How Should We Deal With New Outbreaks of COVID-19?

Series COVID-19 & response strategy

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This is the seventeenth document in a series of discussion notes addressing fundamental questions about COVID-19 and response strategies. These documents are based on the best scientific information available and may be updated as new information comes to light.

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Authors: Clara Prats (UPC), Daniel López-Codina (UPC), Anna Vilella (Hospital Clínic-ISGlobal) and Antoni Trilla (Hospital Clínic-ISGlobal)*

The phased relaxation of confinement measures has led to an increase in mobility, greater contact between people and the arrival of small numbers of tourists from countries that are currently in an epidemiological situation similar to that of Spain. These developments will lead to an increased risk of infection, especially if people do not carefully follow the recommended personal preventive measures (physical distancing, hand hygiene and mask wearing) and avoid prolonged close contact and crowds, particularly in closed and poorly ventilated spaces. People are being encouraged to avoid the "3 Cs": closed spaces, crowded spaces and close-contact settings. SARS-CoV-2 is still with us: new cases are reported every day, in smaller but still significant numbers. If the virus is present and we are in contact with each other, the infection will spread.

In public health strategy, it is important to differentiate between containment and mitigation phases. During containment phases-before and after the peak or the first wave or successive waves-contact tracing is the main mechanism for attempting to control the spread of the virus. Contact tracing is carried out on a case-by-case basis. Chains of transmission are identified and monitored to detect new cases. Diagnostic testing, currently based on the polymerase chain reaction (PCR) technique, is performed as soon as possible (within 24 hours) and individuals who test positive are isolated. Contact tracers also try to identify all or most of the infected person's close contacts-those at highest risk-and quarantine them for 10 to 14 days. While in quarantine, these close contacts are monitored for symptoms.

* Clara Prats is an Assistant Professor at the Polytechnic University of Catalonia, the head of computational modelling at the Centre for Comparative Medicine and Bioimaging of Catalonia and a member of the Research Group on Computational Biology and Complex Systems. Daniel López-Codina is an Associate Professor at the Polytechnic University of Catalonia and a member of the Research Group on Computational Biology and Complex Systems. Anna Vilella is an Associate Researcher at ISGlobal, a physician in the Preventive Medicine and Epidemiology Department at Hospital Clínic de Barcelona and a Lecturer at the University of Barcelona. Antoni Trilla is a Research Professor at ISGlobal, a physician in the Preventive Medicine and Epidemiology Department at Hospital Clínic de Barcelona and a Professor at the University of Barcelona.

In certain epidemiological settings-in elder care facilities, during outbreaks, etc.--all close contacts should undergo diagnostic testing to rule out asymptomatic infection. The same strategy can also be applied when the incidence rate is relatively low. If new cases are not quickly detected and confirmed by diagnostic testing and their close contacts are not required to isolate (if they test positive) or go into quarantine (if they test negative), the chain of transmission grows rapidly and the outbreak becomes more difficult to control. To make matters worse, 40% of COV-ID-19 transmissions occur before the carrier develops any symptoms, which on average appear 5 to 7 days after infection. This incubation period provides a long window of opportunity during which a carrier who does not yet feel ill can come into contact with other people and perhaps infect them. Not everyone is equally infectious: between 10% and 20% of carriers are responsible for nearly 80% of the spread of COVID-19.

Once there is sustained community spread, it usually becomes impossible to track all the chains of transmission. This change marks the start of the mitigation phase, during which the number of new cases increases sharply before eventually reaching a peak and starting to decline, usually at a slower pace. During the mitigation phase, control measures are applied to the population as a whole and typically involve enforcing physical distancing between people. This is a strategy that can be considered and applied when the incidence rate is high. It is the only way to stop the spread of the disease when it is no longer possible to trace every chain of infection.

