# COVID-19 Evidence Update

COVID-19 Update from SAHMRI, Health Translation SA
and the Commission on Excellence and Innovation in Health

25 June 2020

## *Responding to increased cases*

### Executive Summary


**Context:** South Australia has had no new cases of SARS-Cov-2 for weeks and no cases of community transmission for months, effectively eliminating the virus. Until it is eradicated globally, via either a vaccine or effective anti-viral treatments, there will continue to be cases and disease. Cases will inevitably be 'imported' from other jurisdictions. Like SA, a number of jurisdictions have effectively eliminated or supressed the virus and are not in lockdown. Primary strategies for sustained control are: Test-Trace-Isolate; (international) border control and quarantine; public behaviour on physical distancing, staying home when sick and hand hygiene.

**COVID-19 control case studies of success:** Several countries have had notable success: New Zealand; Taiwan; Vietnam; South Korea, Montenegro.

**Key control measures employed**: Control mechanisms vary by country. Unlike Australia and New Zealand, South Korea, Taiwan and Vietnam have not used widespread "lockdown". Strategies: border control and quarantine (all); test-trace-isolate (all, with variability in vigilance around isolation); widespread testing (NZ, Taiwan, Sth Korea); extreme lockdown (NZ, regional in Vietnam); heavy compliance monitoring (Taiwan); public identifying of cases (Sth Korea); widespread masks wearing (Vietnam, South Korea, Taiwan); population self-monitoring of movements (NZ); public messaging: physical distance, stay home when sick and hand hygiene (all).

**Outbreak Threshold (To)** describes a critical point at which an outbreak may become uncontrolled or uncontrollable without implementation of controls. Potential trigger points for determining an Outbreak Threshold:

- Number of cases (in a time period), with consideration to whether cases are from community transmission
- Number of active cases
- Health system capacity (and proximity to exceeding that capacity).
- Effective Reproduction number ($R_0$) - average number of new cases infected by source case

**State of evidence:** Retrospective analyses, modelling studies and non-peer reviewed discussion papers have attempt to predict Outbreak Thresholds for COVID-19. Most studies present models and important input parameters but don't offer estimates for thresholds. Suggested thresholds which are presented include: 30 new cases [1]; 3 cases per 100,000 of population [2]; and $R_0$>2 (two separate discussion papers [3, 4]).



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**Policy positions**: Most countries have not identified their Outbreak Threshold criteria or their contingency plans.

South Korea has experienced a recent spike in cases linked to nightclubs. The Vice-Health Minister reportedly said the new outbreak would not see the country brought back under strict containment as long as the country remained **below 50 new cases daily** and officials were able to **trace 95 per cent of all infections.** The Seoul mayor reportedly nominated a threshold of **30 new cases per day over three consecutive days** and the **hospital bed occupancy rate exceeds 70%.**

New Zealand has retained its 4 Levels of Alert Plan for future lockdown if required. Criteria for future controls relate to **community transmission** and outbreaks (rather than household transmission) but are not quantified.

## Context

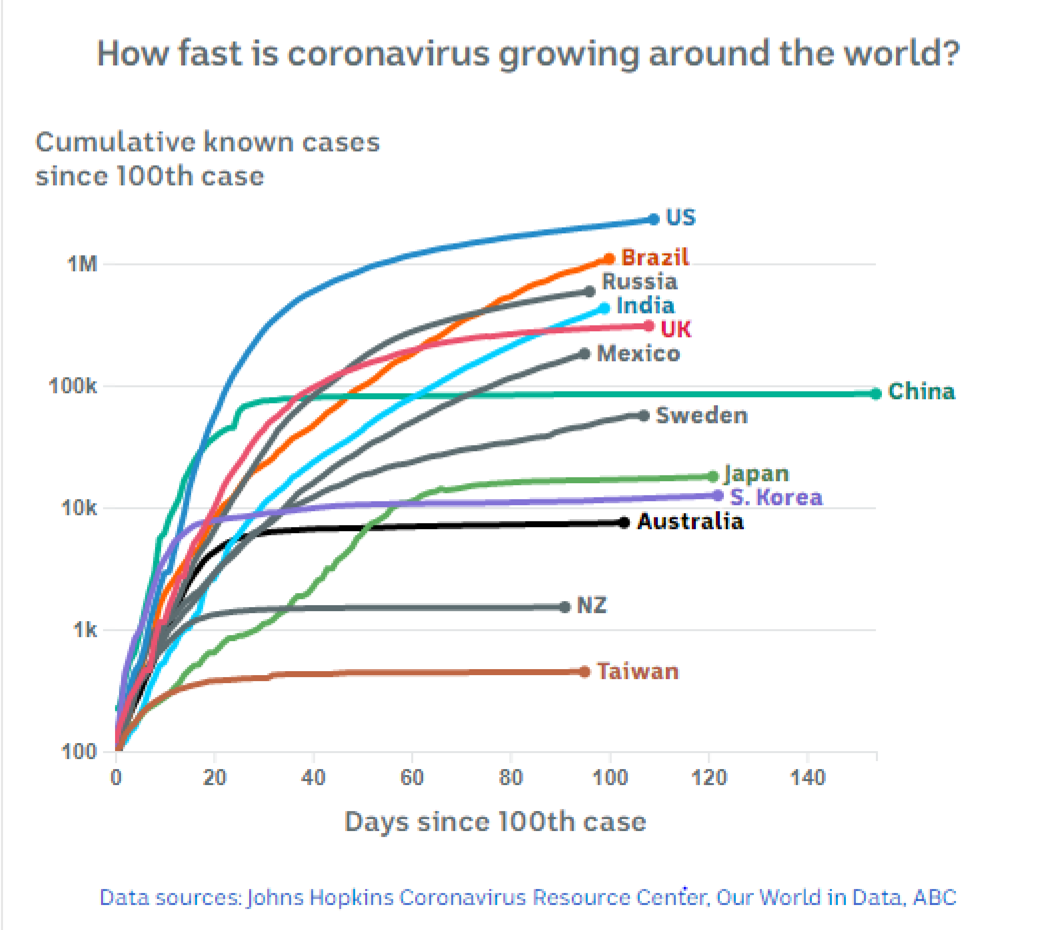
- Key points for risk management / control of COVID-19:
    - The presence and prevalence of transmissible virus in the whole community, or in a geographical area, drives risk.
    - Features of disease:
        - The virus will not circulate silently without cases presenting.
        - While the proportion of symptomatic cases is unknown, it is likely to be the majority. There is a lag between infection and onset of symptoms and symptoms present after an average of 5 days.
        - The majority of cases are mild to moderate and do no not require hospitalisation (~80% known cases). ~20% of cases will present requiring medical attention.
        - There are marked distributions of serious disease linked to: older age; obesity; and health comorbidities (chronic diseases); making specific cohorts more vulnerable.
    - Major transmission routes:
        - is via droplet spread between people in close proximity for a duration of time
        - Symptomatic transmission is more likely and common than transmission by those without symptoms (yet)
        - Virus may live on surfaces for hours to days
    - Test-trace-isolate strategies are fundamental to infection control, and a strength for Australia. Other countries implement these strategies with more "aggressive" isolation monitoring than Australia including surveillance via phone.
    - Different cases present different levels of risk for infection control:
        - Cases in well-supervised quarantine (e.g. overseas arrival) are very low risk
        - Cases among people in unsupervised self-isolation / quarantine are low risk (e.g. family members or close contacts of known cases; interstate arrivals where required)
        - Cases in people who are not self-isolation but who are linked to known cases are medium risk
        - Cases of community (unknown source) transmission are highest risk
    - Effective control mechanisms:
        - **Physical distance** of <1.5m between people significantly reduces risk (Some activities will increase droplet reach: speaking; singing; coughing and sneezing; physical exertion).
        - Temporarily **separating suspected cases** (people with symptoms) from workplaces and the wider community. This involves encouraging people with symptoms to self-isolate and minimising social and financial disincentives for doing (such as loss of earnings).
        - **Hand washing** is protective against virus being picked up from surfaces
        - **14-day quarantine** time is sufficient to detect ~99% of symptomatic cases

