Coronavirus: scientific insights and societal aspects

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Abstract. In December 2019, the first case of infection with a new virus COVID-19 (SARS-CoV-2), named coronavirus, was reported in the city of Wuhan, China. At that time, almost nobody paid any attention to it. The new pathogen, however, fast proved to be extremely infectious and dangerous, resulting in about 3-5% mortality. Over the few months that followed, coronavirus has spread over entire world. At the end of March, the total number of infections is fast approaching the psychological threshold of one million, resulting so far in tens of thousands of deaths. Due to the high number of lives already lost and the virus high potential for further spread, and due to its huge overall impact on the economies and societies, it is widely admitted that coronavirus poses the biggest challenge to the humanity after the second World war.

The COVID-19 epidemic is provoking numerous questions at all levels. It also shows that modern society is extremely vulnerable and unprepared to such events. A wide scientific and public discussion becomes urgent. Some possible directions of this discussion are suggested in this article.

Key words: COVID-19, epidemic progression, mathematical models, crisis management, open questions

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1 Current situation

On April 1, 2020, there are more than 900 thousand confirmed cases in the world and more than 46 thousand deaths. The real situation on the number of infected can be much worse, and the total number of cases continues its exponential growth. World Health Organization publishes daily reports on the situation with COVID-19 since January 20, 2020. It was written in the first report [1]: *WHO is working with our networks of researchers and other experts to coordinate global work on surveillance, epidemiology, modelling, diagnostics, clinical care and treatment, and other ways to identify, manage the disease and limit onward transmission. WHO has issued interim guidance for countries, updated to take into account the current situation.* The sufficiency of those recommendations to avoid the dramatic developments that followed have been disputed by experts and the public; also it remains questionable whether they were followed strictly enough by the national governments. Even more important questions now are how to stop pandemic, how to overcome its consequences, and what lessons should be learnt for the future.

Coronavirus pandemic has apparently taken the world completely unprepared, but is it really so? After the first SARS epidemic in 2003 and the H1N1 flu pandemic in 2009, a large body of research and technical work has been done to design accurate and effective plans to prevent and to curb a possible future pandemic [3, 4, 5], including even communication-related issues [6, 7]. Regretfully, these measures were not fully taken into account.

Presently, there are several important issues arising:

- A key consequence of the epidemic is its impact on the national health systems, probably more than its direct mortality. Indeed, if one takes into account the asymptomatic and the mildly symptomatic cases, the percentage of serious cases is small, yet it requires a huge number of hospital beds equipped with ventilators. Thus, the whole bed capacity of Intensive Care Units is rapidly saturated. As an immediate consequence, this near-collapse of national health systems causes a large amount of indirect deaths and critical health conditions. Medical doctors in ICUs are today facing terrible choices due to the lack of necessary equipment and the enormous work pressure on them.

- Many countries around the world decided to introduce strict quarantine, eventually leading to complete lockdown. However, these measures could have been adopted earlier [8, 9], so that the quarantine was often "too late, too little".

- Once introduced, lockdown will certainly be effective in reducing the transmission rate of COVID-19 and eventually its prevalence. However, its effectiveness in disease eradication is much less obvious as it critically depends on the actual value of the COVID-19 Basic Reproduction Number (BRN), which is currently poorly known. Indeed, one third of contagions are in households [2]. Many people continue to work to provide essential services and they can be infected and transmit the disease to their family members. This mean that if the BRN is 2.4, in the best of cases, lockdown can bring it down to 0.9. This implies a slow reduction of the prevalence, thus requiring longer period of lockdown. If the BRN is larger than 3, reducing it under the value of 1 is most challenging.

- There has been blatant lack of coordination between national governments in the implementation of the home quarantine and the nationwide lockdown decisions. In any particular country, the effectiveness of quarantine can be seriously hampered if the quarantine has not been adopted, or adopted in a much milder form, in the neighboring countries. In other words, there has been a dramatic lack of understanding that coronavirus pandemic is a global phenomenon and, as such, requires decision-making coordinated on the global scale.

