

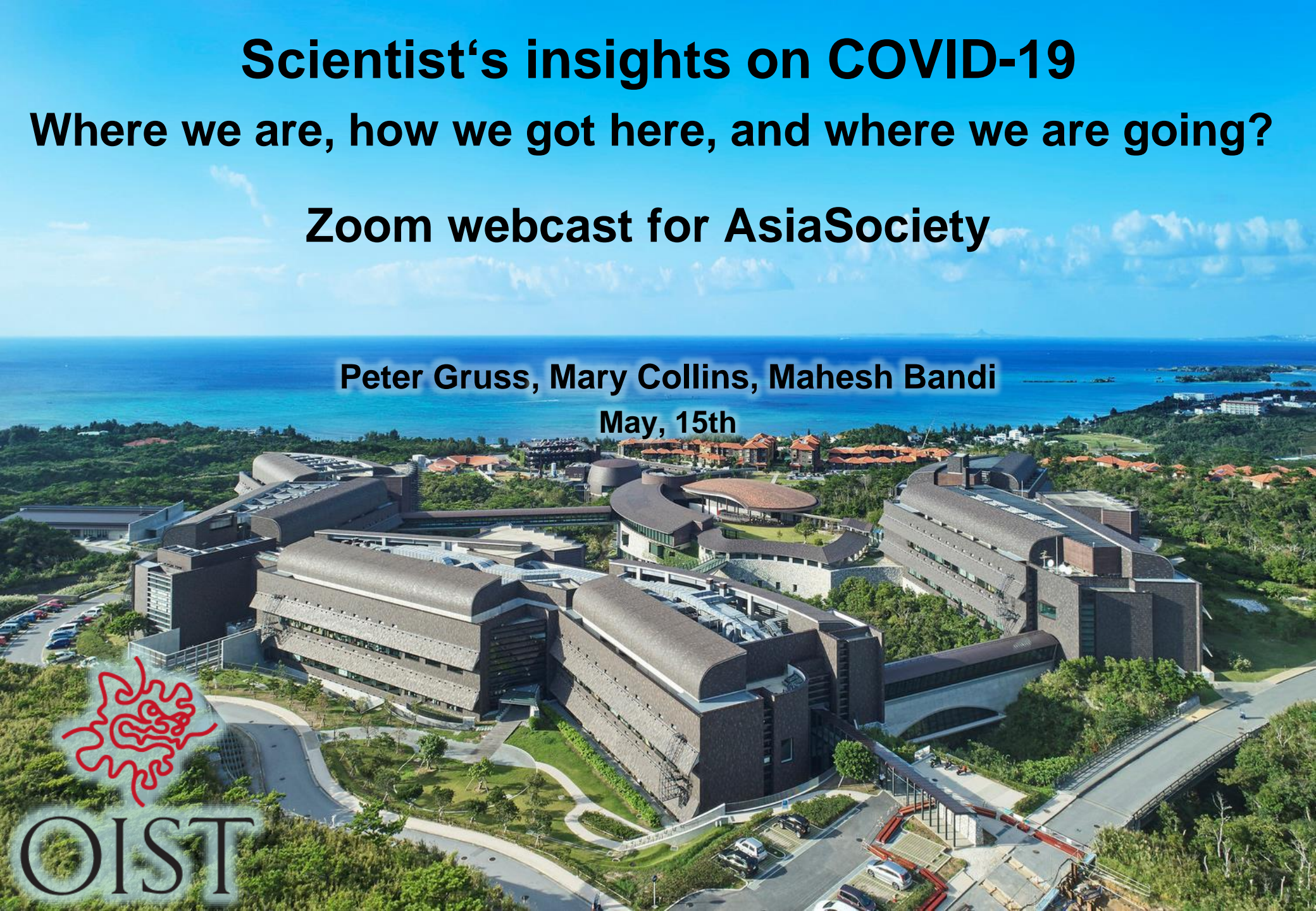
Scientist's insights on COVID-19

Where we are, how we got here, and where we are going?

Zoom webcast for AsiaSociety

Peter Gruss, Mary Collins, Mahesh Bandi

May, 15th



OIST

Key points to be addressed

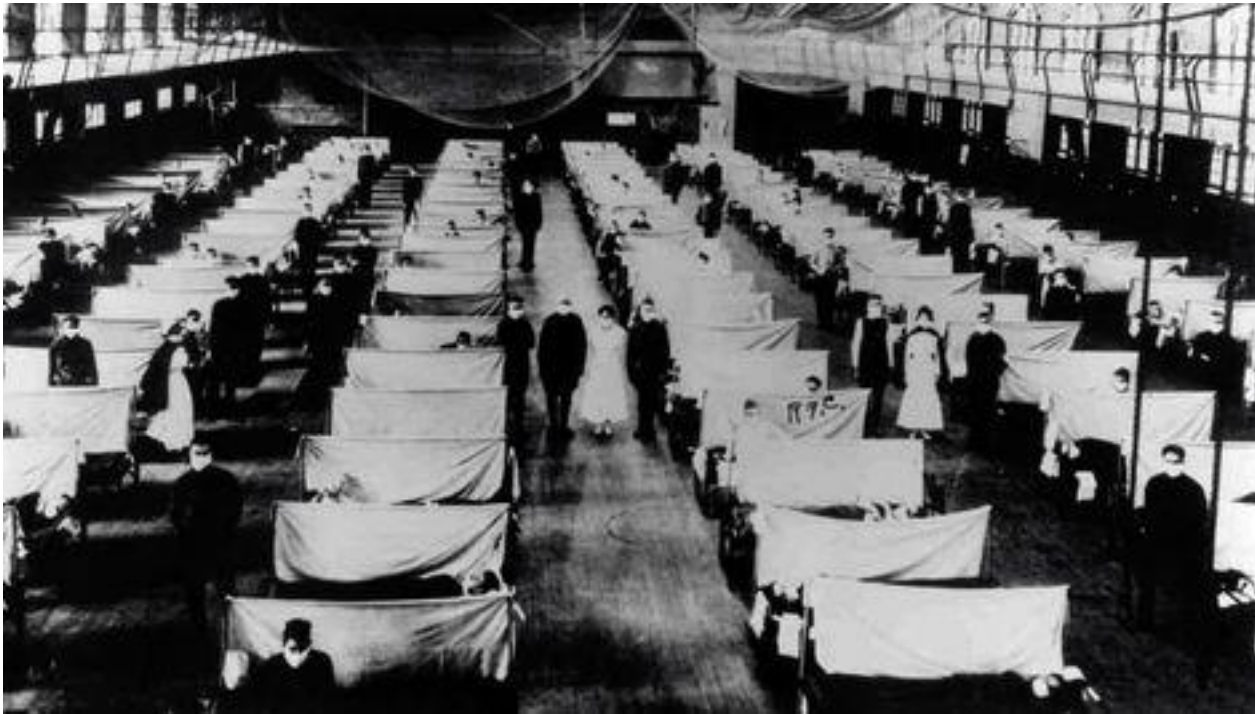
- What is causing COVID-19? How does SARS-CoV-2 infect and spread?
- How can infection be prevented?
- How to test for infected people?: PCR and serological assays
- Research to develop a vaccine
- Infected people respond differently, why?
- Lessons learned from other countries
- 2nd and 3rd waves and when will virus disappear?
- Scenarios for a new normal

History of Infectious Diseases: COVID-19 is not the first pandemic

- Communicable diseases existed during humankind's hunter-gatherer days
- Shift to agrarian life 10,000 years ago created communities that made epidemics more possible.
- Malaria, tuberculosis, leprosy, influenza, smallpox and others first appeared during this period.
- Here in Japan, the smallpox epidemic of the Tenpyo Era, from 735 to 737, killed approximately one third of the Japanese population.
- A host of **bacterial diseases** like cholera, tuberculosis, typhoid fever, some ulcers, respiratory infections, or food poisoning are today treated with antibiotics.
- **Viruses**, however, are much harder to treat because they rely on entering host cells.

