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Perspective

Covid-19 Crisis: How Tortuous is the Coronavirus Road Ahead?

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Covid-19 disease is the third betacoronavirus zoonotic infection affecting humans in two decades, and has been by far the most catastrophic in terms of human lives and economic wreck. The global pandemic that started in the meat market in Wuhan, China, has already claimed 116,000 lives and infected 1,8 million people and counting [1]. The first Indian to test positive for covid-19 was a medical student who had arrived in Kerala from Wuhan at the end of January [2], which is around the same time the first American and the first Korean were tested. The response was mapped out immediately by a group of government officials in Kerala as their experience with the outbreak of Nipah in 2018, a brain-damaging virus originating from bats and transferred to humans, was still fresh [2]. That outbreak was successfully managed despite technical shortfalls. This time they put forward a plan of contact tracing, isolation and surveillance state-wide, until the whole country went into confinement with more than 12,000 cases two months later, in an attempt to curb viral spread.

De-confinement in developing countries will be very different from the developed world, and difficult for other reasons. In India, for example, the population of 1,4 billion residents live in large families and don't have running water making it difficult to sanitize things and maintain social distancing [2]. With a total of only 30,000 to 40,000 ventilators nationwide, in addition to short supply of testing kits, personal protective equipment for health-care workers and oxygen flow masks, the clear path forward is to break chain in the control of transmission [2]. As for a lockdown exit strategy, the government of India launched a Covid-tracker app, Aarogya Setu, which has been downloaded more than 10 million times, with the goal of expanding to the majority of the 500 million smartphone users in India [3]. The app raises one's alert level if one was in vicinity of a person tested positive for Covid-19. The government-appointed expert panel said findings from the aggregated, anonymised data will be a factor in helping decide when to end the lockdown and set policy beyond.

India and other developing countries have not yet seen the deadly wave observed in Europe and America, and the situation will be difficult in many countries at once in the coming months but perhaps at different degrees. The west African country of Senegal is reportedly turning coronavirus tests around within 4 hours with a quick test kit [3]. Senegalese scientists are at forefront of testing in partnership with UK-based Mologic. There are big ideas but the common obstacle remains that there is no clear path on how to go about de-confinement. A strategy based on prophylaxis in the developing as well as developed countries using off-label repurposing of drugs such as hydroxychloroquine have been proposed as well [4]. A number of randomised control trials are ongoing in multiple countries right now, one of the largest being the Discovery trial in France, with results expected shortly.

As Eric Topol put forward, the mantra for preparing for a lockdown exit strategy has two big drivers namely massive testing and tracking. This endeavor will need real-time point prevalence of Covid-19 so that any possible re-introduction of infected cases could be swiftly identified and isolated, and their contacts traced and quarantined. In doing so, that is close watch on real transmissibility, it will also help ensure the infection prevalence does not exceed the surge capacity of the health system. Close monitoring of the instantaneous effective reproduction number and real-time tuning of policy interventions to ensure a manageable second wave remains the over-riding public health policy challenge. The speed of the virus and the response it demands should not seduce us into thinking we need to build solutions that last forever [5].

The discussion rages as to the modalities of tracking and hover around privacy issues that are very sensitive in western countries. The technology proposed here using bluetooth and GPS is not particularly complicated [6]. The apps proposed using phone's GPS and bluetooth signals have been developed and are already successfully used in South Korea, Taiwan, Singapore and Germany spearheaded by the Koch Institute in Berlin, and have been successful in monitoring Covid-19 as witnessed by the lowest rates of fatalities in the world by far in those countries. MIT and Oxford have developed tracking applications of their own, and Google in collaboration with Apple will make tracking perhaps cover the 3 billion cellphone users on the planet.