Timely and efficient solution to the above issue requires a joint effort of medical professionals, health care practitioners and scientists across a broad spectrum of life sciences and biology. An important contribution to this effort can be made by data analysis and mathematical modelling.

2 Epidemiological data and models

Epidemiological data have a crucial importance for the evaluation of the current situation and for making a prediction of its possible progression. There are available data on the situation in different countries (see, e.g. [17, 18]). However, it is not clear whether these data describe the real situation. Obviously, the number of reported daily cases depends on the number of tests performed but the approach to testing is considerably different in different countries ranging from testing only the patients with severe symptoms (e.g. in France), hence in many cases confirming the obvious, to the blanket testing (e.g. in the USA) to include patients with mild symptoms and even people with no symptoms if they were in contact with infected. Numerous media reports in many countries as well as personal evidences indicate shortage of tests and lack of availability of test kits, and hence difficulties to perform the sufficient number of examinations. Thus, one has to evaluate the situation under considerable uncertainty, with only partial, unreliable information available. In particular, there are some estimates suggesting that the actual number of infected individuals can be several times larger than those officially reported [14, 15].

One of possible ways to proceed is to compare the data from different countries. All of them show that, after some initial period, the growth rate of the number of infected individuals becomes exponential. Typically, the number of infected increases from 100 to 1000 in 7-8 days. After that, exponential growth continues with the same of with a slightly lower rate.

The exponential growth of the number of infected individual that can be seen in the data is a common feature predicted by the various possible models for the spread of a disease in a population, which suggests a certain universality of this dynamics. It therefore provides a framework to show and compare the data from different countries regardless the national specifics of testing and data collection, even though the total number of infected can be underestimated (preserving the same growth rate).

The main question is how we can predict the further development of the epidemic, in particular by using mathematical modelling. There are several possible ways to do it.

Modelling epidemic without public health intervention (Scenario E). Keeping the main focus on the number of infected individuals, classical epidemiological models suggest that new cases appear with the rate $\lambda I(t)S(t)$, hence proportional to the average number $I(t)S(t)$ of possible contacts between the infected individuals ($I(t)$) and the susceptible individuals ($S(t)$) in the given population at time t, where λ quantifies the rate at which the disease is transmitted along each single connection due to social contacts. Note that this model has several simplifying assumptions, for instance that the population is well mixed. Refinements and more elaborated models can also include the age structure, a finer modelling of contact pattern between individuals (e.g. to account for the structure of social networks), etc.

At the initial stage of epidemic development, when the number of infected is relatively small, S can be approximated by a constant. Essentially, it is this approximation that gives the exponential growth in the number of infected. The period of exponential growth eventually turns into a slower growth, because the number of susceptible individuals $S(t)$ decreases. One typical pattern of the epidemic development over time predicts that the total number of infected individuals reaches its maximum and then starts exponentially decaying, to 0 in the case where the disease becomes eradicated or to some small background density if the disease becomes endemic.

This situation implies that the majority of the population that became infected and survived the disease develops immunity to the pathogen. Some of the infected individuals can overcome the disease in a weak form without manifestation of the symptoms due to the strong immune response which keeps the level of infection within the human body at a low level.

Comparing with the influenza epidemic (Scenario I). There are abundant statistical data about seasonal influenza epidemic. It is known to have three clearly identified stages: (i) slow exponential growth during first 3-4 months followed by (ii) fast exponential growth for about one month, and then (iii) fast decay for about two months (e.g. see [11]). The proportion of infected when slow exponential growth changes to the fast exponential growth is called the epidemic threshold. It varies from year to year but usually is of the order of magnitude of one new case per one thousand individuals per week. The estimates of the total number of infected vary; one estimate available for France shows that, in the worst case scenario, 10 million people can become infected with influenza (out of 67 million total population in 2020) resulting in about 10,000 deaths. Thus, about 1/6 of the population falls ill. On top of that, a certain number of others can get the pathogen without symptoms or with mild symptoms and develop the immunity. Another fraction of the population may have (partial) immunity resulting from previous infections if the new pathogen is not completely different. These three sub-populations are subtracted from the total number of susceptible people, eventually changing the fast growth mode to the fast decay mode. If a vaccine is available, then it can also essentially decrease the number of susceptible people by making them immune.