- Lockdowns (selective by geography or activity; and general)

- Masks for general community:
  - Masks are of questionable effectiveness as a whole of population control strategy
  - When used properly, surgical masks are of benefit for source control, notably for symptomatic cases
  - Used and disposed of properly, masks may offer some value in setting where physical distance cannot be achieved e.g. crowded public transport, when virus is present.

## Case studies – countries

Many countries are noteworthy in their suppression of transmission of COVD-19, to date.
These include: Australia, New Zealand, Taiwan, South Korea, Vietnam (not shown – sits below Taiwan)



## Taiwan

Pop$^{n}$: 23m Cases: 446; Deaths: 7; active cases: 4

- Taiwan is currently seen as a COVID-19 success story.
- With its close proximity to China (130 kms) and with a population of 23 million citizens, 404,000 of which were working in china in 2019 and more than 2.7million Chinese nationals travelling to Taiwan in 2019, there were concerns that an outbreak was inevitable [5].
- Estimates indicate that approximately 80% of confirmed cases were imported.
- Features of Taiwan's control efforts, and reported reasons for their current success:
    - Daily press briefings and announcements about when and where to wear masks, the importance of handwashing and the effects of hoarding masks for frontline workers;
    - National Health Command Centre established in response to experience of SARS-CoV-1 in 2003.
    - The Central Epidemic Command Centre which coordinated efforts by a number of ministries (e.g. economics labor, education etc) and banned export of surgical masks (one month before South Korea did the same);
    - Early action on screening (31 Dec) then restricting (Jan) travellers from Wuhan and China [6];
    - Health insurance and immigration data was combined with individuals' identification cards. Individuals identified as high risk because of travel in affected areas (under home quarantine) were monitored electronically through their mobile phones;
    - All hospitals, clinics and pharmacies had access to patients' travel histories;
    - Schools and universities reopen after winter break;
    - Ban of all foreign visitors, imposes mandatory 14- day self-isolation for all arriving passengers;
    - Masks become mandatory on public transport (1 April);
    - Social distancing alerts over text messaging;
    - April: Closure of selected venues and limitations on gatherings (100 indoors and 500 outdoors);
    - Late May: Plans to ease social distancing, mask wearing (flights and public transport) and limits on mass gatherings.

## New Zealand

- Pop$^{n}$: 4.9m; Cases: 1515; Deaths: 22; Active cases: 10.
- New Zealand has international border controls similar to Australia, but went into nationwide "Alert Level 4 - Lockdown" at 11:59pm on Wednesday 25 March.
- On 8 June NZ declared it had eliminated the virus and lifted all restrictions on movement and distancing (Alert Level 1 – Prepare).
- NZ System emphasises: stay home when sick; personal hygiene (handwashing, covering sneezes and coughs) heavy emphasis on personal and organisational record keeping to enable contact tracing; plus intensive testing, contact tracing and border restrictions.
- New Zealand retains its 4 level system:
    - Alert Level 1 – Prepare. Disease is contained in New Zealand; COVID-19 is uncontrolled overseas; Isolated household transmission could be occurring in New Zealand.
    - Alert Level 2 - Reduce. The disease is contained, but the risk of community transmission remains. Household transmission could be occurring. Single or isolated cluster outbreaks.
    - Alert Level 3 – Restrict. High risk the disease is not contained. Community transmission might be happening. New clusters may emerge but can be controlled through testing and contact tracing.
    - Alert Level 4 – Lockdown. Likely that disease is not contained. Community transmission is occurring. Widespread outbreaks and new clusters.
- Alert Level 1 (current controls):

- Border entry measures to minimise risk of importing COVID-19 cases;
- Intensive testing for COVID-19, Rapid contact tracing of any positive case; Self-isolation and quarantine required;
- Schools and workplaces open and must operate safely;
- **No restrictions on personal movement** but people are encouraged to **maintain a record of where they have been**;
- No restrictions on gatherings but **organisers encouraged to maintain records to enable contact tracing**;
- Stay home if you're sick, report flu-like symptoms;
- Wash and dry your hands, cough into your elbow, don't touch your face;
- **No restrictions** on domestic transport — avoid public transport or travel if you're sick;
- No restrictions on **workplaces or services but they are encouraged to maintain records** to enable contact tracing.

- Alert Level 2 - Reduce
  - 100 people in a defined space.
  - 2m from people you don't know and in public; 1m in 'controlled environments like workplaces" and public spaces with "record keeping".

### Viet Nam

- Pop$^{n}$: 97m; cases: 349; deaths: 0; active cases: 21.
- Long border with China.
- BBC Coronavirus: How 'overreaction' made Vietnam a virus success 15 May 2020.
  - Vietnam's approach has been described as: "Cost effective, but intrusive and labour intensive approach";
  - Vietnam acted earlier than many countries with health checks / screening at the shared border with China and "other vulnerable places", then travel restrictions;
  - "By mid-March, Vietnam was sending everyone who entered the country - and anyone within the country who'd had contact with a confirmed case - **to quarantine centres** for 14 days";
  - **Everyone in quarantine was tested, sick or not**, and he says it's clear that **40% of Vietnam's confirmed cases** would have had no idea they had the virus had they not been tested;
  - While Vietnam **never had a total national lockdown**, it swooped in on emerging clusters;
  - In February after a handful of cases in Son Loi, north of Hanoi, more than 10,000 people living in the surrounding area were sealed off. The same would happen to 11,000 people in the Ha Loi commune near the capital, and to the staff and patients of a hospital;
  - **No-one would be allowed in or out until two weeks** had passed with no confirmed cases.

