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Updates and first lessons on COVID-19

Abstract

Our purpose is to provide an update on the epidemiology of the COVID-19 pandemic and a general overview on its evolution in the world. Most parts of the Northern hemisphere temperate zone are facing a huge surge in cases whereas in most Asian countries, the COVID-19 wave is very well-controlled. On the other hand, Africa is a grey zone because we do not have sufficient tests to analyze the trends in many countries, but it seems to have been less affected by the virus. It is important to understand the basic reproductive rate is a variable. We must focus on the 10% of the cases who contaminate more than one person because they are the only ones who contribute to the pandemic. There are two tracing approaches in the world: forward tracing and backward tracing which is more efficient. Regarding the three main routes of transmission of COVID-19, small droplets are probably the major route. Besides, preventive measures, lockdown measures, seasonal force/environment and immunity are the four available brakes that can slow down the spread of the pandemic. Of course, the aim is also to explore some pharmaceutical and non-pharmaceutical treatments, as well as the different vaccines under development, and, apart from medical solutions, to identify digital solutions like tracing applications. We will eventually imagine different scenarios for the coming months.

In a collaboration between the University of Geneva and the two engineering schools of Zürich and Lausanne (ETHZ and EPFL), we provide on a dashboard (<https://renkulab.shinyapps.io/COVID-19-Epidemic-Forecasting/>) with daily updates of COVID-19 forecasts for 209 countries and territories. We can see at this time of the year that most parts of the Northern Hemisphere temperate zone are facing a huge surge in cases. However, in Asia, where the surge continues in Japan and South Korea, but not China, it is very well-controlled and at a safety level that is far below the incidence we are seeing in Europe, the USA or Canada. Neither the USA nor Canada have yet got their wave under control, while for the moment, Europe is trying to take control of the second wave of the epidemic.

In some parts of Sub-Saharan Africa, we do not have sufficient data on tests to analyze the trends in many countries, but we can say that there are three different profiles in the continent. The northern part of Africa has a very similar trend to Europe, with a recent winter COVID season second wave, as in Morocco, Libya, or Tunisia. For the countries where we do have data in Sub-Saharan Africa, such as Senegal, Ivory Coast, Ghana, Togo, Nigeria, Ethiopia, Kenya, and others, they report very little activity up to now and it seems that these countries are not facing such a dynamic wave. The reasons are not clear, though of course there is the shortage of testing as reminded above, but a burden of infection would have been detected and it has not. Is it the role of the climate since of course there is no winter season? It is not clear, but we see other respiratory viruses such as influenza in all parts of inter-tropical zones and there were high levels of coronavirus activity in Latin America and Singapore in the recent months, so this hypothesis is not very convincing. The role of demography could be more convincing because the median age is much younger in Sub-Saharan Africa (18 years) than Europe (42 years). It is true that there are still some elderly people in Sub-Saharan Africa but fortunately, we do not see them massively in hospitals. Cross-immunity has been suggested as playing a role against the coronavirus, which would be the immunity provided by other viruses that could block the propagation of this virus, but so far none has been documented. A protective genetic susceptibility among black people is also not convincing because black people in South Africa, North and South America have been hit very hard by the virus. Since there is no clear explanation, we should explore it more and keep vigilant, it may be a question of time. The relative lower connectivity of the continent with the rest of the world may have only delayed the progression of the pandemic in Africa. The third profile is South Africa, which behaved like Australia, Pacific islands, and South America with their strong winter wave between June and September, which was successfully controlled. However, there are worrying signals of a new surge in South Africa, as well as South America (Brazil, Argentina, Chile and even Uruguay), which may be a cause of concern in the coming weeks.

We do not make long-term predictions, we only provide daily seven-day predictions for the 209 countries and territories worldwide. We restrain ourselves when it comes to mid- or long-term predictions. We remember the US CDC forecasts for Ebola in 2015, when they predicted one million plus cases for Liberia alone, but fortunately there were less than 30 000 cases all over the world. Of course, it was far too many but not of the same order of magnitude. Wrong three-month predictions have been released for COVID-19 too, so let us avoid long-term and even mid-term predictions because with the current models available in the world today, we cannot really know what will happen with this pandemic in the coming months.

