Responses to COVID-19 in the world

Minato NAKAZAWA, Ph.D.
Kobe University Graduate School of Health Sciences &
Graduate School of International Cooperative Studies
<minato-nakazawa@umin.net>

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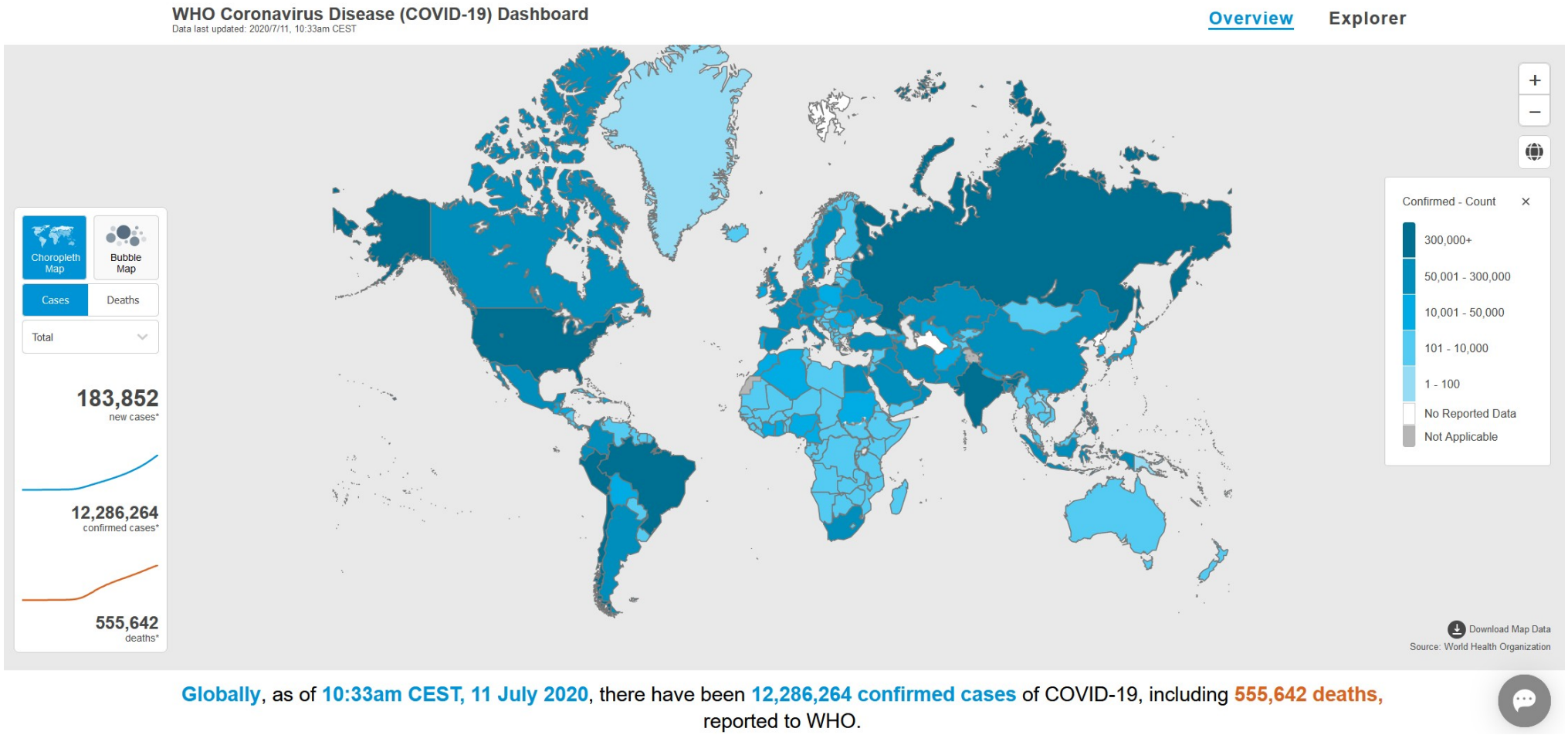