Most European Union countries are now in a low-incidence phase of the COV-ID-19 pandemic, during which **there will surely be new outbreaks** of various magnitudes. An outbreak is an abnormal number of cases of a disease affecting a relatively limited number of people in a particular place and at a particular time. Spain has provisionally defined an outbreak of COVID-19 as three or more cases grouped together in space and time, except at long-term care facilities, where the appearance of a single new case is defined as an outbreak.

Most of the new COVID-19 outbreaks have been the result of large groups of people gathering in closed spaces and remaining in close contact for a long period. The risk of transmitting COVID-19 in closed spaces is thought to be approximately 18 times greater than the risk of contagion outdoors.

The settings where most of the outbreaks have occurred include longterm care facilities for older people and for people with intellectual or behavioural disabilities, hospitals, churches¹ and other places of worship, cruise ships², nightlife venues (bars and dance clubs), workers' living quarters or dormitories (higher risk if workers also share transport), food-processing plants³ and prisons⁴. The risk of contagion in homes is lower: a Chinese cohort study⁵ found that household contacts developed the infection in less than 15%-17% of cases. Household outbreaks involving small numbers of infected or exposed people are less difficult to control •

² Moriarty LF, Plucinski MM, Marston BJ, Kurbatova EV, Knust B, Murray EL, et al. Public Health Responses to COVID-19 Outbreaks on Cruise Ships - Worldwide, February-March 2020. *MMWR*. 2020; 69:347-352.

³ Dyal JW, Grant MP, Broadwater K, et al. COVID-19 Among Workers in Meat and Poultry Processing Facilities - 19 States, April 2020. *MMWR*. 2020; 69:10.15585/mmwr. mm6918e3.

⁴ Okano JT, Blower S. Preventing major outbreaks of COVID-19 in jails. The Lancet. 2020; 395:1542-1543.

⁵ Jing QL, Liu MJ, Zhang ZB, et al. Household secondary attack rate of COVID-19 and associated determinants in Guangzhou, China: a retrospective cohort study [published online ahead of print, 2020 Jun 17]. Lancet Infect Dis. 2020; S1473-3099(20)30471-0.

Can Epidemiological Models Predict Outbreaks?

"It is impossible to predict when and where a new outbreak will occur or how serious it will be. It is, however, possible to model an outbreak once it is underway, provided that sufficient valid data are available." **The answer is no.** This pandemic has amply demonstrated the usefulness of epidemiological modelling, including predictive models and models designed to help us understand the epidemiological dynamics of COVID-19 and the different scenarios that could arise^{6,7,8,9}. However, **it is essential to understand both the scope and the limitations of epidemiological models**, which vary a great deal from one phase to the next:

• During widespread community transmission, models can be highly predictive. They are a key decision-making tool because they allow us to compare different scenarios. In health care resource planning, they can be used to quantify the need for special resources such as intensive care beds.

• **During containment phases**, models lose their predictive power. When effective contact tracing strategies are in place, small outbreaks appear and are contained at the local level. Outbreaks are difficult to predict because their appearance depends essentially on the behaviour of individuals or groups of individuals. Figure 1, based on data from Aragon published by the Carlos III Health Institute, shows how the predictive power of models changes over the course of the epidemic cycle. The exact timing of the start of an outbreak is highly unpredictable, as is its growth rate. However, once an outbreak starts to spread exponentially, models can effectively track the epidemic and predict scenarios. At the end of the first wave, the situation is similar to what it was before the epidemic but with much greater testing and control capabilities. It is impossible to predict when and where a new outbreak will occur or how serious it will be. It is, however, possible to model an outbreak once it is already underway, provided that sufficient valid data are available •

⁶ COVID-19 in Spain. Map of cumulative incidence by province and epidemiological week. Spanish Ministry of Health and Spanish Ministry of Science and Innovation.

COVID-19 Pandemic. Epidemiological updates and risk assessment. European Centre for Disease Prevention and Control.