- World Economic Forum. Here are 4 ways Viet Nam has managed to control COVID-19
  1. Quick, strategic testing.
  2. Aggressive contact tracing:
     - "Using the Ministry of Health's records of infected, suspected and exposed cases of COVID-19, extensive contact tracing was possible thanks to the rapid mobilisation of health professionals, public security personnel, the military, and civil servants. **Perhaps unpopular in some more open countries, neighbours were encouraged to report** if they knew of someone returning from a foreign country."
     - "Contact tracing was also successfully implemented with technology. A mobile app called NCOVI was developed by Vietnam's Ministry of Information and Communications (MIC). This

lets the public update their health status daily. It also shares 'hotspots' of new cases and gives its user 'best practices' for staying healthy."
    - "This was supported by an online reporting system, developed by the Health Ministry, to monitor suspected and confirmed cases of COVID-19. These combined efforts have ensured that new infections are reported and subsequently isolated."
3. Effective public communications campaign.
4. Swift development of testing kits:
    - The Vietnamese COVID-19 test kit was developed by scientists within a month. It is effective, affordable and fast, diagnosing suspected COVID-19 infections in just an hour. Unlike other countries that rely on mass testing, in Vietnam, tests are only done on those likely to be infected.

### South Korea

- Pop$^{n}$: 51m; cases: 12,535; deaths: 281; active cases: 1324*
- Reduced numbers form a peak of 900 cases per day in February to single digits by late April, via intensive tracking and testing. No lockdowns reported, but rather relied on compliance with physical distancing.
- Currently experiencing an outbreak of cases after a holiday weekend.
- ABC 23 June 2020: *South Korea says it is in the middle of a coronavirus second wave — and it arrived earlier than predicted*
    - Officials report: "The infections were caused by young people who visited nightclubs and bars in Seoul"
- ABC 15 May 2020: *South Korea's coronavirus outbreak in Seoul's club scene shows the dangers of stigma during a pandemic:*
    - At least 148 cases have been linked to outbreaks in bars and clubs in Seoul's Itaewon neighbourhood;
    - Concerns reported about fears in Korea's gay community that getting tested for COVID-19 could lead to being outed in a country where homosexuality is widely considered taboo;
    - In South Korea when someone tests positive for COVID-19, the country typically releases **information about a patient's age, gender and the places they visited**;
    - In some cases, even the patients' **last names and occupations are made public** on a Ministry of Health and Welfare website;
    - The Vice-Health Minister said the new outbreak would not see the country brought back under strict containment;
    - Social distancing rules are unlikely to return as long as the **daily number of new cases remained below 50** and **officials were able to trace 95 per cent of all infections**.

- BBC News 22 June 2020: *Coronavirus: South Korea confirms second wave of infections*
    - The mayor of Seoul also warned that the capital may have to return to strict social distancing, should **cases top 30 on average over the next three days** and the **bed occupancy rate of the city's hospitals exceeds 70%**.
    - South Korea has managed to **avoid locking down** the country and has instead relied on **voluntary social distancing measures** alongside an **aggressive track, trace and test strategy** to combat the virus.

- BBC News 30 April 2020: *Coronavirus and South Korea: How lives changed to beat the virus*
    - South Korea also started aggressively contact tracing, finding people who had interacted with a confirmed case, isolating and testing them too.

- When someone tested positive, authorities would send out an alert (via text message) to those living or working nearby.
- Cases linked to the Shincheonji (church) cluster at one point accounted for about half of South Korea's total.
- All churches in South Korea were shut. Officials limited public gatherings. Churches have reopened, but worshippers are required to keep a distance and wear masks.
- 14-day quarantine for arrivals.
- Mask wearing is widespread.

## Other countries

- ABC news (9 June 2020) "New Zealand may be COVID-free, but these other countries beat coronavirus first"
    - New Zealand wasn't the first country to eradicate the virus
    - Only counted countries that reported cases and got down to zero active cases (based on 188 countries and regions that have reported cases). Note that most of the countries listed below have small populations and most only reported a handful of cases
    - Montenegro (shares borders with Albania, Serbia, Croatia):
        - Zero active cases: May 25 (69 days of active cases)
        - Total cases: 324
        - Population: 620,000
        - Foreign nationals have been able to enter without needing to quarantine since June 1, but public gatherings are still capped at 200 people
        - Additional info: Key criterion for entry is <25/100,000 active cases in location of origin. In locations with >25/100,000 active cases, 14 days quarantine remains mandatory.
    - Eritrea (shares borders with Sudan, Ethiopia):
        - Zero active cases: May 15 (active cases started in March) reports of 1 case (and then 1 close contact) picked up through random testing on June 2.
        - Total cases: 39
        - Population: 5.2 million
        - Flights stopped but travel through land and sea routes continue.
    - Timor-Leste (surrounded by Indonesian islands):
        - Zero active cases: May 15 (active cases started March 21)
        - Total cases: 24
        - Population: 1.3 million
    - Fiji (Pacific island):
        - Zero active cases: 5 June (active cases started March 19)
        - Total cases: 18
        - Population: 899,000
    - Papua New Guinea
        - Zero active cases: May 3 (active cases started March 20)
        - Total cases: 8
        - Population: 8 million

## Key summary from the evidence

## Outbreak Thresholds

### COVID-19

- Zhang 2020 [1] (Int J of Infect Dis)
  - Retrospective analysis (16 Jan - 15 Mar), investigated how early characteristics of the COVID-19 outbreak predicted its subsequent size. Based on 45 cities in China with different reproductive rates, the modelling suggested that **30 cases might be a critical threshold for switching from a relatively slow-growing phase to a fast-growing phase,** which grows 5 times faster. Early stage characteristics that were important for predicting the size of the outbreak included the time from the 30th to the 100th case and the case-fatality rate in the first 100 cases.

- Ameudo-Doreantes 2020 [2] (Discussion paper)
  - Lockdown (school closures, closure of non-essential business and stringent shelter in place order) was mandated on 14 March regardless of stage of outbreak in Spain. The relative impact of the lockdown across regions was modelled to estimate the mortality impact of acting earlier. The outbreak was defined as the day when **3/100,000 COVID-19 cases were confirmed,** and speed of lockdown response was the number of days elapsed between the outbreak and lockdown. Results showed that imposing a nationwide lock down 1 day earlier would have lowered COVID-19 deaths by 11%.

- Ma 2020 [7] (arXiv pre-print)
  - "Coronaviruses appear to have a specific heterogeneity/stability scaling parameter (TPL-b) slightly exceeding 2 for cumulative infections or exceeding 1 for daily incremental infections, suggesting their potentially 'chaotic', unstable outbreaks"
  - "TPL parameter ($M_0$) (i.e., infection critical threshold) depends on virus kinds (COVID-19/SARS), time (disease-stages), space (regions) and public-health interventions (e.g., quarantines and mobility control)."
  - $M_0$ indicates the threshold at which infections become random. Below this threshold, infections follow uniform distribution and may die off, depending the level of Allee effects.
  - **$M_0$=5.758 for COVID-19 in China, when converted to total national infection level, would be 5.758x34 (provinces)=196**. When infections exceed this threshold level, the infections can be non-random and highly unstable. However, it remains unknown whether infections will die off below this level as it depends on the level of Allee effects. Note that the **$M_0$ for COVID-19 worldwide was 2.701.**
  - Modelling showed the critical importance of controlling migration (mobility) in suppressing the outbreak, although migration may have been a primary driving force for the initial outbreaks in several regions of China.