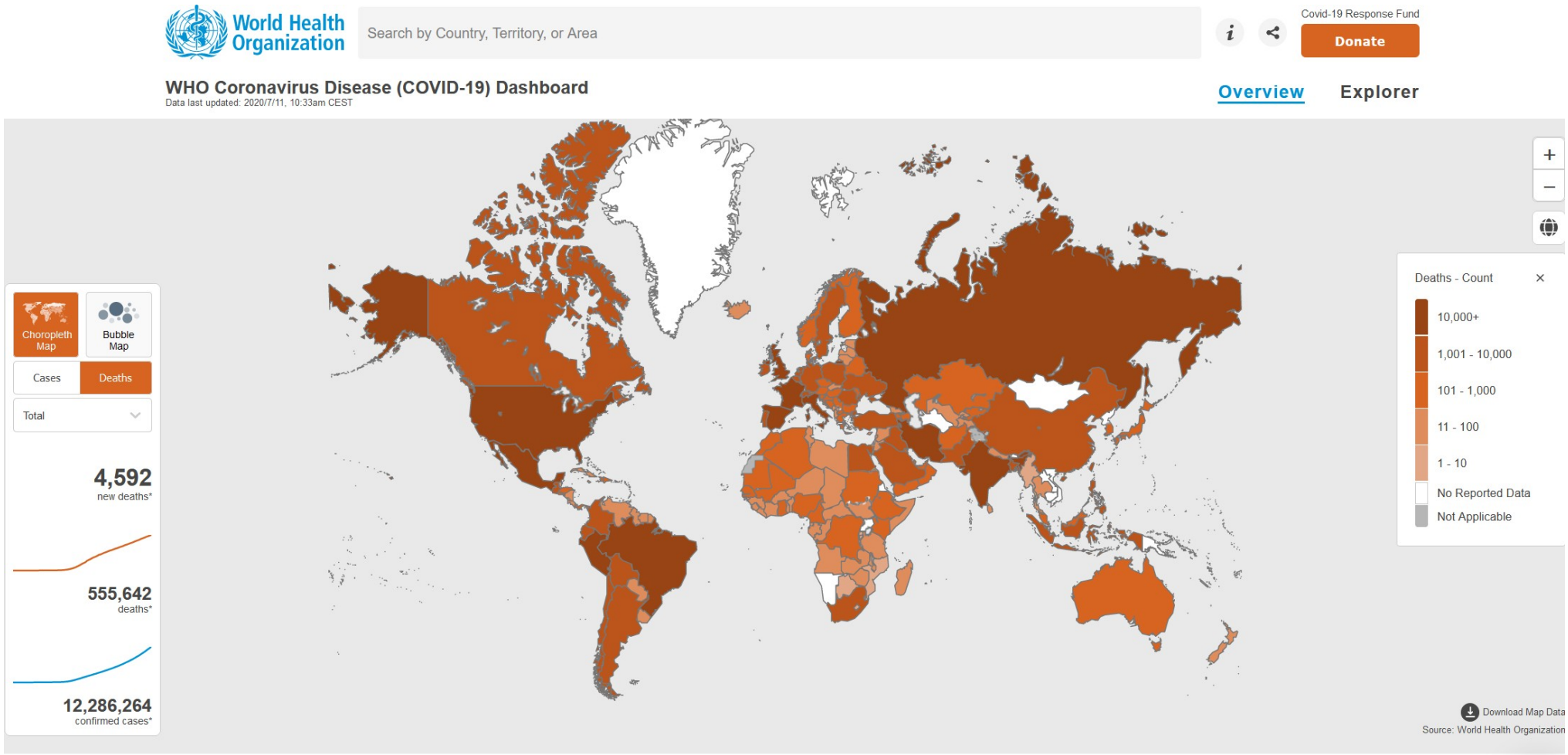
Global situation of COVID-19 cumulative cases (https://covid19.who.int/)



Global situation of COVID-19 cumulative deaths (https://covid19.who.int/)



No death in Namibia, Mongolia, Vietnam, Laos, Cambodia, PNG, ...

