Predictions and role of interventions for COVID-19 outbreak in India

The COV-IND-19 Study Group

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Crisis Of Virus in INDia (COVIND)

As the COVID-19 crisis unfolded around the world, a team of scientists and scholars have prepared this report by analyzing the existing data that are available for case-counts in India using standard epidemiologic models to arrive at a numerical projection and situational assessment of the COVID-19 crisis in India. This report has not undergone peer review. As we prepare this article for peer-reviewed journal submission, given the time sensitive nature of the growing crisis, we are making the report available online.

INTRODUCTION

A 55-year-old individual from Hubei province in China may have been the first person to have contracted COVID-19, ["1st known coronavirus case" - Live Science] the disease caused by the new coronavirus spreading across the globe. That case dates back to Nov. 17, 2019, according to the South China Morning Post, with confirmation on December 7. [Wang et al. 2020] In December, 2019, a series of pneumonia cases of unknown cause emerged in Wuhan, with clinical presentations greatly resembling viral pneumonia. Deep sequencing analysis from lower respiratory tract samples indicated a novel coronavirus, which was named 2019 novel coronavirus (2019nCoV). [Huang et al. 2020] In exactly four months, the coronavirus has caused a global pandemic. [WHO media briefing 11 March 2020] On March 19, 2020, the staggering number of confirmed cases of coronavirus worldwide stands at 275,864 [Microsoft bing coronavirus tracker, 10:45 pm EST March 20] with the number of active cases at 172,554 (62.6%), recovered cases at 91,912 (33.3%) and fatal cases at 11,398 (4.1%). Of these, only 236 confirmed cases are from India with 209 active cases (88.6%), 23 (9.7%) recovered and 4 fatal cases (1.7%). India being world's largest democracy with a population of 1.34 billion (compare China at 1.39 billion and USA at 325.7 million) is being vigilant and wise in instituting the right interventions at the right time including sealing the borders with travel ban/canceling almost all visas, closing schools and colleges in certain states and diligently following up suspected cases/exposed individuals with respect to adherence of quarantine recommendations. **Table 1** presents a timeline of the prevention/policy recommendations as they have been rolled out in India in the last month. Figure 1 shows a description of the cases/recoveries and fatalities in the early phases of the disease till March 19 in reference to the introduction of the intervention. Figure 2 shows that in the early phase of the epidemic, India has done well in terms of rolling out strict intervention and controlling the number of confirmed cases compared to other countries.

Fast forward: The numerical and social dilemma

As we try to project the expected number of cases in the pandemic in India, we have to be cautious with interpreting the low number of cases and the slow growth of the incidence curve up to this point. There is a critical missing or unknown component in all these calculations and assessments: "The number of truly affected cases," which depends on the extent of testing, the

accuracy of the test results and in particular frequency and scale of testing of asymptomatic cases who may have been exposed. Transmission data shows that 83% of the confirmed cases are Indian nationals while 17% are foreign nationals, 59% transmission are labeled as imported and 41% are local. [covid19 India] The frequency of testing for India has been very low, according to the associated press only 11,500 subjects have been tested as of March 18. ["India's poor testing rate" - Al Jazeera] According to a recent article in the New York Times ["India scrambles to escape coronavirus" - NY Times] the limited number of cases detected so far in India can have two explanations. It is either that there are many more cases in India that have not been detected, because of the difficulties of getting tested, or that India has indeed managed to so far escape the worst, possibly because of quick and strict efforts right from the start.

Specific vulnerable populations have been identified to be at higher risk of severity and fatality from COVID-19 infection: older persons and persons with preexisting medical conditions (e.g., high blood pressure, heart disease, lung disease, cancer, diabetes, immunocompromised persons). ["Q&A on coronavirus" - WHO; "Coronavirus: Are You at Higher Risk?" - CDC] Table 2 provides a description of the approximate number of individuals in these high-risk categories in India which in hundreds of millions (e.g., roughly 122 million people with diabetes related conditions). India has the most overstretched healthcare system where it is hard to provide care in times of "normal" patient volume. The number of hospital beds per 1000 people in India is 0.7, compared to 6.5 in France, 11.5 in South Korea, 4.2 in China, 3.4 in Italy, 2.9 in the UK, 2.8 in the USA, and 1.5 in Iran. [World Bank] With a surge in the number of cases, it will be impossible for the healthcare providers to support the sheer volume of cases. Thus, it is incredibly important to slow down the spread or flatten the curve. [Pueyo 2020] It is highly appropriate to adopt draconian measures for the largest democracy in the world, acting early, before the gradient starts to accelerate. The 50th COVID-19 case in India was reported on March 10th, 41 days after the first case was reported in Kerala on January 30, the 100th case was reported on March 14th, 45 days after the first case was reported, the 150th case was reported on March 17th, 48 days after the first case. Though this is clearly the early phase of the epidemic, entering phase 2 or phase 3 of escalation will have devastating consequences. Even with the relatively small counts and sparse data, this study group took a close look at what might be coming in the next few weeks and months, based on what we have seen in other countries and a susceptible-infected-removed (SIR) state-space epidemiological model that have been gainfully employed to assess the effect of interventions in Hubei province in China. [Song et al. 2020]

We must acknowledge that there is a substantial degree of uncertainty in our predictions due to rapidly emerging data on community transmission, policy changes, interventions, scale of testing and adherence to interventions. The fundamental premise of our work is to conduct a counterfactual study or a quantitative projection experiment where we compare a world with various degrees of intervention to one without and conduct a range of sensitivity analyses to the assumptions we make. We conclude with an assessment of the economic, social and healthcare implications of these interventions that are very unique to the Indian context.

The rest of the report is organized as follows. We first briefly review the historical data on similar flu pandemics and what happened in India during those times. Second, we review the potential interventions that have been rolled out and what is known about their protective/preventive benefits from other countries that are in a later phase of the epidemic. We then construct a predictive model for case-counts in India and conduct a sensitivity analysis with hypothetical interventions with various intensities and provide projections over a time horizon. We finally conclude with an assessment of the economic, social and healthcare implications for such interventions in India. We conclude that till we acquire biological herd immunity from COVID-19, there is need for social and economic immunity: not just universal coverage for testing and treatment for COVID-19 for everyone in India, but subsidies and incentives for the common public to survive the consequences of the severe interventions that are needed to stop the virus from creating a havoc in India.