It is important to understand the basic reproductive rate because it is not a constant, it is a variable. When we say it is two to three, it is an average. We have to realize that maybe almost 70% of cases will not contaminate anyone and maybe 20% will contaminate just one person and will not contribute to the pandemic at all. We have therefore to focus on the 10% who contaminate more than one person because they are only ones who contribute to the pandemic dynamic. As a consequence, there are two tracing approaches in the world. The Western style of forward tracing, searching for contacts of reported cases, is not very efficient because 90% of the reported cases will not contaminate anyone. Backward

tracing is a lesson we can learn from the Japanese and other democratic Asian countries, where they look for the person who has contaminated the reported case. Because of this so-called “over-dispersion”, the asymmetry between the 90/10 described above, they do not waste their limited time and resources in tracing all contacts, they prioritize the contacts of potential superspreaders (i.e., those 10% who contaminate more than one person). If someone has already contaminated one person, i.e., the reported case, of course, the probability that he or she contaminates another person is much higher.

The main rules of transmission for Sars-Cov-2 are still being debated and even hotly debated. Of course, there are a number of potential routes, but let's focus on the following three major routes:

- Large droplets – This is the ballistic route when you cough, sneeze or sometimes even speak and may expel some large droplets more than 100 micrometers. These may just hit someone in the nostrils, eyes or mouth and contaminate them. It is probably not very frequent when you respect physical distance which may not be easy in homecare facilities, childcare and of course, sometimes in hospital settings.
- Small droplets – These are the droplets below 100 micrometers you expel when you breathe or 10 times more when you speak, and 50 times more when you sing or yell. Small droplets are aerosolized and can float in the air for a couple of minutes or even hours in poorly ventilated, closed settings, these aerosols may contain some coronavirus.
- When these droplets fall on top of surfaces, these small droplets contaminate fomites, which make a route of transmission.

It is not clear that virus attribute a part of each route and it depends on the settings. Outdoors the aerosols most probably do not play any role, but they seem to play a leading role indoors. Intensive handwashing programs have been assessed through randomized clinical trials for other respiratory viruses and they show a risk reduction of 16%, which is substantial but not dominant. Small droplets are probably the major route indoors.

There is not one COVID-19 disease, there are at least three different type of diseases according to its prognosis. A Danish series of more than 10,000 cases of confirmed COVID-19 show that cases under 50 do not have a high risk of having severe complications or dying from COVID-19; at the most, they were as safe as for many viral, respiratory diseases. Between 50 and 70 it becomes a very severe disease and with comorbidities (50% of the population at this age have comorbidities such as hypertension, diabetes or are overweight), having a risk of dying that is close to that of SARS in 2003, around 10%. It is a very severe disease. Above 70 it becomes a highly dangerous disease, like Ebola in West Africa, with mortality rates sometimes close to 50% or above.

There are four available brakes that can slow the spread of this pandemic.

- Preventive measures – handwashing, wearing masks, physical distancing, ventilation of closed rooms.
- Lockdown measures – homeworking, closure of schools, universities, bars and restaurants, non-essential businesses, restrictions on mass gatherings, limitations of movements. More personalized lockdown measures are in fact the testing/tracing/isolating process because you lockdown those you find are infected or at risk.
- Seasonal force/Environment – We have seen the seasonal force in the Southern Hemisphere during their winter and we are now observing it in the cold seasons in the Northern Hemisphere. The seasonal force in summertime in temperate zones is not a blockage it is a brake, and it may happen that it slows the process. I will come back to the environment component below.

- Immunity – Of course, the more the disease progresses without any substantial mutation gives an acquired immunity. Today, in Paris, London, and Geneva we have probably reached almost 20% of the population being immunized. It is not enough to block, but it is a brake that slows down the process. Of course, vaccines and treatments will help a lot completing it.