What's known about COVID-19

- The pathogen of COVID-19 is SARS-CoV-2, which is the 7th corona virus for human host.
  - Among the corona viruses for human host, 4 types cause common cold.
  - Other 3 types are SARS-CoV, MERS-CoV, and currently prevailing SARS-CoV-2 (it was called as 2019-nCoV at first). The genomes of SARS-CoV and SARS-CoV-2 have similarity of 80%. A kind of bat CoV genome showed almost complete similarity with SARS-CoV-2 genome.
    - SARS-CoV originated from bat, through other animal, then human to human
    - MERS-CoV originated from camel, rarely human to human
    - SARS-CoV-2 originaned from bat, probably through pangolin (*Manis javanica*), human to human
- Characteristics of SARS-CoV-2
  - Latent period (from infection to symptom) is 5 days in average (Linton et al. 2020)
  - Serial interval (between the occurrence of symptoms of first case and second case) is 4 days in average, which means infection occurs in presymptomatic period. Contact tracing is difficult (Nishiura et al., 2020)
  - About 80% of the infected persons are asymptomatic or showing mild symptoms.
  - The risk of severe symptoms or deaths depends on the patients age. Elderly and the people with underlying diseases show high risk, but some young patients without any underlying diseases may also die at much higher risk than influenza.
  - The periods from admission to the hospital to either getting well or death are about 20 days, recently shortened.
  - Because of no vaccine nor effective medicine, severe cases have to be treated by ventilator or ECMO in ICU, otherwise die at high risk. The risk of death depends on medical standard.

Severity

- The common indicator of severity is CFR (Case Fatality Ratio/Risk).
  - Definition: [number of deaths caused by a disease] / [number of confirmed cases of that disease]
  - CFRs for SARS, MERS, Spanish flu and Asian flu were 10%, 35%, 3% and 0.5%, respectively.
  - CFR of seasonal flu is "less than" 0.1%. In Japan, the estimates of confirmed cases is about 10 million, and the number of death due to seasonal flu is 2000 to 3000, so that CFR is 0.02-0.03%.
  - The CFR of COVID-19 ranges from 1 to 10%.
    - The wide range of CFR is caused by large difference of examination ability, medical capacity, and the age distribution of the patients.
    - Like in South Korea and Germany, extensive RT-PCR examination for many people leads to large number of confirmed patients, subsequently smaller CFR estimates. In South Korea, younger patients with lower fatality shared majority of positives, which made CFR lower.
    - Like in Italy and France, if the number of patients went beyond the medical capacity with rapid increase (so-called "overshoot" in Japan, analogously with "overshoot" in ecology, which means excess population growth beyond the carrying capacity), CFR goes higher.
- New indicator of severity is IFR (Infection Fatality Ratio/Risk).
  - Definition: [number of deaths caused by a disease] / [number of all infected cases of that disease]
  - Based on the data from China, estimated CFR ranged 3-6% and the confirmed cases were considered to share about 10% of all infected patients, IFR was suggested as 0.3-0.6%. IFR may be applicable as universal indicator of disease severity (Nishiura 2020).
  - The IFR of seasonal flu seems to range from 0.005 to 0.01%.

Age dependency of CFR

Age-specific CFRs in Mainland China up to 11 Feb 2020. http://weekly.chinacdc.cn/en/article/id/e53946e2-c6c4-41e9-9a9b-fea8db1a8f51			
	Confirmed cases	Deaths	CFR(%)
0-9yr	416	0	0
10-19yr	549	1	0.2
20-29yr	3619	7	0.2
30-39yr	7600	18	0.2
40-49yr	8571	38	0.4
50-59yr	10008	130	1.3
60-69yr	8583	309	3.6
70-79yr	3918	312	8.0
80yr+	1408	208	14.8
All	44672	1023	2.3

- Age-specific CFR of Pandemic flu 2009
  - MHLW data in Japan (https://www.mhlw.go.jp/bunya/kenkou/kekkaku-kansenshou04/dl/infu100608-03.pdf)