History of major Flu-type Pandemics in India

The first seven cases of the 1918 Flu Pandemic, referred to as "The Bombay Influenza" or "The Bombay Fever", was reported on June 10. ["Deja flu" article - The Times of India] They were all police sepoys at the Mumbai (then Bombay) docks. Within two weeks, this flu crippled Mumbai and quickly moved North to Punjab and Uttar Pradesh via railway lines. The flu resurfaced violently in September 1918, ["Deja flu" article - The Times of India] believed to have been brought by returning flu-infected World War I soldiers, [Kant & Guleria 2018] and quickly spread all over the Indian subcontinent. It claimed an estimated 10-20 million lives in India, the largest number of deaths in a single country. [Murray et al. 2006] Just as we knew nothing about SARS-CoV-2 (the COVID-19 causing virus) when it first struck in Wuhan, China in 2019, nothing was known about the influenza virus in 1918. In fact, the influenza was thought to be caused by a bacteria, [Kant & Guleria 2018, Phipson 1918] and needless to say, there was neither a vaccine nor anti-viral drugs. [Kant & Guleria 2018] Multiple possible prevention strategies were discussed in India Sanitary Commissioners Reports from 1918 [Phipson 1918] and 1920 [Indian Medical Gazette 1920] (e.g., "strict isolation, at home, of the first case occurring in a household", "Personal prophylaxis", "avoidance of churches, crowded railway carriages, theatres, cinemas and other large aggregations of people", "regular use of an antiseptic nasopharyngeal douche") but it is unclear if any of these measures were successfully undertaken. In fact, Dr. Phipson expressed their apprehension about being able to implement either of these measures in their report from 1918 [Phipson 1918]: "No country and no city, which has lain in the natural path of influenza in its pandemic form, has ever succeeded in avoiding its incidence, and in the present state of our knowledge there is no prospect of doing so, except by the imposition of restrictions of such severity that no community could be expected to tolerate them. With a disease of low mortality like influenza, the public prefer to take their chance, and preventive measures on a large scale in Bombay or any other Eastern city demand a degree of public enlightenment and co-operation which is not likely to be realized before the millennium."

Severe Acute Respiratory Syndrome (SARS) was a multi-country outbreak that was recognized at the end of February 2003. In India, the first SARS case was reported on 17 April 2003 in a person stopping over in Mumbai after visiting Singapore and Hong Kong. [WHO SARS outbreak report 18 April 2003] According to Wikipedia, only 3 cases were reported in India and no fatality was reported [SARS - Wikipedia]. Middle East respiratory syndrome (MERS) was another multi-country outbreak first recognized in 2012. There seems to have been no reported MERS case in India between 2012 and 2017. [WHO MERS-CoV map and epicurves]

PUBLIC HEALTH PREVENTIONS AND NON-THERAPEUTIC INTERVENTIONS

Testing for COVID-19

"We have a simple message to all countries - test, test, test," WHO Director General Tedros Adhanom Ghebreyesus told a news conference in Geneva, calling the pandemic "the defining global health crisis of our time". "All countries should be able to test all suspected cases, they cannot fight this pandemic blindfolded." [WHO Director-General 16 March 2020] Without testing, cases cannot be isolated and the chain of infection will not be broken, he said. Even countries with advanced health systems have struggled to cope with the outbreak, Tedros said, adding he was deeply concerned about its effects on low-income countries where people already struggled with malnutrition and other health problems. [WHO Director-General 16 March 2020] Furthermore, although the quality and capacity of a country's health care system are crucial drivers of mortality in the wake of an outbreak, it is important to understand that all other things being equal, more testing will give us more accurate estimates of the mortality rate in a country.

According to the WHO-China Joint Mission on COVID-19, "in the face of a previously unknown virus, China rolled out perhaps the most ambitious, agile and aggressive disease containment effort in history. The strategy that underpinned this containment effort was initially a national approach that promoted universal temperature monitoring, masking, and hand washing. However, as the outbreak evolved, and knowledge was gained, a science and risk-based approach was taken to tailor implementation." [Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19)] The joint commission reported systematically collected data on COVID-19 testing from routine respiratory disease surveillance systems. These included RT-PCR testing of the COVID-19 virus in influenza-like-illness and severe acute respiratory infection surveillance systems, as well as testing of results among all visitors to fever clinics. Chinese authorities have reported testing some 320,000 people in Guangdong province, but the total number of people tested across the country remains unclear.

William Schaffner, a professor of preventive medicine and infectious diseases at Vanderbilt University School of Medicine argues for testing more broadly, because with broader testing "we discover, almost always, that there is a broader spectrum of illness," he said. ["South Korea's aggressive testing" - This Week In Asia] In this regard, South Korea emerged as a "wonderful laboratory" for studying the virus. More widespread testing allows scientists to complete the picture

of the entire pyramid. "If we can test more people – whether they have no symptoms, mild or severe disease – the results, including the case fatality rate, are more accurate and representative when the whole disease spectrum is taken into consideration," said David Hui Shu-cheong, an expert in respiratory medicine at the Chinese University of Hong Kong. "Most countries just focus on testing the hospitalized patients who obviously have more severe disease, and [thus] the fatality rate is high."

The first case of COVID-19 in South Korea was confirmed on January 20, 2020. Within a month, the country had tested nearly 8,000 people suspected of infection. By the end of February, that number had reached 82,000 as health officials mobilized to carry out as many 10,000 tests each day. ["South Korea's aggressive testing" - This Week In Asia] Till date (March 16, 2020), 274,000 people have been tested in South Korea, bringing the overall rate to 5,250 tests per million people. ["US lags after slow response" - The New York Times] The scale and speed of South Korea's screening regime has been applauded by the international community, and can serve as a model for other countries. President Moon Jae-in declared "war" on the virus. After the outbreak of the Middle East Respiratory Syndrome in 2015, South Korea had introduced a system to grant the rapid approval of testing kits for viruses. Health officials in the country tracked down symptomatic people and their contacts. Drive-through stations were set up, where members of the general public could be tested in minutes. Government websites and mobile apps disclosed how many people had been tested and where. ["US lags after slow response" - The New York Times] Through such intensive testing and monitoring efforts, South Korea was able to arrest the emergence of new cases.

In terms of aggressive testing strategy, Italy came second with 2,200 tests conducted per million people. In Lombardy, Italy's hardest-hit region, health officials carried out swab tests on people who were sick, as well as contacts of infected people, even if they were asymptomatic. Australia is testing at the rate of 1,900 per million people. ["US lags after slow response" - The New York Times] Recent data (March 16, 2020) shows that in the United States only 125 people per million are being tested, [The COVID Tracking Project] far fewer than most other countries where data is available. Lack of testing and testing delays have set back the response to coronavirus in the United States.