We have recently published a work showing four different weather conditions all linked with accumulation of fine particles in the air. In Tenerife in the Canaries, we found that sandstorms led to fine particles in the atmosphere and were followed by an outbreak of COVID. In London, Paris, and Ticino in Switzerland, we have seen that the atmospheric conditions led to fine particles in the air and were associated with a spike in outbreaks of COVID-19 concomitantly or soon after. We have seen that for the first wave, and it seems to have also been reproduced in the second, so climate and seasonal conditions may play a role, as well as the environment. When we cannot act against weather conditions, we certainly can contribute to avoid air pollution in these specific atmospheric conditions.

Like all other European countries, Ireland has experienced a second wave during the Autumn and on October 21 the government decided to lockdown again. On October 25, four days later, we saw a break in the exponential trend. It is quite exceptional to see the effectiveness of a political intervention on this pandemic in just four days. In fact, we can say that there was a citizen participation anticipating this policymaking. The Google mobility data show a 40% reduction in mobility using public transportation from October 4th, i.e., a couple of weeks before the second official lockdown. It is interesting to see the self-lockdown that people in Ireland used to anticipate the political decision, which has also been shown in France. In democracies, governments often follow and endorse their people's own decision and perception of the risks.

When it comes to treatments, we have not got very far, we have only confirmed the efficacy of Dexamethasone, an old and cheap corticosteroid. We are on the verge of seeing some interesting results from monoclonal antibodies, which were administered to President Trump when he had COVID. There have also been some non-pharmaceutical treatments such as appropriate timing of assisted ventilation and oxygen, and the prone position when ventilated. However, some others may be promising and are still being assessed in clinical trials, so for the moment, we do not know if other products will significantly contribute to the treatment. More optimistically, we can say that the survival rates in hospitals have dramatically improved over the previous six months, with survival rates being 30% to 50% higher, just using Dexamethasone and better care with non-pharmaceutical treatments.

We are much more advanced with vaccines with some very promising results. We have not seen any publications for the moment, but the dossiers are being evaluated by regulatory agencies and the UK agency already approved the BioNtech-Pfizer mRNA vaccine. The Moderna vaccine is following soon and AstraZeneca, which is a vector borne vaccine, will probably also follow very soon, but could be delayed a bit by some difficulty in accessing some data. BioNtech-Pfizer and Moderna produced two very promising vaccines, but there are many others, about 150 in development and 50 of them currently in clinical trials, some may come to the market soon.

We do not know exactly how long immunity will last. We can hope that it will last for a couple of weeks or months, but of course we do not have enough experience of that.

When it comes to the scenarios for the coming months as we are waiting for the effect of these vaccines. First, we have to land towards our safety zone before easing and lifting the lockdown measures. After that, we will have to change and adjust our testing strategy towards a backward tracing strategy, prioritizing while not giving up on the other one if we have enough resources and time. We will also have to improve the isolation of contagious people in dedicated hotels, as the Asians and Australians did. We

also need to use more and better apps and digital traces because they are very useful partners for catching cases and contacts. Afterwards, we will have to conduct seroprevalence studies to know exactly what the acquired immunity is. If we have still low immunity levels, i.e. below 10%, in some areas, the risk of resurgence would be very high, and it will be very difficult to ease the restrictions. If we have higher prevalence, maybe above 25% or 30%, that will represent a beneficial brake and a sufficiently low risk to open bars and restaurants and other non-essential businesses, with some caution and maintaining some preventive measures. In between, we have moderate risk, and we will have to be cautious. Wintertime, the cold season in the Northern Hemisphere, will remain a dangerous period and we keep most of the existing preventive measures.

In conclusion to avoid COVID-19, please remember to:

- Avoid crowding indoors,
- Avoid poorly ventilated areas,
- Avoid going unmasked,
- Keep your distance even when wearing masks, since aerosols close proximity is a risk factor,
- Avoid long periods of exposure in these rooms, which is why we are not all in the same theatre with Thierry de Montbrial today,
- Avoid singing and yelling. In Japanese railways, passengers are not allowed even to speak!

And hopefully, with the vaccine, we will be free of all these measures and constraints in a coming future.