    0-4yr 0.0007%
    5-9yr 0.0003%
    10-14yr 0.0001%
    15-19yr 0.0001%
    20-29yr 0.0005%
    30-39yr 0.0009%
    40-49yr 0.0031%
    50-59yr 0.0066%
    60-69yr 0.0147%
    70yr+ 0.0282%
  - NY city H1N1pdm2009 (https://doi.org/10.1371/journal.pone.0011677)

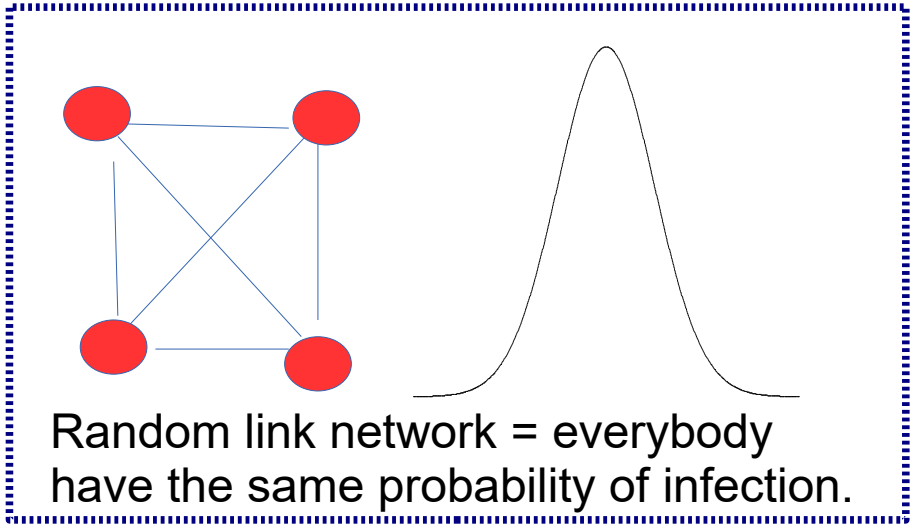
    0-17yr 0.0008-0.0012%
    18-64yr 0.0081-0.0132%
    65yr+ 0.0094-0.0147%

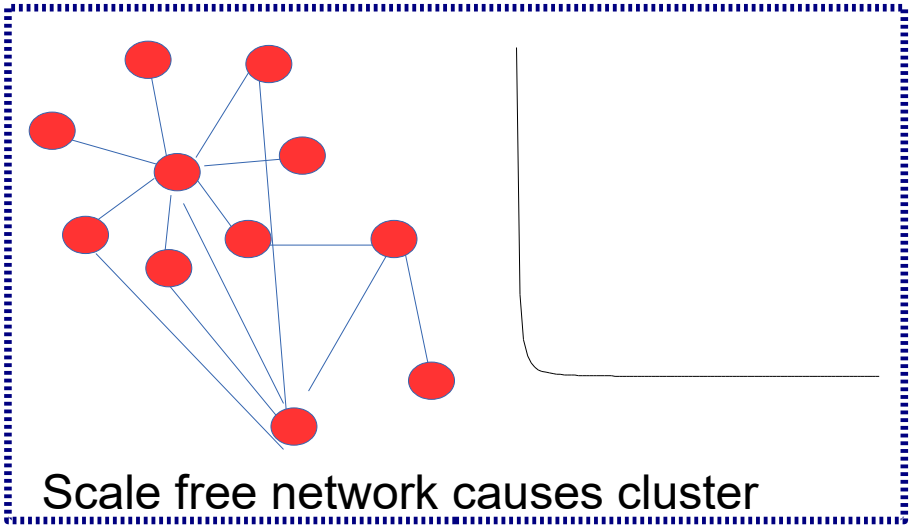
Infectiousness (ability of transmission)