Nevertheless, the human capital at the disposal of society at the moment, having undergone massive layoffs, remains an untaped capital that can be used by the governments in tracking as well [6]. Privacy issues will be a major obstacle in implementation of sys-

tematic tracking in the west. In the western countries such as the US, cultural expectations around privacy prevents sending out the equivalent of South Korea's emergency alerts [7]. But in collectivist societies such as India, China and South Korea, the desire for privacy has a lower threshold than in Western countries, especially when there is an argument for the greater public good. Further, the data protection law currently in place in Europe was designed to emphasize upon privacy. The German example would be a good one to follow, unique as the cultural differences just within Europe are striking. The good news is that there are a lot of people currently out of work who are looking for new career opportunities. This is an untaped source at the disposal of the governments as soon as the lockdown would be lifted and can serve as human quarantine enforcers especially in countries with cultural obstacles to implementation of a tracking by bluetooth and GPS.

A vaccination strategy in order to fully overcome the disease is unlikely before another year. As of early April 2020, there are some 50 potential vaccines in development in addition to some 100 potential drugs [8]. Hundreds of clinical trials registered with the World Health Organisation are underway [3]. Some could already yield results by this summer. But realistically, even in the best of estimates, it is hard to imagine a vaccine that is proven effective before a year, and even then, nobody can tell how long that vaccine will remain effective as the virus can genetically alter by spontaneous mutations for its evolutionary survival. Apart from the traditional platforms of vaccination namely DNA, viral vector, subunit, virus-like particles, inactivated and live-attenuated viruses, the newest mRNA vaccine designs have improved stability and protein translation efficiency and stand the chance of an unprecedented fast-track clinical trial, currently ongoing in the US and will shortly start in Germany [9]. But the real possibility remains that the world is without a standout effective vaccine or drug for a while.

The BCG vaccine has been proposed as a strategy after it was noticed that countries with BCG vaccination in their universal immunization had less mortality. Researchers at the Murdoch Children's Research Institute in Australia are set to conduct a randomised, multi-center clinical trial to test the use of tuberculosis vaccine BCG against covid-19 [10]. Termed the BRACE trial, it is intended for healthcare workers and is based on previous reports that BCG decreases the level of virus in patients infected by viruses similar to SARS-Cov-2. BCG will be assessed to mitigate the prevalence and severity of Covid-19 symptoms. Similar efforts have been deployed in Boston and in the Netherlands in spite of the WHO saying there is no evidence it will help. In the same line of thinking, the malaria vaccine, Mosquirix, developed in 2015, which has a low efficacy for malaria, has yet to be proposed for a trial for Covid-19.

De-confinement is western countries will not be a return to normal, rather a new normal, with new rules of social behavior and social organisation, some of which will persist long after the crisis would be over [8]. There will be aspects of contact tracing and disease monitoring adopted from the successful Asian models namely South Korea and Singapore [3]. Other aspects will entail regularly testing chunks of the population, and to start with health care workers, and putting movement restrictions based on negative testing and proof of immunity having been exposed to coronavirus, which will be arbitrary at best for the medium term. This considerable degree of social overhaul with surveillance and control will be certainly different in western countries due to social values being different related to privacy. There will also be divisions between who is going to work from home and who is allowed to move freely.

From a health perspective, the changes brought will affect who will have medical care and who will be left with a hefty bill, especially in countries without universal health coverage such as the United States. The new social order will seem unimaginable to most people in the democratic countries, mostly in Europe, concerning privacy, the uses of personal data, and algorithmically enhanced decision making [9]. Germany has launched a smartwatch app backed by the Koch Institute and more than 160,000 people have already enrolled, which plans to capture body temperature in an attempt to map out flu hotspots breaking out [11]. The German case is noteworthy due to the newly enacted European laws on data protection and privacy limiting digital data collection [11]. Eric Topol's group has launched an initiative of the same sort in the US with far lesser enrollment at this stage. However, changes will become normal once people start accepting them. As Jeremy Farrar, head of the Wellcome Trust, said that a path out of the dilemma now facing the world will come from research. Science is the exit strategy [12,13].

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