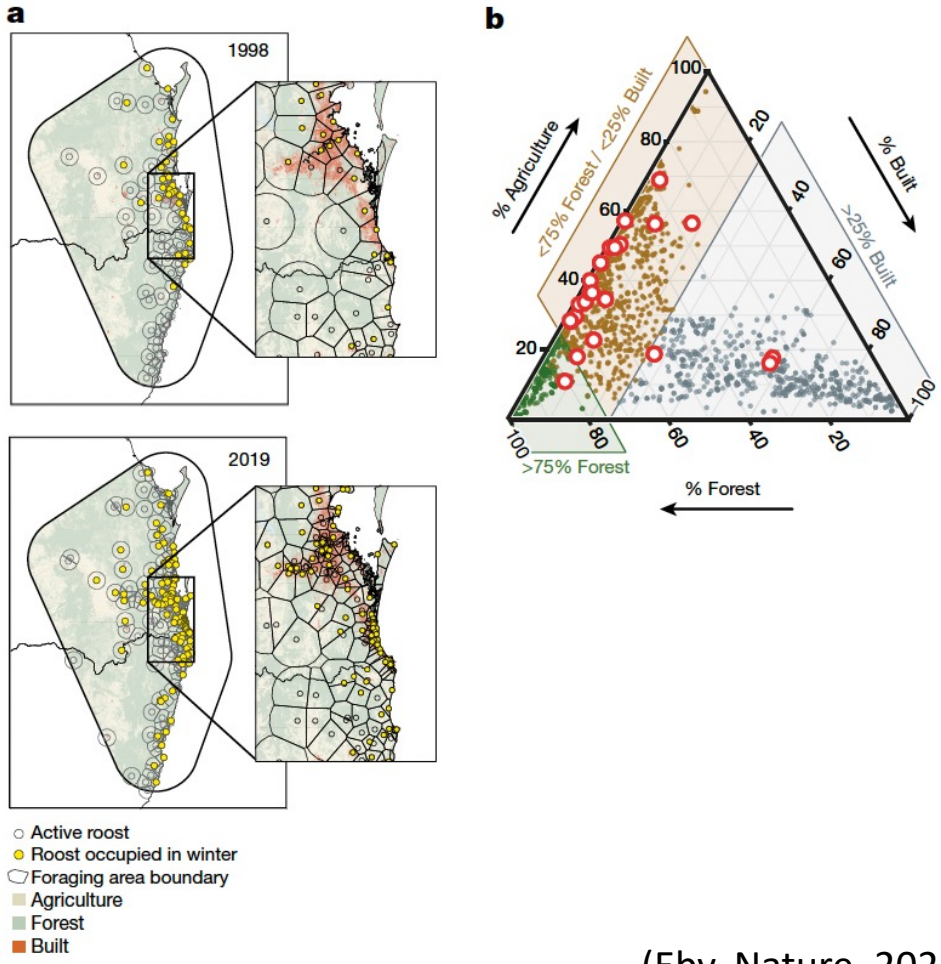
(Carlson, Nature, 2022)

Hendra virus transmission – Forest clearing - Australia



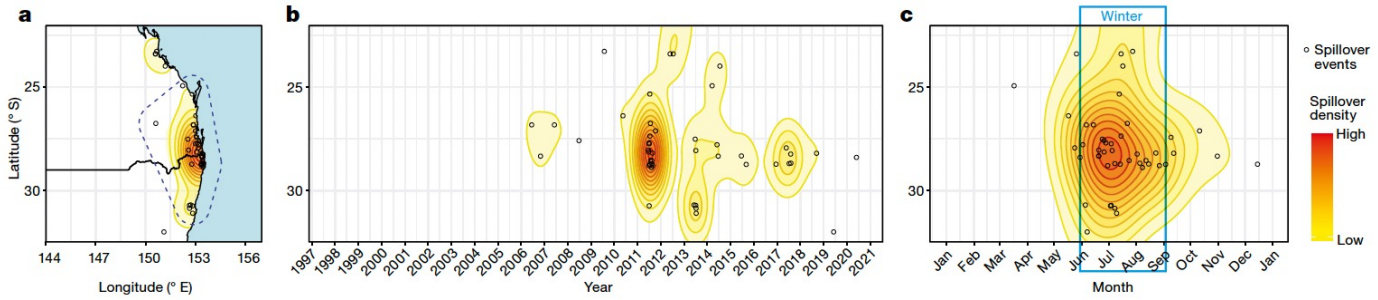
(Kushro, J Equine Vet Sci, 2020)

Distribution of *Pteropus alecto* roosts during winter



(Eby, Nature, 2022)

Distribution of Hendra virus spillovers to horses, Australian subtropics

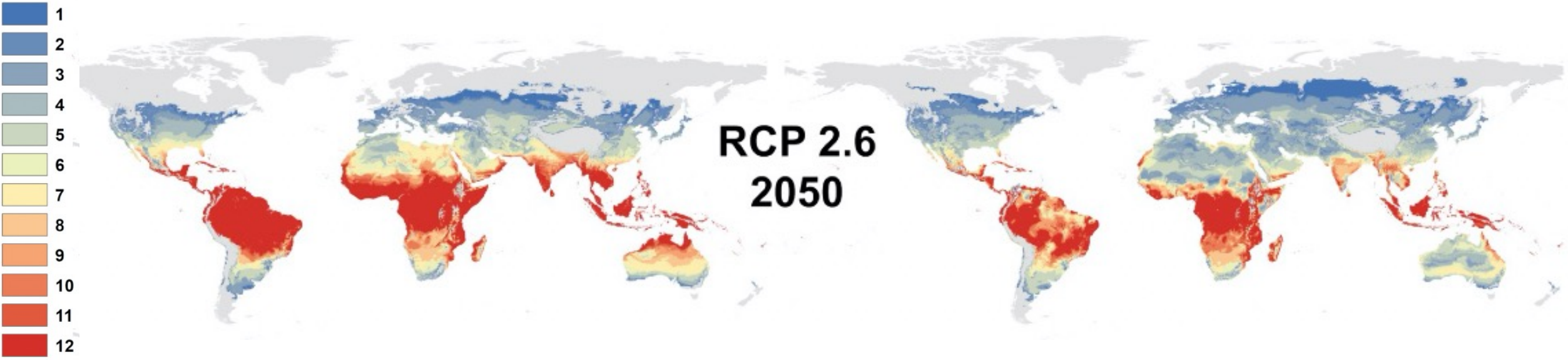


Mapping future temperature suitability for transmission scenarios for *Aedes aegypti* and *Ae. albopictus* – RCP 2.6

Months

Ae. aegypti

Ae. albopictus



Yellow fever, dengue, Zika, Chikungunya

(Ryan, PLoS NTD, 2019)

El Niño / Southern Oscillation (ENSO) and cholera peaks in Bangladesh

El Niño

↓ 6 months

Warming in Northern Bangladesh

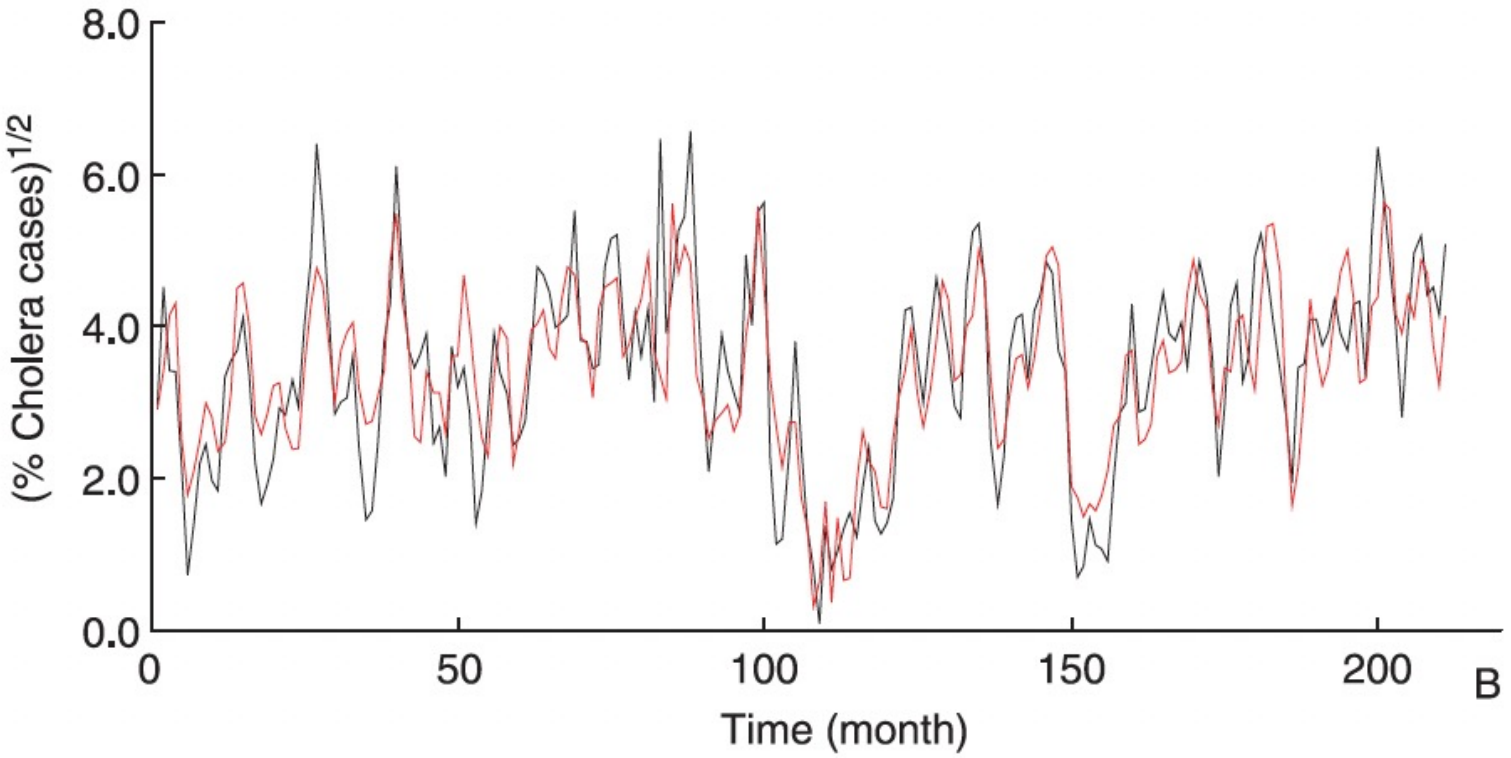
↓ 4-6 months

Higher water temperatures in the South

↓

Cholera rises

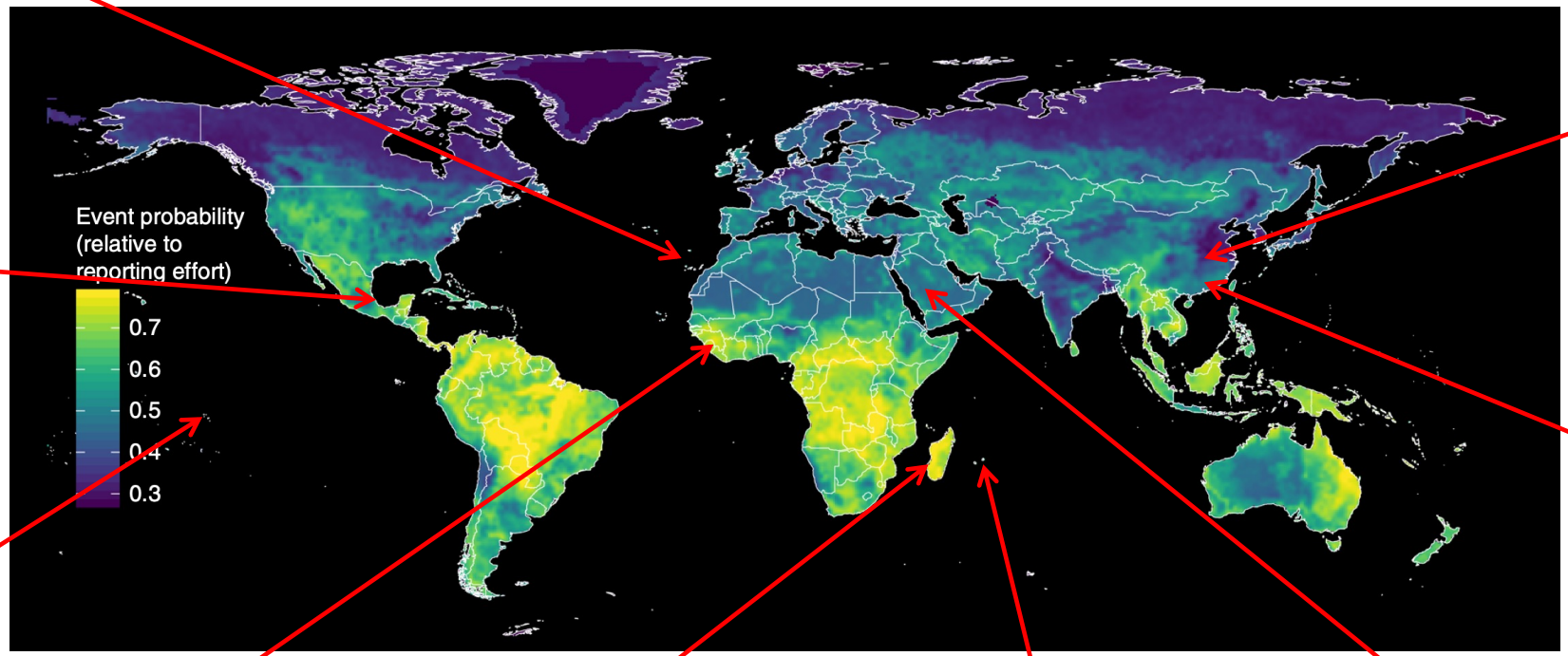
Cholera data (black line) and predicted (red line) based on ENSO with 11 months lag time



(Pascual, Science, 2000)

What about the unknown threats ?