According to the latest guidelines published by the Chinese government, the diagnosis of COVID-19 must be confirmed by reverse-transcription polymerase chain reaction (RT-PCR) or gene sequencing for respiratory or blood specimens, as the key indicator for hospitalization. [Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19)] However, with limitations of sample collection and transportation, as well as kit performance, the total positive rate of RT-PCR for throat swab samples has been reported to be about 30% to 60% at initial presentation. [Yang et al. 2020] In the current public health emergency, the low sensitivity of RT-PCR implies that a large number of COVID-19 patients won't be identified quickly and may not receive appropriate treatment. In addition, given the highly contagious nature of the virus, they carry a risk of infecting a larger population.

In a study of more than 1,000 patients published in the journal *Radiology*, chest CT outperformed lab testing in the diagnosis of COVID-19. [Ai et al. 2020] Chest CT, a routine imaging tool for pneumonia diagnosis, is fast and relatively easy to perform. The researchers found that the sensitivity of CT for COVID-19 infection was 98% compared to RT-PCR sensitivity of 71%. They concluded that "chest CT imaging is a more reliable, practical and rapid method to diagnose and assess COVID-19, especially in the epidemic area." ["CT provides best diagnosis for COVID-19" - Science Daily]

So far, the number of people tested in India has been relatively small. ["India's Handling of Coronavirus" - NDTV] In the absence of widespread testing, it is impossible to quantify the magnitude of "community transmission", in other words, estimate how many are infected outside hospitals and health care facilities. As we speak, those infected but not tested are infecting thousands of others. Currently all testing in India is being conducted under the jurisdiction of the government. People are queuing up at government hospitals to get tested, and potentially infecting each other. Allowing the private sector to test will boost the collector workforce, scale up operation, and reduce further person-to-person transmission. Currently, private labs are banned from conducting these tests after the government invoked an 1896 Act, which was designed and enacted to tackle the plague. ["India's Handling of Coronavirus" - NDTV]

Social Distancing

As we have seen in multiple countries across the six continents, COVID-19 has a rapid spread rate with dire repercussions. Fortunately, the most effective and simple way to stop the transmission is via the (now ubiquitous) term: #SocialDistancing: the simple expedient of maintaining distance, so we can be out of range of the respiratory droplets that are considered the principal source of the spread. This allows for "flattening the curve" of the number of exponentially rising cases and effectively slowing the spread rate through community isolation measures -- so that healthcare facilities can accommodate and treat serious cases at their current capacities. In the absence of therapeutic and pharmaceutical interventions such as vaccines, this has proved effective in the early areas of outbreak in China and South Korea. As of March 17th, China reported no new cases and rates are declining in South Korea. India is currently in stage 2 of the pandemic, where stage 3 is community spread, and effective community isolation strategies can arrest (and possibly avoid) this situation. Self-quarantine followed by centralized quarantine strategies have been implemented in both China and Italy to contain the disease, but when the number of cases reach a certain point, one has to move to more drastic community mitigation as tracing the contacts as a strategy is no longer feasible. ["California county turns to mitigation" - CIDRAP]

Unfortunately, humans are a social race -- unused to keeping social distance -- especially on demand. In an inherently community-based culture like India where 1.3+ billion people inhabit with a relatively high population density (~460 per sq km), and inter-generational extended families are still common - the community tends to be relatively tight-knit. In this context mandating social

distance is problematic and difficult to implement, in some respect, much like Italy. Additionally, with a large rural population- a campaign based on scientific literacy would not go far via standard channels. What could work is a campaign centered around the inherent respect that Indians have for their older generations and families and tap into the culture of taking care of "families" rather than individuals. Much of India is still young with an average age of 29. [Financial Express] Increasing evidence suggests COVID-19 has a higher mortality rate in older populations, [Wang et al. 2020] but the key issue is that the younger population become vectors or vehicles to spread the disease. As recently suggested, almost 86% of all infections were undocumented and can be ascertained to healthy carriers and also partly explain the rapid geographic spread -- which makes containment challenging. [Li et al. 2020]

Investing in the simple mechanism of social distancing in these uncertain times could have an exponential effect, and warrants multiple rounds of building literacy and policy for immediate implementation. ["Coronavirus here to stay - now what?" - NY Times] This has enormous long and short term social, economic and political implications, which are difficult to predict for India, but, nonetheless drastic situations call for drastic measures.

Travel Ban

The general sense in the epidemiologic community is that travel bans -- local, domestic and international -- can slow down the spread of an infectious disease outbreak but cannot really prevent it. ["Blocking Travelers Won't Prevent Spread" - Vox; Chinazzi et al. 2020] China restricted travel to the Hubei province fairly quickly and Italy was one of the first countries to impose a travel ban to China. This helped slow down the epidemic and gave other countries some more time, but both countries failed to avert the epidemic. Travel bans are most effective in the early part of the epidemic and India has taken very prompt and strict measures in the early phase. The ultimate drop in the number of cases in China has been through lockdown of the city, ban traffic, rapidly identify cases, isolate them and educate the public. As shown in **Table 1**, some steps have been taken but more stringent regulations and implementation is required.

Personal Hygiene and Sanitation

Based on what is currently known about the COVID-19 virus, the Centers for Disease Control and Prevention (CDC) has issued numerous guidelines on personal hygiene and sanitation - what to do at homes, schools, businesses to battle the disease. Even though information is limited, early data seems to indicate that COVID-19 can seriously affect the elderly, immunosuppressed and immunocompromised populations more than others, which is why the CDC recommends every individual to identify vulnerable people and make emergency contact lists for everyone in their households so that swift action can be taken in case of an infection. This includes chronic comorbidities such as diabetes and India has one of the highest rate of diabetes incidence (**Table 2**). [Epidemiology of diabetes - Wikipedia] The CDC has urged everyone to follow simple personal

hygiene and sanitation practices, such as regularly washing hands with soap and water for at least 20 seconds or using an alcohol-based hand sanitizer that contains 60-95% alcohol, avoiding touching nose, eyes and mouth with unwashed hands and disinfecting all 'high touch' surfaces such as counters, tabletops, doorknobs, toilets, keyboards and phones. Infected people have been asked to isolate themselves in their homes and restrict outside activities, except for getting medical care. These guidelines are similar to the findings described in, [Srivastav et al. 2018] where the authors reported that other than timely vaccinations, preventive measures taken by the non-institutionalized US adult population to avoid catching or spreading influenza were washing hands often, covering coughs and sneezes, using hand sanitizers, staying home if sick and avoiding people who are sick with a respiratory illness.