Spanish Flu

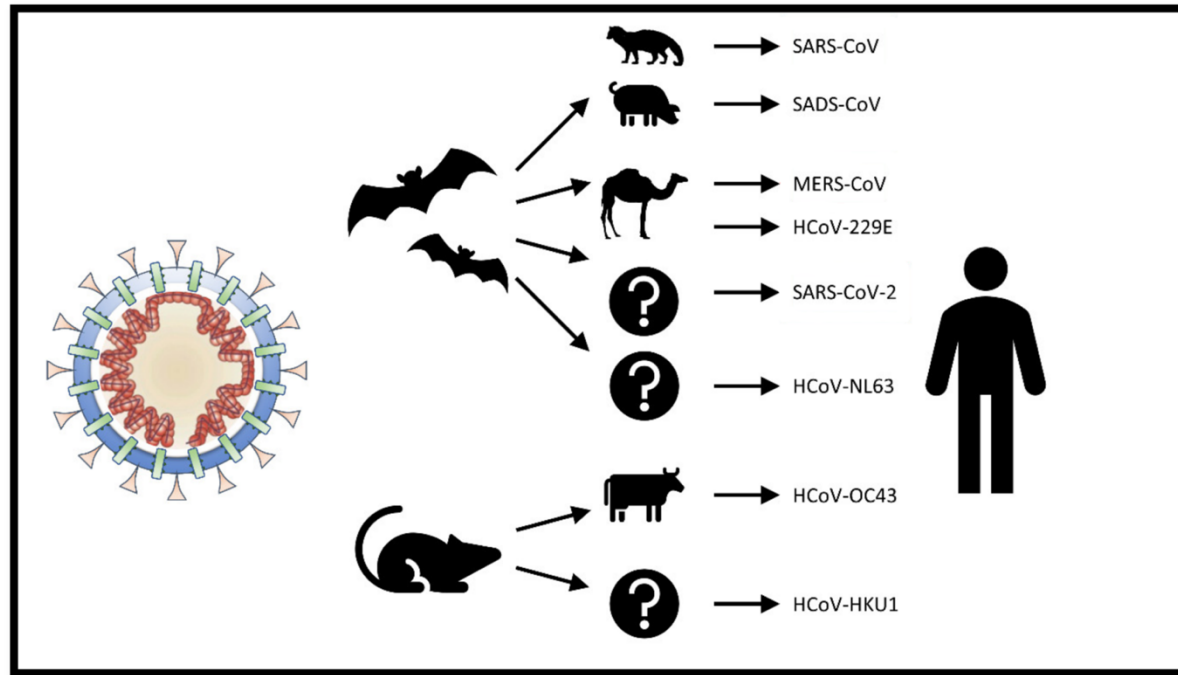
- Spanish Flu is thought to have infected around one third of the world's population and killed at least 50 million people. It is the deadliest pandemic in modern history.



But.....

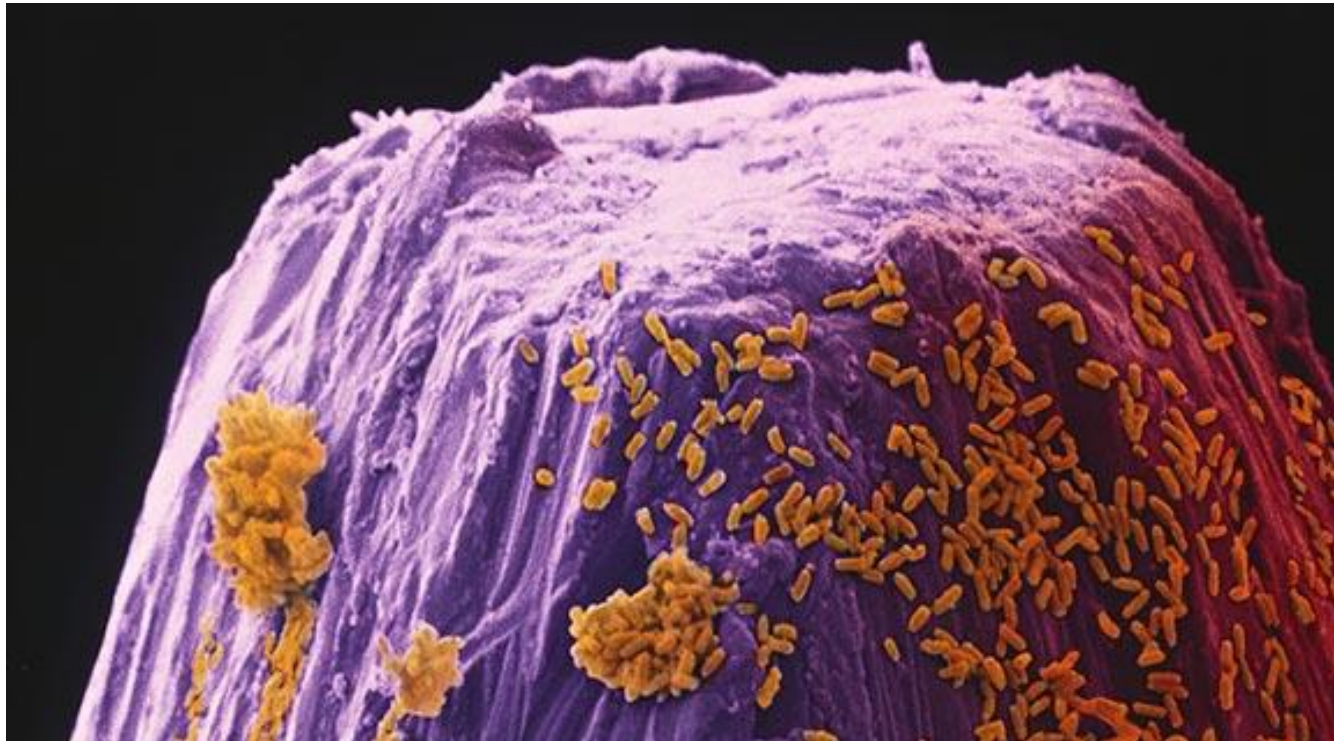
- Without microorganisms, we would cease to exist. There are 37 trillion cells in our bodies. The same number of bacteria in our gut help us digest the food we eat in order to survive.
- There are more microbes in a teaspoon of soil than there are people on the earth.
- Viruses also emerged at an early stage in the evolution of life.
- There are approximately **10 million viruses** in every drop of surface seawater,

SARS-CoV-2 has it's origin in animals

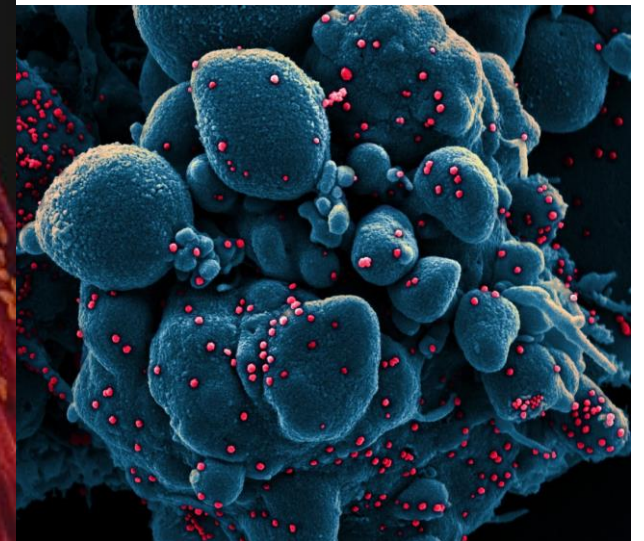


- Coronaviridea are also ancient. They originated 55 million years ago, and they are closely associated with the evolution of bats and birds.
- Their genetic material is RNA
- Mutations occur during replications
- Some mutations allow infections across the species barrier