Places and timing of emergences cannot be predicted yet



Monkeypox 2022

« Mexican » flu
A(H1N1) 2009

Zika 2013

Ebola 2014

Plague 2017

Chikungunya 2005

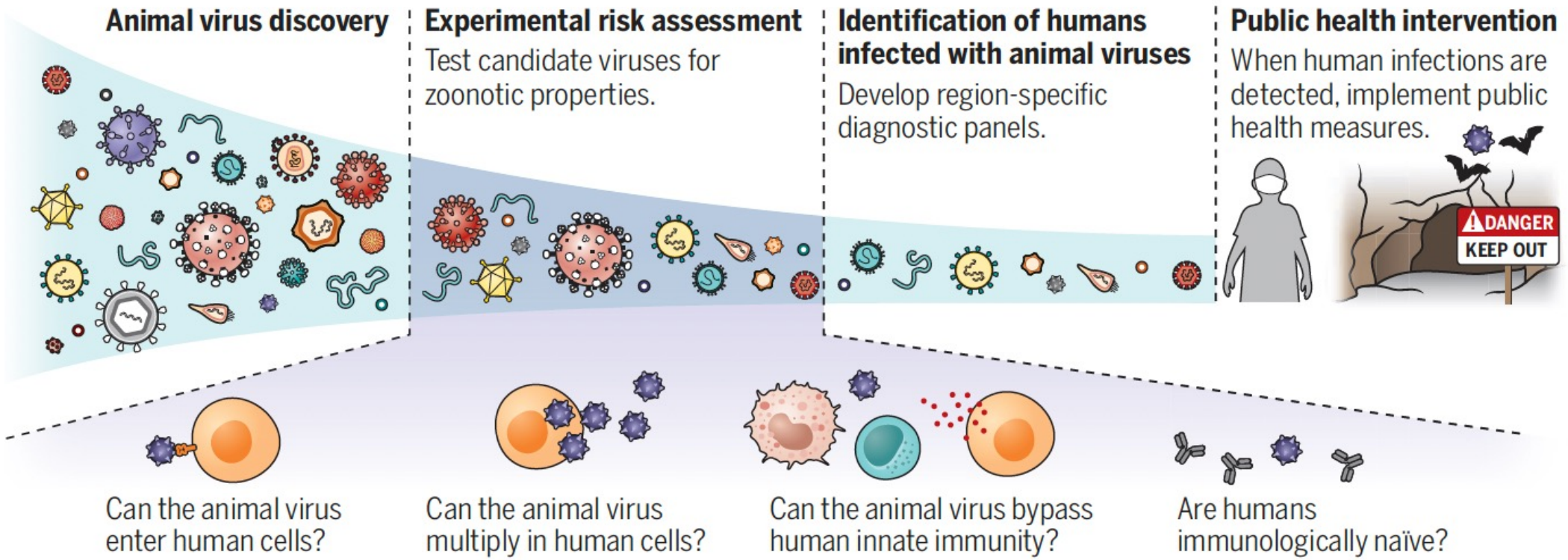
MERS 2012

SARS 2003

COVID 2019

(Adapted from Allen, Nature Comm, 2017)

A framework for getting ahead of future pandemics



structural analysis
in silico docking analysis
« pseudotype » entry assay

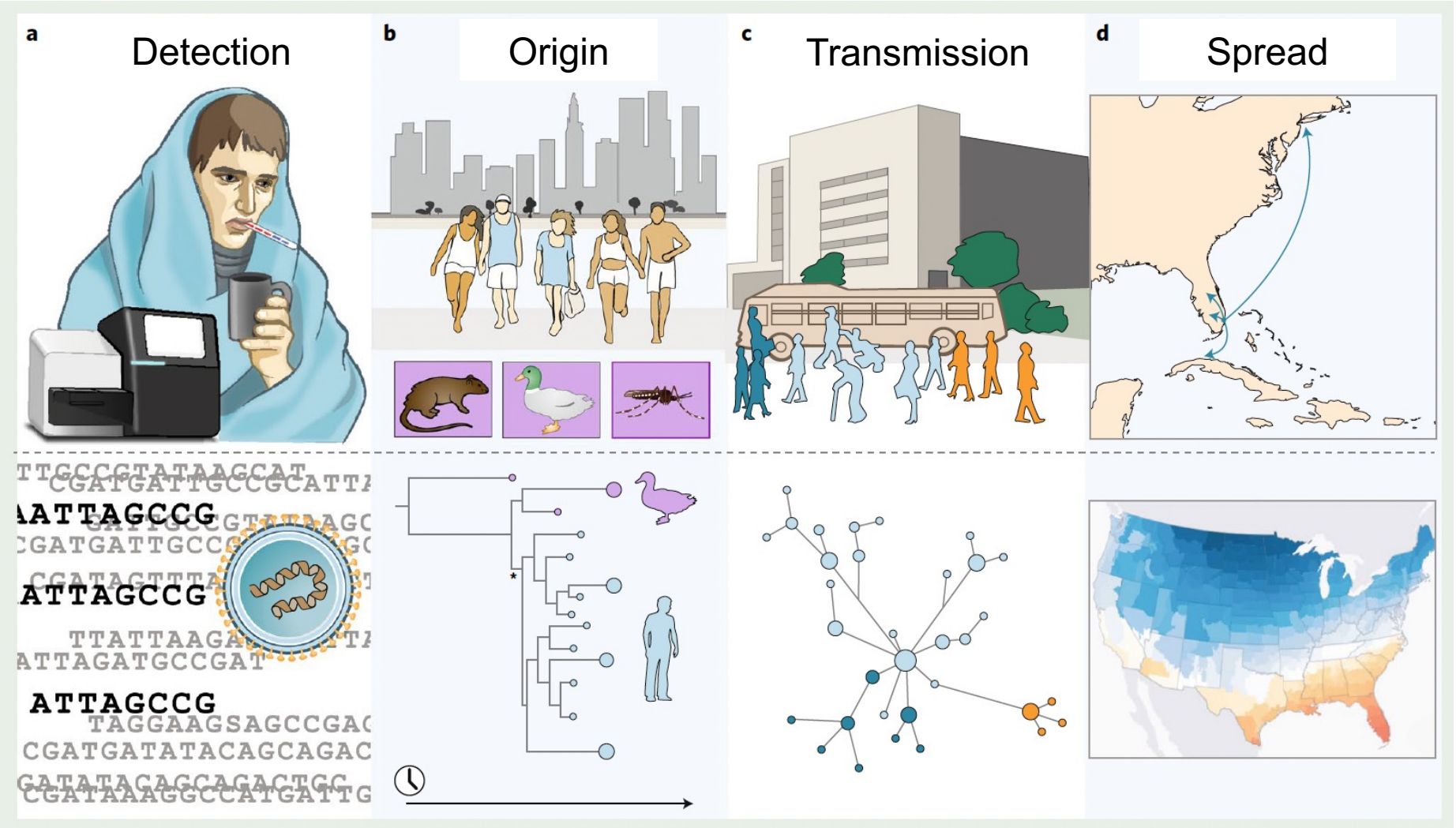
viral isolation
reverse genetics
human organoids

little known beyond
IFN response

Ab and T-cell response

(Warren & Sawyer, Science, 2023)

Real-time genomic investigation of Disease X



(Grubaugh, Nature Microbiol, 2019)

Pre-positioning of vaccines for human experimentation

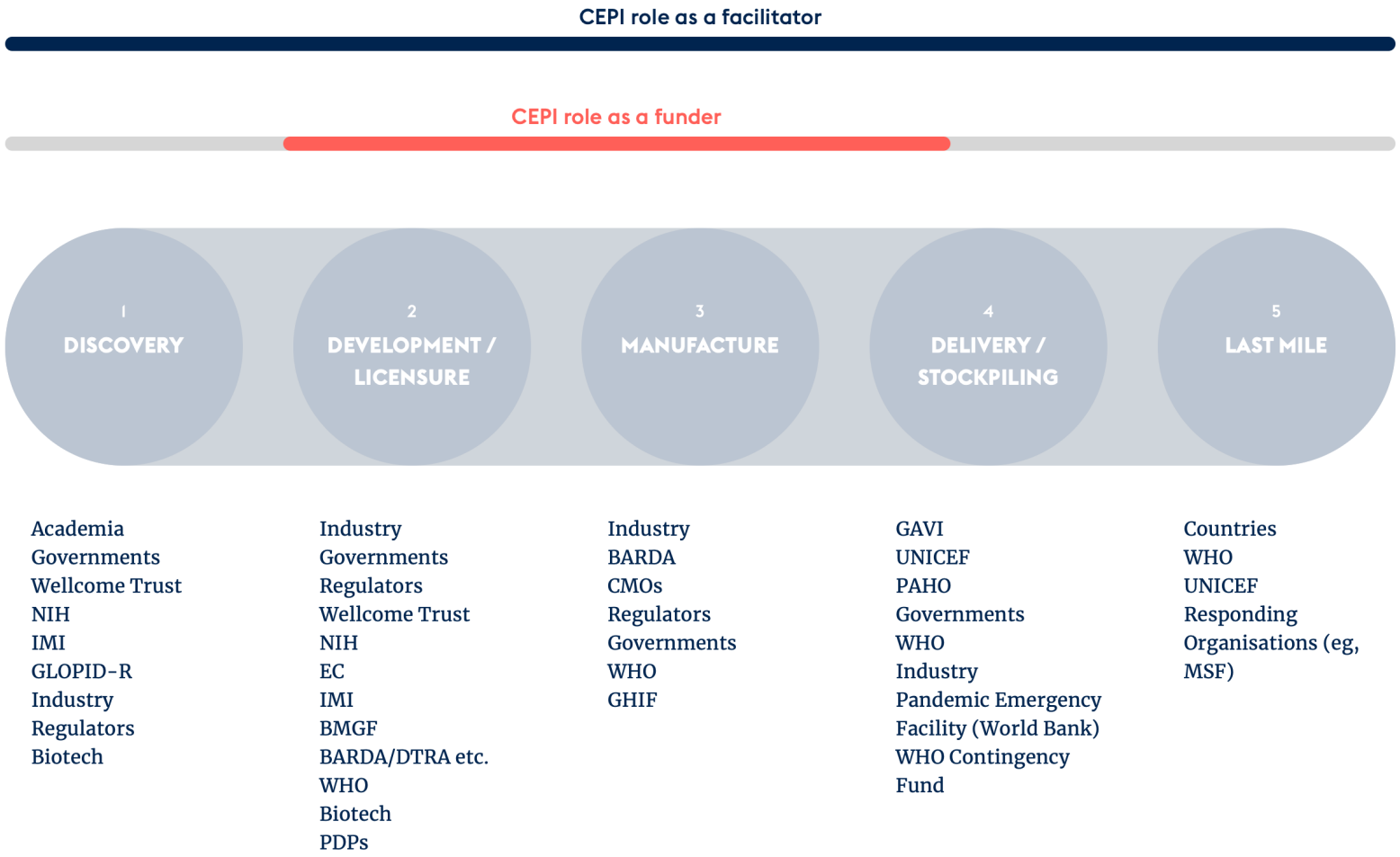
Coalition for Epidemic Preparedness Innovations (CEPI)

Public-private partnership

Vaccines development up to phase 2/3:

- Chikungunya
- Coronavirus (MERS, COVID-19)
- Filovirus (Ebola)
- Rift Valley fever
- Lassa
- Nipah

Vaccine platforms against Disease X



COVID-19 vaccine – All this would not have been possible without years of basic research on mRNA and coronaviruses

NATURE May 13, 1961 Vol. 190

AN UNSTABLE INTERMEDIATE CARRYING INFORMATION FROM GENES TO RIBOSOMES FOR PROTEIN SYNTHESIS

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UNSTABLE RIBONUCLEIC ACID REVEALED BY PULSE LABELLING OF *ESCHERICHIA COLI*

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The Biological Laboratories, Harvard University

mRNA discovery 1961

10 January 2020 — Release of the SARS-CoV-2 genome

11 January 2020 — 2P mutations in S protein residues 986-987 → prefusion-stabilized SARS-CoV 2 S(2P) protein for structural analysis in silico