Like the MERS-CoV and the SARS-CoV, COVID-19 is also a betacoronavirus (enveloped, positive-sense, single-stranded RNA viruses of zoonotic origin) and has its origin in bats. [Betacoronavirus - Wikipedia] COVID-19 is much less deadly than both SARS-Cov (~11% fatality) ["Consensus on SARS" - WHO] and MERS-CoV (~35% fatality) ["MERS Clinical Features" - CDC] with current reports suggesting that its fatality rate is roughly 3.7% [Roser et al. 2020]; however, what is frightening about this disease is how difficult it is to contain. COVID-19 shares similar symptoms (fever, coughing, respiratory problems) as the other two coronaviruses. ["Coronavirus" - WHO] Even though the symptoms make it harder to differentiate between COVID-19 and common cold or influenza, it is to be kept in mind that shortness of breath is a characteristic of COVID-19 and not common cold or influenza, and COVID-19 has not been observed to cause sneezing which is a symptom for common cold or influenza. ["How does coronavirus compare with flu?" - Live Science]

It is encouraging that the Ministry of Health and Family Welfare in India has started to take action, issuing guidelines to the public similar to those issued by CDC (regular washing of hands, avoid non-essential travel, social distancing, etc.) so that we can nip this in the bud before it becomes an outbreak. Most educational institutions and private sector companies have been closed with the aim of working online. Closure of restaurants, gyms, movie theatres, swimming pools, cultural and social centres in the country has also taken place. Currently, the Indian Council of Medical Research has engaged with other institutions like the CSIR, DBT, DRDO and government medical colleges to offer free testing to those individuals who are required to be tested with the aim of providing free and reliable diagnosis to all individuals who meet the inclusion criteria of COVID-19 testing.

Therapeutic Interventions/Treatments

As of March 18, no treatment or vaccine for COVID-19 exists; [WHQ ("no current evidence to recommend any specific anti-COVID-19 treatment"); CDC ("no specific treatment for COVID-19 is currently available"); FDA ("no FDA-approved vaccines or therapeutics to prevent or treat COVID-19 or other coronaviruses")] however, there are several initial efforts to test the efficacy of

various treatments. In a letter to the editor published in *Cell Research* on February 4, Wang et al. [2020] suggest that "an efficient approach to drug discovery is to test whether the existing antiviral drugs are effective in treating related viral infections." Antiviral drugs used to treat patients during the MERS and SARS outbreaks were tested and they concluded "remdesivir and chloroquine are highly effective in the control of 2019-nCoV infection in vitro," indicating promise for treating COVID-19 patients. Another exciting prospect is the Japanese anti-flu drug *favipiravir*. ["Japanese drug 'clearly effective" - The Guardian]. There are emerging reports warning against the use of *ibuprofen*, a household drug commonly used to treat cold and flu-like symptoms, as a treatment for COVID-19. The French Health Minister, Olivier Veran, issued a warning against its use based on a recent Lancet article that hypothesized an enzyme boosted by anti-inflammatory drugs could facilitate and worsen COVID-19 infections. ["Avoid ibuprofen" - France24, 3/18] Despite insufficient evidence in support of this warning, the WHO spokesperson recommended the use of *paracetamol* (also known as *acetaminophen* or Tylenol) to self-medicate for fever, as opposed to *ibuprofen*, as they further evaluate the claim. ["Avoid ibuprofen" - France24, 3/17]

Again, while a vaccine does not yet exist, the race to develop and test one is quickly heating up with the first human trial in the US, which began March 16. ["Coronavirus vaccine test" - AP News] At least two other companies, both based in Germany, are also developing experimental vaccines. ["Hopes of coronavirus vaccine mount" - CNBC] However, even if development goes well, Anthony Fauci of the US National Institutes of Health says a vaccine will not be available for widespread use for 12 to 18 months. ["Coronavirus vaccine test" - AP News]

Prediction of Future Case Counts Based on Current Data

In the next section we proceed to analyze the data from India with standard epidemiologic tools of modeling disease transmission and estimating the theoretical number of infected at a time t, namely, I(t). The model known as SIR model is a compartmental state-space model guided by a set of equations relating the number of susceptible people S(t), number of people infected I(t) and number of people who have recovered R(t). Though there are numerous websites that displays the data, [Microsoft bing COVID-19 Tracker, "Novel Coronavirus (COVID-19) situation" - WHO, "COVID-19 Coronavirus Outbreak" - worldometer] we used current daily data from the 2019 Novel Coronavirus Visual Dashboard operated by the Johns Hopkins University Center for Systems Science and Engineering (JHU CSSE). [Dong et al. 2020; JHU CSSE COVID-19 Github]

Brief Outline of the Model

The standard SIR model has three components: susceptible, infected, and removed (includes the 'recovered' and the 'deaths'). Wang et al [2020] recently proposed an extension of this model, called the eSIR model, to incorporate time-varying transmission rates or time-varying quarantine protocols. The proportions of infected and the removed cases are modeled using a Beta-Dirichlet state-space model while a latent Dirichlet distribution is assumed for the underlying unknown

prevalence of the three states. Priors for the disease transmission rate, removal rate (consequently, the reproductive number) and the underlying unobserved prevalence of the susceptible, infected and removed states at the starting time are considered. Using the current time series data on the proportions of infected and the removed cases, a Markov Chain Monte Carlo implementation of this Bayesian model provides predicted proportions of the infected and the removed cases at future time points, and posterior median estimates of the unobserved prevalence at both observed as well as future time points along with credible intervals (CI). Additionally, when using the eSIR model with time-varying disease transmission rate, it can depict a series of time-varying changes caused by either external variations like government-initiated macro isolation measures, community-level protective measures and environment changes, or internal variations like mutations and evolutions of the pathogen. The second eSIR model that accommodates time-varying quarantine allows us to move a certain proportion of susceptible subjects to the quarantine stage. This model, however, does not allow the transmission rate to vary with time; only lets the proportion of susceptible people to decrease at certain time points. The R package for implementing this general model for understanding disease dynamics is publicly available here: https://github.com/lilywang1988/eSIR.