Viruses are small and have to attack cells to survive

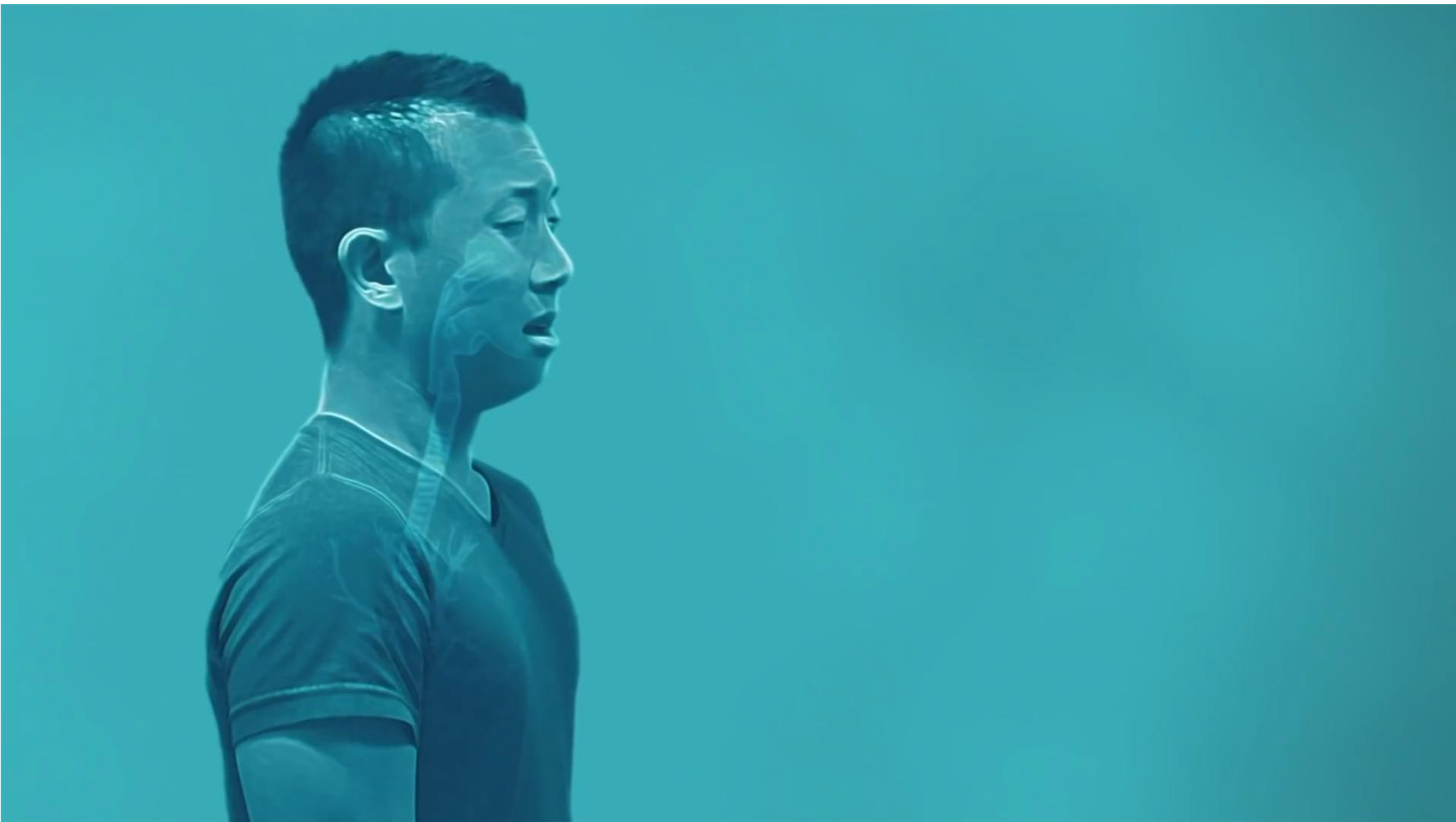


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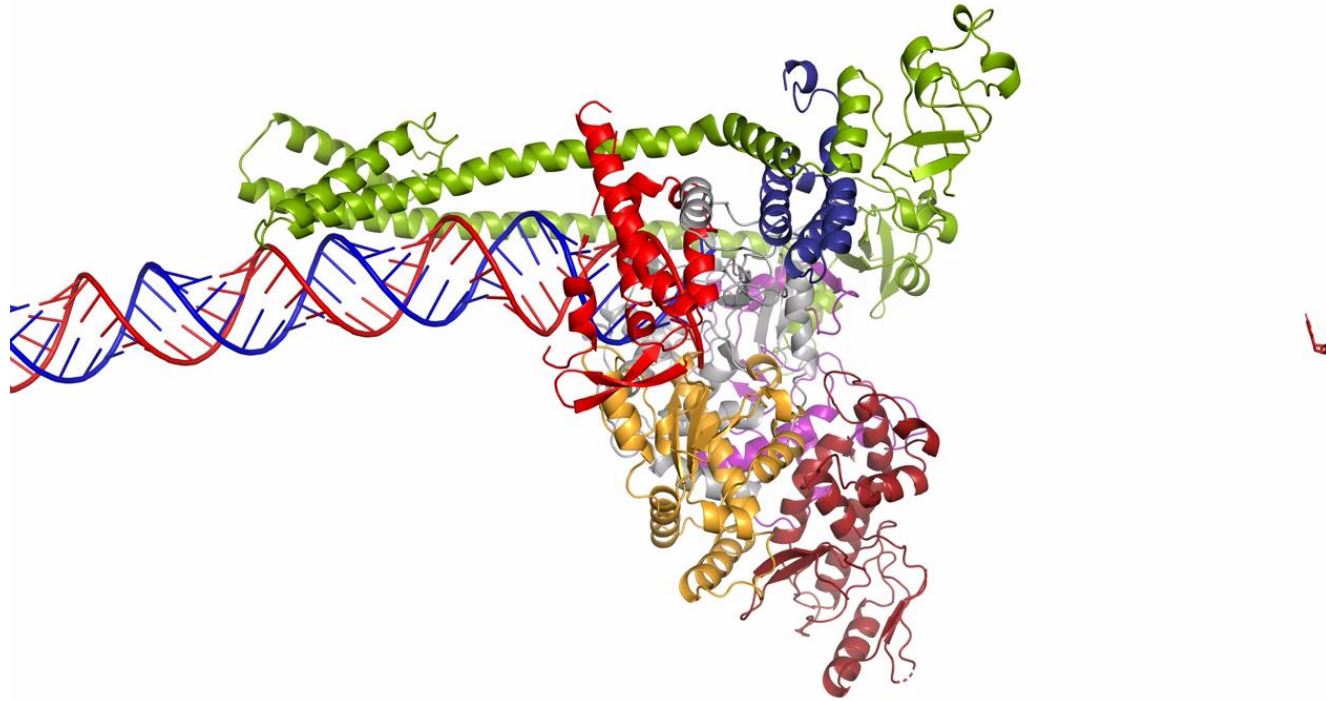


- Bacteria (on the tip of a needle) are ten times smaller than an average body cell.

- A virus is five hundred times more tiny.



SARS-CoV-2 has a virus specific enzyme for replication

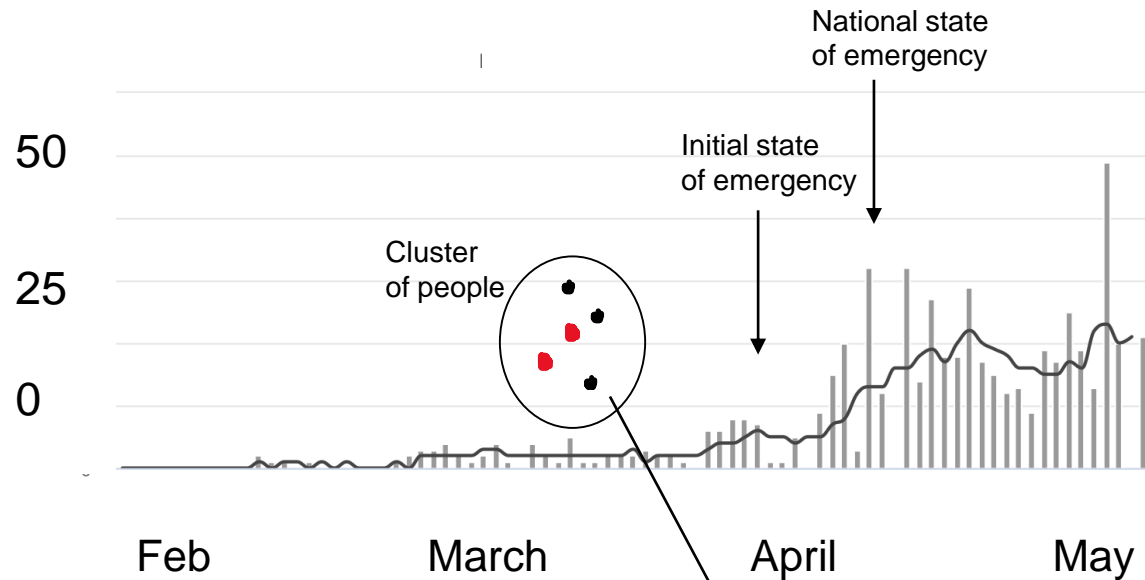


- Many hopes rest on **Remdesivir** (Gilead) and Avigan (Fujifilm), which selectively inhibit the viral RNA-dependent RNA polymerase.

How to prevent SARS-CoV-2 infection?

