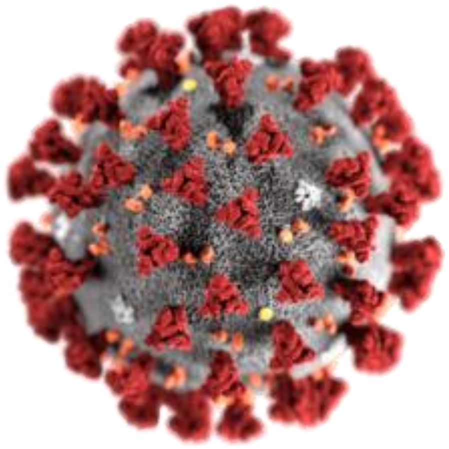

COVID-19 Science Report: Exit Strategies

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As of 17 July 2020

DOI: 10.25540/g7z2-sy92

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Executive Summary

In response to the worldwide outbreak of COVID-19, 186 countries thus far have instituted some form of movement restriction and 82 countries have full or partial lockdowns. While lockdowns may be necessary in cases where widespread community transmissions exceed the ability of health systems to cope, they impose a heavy cost on societies and economies.

Countries imposed lockdowns of varying degrees in response to a sudden sharp rise in cases and deaths, many without planning how to later remove the lockdown. A comprehensive and clear approach to de-escalate a lockdown is required to ease these societal and economic burdens without provoking a rebound rise in infections.

In the context of this report, the “exit plan” is the intentional combination of steps a country designs to exit from a lockdown, based on one or more “exit strategies” (or conceptual approaches) to bring about a sustainable long-term outcome. Some countries have shared their intended path out of lockdown while others have announced selected elements. The case series COVID-19 Science Report: Country Journeys describes the reported “exit scenarios” of selected countries or cities.

Key factors in the design of an exit plan include the following:

1. Disease characteristics. The “novel coronavirus” is different in many ways from other viruses, even those in its coronavirus family. Beyond its clinical management, we must understand its clinical characteristics to interrupt its transmission through appropriate measures. New evidence, as it arises, must be constantly evaluated and incorporated, and the exit strategy and plan adjusted to accommodate our new findings. Key elements of exit strategies pivot on our understanding of the disease characteristics of COVID-19. Presymptomatic and asymptomatic transmission has been suggested. The degree and nature of these transmissions may play a big role in the management of the outbreak.

2. Close monitoring of the spread of the outbreak to guide the exit measures, with epidemiological data, surveillance of the population at risk and at large, and factors that promote or inhibit spread.

3. Health system capacity, especially intensive care, protective equipment and supplies, and manpower and facilities to look after the infected, exposed, vulnerable and non-COVID patients in different contexts. The overwhelming of health system capacity (and the threat thereof) initiated lockdowns in many countries.

4. Compliance and response capabilities. Healthcare facilities and central agencies cannot manage the outbreak without the support and compliance of the general population. Communications and community engagement become critical elements of the exit plan.

5. Global situation. The virus crosses borders easily in our interconnected world. In the long run, the pandemic must be defeated across the whole world to be beaten at all.

6. Other societal sectors, including the environment, food supply, trade and industry, security, communications and technology, mental health, social support, food and nutrition, to name a few.

7. Strategic oversight. Placed last because it is the pivot around which all the factors above move, a mechanism for strategic oversight with the right knowledge, skills and capabilities to focus and coordinate an *architected* exit plan that adapts and responds to outbreak trends and new information and insights, dropping measures of low

impact when appropriate, and most importantly synchronises, synergises and synthesises multiple agencies in action.

WHO suggested the following prerequisites for a successful transition.

1. Control of spread to a level of sporadic cases and clusters of linkable cases.
2. Presence of health systems and public health capacities to detect, test, isolate and quarantine all cases, regardless of disease severity and origin.
3. Minimisation of risks in settings that may be vulnerable to outbreaks.
4. Established preventive measures at workplaces.
5. Management of risk of imported cases.
6. Engagement of communities to achieve a common understanding of the shift to detection and isolation of all cases and the maintenance of behavioural prevention measures.

Potential exit strategies are summarised in the following table. For any one exit strategy, all critical success factors need to be met. For now, highly accurate low-cost rapid point-of-care testing has not been developed and sustainable immunity has not yet been demonstrated in order for immunity passports to be implemented. Lockdown until vaccines are available will be extremely painful.

The exit strategies actually doable at this time will be one or a combination of gradual easing, adaptive triggering and/or mass testing with contact tracing. The exit plan may involve a combination of the strategies above, either in parallel or in sequence.

Options	Advantages	Disadvantages	Critical Success Factors
Gradual easing	Allows reconstruction of the economy, and gradual return to normal life while minimising the risk of a sharp spike in cases.	Potential resurgence of cases if too fast a release or if remaining measures are inadequate. Unequal burden, with higher social and economic costs for groups that are subjected to prolonged isolation Potential unnecessary burden if done slower than actually needed. Some population vulnerable to new imported infections until vaccine is available.	• Ability to sustain lockdown until pre-requisites for lifting lockdown are met. • Judicious combination with other exit strategies to minimise impact. • Good surveillance, and good judgement on what measures and when to relax. • Ability to reimpose measures if relaxed too quickly at some point.

Options	Advantages	Disadvantages	Critical Success Factors
Adaptive triggering	Allows economy and society to run while avoiding exceeding the health system capacity.	Management of public confidence will be challenging with cycles of strict measures imposed and lifted. Businesses and communities unable to plan ahead. Population vulnerable to new imported infections until vaccine is available.	• Robust monitoring system. • Ability to activate and deactivate interventions multiple times. • Adaptability and compliance of population.
Mass testing with contact tracing	Early isolation, treatment, and contact tracing which reduces transmissions. Keeps infection rate low.	False positives will strain health system. False negatives risk more transmissions. Feasible only when number of cases remain small relative to contact tracing capabilities. Population vulnerable to new imported infections until vaccine is available.	• Availability of appropriate tests with adequate sensitivity. • Ability and resources to do extensive testing. • Good uptake of testing by population. • Efficient contact tracing and isolation of close contacts following testing.
Immunity Passports	Allows partial recovery of economy by allowing immune individuals to return to work while shielding susceptible individuals	Potential reinfection if immunity wanes. False positives susceptible to infection. Some population vulnerable until vaccine is available.	• Demonstration of adequate and sustained immunity levels. • Highly specific antibody test. • Tight control against abuse and gaming.
Lockdown until Vaccines	Most aggressive way to ensure control of disease spread	Heavy social and economic costs in the meantime.	• Enforcement of compliance. • Eventual availability of safe, effective, widely available vaccine.

Exit Strategies

The report explores exit strategies. Because of the time limitation, the rapid scan approach, and the variability of available information, the descriptions of exit strategies may vary in detail. This report should be read alongside the evidence summaries related to Containment Measures, Lockdowns and Country Journeys.

For regular readers of this report, the latest additions have been highlighted in purple.

Background

According to a UNICEF statement on 9 April 2020, 186 countries have instituted some form of movement restriction, and 82 countries have a full or partial lockdown.[1] While lockdowns may be necessary in cases where widespread community transmissions exceed the ability of health systems to cope, they impose a heavy cost on societies and economies. Politically and socially, lockdowns are subject to contention, with groups that protest against lockdowns pitched against others that prefer restrictions to be in place for longer.[2] Until safe, highly effective, and affordable therapeutics and vaccines are available in sufficient quantities, societies need to limit the spread of COVID-19. Therefore, a comprehensive and clear approach to de-escalate a lockdown is required to ease the societal and economic burdens without provoking a rebound rise in infections.

In the context of this report, the "exit plan" is the intentional combination of steps a country designs to exit from a lockdown, while an "exit strategy" is the method or approach within that plan. Not all countries have officially shared their formal exit plans. We are therefore able only to describe their apparent exit scenarios (that is, what has been happening) rather than their exit strategies (that is, what their intents and plans are) in the COVID-19 Science Report: Country Journeys.

Key factors in design

While balancing societal and economic costs, the exit plan should ensure the protection of public health in both the short and long term. There is much unknown and uncertain for this novel coronavirus and the following key factors (drawn primarily from the European Commission roadmap towards lifting COVID-19 containment measures[3] and supplemented by other sources as cited) are key considerations in the design of the exit plan.

Disease characteristics

COVID-19 was originally termed the "Novel Coronavirus" and true to its first name is different in many ways from other viruses, even those in its coronavirus family. From the first clinical presentation as a SARS-like condition, we have been discovering new facets of this disease, from its severity in the elderly discovered early to the presenting symptom of anosmia (loss of smell) only realised much later. Measures that proved useful (eg temperature monitoring because fever is not consistently present) have proved less reliable and models of its spread have been found to differ significantly from the earlier SARS virus (eg viral shedding is much earlier compared to the first SARS), with much impact on populations contained in high density accommodations.

Our understanding of the virus' clinical characteristics has changed in many ways over the last three months and may continue to evolve. New evidence, as it arises, must be constantly evaluated and incorporated, and the exit strategy and plan adjusted to accommodate our new findings. Key elements of exit strategies (eg protecting the vulnerable) pivot on our understanding of the disease characteristics of COVID-19.

Monitoring and testing capacity

The spread of COVID-19 should be monitored closely. Epidemiological data should be assessed in detail prior to, and continually upon, relaxation of confinement measures, as any degree of gradual relaxation may lead to a rise in new cases. Testing capacity and public health capacity (including contact tracing capabilities and support from other agencies) should be considered.[4]

Level of transmission and transmission dynamics

The exit plan should be based on updated, reliable data on the rate of transmission, duration and level of immunity (including risk of reinfection) and the groups of individuals at risk of COVID-19. Transmission rates may be affected by:

1. Pathogen-specific factors such as SARS-CoV-2 binding sites, environmental persistence, dose and virulence (which may be influenced by mutations and strains).
2. Host factors including susceptibility, length of infection, course of infection (eg incubation period, duration of infectiousness) and symptoms.
3. Environmental factors including population density and infection control.
4. Behavioural factors such as personal hygiene and health-seeking behaviour.

In line with the goal of the public health response to reduce the overall basic/effective reproduction rate R to below 1, super spreading events (SSEs) should be avoided. Super spreading events are most commonly caused by a delay in diagnosis. Prevention of SSEs include early recognition and detection (including atypical symptoms), early institution of control measures, proper infection control measures in healthcare settings, and community wide NPIs (eg risk communication).[5] The dispersion factor (k) is a measure of variability in empirically observed cluster sizes. A low dispersion results in a steadier growth of the epidemic, while a larger dispersion may imply that some cases account for a disproportionate number of secondary cases[6] with individual-level variation in the risk of secondary transmission.[7] The estimated k values for Hong Kong, Japan and Singapore are estimated to be 2.3, 0.51 and 1.78 respectively. With a hypothetical seeding of 50 infections, the probabilities of a SSE with cluster size of 30 or more are 0.114, 0.0411, and 0.412 respectively.[8]

Transmission dynamics should also be explicitly considered if the exit plan is graduated across different groups of people (eg school children and workers first, the elderly and vulnerable later). People considered less at risk who are allowed to move early may inadvertently allow transmission to those at risk. Care should be taken to think of groups of people of higher risks who might otherwise not be catered for.

Presymptomatic and asymptomatic transmission

There have been reports of presymptomatic transmission[9,10] as well as suggested asymptomatic transmission.[11] One study found rapid transmission of COVID-19 by an initially asymptomatic youth to a cluster of youngsters with a median incubation period of 2 days (range 1-4) and median serial interval of 1 day (range 0-4).[12] He et al reported that (95% CI 25–69) of secondary cases were infected during the index cases' pre-symptomatic stage.[13] WHO has reported that most asymptomatic cases go on to develop symptoms, thus truly asymptomatic infections are rare. The true proportion of asymptomatic cases is however unclear.[14]

Health system capacity

The health system capacity includes the intensive care (or critical care) capacity, number and occupancy of available hospital beds, access to medications and care in particular for vulnerable groups, availability of stocks and equipment, number of adequately trained staff both in hospitals as well as in primary care, and resources to manage patients before and after hospital discharge (eg in community isolation facilities or at home). There should be adequate capacity for a possible increase of cases after lockdowns are lifted.

Healthcare workers and support staff should be protected, including those working in the community, and in residential and care homes. PPE guidelines should be communicated and supported and adopted by staff.[15]

Sufficient capacity should be considered not just for the management of COVID-19, but also to manage the backlog of elective procedures that were postponed. There may be an approximately 3-week time lag between distancing measures and peak critical care demand, and surge critical care capacity should be planned accordingly.[16,17,18] A report by the John Hopkins Center for Health Security noted that excess capacity should be maintained given a potential rebound in COVID patients, and an expected increase in non-COVID patients who present to emergency departments as social distancing eases. Priority systems for resuming deferred healthcare services should also be developed. These near-term priorities should include surgical procedures with a negative impact on the condition of patients, and are least disruptive to existing services to manage COVID-19.[19]

Compliance and response capabilities

Given changes in disease spread over time, clear, transparent and timely communication is essential. Dialogue with social partners may be key to facilitate adaptations. Public sentiment (eg perceived threat and behavioural fatigue) may affect compliance and therefore the effectiveness of social distancing measures.[20] The exit plan should explicitly consider the options of gradual or adaptive exits (more later), and the community and businesses should be prepared for reinstitution of lockdowns across the country or in local areas as needed.

Global situation

Exit plans should take into account the epidemic situation in the region and globally, as well as border control policies and travel restrictions. Coordinated action is important in the control of imported cases.[21] Exit strategies that keep the number cases down also maintain the lack of immunity in a population, which then remains susceptible to new cases imported from other countries.

Societal costs

Other costs include supply chains (for example, of personal protective equipment, healthcare equipment and other logistics), economic repercussions and costs,[22] and political implications. Societal costs include but are not limited to lost education,[23] access to other healthcare services, preventive health programmes, mental health, food, nutrition programmes, security, exploitation, violence and abuse,[24] loneliness, and gender safeguarding issues during the pandemic.[25] The deferment of non-emergency and non-urgent treatments for non COVID-19 related health conditions and chronic diseases imposes a cost on patients as well as health care systems in the long run.[26] Potential issues of disenfranchised grief, or unresolved grief due to the lack of support for family members of the deceased have also been raised.[27] Community acceptance of containment measures should be taken into account.[28]

Strategic oversight

Placed last in this list because it is the pivot around which all the factors above move, a mechanism for strategic oversight with the right knowledge, skills and capabilities to focus and coordinate an *architected* exit plan that adapts and responds to outbreak trends and new information and insights, dropping measures of low impact when appropriate, and most importantly synchronises, synergises and synthesises multiple agencies in action.