- Commonly used measure of infectiousness is the Reproduction Number (R), which means the average number of secondary infected people from the first case.
  - In the beginning of epidemic, nobody has immunity. Under such situation, where everybody is susceptible, if one index case invades, R is called as Basic Reproduction Number (R0). R0 depends on the nature of pathogen, host behavior, and environment.
  - After the progress of epidemic, recovered (immune) people increase. Some of the population are vaccinated, immune people also increase. In either case, the proportion of susceptible people decreases and thus R decreases, which is called as Effective Reproduction Number (Rt or Re). Rt depends on R0, protective measure, and the size of the population.
- If R<1, the epidemic will be suppressed.
- The R0 of SARS was about 3, but the variance of R0 was very large because of many cluster infection occurred in the airplane or hospital, where superspreading event may occur. The R0 of MERS was generally less than 1 except for nosocomial infection.
- The R0 of Spanish flu was estimated around 2. The R0 of seasonal flu or Influenza (A) H1N1pdm2019 ranged 1.1-1.5.
- The R0 of COVID-19 was initially estimated as 1.4-2.5 based on the data obtained Wuhan (WHO, 23rd Jan 2020). With accumulation of data, the estimates of R0 largely varied by model or data, at highest, 6.47 (Tang B et al. 2020). However, inter-individual difference was very large, so-called "overdispersion" (Voltz E et al. 2020; Grantz K, Metcalf CJE 2020; Nishiura H et al. 2020).

The routes of infection

- Random link routes of infection, where everybody have the same risk of infection (same as flu) → handwashing, sanitation and social distancing are effective, probably culturally very different
  - Droplets: face-to-face conversation without mask with distance within 2m.
  - Contact with contaminated material surface: touch the material surface contaminated by droplets, saliva or something else excreted from patients
  - Fecal-oral: The viral shedding occurs to feces, so that without washing hands after defecation, the patients touch something, which become source of contact infection
- Scale free route of infection (The cause of overdispersion of R) → paid attention in Japan since February, but very recently become popular by 239 scientists appeal (https://doi.org/10.1093/cid/ciaa939).
  - Cluster infection due to suspended micro-droplets, which likely occur under 3Cs env.
    - Closed space (poor ventilation)
    - Crowded (high population density)
    - Close contact with conversation





Responses by the governments (https://www.coronanet-project.org/)

Policy	Median activity index
Closure of shopping malls	1.7
Restriction commercial business	1.7
Closure of retail stores	1.5
Closure of personal grooming	1.4
Primary school closure	1.3
High school closure	1.2
Higher education closure	1.1
Restriction of other business	1.1
Sanitizer policies	1
Closure of restaurants	1
Quarantine at home	1
Pre-school closure	1
Mobilization of volunteers	0.9
Other health staff	0.9
Restriction of mass gatherings	0.9
Test production	0.8
Mobilization of doctors	0.8
Mobilization of nurses	0.8
Internal border restrictions	0.8
Limited quarantine	0.8
Other health resources	0.8
Social distancing	0.8
Other health facilities	0.8
Other health resources	0.8
Mobilization of ventilators	0.8

Policy	Median activity index
Masks policies	0.7
Restriction government services	0.7
Other health facilities	0.7
PPE mobilization	0.6
External border closure	0.6
Supporting hospitals	0.6
Other quarantine	0.6
Quarantine in hotel	0.6
Curfew	0.5
Biomedical research	0.5
Declaration of emergency	0.5
Temporary medical units	0.5
Quarantine/lockdown	0.4
Building quarantine facilities	0.4
Public testing mobilization	0.4
Quarantine in government facility	0.4
Border health certificates	0.4
Monitoring population health	0.4
Public awareness measures	0.3
Suspend visa issuance	0.3
Mobilization of testing	0.3
Task force	0.3
Other border restriction	0.2
Border health screenings	0.2
Travel history required	0.1