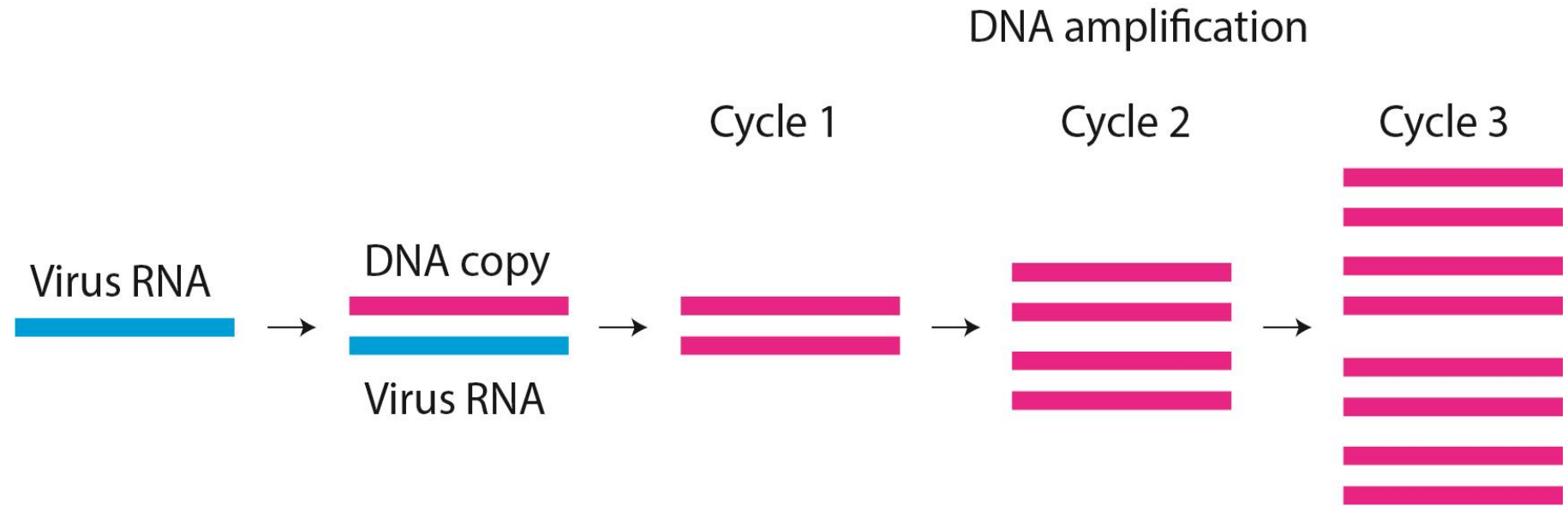
- There is no vaccine available as yet to combat COVID-19.
- The critical task is to prevent transmission of the virus from contact with infected people, whose breathing and coughing will expel it into the air you inhale.
- Measures like wearing face-masks, closing schools, or cancelling public events, can of course help, but they will only have a moderate effect.
- The most effective way to prevent infection is through a 'lockdown', requiring people to stay at home whenever possible, avoiding groups, and leaving only for essential tasks like grocery shopping or taking exercise.

Daily COVID-19 deaths in Japan



- PCR test based on symptoms + risk
- Trace contacts and test
- Isolate infected people in hospital

The PCR Test



After 20 cycles, 1 million copies

Just 1 Virus Gives...

After 30 cycles, 1 billion copies

After 40 cycles, 1 trillion copies

No Virus Gives...

NO copies, no matter how many cycles

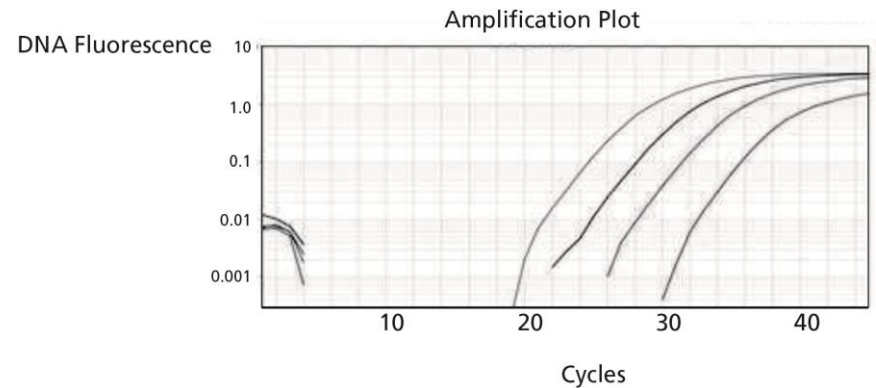
COVID-19 PCR at OIST



- Commissioned by Okinawa Prefecture
- Using WHO recommended method
- Samples from Hokubu, Yaeyama's and Miyako every day
- Throat and nasal swabs, and sputum

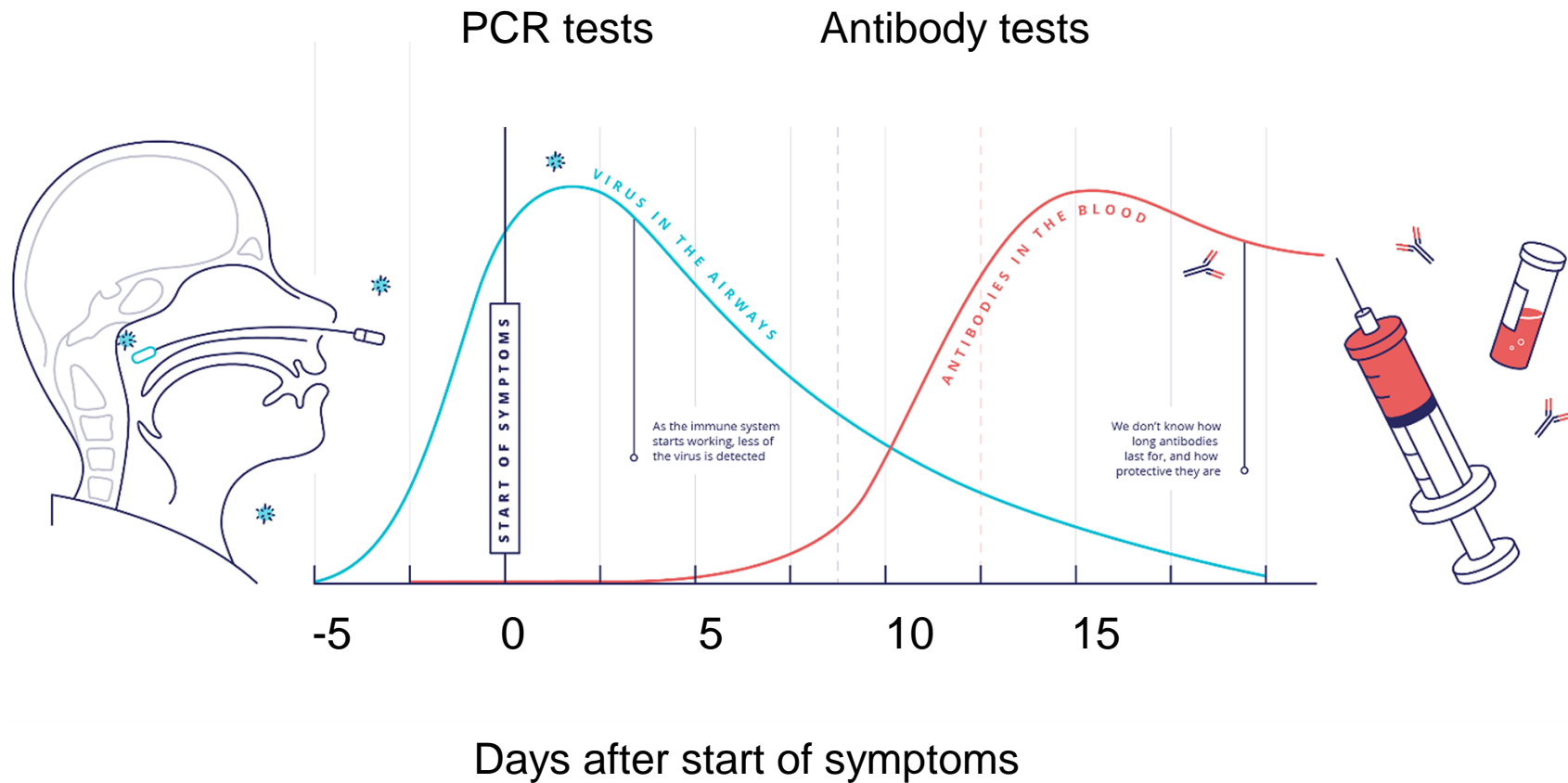
Planned developments

- Faster- under 1 hour
- From saliva
- Automated

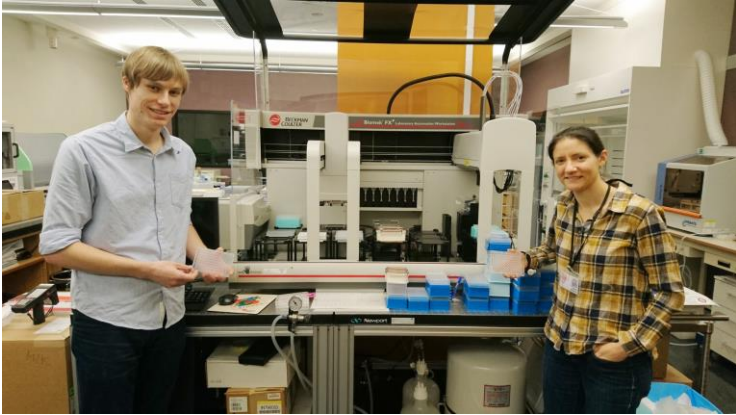


OIST data

Antibody tests to see where the virus has been



COVID-19 antibody tests at OIST



Christian Butcher and Melissa Matthews

- Prof Matthias Wolf is implementing a test developed by Florian Krammer at Mt Sinai Hospital, NY
- OIST is commissioned by Okinawa Prefecture to survey patients from 5 hospitals