The scenario of influenza epidemic is close to the previous Scenario E with one difference that the transition to the fast exponential growth is not described by baseline epidemiological models. It can be related to the heterogeneity of the population. For instance, disease spread can begin among people with a weaker immune response and continue in the whole population [10].

We do not yet know whether COVID-19 can manifest the acceleration in its growth when the fraction of infected individuals becomes sufficiently large. However, the possibility of such development should be taken into account, because its apparent disastrous consequences. Another unknown factor is whether COVID-19 is a seasonal epidemic, similar to influenza, e.g. how it will evolve during the summer season.

Applying quarantine measures (Scenario Q). Strong quarantine measures were introduced in China on January 23, 2020 (Q-day) when the total number of infected individuals was just about 830. However, due to the long incubation time of the disease, the effect was not seen until after two weeks: the maximum number of daily new cases was reached on February 4 (M-day). A singular large outbreak occurred on February 12 but its origin is not clear; it can also be related to the way the data were collected. Restrictions in South Korea were introduced on February 22 when the number of infected was 436. The M-day was on March 3. Thus, the M-day was reached 12 days after the Q-day in China and after 10 days in South Korea. These two examples are hardly sufficient to draw general conclusions but they allow to work out a working hypothesis, for instance about the importance of the time lag [16].

We want to mention here that, if the number of infected people remains relatively small in comparison with the total population (e.g. during early stages of the epidemic development), number S of susceptible individuals can be regarded as constant. Epidemiological models then become linear and the exponential growth is their generic solution. This means that all numbers are proportional. It also suggests that, to model the growth during the early stages, there is no qualitative difference between simple (conceptual) and complex ('realistic') epidemic models.

In Italy, the Q-day was March 10 (with some softer measures being adopted prior to that) with about 10,000 total cases at the time. The M-day was reached on March 21, that is, 11 days after the Q-day. During several days after the M-day, there was stabilization at the level of about 5000 new daily cases, with a tendency to decrease. In France, the Q-day was March 16 with about 6500 total reported cases. The M-day can therefore be expected on March 26-27, however there has been no reliable data so far to check this prediction. The number of daily cases undergoes strong oscillations, probably due to a variable daily number of administered tests.

We also note here that the daily multiplication coefficient on the Q-day was 1.19 in Italy and 1.23 in France (1.23), which is less than in China (1.4).

What can happen next under Scenario Q? In China and South Korea, a rather rapid transition to the exponential decay mode was observed. It continued for about 2-3 weeks being then followed by the stabilization at a low level of newly infected individuals, several dozens of daily cases in China and about 100 in South Korea. Most of the new cases were imported to have been brought from abroad by the citizens returning from international travel. Quarantine models [13, 16] present all three regimes: exponential growth, exponential decay, and constant number of daily cases (linear growth of the total number of infected) [16]. One can expect the transition to the decay and stabilization modes after the M-day. If this stabilization occurs, then it is important to know what the new growth rate is going to be, in order for the public health system to get prepared and be able to manage it. Importantly, stabilization is likely to require prolongation of the quarantine over considerable time. Otherwise, the disease dynamics can return again to the exponential growth mode. This seems to have happen in Iran where the number of daily cases stabilized at about 1000 per day during 20 days period, followed by a new period of growth.