The Tony Blair Institute for Global Change highlighted three key considerations in the planning of a "roadmap" or exit plan: costs and benefits of lockdown, risks of transmission, and vulnerability.[29]

Components of exit plan

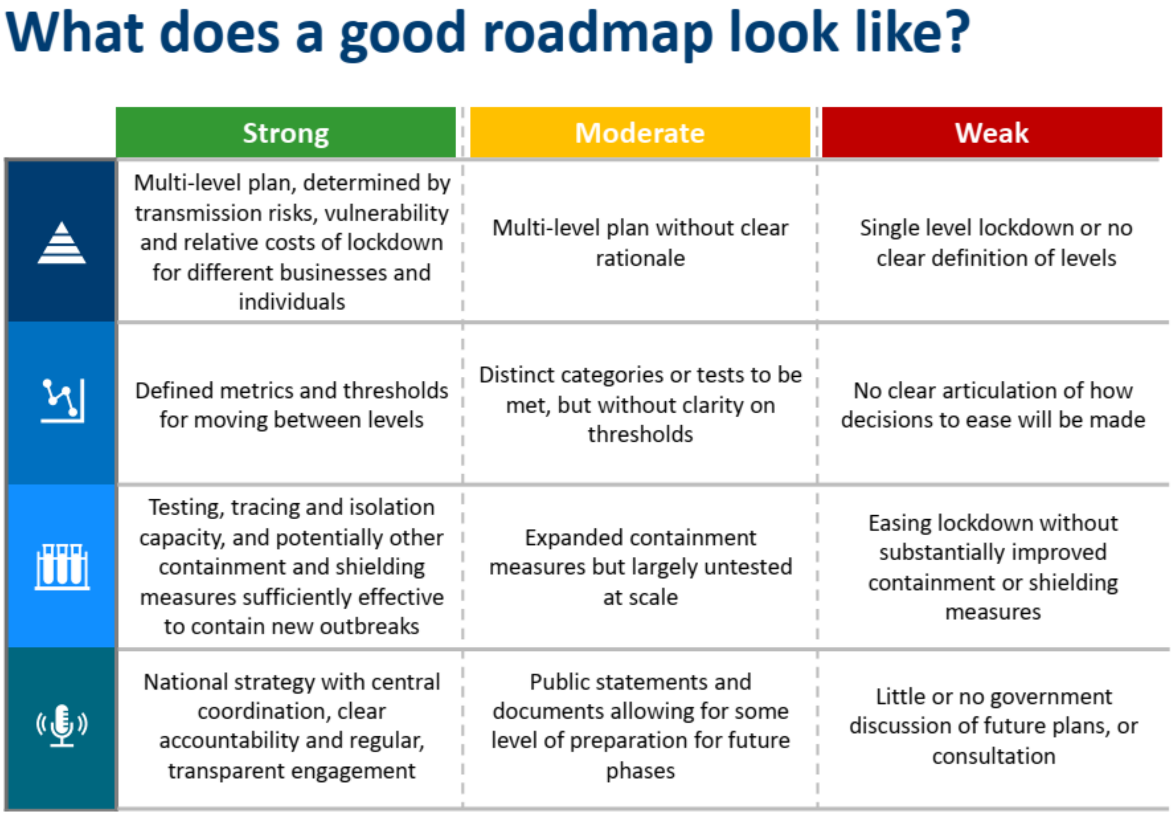
It has been proposed that a well-structured exit plan can reduce uncertainty for individuals and businesses, and improve compliance with measures to save lives and livelihoods.[30] It should provide clarity on:

(1) Levels of exit
This could include the phases of exit that may range from lighter restrictions ("normal") to lockdowns, and the impact of each on individuals and businesses in society.

(2) Triggers for each level
This should include clear metrics and thresholds for transitions to another level. Triggers for transition could include health system capacity, health system demand, death rate, mode of transmission, and cost-benefit analysis (eg well-being framework). The Centre for Economic Performance, London School of Economics, proposed the use of Wellbeing Years (WELLBYs), which is analogous to QALYs (quality-adjusted life years), as a metric to evaluate the net benefit of lockdown measures. This metric could include factors such as income, unemployment, mental health, public confidence, schooling, COVID-19 deaths, road deaths, commuting, CO2, emissions, and air quality. Nonetheless, such a metric requires all relevant societal costs and benefits to be captured, and a judgement about the effects of measures on the level of outcomes, as well as the relative importance of individual outcomes.[31]

(3) Containment measures at each level
This should include measures to avoid a second spike in cases after a lockdown. Appropriate responses may be tied to various transmission scenarios and/or epidemic phases (eg no/emergent cases, sporadic cases, clusters of cases, widespread cases).[32]

(4) Organization and communication plans
This should be clear and coordinated (with individual accountability for execution). Communications should be tailored, and involve stakeholder liaison. A strong risk communication strategy that informs and engages the public, businesses, and vulnerable groups, and explains the rationale behind the adjustment of measures, is required to obtain buy-in.[33]



What does a good roadmap look like?

	Strong	Moderate	Weak
	Multi-level plan, determined by transmission risks, vulnerability and relative costs of lockdown for different businesses and individuals	Multi-level plan without clear rationale	Single level lockdown or no clear definition of levels
	Defined metrics and thresholds for moving between levels	Distinct categories or tests to be met, but without clarity on thresholds	No clear articulation of how decisions to ease will be made
	Testing, tracing and isolation capacity, and potentially other containment and shielding measures sufficiently effective to contain new outbreaks	Expanded containment measures but largely untested at scale	Easing lockdown without substantially improved containment or shielding measures
	National strategy with central coordination, clear accountability and regular, transparent engagement	Public statements and documents allowing for some level of preparation for future phases	Little or no government discussion of future plans, or consultation

Figure 1: Illustration of strong and weak roadmaps. Source: Alvis S et al (2020) [34]

It has been proposed that the UN Disaster Resilience Scorecard for Public Health can be applied in the assessment of risks during re-opening.[35]

Selective sections of the Disaster Resilience Scorecard for Public Health

#	Assess
A1.1/9.2	Governance mechanisms for disaster risk and emergency management include public health professionals
A2.1	Disaster risk planning includes public health emergencies
A2.2	Consideration of public health impacts arising from other disasters
A3.1	Funding earmarked for addressing public health implications of disasters
A6.1	Sufficient, skilled health professionals to maintain public health around disasters
A6.2	Public health data shared with all stakeholders that need it
A7.1	Communities are prepared to maintain public health levels after a disaster
A7.1.2	Community can access and trust public health information
A8.1	Existence of health infrastructure besides hospitals (E.g., isolation, clinics, labs, supplies)
A8.2	Health facilities can manage a surge of patients
A9.1	Early warning systems exist for impending healthcare emergencies
A9.5	Existing stockpile of public health items, PPE, medications and equipment

Surveillance

While surveillance is not a strategy in itself, it is a crucial element of any exit strategy. A robust surveillance strategy monitors both the intensity as well as the geographical spread of COVID-19, identifies outbreaks, monitors changes in transmission levels across various risk groups, monitors age-specific population immunity levels, tracks the impact on health systems, and the impact of measures.[36] Beyond existing indicators (eg prevalence of current and past COVID-19 infections in the community, and hospital and ICU occupancy rates), other indicators to be monitored include the effective reproduction number, trends in population movement (via proxy indicators), and new mutations or strains of SARS-Cov-2 that may influence the transmission of disease. Excess deaths (comparing all-cause weekly mortality rates relative to that in previous years) has been suggested as a measure of the impact of not only COVID-19, but also delays to seeking care for other medical conditions.[37] The response to COVID-19 should be assessed through in-action and after-action reviews to determine capabilities and capacities to implement response strategies.[38]

Sentinel surveillance enables nations to determine if herd immunity has been acquired, and thus the risk of further transmission. When herd immunity is achieved, the risk of further viral transmission within the community is low.

Monitoring level of transmission

Measures of the level of transmission include health system demand such as ICU admissions, case rates, R proxies such as Koch Institute's surveys and TBI's early warning model.[39]

Beyond the number of cases, ICU admissions and crude case fatality rates, some studies have recommended that the effective reproductive number (R_t) be constantly kept below 1 until effective vaccines are available, and that real-time estimates of R_t should be monitored in routine dashboards and situation reports.[40]

There is a lead time between actual changes in R_t and the detection of changes, which is roughly equivalent to the incubation period plus delays in testing and reporting.[41] Real time reporting of R_t based on the epidemic curve and corrected by statistical methods ("nowcasting") is being carried out in Hong Kong.[42,43] The R_t threshold should be lowered with more aggressive measures in the event of an explosive outbreak that threatens to exceed the health system capacity.[44]

A combination of daily counts, averages (across days, weeks), and trend lines for new cases and deaths are used to monitor transmission. Changing case definitions and testing strategies would need to be accounted for when making inferences on epidemic growth rates and R.[45]

Across countries and states, there are also variations in terms of definitions and methods for counting deaths attributed to COVID-19. Extra time taken in the coding and reporting of deaths may also contribute to time lags in certain countries.[46]

The Pandemic Recovery Acceleration Model (PRAM) analytic tool was developed and implemented in Nebraska. It consists of 3 disease specific values, namely daily new cases, newly reported deaths and percentage positive tests per day, and 3 health care resource specific values, namely daily percentage total of acute care hospital beds, ICU beds and ventilator capacity used by COVID-19 positive patients. For each measure/value, rolling averages over past 1-3 days (5-7 day averages have also been proposed; reflective of current position) and 8-14 days (reflective of past position), along with the ratio of the two rolling means (trend index reflective of velocity of change) are tabulated. The Recovery Composite Index indicates the rate of acceleration or deceleration of pandemic recovery, while the Recovery Ratio Index indicates the velocity of the impact on health care resources relative to the velocity of the pandemic spread.[47]

Self-reporting

A study in Wuhan China found that an online questionnaire of symptoms and history of contact or travel history can be used as a proxy to identify trends in disease prevalence, and identify risk factors for disease.[48] Similarly symptom checkers such as the COVID Symptom Tracker can be used to track disease prevalence among the general public, with geospatial data for identification of hotspots. These can then be used to develop weighted prediction models. In Southern Wales, user reported symptoms predicted two spikes in cases 5-7 days in advance of official reports. Real-time tracking can also be used among vulnerable populations such as healthcare workers to monitor the intensity and type of direct patient care experiences, use of PPE, and work-related stress and anxiety.[49] COVID-19 related knowledge, attitudes and practices of the population can be monitored through social media advertisement campaigns.[50]

Herd immunity

The minimum ('critical') level of population immunity (P_{crit}) required to stop further disease spread may be derived using the formula: $P_{crit} = 1-(1/R_t)$, where R_t is the effective reproduction number. R_t can be derived by multiplying R_0 by the percentage of the population that remains susceptible to COVID-19.[51] Based on early estimates, at least 70% of the population requires immunity to achieve herd immunity.[52] A preprint study suggested that elimination of SARS-CoV-2 infections annually over 5 years was only achieved if large proportions of infected individuals become immune (>70%) with long-term sustained immunity (>15 years). The study highlighted the endemic potential of SARS-CoV-2 in the event of seasonal variability of infectivity and incomplete sustained immunity.[53] A preprint study in Japan noted that at R_0 of 2 or more, herd immunity approaches are unlikely to be socially acceptable (based on an upper bound of overall mortality) assuming current infection fatality rates are not overestimated.[54]

Given that population immunity may be acquired either through vaccination or natural infection, surveillance using serological tests may allow countries to gauge the proportion of population who were previously infected (symptomatic or otherwise) and have developed immunity.

However, the proportion of the population across countries that has been infected and has recovered with antibodies appears to be much lower than that required to achieve herd immunity. WHO recently announced that early data from studies using antibody testing suggest that only approximately two to three percent of the world's population had previously been infected.[55]

A preprint of a study by Bendavid et al presented serological test findings of a representative cohort of 3,300 in Santa Clara County, California, USA.[56] The prevalence of antibodies to SARS-CoV-2 in Santa Clara County was 1.5% if unadjusted and 2.81% if population-weighted. With further adjustment accounting for the performance (sensitivity and specificity) of the serological tests used, the prevalence of COVID-19 in Santa Clara ranged from 2.49% to 4.16%. The estimated population prevalence translates to 48,000 and 81,000 people infected in Santa Clara County, which is 50 to 85-fold more than the 956 confirmed cases.

This finding of the infection being more widespread than the reported number of confirmed cases is echoed in a similar study in a village in Germany, with an estimated 14% of the village having been infected.[57] Similar work has started in Wuhan, China, which was the first epicenter of COVID-19.[58] However, preliminary findings indicated only 2% to 3% of all recent patients and other visitors have antibodies for SARS-CoV-2.