Testing strategy

- Presumption
  - Testing performance is not perfect (RT-PCR cannot detect positive patients if the nasal/ throat swab could not sample viral RNA particles)
  - Early detection cannot lead to effective early treatment to prevent severity or death
- The 3 purposes of RT-PCR to confirm infection (A is crucially needed, B is more effective than C when contact tracing is successfully conducted. If the disease becomes prevailing, B is difficult because it may excess the capacity of manpower of health center)
  - (A) When doctor judged the necessity of confirmation from atypical pneumonia or other results of clinical inspection, to prepare ICU beds, respirator, and ECMO (WHO recommends, many countries incl. Japan do)
  - (B) Detect positive patients (incl. asymptomatic, or with only mild symptoms) from all closely contacted people with patients [active case detection] to prevent spread by isolation of detected cases. (Also WHO recommends, impossible after excess number of new patients as in Europe/USA, Singapore and Taiwan succeeded, Japan did until mid-March and try to continue)
  - (B') Frequent checkup for high-risk people especially medical and health care providers
  - (C) Widely examine suspected people to detect all cases (under low prevalence situation, efficacy is low) to prevent spread by isolation (Iceland, South Korea and Germany did)

Contact Tracing

- Field epidemiologists or public health nurses conduct contact tracing, which requires large man-power and not sustainable under high level transmission.
- Use of big data automatically collected by smartphone apps
  - China seems to have enhanced the information collection system using GPS tracking and surveillance camera since Beijing Olympic. The report 11 from the group of Imperial College used the population movement data from GPS record by Baidu.
  - South Korea has a strong regulation based on the law of infection control, by which the movement of the infected cases using GPS data is visualized and opened to public.
  - In Singapore, the smartphone app "TraceTogether" is recommended to install for everybody. When the smartphone with the TraceTogether running comes close each other, the other's information without location information is automatically detected using bluetooth and recorded with time in each smartphone. The information is kept for 21 days within each smartphone. When a person is proved to be infected, it's possible to find all close contactees of the person during previous 21 days.
  - Apple and Google developed "TraceTogether" like smartphone API, which allows the use of one application for each country. In Japan, it's COCOA. Australia and Switzerland opened to the public very early.
- According to the paper by the groups Prof. Fraser in Science (Ferretti et al., 2020), "digital contact tracing" using smartphone app may enable the suppression of epidemic to avoid "overshoot" without "lockdown". They also discussed ethical issue in that paper.

Behavioral restriction

- According to the basic strategy to tackle the pandemic of infectious diseases by CDC in 2007 (https://stacks.cdc.gov/view/cdc/11425), community mitigation (see the top right) is the important measure
- According to the report 9 from Imperial College of London (https://www.imperial.ac.uk/media/imperial-college/medicine/mrc-gida/2020-03-16-COVID19-Report-9.pdf) and so-called "Hammer and Dance" article (https://medium.com/@tomaspueyo/coronavirus-the-hammer-and-the-dance-be9337092b56), **repeated sets of suppression period** by relatively strict behavioral restriction **and granted period** may become a central strategy.
  - "When the behavioral restriction is granted?" is the matter.

Figure 1.