3 Question to be answered to improve the understanding of pandemic

The above overview of the coronavirus pandemic brings forward several questions that are crucial to improve our understanding of this phenomenon:

- What is the actual total number of infected individuals with respect to the identified infected individuals and the number of death cases? Are there individuals that are resistant (immune) or may become infected without becoming infectious? These questions concern the estimation of the unobserved part of the epidemic (asymptomatic infectious individuals and non-reported/nonidentified cases).
- How the huge differences between the fatality rates in different countries should be explained?
- What is the effective death rate?

A heuristic estimate that has been widely used so far is obtained by dividing the current cumulative number of deaths by identified infected individuals. However, this definition fails in the exponential growth phase. The delay between the detection of infection and the instance of death leads to substantial underestimation of the true fatality rate.

When the average time between the onset of symptoms or positive test and death is m days, the current cumulative number of deaths should be divided by the cumulative number of cases recorded m days before. In Germany, where the lowest fatality rate has been observed (among countries with a high number of reported cases), the program of identification of infected people by testing them at early stages of the disease and the high standard of public health care may have resulted in large m. Together with high daily growth (of about 30% during March 14-20, 2020), that may have resulted in significant underestimation of the true fatality rate. Assuming m between 10 and 14 days, one can find that the reported fatality rate may be smaller than the true one by the factor between 1.3^{10} and 1.3^{14}, that is 14-40 times.

On the other hand, the unknown fraction of hidden infected individuals may substantially lower the effective death rate. A possible way to answer the question could be obtained by tracing disease development in a group of selected individuals in which infection was detected by testing only.

• What is the basic reproduction number (BRN) in the case of free epidemic growth?

BRN is the mean number of infectious contacts that an infected individual has, on average, during the early stage of the outbreak. Its value determines the exponential growth phase. Supercritical values BRN > 1 are associated with an epidemic outbreak, BRN < 1 corresponds to a subcritical regime where the epidemic will decay exponentially. In order to restrain the epidemic, estimation of this parameter is thus crucial. However, its mathematical expression depends heavily on the choice of the model: although the exponential growth at the early stage is generic, the dependence of the exponent on the parameters is not.

• Based on the existing experience, what should be the most efficient measure to quickly suppress the disease spread in newly affected countries?

Arguably, this question should best be addressed by taking into account the costs and/or potential economic impact of the suggested measures. At the very early stage of disease development when there are just a few infectious individuals, tracing all their contacts (like it was successfully implemented in Singapore) and to place them into mandatory isolation may be expensive, but it can prevent the huge negative impact on the economy if the nationwide lockdown become necessary. Thus, epidemiological modelling should be combined with a cost-benefit analysis.

• Can we estimate the level of immunity in the population at the end of the quarantine, in particular with then purpose to predict a possibility of the 'second wave', its specific features and an efficient and least costly way to suppress it?

• What is the potential for evolution of the virus and could it have an impact on the future of the epidemic?

Practical questions regarding containment. While it is conceivable that the above questions can be successfully addressed by using epidemiological modelling (in combination with data analysis and necessary insights from biology and especially virology), there are also a number of broader, societal, economic and political issues and questions that may require a more interdisciplinary approaches and different types of mathematical modelling.

• There are urgent needs to better understand the effect of different ways of the quarantine introduction, e.g. through partial or complete lockdown, in the abrupt (as in China) or progressive manner (as in Italy), at the local, national and international levels. Similarly, scientifically checked advise must be provided as to how the quarantine is lifted and the borders are reopen, for instance what could be the global consequences of this, in particular for countries that are at the early stage of the epidemics?

• What social/professional groups should be tested extensively? Doctors? Salesmen? Essential service providers? Other people that have high number of contacts per day? People that had primary (or secondary) contact with infected person? How frequently these people should be tested?

• How we should restrict contacts? - only for people above given age (e.g. children and/or senior citizens), for people with potentially high number of contacts, everybody?