For creating our prediction figures, we used the eSIR model with time-varying transmission rate. Our chosen prior for the transmission rates during the no intervention period, the period with travel ban in effect only, the period with travel ban and social quarantine, and another period with an additional hypothetical intervention of nationwide lockdown were respectively 1, 0.8, 0.6 and 0.2. The prior for the reproductive number R_0 (the expected number of cases generated by one infected person in the absence of any intervention) was taken to be 2 in all scenarios. All calculations were carried out in the *RStudio* platform.

Prediction Results

Figure 3 is central to the story where we project the cumulative number of cases on a daily basis over time till May 15. The predicted cumulative number of cases in India, US and Italy on March 31 is 379, 394 thousand and 550 thousand, on April 15 is 4.8 thousand, 10.4 million, and 8.4 million and on May 15 is 58.6 thousand, 39.6 million and 44.5 million. However, the upper confidence bound for the counts for India is close to 915 thousand. Note that these predictions are based on the assumption of having no intervention and Italy and USA are in a more advanced stage of the epidemic. If the same rate of exponential growth continues with no intervention these numbers for India will be at 100,175 on June 1 (upper CI 1.46 million) and to a staggering 131,328 by June 15 (upper CI 1.63 million). When we ran the model, we used observed data up to March 16. For March 17, 18 and 19 our model predicted 119, 126 and 133 cases in India whereas the observed case counts were 142, 156 and 194 respectively, giving some credence to the predictions and also showing that we are underestimating the case-counts which will accumulate as we progress in time. **Thus our current estimates are at best underestimates for India based on early phase data.** This underestimation pattern holds for USA as well but for Italy we overestimate (**Figure 3**). The uncertainty in the predictions for India are large with many unknowns, thus we present not

only the posterior median of the predicted counts but also the upper CI in **Figure 3**. Note that we have very low estimated prevalence considering the huge population size in India (1.339 billion by 2017 according to the data from World Bank and United States Census Bureau), and this method itself accumulates uncertainties from results of previous time points, which altogether lead to the large uncertainty in the prediction. Under-reporting/testing can also be a cause of the small counts. The findings in **Figure 3** suggest that a slower rate of growth is predicted in India based on the current data when compared to Italy and USA. However, availability of testing and community transmission may lead to a spike in a single day and that will shift the projection curve significantly and India can start looking like USA or Italy in terms of case-counts.

Figure 4 focuses only on India and creates hypothetical interventions of various severity in the eSIR model. Here, instead of adjusting the case counts for the total population of India (as in **Figure 3**), which is perhaps leading to the underestimation in Figure 3, we adjusted using the total population from major cities of the Indian states or union territories that are currently COVID-19 hotspots in India (namely, Kochi, Mumbai, Pune and Bengaluru). We see that without enforcing the interventions, the predicted counts are going to exceed the estimated capacity of hospital beds in India (estimated at 0.7 per 1000). It should be noted that 70 hospital beds per 100,000 people is an upper bound on treatment capacity. Given an average occupancy rate of 75%, only a quarter of these are available. (Sindhu et al. 2019) Moreover, critically ill COVID-19 patients (about 5-10% of those infected) will require ICU beds, which constitute between 5 and 10% of bed capacity in Indian hospitals (Yeolekar & Mehta 2008) with very high occupancy rates

We also note from **Table 3**, for example the predicted number of cases by May 15 will be at 161 per 100,000 without any intervention (2.2 million total cases nationwide) and will reduce to 1 per 100,000 (13,800 total cases nationwide) with the most severe form of intervention. We also consider Italy and USA under similar degree of interventions in **Table 3** and in **Figure 5**, and drastic reductions are noted, particularly with the large number of currently confirmed cases in these two countries.

Limitations

Our statistical modeling and forecasts are not without limitations. The uncertainty in our predictions is large due to many unknowns arising from model assumptions, population size, accuracy of the diagnostic tests for COVID-19, heterogeneity in implementation of different government-initiated interventions and community-level protective measures. While we do observe a similar pattern in the daily growth rate of cases between US and India based on data until March 16, with India being behind US by around 13 days in terms of case counts, we need to keep in mind that growth rates may depend on factors such as the number of diagnostic tests administered per day, accuracy of test results, population demographics, exposure, and the policies undertaken already to curb the spread of the disease. Regardless of the biases, the analysis shows the impact and necessity of interventions worldwide.

Will Summer make it better?

There is some conjecture that India is less at risk of COVID-19 spread due to the rising temperatures in March. This has brought about speculations about the effect of temperature on the incidence of COVID-19 with some reports indicating negative association of temperature and incidence. [Wang et al. 2020 (medRxiv), Wang et al. 2020 (SSRN)] Other studies have also identified significant community outbreaks along restricted latitude, temperature, and humidity, similar to the behavior of a seasonal respiratory virus. [Sajadi et al. 2020] We explored to find any similar trends in the associations between the average monthly temperature and the incidence counts with worldwide data.

We obtained data available from Kaggle [Novel CoronaVirus 2019 Dataset] which was curated from Johns Hopkins University public data dashboard to result in a day-level database on COVID-19 cases. We aggregated these cases to a month-level for each country, that is, we look at the total number of new cases in the months of January, February and March (until March 15, 2020) for each country. Additionally, we obtained the monthly average temperature of major cities across the world, ["Cities by average temperature" - Wikipedia] and used it to compute the monthly average temperature for each country. We computed the correlation between the average monthly temperature and total monthly incidence and it was indeed negative in sign. The estimates and the 95% confidence interval for the correlation coefficient for (a) January was -0.213 and (-0.600, 0.253) with 20 countries having non-zero incidence, (b) February was -0.118 and (-0.392, 0.179) with 47 countries having non-zero incidence, and (c) March was -0.129 and (-0.308, 0.058) with 111 countries having non-zero incidence. Although the estimates were negative, the 95% confidence interval includes zero indicating weak evidence for any claim of confirmed negative association. Any such affirmation will require further data and investigation.

To further elaborate, we show spatial plots for the average monthly temperatures from January through March across all countries, as can be seen in **Figure 6**. These are accompanied by total monthly incidence across all countries from January until March 15. These plots indicate a suggestive pattern of increase in community spread across cities and regions specifically along narrow north east-west directions. Countries in these regions consistently exhibit similar weather patterns. However, in the context of India we clearly see a gradual rise in the number of incidences starting from January through March. Although the temperatures in India are very high during the months from March onwards, the focus should be on interventions as they play an important role in reducing the incidence while the scientific community further explores the effect of temperature. We cannot rely on the hypothetical prevention (with inconclusive evidence) governed by meteorological factors and need public health actions, regardless of the weather.