⁸ <u>COVID-19 surveillance report</u>. European Centre for Disease Prevention and Control.

Rapid Risk Assessment. Coronavirus disease 2019 (COVID-19) in the EU/EEA and the UK - tenth update. European Centre for Disease Prevention and Control. 11 June 2020.



Figure 1. Course of the COVID-19 epidemic in Aragon and usefulness of epidemiological models at different stages.

Source: Carlos III Health Institute.

Can We Estimate the Likelihood of an Outbreak Using Data Analysis?

"The primary indicator for assessing the likelihood of an outbreak is the number of active cases. also known as the infectious population. This population cannot be measured with absolute precision, but it can be estimated by counting all cases diagnosed in the last 14 days."

The answer is yes. The primary indicator for assessing the likelihood of an outbreak is the number of active cases, also known as the infectious population. This population cannot be measured with absolute precision, but it can be estimated by counting all cases diagnosed in the last 14 days. The indicator recommended by the European Centre for Disease Prevention and Control is the number of new cases reported per 100,000 population over the past 14 days, also known as 14day incidence. If the number of active cases is very low, the likelihood of an outbreak is also very low; if the number of active cases is high, the likelihood of a new outbreak is also high¹⁰.

Other indicators of virus circulation may also be useful for assessing the likelihood of new outbreaks:

a) Wastewater analysis. The presence and concentration of viral genetic material in wastewater can be analysed to determine whether SARS-CoV-2 is circulating in a given population¹¹. Wastewater surveillance is a useful complement to traditional clinical epidemiological surveillance because it provides population-level information. Since wastewater can include viral genetic material excreted through faeces and urine, samples taken from local wastewater networks can be used to estimate the infected population in a given area. This population includes symptomatic, asymptomatic and presymptomatic individuals who may or may not have been diagnosed as well as infected individuals who have not (and may never) come into contact with the health system (remember that 80% of COV-ID-19 cases are mild or very mild).

¹⁰ Horton R. Offline: The second wave. *The Lancet.* 2020; 395:1960

¹¹ Lodder W, de Roda Husman AM. SARS-CoV-2 in wastewater: potential health risk, but also data source. The Lancet Gastroenterol Hepatol. 2020; 5:533-534.

Early studies¹² in the Netherlands, Australia and other countries suggest that wastewater surveillance could be used to detect the presence of SARS-CoV-2 before the virus begins to spread through a population. These studies further suggest that viral concentrations in wastewater largely correlate with increases in reported clinical cases of COVID-19. The findings reported demonstrate the potential of wastewater surveillance as an early-warning tool for alerting communities to local outbreaks. They also underscore the need for improved predictive modelling and better techniques for detecting SARS-CoV-2 in wastewater to clarify the relationship between viral material concentrations in wastewater and active infections in the population.

b) Systematic diagnostic testing. Systematic PCR diagnostic testing of a representative or random sample of a population or a specific population group (e.g. health professionals or pregnant women) is a useful screening method for estimating the overall prevalence of the virus because it identifies asymptomatic or presymptomatic cases in addition to symptomatic cases. In Wuhan, the Chinese authorities recently conducted mass testing after a slight increase in cases was detected. Between 6 and 11 million tests were administered over two weeks and 300 cases-nearly all of them asymptomatic-were detected. This does not, however, appear to be a very efficient strategy and it is certainly very difficult to carry out in practice.

In low-prevalence situations, pool testing can be used to detect asymptomatic carriers and support contact tracing. The technique involves combining samples from multiple individuals-usually around 10-and performing the diagnostic test on the pooled sample. If the result is negative, it is highly likely that all ten individuals are negative. If the result is positive, then the 10 original samples can be analysed individually to identify and isolate the infected individual(s). Although pool testing slightly increases the probability of a false negative-because the viral concentration in any individual sample becomes diluted when combined with other samples- this methodology can save time and resources •

¹² Mallapaty S. How sewage could reveal true scale of coronavirus outbreak. Nature. 2020; 580: 176-177.