A study on blood donors in Stockholm noted that 11 out of 100 had antibodies against SARS-CoV-2.[59] Another recent study in Sweden estimated that while 2.5% of the population in Stockholm was reported to have been infected between 27[h] Mar and 3 Apr, it is possible that assuming 99.9% of cases are unconfirmed, up to a third (32.0%, 95% CI 18.4-47.7) of people in Stockholm would be infected by 1 May.[60]

A pilot street study found that 64 out of 200 residents tested in Chelsea, Massachusetts, tested positive for antibodies, but the results may not be representative given the limited scale of the study. In addition, the tests were carried out using an unapproved rapid diagnostic test of uncertain accuracy.[61]

Monitoring population movement

It has been suggested that through social media, mobile network operators, online payment platforms, location-based data from public transport systems and other technology platforms, information can be gathered on mobility patterns and social interactions.[62,63] Aggregated human flows may be charted in a real-time map to support the implementation of effective social distancing measures.[64] A paper by the Tony Blair Institute for Global Change suggested that mobility can be used as an early-warning signal; a percentage point increase in mobility can result in a 2.2 percentage point change in acceleration of virus transmission. This percentage may be limited by parameters such as transmission within institutions.[65]

Several studies (some preprints) and some countries have started using and tracking such platforms and indicators to monitor outbreak risks and implementation of measures:

Use of platforms and proxy data indicators to monitor risks/assess impact of measures

Platforms/ Indicators	Description
Smartphone apps and user locations (Austria and Italy)	Smartphone apps are used by public health officials and researchers in Austria and Italy to monitor social distancing behaviour and outbreak risk (based on how much time residents spend in a location and location of medical facilities reporting infections). Data is used to stratify zones into risk levels with accompanying appropriate measures implemented in the respective zones.[66]
Smartphone apps and user locations (US)	Similarly, in US, a “Social Distancing Scoreboard” measured the reduction in travel among residents using location data. A preprint study in US found that the adoption of better social distancing practices (measured with smartphone location tracking) was associated with counties with better financial and community health resources.[67]
Average daily contact per person (UK)	A UK survey study noted a 73% reduction in average daily number of contacts per participant after implementation of the lockdown. Pointing out significant delays between infection, onset of symptoms, hospitalisation and reporting, the study recommended tracking such behavioural change data for rapid assessment of the impact of distancing measures.[68]
Average daily contact per person (US)	A Berkeley Interpersonal Contact Study (BICS) noted that 85% of respondents reported having contact with 4 or less people and 50% reported no contact outside of their household. This was a 70% decrease in daily average number of contacts per person when compared to a similar survey study in 2015. The study was able to provide a rapid assessment of social distancing policies.[69]

Platforms/ Indicators	Description
Mobility data in certain sectors (Europe)	A study models the impact of changes in mobility patterns in 11 European countries and their effect on the R_0. Mobility patterns were measured in 5 different sectors, with grocery and pharmacy being the clearest indicator for R_0 change, with a narrow confidence interval. This suggests that relative change in mobility in the grocery and pharmacy sector can provide an easy and straightforward way for governments to analyse the effectiveness of their non-pharmaceutical interventions (NPIs), as the sector accounts for over 90% of the change in R_0.[70]
Mobility data (Brazil)	This study calculated an “isolation index” as a ratio of the number of individuals staying at home over the number of cell phone users. The study found that mobility data can predict the time-dependent reproduction number (R_t). Isolation indexes above 50% led to R_t below 1 in most cases (89%).[71]
Residential parking data and public transportation mobility data (Singapore)	A paper pointed to the analysis of mobility data as an indication of public response to social distancing guidance/policies and the ‘Circuit Breaker’. Charting of residential parking data (as a proxy for traffic) and Citymapper public transportation mobility data suggested that measures were taken seriously (decreased availability of carparks and % of city moving), even in the week leading up to Circuit Breaker.[72] (Figure 2).
Environmental impact and air pollution (UK)	A UK study conducted an ecologic analysis of the correlation between air pollution and COVID-19. The study reported that air pollution levels are correlated with risks of transmission in London boroughs. It suggested that air pollution levels can be used as an indicator to assess a region’s vulnerability to COVID-19.[73]

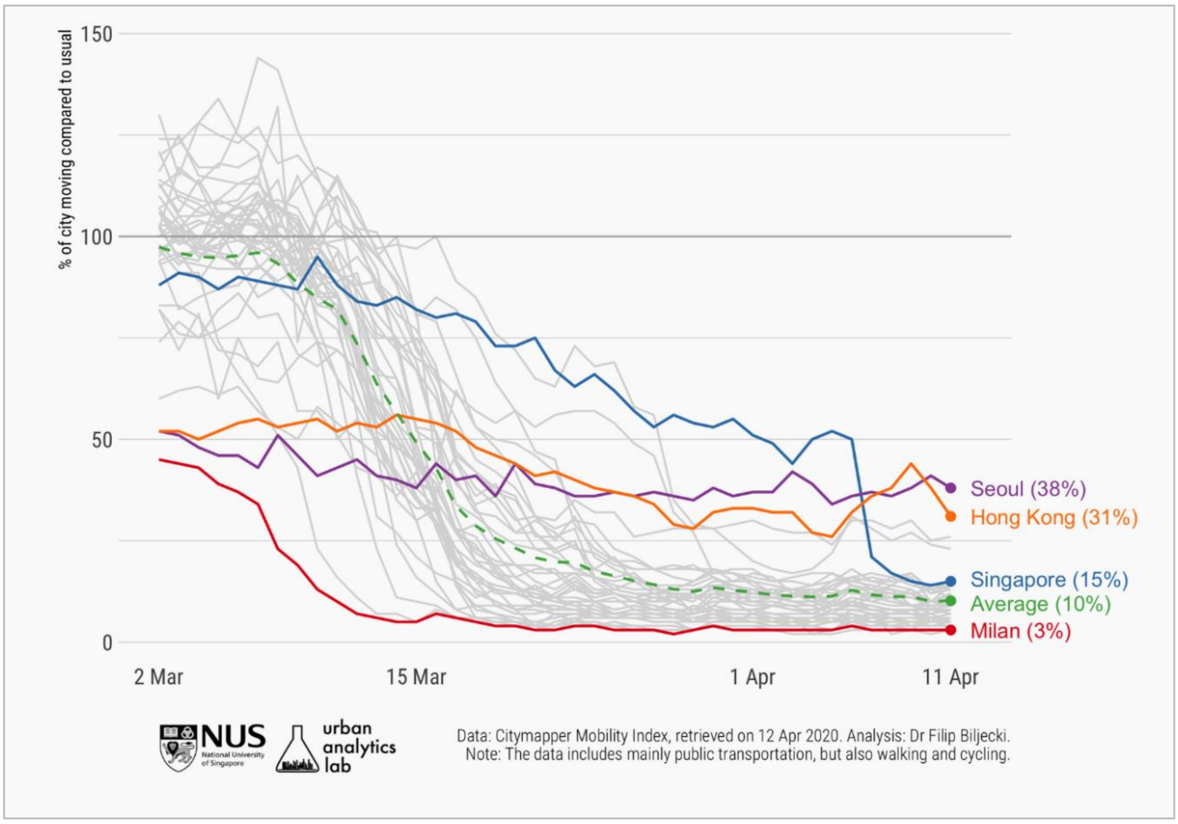


Figure 2: Comparison of mobility data trending (mainly public transportation but also walking and cycling) with global trends. Source: NUS

Monitoring changes

An early warning system should be in place to detect the emergence of new or mutated diseases.[74]

Prerequisites for lifting a lockdown

World Health Organization noted in its Strategy Update that every country should implement comprehensive measures to slow down transmission and reduce COVID-19 associated mortality, with the ultimate aim to transition to and maintain a "steady state of low-level or no transmission of COVID-19".[75]

Prerequisites for a successful transition may be classified in the following six categories:

1. Control of spread to a level of sporadic cases and clusters of linkable cases.
2. Presence of health systems and public health capacities to detect, test, isolate and quarantine all cases, regardless of disease severity and origin.
    a. Detection measures should include active case finding in addition to entry screening and other approaches.
    b. Sufficient capacity for testing (with results within 24 hours of identification).
    c. Isolation of confirmed cases until patients are deemed non-infectious.
    d. Isolation and monitoring of close contacts are recommended for 14 days.

3. Minimisation of risks in settings that may be vulnerable to outbreaks (eg intermediate and long-term care facilities, army barracks, and other populations contained in high density accommodations).
    a. Identification of all major drivers and amplifiers of disease transmission.
    b. Presence of measures to minimise the risk of new outbreaks.
    c. Adaptation of sites, if feasible, to ensure safe distancing and proper crowd management, enforcement of infection control, risk communication, community engagement and surveillance.
4. Established preventive measures at workplaces.
5. Management of risk of imported cases.
    a. Analysis of origins and pathways of importations.
    b. Measures to detect and manage suspected cases among travellers rapidly.
    c. Barriers to identified sources and/or channels of importation.
6. Engagement of communities to achieve a common understanding of the shift to detection and isolation of all cases and the maintenance of behavioural prevention measures, wherever possible, through intermediaries (like non-governmental organisations and social service agencies) already familiar to the communities.

The European Commission roadmap emphasised the need for signs of a decrease and stabilisation in the spread of disease based on epidemiological data prior to the easing of lockdowns. Indicators may include the number of new infections, hospitalisations, and ICU cases. Other indications include a sufficient health system capacity, and appropriate monitoring capacity.

Individual countries have also set out similar conditions before easing restrictions, some of which are listed in the following table.

Australia[76]	1. Increased testing for asymptomatic and presymptomatic individuals. 2. Enhanced contact tracing “to industrial capability” through the use of technology (an application). 3. Enhanced local response capabilities, such as the lockdown localised areas, involving multi-agency forces.
United Kingdom[77]	4. Confidence that the NHS can still provide sufficient critical care and specialist treatment across the UK. 5. Evidence of a sustained and consistent fall in the daily death rate to be confident that UK is beyond the peak 6. Reliable data from SAGE that the infection rate has decreased to manageable levels 7. Testing capacity and PPE are in hand to meet supply for future demand 8. Confidence that a second peak of infection that overwhelms the NHS will not be triggered by adjustments

Key strategies

The Tony Blair Institute for Global Health[78] proposed six (alternative) exit strategies for UK:

1. Lockdown until a vaccine is developed.
2. Gradual easing from suppression measures.
3. Adaptive triggering, through easing of suppression measures with declines in infections, and reimposition with increase in infections.
4. Immunity Permits.
5. Weekly testing with active case finding.
6. Contact tracing through an application along with widespread testing.

The American Enterprise Institute[79] proposed a single (sequential) process for United States:

1. Slow the spread. This including social distancing measures, increasing diagnostic testing capacity and rapid sharing of results for contact tracing, capacity building in the health care system, comprehensive surveillance systems, and instituting public health hygiene measures eg mask-wearing.
2. Reopen, State by State. This includes relaxation of physical distancing measures and special care for vulnerable populations, and identification of immune individuals to return to work.
3. Establish protection then lift all restrictions. This includes global vaccination, and serological surveys to determine population immunity.
4. Rebuild readiness for the next pandemic. This includes scaling up capabilities for vaccine development, strengthening of health care systems, the establishment of infectious disease forecasting centres, and governance.

This report focuses on the following key exit strategies. As framed in this report, these may not be mutually exclusive and may be combined in various ways in the final exit plan. We describe the rationale, implementation, risks, and critical success factors for each strategy. We also discuss the implications of a prolonged lockdown until vaccines are available.

1. Gradual easing.
2. Mass testing with active case finding, contact tracing and isolation.
3. Immunity passports.
4. Adaptive triggering.

Gradual easing

This involves a gradual relaxation of containment measures and the replacement of general measures by targeted measures. Measures that contribute relatively less to transmission in real-world terms should be prioritised ahead of others for relaxation. As much as possible, people should be educated on the mechanisms of spread and how to interrupt transmission so that they behave appropriately to reduce infections rather than have to be compelled to adhere to overly stringent rules that make no difference to actual transmission.

Rationale

Most countries appear to be gradually easing their lockdowns to allow for reconstruction of the economy and gradual return to normal life, while minimizing the risk of a sharp spike in cases. The European Commission recommends a stepwise approach, with ample time between the lifting of different measures, as the effect of relaxation of measures can only be detected over time. Effective action should be tailored to local condition and national specificities, with relaxation of measures that have a greater impact on people's lives.[80]

Implementation

The key consideration in the employment of this strategy is the selection and timings of the measures to relax. It is important in this strategy to guide the relaxation very carefully, on one hand relieving the societal and economic stresses of the lockdown as much and as quickly as possible without allowing the reproduction rate to rise and provoking an explosion of cases. Overly tight as well as overly lax controls are both extremes to be avoided. Finding that right trajectory will be informed by science but much art is also required because the socio-political and economic dimensions will factor greatly in how well the population copes and the economy recovers. The aim, as stated by Switzerland, will be remove control measures "as soon as possible and as slowly as necessary".

Gating criteria for each phase transition may include decrease in newly identified COVID-19 cases, decrease in ED or outpatient visits for COVID-like illnesses and influenza-like illnesses, decrease in percentage of positive SARS-CoV-2 tests, capacity to treat all patients without crisis care (including relatively lower ICU bed occupancy, absence of staff shortage, and adequate PPE supply), and robust testing programmes (measured by test availability, percentage of positive tests, and median time from test order to results). Rebounds may be identified by increase in trajectories or cases, influenza-like or COVID-like illness visits or activity levels (through daily statistical anomaly detection methods, or regression methods to classify time series trends), and/or coupled with other early warning indicators. The definition of a rebound should be clear for early identification.[81]

A preprint paper has proposed a composite index that provides real-time guidance of when to ease social distancing and exit from lockdowns.[82] The simple index quantifies the combined effects from three areas: 1) social distancing for reducing confirmed infected cases, 2) optimal triage and care of patients for recovery, and 3) critical care capacity for reducing death from COVID-19. The index, named easing social distancing (ESD) index, is calculated as [(cumulative confirmed cases)/(cumulative recovered patients without dying from COVID-19) – 1]. The cumulative recovered patients without dying is calculated by multiplying the number of recovered patients by (1 – case fatality). The ESD index approaches 0 when the ratio component of (cumulative confirmed cases) :(cumulative recovered patients without dying from COVID-19) is close to 1. This means most of the confirmed cases have recovered without dying. The global ESD index was found to have peaked at 3.87 at the end of March and dropped to 1.35 by the end of May. In May, low ESD index as found for Iceland and Taiwan, moderate for Germany, and high for France. It was proposed that easing of social distancing does not need to occur with the unrealistic expectation of ESD index being close to 0 (which requires very little case fatality), and can occur when the ESD index is lower than 1.