- Arenas 2020 [8] (medRxiv pre-print)
  - Key parameter for tracking the progression of epidemics is the effective reproduction number R(*t*), defined as the number of secondary infections generated by an infected individual after becoming infectious at time *t*. **The suppression of epidemics is directly related to this value and is attained when R<1**.
  - The authors reported an analytical expression for R(*t*) as a function of mobility restrictions and confinement measures based on data from Spain. The analysis focusses on different levels of confinement needed to 'flatten' or 'bend' the curve.

- Yue 2020 [3] (Science Bulletin; news and views section)
  - The basic reproduction number $R_0$ is a critical indicator, defined as the average number of new infections caused by a single infected individual when introduced into a wholly susceptible

population over the duration of the infection of the individual. In the formula for $R_0$ the transmission rate is not directly observable and can be difficult to measure.

- The time-dependent transmission rate (TDTR) can yield useful information about disease outbreaks. The formula for TDTR includes the proportion of susceptible people, infected people, recovery rate and fatality rate.
- **“It has been universally accepted that if $R_0$ is <1, the introduction of an infected individual would not result in an outbreak, but only a localised infection…However, when $R_0$>1, then an epidemic will occur and the infection will spread in the population no matter how small the initial number of infected individuals is. When $R_0$>2, a major outbreak is possible. If $R_0$>3, the emergence of a pandemic is generally considered to be inevitable.”**
- The application of this new model to data from China showed that the epidemic oscillated while the $R_0$ was above 1 and was not under control until the $R_0$ dropped below 1 (see figure below).

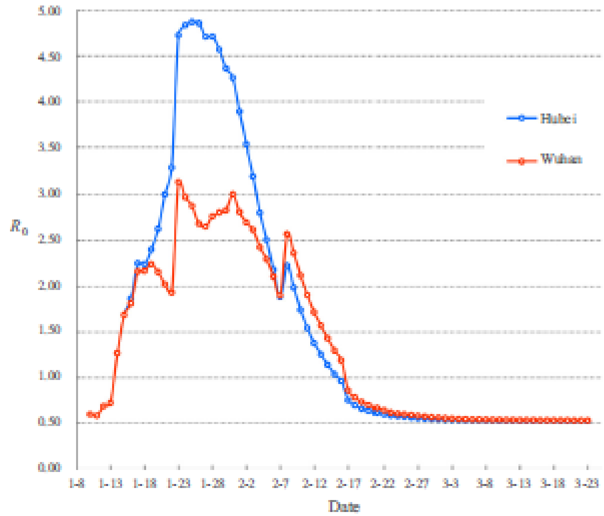



**Fig. 1.** The $R_0$ values based on the new model in Wuhan and Hubei.

- “A robust temporal model for the spread of an infectious disease should incorporate the following information: the patterns of contacts among infectious and susceptible individuals, the latency period from being infected to becoming infectious, the duration of infectiousness, and the extent of immunity acquired following infection. Once all of these factors are formulated in a model, we will be able to construct the entire epidemic curves describing the expected number of individuals who will be infected, the duration of the epidemic, the peak incidence, and the expected number of cases at each point in time.”

- Huang 2020 [9] (Science Bulletin, news and views)
  - Discusses some of the limitations of $R_0$ as a tool during the developing phase of an epidemic.
    - Requires too much information to be realistic;
    - Rarely observed in the field and is usually calculated via a mathematical model relying on tuning;
    - Cannot account for the dynamic of epidemics where different transmission patterns may occur at different phases of the event, or interventions.
  - There is a need for a quick and robust tool to detect minute and subtle changes of the epidemic course for effective management. The authors propose a simple and data driven model based on the physics of natural growth algorithm:

$$N(t) = N_0 \cdot \exp\{a_t(t - t_0)\},$$

  - $N(t)$=current existing infected case number at time $t$; $N_0$ is the initial number of existing infected case number at time $t_0$, and at is the growth rate $a_t$ time $t_0$.

- The transmission rate ($c_t$) was defined as 1+ $a_t$, where $c_t$ >1 indicates that the existing infected number would increase.

- Zhao 2020 [10] (Quantitative Biology)
    - Distinct features of COVID-19 that make it hard to describe with the existing epidemic models (e.g. SIR, SEIR): long incubation period causing time delay between real dynamic and daily-observed case numbers; the epidemic trend depends on local medical resources, quarantine measures and the efficiency of confirmation approaches all which need to be explicitly modelled.
    - The authors propose to use a simple SUQC model instead (Susceptible, Un-quarantined infected, Quarantined infected, Confirmed infected). **Only un-quarantined infected have ability to infect susceptible individuals.** The model also has a quarantine rate parameter (strength of quarantine policy) and a confirmation rate parameter (efficiency of confirmation based on released data).
    - The SUQC was applied to data from China and demonstrated accurate prediction of trends.

- Maier 2020 [11] (Science)
    - Introduced a parsimonious model that captures both quarantine of symptomatic infected individuals, as well as population-wide isolation practices in response to containment policies or behavioural changes, and showed that the model captures the observed growth behaviour accurately.
    - The model assumes that containment efforts effectively remove individuals from potential transmission, and also accounts for the removal of symptomatic infected individuals who are quarantined. The transmission rate and recovery rate are quantified.
    - The key mechanism of the model is the exponentially fast depletion of susceptibles in addition to isolation of infected. Model:

$$\partial_t S = -\alpha S I - \kappa_0 S \quad (1)$$

$$\partial_t I = \alpha S I - \beta I - \kappa_0 I - \kappa I \quad (2)$$

$$\partial_t R = \beta I + \kappa_0 S \quad (3)$$

$$\partial_t X = (\kappa + \kappa_0) I \quad (4)$$

    - The analysis suggests that nonexponential growth is expected when the supply of susceptibles is depleted on a time scale comparable to that of the infectious period of a disease.

- University of Philippines COVID-19 Pandemic Response Team (13 April 2020) [4].
    - **Outbreak Threshold is when $R_0$=2.**
    - Risk matrix and recommended course of action when cases indicate proximity to Outbreak Threshold:

| Ratio of confirmed cases to estimated outbreak threshold | Probability of outbreak | Recommended action for the LGU |
|---|---|---|
| <0.75 | Less than 80% | No community quarantine needed, but continue other interventions such asinformation campaigns, healthcare system strengthening, general physical distancing, testing and contact tracing, home quarantine for probable cases, and hospitalization for patients needing care and treatment |
| 0.76-0.99 | 80% to less than 90% | General Community Quarantine |
| 1-2 | 90% to less than 99% | Enhanced Community Quarantine |
| >2 | 99% or more | Extreme Enhanced Community Quarantine |

*Table 1.Example of a Decision Matrix for Graduated Community Quarantine Implementation*

## Pre-COVID-19

- Thompson 2018 [12] (PLOS computational biology)
    - Decision-making involves continuously balancing the potential benefits of waiting (to learn more about transmission) against possible costs of further spread.
    - The authors propose the “Control Smart Algorithm” (CSA) as an alternative to using pre-specified thresholds. The CSA generates an estimate of the expected cost of an ongoing outbreak if control is introduced immediately (i.e. at t = T), and the expected costs if control is instead introduced at each possible time in future (i.e. at t = T+τ, a delay of τ days before introducing control). If the expected outbreak cost is lower with control deployed now rather than at any time in future, then the decision to control immediately should be taken. If not, then a decision of waiting to learn more and reassessing at the following possible decision time is recommended.