Can We Assess the Risk of an Outbreak Getting Out of Control?

"In a given population, the likelihood of an outbreak getting out of control is ultimately determined by the capacity for diagnostic testing and contact tracing." The answer is yes. To assess the risk of an outbreak getting out of control, the first thing we need is a good warning system capable of detecting the early signs of an expanding outbreak. The second priority is to identify the factors that may fuel the expansion of the outbreak or help to get it under control. In a given population, the likelihood of an outbreak getting out of control is ultimately determined by the **capacity for diagnostic testing and contact tracing**. Once the incidence rate rises to a higher levels, the primary care and public health system may no longer be able to follow up infected individuals on a caseby-case basis and keep track of chains of transmission. Table 1 outlines key aspects involved in detecting an outbreak and assessing the risk associated with it •

Table 1. Key aspects to consider when assessing the risk of an outbreak.

• **Significant increase in case count**. A sharp increase in the number of cases is the first warning sign.

• **Consolidation of the rising case count over several days.** A sustained increase over time indicates a significant increase in the number of active cases— in other words, an infection hotspot that can generate new chains of transmission.

• **Simultaneous increase in case counts in nearby areas**. Small increases happening at the same time in adjacent regions can indicate a certain level of community spread.

• **Mobility in the affected area**. A high level of mobility implies a higher level of interaction among people and can contribute to the emergence of new hotspots in other areas.

• **Population density in the affected area**. High population density increases the risk of community spread and makes it difficult to trace every chain of contacts.

Tools for Early Detection and Risk Assessment

"In the current phase of the epidemic, it is essential to work at the smallest possible scale. If containment measures are necessary. it is always preferable to apply them to a single building than to an entire neighbourhood, town, county or province. However, it is difficult to analyse the whole situation thoroughly when working with small numbers."

In the current phase of the epidemic, **it is essential to work at the smallest possible scale**. If containment measures are necessary, it is always preferable to apply them to a single building than to an entire neighbourhood, town, county or province. However, it is difficult to analyse the whole situation thoroughly when working with small numbers. It is important to strike a good balance between scale and analytical capacity.

When detecting outbreaks and assessing the risk that they will spiral out of control, there are three essential indicators to consider:

a) Is the number of cases increasing? At what rate? To answer these questions, we must consider several variables. For an area of a certain size-a health care region, a province or some larger entity-one possibility is to use the effective reproduction number (R_e) , a measure that expresses the "real" susceptibility of a given population. The value of Re takes into account additional factors, such as the fraction of the population that is immune to the disease, and is therefore typically lower than the value of the basic reproduction number (\mathbf{R}_0) . The effective reproduction number changes over time and provides a more accurate estimate of the real situation based on the actual conditions of the population in question. A similar indicator that can be used in this context is the empiric reproduction number. When dealing with a smaller geographical area, it is better to consider the relative increase in number of cases, for example by comparing the number of new cases recorded over two successive weeks.

b) How big is the population in which the disease is spreading at this rate? An increase from three to six cases is not the same as an increase from 300 to 600 cases, even though the number of infected people has doubled in both scenarios. The number of new cases reported per 100,000 population over the past 14 days—i.e. 14-day incidence—is therefore a useful indicator.

c) What is the testing and contact tracing capacity of the system? As long as the number of new cases is within the capacity of the detection and surveillance system, the outbreak can be contained. A good indicator of this capacity is the number of diagnostic tests that can be performed each day per 100,000 population. This number can tell us whether we are dealing with a low-, intermediate- or high-risk area.

These three indicators can be represented in a **risk diagram**—a visual tool that can help us understand an outbreak. Figure 2 shows the risk diagrams for two Catalan health regions. The diagram for Camp de Tarragona depicts an incipient outbreak that was brought under control without complications, whereas the diagram for Lleida shows an outbreak that forced the health authorities to postpone the easing of lockdown measures.