We mention here that, given the high negative impact that quarantine has on the economy, this is a highly nontrivial question that has no intuitive answer. The approach taken by the national governments was sometimes contradictory and inconsistent. For example, the UK government first advocated the idea of developing the 'herd immunity' where only people from vulnerable, high risk groups (such as senior citizens and people with underline health conditions) would be isolated while the rest of the population was expected to get infected and to develop immunity. However, that idea was later dropped, as it was estimated that the number of infected that could need intensive care would lead to the collapse of the NHS. In the USA, soon after the quarantine was introduced in most parts of the country, it was announced that 'cure cannot be worse than the disease' and hence the economy should restart (and hence quarantine lifted) in a short time. That idea however was later suspended.

• Whether people will voluntarily reduce contacts? What can be an acceptable level of risk and how it will change in time?

4 Crisis management

Coronavirus pandemic induces a large scale crisis across the globe with many immediate and long-lasting consequences for public health and economy. The choice of efficient strategies and their timely implementations are crucial for the crisis management. Clearly, it is hardly possible to be prepared for all situations; however, there are only a relatively small number of major risks and some common rules to manage them. Crisis management should primarily focus on public health, the availability of basic daily food, products and needs including regular and essential medicines and transportation.

Public health. In many countries with significant number of reported cases, the situation is almost disastrous. Not only the essential equipment (such as ventilators) for severe cases are lacking and there is shortage of beds in hospitals, but even simple protective masks are often lacking even for the medical personnel who are at the frontline of this battle. For the general public, masks are even less available, also there are no clear guidelines from the medical authorities about the necessity to wear them. The situation is further exacerbated by the confusing statement made by WHO during the early stages of the epidemics when it was officially announced that masks are not needed. That statement was later revoked.

Production and shipping of food and basic consumables. Another question of major importance is the production and distribution of food and basic goods during the quarantine.

In particular, they should be considered taking into account of the geographical location in order to minimise the shipping effort. There should be a sufficient number of production lines that could be quickly changed/redesigned for the production of alternative products required during the pandemic and under quarantine conditions, for instance, medical masks, sanitizers, etc.

Internet, distant work and communication. One of the very few positive elements in this otherwise sombre picture is the quite remarkable progress in distant work and education. While it still faces many technical difficulties (some of them being stressful and time consuming, e.g. because of insufficient capacity of networks or inadequate teleconferencing software), the quarantine seems to have a significant positive impact on their development and broad use. This arguably provide a valuable asset that authorities and business companies should further build after the quarantine is lifted and life returns to normal, in particular to reduce unnecessary travel. Further development of online platforms to share pedagogical content with simpler and more efficient access would also be useful.

The surge in the use of online facilities has revealed some difficulties and inconsistencies too. The capacity for online shopping and especially shipping to residences of ordinary people (mainly senior citizens) should be massively increased.

Mental health. For many people, spending a prolonged time in self-isolation poses a significant challenge. In effect, it amounts to a jail service (albeit spent in a comfortable surrounding) and it can have a considerable negative effect on the mental health of the general public. Increasing stress can result in antisocial behaviour and violation of the quarantine riles, which is of course unacceptable. This problem could to some extent be moderated through social contacts using internet and various social media. However, its solution should not be left to a chance. While it does not seem possible that the governments take care of this issue directly, at least they should delegate it to local authorities and social care departments.

5 Conclusions

Coronavirus epidemic has exposed the vulnerability of the modern world and put the humanity to a global crisis. The epidemics brought forward a number of great challenges, some of them apparently incompatible, for instance, how to minimize the number of infections by a strict quarantine and yet not to cause an irretrievable damage to the economy. While we believe that all these challenges can be solved, it will require careful, efficient and well-informed decision making. In its turn, this will require a good understanding of the epidemic dynamics and of the subtle interplay between numerous factors and processes involved. Mathematical modelling is an efficient tool to achieve this goal.

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