CONCLUSION

Though the epidemiologic and mathematical calculations make a convincing case for enforcing severe interventions, they come at a tremendous price to the social and economic health of the people of India. The management of this crisis requires strong partnership of government, scientific community, health care providers and all citizens of India (and all global citizens).

COVID-19: Economic Impact and Mitigation

Social distancing measures to slow down the coronavirus outbreak will have very serious economic repercussions. Recently released data from China ["Coronavirus devastates China's economy" - CNN] show that in the month of January and February, compared to the same period a year ago, retail sales fell by 20.5% and industrial output by 13.5%. Economic losses can spread from directly impacted sectors (like hospitality and transportation) to others (like online retail and apparel) through a contagion process not dissimilar to that of the virus itself. It can last months or even years after the restrictions on social mobility are lifted, because the damage from business closings and layoffs are often irreversible.

There are three broad classes of policies that may be used to counteract this: (a) monetary easing (lowered interest rates and increased money supply) and fiscal stimulus (increased government spending) to revive overall macroeconomic health (b) more targeted relief for sectors which are heavily impacted to keep them afloat till demand revives (c) even more targeted livelihood assistance for infected individuals who have to go into quarantine.

(a) Monetary and fiscal policy

The Indian economy was in a long slowdown even before the crisis hit. Many commentators have been urging stronger monetary and fiscal measures, a step which assumes increasing urgency now. The Reserve Bank of India has not yet gone for the kind of sweeping rate cuts and liquidity infusion that the U.S Federal Reserve has recently undertaken, ["Federal Reserve cuts rates" - CNN] so there is room for maneuvering there. Corporate and personal income tax cuts have been the government's favored fiscal instrument in the last Union Budget. However, since only 1.1% of Indians pay any income tax, ["How many people in India pay tax?" - Financial Express] the overall stimulus will be much weaker compared to something like the payroll tax holiday proposed in the U.S. The government should seriously consider increasing allocation in MGNREGA, the employment guarantee program, which reached 77 million mostly poor workers in 2018-19.

(b) Sectorally targeted assistance

In the context of the U.S, some economists have advocated virtual demand creation [Saez & Zucman 2020] by the government – firms should be paid their lost revenues over the duration of

the lockdown. This takes care of heterogeneous impact (after all, grocery stores and pharmacies will not be as badly hit as movie theaters and restaurants) but raises difficult issues of loss estimation. This is especially true in India where small informal sector firms dot the economic landscape. Nevertheless, the GST (Goods and Services Tax), whose introduction in 2017 caused quite a few hiccups, can be put to good use now. Firms may be allowed to claim a tax credit based on the difference in average monthly sales before and during the lockdown. Some struggling sectors like airlines and infrastructure companies need to be closely watched and possibly given additional assistance. These sectors are the source of loan defaults, which have precipitated an ongoing banking crisis. ["Key lessons from NPA crisis" - Hindu Business Line] Compounding that problem will be costly.

(c) Individually targeted livelihood assistance

This has received surprisingly little attention but may be the most important instrument for not only economic relief but also effective social distancing. Near universal lockdowns of the kind adopted in more affluent nations is going to be both extremely burdensome and impossible to enforce in India, because a lot of essential services are very labor intensive. For example, about 20 million people work in food retail, ["Indian Retail Industry - Current Status"] manning the country's bustling bazaars, small grocery stores, vegetable carts, etc. Shutting them at home will not only lead to livelihood losses for millions of families but also starvation for others. It is of utmost importance, therefore, that India adopt widespread testing to identify and quarantine the infected rather than go for the blunt instrument of isolating nearly everyone.

For people living hand-to-mouth, without paid leave, health insurance or opportunity to work from home, the economic consequence of testing positive can be disastrous. It is a reasonable expectation that barring those in secure, salaried jobs, most will try to evade it. To ensure compliance, it is critical to generate the right incentives. This means not only making testing and treatment free, but also providing livelihood assistance for the period of quarantine. To get a ballpark idea of the fiscal burden involved, assume 10 lakh detected cases, quarantine of 6 weeks per patient, and Rs 10,000 monthly compensation. This adds up to a bill of Rs 1,500 crores, which is roughly 2.5% of the annual healthcare budget of the central government. There is also the need to improve the facilities in quarantine centers – there are already reports ["Why Indians run from isolation" - Scroll.in] of people escaping confinement due to the poor conditions.

Public expenditure on healthcare in India is 1.28% of GDP, which is very low by international standards. There are 0.7 hospital beds per thousand population, 0.8 doctors and 2.1 nurses. In comparison, the averages for middle-income countries are 2.4, 1.3 and 2.6 respectively. [World Bank] The coronavirus pandemic has overwhelmed the well-funded health care systems of advanced nations, so the strain on India's ragtag medical infrastructure will be unimaginable. Since one should never let a good crisis go to waste, the most important lesson to take away from this one is that we need a paradigm shift in healthcare spending.

Health Care Infrastructure

As we have argued, quantitatively and qualitatively, this is a tipping point in our history, escalated by a pandemic that the living generation has not seen. The pressure on the health care system, small and large, will be enormous, impacting both the health care receiver and giver alike. Health care workers and first responders are at the front line of this pandemic, and we, as a community, should ensure they are not over-burdened, safe and have adequate resources to function in the most effective and efficient manner. This involves better triaging of non-essential health care, sustaining a steady supply chain of medical resources (masks, gloves, gowns, ventilators), and protecting our healthcare workers (physically and psychologically). Given the long term uncertainty of this virus strain, it is now imperative to have structured plans in place to build scalable health infrastructure and capacity, and create access to universal coverage for testing and treatment across the entire socio-economic spectrum to diseased as well as healthy, asymptomatic carriers. This would require an expansive buy-in from many sectors, both government and industry. COVID-19 has held up a mirror to the many inadequacies of our current health system. We would be wise to take a long, hard look, and make foundational and systemic changes, even as we move quickly to address the immediate & urgent needs.