15 January 2020 — Production of mRNA in lipid nanoparticles encoding SARS-CoV-2 S(2P) (mRNA-1273)

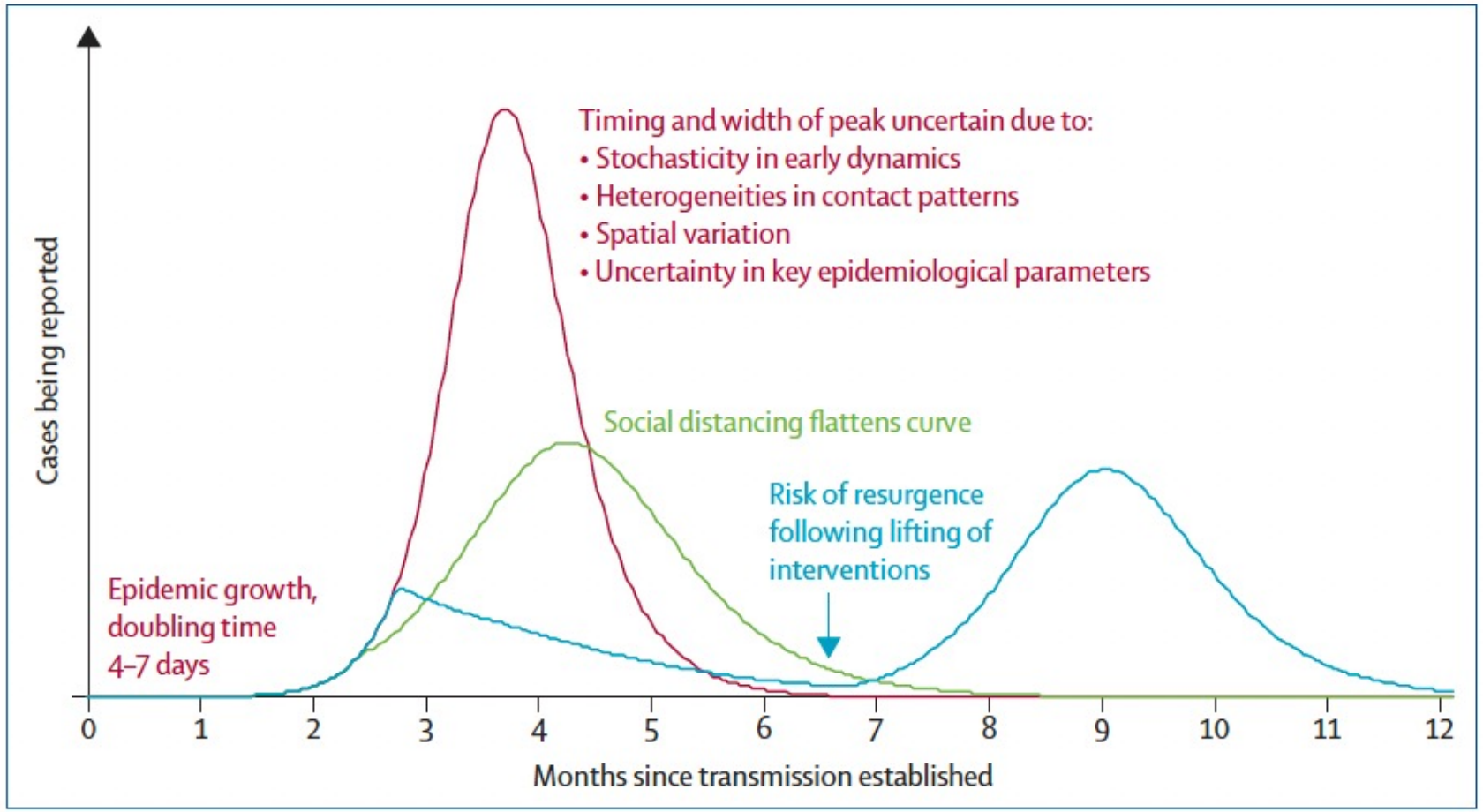
16 March 2020 — In-human phase 1 clinical trial

29 May 2020 — In-human phase 2 clinical trial

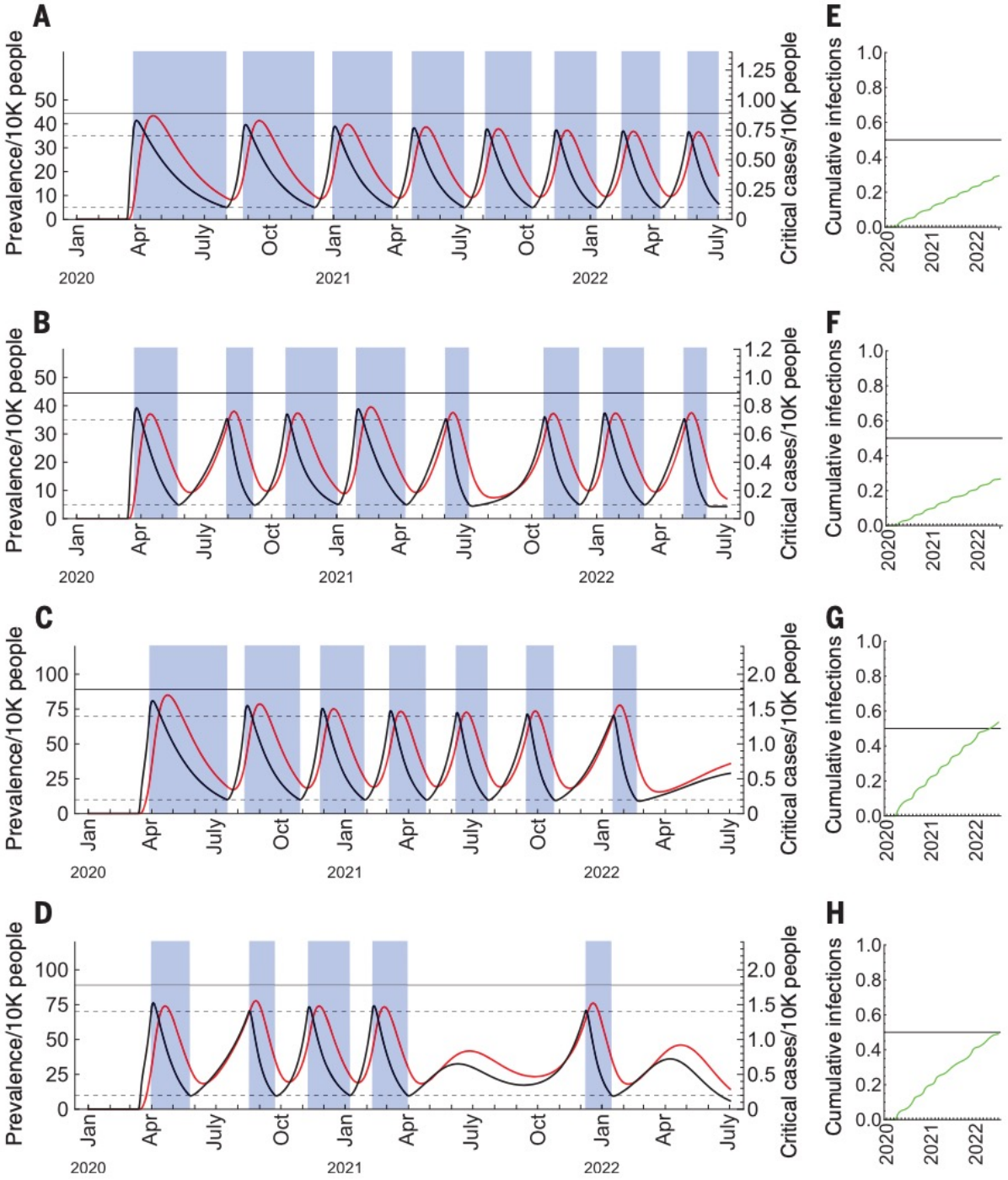
(Corbett, Nature, 2020)

Back-up slides

Flattening the curve and reach herd immunity ?



(Anderson, The Lancet, 6 March 2020)



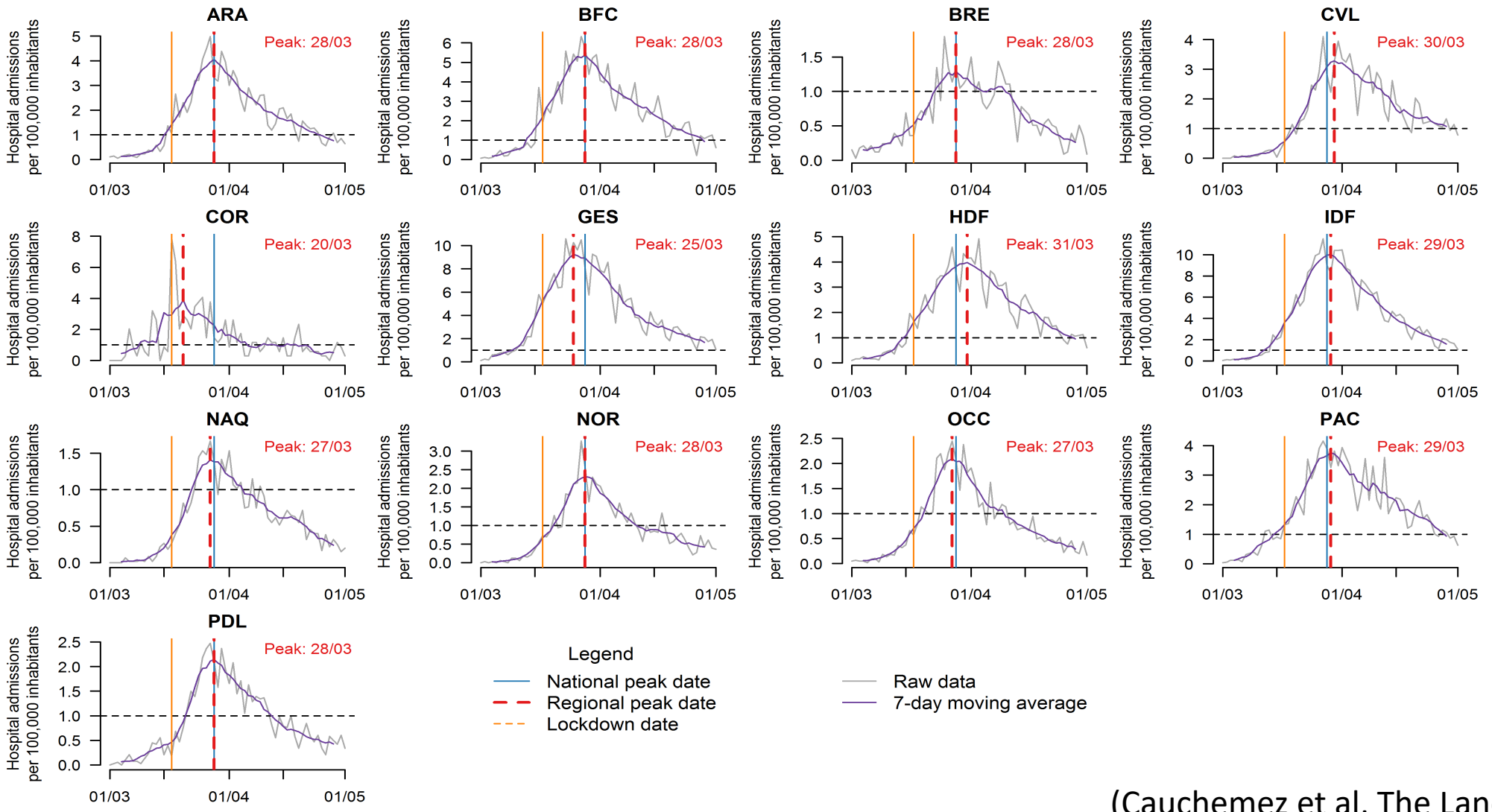
SARS-CoV-2 scenarios 2020-2022

Herd immunity acquisition by alternating « social distancing » and « non intervention » periods

(Kissler et al., Science, 2020; preprint on 6 March 2020)

How did the lockdown work in France?

COVID-19 hospital admission data by regions, March-April 2020

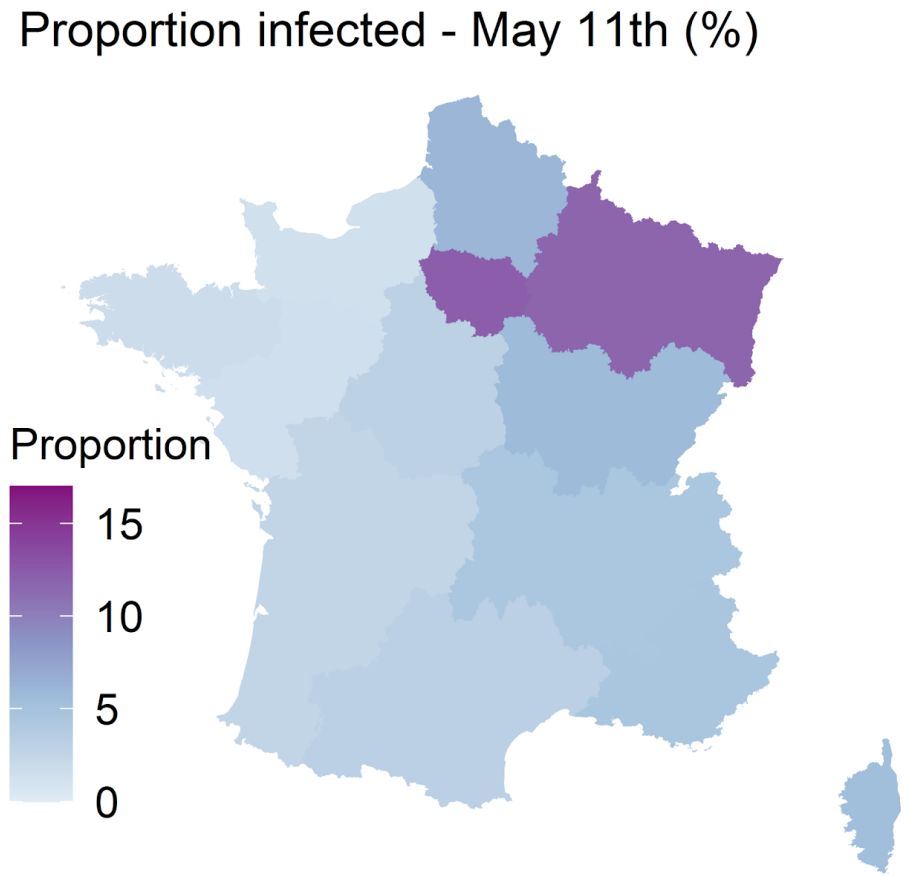


(Cauchemez et al, The Lancet)

Transportation of patients in critical condition

- By train, helicopter, plane
- Unique in the world

COVID-19 1st epidemic wave, France, 2020



5.3% of the population infected

(Salje et al., 2020, Science)