- Thompson 2019 [13] (bioRxiv pre-print)
    - Thresholds can be: **cases infected**; **health system capacity for treatment**; number **simultaneously infected**. These are relevant in different situations (different outbreaks).
    - "The definition of a major epidemic should be designed to match the questions of interest in the particular setting being considered."

- Orbann 2017 [14] (Epidemics)
    - To understand disease dynamics, modelers have focused on epidemic thresholds, generation times, growth rate, and model design.

- Hartfield 2013 [15] (PLOS Pathogens):
    - The concept of outbreak threshold (T0) of an epidemic has been proposed. It is defined as the **number of infected hosts above which there is very likely to be a major outbreak**, and can be estimated using simple formulae. However, modifications are needed to set a specific cutoff value or to capture host heterogeneity in transmission or incomplete sampling. Examples of how the outbreak threshold works are shown in the figure below:

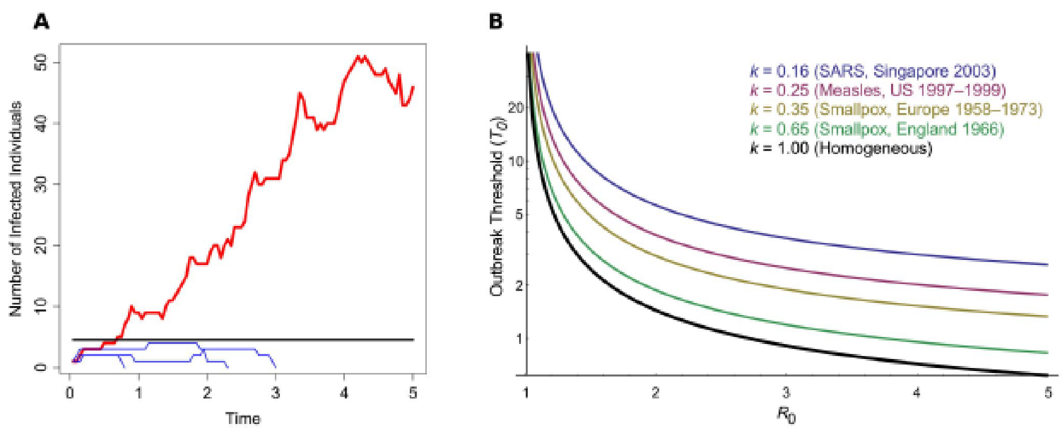



**Figure 1. The outbreak threshold in homogeneous and heterogeneous populations.** (**A**) A schematic of pathogen emergence. This graph shows the early stages of several strains of an epidemic, where $R_0 = 1.25$. The black line denotes the outbreak threshold ($T_0 = 1/\mathrm{Log}(R_0) = 4.48$). Blue thin lines show cases in which the pathogen goes extinct and does not exceed the threshold; the red thick line shows an epidemic that exceeds the threshold and persists for a long period of time. Simulations were based on the Gillespie algorithm [22]. (**B**) Outbreak threshold in a homogeneous (black thick line) or in a heterogeneous population, for increasing $R_0$. The threshold was calculated following the method described by Lloyd-Smith et al. [11] and is shown for different values of *k*, the dispersion parameter of the offspring distribution, as obtained from data on previous epidemics [11]. If the threshold lies below one, this means that around only one infected individual is needed to give a high outbreak probability.
doi:10.1371/journal.ppat.1003277.g001

    - The authors applied the concept to a case study: **SARS**, Singapore 2003: “outbreak with known super-spreaders, with an estimated initial R0 of 1.63 and a low k of 0.16 (k is the dispersion parameter which determines the level of variation in the number of secondary infections; k=1 is homogenous outbreak, heterogeneity [e.g. number of ‘super-spreaders’ that are present] increases as k drops below 1). **T0 is estimated to be around 27 infections**. The first cases were observed in late February, with patients being admitted for pneumonia. Strict control measures were invoked from March 22nd onwards, including home quarantining of those exposed to SARS patients and closing down of a market where a SARS outbreak was observed. By this date, 57 cases were detected, although it is unclear how many of those cases were still ongoing on the date. This point is important, as it is the infected population size that determines T0...Quick containment of the outbreak was difficult to achieve since SARS was not immediately recognised, as well as the fact that the incubation period is around 5 days, by which point it had easily caused more secondary cases. However, in subsequent outbreaks super-spreaders might not be infected early on, allowing more time to contain the spread."

- German 2020 [16] (medRxiv pre-print): Two epidemiological models were developed to study the disease dynamics of the COVID-19 pandemic and exit strategies from lockdowns [22]. The authors concluded adaptive triggering, or repetitive short term contact reductions when relevant figures (e.g. **deaths, need for ICU) exceed a threshold,** could be used to manage the virus until a vaccine was available. Antibody tests would also add benefit if they allowed people with antibodies to be excluded from contact reductions.

- Imperial College London 2020 [17] (Report): Modelling of containment strategies to reduce COVID-19 mortality and healthcare demand in the UK suggested that **adaptive hospital surveillance-based triggers** for switching on and off population-wide social distancing measures offer greater robustness to uncertainty than fixed duration interventions, and can be adapted for regional use. The results suggested that **social distancing would need to be in force for at least ⅔ of the time** given a R0 of 2.4 until a vaccine was found. The figure below illustrates adaptive triggering over time, which can be adjusted for proportion of time social distancing is in place, on and off triggers and R0:

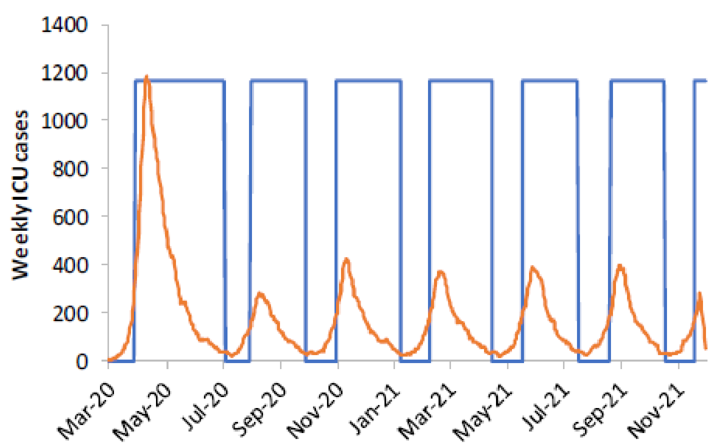



**Figure 4: Illustration of adaptive triggering of suppression strategies in GB, for $R_0$=2.2, a policy of all four interventions considered, an "on" trigger of 100 ICU cases in a week and an "off" trigger of 50 ICU cases. The policy is in force approximate 2/3 of the time. Only social distancing and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

- Fraser 2004 [18] (PNAS)
  - Measures the effectiveness of contact tracing and isolation of symptomatic cases to prevent an epidemic, and when other controls are necessary.
  - Show that the success of these two measures is determined as much by the proportion of transmission occurring prior to the onset of overt clinical symptoms (or via asymptomatic infection) i.e. $\theta$, as the inherent transmissibility of the etiological agent (measured by the reproductive number $R_0$).