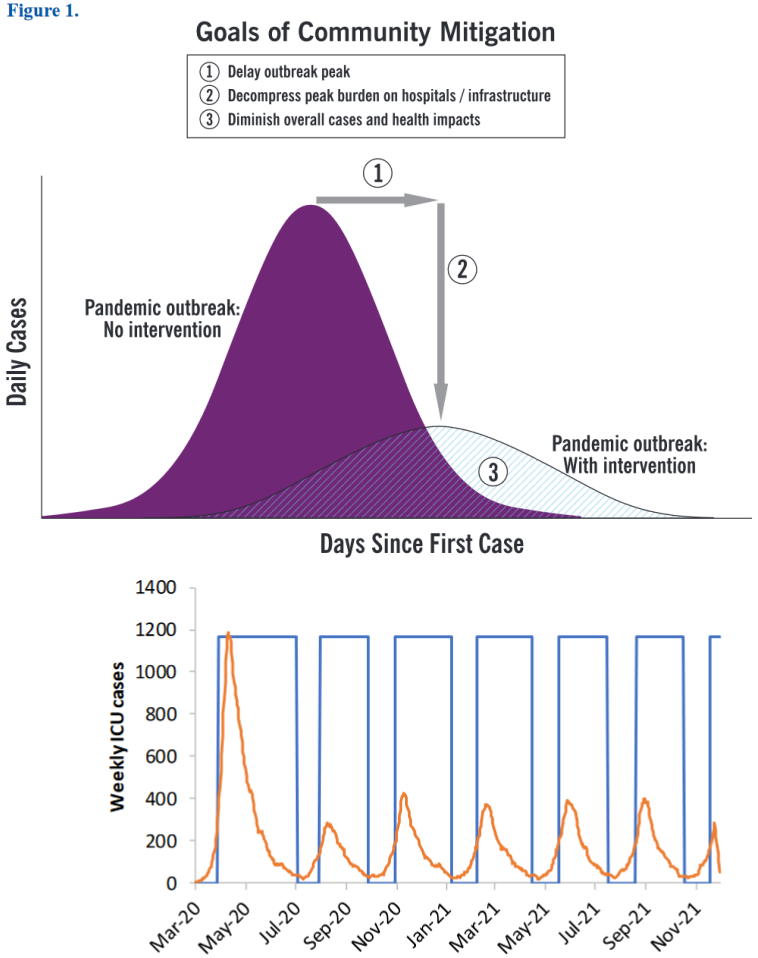


Figure 4: Illustration of adaptive triggering of suppression strategies in GB, for R_0=2.2, a policy of all four interventions considered, an "on" trigger of 100 ICU cases in a week and an "off" trigger of 50 ICU cases. The policy is in force approximate 2/3 of the time. Only social distancing and school/university closure are triggered; other policies remain in force throughout. Weekly ICU incidence is shown in orange, policy triggering in blue.

Factors related to the different policies (very rough view)

- Age structures
  - LMICs have more youth than elderly. Relatively lower IFR
  - HICs have more elderly. Even with more medical treatment including ventilator and ECMO in ICU, IFR is higher
- Governmental strategies to avoid the restriction for economics
  - Coverage of counteraction such as diagnostic testing, isolation, treatment, contact tracing, behavioral restriction varies by the strategy
  - For counteraction, materials (incl. PPE) and equipment have to be secured
  - Counteraction affects the mental and socioeconomic status
- Social gradient
  - Absolutely or relatively poor people living in slums or ethnic minority living in remote area are more vulnerable, if the covid-19 invades into the community, IFR become higher

- Possible strategies by LMICs tended to become either of 2 extremities
  - Do nothing to establish herd immunity, because due to population structure is young, other causes of death share more, then IFR of covid-19 is socially acceptable
  - By strict quarantine and external border closure, prevent invasion. However, no country can continue border closure forever, and longer asymptotic period and infectiousness of asymptotic carriers make it difficult.

Policy sets by some countries (very rough view)

- Do little counteraction (non-pharmaceutical intervention: NPI) to establish herd immunity (aiming to minimize the restriction for economic activity)
  - Brazil: Almost no restriction
  - USA, India: Once conducted NPI including lockdown, but banned such control too early when considerable new cases occur everyday
- Do some NPIs without focusing on 3Cs
  - Sweden: Relatively few NPIs
  - Most European countries: Lockdown kept until the new cases decrease enough
- Do some NPIs focusing on 3Cs
  - Japan: In most area, strict behavioral restriction was done until the new cases decrease enough, but in some area including Tokyo, NPIs were granted too early
  - Malaysia
- Do more NPIs with extensive testing, contact-tracing, quarantine and isolation
  - South Korea, Germany, Iceland: Extensive testing
  - New Zealand, Taiwan: strict NPIs were taken until elimination (followed by 2 weeks of no new case) and keep strict quarantine
- Do strict quarantine and external border closure to prevent invasion
  - Vietnam, Laos, Cambodia, PNG, FSM, ...

Situation of COVID-19 in some countries based on COVID-19 Data Hub

- USA, Brazil and India still show rapid increase (For Brazil and India, since May, for USA, since June, exponential growth).
- Russia, Sweden and most European countries showed rapid increase in the past, but gradually decreased, whereas rapid increases of new cases are sporadically reported in some localities.
- Japan showed decline of new cases during April and May under the declaration of emergency, but started to increase again since June (probably because the restriction was granted too early).
- New Zealand, Taiwan and some other countries (not shown here, but including Laos, Vietnam, ...) successfully contained.