Majority of the Indian population do not have any health insurance coverage. According to the latest National Family Health Survey only 29% of Indian households have at least one member covered under health insurance or health scheme. [National Family Health Survey, India] More than 55% of households do not generally seek healthcare from the public sector due to lack of trust in the quality of care received at government hospitals. Private health sector is the primary source of healthcare in urban areas. In rural India, the situation is further exacerbated by poverty and lack of health consciousness. Moreover, in suburban and rural India, a substantial chunk of the working class population are daily wage earners with no benefits that would allow them to practice social distancing. COVID-19 has emerged as the defining health crisis amidst this socio-economic fabric. To handle a crisis of this scale in the context of the Indian economy, different sectors of society have to come together to roll out free universal coverage for testing and treatment. It is critical that all stakeholders: the public, government, and the private sector come together now to create a partnership.

In the words of the WHO Director General "the days, weeks, and months ahead will be a test of our resolve, a test of our trust in science, and a test of solidarity." It will be unwise to be complacent based on current case-counts in India as the past four months have been a complete failure of our societal imagination. As Obelix said, the Sky is Falling -- and we hope to be proved otherwise! [Obelix — Wikipedia] In this moment of pause, reflection and disbelief, the world is getting its education on the difference between the exponential versus the linear.

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FIGURES

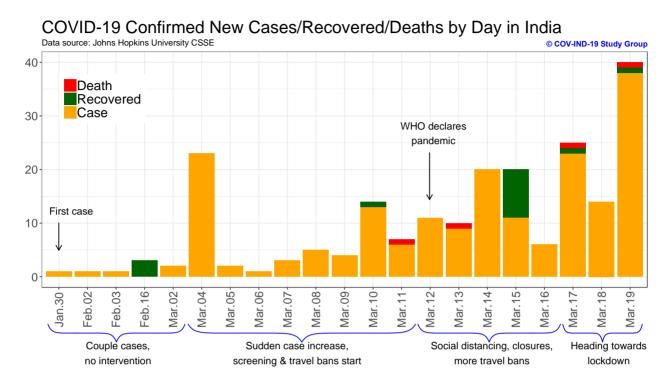


Figure 1. Description of the cases, recovered and fatalities in India with landmark policy/recommendations.

Data Source: JHU CSSE Cumulative number of COVID-19 infections updated on March 19

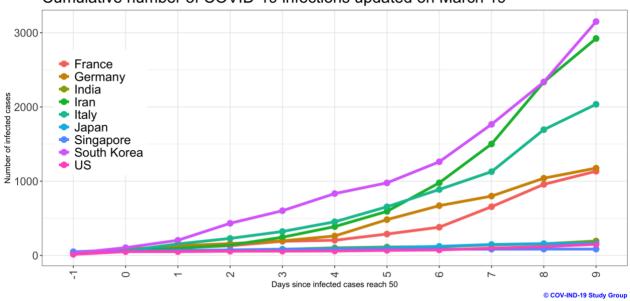


Figure 2. Early phase of the epidemic and daily growth in cumulative case-counts in India compared to other countries affected by the pandemic. The zero on the horizontal axis is the day where cumulative confirmed cases exceeded 50.

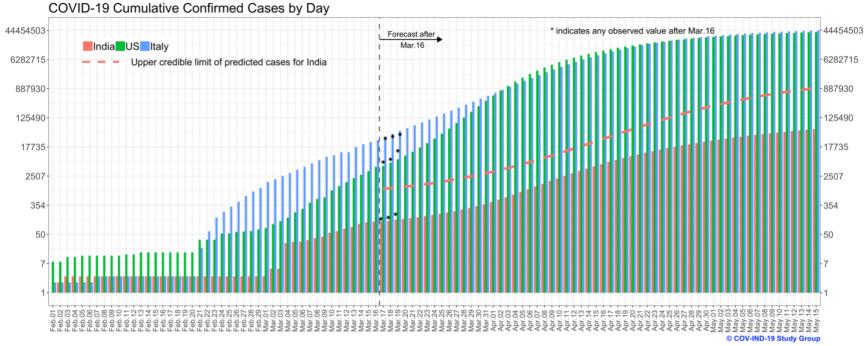


Figure 3. Daily growth in cumulative case-counts in India compared to the US and Italy (all affected by the pandemic) up to May 15. Observed data are shown for days up to March 16. Predicted future case counts for March 17 and onwards based on observed data until March 16 using the eSIR model assuming no intervention has been implemented. Observed case-counts for March 17, 18 and 19 are also plotted that show how close these predictions are. The counts are adjusted for the total population of each country (data from World Bank and United States Census Bureau).

Data source: JHU CSSE, censusindia.gov.in Adjusted for the total population of Kochi, Bengaluru, Mumbai, Pune: 32 millions Predicted number of COVID19 infections based on data upto Mar 18

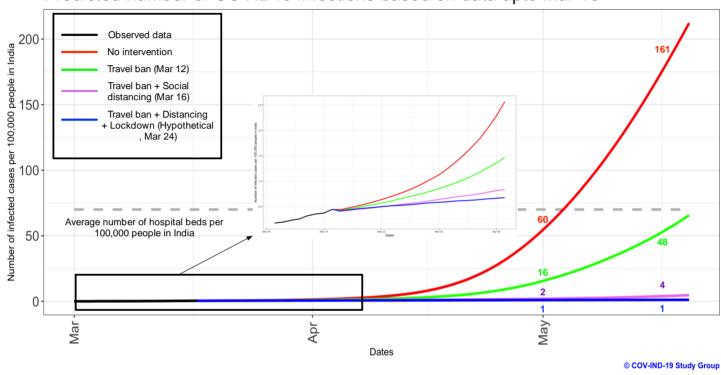


Figure 4. Daily growth in case-counts in India per 100,000 people and how that is affected by different non-pharmaceutical intervention strategies. Observed case-counts are shown until March 18, after which the predicted future case counts from the eSIR model are shown. The case-counts are based on the total population of the cities Mumbai, Pune, Kochi and Bengaluru since the current COVID-19 hotspots of India are in the states of Maharashtra, Kerala and Karnataka.