Planned developments

- Improved antigens
- From finger pricks
- Home kit format?
- Automated

Local testing development costs



Join the OIST Foundation for our 3rd U.S.-Japan Science Webinar on Thursday, May 14 at 6:30 PM EST

The future of COVID-19 tests

-they will be with us for years to come

- Faster virus genome test for even mild symptoms
- Trace contacts by phone app, test, and home isolation
- Test for travelers
- Test for OIST visitors
- For olympic athletes and spectators
-

- Antibody tests to see who in population has been infected

Do antibodies protect you?

- Health and care workers?
- Teachers?
- Travellers?

Antiviral drugs or vaccine?

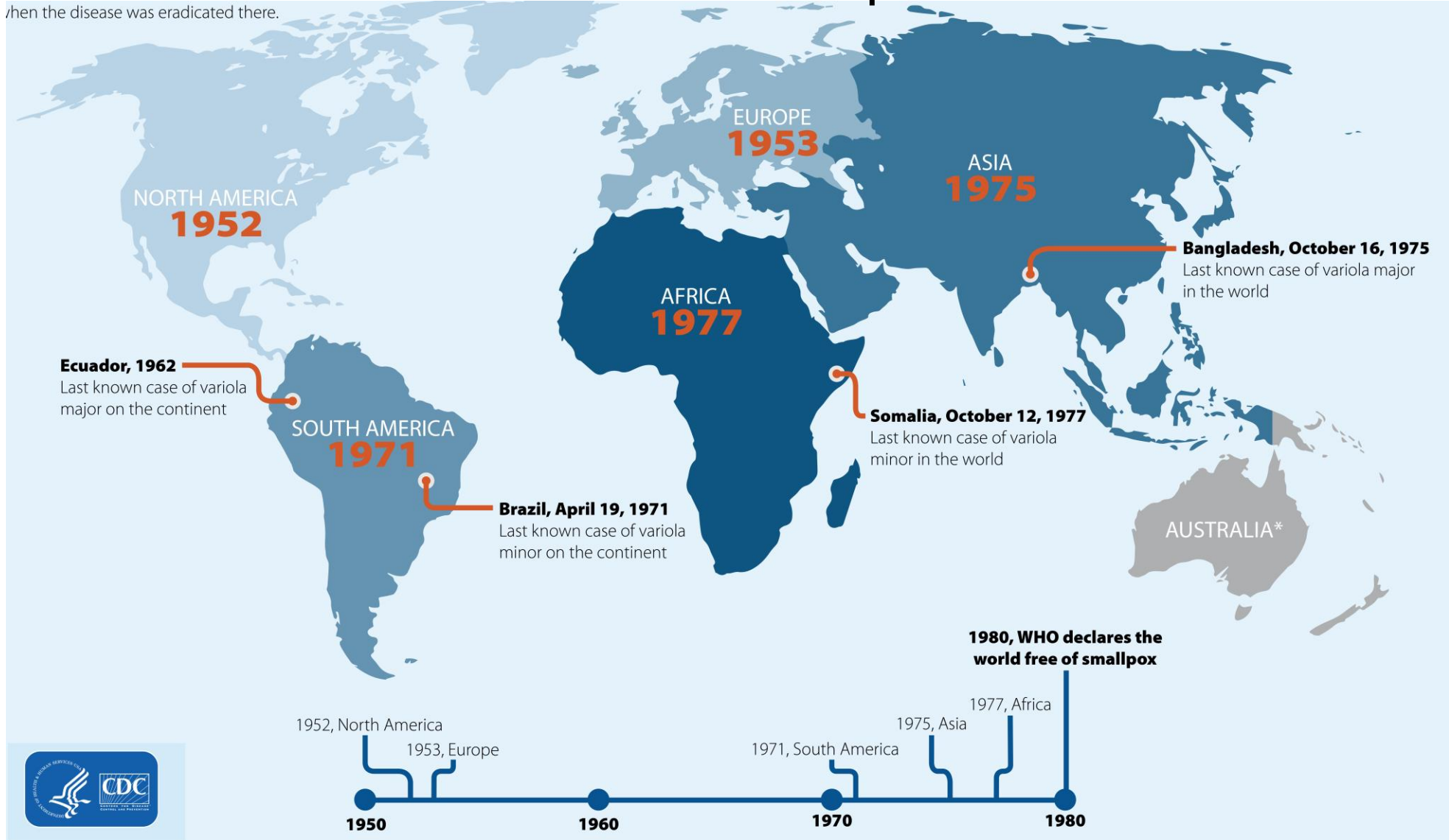
Global problem, solution should be deliverable, affordable

Antiviral drugs can lessen disease in developed world

Optimal testing worldwide will be needed for many years

Eradication of smallpox

when the disease was eradicated there.



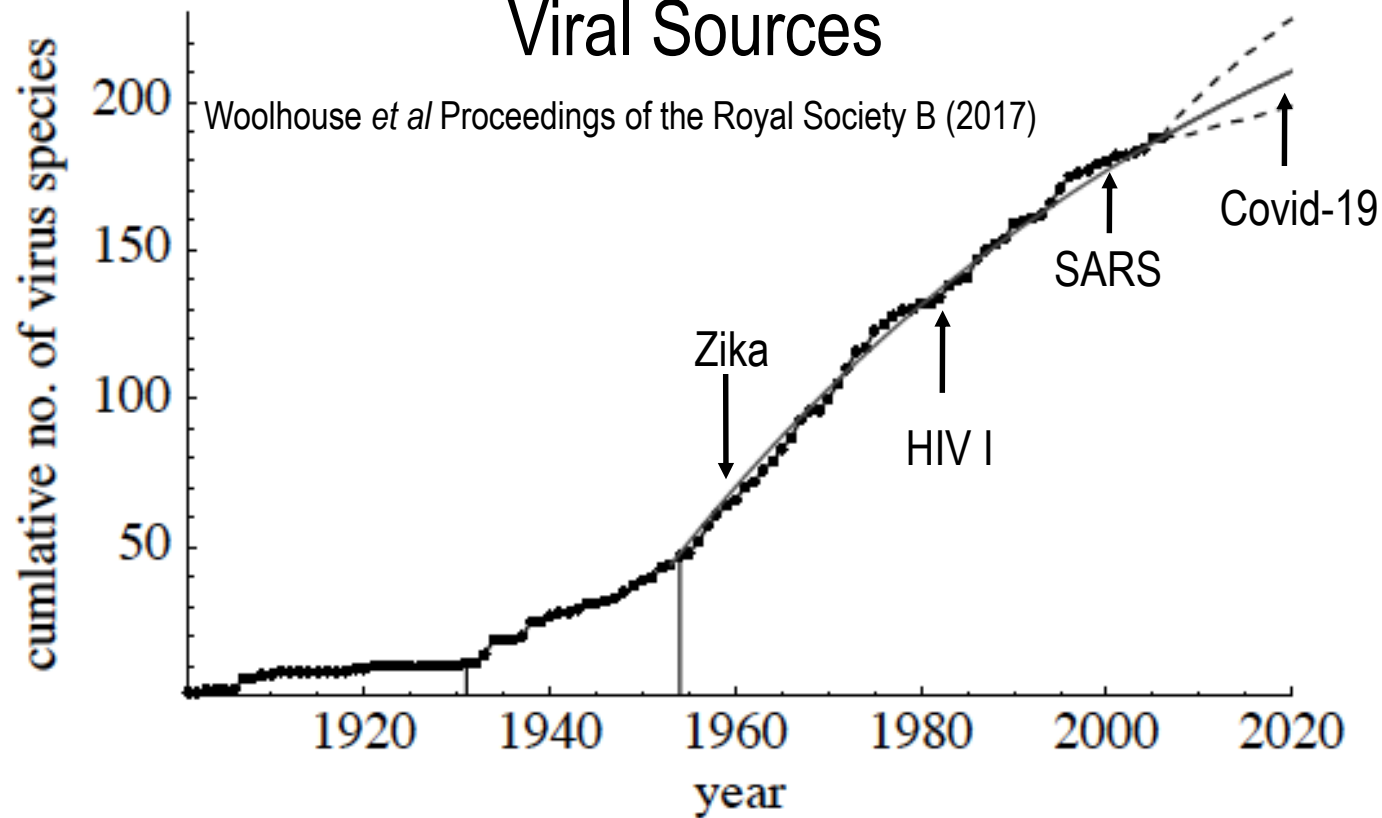
COVID-19 vaccine prospects

- Over 100 teams working on the problem
- Virus is not mutating substantially as it spreads
- Virus does not persist