Risk stratification

Vulnerable groups may be protected for a longer period of time ("shielding"),[83] while restrictions are lifted for other groups. These vulnerable groups include those at a higher risk of severe disease and mortality, such as the elderly and those with chronic diseases and mental illnesses.[84] Individuals living in care institutions should also be protected. [85] Segmentation may be by age, sector and geographical region.[86] A preprint modelling study showed that segmentation by age to limit interactions across groups of different age bands can help reduce mortality by 66%.[87] Therefore, age-related restrictions to allow only those in the same age group to interact in settings such as supermarkets, could be protective for the elderly as social distancing measures get eased. While social distancing measures for elderly over the age of 70 have a lower impact on transmission as compared to other age groups, they help to reduce the demand for intensive care in hospitals and overall mortality rates. In New York, the “Matilda’s Law” requires that vulnerable populations stay home, with home visitations limited to immediate family members or close friends who require emergency help, and pre-screening of visitors for flu-like symptoms.[88] A score-based risk classification may also be considered in the classification of vulnerable subgroups.[89]

Schools may open first, given the lower risks of mortality to children, and the high costs of school closures.[90] The reopening of schools and universities should be with strong social distancing measures, enhanced disinfection, smaller class sizes, and increased reliance on e-learning.[91] Strong social distancing measures such as staying in the same classroom, restricting movement in corridors, segregating recess areas by class, staggering of recess times, segregating of cafeteria by class, and staggering of lunch periods, have been found to be feasible to implement and more so for lower grade levels.[92] Other recommendations include donning of PPE by teachers and adults, phasing the reopening of schools, rapid detection and response to localised outbreaks in school with adequate testing and tracing infrastructure, and gathering feedback from schools and key stakeholders.[93]

With the COVID-19 pandemic, several countries across the world closed schools and are currently managing their safe reopening after national COVID-19 cases have peaked and come down. While there are some modelling studies that predicted that school closures alone would only prevent 2-4% of deaths[94], the effect on transmission (including back to the families) is unclear. In the initial phase of exits, most countries have either kept schools and kindergartens or nurseries closed, or reopened schools with strict social distancing measures (eg small groups, one-to-one consultations) and a continued focus on online learning. A review article pointed out that the uncertainty of whether most children evade infection or are largely asymptomatic when infected requires caution when reopening schools.[95] Considerations to guide safe reopening include:

- Exploration of surveillance methods (eg large scale testing approaches in children with ‘child-friendly’ self-collection methods).
- Consideration of children with chronic conditions, vulnerability to COVID-19 or conditions that often present with COVID-19 symptoms (eg asthma), who may face barriers to school re-entry.
- The benefits of after-school activities and physical education, and innovative ways to safely conduct them rather than defer/abandon them.
- Privacy considerations with viral surveillance and contact tracing efforts.

The measures and considerations for the safe reopening of schools are further discussed in the Appendix – Safe Reopening of Schools.

University campuses, unlike grade schools below tertiary education levels, present a different unique situation. Many universities have residential campuses, functioning like a mini microcosm with a campus town, drawing students from around the country, region and the world. The risks that exist with reopening of these campuses after lockdown and the return of students after the long summer break is thus parallel to a country reopening its borders to travellers. Multiple preprint studies have modelled different combinations and variations of strategies, with a focus on regular testing.[96,97,98] A pre-semester mass testing of all students before return to campus has been highlighted to be able to help delay and reduce the size of any eventual outbreak.[99]

Return to workplaces should be staggered. Groups at a lower risk and in sectors that are more economically essential resume first. Other businesses that can maintain social distancing may open.[100] Occupational health and safety measures should be continued. Teleworking should continue where possible. A policy paper from Warwick University suggested releasing young citizens (between 20 and 30 years) who do not live with their parents back to work, but noted the potential for social discontent and abuse of the system.[101] In the initial phase of exit, most countries have opened selected businesses, including those in shopping malls where social distancing is maintained.

The resuming of social and dining activities may be considered with restricted opening hours and restrictions on the number of people per setting. Individualised transport mediums (eg private cars) may be permitted, followed by public transport with health-oriented measures (eg reduction of density of passengers, higher service frequency, personal protective equipment for transport personnel, protective barriers, availability of disinfectants etc). Community hygiene should be sustained. Risk management strategies may include intensified disinfection.[102]

The measures and considerations for the resuming of dining activities in food and beverage establishments are further discussed in the Appendix – Safe Reopening of Dining In.

Across countries, some sports venues have been reopened in the initial phases of the exit. Some places of worship may be reopened provided plans for strict social distancing are in place. Mass gatherings are potential super-spreading events and most countries do not permit mass gatherings until the later phases.[103]

A preprint simulation study found that with partial lifting of measures in exiting from a lockdown, if school, work, and leisure interactions can be kept to levels that are 50%, 50% and 60% lower compared to pre-COVID-19 levels.[104] The susceptibility to infection would be lowered by 5 to 30%, and if lowered by 20% or more, R_t could potentially be maintained at below 1. This study utilised retroactive self-reported data of social interactions from before the epidemic broke out in Greece and during the country's lockdown.

In a comprehensive preprint simulation study by Scott et al (2020), various scenarios of reopening of sectors and activities were modelled.[105] The study used disease-specific parameters from global published estimates, as well as contact networks parameters and policy change effects parameters from were obtained from a combination of the literature and a modified Delphi process. This modified Delphi process generated a median and range of the parameters from independent estimates by the panel of 12 experts, which included modellers, epidemiologists, qualitative researchers, social network researchers, infectious disease physicians and public health physicians. The modelled scenarios found that reopening pubs and bars without additional restrictions, withdrawing work from home directives (resulting in greater public transport use as well as more work interactions), and permitting large-scale events like concerts led to the fastest increase in infections. Making these reopening steps would more likely introduce increase in random one-time interactions, or big unstructured meetings with unknown individuals. Cumulative infections increased less for the other reopening steps in the following descending order: reopening cafes and restaurants, reopening entertainment venues (eg cinemas, performing arts), allowing community sports again, reopening schools, and allowing small social gatherings of less than 10 people.

In another preprint study, a SEIR (Susceptible, Exposed, Infectious, Recovered) framework was used to model the different types of transmission scenarios.[106] Based on trends in Los Angeles and Seattle, the models tested lifting all shelter-in-place (lockdown/social distancing) measures completely, continuing of shelter-in-place measures, keeping to isolating only known infected persons with partial lifting shelter-in-place measures, and stopping superspreading events. Factors promoting superspreading events include: "(1) high rates or intensity of contact between people or with surfaces; (2) large aggregations of people; (3) poorly ventilated physical environments, especially indoors; (4) highly infectious individuals; (5) highly susceptible recipient population". The models found that stopping high-risk superspreading events could allow for easing of some shelter-in-place measures without causing a resurgence of cases. Therefore, the authors suggested postponement in resumption of voluntary, large, indoor events that are mainly for entertainment such as gyms, clubs, sporting events, concerts, and large lecture.

Phased opening of external borders should take into account the epidemic situation in the region and globally as well as border control policies and travel restrictions.[107] Most countries have not eased external border controls, although countries such as the Baltic nations, and New Zealand and Australia, are moving to establish "travel bubbles".[108] Options proposed beyond post arrival quarantine include risk based approaches of lifting restrictions between countries with low transmission rates, good surveillance and transparent reporting, and a proof of immunity from travellers under the International Health Regulation.[109]

No country operates in isolation in our highly-globalised world, and particularly amongst the inter-connected European countries. A preprint simulation study used Vodafone Telcom and Google mobility data before and during Europe's implementation of non-pharmaceutical interventions (NPIs) of lockdowns and major social distancing.[110] The simulations found that coordination of NPIs across various countries were key to helping control and halt community transmissions. However, any country prematurely removing NPIs and creating unsynchronised NPIs across the different countries would lead to earlier subsequent epidemic peaks.

Phased Implementation

The lifting of restrictions may be carried out in phases. The sequencing of the types of restrictions to lift should consider the following:[111]

1. Degree of impact of containment measure or restriction on society and economy.[112]
2. Disease susceptibility and risk of morbidity and mortality among individuals in the target group.
3. Risks of transmission (including downstream risks to at-risk groups).
4. Effectiveness of various containment measures.

The John Hopkins Bloomberg School of Public Health Centers has published a document on risk assessment in 3 dimensions (contact intensity, number of contacts, and modification potential) across 7 categories (non-essential businesses, schools and childcare facilities, outdoor spaces, community gathering spaces, transportation, mass gatherings and interpersonal gatherings). The document provides a qualitative assessment for risk stratification across various sectors based on expert opinion, which may be adapted for the local context.[113]

A preprint modelling study using demographic data from New Zealand considered a strategy in which all of society (bar essential workers) are locked down for 2-4 weeks to brake uncontrolled epidemic spread, after which those with no risk factors are encouraged to return to work and socialise while at-risk individuals remain at home under strict quarantine, resulting in controlled ICU admissions while the infection passes through the larger low-risk population. The modelling suggests that lowering the age threshold for quarantine to 50 years of age reduces ICU admissions drastically and isolating one-third of the population for six months is sufficient to avoid overwhelming ICU capacity throughout the entire course of the epidemic. Quarantine measures can then be lowered in stages, with each stage exposing successively higher risk populations.[114] Similar findings may be expected to hold for other countries, but will need to be adapted for local age demographics and hospital facilities.

The study pointed out a number of pressing logistical issues to be resolved in real-life implementation:

1. Establishing food delivery infrastructure for quarantined individuals.
2. Partitioning health care facilities so as to prevent mixing between quarantine groups.
3. Communication and public education.
4. Rearranging the workforce, given the large number of senior staff who will no longer be available in person.
5. Identifying new jobs needed to maintain effective quarantine.
6. Investigation and community engagement with ‘de-mixing' households, so that people in different quarantine groups are no longer living with one another. Such measures may be disruptive but are likely necessary. Individuals in the quarantine group currently living alone might consider moving in with other quarantined persons, and university students would be required not to return to their homes.

A preprint modelling study projected that a similar exit strategy with vertical confinement of population over 50 years old in Brazil would keep infections within healthcare capacity.[115] Another preprint study noted that the use of personalized clinical risk prediction models to guide restrictions may reduce the number of people kept in isolation, and allow restrictions to be relaxed faster without exceeding ICU capacity. However, this requires compliance with differential isolation policies.[116]

Another preprint study found that greater reductions in hospital burden and fatalities are achieved with more gradual relaxation of social distancing measures. It was also noted that herd immunity cannot be practically achieved with gradual relaxation of controls. The study found that for mitigation to work, social distancing measures must i) initially lower transmission rates to a narrow range, ii) vary in a precise and unfeasible manner, and iii) be maintained for a long period of time (over 6 months).[117]

The effectiveness of individual measures is available in the COVID-19 Science Report: Containment Measures Report (under Decreasing Social Mixing, Workplace and School Closures, Decreasing Social Mixing/Increasing Social Distance, and Community Hygiene).

Detailed plans on phased implementations of gradual easing were announced by countries such as Switzerland, Czech Republic and Austria. Some countries (eg New Zealand) have structured measures based on alert levels, while others have gradual time-based reopening without distinct phases. These are described in detail in the COVID-19 Science Report: Country Journeys.

Across countries, it has been proposed that a “new normal” is required[118], as opposed to a simple return to pre-COVID-19, given increasing instances of new cases in areas thought to have eradicated the virus. There is a need to proactively identify vulnerable populations, including marginalized sections of the society (eg homeless, migrant workers, LGBT communities, sex workers, refugees, elderly in nursing homes etc), as well as populations that avoid seeking healthcare, and/or avoid testing and their consequences.[119,120] Levels of containment measures vary across regions, and may be tailored according to local risk levels.

Risks

Easing lockdown measures runs the risk of the effective reproduction rate exceeding 1 and a resurgence of community spread. Social distancing should be maintained to the extent at which hospitals can cope with providing the clinical care needed.[121] In UK and US, the social distancing of elderly alone was projected to still result in a ICU peak demand that is 8 fold higher than available surge capacity.[122] A contingent exit plan is thus recommended.[123]

While there are studies that model the impact of the introduction of individual containment measures on COVID-19 transmission, these should be interpreted with caution given that most measures were introduced in countries concurrently or in quick succession.[124] It is unclear if there are synergistic or multiplicative effects gained from particular combinations of interventions, or if reversals of containment measures exert the same magnitude of effect on transmission as their implementation. A preprint study using the Oxford COVID-19 Government Response Tracker non pharmaceutical (NPI) stringency index found that the average intervention leverage across 23 countries is 0.01 (95% CI 0.0102 – 0.0112), and highlighted the need to monitor intervention leverage as NPIs are released.[125]

Several modelling studies have projected that rapid or earlier relaxation of measures can lead to subsequent outbreaks and/or increased deaths. A modelling study found that the relaxation of interventions may result in a second-wave exponential increase of cumulative case count when the effective reproduction rate (R_t) exceeds 1, even if control interventions were reintroduced thereafter. A duration longer than the duration of intervention relaxation would almost always be required to reduce disease prevalence to prerelaxation levels, along with more aggressive control interventions to drive R_t below 1.[126]

A preprint modelling study projected that a 15 day extension to lifting lockdown measures in Spain would limit the current epidemic peak to around 100,000 active cases and a 60 day lockdown period would delay a second peak till 2021.[127] Another preprint modelling study compared scenarios of rapid versus gradual relaxation of measures in the US, and projected that rapid relaxation results in a second outbreak with 788,815 deaths and shrinking of the economy by 28.2%, while gradual relaxation results in 221,743 deaths and shrinking of the economy by 29.4%. The study recommends very gradual lifting of quarantine measures for non-seniors as the best case in terms of limited deaths and less economic damage.[128] This is corroborated by a preprint modelling study in Australia that suggested that a staged relaxation of social distancing in a low transmission setting by increasing school attendance (to 60%), then lowering community-wide contact reductions and increasing workforce attendance (to 80%), with continued increased case isolation, may not result in a severe spike in cases. However, containment measures should be held longer before being eased if widespread community transmission was present.[129]

Another preprint modelling study also provide evidence that with other social distancing measures in place, the reopening of schools alone are not likely to majorly increase transmissions in England.[130] By nature of increased interactions between children, there will be some increase in transmissions, but the magnitude is also dependent on the age groups of children that return to schools. Older children in secondary schools would have more social interactions and pose higher risks of transmissions than children in primary schools. However, the measures in place for safe reopening of schools, such as only allowing select cohorts to return, reducing class sizes, and maintaining social distancing will further keep transmissions low.

Another preprint study simulated a scenario of early relaxation of measures in early May for the US, and found that further delays by one week in the re-implementation of control measures could result in 32,379 additional deaths in the US by July 1 2020.[131] The authors cautioned that daily cases can continue to decline for up to two weeks even after measures have relaxed, and is resultant from lag time in infection acquisition and case confirmation. Therefore, such a situation could lead to false hope and delays in re-implementation of control measures.