- Authors present data for SARS, HIV, Influenza and Smallpox and levels of efficacy of isolating symptomatic people for controllability of epidemic (see figure 3 below).
- The lesson from the SARS outbreak is that, the proportion of transmission that occurs before the onset of clinical symptoms or in asymptomatic infection, may be equally as important for determining the ease of control of a novel outbreak as the intrinsic transmissibility, R0.
- Note: this is difficult to apply to SARS-COV-2 until R0 and θ are known.

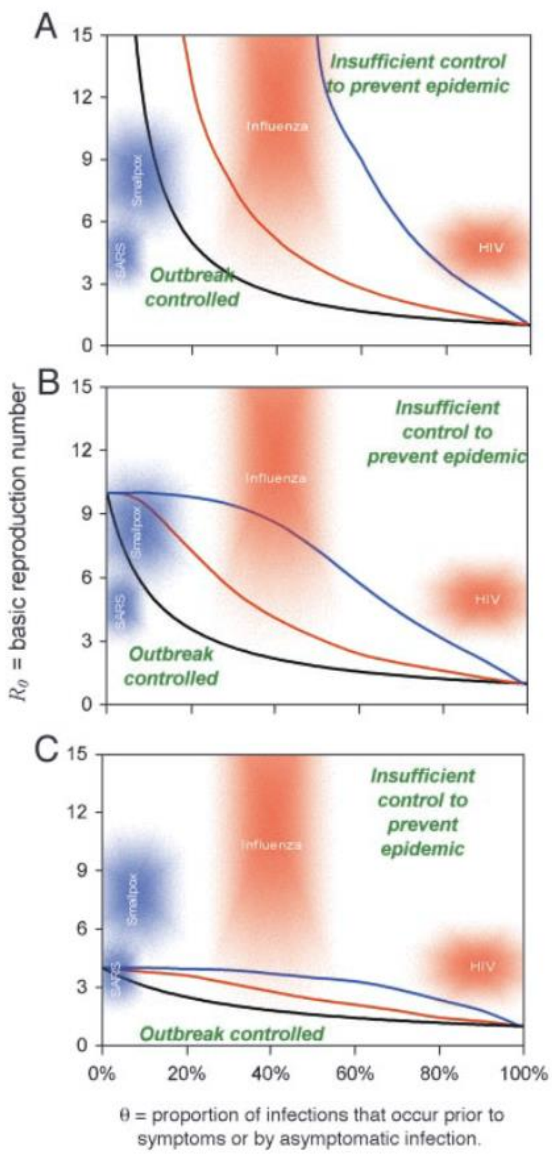



**Fig. 3.** Criteria for outbreak control. Each curve represents a different scenario, consisting of a combination of interventions and a choice of parameters. For each scenario, if a given infectious agent is below the $R_0$–$\theta$ curve, the outbreak is always controlled eventually. Above the curve, additional control measures (e.g., movement restrictions) would be required to control spread. Black lines correspond to isolating symptomatic individuals only. Colored lines correspond to the addition of immediate tracing and quarantining of all contacts of isolated symptomatic individuals. The black (isolation only) line is independent of distributional assumptions made (low or high variance), whereas the colored (isolation + contact tracing) lines match the variance assumptions made in Fig. 1 (red = high variance; blue = low variance). The efficacy of isolation of symptomatic individuals is 100% in *A*, 90% in *B*, and 75% in *C*. Contact tracing and isolation is always assumed 100% effective in the scenarios in which it is implemented (colored lines). Curves are calculated by using a mathematical model of outbreak spread incorporating quarantining and contact tracing (see main text).

## Second wave strategies and risks

- Lopez 2020 [19] (Nature Human Behaviour):
  - Used a modified SEIR model to assess post-confinement strategies. Simulations were generated with observed data from Spain. Simulations were also conducted for other countries such as Japan, US, Indonesia, and Argentina.
  - The results showed the importance of taking prompt and efficient actions to both limit the epidemic spread and prevent disease recurrence. Gradual deconfinement strategies always result in a lower number of infections and deaths, when compared to the sudden release of moderate to large portions of the population. If it is an economic necessity to remove lockdowns, then a mixed deconfinement framework can be considered, such as allowing low-risk people to exit lockdown providing that they follow social distancing and other NPI measures.
  - In terms of successful containment, early enforcement of lockdowns, effective implementation of social distancing measures and personal protection are the most effective interventions.
  - With respect to the role of social distancing specifically, Japan's mild restrictions appear to have had a marked containment effect by the end of May, due to social distancing. This is despite the fact that Japan conducted only 2.2 tests per 1,000 people (as compared to 16 in South Korea and in the United States, for example).
  - Although widespread test–trace–isolate strategies may be equally or locally more effective and may minimize the economic and social costs of lockdowns, these are outside the reach of most countries (and are not modelled in this work).

- Zhang 2020 [20] (medRxiv pre-print)
  - Aimed to determine what level of social distancing and facial mask usage were necessary to prevent second wave of infections in Wuhan.
  - Results indicated that returning to pre-quarantine levels of social interaction would require facial mask usage (or other powerful interventions) of 85%.
  - Prior to quarantine, most transmission was public but after quarantine, household transmission was the dominant route. In cases where the epidemic results in a second major outbreak, it would be driven mostly by household transmission.

- Pedro 2020 [21] (medRxiv pre-print)
  - Analysed a simple theoretical model of the interplay between SARS-CoV-2 transmission and social dynamics (e.g. public support for physical distancing and school and workplace closure). Results indicated that a second wave of COVID-19 (and sometimes also a third wave) was likely across a broad range of epidemiological and behavioural parameters. In some cases, the second peak was higher than the first peak, while for other parameter combinations it was lower. Authors conclude that that more effort in transmission modelling of COVID-19 should consider the effect of interactions between the dynamics of disease spread and social processes.

- de Castro [22] (medRxiv pre-print)
  - Used an SEIR model to simulate predictions of a second wave of infections using Spain and Germany as case studies. The simulations of the post-confinement period showed that a second wave was probably inevitable, no matter how gradually or carefully the confinement was lifted due to the large pool of infected (mostly undetected) still present in the population when the lifting of confinement measures started. The model estimated that the number of infected at the end of the confinement was $775 \times 10^3$ and $149 \times 10^3$ in Germany.