Notes of caution:

- How to test, field test vs challenge volunteers?
- How long will protection last?
- Vaccine could enhance inflammatory disease like Dengue fever or RSV

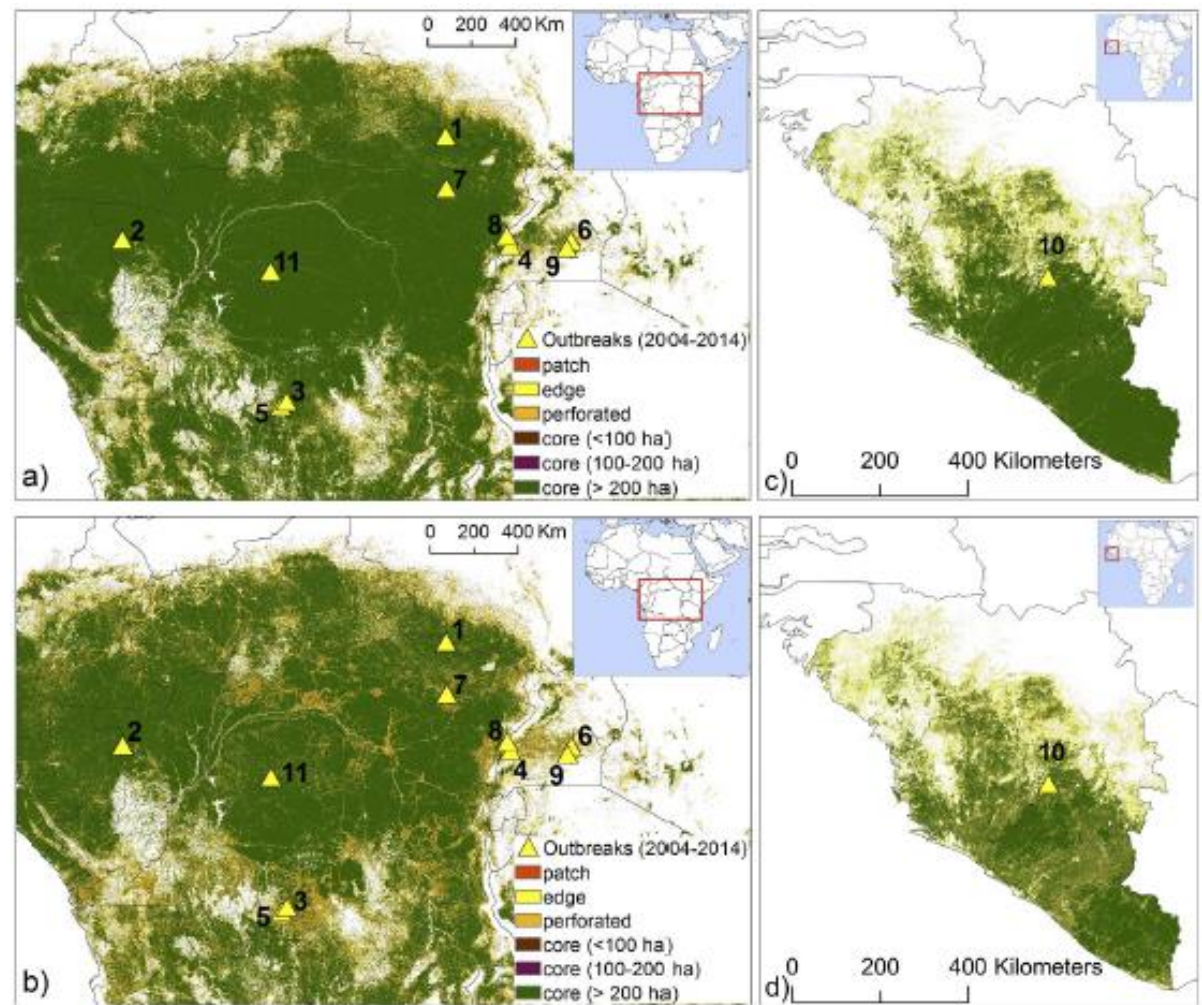
Viral Sources



- Viruses regularly jump from animals to humans, roughly 2 viruses/year since the 1960s.
- Examples: Zika, Nipah, Hanta, Ebola, Dengue, SARS, MERS, and now Covid-19.
- Why is cumulative number of virus species flat before 1940s? Three reasons:
 - Viral detection tools matured in 1940s - 1960s.
 - Lifestyle improvements translated to increase in wildlife trade (Source: CITES).
 - Wuhan seafood market seen as source of current outbreak. Remark: US vs. China wildlife trade.

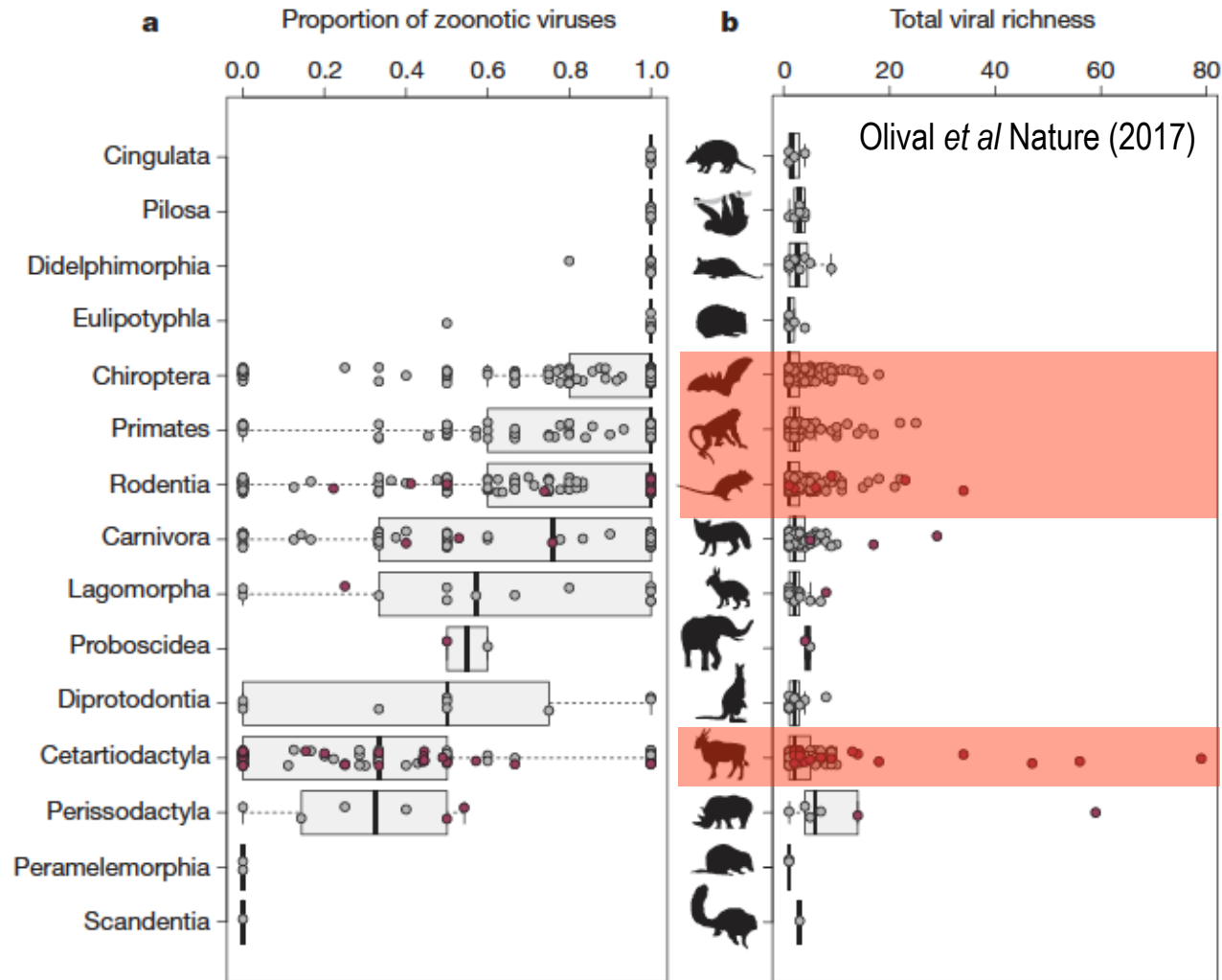
Reason 3

Rulli *et al* Scientific Reports (2017)