Hoffman B suggested that a reduction in social distancing of more than 50% will result in a rapid second wave in New York State. The preprint study also suggested that while one-time relaxations are comparable to phased relaxations for the majority of relaxation magnitudes, for large magnitude reductions, phased relaxation resulted in fewer deaths by September 1, 2020 as compared to a one-time relaxation in social distancing. Recurrent outbreaks into 2021 are likely, and cannot be avoided entirely although they may be mitigated through strong social distancing measures that are instituted early.[132]

A preprint study suggested that a second wave is commonly noted in modelling scenarios (with a peak that tends to be higher than the first peak if R_0 is less than 2.4), and a third wave is possible when 1/inverse of the average duration of infectiousness is between 5-7 days, and the transmission rate is up to 0.4 per day. An increase in the level of adaptation of the population to containment measures (novel social behaviour) increases the number of waves (from 2 to 6/7); no second wave occurs in the event of slow adaptation such that the first wave confers herd immunity.[133]

A preprint modelling study suggested that in the absence of testing of asymptomatic individuals and those without severe symptoms, an optimal response may involve 4 consecutive phases: quick activation of strong lockdown, light lockdown (above 60% intensity to keep R below 1) with decrease in disease prevalence but increasing ICU admissions, long period (1 year) with stable prevalence and sustainable ICU capacity (with contact rates increasing gradually from 40 to 80%), and terminal slow progressive release of lockdown with elimination of disease.[134]

A preprint modelling study highlighted that insufficient broader testing and contact tracing will mask rebound and exponential growth in cases in the context of a premature increase in contact rates.[135]

Notwithstanding, prolonged targeted isolation of certain vulnerable groups carries social and health costs, a decrease in adherence to isolation policies is expected over time.[136]

Critical success factors

Premature lifting of interventions should be avoided avoid a spike in cases and a second wave.[137,138] Gradual easing of lockdown measures should be carried out in conjunction with other exit strategies such as the ramping up of testing and rigorous contact tracing. Quarantine and treatment of infected individuals, including those with mild symptoms, should remain to limit further transmission.[139] The measures should be continuously monitored, with room for stricter containment measures (eg “cordon sanitaire”) to be reimposed as necessary.[140]

Adaptive triggering

The adaptive triggering exit strategy[141] is the easing of interventions and reinforcement of strict social distancing measures when a threshold is met. It is similar to gradual easing except that, instead of a single slope towards the lifting of all measures, adaptive triggering plans for a series of guided fluctuations of that slope.

Rationale

Modelling studies have shown that adaptive triggering measures may be effective in the control of the COVID-19 pandemic. A modelling study in UK pointed out that intermittent social distancing measures can maintain control of the COVID-19 epidemic in the United States.[142] Such an approach may represent a more palatable and sustainable control strategy, allowing populations and the economy to "come up for air" at intervals.[143]

Implementation

Adaptive triggering involves the initiation of social distancing (with or without school and university closures) when a threshold (such as weekly confirmed case incidence in ICU) is met. Social distancing measures are relaxed when cases fall below the threshold (Figure 3), and reintroduced again when they rise.[144]

Social distancing measures that are relatively less likely to contribute to transmission (eg walking alone with or without a mask in the open air) should be prioritised ahead of others (eg mass gatherings, crowds, cross-household visits) for relaxation. As much as possible, people should be educated on the mechanisms of spread and how to interrupt transmission so that they behave appropriately to reduce infections rather than to follow strict do's and don'ts without regard to context or contribution.

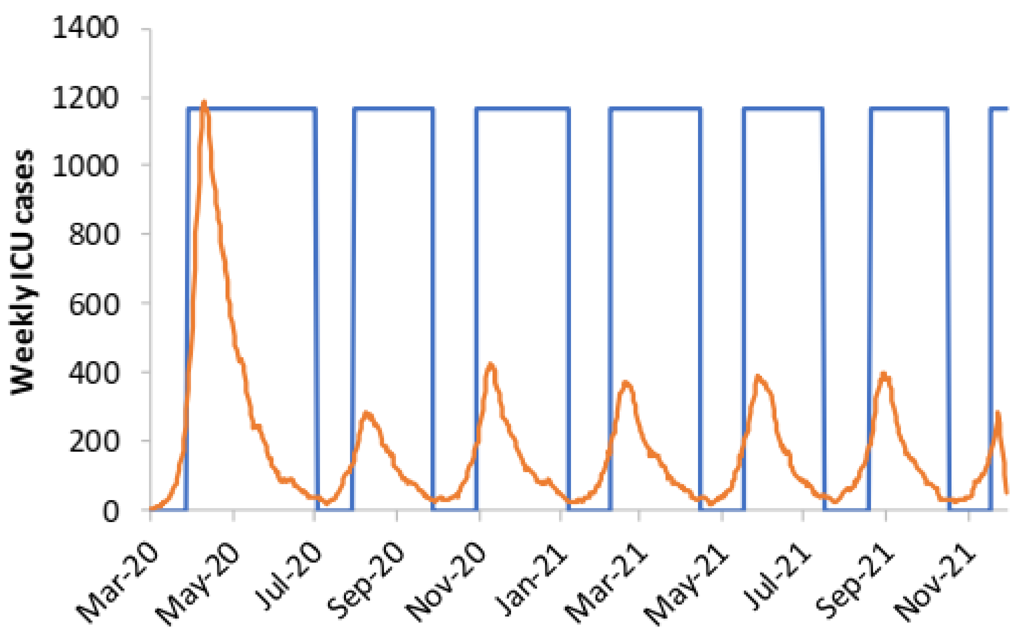


Figure 3: Illustration of adaptive triggering. Source: Ferguson N et al (2020)[145]

Widespread surveillance will be necessary to monitor when prevalence thresholds that trigger the start/end of distancing have been crossed. Critical care bed availability might be used as a proxy in the absence of widespread surveillance but the lag between distancing and peak critical care demand (approximately 3 weeks between start of social distancing and peak critical care demand) can lead to over-running of critical care resources. Over the course of the epidemic, the duration between distancing measures increases, as the build-up of immunity in the population slows infection resurgence.[146]

Several modelling studies (mostly preprints and on Western countries) have projected the workable impact of the adaptive triggering strategy over an approximate 2 to 2.5 year period, with infected cases kept within current medical care capacity. Most of the studies assumed use of widespread surveillance or critical care bed availability as indicators for the triggering/relaxing of distancing measures. The necessary duration of distancing measures required within a 2-2.5 year period varies within and across studies (ranging from 25% to as high as over 80% depending on virus transmissibility), and depends on the strength of measures, and the scenario.

Modelling studies projecting the impact of adaptive triggering strategies

Study	Description
Kissler S et al (preprint)	The study proposed that under current critical care capacities in United States, and using widespread surveillance or critical care bed availability to monitor and trigger the start/end of distancing measures, social distancing could last into 2022. Distancing measures are required to be in place 25-70% of the time (for varying scenarios of R and seasonality). Longer social distancing measures may need to be enforced if SARS-CoV-2 immunity wanes rapidly. The study incorporated population immunity into projections and pointed out that the length of time between distancing measures increases as the epidemic continues, as accumulation of immunity slows infection resurgence.[147]
Tuite A et al (preprint)	For the Ontario population, it was estimated that cycling on and off of distancing measures (with interventions triggered based on ICU capacity crossing a given threshold) kept the median number of ICU cases reduced below current ICU capacity. 13 months of social distancing, cycled on and off, reduced the percentage of population infected at the end of the 2-year period to 2%.[148] A combination intervention where enhanced case isolation/quarantine is applied with less restrictive social distancing in the adaptive triggering approach is promising. With increasing testing capacity, such a combination intervention can possibly strike the right balance between disease control and societal disruption.[149]
Karin O et al (preprint)	The modelling study proposes a related concept. The adaptive cyclic exit strategy involves a cyclic schedule of 4 workdays and 10 lockdown days, or any similar variant, which allows for control of the epidemic, along with predictability for businesses and the economy.[150]
Liu P et al (preprint)	The modelling study showed that implementation of an intermittent social-to-no-distancing arrangement in 50 US states would reduce medical demands by up to 80%, provided the duration of social distancing is less than or equal to five times that of the recurring normalcy period.[151] The study noted that there is a diminishing marginal benefit (negligible incremental benefits) of increasing the duration of distancing measures beyond the distancing to normalcy period ratio of 5:1.[152]

Study	Description
James A et al (preprint)	A modelling study on New Zealand simulated the combination of a low level of control (case isolation with household quarantine, that reduces R to 1.75) with periods of high control (that reduces R to 0.75) to keep the number of cases under hospital capacity. The switching strategy could involve strong control when ICU cases are close to capacity, and lifted restrictions when ICU cases fall to 50%, and would need to be continued for 750 days. It was suggested periods of high control should be triggered earlier (eg when ICU cases reach 50% instead of 100%) to address the time lag between infections becoming symptomatic and then requiring ICU admission, and the uncertainty about the effectiveness of strong control measures. The mitigation strategy fails if strong control measures only reduces R to 1.5.[153]
Duque D et al (preprint)	The study modelled that an optimal strategy to manage surge in hospital care demand in Austin, Texas will involve toggling between multiple periods of lock downs (90% reduction in transmission) and relaxed states (40% reduction in transmission)). The former would involve voluntary social distancing and testing-based containment. While triggers for enacting lockdowns are robust to lower compliance to social distancing measures during relaxed states, they are not robust to “leaky” cocooning of vulnerable populations (ie <95% level of effectiveness).[154]

Concurrent interventions that can reduce the overall duration of the epidemic while ensuring adequate care for the critically ill are:

- Increasing critical care capacities which in effect raises the threshold of the trigger for the reintroduction of measures (substantially reducing overall duration of epidemic).
- Treatments that can reduce proportion of infections requiring critical care/duration of infectiousness, which both reduces the load on healthcare facilities as well as raise the threshold for the trigger.
- Vaccines that can accelerate the accumulation of immunity in the population.[155]

Risks

If interventions cannot be reimposed in a timely and effective manner, there may be a negative impact on mortality and strain on health systems.[156] There are concerns on how acceptable it would be to the population to not only suffer intense quarantine once but repeatedly. Because of the lag between the imposition of measures and their effect, this strategy runs the risk of increasing oscillations between measures and relaxations.[1]

The strict social distancing measures that need to be reimposed regularly over a long period may have the same effects socially and economically as a permanent lockdown. Socially and economically, operations and planning ahead will be difficult for businesses, communities and individuals.

Modelling studies simulating adaptive triggering strategies have cautioned about the workability of the strategy. A preprint modelling study compared the impact of NPIs implemented in China, Italy, Belgium and Spain and pointed out that any significant reduction of R that does not bring it extremely close to 1 would overwhelm the healthcare

[1] Where severe measures which are introduced to manage the increase in cases substantially drive community transmissions down to very low levels, leading to relaxations of said measures which in turn allow the cases to rise again. The lag between measure and effect can create increasing oscillations between highs and lows (similar to how Cheyne-Stokes breathing is caused in some patients).

system because the height of the epidemic peak in an immunologically naïve population far exceeds the current ICU capacity anyway. Even if the epidemic could be controlled at the precise R level without overloading ICU capacity, the time needed to achieve herd immunity would be in years. They conclude the only viable plan currently is immediate quashing and containment of the epidemic at a minimal level driven by imported cases (as deployed in countries like South Korea, Hong Kong and Singapore) while awaiting arrival of medical solutions. If such strategies fail, heavy quarantine measures have to be imposed again quash the new epidemic flare.[157] Other studies have similarly pointed out that while the approach is tempting in theory, uncertainties in case trajectories and the effectiveness of control measures can lead to incorrect timing of implementation and drastic overshooting of hospital/ICU capacity.[158] There is also only a narrow feasible interval of epidemiologically relevant parameters within which a mitigation strategy, while keeping hospitalisation below available capacity, also facilitates the achievement herd immunity in the long term.[159]

Critical success factors

The adaptive triggering strategy requires a robust monitoring system, and rapid activation and reimplementation of aggressive interventions to prevent further disease transmission. The adaptability and compliance from the population is critical to its success.[160]

In a study using a modified SEAIR (susceptible-exposed-asymptomatic-infectious-recovered) model, optimisation-based decision making was used for the containment measures of social distancing, extensive testing, and quarantining of confirmed infected subjects.[161] The importance of keeping to quarantining of infected individuals had greater impact than social distancing, with both having greatest impact when implemented early. Extensive testing was also found to be less impactful during periods with major social distancing or lockdown. It is not meaningful for active surveillance with extensive testing of the general population to detect asymptomatic cases, since social interactions are minimal. However, extensive testing was found to be crucial in the period right before relaxation of social distancing or lockdown.

Mass testing

Rationale

Large scale, mass-testing (or universal testing) has also been proposed. Given reports of asymptomatic and presymptomatic transmission, testing for infection should be extended beyond just symptomatic individuals. As part of the testing, tracking, tracing strategy (TTT), testing enables rapid contact tracing and isolation to reduce the risk of disease transmission.[162,163]

Testing

Current tests include full genome sequencing, detection of viral RNA through nucleic acid amplification (eg PCR), as well as antibody testing. This section will focus on the detection of current infection. Antibody testing will be elaborated on in the section Immunity Passports. A combination of antibody, antigen and RT-PCR tests for mass testing has been recommended.[164]

Two varying approaches have been proposed:

1. Random testing, eg sentinel surveillance.

2. Targeted testing, eg of healthcare workers and workers providing essential services or community-facing roles, close contacts of confirmed cases and patients with symptoms[165], followed by testing to support deconfinement based on risk profile and risk of disease transmission.[166]

Paul Romer proposed that a nonspecific policy is much more disruptive than a targeted policy guided by frequent testing.[167] Through hypothetical simulations, he suggested that the following combinations may achieve a cumulative infection rate of below 20% over 500 days:

1. Random testing of 7% of the population daily, or approximately once every two weeks per person, assuming a Type I error (false positive) of 1%, and Type II error (false negative) of 20%.
2. Random isolation of 3% of the population daily, which translates to an average isolation rate in the population of 50% after accounting for isolation period.