Effective reproduction number R_t

Target is « 1 »

$$R_t = R_0 * (1 - \%\ \text{immunized}) * (1 - \%\ \text{contact reduction})$$

Proportion « immunologically » susceptible

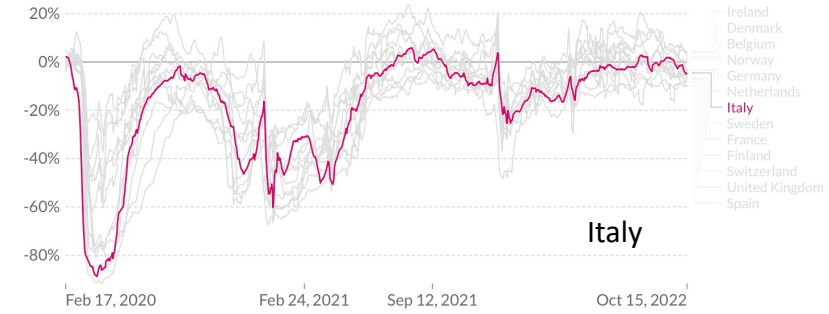
Proportion « socially » susceptible

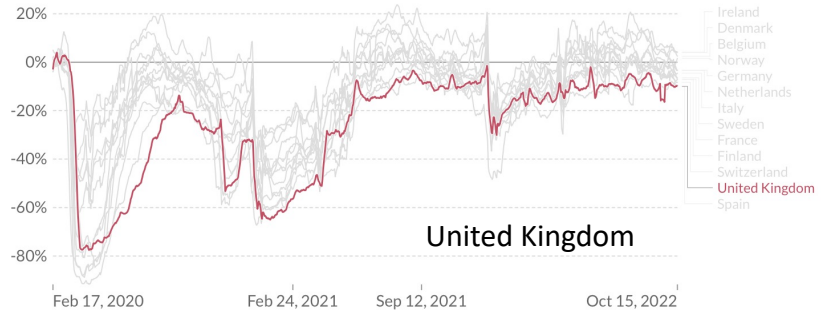
(Under simplifying assumptions)

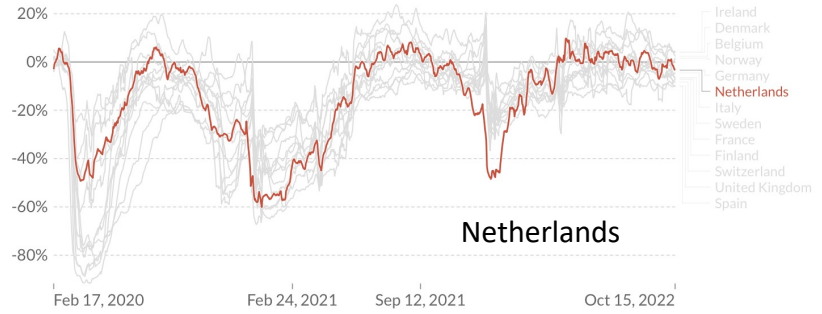
(Fontanet & Cauchemez, Nat Rev Immunol, 2020)

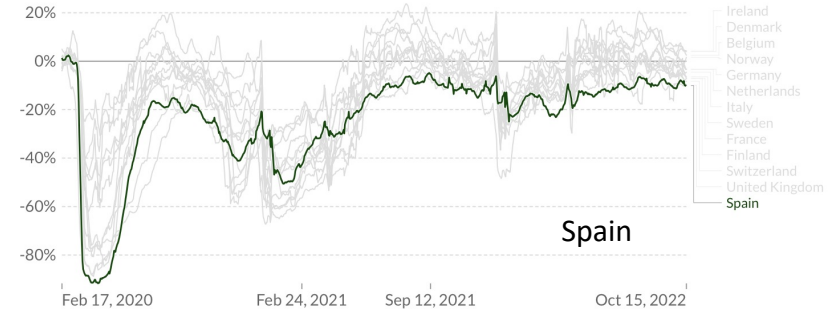
Control measures intensity & reduction in mobility

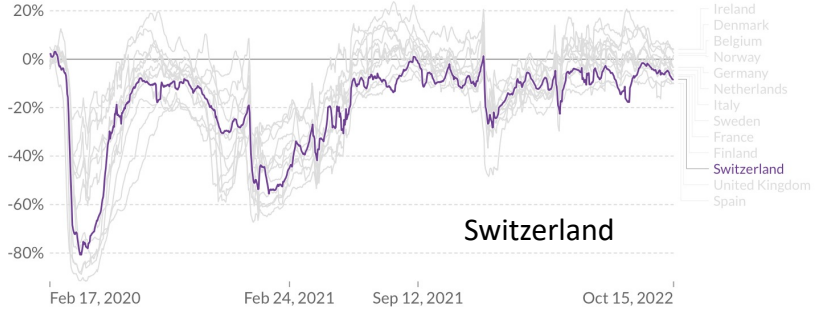
Retail and recreation : How did the number of visitors changed relative to the Jan 3 - Feb 6 2020 period ?

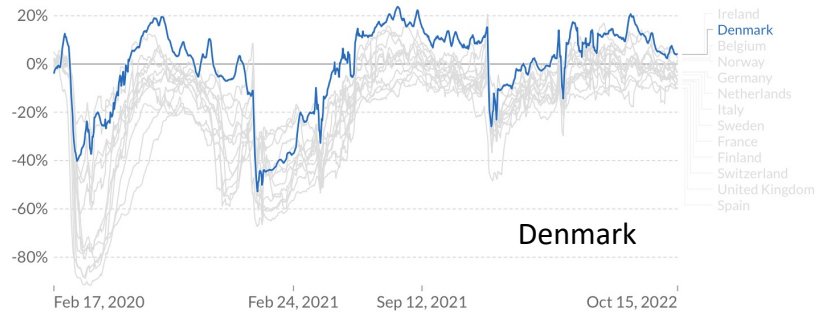


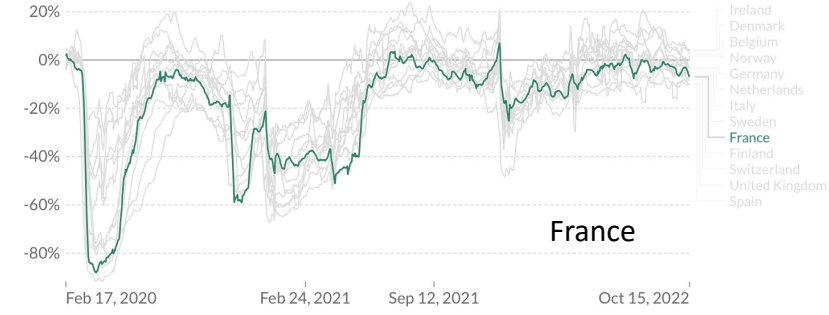


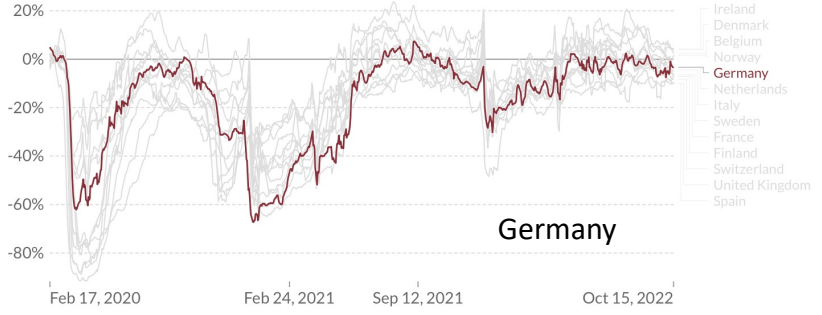


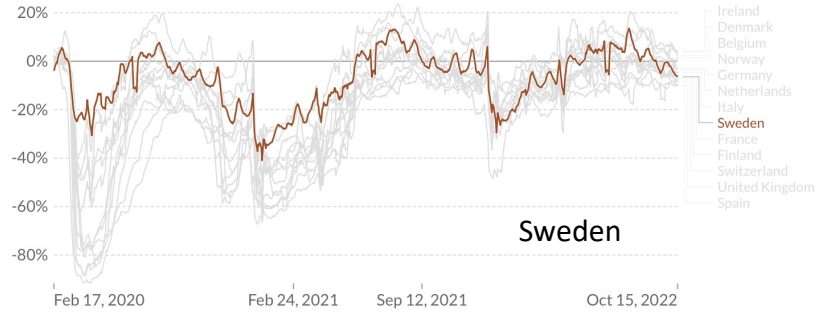










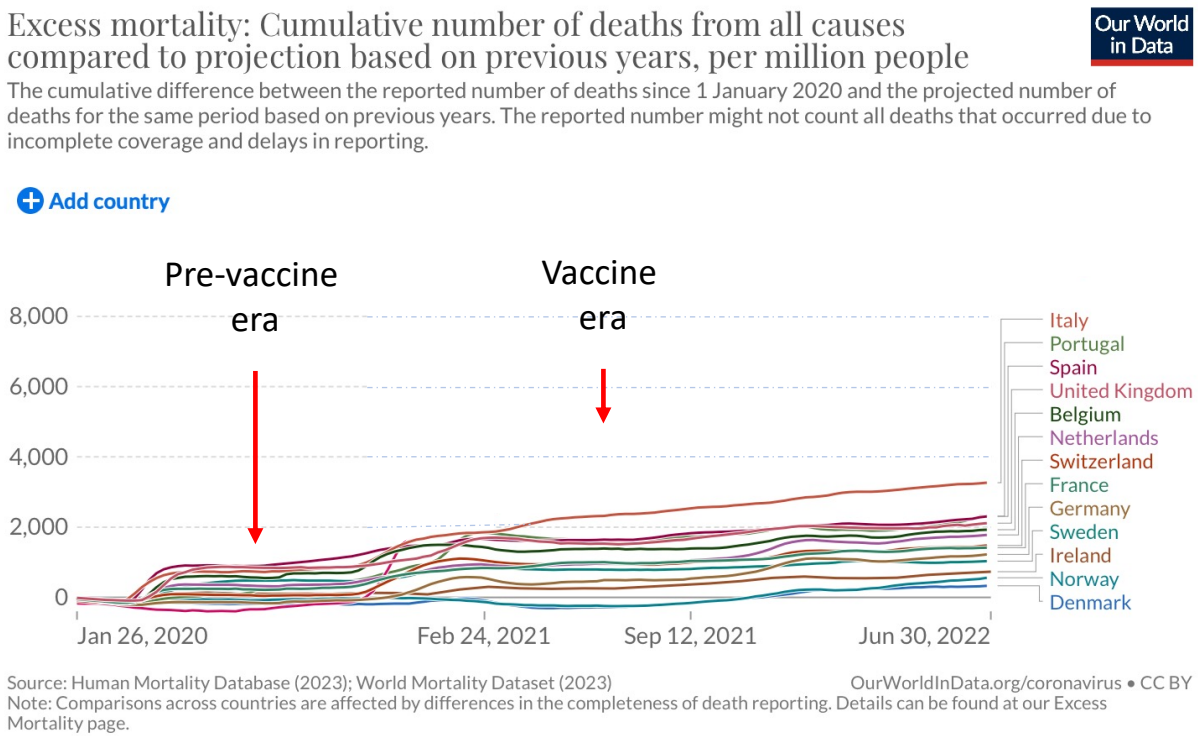


(Source: Google COVID-19 Community Mobility Trends / OurWorldInData.org/coronavirus)