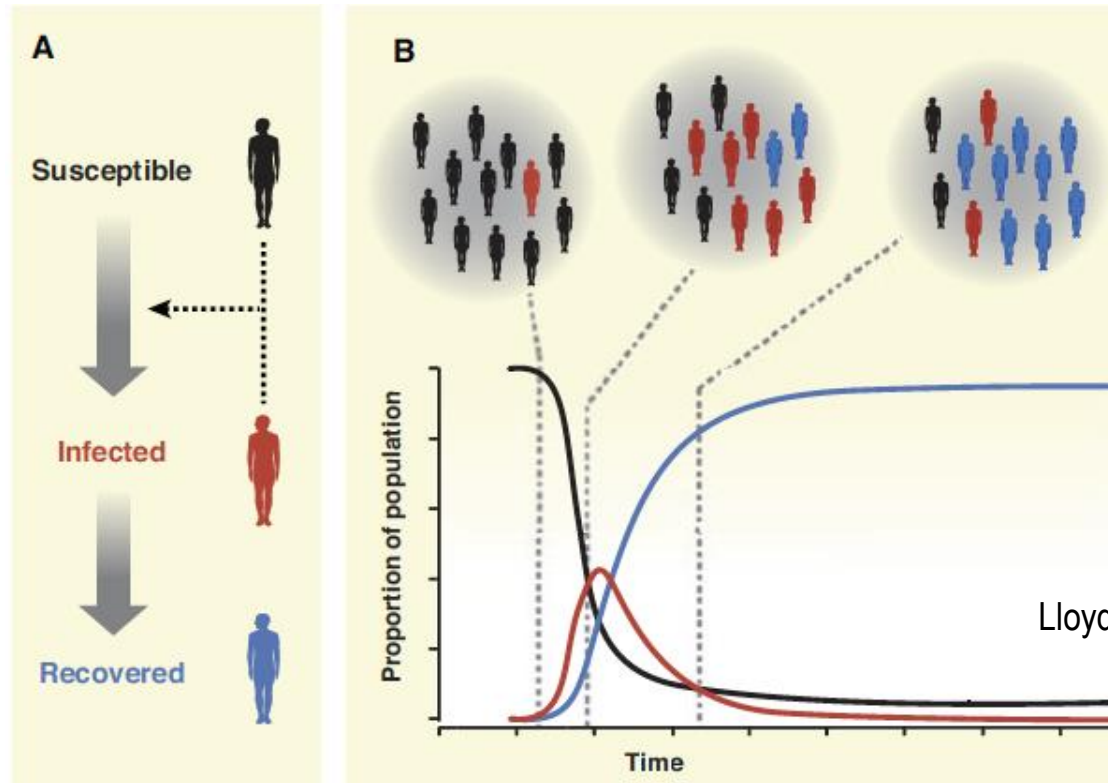
- Global population increase forest land encroachment for agriculture.
- Case in point: Ebola outbreaks first appeared at forest-farm perimeters in Africa.

Viral Sources



- Unfortunately, animals rich in viruses also ones humans come in close contact with.
 - e.g. Mammals & Primates (closely related to us), rodents & domestic animals.

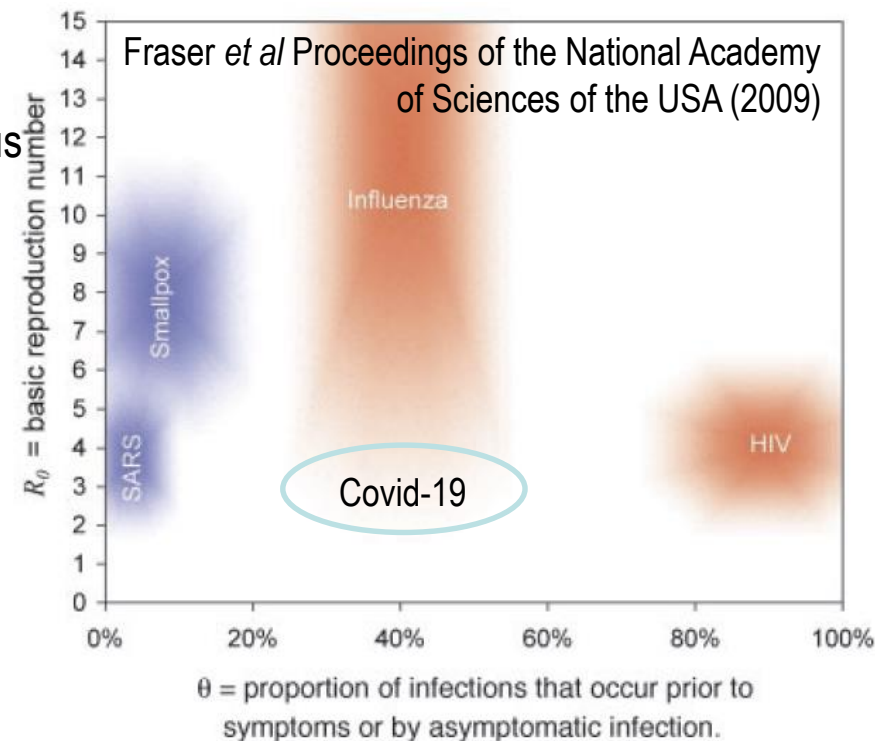
Viral Transmission



- Initial: We have population of un-infected humans, all susceptible to infection (BLACK).
- Start: Virus jumps from animal to human and seeds an infection (RED).
- Transmission: Infections rise exponentially until infected people (RED) exceed un-infected people (BLACK) and recoveries begin (BLUE).
- Recovered people (BLUE) are immune for some period.

What is the risk?

- R_0 : Average number of people an infected person transmits virus to.
 - $R_0 > 1$: Exponential rise, $R_0 < 1$: Infections die.
- Media quotes this number only, but not enough.
- % of asymptomatic infections equally important.
- Disease virulence depends on both numbers.
- Together, they decide the degree of risk.



- SARS $R_0 \sim 2.5 - 5$, COVID $R_0 \sim 2 - 4$, HIV $R_0 \sim 3 - 5$ all in similar range, but virulence varies.
- SARS: not widespread because viral shedding happens after symptom onset.
- HIV: $\sim 100\%$ asymptomatic transmission. Covid: 30-50% asymptomatic transmissions.

Near-term risk reduction: Personal hygiene — within individual control.

Social distancing (most important) OR Herd Immunity (dangerous concept, Sweden).

Test, Test, Test: Only way out. Clueless without numbers.

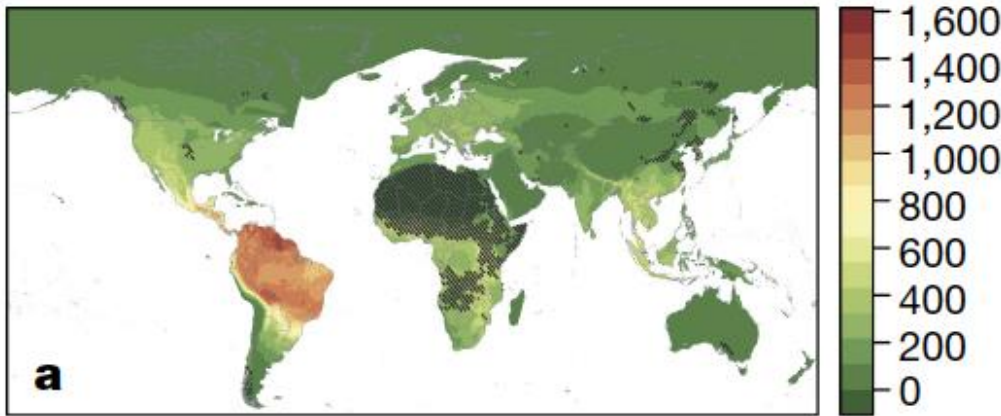
Importance of social distancing: A sample.