The extent of testing plans can range from minimal to universal, with different scales in terms of the segment of the population (eg only symptomatic vs all individuals) tested, frequency of tests, percentage of population tested, and total costs of tests.[168] To scale up testing, Paul Romer further suggested that testing start with essential workers, followed by categories of people that are keen to return to work urgently, followed by everyone.[169] A timeline of testing solutions (short-term, medium-term and long-term) has also been proposed.[170]

In contrast, Cleevy et al suggested that at least 21% of the population has to be tested to everyday (or approximately once every five days per person) to obtain a R' below 1. Stratified periodic testing (over 25% of specific groups such as healthcare workers, key workers, and at high risk of disease transmission daily) was suggested as a feasible method to eliminate disease transmission.[171]

There is currently little scientific evidence on the optimal mass testing strategy, with mostly only preprint papers that present analyses of impacts from existing testing strategies or model possible strategies.

Optimisation

Mass testing is a very costly exercise and not all countries have the financial and manpower resources to support such a strategy for prolonged periods. Multi-layered surveillance approach with priorities to patients presenting in fever clinics in China have been found in a preprint study to be more sensitive.[172] Improving flu vaccination coverage has also been proposed to help with the screening and surveillance efforts as it helps limit testing of patients presenting similar symptoms due to influenza.[173]

A preprint paper by researchers in Google presented results from simulating various scenarios of different testing strategies.[174] For mass testing of the general population alone, testing of 30% of the population daily was needed to achieve containment. This was deemed inefficient since it is such a high rate that requires a large amount of resources. Therefore, the authors suggested that the same amount of tests and resources could be used on symptomatic patients and their contacts, which would be is much more efficient. However, simulating testing of symptomatic patients and their contacts, they showed containment can only be achieved when testing was done within 0.2 days of symptom onset to allow for speedy quarantine and contain spread, which is not possible to achieve.

The authors simulated a scenario of taking two days to detect an infected individual, and showed that containment was possible if 100% of the contacts were traced and tested. The authors concluded that to safely exit lockdowns, swift testing and tracing with large coverage can drive *R* below 1 to achieve containment. Otherwise, mass quarantining with lockdown and social distancing would need to continue and an exit is not possible.

Some studies have suggested testing pooled samples for community surveillance, ie pooling samples of groups (of 9-10, or even up to 48 samples per group), to increase the efficiency of tests. However, this is only feasible if disease prevalence is low.[175,176] One published study simulated different combinations of sample pooling and stages of pooling before testing of individual samples within a positive pool.[177] The study found that the optimal strategy combination varies with the prevalence of infection, with pooling of 16 samples in 3 stages of testing optimal for low prevalence of 0-3.5%, while pooling of 3 samples in 2 stages is optimal for high prevalence of 12-30%. Beyond 30% prevalence, pooling of samples for testing should not be done. Results of studies on test efficacies and pooled testing are detailed in the COVID-19 Science Report: Containment Measures.

A preprint modelling study comparing social distancing and mass testing (with subsequent isolation of cases) found that mass testing alone can be just as effective in reducing R_0 as social distancing. A 1.7666 times higher detection rate can bring R_0 down to one. This is equivalent to testing the entire susceptible population roughly once every 10 days. Mass testing should be continued even after the number of infected cases falls and an increasing proportion of survivors become immune, albeit at a reduced frequency, unless the virus has been defeated completely globally. Where testing capacity can be ramped up, mass testing alone or coupled with less severe social distancing measures can be an effective strategy which results in far less disruption to economy and societal functioning.[178] Another preprint modelling study in Brazil noted that an increase in proportion of testing above 40% of the infected population (up from the estimated 20% at present) through expanding the testing criteria to include mild/moderate/asymptomatic cases, can decrease confirmed cases with immediate isolation of confirmed cases.[179] A preprint modelling study in Mendoza, Argentina reiterated the importance of detecting asymptomatic infected individuals (at least 45%) to avoid mass quarantine.[180]

Another preprint study compared active testing and isolation (ATI) with random testing and isolation (RTI), deterministic testing and isolation based on contact tracing (DTI), and isolation based on symptoms without testing (NTI) in 3 simulations, with testing capacity up to 5% of the population. It found that ATI outperformed other strategies on 3 measures – burden on healthcare system, total morbidity, and economic and social impact. With 0.1% of the population previously infected, and up to 0.3% of the population tested daily, ATI can reduce the quarantine period of large populations of the population, and the peak load in healthcare system by 18% as compared to random testing, and by 10% compared to contact tracing without controlled testing. ATI involves identifying infected individuals based on symptoms or preceding test results and isolating them, isolating first-order contacts for 14 days or more, updating the beliefs over the population graph, and actively testing people who have the highest likelihood of infection (probabilistic analysis based on contact data – eg number of contacts, duration of contact).[181]

Another preprint modelling study assessed the various strategies with reopening of schools together with relaxation of lockdown measures in the UK.[182] The study found that a second COVID-19 pandemic wave can be prevented with an enhanced test-trace-isolate (TTI) strategy, by testing between 25% and 72% of symptomatic individuals, tracing between 40% to 80% of the contacts of symptomatic individuals, and isolating both symptomatic and confirmed cases. Specifically for the reopening of schools, prevention of a second wave would require testing 51% of symptomatic individuals and tracing 40% of their contacts. A key main assumption of this study is that 70% of the cases are symptomatic, while 30% are assumed asymptomatic.

A preprint study highlighted that social distancing alone will result in very slow release of quarantined individuals who are susceptible. Universal testing alone will need to be done at an average testing frequency of once every 2 days (Italy) to once a day (USA) for each person. If combined with contact tracing and/or if testing can pick up infections during the latent phase, the testing frequency required is reduced to between once every 5 days (Italy) to once every 3 days (USA). These estimates assume test sensitivity of close to 100%, and immediate isolation following positive test results.[183]

Considerations

Test sensitivity and specificity

The impact of the sensitivity and specificity of diagnostic tests on the number of false positives and negatives must be analysed. Given the multiple combinations of the types of samples (eg nasopharyngeal swabs, oropharyngeal swabs, sputum, oral swabs, bronchoalveolar lavage fluid, rectal swabs), types of test kits (each with varying sensitivities and specificities, as well as stability issues), as well as combinations of testing strategies (eg weekly vs twice weekly testing, targeted vs random testing among different groups), surveillance information on the current prevalence of infection (including asymptomatic infections) and a consolidation of feasible testing options will guide further modelling.

A list of currently available test kits, along with their reported sensitivities and specificities, is available in our COVID-19 Science Report: Diagnostics report, and a list of rapid-test kits is available in the report by the Tony Blair Institute of Global Change.[184]

Technology may assist in the prioritisation and triage for testing, coordination of testing, delivery and distribution of test kits, automation (eg in Spain), and aggregation of data for R&D.[185]

Implementation

Principles for mass testing include diversity and decentralisation, transparency, innovation, oversight, quality accreditation with rapid approval, and communication.

To scale up, diagnostic tests should be rapid, available at point-of-care in hospitals and primary care along with distributed network testing, involve decentralised lab processing but with oversight and coordination, and should be supported by global supply chains.[186,187,188] The optimization of lab space, use of white-label reagents instead of proprietary reagents, harnessing of multiple suppliers, and development of proper infrastructure have also been recommended.[189] Beyond healthcare facilities, testing can be carried out at drive-through or walk-through testing facilities[190], and via mobile testing for at risk seniors at their homes. Self-testing kits may be considered after validation to reduce the burden on healthcare services.[191,192] Pharmacies may also be considered as testing hubs for expanded access.[193]

Test results should be supplemented with clinical and sociodemographic information of both those who test positive and negative[194] where possible to enhance epidemiological surveillance. The feasibility of a universal testing programme has to be first assessed.[195]

Testing parameters should be monitored, and can be used as an indicator for transition to another phase. For example, CDC has suggested phase transition thresholds – percentage of positive tests below 10-20% over 14 consecutive days, and median time from test order to results of ≤2-4 days.[196] Others have suggested a 5% threshold for rate of positivity in testing.[197] Combining test results from RT-PCR tests and serological tests for reporting can hamper surveillance efforts, as only positive RT-PCR tests are an indication of active infection.[198]

Population-wide testing

In Iceland, following initial targeted screening of persons suspected to be at high-risk of infection, population screening was opened for all other residents. Registration was conducted online, and sample collection was done in the capital. 9199 individuals (6% of the population) were screened. Nasopharyngeal and oropharyngeal samples were combined in a single tube for each individual. Viral RNA was isolated and extracted within 24 hours, and testing was done with quantitative RT-PCR with sequencing. Random testing can enable an understanding of risk factors for viral susceptibility. Haplotype analysis showed concordance (difference of less than 3 mutations) between 295 out of 369 pairs of individuals identified by contact tracing and may support the identification of clusters.[199]

In Vo'Euganeo, a town in Italy with approximately 3000 residents, full quarantine and blanket testing with nasopharyngeal swabs was performed. A second round of test was performed less than two weeks apart (~after 9 days).[200,201] Based on data presented in a preprint study, 85.9% and 71.5% of the 3275 residents were tested in the first and second test respectively. 2.6% of the population tested positive for SARS-CoV-2, and 43.2% (95% CI 32.2-54.7%) of confirmed SARS-CoV-2 infections were asymptomatic.[202]

While testing is not conducted population-wide in South Korea as reported on 7 April 2020, testing is conducted at a rate of 8996 per million of its population (compared to 6666 per million in Singapore).[203] Testing was done in drive-through testing stations nationwide, and negative pressure and positive pressure walk-through booths.[204]

With a recent rise in cases in Wuhan, China embarked on an ambitious exercise of testing all 11 million people in the city. In just under two weeks, about 6.68 million have been newly tested, with 200 found to be actively infected but not currently with symptoms.[205] This massive effort relied on pooling of 10 samples into a batch to be tested, which optimised the number of tests needed and time taken.[206] Results were then made available to individuals after 3 days via popularly social media platform app WeChat. This exercise is estimated to have cost at least 1 billion yuan (USD $140 million).

New approaches in testing[2]

Project	Description
Mobile or home testing to reduce unnecessary ambulance use and hospital visits in the detection process (London, US)	Potential cases referred from GPs, National Health Service's (NHS) hotline or local emergency departments are triaged over the phone to ensure that they are well enough to remain at home and self-isolate. A healthcare professional with PPE training is then sent to their homes to perform the test within 24 hours of referral, after which those who are found to be infected are admitted to hospital. Such a practice reduces the downtime for ambulances which can be out of service for up to eight hours for decontamination after carrying potential cases to hospital for testing.[207] Other NHS trusts, and states in US have adopted this as well.[208,209]
"Drive through" scheme to relieve pressure on hospital and ambulance services	Patients referred by NHS 111 will be sent to the "drive thru" service, with pregnant women and those seriously ill excluded under its protocols. Nurses based at the centre will put on PPE before travelling outside to collect swabs from patients in their cars. There has been some concern that those unable to drive may end up having someone

[2] Adapted from COVID-19 Science Report: Containment Measures report.

Project	Description
(London, Community Healthcare NHS trust, Edinburgh, Scotland, South Korea)	bring them to the centre, potentially putting another person at risk of infection.[210] A "drive through" testing centre has recently opened in Edinburgh.[211] "Drive through' coronavirus testing facilities are also open to the public in South Korea.[212] Some of South Korea's testing centres are located in less populated areas in preferably large parking lots. Features include: • All communication made by mobile phone except for specimen collection, with use of contactless thermometers and electronic payment systems. • Open tents of temporary buildings used for work booths. • PPE of inner and outer gloves, N95 respirator, eye–shield/face shield/goggles, and hooded coverall/gown required for HCWs with direct contact with testees. Additional disposable apron gown and gloves are changed for every testee with hand disinfection with 70% alcohol. • Nasopharyngeal and oropharyngeal swabs taken by HCWs at the specimen collection booth through opened car window. Car ventilation mode should be kept as internal circulation. • Sputum samples collected in the testees' cars by themselves with windows closed. Advantages and disadvantages: • 10 minutes per test (one-third shorter than conventional screening, which requires 30 mins for cleaning of specimen collection rooms) with 100 tests per day being able to be done. • Excludes risk of cross-contamination between testees. • Possibility of specimen contamination by HCWs' PPE as HCWs do not change PPE for every testee. • Protection of HCWs from bad weather conditions. • Dehydration from long working time wearing PPE. • Limited prompt management of medically unstable testees with hospitals located some distance away.[213]
Walk through testing (South Korea)	In negative pressure booths, testees stay inside the disinfected booth while healthcare workers stay outside the booth to disallow a direct contact between the two. This reduces the risk of transmission of infection to the tester as there is no direct contact. PPE donned by the healthcare staff include gloves, gown and a disposable face mask. In positive pressure booths, the tester stays inside the booth while the testee remains outside the booth. This reduces the need to disinfect the booth after each test.[214]
Community screening stations (Taiwan)	Taiwan's effectiveness in surveillance, detection, quarantine and isolation is in part due to its tiered primary healthcare model:

Project	Description
	• Tier 1: Walk-in clinics provide general care including for chronic diseases and mental health. Clinics are equipped with standard protection and general diagnostic equipment. • Tier 2: Community Healthcare Groups Prepared Clinics accepts patients from walk-in clinics with upper respiratory symptoms, fever and possible COVID-19 cases. Government provides these clinics with protective equipment and subsidies to recruit more CHGPCs as they are the first responders to public health emergencies. • Tier 3: Community screening stations are equipped with imaging, testing and quarantine facilities. They take in suspected COVID-19 cases from Community Healthcare Groups Prepared Clinics and treat mild cases. • Tier 4: Medical centres/designated hospitals treat serious cases referred by community screening stations. 90% of Taiwan's clinics participate in National Health Insurance, allowing for rapid response via education, diagnosis, isolation and referrals. Through this tiered model, COVID-19 management will ideally not be at the expense of other acute and chronic care functions.[215]

Case finding and contact tracing

While it has been proposed that serological tests can be used to supplement case finding (including the detection of asymptomatic patients), there is a time lag between the onset of symptoms and the development of antibodies, and therefore a window when tests are negative for infected persons.