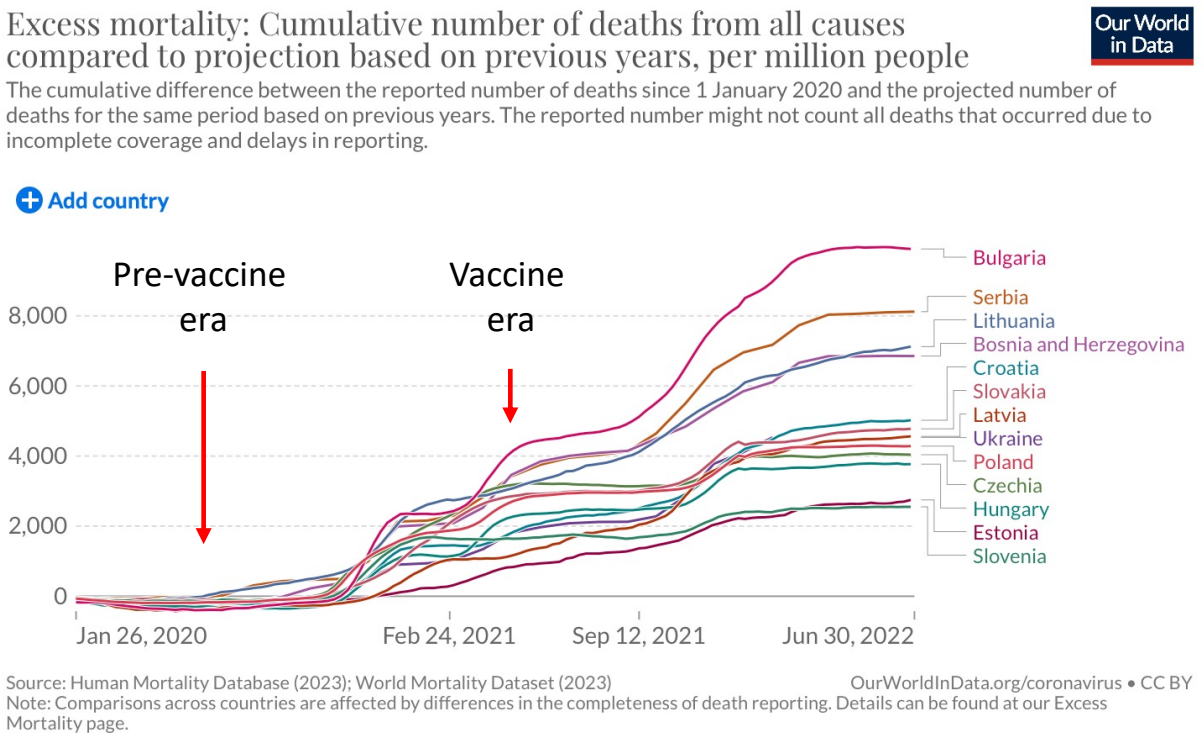
The impact of vaccines

Excess mortality per million people, Europe, Jan 2020-Jun 2022

Western Europe



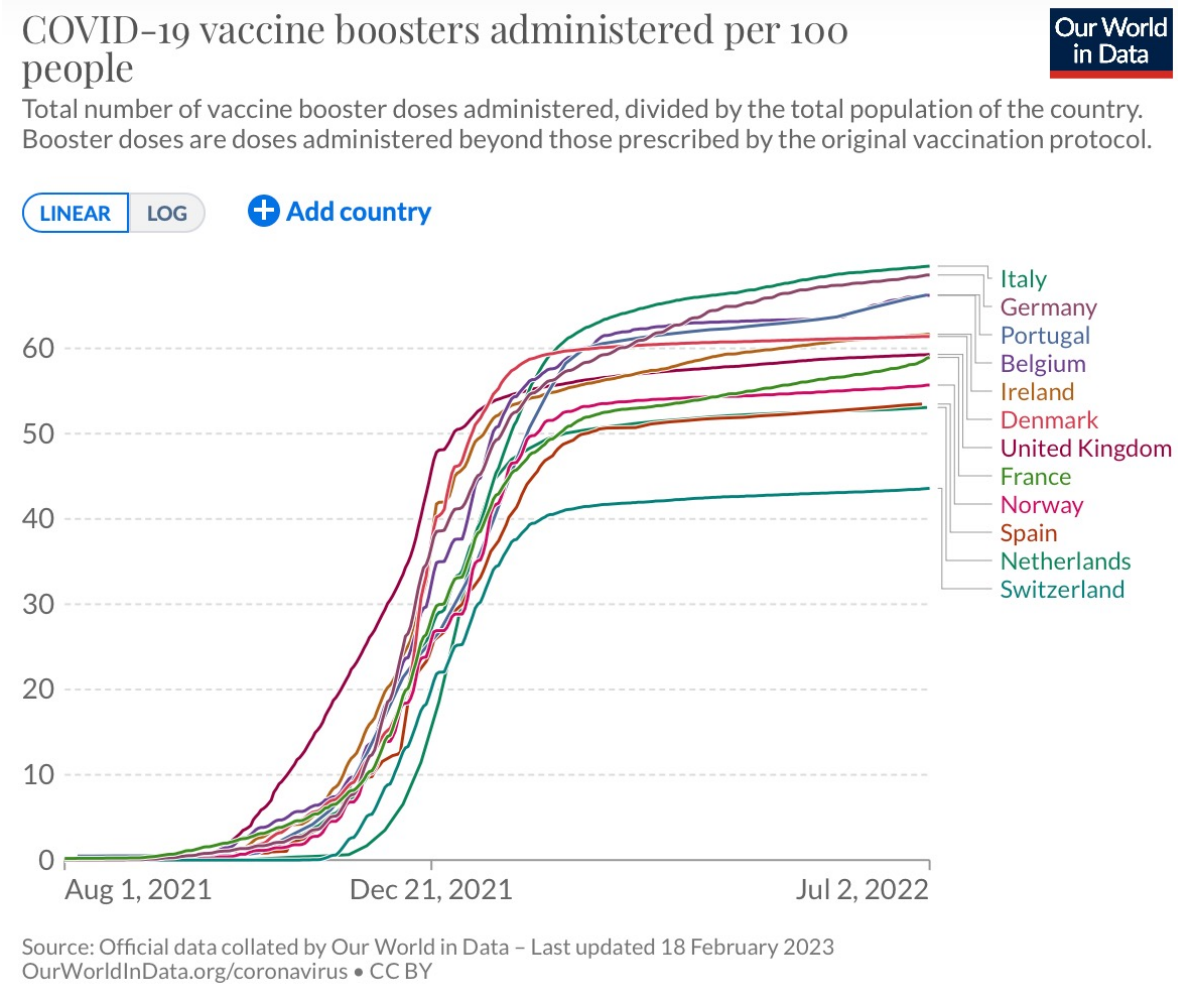
Eastern Europe



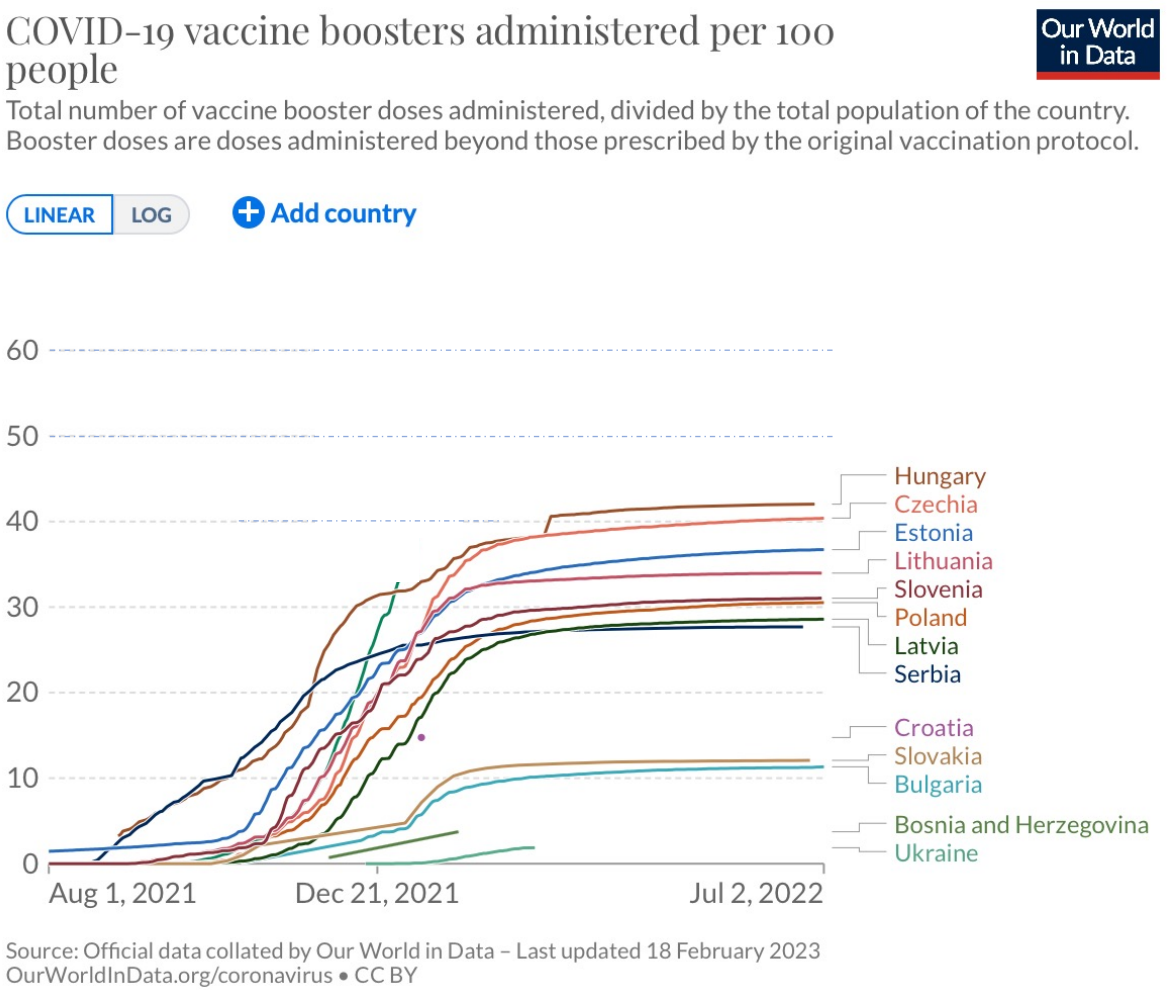
The impact of vaccines

COVID-19 vaccine boosters administered per 100 people, Europe, 2021-2022

Western Europe

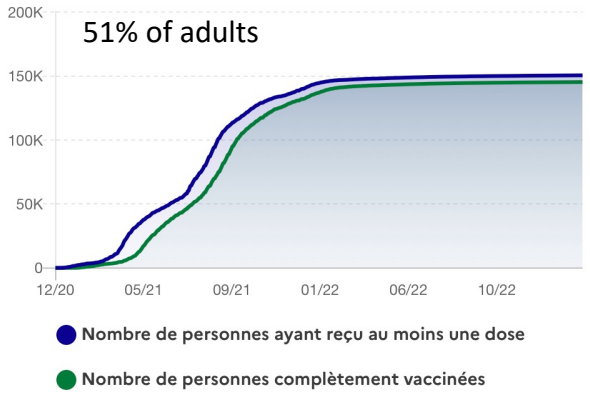


Eastern Europe (ref Italy)

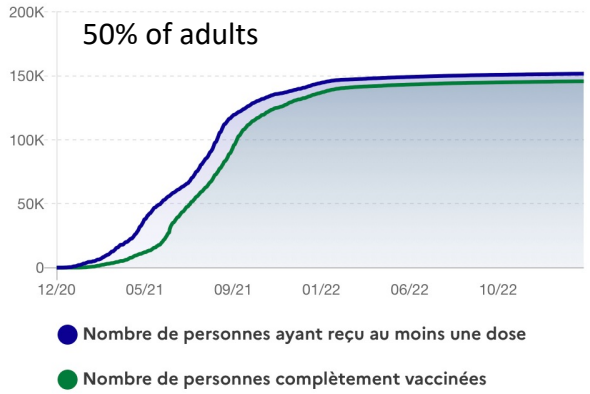


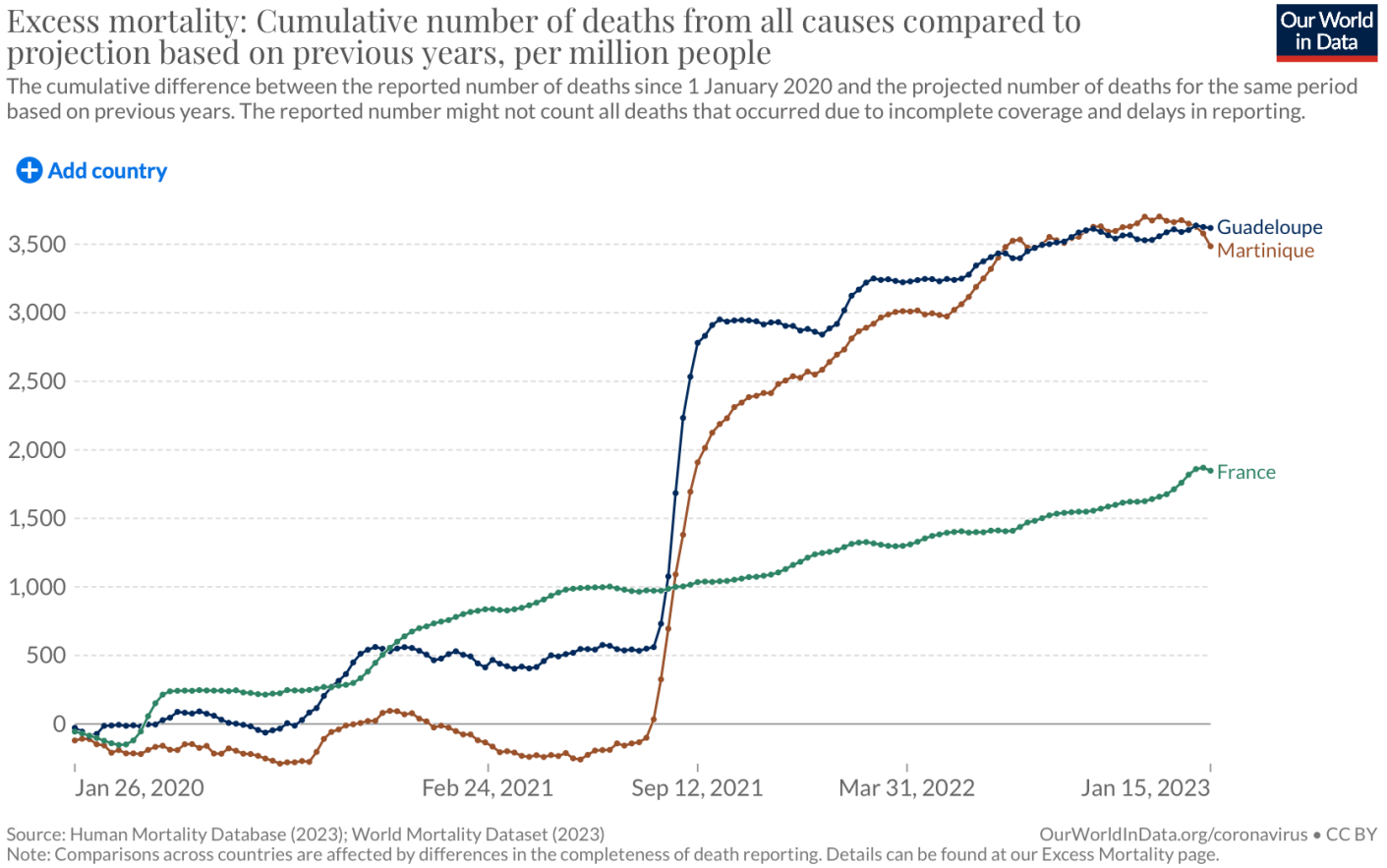
The impact of vaccines
French overseas department, 2020-2023