AI-based tracing at Ft. Lauderdale beach during spring break (after US was in full COVID crisis).

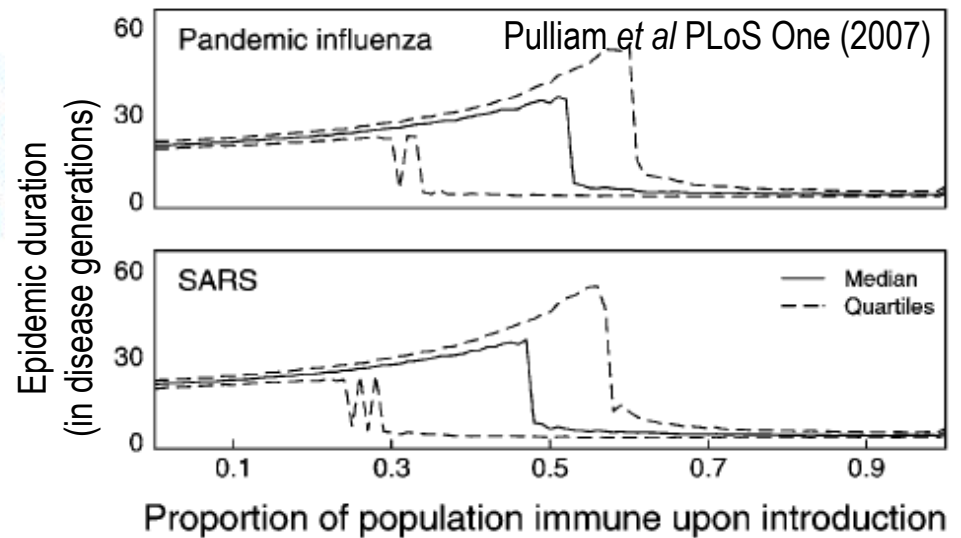


Long-term Risk reduction

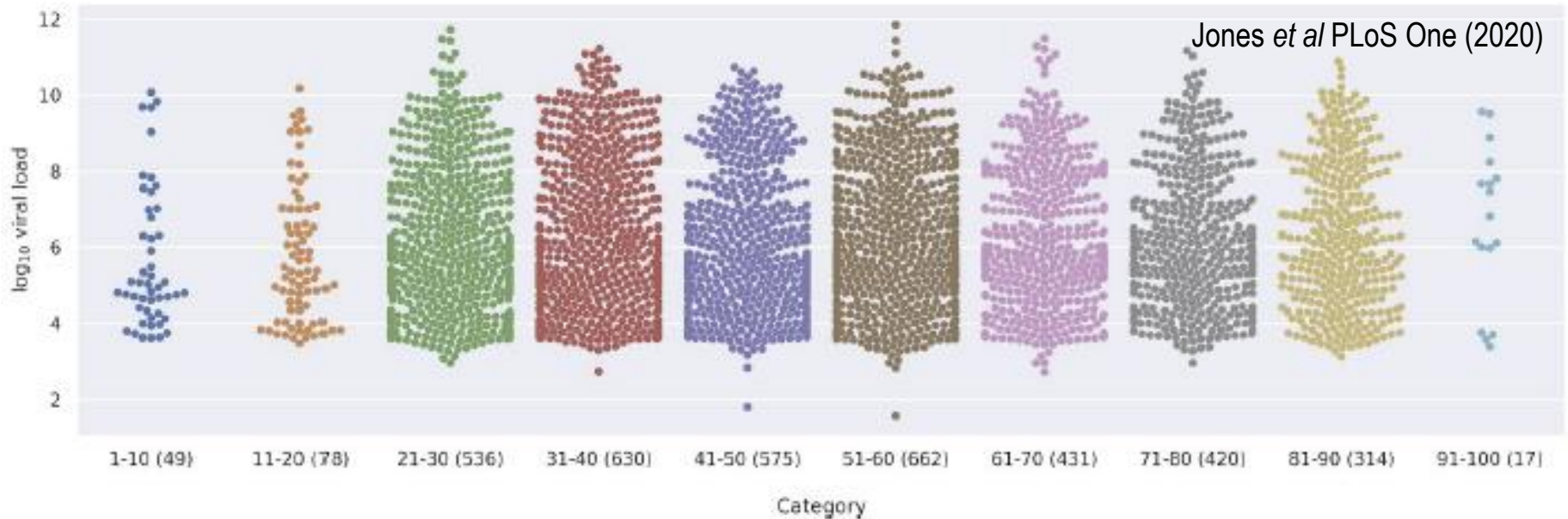
- Vaccine: Likely, but will take ~ 2 years.
- Stamp out virus: Possible, but requires extreme measures. Smallpox/Polio took long.
- Improve health care: Strong correlation between healthcare quality and mortality rate.
- Prepare for future waves: 1st wave always stronger, but later waves linger longer.
- Control wildlife trade: Viral jumps to humans come from contact with wildlife.
- Control deforestation: Reduces wildlife contact, but solution too maybe hidden in forests.



Olival *et al* Nature (2017)



Long-term risk reduction



- So much more to learn, will take 2-5 seasons to answer many pressing questions:
 - Why is there huge variation in how infected people respond to virus?
 - Why the huge variation in detected viral particles (few - 100 million per ml)?
 - How long does immunity last?
 - Does Covid-19 depend on climate (temperature, humidity etc.)?
 - How fast does the virus mutate? Not a high mutation rate so far...

The New Normal Coronanomics: lasting shifts

“ Flatten the curve“

Any step to ease restrictions and transition must ensure:

- That evidence shows COVID-19 transmission is controlled;
- That public health and health system capacities including hospitals are in place to identify, isolate, test, trace contacts and quarantine them;
- That outbreak risks are minimized in high-vulnerability settings – particularly in elderly homes, mental health facilities and people residing in crowded places;
- That workplace preventive measures are established – with physical distancing, handwashing facilities, respiratory etiquette in place, tracing apps useful.
- That communities have a voice and are engaged in the transition.

The New Normal „Corononomics“: lasting shifts

Many countries are embarking on a two-stage approach to overcome the crisis

- Cushion the downfall
- Accelerate the recovery

The New Normal „Corononomics“: lasting shifts

Many countries are embarking on a two-stage approach to overcome the crisis

➤ Cushion the downfall

- As governments step up to serve, or save, the private sector, the means they choose will differ.
- Some will outright nationalize, some will take equity stakes,
- some will provide loans, and
- others will choose to regulate.
- Helicopter money for all

The New Normal „Corononomics“: lasting shifts

Many countries are embarking on a two-stage approach to overcome the crisis

- Cushion the downfall
- Accelerate the recovery
 - ✓ Globalization and trade
 - ✓ Technology and Innovation
 - ✓ Societal impacts
 - ✓ Behavioral shifts

✓ Globalization and trade

- Automation and additive manufacturing offer promise as global supply chains lose some of their luster
- It may also cause businesses to move from offshoring to near-shoring and even reshoring of production.
- This could boost the anti-globalization trend that has been visible for the past few years.

The New Normal „Corononomics“: lasting shifts

✓ Globalization and trade

✓ Technology and Innovation

The pandemic may lead to a fundamental rethink of where, and how, we work.

- Social distancing enforces videoconferencing, virtual classrooms and telemedicine, digital commerce.
- Accelerate development of next-gen remote working technologies, such as augmented and virtual reality.
- .
- Governments are deploying surveillance technologies to track those infected and identify those who came into contact with them.
- Researchers are employing AI and synthetic biology in drug and vaccine R&D. 3D printers are printing parts for ventilators, hands-free door openers and more.

The New Normal „Corononomics“: lasting shifts

- ✓ Globalization and trade
- ✓ Technology and Innovation
- ✓ Societal impacts
 - As the pandemic exposes gaps in the safety net, society's expectations of who should provide what may be changing
 - Health coverage, gig workers, more jobless people, Gen-Z

The New Normal „Corononomics“: lasting shifts

- ✓ Globalization and trade
- ✓ Technology and Innovation
- ✓ Societal impacts
- ✓ Behavioral shifts
 - The lasting impacts on society are as inevitable as they are hard to predict; behavioral economics might prove useful in responding.
 - In-person connection over social media,
 - Remote shopping
 - Trust is low, polarization high, and **xenophobia** surging.