- Mahadevan 2020 [23] (Report, non-peer reviewed)
  - Aim was to identify groups at risk of reintroducing COVID-19 in Taranaki, a region in New Zealand, once Alert Level 4 was downgraded. A total of 31 groups were identified, of which 9 had high overall population health risk. The highest risk group was New Zealanders visiting family/whanau (Māori and Pacifika). See table below showing part of the health risk assessment matrix:

Table One – Population Health Risk Assessment Matrix

| Category of people travelling to Taranaki | Number of people within category [large, medium, low] | Exposure risk outside of Taranaki (area with community transmission of COVID-19, size of bubble, transmission risk – duration and degree of exposure) [high, medium, low, very low] | Transmission risk within Taranaki (size of bubble, transmission risk – duration and degree of exposure) [very high, high, medium, low] | Barriers for early detection [high, medium, low] | Community vulnerability of the exposed population in Taranaki [high, medium, low] | OVERALL POPULATION HEALTH RISK [very high, high, medium, low, very low) |
|---|---|---|---|---|---|---|
| **Community/Social** | | | | | | |
| New Zealanders visiting family/whānau (Māori and Pacifika) | Large | High | High | High | High | Very High |
| New Zealanders visiting family/whānau (Non-Māori) | Large | Medium | Medium | Medium | Medium | High |
| Students coming home for the holidays (during educational facility closure) (8) | Large | High | High | Medium | Medium | High |
| Young people coming home after losing jobs in major centres | Medium | High | High | High | Medium | High |
| Students who board in Taranaki | Low | High | High | Medium | Medium | Medium |

- Rapid case detection and contact tracing, combined with other basic public health measures, has over 90% efficacy against COVID-19 at the population level, making it as effective as many vaccines. This intervention is considered to be central to COVID-19 elimination in New Zealand.
- Early detection of COVID-19 within Taranaki therefore requires us to actively test the above identified groups because they pose the highest overall population health risk for COVID-19 infection. This means having a low threshold for testing people with symptoms and actively testing within populations where there are barriers for early detection and community vulnerability. It is recommended that an equity lens is applied regularly to the testing data to ensure that high risk groups are being tests. Focused testing of asymptomatic people is also recommended for those at high-risk of exposure.

- Aleta 2020 [24] (MedRxiv pre-print)
  - Used agent-based model to describe transmission of SARS-CoV-2 in the Boston metropolitan area. Found that enforcing strict social distancing followed by a policy based on a robust level of testing, contact-tracing and household quarantine could keep the disease at a level that does not exceed the capacity of the health care system.
  - Assuming the identification of 50% of symptomatic infections and tracing 40% of their contacts and households (corresponding to 9% of individuals quarantined), the ensuing reduction in transmission will allow the reopening of economic activities while managing the health care system.
  - Note: the authors used a R(t) of 1 and hospitalisation and the ICU basal capacity as important considerations for containment.

- Hazem 2020 [25] (medRxiv pre-print)
  - Studied the implications of loosening the lockdown conditions in the US, Germany, UK, Italy, Spain, and Canada using a modified version of the SIR model.
  - The results varied by country. The US and the UK were more affected by reopening as they had not fully conquered COVID-19 yet. There was a correlation between the turning point date, reopening date, and second-wave peak infection rate. The authors recommended that loosening of the measures should occur at least 3 months from the turning point date.

- Friston 2020 [26] (arXiv pre-print; technical report)
  - Investigated how social distancing strategies may affects a second wave of new cases that may result from loss of immunity and exchange of people between regions in the US.
  - The provisional results suggest that social distancing and loss of immunity are the two key factors that underwrite a return to endemic equilibrium.

- Leung 2020 [27] (Lancet)
  - Estimated the instantaneous reproduction number (Rt) of COVID-19 in Beijing, Shanghai, Shenzhen, Wenzhou, and the ten Chinese provinces that had the highest number of confirmed COVID-19 cases and used an SIR model to show the potential effects of relaxing containment measures after the first wave of infection, in anticipation of a possible second wave.
  - In all selected cities and provinces, the Rt decreased substantially since Jan 23, when control measures were implemented, and have since remained below 1.
  - Relaxing the interventions (resulting in Rt>1) when the epidemic size was still small would increase the cumulative case count exponentially as a function of relaxation duration, even if aggressive interventions could subsequently push disease prevalence back to the baseline level.
  - Stage 1, interventions were implemented, such that *Rt*=1. Stage 2, interventions were relaxed, resulting in *Rt*=*R*2>1 when stage 2 began. Stage 3, interventions from stage 1 were again implemented, such that *Rt*=1. Stage 4, interventions more aggressive than those in stages 1 and 3 (when *Rt*=*R*4<1when stage 4 began) were implemented to bring the disease prevalence back to pre-relaxation level (ie, stage 1 level).
  - The relaxation of intervention increased the cumulative case count exponentially with the duration of relaxation, even if aggressive interventions could subsequently push prevalence back to pre-relaxation level; and the required duration of such interventions would always be longer than the duration of intervention relaxation unless Rt was below 1.5 during intervention relaxation, and could be pushed below 0.5 during stage 4. Taken together, these results suggest that allowing Rt to rise above 1 when the epidemic size was still small (ie, no herd immunity) would likely incur both health and economic loss even if aggressive interventions could push the prevalence back to pre-relaxation level afterwards.
  - **Given the pivotal role of *Rt* in epidemic control, we suggest that real-time estimates of *Rt* should be presented in the routine COVID-19 dashboards and situation reports for provincial, national, and supranational health agencies.**

- Block 2020 [28] (Nature Human Behaviour)
  - Adopting a social network approach, the effectiveness of three distancing strategies designed to keep the curve flat and aid compliance in a post-lockdown world were evaluated using simulations: limiting interaction to a few repeated contacts akin to forming social bubbles; seeking similarity across contacts; and strengthening communities via triadic strategies.
  - All three strategies substantially slow the spread of the virus compared with either no intervention or simple, non-strategic social distancing. The most effective approach is the strategic reduction of interaction with repeated contacts. Compared with the random contact reduction strategy, the average infection curve delays the peak of infections by 37%, decreases the height of the peak by 60% and results in 30% fewer infected individuals at the end of the simulation.
  - When a firm lockdown is no longer mandated or recommended, individuals will want or need to interact in different social circles (for example, at the workplace or with wider family). results show that a mix of strategies still provide comparable benefits to single strategies, and all work considerably better than simply releasing a floodgate of full non-strategic contact; however, further modelling is needed to assess the implications across a variety of contexts.