Vaccine coverage Martinique



Vaccine coverage - Guadeloupe



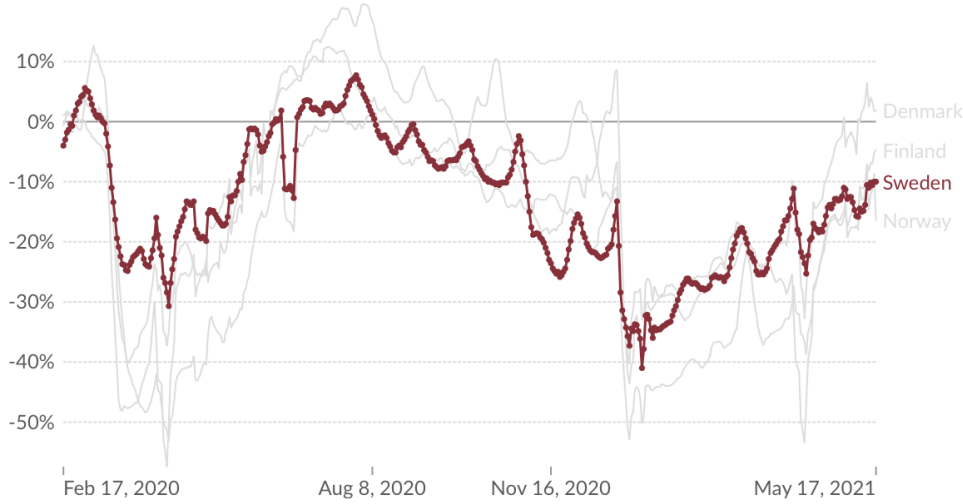


Scandinavian countries – control measures

Date of	Sweden	Denmark	Finland	Norway
Borders closed	Never undertaken*	13 March	18 March	14 March
Junior school closed	Never undertaken	13 March	16 March	12 March
High school / Uni changes	Distance education 17 March	13 March	16 March	12 March
Ban on gatherings	>500 11 March >50 27 March	>500 13 March >10 17 March	>500 13 March >5 16 March	>5 24.3
Pubs, bars, restaurants closed	Never undertaken: Some restrictions recommended	13 March	16 March	12 March
Non-essential shops closed	Never undertaken	18 March	4 April	12 March
Shielding of vulnerable (>70 years)	16 March	13 March	17 March	12 March
Population lock-down (not medicine/food)	***Never undertaken***	***11* March**	***16* March**	***13* March**
Travel restrictions	International 11 March National 19 March	13 March	International National 25 March	13 March then 16 March
% Journeys to work in April (compared to Jan/Feb 2020)	70%–80%	40%–60%	50%–60%	50%–60%
Use of parks and recreation % usual	240% (all regions)	170% (all)	220% (all)	140% (all)
Travel by vehicle within/to capital in April % usual	~25% Stockholm	~10% Copenhagen	~10% Helsinki	~10% Oslo

*The Swedish border never officially closed, but as neighbouring countries' borders were all closed, this resulted in a *de facto* border closure. European directive recommending curtailing travel among Schengen group countries was imposed on 17 March.

Google mobility to Retail and recreation



(Orlowski, J Roy Soc Med, 2020)

Public apologies from the King & PM of Sweden – December 2020

"Svenska folket har lidit" – hör kungens beskrivning av 2020. Foto: Rikard Collsiöö/SVT

"I think we have failed. We have a large number who have died and that is terrible. It is something we all suffer with," the king told Swedish broadcaster SVT.

"The Swedish people have suffered enormously in difficult conditions," Carl said. The monarch described 2020 as a "terrible year."

DECEMBER 17, 2020

Swedish PM says officials misjudged power of Covid resurgence

Major report finds nation failed to protect elderly and criticises response to the pandemic

- Coronavirus - latest updates
- See all our coronavirus coverage

AP in Stockholm

Tue 15 Dec 2020 23.46 CET

Share

Sweden's prime minister, Stefan Löfven, said: 'I think that most people in the profession didn't see such a wave in front of them.'
Photograph: Henrik Montgomery/AP

Health officials in Sweden, which opted not to respond to the first wave of Covid-19 with a national lockdown, misjudged the power of the virus's resurgence, the country's prime minister has said, as independent commission criticised the country's strategy.

How close from herd immunity after one year ?

Sweden - weighted seroprevalence – April-May 2021

	Proportion with SARS-CoV-2 IgG antibodies			
	Total study population (n = 2860)		Non-vaccinated (n = 1876)	
	%	95% CI	%	95% CI
Total	32.6	(30.3–34.9)	20.1	(17.6–22.8)
0–10 years	20.5	(12.0–31.4)	20.5	(12.0–31.4)
11–19 years	30.5	(23.6–38.2)	30.5	(23.6–38.2)
20–64 years	24.8	(22.0–27.8)	18.0	(15.3–20.9)
65 + years	62.2[a]	(58.6–65.8)	18.1	(9.5–29.6)
Female	34.7	(31.7–37.9)	19.8	(16.6–23.3)
Male	30.4	(27.0–34.0)	20.4	(16.6–24.6)

(Beser, Scientific Reports, 2022)

Norway – seroprevalence – January 2021

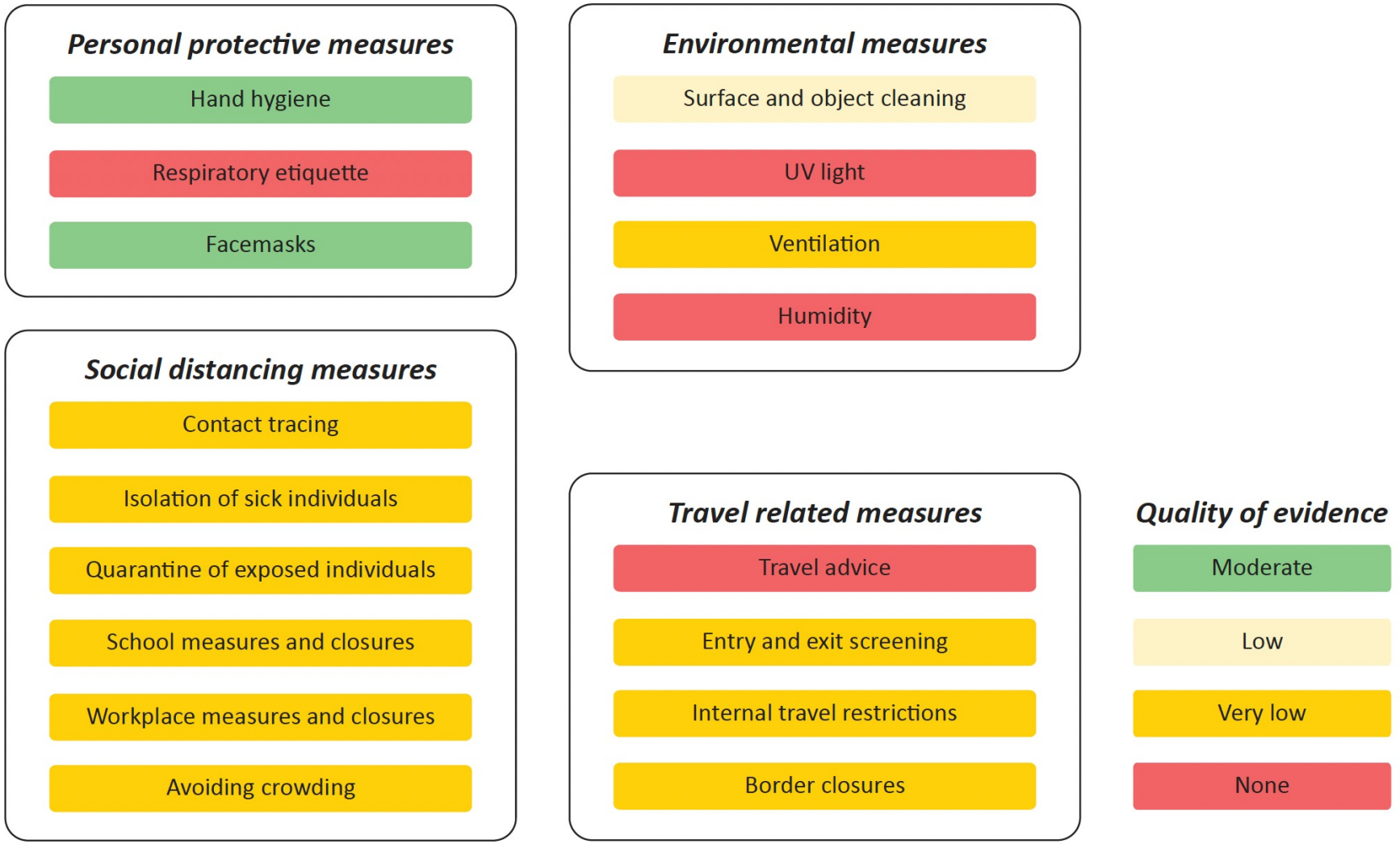
Age groups	
0–4 years	6.3 (2.8–10.7)
5–14 years	4.4 (2.3–6.9)
15–24 years	2.7 (1.1–4.9)
25–59 years	2.1 (1.1–3.4)
≥60 years	4.0 (2.2–6.2)

Denmark – seroprevalence – February 2021

	Prevalence(%)	(95% CI)
Age group		
12–17 years	8.3	(6.1–11)
18–29 years	10.0	(8.4–12)
30–39 years	7.6	(6.0–9.1)
40–49 years	9.2	(7.7–10.7)
50–64 years	6.7	(5.4–7.5)
65+ years	4.4	(3.2–5.4)

(Krogsgaard, Infection & Drug Resist, 2023)

Non-pharmaceutical public health measures included



WHO
NPIs influenza
2019

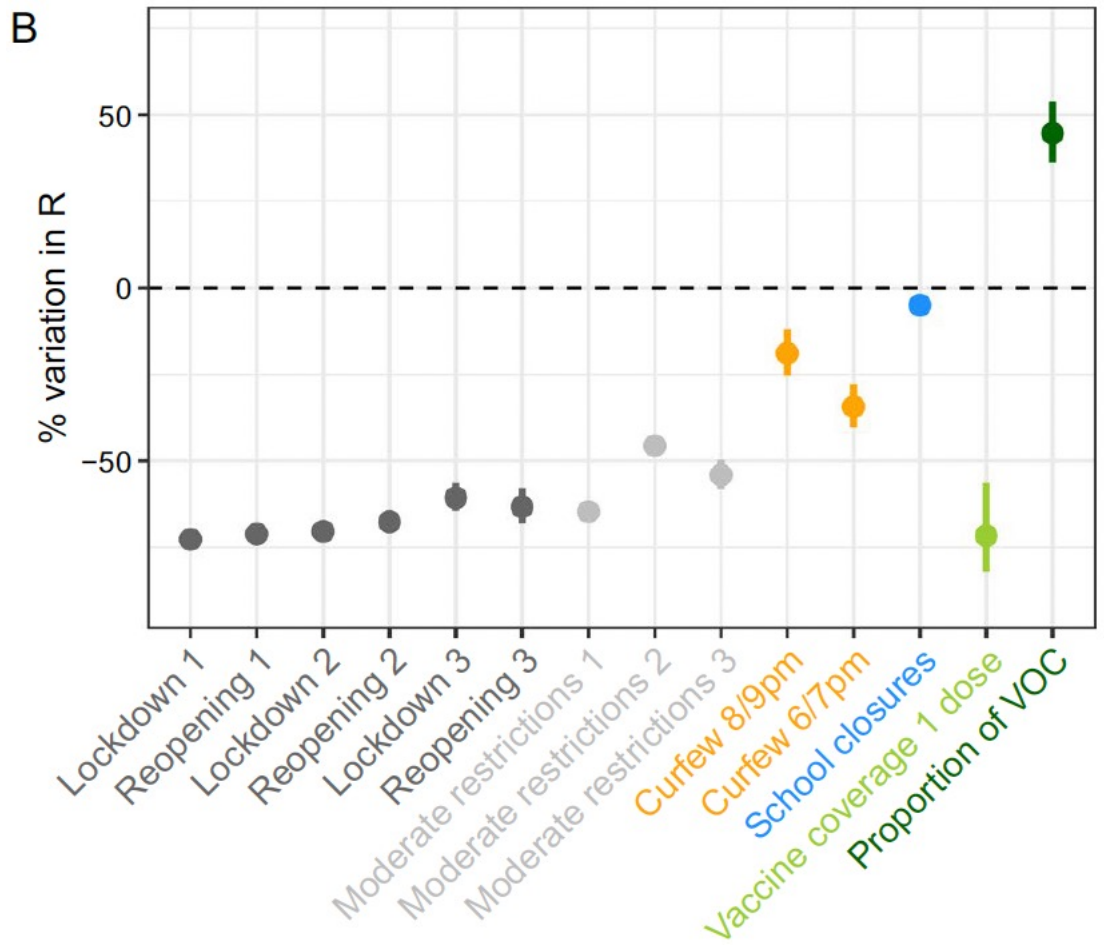
https://apps.who.int/iris/handle/10665/329438

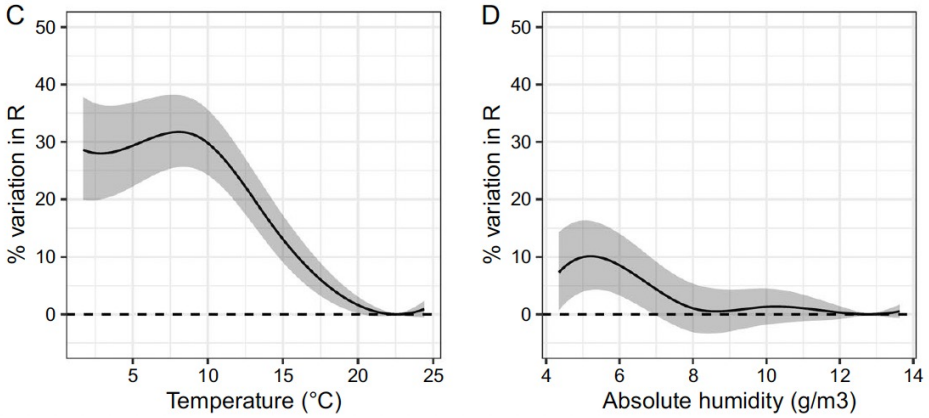
Recommendations on the use of NPIs by pandemic/epidemic severity