The horizontal axis represents the infectious potential in the population, i.e. the number of active cases per 100,000 population (14-day incidence or equivalent indicator). The vertical axis represents the rate of transmission (empiric reproduction number or equivalent indicator). Finally, the colour-coded background represents the daily testing capacity of the local health authority and tells us whether the situation in the area is lowrisk (green), intermediate-risk (yellow) or high-risk (red). When the risk is low or intermediate, the system in place has the capacity to follow up on all cases and trace all contacts. In an area at high risk, the system is no longer capable of keeping track of all cases and contacts; in such cases the health authorities should consider enforcing physical distancing to break the chains of transmission. Each point in the diagram represents one day.

A **sharp increase** in the number of cases appears as a steep curve on the risk diagram, i.e. an increase in the empiric reproduction number. If this spike does not trigger additional cases, the curve goes back down, which means that an incipient outbreak has been brought under control without further complications. **If additional cases do appear**—i.e. the 14-day incidence increases—the curve shifts to the right. As long as the curve stays within the green and yellow risk areas, case-by-case control is possible. If the number of chains of transmission increases, the curve may enter the red risk zone. At that point, case-by-case control may no longer be possible and the health authorities should consider taking measures to reinforce the primary care system, enforce physical distancing, etc.

Figure 2. Risk diagrams for the Camp de Tarragona (left) and Lleida (right) health regions.

In each of the risk diagrams, an outbreak can be seen at the later end of the curve (late May to early June). The Camp de Tarragona diagram shows that the incipient outbreak was resolved without incident. The Lleida diagram depicts an outbreak that required an extension of lockdown measures. Arrows indicate the start and end dates of the outbreaks.



Source: Research Group on Computational Biology and Complex Systems, Polytechnic University of Catalonia.

Figure 3 provides an additional explanation using the analogy of forest fires. Forest fire risk assessment includes two components: **risk of ignition**, which may depend on temperature and humidity, among other factors; and **risk of spread**, which may also depend on temperature and humidity but can increase with wind or with the density of fuel available for combustion. For COVID-19, the appearance of new cases is the equivalent of ignition; the corresponding risk depends on the 14-day incidence value. The risk of spread can be estimated using the empiric reproduction number and depends on population density, people's behaviour and mobility, and the quality and speed of response of the epidemiological surveillance system. The product of these two values (14-day incidence and empiric reproduction number) is not only an indicator of the likelihood that new cases will appear but also of the likelihood that these cases will result in an outbreak that cannot be controlled without implementing containment measures •

Figure 3. The forest fire analogy.



Source: Created by the authors using material from <u>http://efirecom.ctfc.cat/docs/efirecomperiodis-</u> tes_es.pdf.

Summary: The Keys to Controlling an Outbreak

1. Detect the outbreak early. While the number of cases is still very small, monitor the risk diagrams, identify all (or most) of the people who may be affected and administer diagnostic tests to determine their actual status promptly. It is crucial to detect the outbreak as early as possible using good epidemiological data and tools that allow rapid analysis of the geographical and temporal spread of the outbreak.

2. Identify and trace all contacts. Remember that up to 40% of cases may be asymptomatic. Cases must be isolated and contacts must be quarantined for 10 to 14 days to prevent further transmission.

3. Adopt proportionate control measures that are as limited as possible. If necessary, these measures can be scaled up as the outbreak progresses.

"Keys are detecting the outbreak early, identifying and tracing all contacts and adopting proportionating control measures that are as limited as possible."

FOR MORE INFORMATION

• <u>COVID-19 in Spain. Map of cumulative incidence by province and epidemio-logical week</u>. Spanish Ministry of Health and Spanish Ministry of Science and Innovation.

• <u>COVID-19 Pandemic. Epidemiological updates and risk assessment</u>. European Centre for Disease Prevention and Control.

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