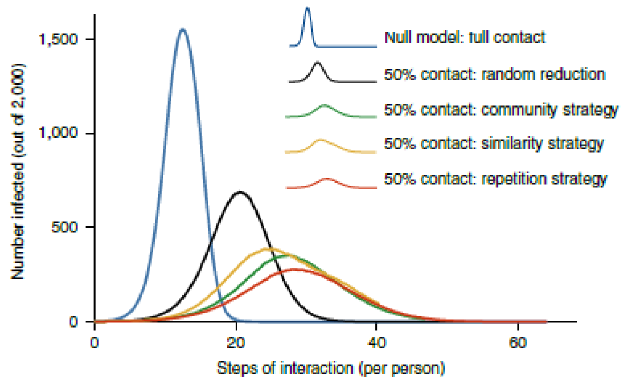



**Fig. 4 | Average infection curves.** Curves compare four contact reduction strategies with the null model of no social distancing. The underlying network structure includes 2,000 actors and the benchmark network characteristics described in the main text.

- "Concrete policy guidelines can be deduced from our network-based strategies. For hospital or essential workers, risk can be minimized by introducing shifts with a similar composition of employees (that is, repeating contact and creating bubbles) and distributing people into shifts based on, for example, residential proximity where possible (that is, seeking similarity). In workplaces and schools, staggering shifts and lessons with different start, end and break times by discrete organizational units and classrooms will keep contact in small groups and reduce contact between them. When providing private or home care to the elderly or vulnerable, the same person should visit rather than rotating or taking turns, and that person should be the one with fewest bridging ties to other groups and who lives the closest (geographically). Repeated social meetings of individuals of similar ages who live alone carry a comparatively low risk. However, in a household of five, when each person interacts with disparate sets of friends, many shortcuts are being formed that are potentially connected to a very high risk of spreading the disease."

- Hirschi 2020 [29] (medRxiv pre-print)
  - A very simple model is used to illustrate the impact the timing of measures can have on the severity of the first wave of the pandemic and the consequences of a weak or a strong first wave once the lockdown rules are gradually relaxed. Modelled on case numbers from UK and Germany.
  - The goal of measures such as social distancing and lockdowns is to reduce R0 in order to get Re below a value of 1 before the number of infected people requiring treatment becomes too large.
  - Modelled scenarios show that both the timing of the first measures as well as the choices made once the first wave is ebbing are crucial. Early action is the most effective way to reduce the amplitude of a first wave. Even delaying measures by a few days can result in many more lives being lost in that first wave. When gradually easing the lockdown, countries which had a mild first wave (e.g. Germany, Austria, Norway, South Korea) may opt for a slightly slower unwinding of measures than countries that experienced a major first wave. Experiencing a major first wave means that there is likely to be a higher "partial herd immunity" and that an effective reproduction rate Re < 1 can be achieved with more relaxed measures than in countries where the partial herd immunity is lower. This effect can already be significant even if less than 10% of the total population have been infected. NOTE: the extent that 'herd immunity' is achieved in the long term remains an open question.

- Duckett, June 2020 (Grattan Institute; Coming out of COVID-19 lockdown: the next steps for Australian health care)
    - Developed a model which simulates the risks of different relaxation strategies, and recommends:
    - Maintain social distancing efforts while there are active COVID-19 cases locally
        - Maintain high levels of testing, contract tracing and isolation.
        - Enforce social distancing in workplaces; workplaces should be re-opened slowly, continue working from home when possible; symptomatic people should not be allowed to go to work (sick leave entitlements should be provided).
        - Close school if case detected
        - Limit shopping in places where community transmission is occurring
        - Community must continue to social distance; masks in public are encouraged if there are active cases in the community
    - Ramp up lockdowns when outbreaks occur
        - State governments must be prepared to reimpose lockdowns to control major outbreaks
        - Local lockdowns should be enacted to control local outbreaks
    - When there are no active cases in Australia
        - Capacity constraints on workplaces, shops, and hospitality can be removed. People can start to move freely within and between states.
        - Testing must remain a routine part of life. If local cases are identified, contact tracers must be at the ready, and widespread testing should restart in affected areas.
        - Current mandatory quarantining of people arriving from overseas must remain in place.
        - Quarantine exemptions could be made with other countries, such as New Zealand, that also have no active COVID-19 cases and that have effective international arrival protocols in place.

    - Coming out of lockdown
      For a susceptible person, the likelihood they will become infected when exposed to COVID-19 in a given situation is called the 'secondary attack rate', which varies by situation
        - HIGH RISK: Home or workspaces, where long times are spent in shared indoor spaces; sharing a meal (at home, or at a restaurant) is particularly risky
        - Lower risk: schools, due to the lower spread and contracting of the virus in children compared to adults
        - In general, the shorter an interaction, the fewer opportunities the virus has to spread (e.g. shops less risky than restaurants). However, outbreaks are still possible from low-probability interactions. Super-spreader events have been documented from the beginning of the pandemic. Shutting down high-risk events – removing the opportunity to have super-spreader events can be highly effective.

    - The strategic design of health restrictions
        - Scenario 1: Elimination: no local transmission – allow all activity
        - Scenario 2: Suppression: **only a few local transmissions – combination of restrictions and effective track-and-trace systems to suppress growth of infections**. This may require that restrictions remain in place indefinitely and relies on the track-and-trace system being highly effective in breaking chains of transmission
        - Scenario 3: Growth and restriction: **track-and-trace system no longer effective** because it becomes practically impossible to trace all contacts of every infected person – need enough restrictions to ensure that infections do not grow rapidly in a 'second wave'. If infections do grow rapidly, community fear is likely to spread quickly and governments would need to re-impose restrictions to bring infections back under control.

**Summary from media reports**

- A report in the Guardian indicates that the rise in $R_0$ after lockdown measures are relaxed is something epidemiologists are aware. Regional differences in the value of $R_0$ are also important where areas with greater health resources or fewer COVID cases may be more practical. *'What's of greater concern to epidemiologists are indications that the R number is rising uncontrollably, or in a way that increases the exposure of the most vulnerable or puts health systems under great strain. In other words, what's as important as the R number is the total number of cases across a population that an increase in R would cause. While the increase in* ***Germany's*** *R number is concerning, this would be far more alarming were it to occur in the UK, where there are currently many more cases of coronavirus.'*

- This same report indicates that in Seoul, a recent outbreak of 170 infections has been linked to bars and nightclubs and while South Korea, who has been one of the most successful countries at controlling the virus has had 170 infections linked to five bars and nightclubs.

- BBC news reports indicate that **South Korea** may be facing a second wave of infections, with 17 new infections being recorded in the last 24 hours. *'The mayor of Seoul also warned that the capital may have to return to strict social distancing, should cases top 30 on average over the next three days and the bed occupancy rate of the city's hospitals exceeds 70%.'*

- In Germany, local outbreaks (that are occurring in meat processing plants and among religious communities) which can have a strong influence on the value of the reproduction number but a nationwide increase in case numbers is not expected.

- An ABC news article indicates that Australia is currently detecting approximately 92% of all symptomatic cases. *"The mechanisms put in place to maintain physical distancing, to reduce the number of people to four square metres in each venue [are] incredibly important in helping to prevent any seasonal increase with COVID-19 cases."* Says Dr Kidd, Deputy Chief Medical Officer.

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**Searchers:** Dr Ingrid Lensink, Nikki May (CEIH)

**Expert input:** Prof Steve Wesselingh

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