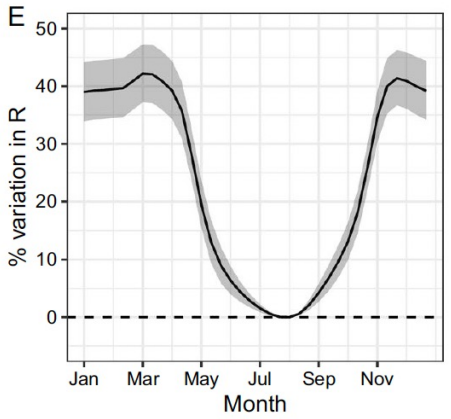
Severity	Pandemic		Epidemic	
Any	Hand hygiene Respiratory etiquette Face masks for symptomatic individuals Surface and object cleaning	Increased ventilation Isolation of sick individuals Travel advice	Hand hygiene Respiratory etiquette Face masks for symptomatic individuals Surface and object cleaning	Increased ventilation Isolation of sick individuals Travel advice
Moderate	*As above, plus* Avoiding crowding		*As above, plus* Avoiding crowding	
High	*As above, plus* Face masks for public School measures and closures		*As above, plus* Face masks for public School measures and closures	
Extraordinary	*As above, plus* Workplace measures and closures Internal travel restrictions		*As above, plus* Workplace measures and closures	
Not recommended in any circumstances	UV-light Modifying humidity Contact tracing Quarantine of exposed individuals	Entry and exit screening Border closure	UV-light Modifying humidity Contact tracing Quarantine of exposed individuals	Entry and exit screening Internal travel restrictions Border closure

(Ben Cowling, adapted from WHO NPI's influenza 2019)

% variation in R associated with interventions and climate, France, 2020-2021

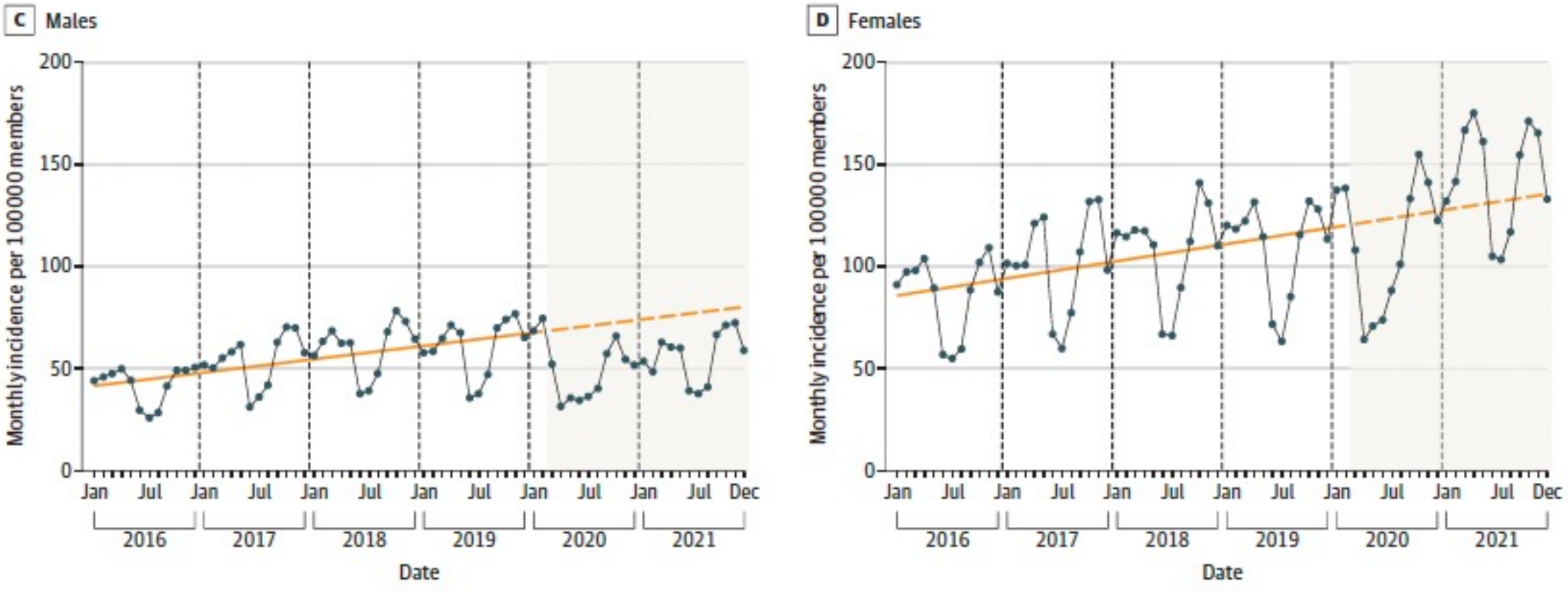






(Paireau, BMC Infect Dis, 2023)

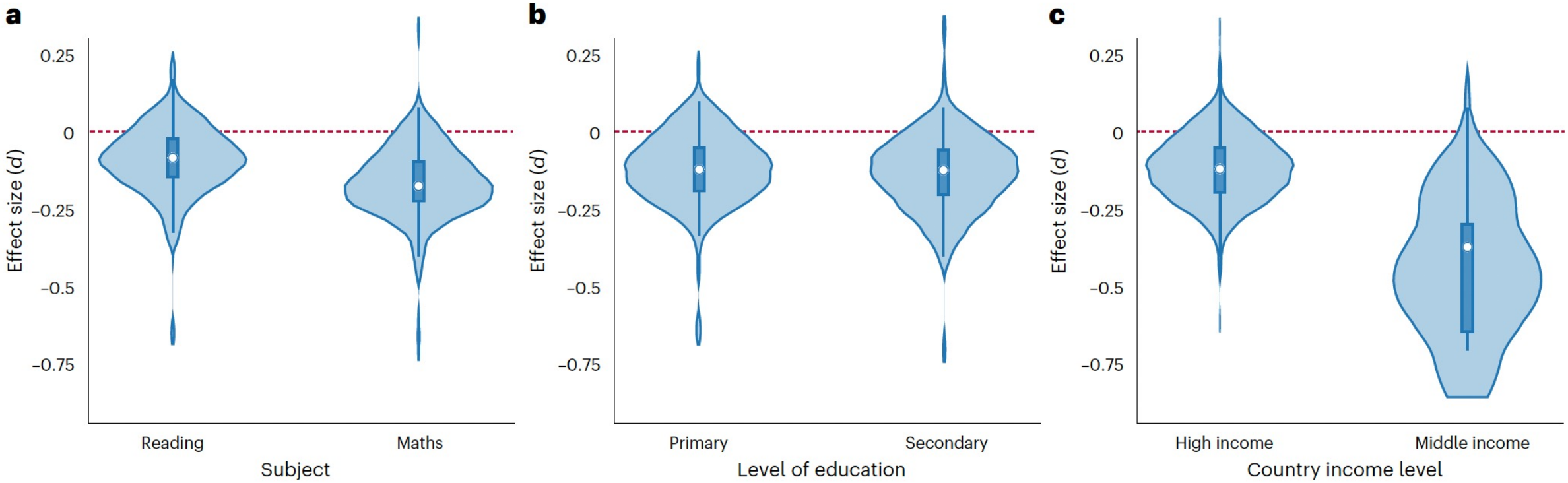
Emergency department visits and hospitalizations for suicidal ideation and suicide attempts among children and adolescents, U.S., 2016-2021



(Health database, 47 million individuals across U.S.)

(Kim, Jama Network Open, 2023)

Educational impact : COVID-19 learning deficits
15 countries, May 2020 – May 2022



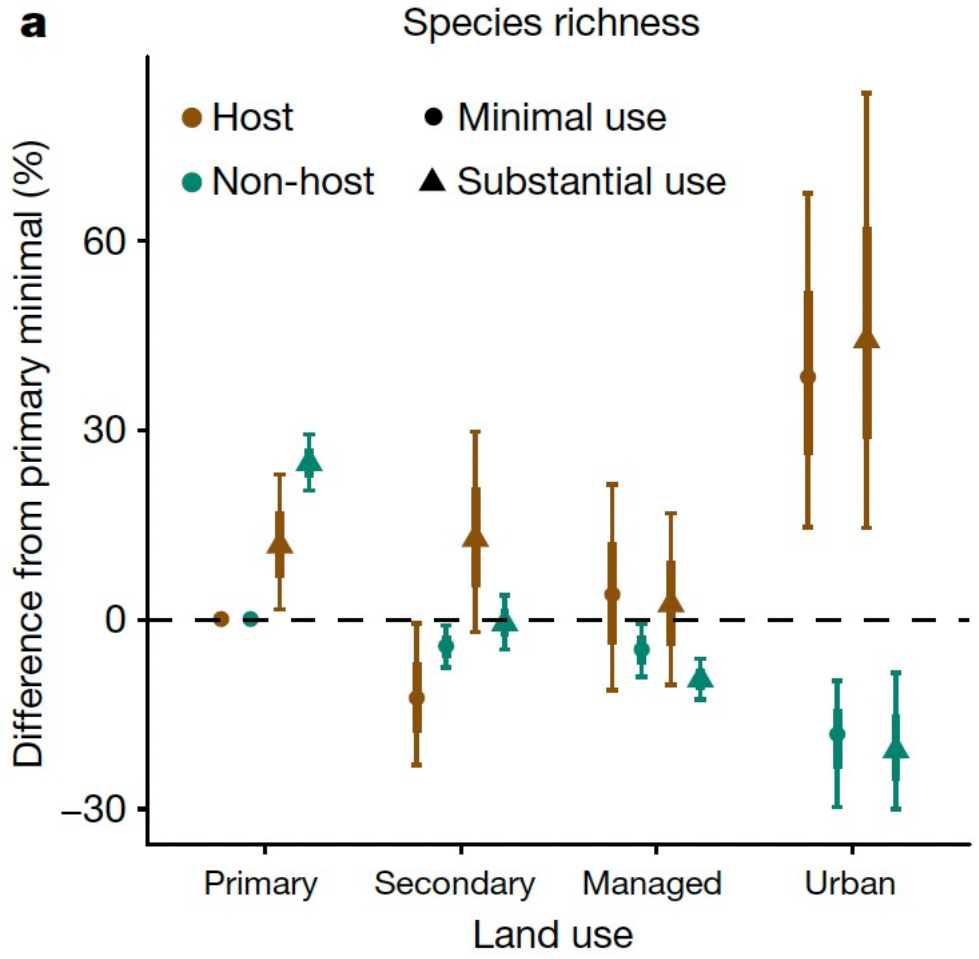
Pooled effect size = -0.14 (about 35% of a normal school year's worth of learning)

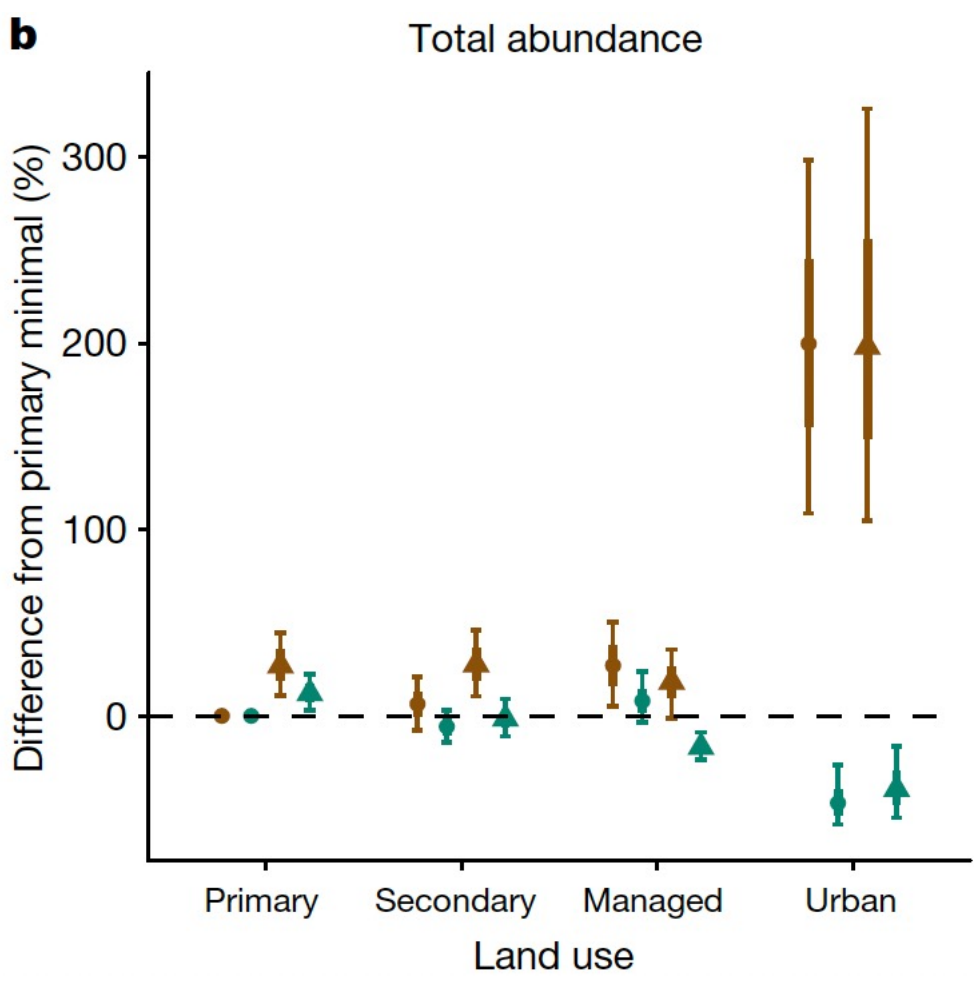
(Betthaüser, Nature Human Behaviour, 2023)