Voluntary reports of mild diseases (such as through participatory surveillance), and/or indirect signals of disease spread (such as a spike in searches for unusual symptoms) may aid in early detection of cases. Pooled and anonymised data, managed with proper steps to ensure data protection and privacy[216], may also aid in modelling and forecasting.[217]

It has been proposed that contact tracing may be scaled up by enlisting the help of non-public health staff and volunteers to carry out contact tracing activities (eg interviewing cases to obtain contacts and following up with the contacts for quarantine), repurposing existing resources (such as call centres or other national hotline services) for contact tracing, and using technology. It should be noted that new staff and volunteers should be trained and supervised during the initial phases. Contact tracing in complex settings such as healthcare facilities should continue to be carried out by public health professionals, with specialist public health input. Modifying the follow-up process of contacts (eg stratifying intensity of follow-up based on contact time and exposure risk[218], as well as occupation, setting, and risk of further transmission to vulnerable populations) may conserve resources, but may also reduce the effectiveness of contact tracing.[219]

Given the limitations of manual tracing, "app-augmented" contact tracing may be considered. Automated and manual contact tracing should be viewed as complements rather than substitutes.[220] App designs may be user-centric or system-centric. The former relies on "decentralised" data storage (of key codes of interactions) on users' handsets, and automated alerts when infected individuals update their diagnosis on apps, which may enhance privacy. The latter relies on "centralised" data collection with the matching process to send out alerts completed on a computer server, which may maximise public health insights, allow for risk scoring,[221] and sidestep issues of false positives and self-reporting errors.[222] Algorithms for contact tracing may be refined depending on disease spread - digital contact tracing may be extended to entire households, or second or third degree contact tracing can be performed if required.[223] Examples of contact-tracing apps include Singapore's TraceTogether, NHSX app, and a Bluetooth-based platform co-developed by Apple and Google. Nonetheless, issues with user privacy, data security (trolls and hacks), operating system (convenience and user-friendliness), and legal safeguards[224] should be addressed. Adequate penetration and uptake rates are required for effectiveness.[225] A report in UK suggested that a containment strategy with app-based tracing is effective with an uptake rate of 80% among smartphone users, or 56% of the entire population. Given low smartphone use among the elderly, it was recommended that shielding (partial lockdown) be continued.[226] It should be noted that some individuals (eg healthcare workers) may not carry their mobile devices with them at work or in social settings.

The use of web-based applications for data entry, followed up by phone calls, has also been proposed. Symptom trackers may also be used for population-level monitoring.[227] Contact tracing management software include Go.Data,[228] which allow for data analysis, visualisation of chains of transmission by category, and export of data for sharing or analysis using other software.[229]

South Korea adopts a COVID-19 Smart Management System (SMS), for contact tracing. Beyond a smartphone app, data from multiple organizations (such as National Police Agency, Credit Finance association, smartphone companies, and credit card companies, CCTV footage) are aggregated in a database to provide a real-time feed for epidemiological tracking. This enables the Korea Centers for Disease Control and Prevention (KCDC) oversees to cut contact tracing time for each individual to approximately 10 minutes. Individuals who have been in close contact with confirmed cases are quickly notified and quarantined.[230,231]

Beyond augmenting traditional interview-based individual-based contact tracing with technology, thought should also be given to designing new approaches to contact tracing. For example, besides obtaining a list of possible contacts from each infected person and calling each one, telecommunication companies can assist by sending messages to all persons whose mobile phones were in a particular vicinity in the same time window to inform them of their risks, to monitor themselves and to recommend actions. Those who detect symptoms could come forward themselves without being individually contacted, and the others would be encouraged to behave responsibly.

In addition, the separate apps created by various agencies to help with the management of the pandemic could be combined into a single utility app with the features of TraceTogether and SafeEntry plus access to services and benefits arising from the outbreak. (This will incidentally increase the needed penetration of TraceTogether for more effectiveness).

A preprint modelling study noted that the timing of quarantine is a major determinant in the risk of community transmission. A quarantine time of half a day before symptom onset of an infected individual is able to reduce the effective reproduction number R from 2.32 to 0.76 (95% CI 0.66-0.86), whereas quarantine one day after symptom onset results in R of more than 1 and thus community spread. Timing to quarantine plays a role in determining detection efficiency. The model estimates that a 1-day delay and 6-day delay in quarantine reduces daily detection ratio from 71% to 60% and 31% respectively.[232] A published study noted that no parameter combination can ensure epidemic control if there is a 3-day delay or more in notification of contacts.[233]

The effectiveness of testing and contact tracing is dependent on

1. Percentage of infected individuals traced and isolated.
2. Percentage of asymptomatic or pre-symptomatic transmission out of all transmissions (related to number of asymptomatic cases).
3. Time from symptom onset to isolation.
4. Number of initial cases (Figure 4).[234]

Mathematical modelling found that highly effective contact tracing and case isolation is enough to control a new outbreak of COVID-19 within 3 months in most scenarios (R_0 1.5, 2.5 and 3.5 were used). For higher R_0 transmissibility scenarios, effectiveness of contact tracing needs to be significantly higher to control the outbreak. More than 50% of contacts need to be traced for R_0 of 1.5, more than 70% for R_0 of 2.5 and more than 90% for R_0 of 3.5.[235]

A preprint modelling study comparing different strategies in the scenarios in London, Wuhan, UK and Hubei projected that with effective contact tracing (with less than 5% of population in contact with infected individuals), a new outbreak can be successfully controlled in under 100 days with no peak time in all 4 regions.[236] However, another recent preprint study indicated that that rapid diagnosis and isolation alone cannot control outbreaks of SARS-CoV-2 but can contribute to reducing the growth rate and doubling time of epidemics, thus buying time by spreading severe cases out over a longer period of time, and potentially reducing the total infected cases, and reduce peak healthcare demand. The potential for containment will be seriously jeopardized when asymptomatic cases comprise more than 30% of infected cases.[237]

Another preprint study noted that the rate of isolation following testing has to be fast (δ^{-1}= 0.5 day) given reporting delays, to eradicate the disease. Given that this may be difficult to implement, carriers of the disease should be identified early through contact tracing.[238]

A preprint study noted that contact tracing of contacts-of-contacts reduces the size of outbreaks beyond that that results from tracing of contacts only. However, a large proportion of the population may have to be quarantined at any one time. This may be reduced by combining contact tracing with testing and releasing of quarantined cases, or physical distancing to reduce the number of links.[239]

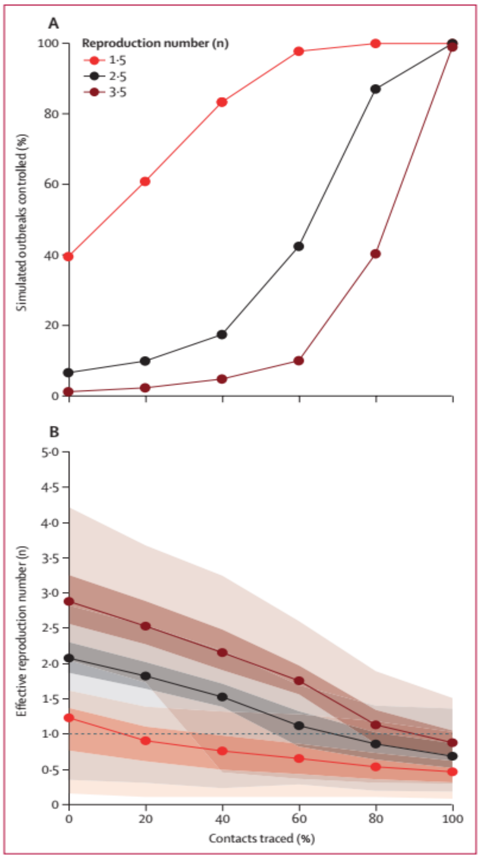


Figure 3: **Effect of isolation and contact tracing on controlling outbreaks and on the effective reproduction number**
(A) The percentage of outbreaks that are controlled for scenarios with varying reproduction number (R_0), at each value of contacts traced. The baseline scenario is R_0 of 2·5, 20 initial cases, a short delay to isolation, 15% of transmission before symptom onset, and 0% subclinical infection. A simulated outbreak is defined as controlled if there are no cases between weeks 12 and 16 after the initial cases. Other scenarios are presented in the appendix (p 2). (B) Effective reproduction number in the presence of case isolation and contact tracing. Median, and 50% and 95% intervals are shown.

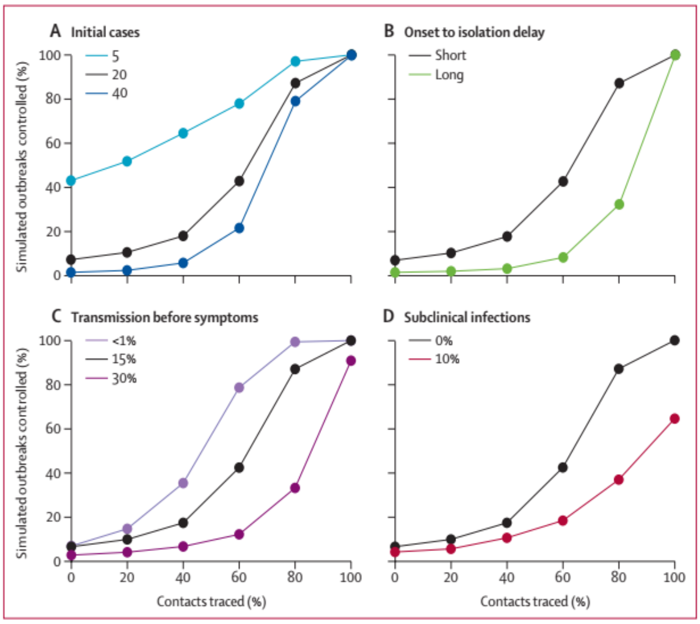


Figure 4: **Achieving control of simulated outbreaks under different transmission scenarios**
The percentage of outbreaks controlled for the baseline scenario, and varied number of initial cases (A), time from onset to isolation (B), percentage of transmission before symptoms (C), and proportion of subclinical (asymptomatic) cases (D). The baseline scenario is a basic reproduction number (R_0) of 2·5, 20 initial cases, a short delay to isolation, 15% of transmission before symptom onset, and 0% subclinical infection. Results for R_0=1·5 and 3·5 are given in the appendix. A simulated outbreak is defined as controlled if there are no cases between weeks 12 and 16 after the initial cases.

Figure 4: Source: Hellewell J et al (2020)[240]

Safe distancing (close contact)

The guideline for a safe distance of 1-1.5 metres takes into account the usual travel distance of droplets; larger respiratory droplets (>5 μm) travel short distances of less than 1m.[241] However, this travel distance before contacting the floor is in part dependent on the size of droplet particles, the speed at which they are expelled, and relative humidity. A smaller particle size, faster expulsion speed and lower humidity (and thus slower evaporation) is associated with further travel distances.[242] A paper published on JAMA suggested that the recommendations of 1-2m distancing from symptomatic COVID-19 patients do not account for long-distance travel by high-momentum turbulent gas clouds carrying droplets that may be produced during sneezing and coughing. With peak exhalation speeds of 10-30m/s, turbulent gas clouds can span approximately 7-8m.[243]

A study of an outbreak in a restaurant in Guangzhou found that transmission occurred even with a distance of more than 1 metre between some of the cases. While the air conditioner did not show traces of the virus, it was suggested that the strong airflow from the air conditioner could have allowed droplets to be transmitted over such long distances. The key factor involved was the direction of airflow.[244]

A preprint simulation study found that, in the absence of external wind, the largest exposure to droplets occurs if a person is positioned directly in line behind and in the slipstream of another person.[245] At a walking speed of 4 km/h, no droplets will reach the upper torso of a person at a distance of about 5 m behind, while at a running speed of 14.4 km/h this distance is about 10 m. The study recommended the avoidance of droplet exposure by increasing social distances and avoiding the slipstreams of other persons.

An investigation in COVID-19 patient rooms in a hospital in Iran using the impinger technique found that all air samples taken between 2 and 5 meters from the patients' beds were negative for SARS-CoV-2.[246] In contrast, a preprint study in Nebraska found that 63.2% of air samples taken from the isolation rooms of patients with COVID-19 tested positive for SARS-CoV-2 (with a mean concentration 2.86 copies/L of air).[247] Air samplers worn by sampling personnel were all positive although patients were not observed to have coughed.

The debate continues on whether viral particles can be aerosolised by sneezing or coughing.

A preprint study conducted in Wuhan involved tests for three different types of aerosols (total suspended particle, size segregated, and deposition aerosol).[248] Public areas outside the hospitals had undetectable or very low concentrations of SARS-CoV-2 aerosol, except in one crowded area near a department store entrance. The study recommended crowd control, ventilation and cleaning of toilets, use of personal protection measures e.g. masks, and sanitization of high-risk areas. In hospitals, workstations showed to have the lowest aerosol concentration (1-9 copies/m^3), while patient mobile toilets had the highest concentration (19 copies/m^3). The peak concentration of SARS-CoV-2 aerosols appeared in 2 size ranges: 0.25-1microM, and >2.5microM. This might be due to different formation mechanisms. In ICUs, the deposition rate is 31-113/m^2/hour. In an experiment, aerosols were generated with a three-jet Collison nebulizer and fed into a Goldberg drum.[249] SARS-CoV-2 remained viable in aerosols for 3 hours (throughout the duration of the experiment). The infectious titre fell from $10^{3.5}$ to $10^{2.7}$ per ml. Nonetheless, it is uncertain if viral materials in small particle aerosols retain their infectivity.[250]

A study of all staff with 'close contact' within 2 metres of a patient for more than 15 minutes, or performed aerosol generating procedures without appropriate personal protective equipment (PPE) ie N95 respirator, face shield, gown and gloves, but wore a surgical mask, did not display symptoms of SARS-CoV-2.[251]

A preprint study reviewed the implications of applying a stricter definition of 'close contact' for COVID-19 (ie longer contact time) which can reduce the burden on contact tracing services. The UK currently defines a close contact as 15 minutes within 2 metres in the two weeks before detection. The study, which utilises data on social encounters in the UK from a survey, found that changing the definition of "close contact" increases the risks of untraced contacts.[252]

Risks

False positives in testing result in unnecessary strain on the health system capacity and undue stress on patients as well as their close contacts, while false negatives run the risk of community spread and a false sense of security among patients. With large numbers of tests carried out, even a small difference in sensitivity and specificity can result in a large number of false positives and false negatives.[253] False positives may exceed true positives when there is a low prevalence of COVID-19 in the tested population even with small errors in tests.[254]

Individuals and groups who test positive may be subject to discrimination. Testing policies should take into account civil liberties, due processes, health ethics and privacy protections. Isolation should be supported by job protections, resources and access to health care.[255]

Critical success factors

Critical success factors for mass testing include the availability of test kits, adequate sensitivity of antigen test kits to detect cases before further transmission, good uptake rates for testing, and efficient contact tracing and quarantine of close contacts following testing.