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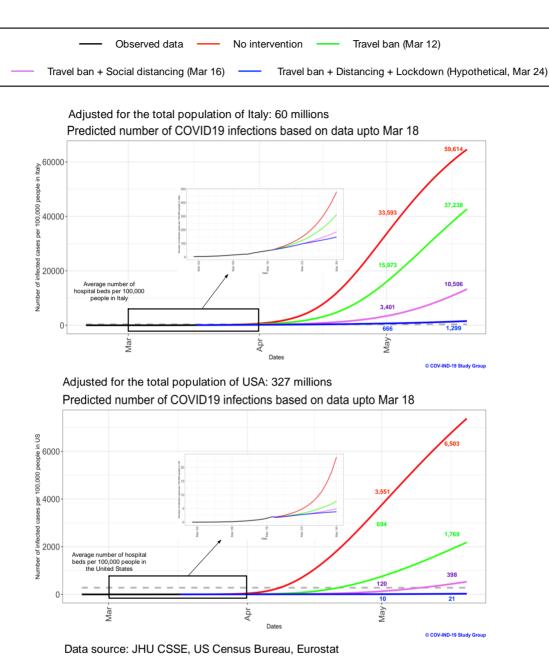


Figure 5. Daily growth in case-counts in Italy (top panel) and US (bottom panel) per 100,000 people and how that is affected by different non-pharmaceutical intervention strategies. Observed case-counts are shown until March 18, after which the predicted future case counts from the eSIR model are shown. The case-counts are based on the total population of the respective countries.

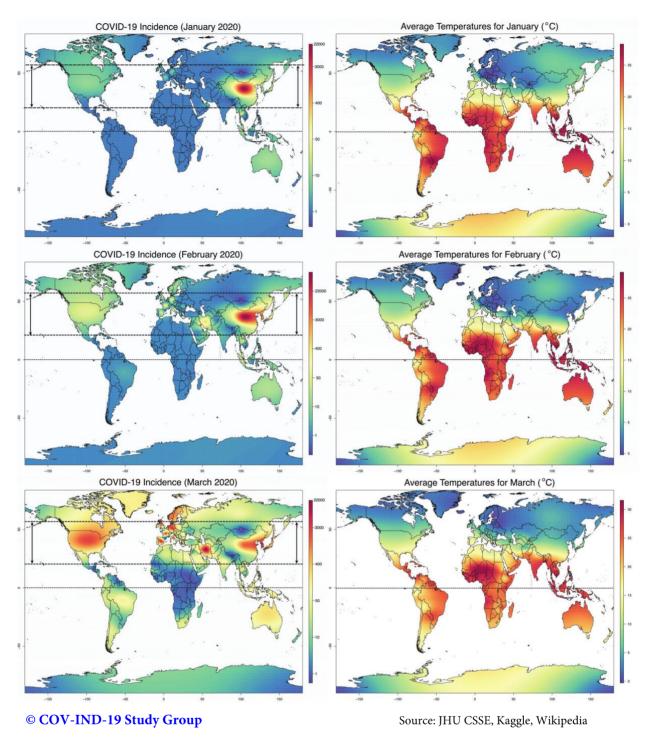


Figure 6. *Left*: Country-wise total monthly incidence of COVID-19 in the months of January, February and March (until 15th). The horizontal lines approximately indicate the equator, the tropic of cancer and the 60N latitude. *Right*: Average monthly temperature (in C) during the months of January, February and March.

TABLES

Table 1. Timeline of COVID-19 interventions in India

Date	Interventions
3 March 2020	• India travel ban has been issued on four countries - China, South Korea, Italy, and Iran
6 March 2020	 Union Health Ministry has issued advisory to avoid mass gatherings
7 March 2020	 Agra Mayor has urged the Union government to close down historical monuments including Taj Mahal Kuwait suspends flights to India
9 March 2020	• Qatar puts India on travel ban list
10 March 2020	• Manipur has closed its border with Myanmar
11 March 2020	 India suspends all visas and e-visas granted to nationals of France, Germany, and Spain on or before 11 March
12 March 2020	 WHO declared the COVID-19 outbreak as 'pandemic' India suspends all visas with the exception of those for diplomatic, UN, or international bodies, official and employment purposes until 15 April India reports 1st death
13 March 2020	 India reports 2nd death Several academic institutions (e.g., JNU, IIT, IIM) cancel classes/convocations, some closed hostels
16 March 2020	 Centre proposes social distancing measures until 31 March India bans passengers from EU countries, UK, and Turkey until the end of March Central government recommends the closure of educational institutions until 31 March
17 March 2020	 Taj Mahal will be shut down until 31 March; ASI closes 3,000 monuments and 200 museums Mandatory quarantine of passengers coming from UAE, Qatar, Oman, and Kuwait India is heading towards a countrywide lockdown mode
19 March 2020	 India halts all incoming commercial international flights for 1 week Some state governments ban public transportation Prime Minister urges people of India to observe self-imposed curfew on March 22

Source: https://www.pharmaceutical-technology.com/news/india-covid-19-coronavirus-updates-status-by-state/

Table 2. Proportion of population in specifically vulnerable subgroups at potentially high risk of COVID-19 severity risk in India

Metric	Number† (in millions)	Year	Source
Uninsured	1,104	2014	Prinja et al. 2019
Population over 65	92.5	2020 (est.) CIA World Factbook
Hypertension (men)*	175.7	2015/16	Gupta & Ram 2019
Hypertension (women)*	132.6	2015/16	Gupta & Ram 2019
People with cardiovascular disease*	78.7	2016	Prabhakaran et al. 2018
Population with COPD*	75.9	2016	Lancet 2018
Population with asthma*	45.5	2016	Lancet 2018
Develop cancer by age 75 (men)**	70.3	2018	NICPR
Develop cancer by age 75 (women)**	62.3	2018	NICPR
Population with diabetes (adult)	122.8	-	IDF
Access to inpatient department facilities***	731.4	2012	IMS Institute 2013
Access to outpatient department***	1,104	2012	IMS Institute 2013

[†] based on 2020 est. of 1.38 billion from <u>UN Department of Economic and Social Affairs</u> * age-standardized; ** risk; *** defined as within 5-kilometer distance of home or work Abbrev.: COPD, chronic obstructive pulmonary disease; IDF, International Diabetes Federation; NICPR, National Institute of Cancer Prevention and Research

Table 3. Predicted number of infected cases per 100,000 people on (April 15, May 1, May 15) under different hypothetical interventions using the eSIR model. Predictions based on observed counts until March 18.

Country	No intervention	Travel ban only	Travel ban + Social quarantine	Travel ban + Social quarantine + Lockdown in 1 week
India*	(7, 60, 161)	(3, 16, 48)	(1, 2, 4)	(1, 1, 1)
Italy**	(6794, 33593, 59614)	(2747, 15973, 37238)	(796, 3401, 10506)	(322, 666, 1299)
US***	(928, 3551, 6503)	(110, 694, 1769)	(21, 120, 398)	(6, 10, 21)

^{*} adjusted for the total population of the cities Mumbai, Pune, Kochi and Bengaluru

^{**} adjusted for the total population of Italy

^{***} adjusted for the total population of US