Conclusion

- Observational evidence and modeling suggest that change in climate and land use will increase the rate of new emergences
- Fighting deforestation, monitoring wild life markets and animal farming are highly cost-effective in preventing pandemics
- Innovative approaches targeting mosquito populations (e.g., *Wolbachia* infection) may become an important player in the fight against mosquito-borne diseases
- Pandemic preparedness, including pathogen discovery, screening for zoonotic properties, and vaccine development should target viruses with pandemic potential
- Basic knowledge on viruses will remain the key to future innovation

Effects of land use on site-level host species richness and total abundance

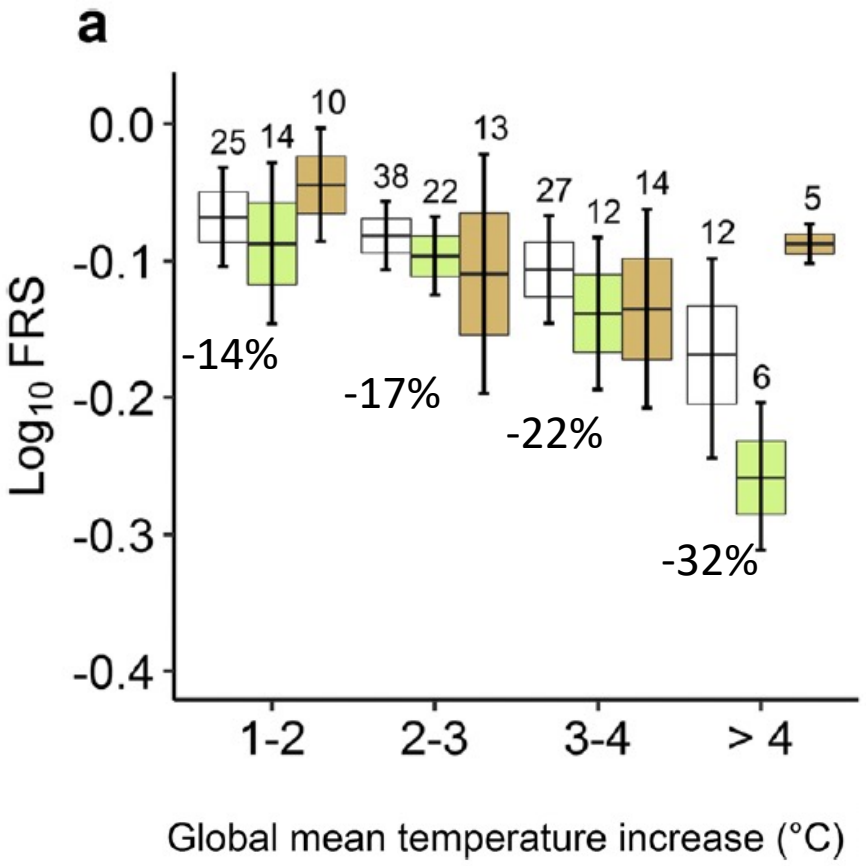




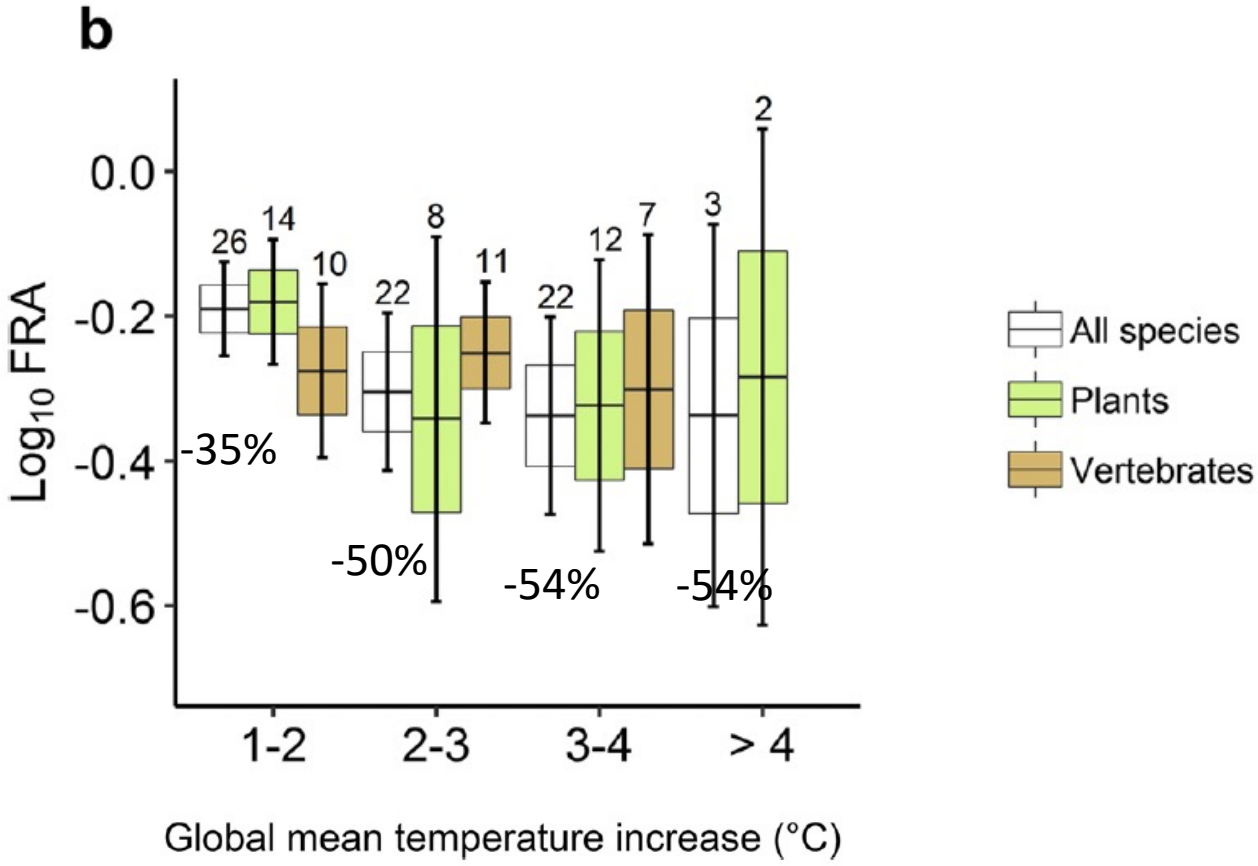
(Gibb et al, Nature, 2020)

Biodiversity - Fraction of remaining species, and remaining area with suitable climate, under temperature increase

Fraction of remaining species (FRS)

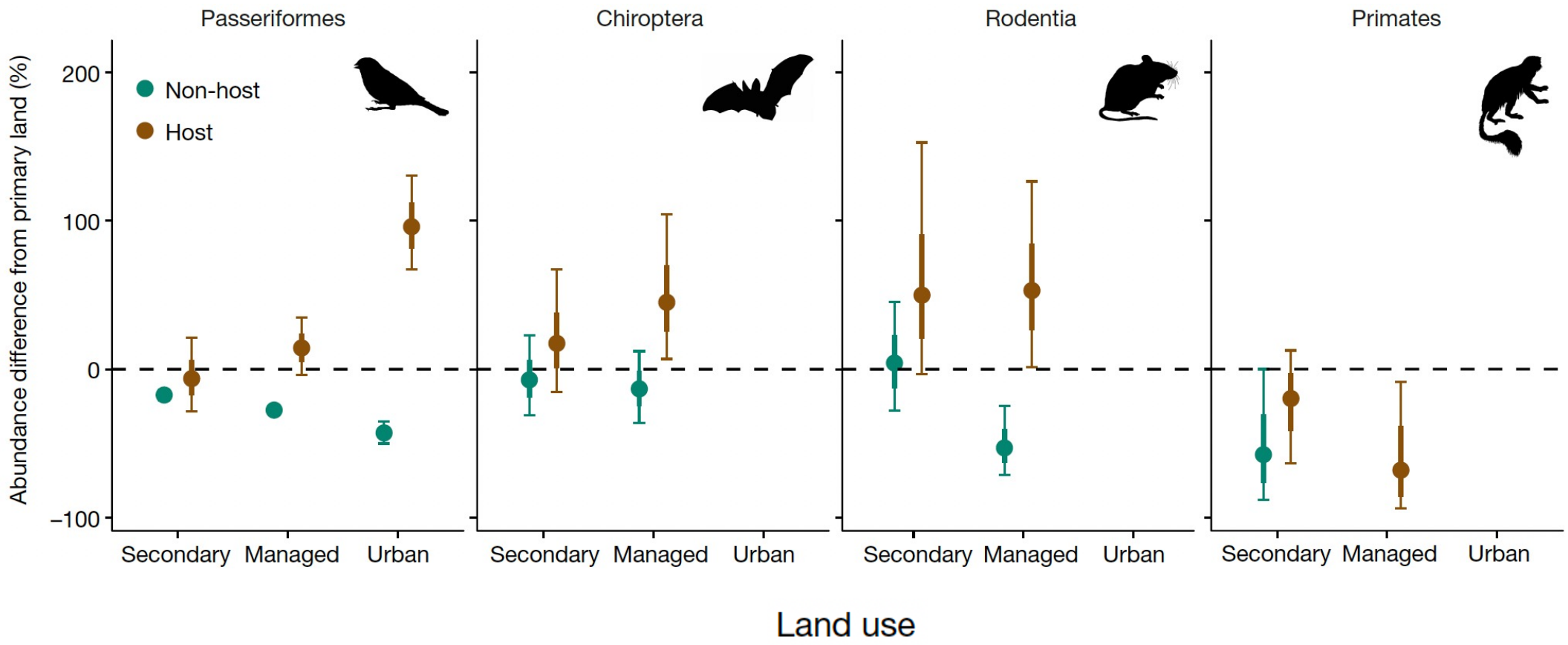


Fraction of remaining area (FRA)



(Nunez, Climatic Change, 2019)

Effects of land use on species abundance of mammalian and avian zoonotic hosts and non-hosts

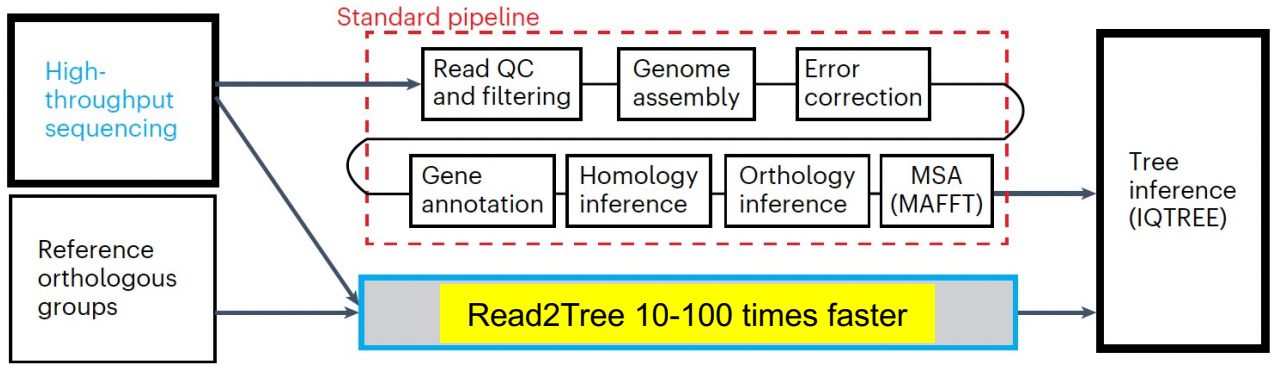


(Gibb et al, Nature, 2020)

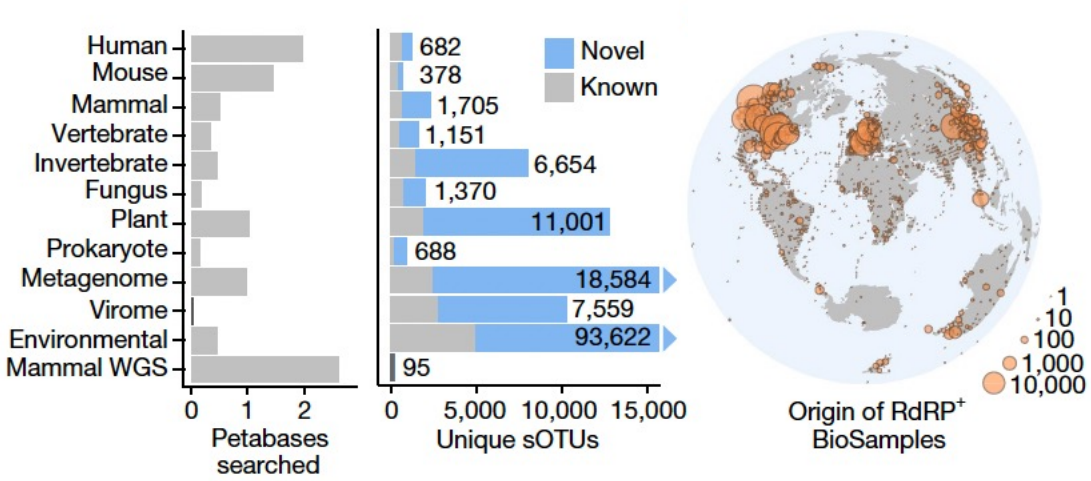
Unknown threats - Pathogen discovery

Improvement in
next-generation sequencing technology

Huge number of viral sequences available



(Dylus Nature Biotech, 2023)



Ultra-high-throughput sequence alignment
at the petabase scale

Viral RNA-dependent
RNA polymerase search

131,957 novel RNA viruses

(Edgar, Nature, 2022)