Immunity passports

Immunity passports are immunity certificates that allow individuals immune to COVID-19 to return to work and the community.

Rationale

The issuance of immunity passports (or "immunity permits" or "immunity certificates") is a possible measure to ease lockdown and social distancing measures. Individuals who have recovered from COVID-19 are assumed to have immunity against SARS-CoV-2 are provided a certificate to that effect. This can be implemented in a physical form such as an ID card or bracelet or in an electronic form such as a secure digital certificate[256] or database record accessible with an application and/or QR code.

This may allow part of society to reopen and resume functions and businesses. Individuals who are immune may return to work, serve in front line roles with higher risks of infection, and take on community roles to support those who remain in quarantine.[257] Frontline healthcare and emergency services workers should be prioritised for testing to determine their eligibility for immunity passports. Those with immunity passports may be exempted from wearing cumbersome full PPE, which may also optimise the use of limited supplies. On April 21, 2020, Chile announced its plans to proceed with the world's first immunity passports.[258]

Available serological tests

There are 3 main types of serological tests currently.

Type of test	Time to results	What it tells us	What it cannot tell us
Rapid diagnostic test (RDT)	10-30 minutes	The presence or absence (qualitative) of antibodies against the virus present in patient serum.	The quantifiable number of antibodies in the patient serum or if these antibodies are able to protect against future infection
Enzyme linked immunosorbent assay (ELISA)	1-5 hours	The presence or absence (quantitative) of antibodies against the virus present in patient serum.	If the antibodies are able to protect against future infection.
Neutralization assay	3-5 days	The presence of active antibodies in patient serum that are able to inhibit virus growth ex vivo in a cell culture system. Indicates if the patient is protected against future infection.	It may miss antibodies to viral proteins that are not involved in replication.

Source: John Hopkins Bloomberg School of Public Health, Center for Health Security (2020)

Venous and fingerstick blood samples (fingerprick assays) have been used for serological tests. A list of serological tests approved and in development in both US and other countries is available on the website of the Center for Health Security at John Hopkins University.[259]

Issues with serological tests and immunity passports

Uncertain levels of immunity

For immunity passports to work, an accurate test that can be used to determine immunity is required. The available serological tests using immunoassays for IgM, IgG, and IgA antibodies have been found to have limited cross-reactivity with other human coronaviruses (such as SARS-CoV or MERS-CoV).[260] While antibody tests are commercially available, further validations are required.[261,262]

It has been less than 6 months since SARS-CoV-2 was first detected in the human population, and uncertainties remain of the human body's immune response to the virus:

1. How quickly does the body take to produce antibodies?
2. How long does the body continue to produce antibodies after infection?
3. Do those that are asymptomatic or with mild symptoms produce detectable levels of antibodies?
4. Are the antibodies neutralising antibodies, ie can they prevent SARS-CoV-2 cell entry and reinfection?
5. Does the presence of antibodies guarantee lack of infectivity by a person?

The presence of IgM antibodies for SARS-CoV-2 has been observed in a cohort study 10 days or later after the onset of symptoms,[263] but has been separately observed as early as after 7 days in a patient.[264] After 14 days or more, seropositivity was noted in serum samples, for anti-NP IgG (94%), anti-NP IgM (88%) anti-RBD IgG (100%), anti-RBD IgM (94%).[265] In a study of a rapid point-of-care serology tests used when potential patients first present at emergency department (and later confirmed positive with real-time RT-PCR), 31 of 38 (81.6%) were found negative for both IgM and IgG.[266] Two studies have found that with their small cohorts, 100% had seroconversion 14 to 15 days after admission.[267,268] In a study of 173 patients, less than 40% of patients had antibodies from 1 week of symptom onset, although the percentage of patients with antibodies increased to 100.0% (Ab), 94.3% (IgM) and 79.8% (IgG) 15 days from symptom onset. The median time to Ab, IgM and IgG seroconversion was 11, 12 and 14 days respectively.[269]

In a study by Jin et al (2020),[270] 27 laboratory-confirmed positive patients (first symptom to serological testing was on average 16 days (mean), IQR 9–20 days) had antibodies tested before they were viral-negative. Of the 27, 13 (48.1%) were positive for IgM and 24 (88.9%) were positive for IgG, and <u>3 of 27 (11.1%) tested negative for both IgG and IgM.</u> In the same study, 34 laboratory-confirmed patients (first symptoms to serological testing was on average 18 days (mean), IQR 11–23 days) had antibodies tested after two oral swabs taken 24h apart tested negative. Of the 34, 19 (55.9%) were positive for IgM and 32 (94.1%) were positive for IgG, and <u>2 of 34 (5.9%) tested negative for both IgG and IgM.</u>

In a study by Du et al (2020)[271], 60 convalescent positive patients were tested for antibodies following 6-7 weeks of disease onset. Of the 60, 47 (78.3%) were positive for IgM and 60 (100%) were positive for IgG, with a higher IgG titre than IgM titre. The study further tested 10 of the convalescent patients twice (1 week apart) after two consecutive SARS-CoV-2 RNA tests were negative. They found that both IgM and IgG titres showed a decrease.

With changing levels of IgM and IgG through the course of SAR-CoV-2 infection, the use of serological tests could complement nucleic acid tests in identifying the stage of COVID-19 progression. While the limited evidence does suggest that the majority of patients had detectable levels of IgG antibodies upon recovery, the long term persistence of antibodies requires further investigation.[272,273] Furthermore, the findings were mostly from patients that were admitted to a hospital and may not be simply extrapolated to asymptomatic or mildly symptomatic individuals.

Risk of viral transmission even with detected antibodies

The presence of antibodies alone does not suggest that patients are no longer infectious, given that viral RNA and antibodies may be detected concurrently during active infection after a window period.[274] Tests for viral RNA should be carried out to confirm that individuals with positive serological test results do not have an ongoing infection. The Edmond J SAFRA Center for Ethics highlighted that immunity certificates should only be provided in cases where individuals have equal access to PCR testing, and where a recent negative PCR test result provides equal access to movement as immunity.[275]

Low sensitivity and specificity of tests

While there were plans to roll out self-administered 15-minute home testing (finger-prick) kits in UK[276], antibody test kits failed to demonstrate acceptable levels of sensitivity and specificity in validation tests. In Spain, failed test kits were also returned.[277] Individuals with false positive serological test results are susceptible to SARS-CoV-2 infections.

Risks of gaming the system

With the rolling out of immunity passports, those without immunity could be discriminated against. Those who are eager to obtain immunity passports in order to return to work and/or to former way of life may consider intentionally seeking to be infected through “infection parties” (much like “chickenpox parties”).[278] There is also the risk of counterfeit certificates or attempts to hack the online systems.

Mass implementation

For immunity passports to be implemented nationwide and internationally, there must be adequate resources for mass testing. A coordinated, standardised, secure yet accessible record system would also be required.

Risks

People run the risk of reinfection and transmission if the presence of antibodies does not translate to full immunity or if the immunity wears off with time. Given reports of patients who have tested positive for SARS-CoV-2 again after testing negative twice,[279] there is a need for more information on the risks of viral reactivation and reinfection among patients who have recovered. Further studies on immunological responses, and the validation of serological tests are required before adoption of immunity passports. With more information, further stratification of risk tiers by immunity status and levels may have to be considered.

Critical success factors

The success of this strategy is highly dependent on adequate and sustained immunity levels over time to ensure protection against reinfection. It is also dependent on a highly specific antibody test to ensure that individuals who are not immune to SARS-CoV-2 infection do not test positive in serological tests. Until further information on infectivity is available, safeguards have to be in place to ensure that individuals who have an active infection (ie with positive antigen and serological tests) are continued to be kept in isolation. Systems should be in place to avoid abuse.

Prolonged lockdown until vaccine

This involves a lockdown and mass isolation of the population until vaccines are administered. While a sustained lockdown would keep the number of infections low (and minimise the impact on the healthcare system), the population remains vulnerable until such time as the virus disappears (as happened with SARS) or herd immunity is acquired either through vaccination or through infections.

Effective therapeutics, including prophylactic treatment, may reduce the mortality and morbidity associated with COVID-19, thereby reducing demands on the healthcare system.[280] While effective therapeutics may reduce the strain on healthcare capacity, this final exit scenario is the development of a safe, effective and widely available vaccine to provide herd immunity on the population.

Rationale

In the absence of herd immunity, interventions are continued to prevent a surge in COVID-19 cases. An intensive suppression strategy with combined interventions will help ensure that critical care demand remains within existing capacity.[281] Relief will eventually come when a viable vaccine is available for the population.

Risks

Severe social and economic costs along with high unemployment are expected with a prolonged lockdown. A longer lockdown may increase the chance of a significant permanent reduction in standards of living.[282] Given that a vaccine may not be ready for another 12 to 18 months,[283] this strategy is not recommended.

Critical success factors

To consider this strategy, the threat and impact of COVID-19 must outweigh the political, economic, psychological, and social costs of a sustained lockdown.[284] The success of this strategy is contingent on the successful development, and widespread availability and adoption, of a safe and effective vaccine.

Conclusion

Potential exit options are summarised in the following table. For any one exit strategy, all critical success factors need to be met. For now, highly accurate low-cost rapid point-of-care testing has not been developed and sustainable immunity has not yet been demonstrated in order for immunity passports to be implemented. Lockdown until vaccines are available will be extremely painful.

The exit strategies actually doable at this time will be one or a combination of gradual easing, adaptive triggering and/or mass testing with contact tracing. The exit plan may involve a combination of the strategies above, either in parallel or in sequence.

Future pandemic preparedness should consider the following: standby diagnostics that are cheap and fast to develop, deep antiviral libraries, systems to rapidly scale up antibodies, vaccine platforms, early warning systems and simulations/germ games.[285,286]

Summary of key exit strategies

Options	Advantages	Disadvantages	Critical Success Factors
Gradual easing	Allows reconstruction of the economy, and gradual return to normal life while minimising the risk of a sharp spike in cases.	Potential resurgence of cases if too fast a release or if remaining measures are inadequate. Unequal burden, with higher social and economic costs for groups that are subjected to prolonged isolation Potential unnecessary burden if done slower than actually needed. Some population vulnerable to new imported infections until vaccine is available.	• Ability to sustain lockdown until pre-requisites for lifting lockdown are met. • Judicious combination with other exit strategies to minimise impact. • Good surveillance, and good judgement on what measures and when to relax. • Ability to reimpose measures if relaxed too quickly at some point.
Adaptive triggering	Allows economy and society to run while avoiding exceeding the health system capacity.	Management of public confidence will be challenging with cycles of strict measures imposed and lifted. Businesses and communities unable to plan ahead. Population vulnerable to new imported infections until vaccine is available.	• Robust monitoring system. • Ability to activate and deactivate interventions multiple times. • Adaptability and compliance of population.
Mass testing with contact tracing	Early isolation, treatment, and contact tracing which reduces transmissions. Keeps infection rate low.	False positives will strain health system. False negatives risk more transmissions. Feasible only when number of cases remain small relative to contact tracing capabilities. Population vulnerable to new imported infections until vaccine is available.	• Availability of appropriate tests with adequate sensitivity. • Ability and resources to do extensive testing. • Good uptake of testing by population. • Efficient contact tracing and isolation of close contacts following testing.
Immunity Passports	Allows partial recovery of economy by allowing immune individuals to return to work while shielding susceptible individuals	Potential reinfection if immunity wanes. False positives susceptible to infection. Some population vulnerable until vaccine is available.	• Demonstration of adequate and sustained immunity levels. • Highly specific antibody test. • Tight control against abuse and gaming.
Lockdown until Vaccines	Most aggressive way to ensure control of disease spread	Heavy social and economic costs in the meantime.	• Enforcement of compliance. • Eventual availability of safe, effective, widely available vaccine.

Search Method

This descriptive review was based on searches of research databases (PubMed and Google Scholar), relevant journals, science reports, preprint servers, expert comment, news sites, relevant government websites and Google. The search strings included a combination of the terms ‘exit strategy’ / ‘control measures’/ ‘pandemic’ / ‘epidemic’ / ’outbreak’ / ‘spread’, ‘COVID’ / ‘COVID-19’ / ‘SARS-CoV-2’ / ‘2019-nCoV’ / ‘coronavirus’ / ‘respiratory illnesses’, ‘border control’ / ‘travel restrictions’, ‘border quarantine’, ‘isolation’, ‘quarantine’, ‘detection’, ‘release’, ‘hospital’, ‘healthcare’, ‘protection of healthcare personnel’, ‘protection of healthcare worker’, ‘infection control’, ‘use of mask’, ‘face mask’ / ‘community hygiene’, ‘hand hygiene’, ‘risk communication’, ‘social distancing’, ‘workplace closure’, ‘school closure’, ‘business continuity plan’ / ‘BCP’, ‘working arrangements’ / ‘HR working arrangements’, workplace’, ‘effectiveness’ / ‘cost impact’ / ‘implications’.

Works reviewed include mainly policy or regulatory documents on general practices and recommendations, epidemiological/modelling studies, systematic reviews and qualitative/case studies that estimate or evaluate effectiveness or analyse influencing factors, and other relevant news articles and related references.

Acknowledgement

We are grateful to the following individuals for their assistance with the review of articles:

Lee Pei Yu

Zander Tay Yong Hong

Aaron Ho Kwun Han

Ho Yi Jie

John Tan Wen Yu

Sylvia Phua Yi Hui

Thng Zheng Huan Javier

Lee Yong Qin

Loh Xin Sheng

Jillian Too Hui Li

Veronica Lim

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