COVID-19

A PROBABILISTIC MODEL AND STUDY

ABSTRACT

The coronavirus disease 19 (COVID-19) is a highly transmittable and pathogenic viral infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It emerged in Wuhan, China and spread around the world rapidly in the beginning of 2020. It has since been declared a pandemic by WHO. All governments and organizations worldwide have been devising methods to deal with the viral outbreak. Here we will attempt to analyze the pathogenicity of the virus, the testing strategies adopted by various countries, the measures taken by governments etc. while also modeling the uncertainty of all these actions and events.

INITIAL PATIENTS OF THE DISEASE

WHO was informed on 31st December 2019 about cases of pneumonia. The cause was still unknown when on 3 January 2020, a total of 44 patients with pneumonia like symptoms were reported by the national authorities in China. Of the 44 cases reported, 11 are severely ill, while the remaining 33 patients were in stable condition.

Patient 'Zero'

"A Wuhan shrimp seller identified as coronavirus 'patient zero' " –said the headline of a Chinese news outlet referring to a 57 year old female shrimp seller from the Huanan Seafood Market. She initially developed a mild cold but on developing severe pneumonia like symptoms she was quarantined at the end of December when doctors started to realize the spread of the virus.

The first case in India was reported in Kerala on January 30. The first patient was a student at a university in Wuhan, China and had returned for vacation.

The first 50 COVID-19 cases in India were reported in a span of 41 days and were spread in 12 states and 18 cities/districts.

SIMPLE TRANSMISSION MODEL

The basic reproduction number (R0), is defined as the expected number of secondary cases produced by a single (typical) infection in a completely susceptible population.

Basic Reproduction Number

1. $R_0 < 1$ Infection die out
2. $R_0 = 1$ Infection become endemic
3. $R_0 > 1$ Infection become pandemic — Death / Immune

- If the R0 <1, for example, 0.5. Then one person will produce 0.5 new cases, the secondary 0.5 cases will pass the virus to the next 0.25 cases. Thus the infected population will be getting smaller and die out without any chance to become global epidemics.
- If the R0 = 1, meaning that one person will only pass the virus to another, then to the next one. We end up having a flat line of the infectious case. Hence we call it endemic (local spread), for example, chickenpox.
- The last scenario is when the R0 > 1, for example, 2, then the growth will be exponential, 2 to 4, 4 to 8 and eventually reach the tipping point that it cannot be contained in a local area. We now call it a pandemic.

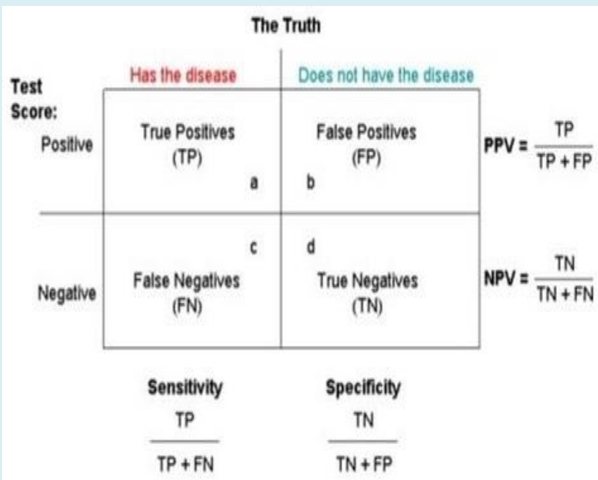
For Covid-19 the basic R0 was found to be 3.28 and the median R0 was found to be 2.79.

TESTING METHODS AND THEIR ADMISSIBILITY

1. **RT-PCR:**
   It is done using real-time reverse transcription polymerase chain reaction and the test can be done on respiratory samples. However the RT-PCR test performed with throat swabs is only reliable in the first week of the disease. Later on the virus can disappear in the throat while it continues to multiply in the lungs. For infected people tested in the second week, a sample material from the deep airways by suction catheter (sputum) can be used.
   The USA has tested millions of people using nasal/ throat swabs. The sputum samples were used only for patients that showed pneumonia like

symptoms. This majorly challenges the accuracy of the test results as more and more asymptomatic patients are getting identified each day.

2. **<u>Serological Tests:</u>**
These tests detect two types of protective antibodies that are produced by the body when the immune system recognizes a foreign structure, in this case SARS-CoV-2. Since these tests are rapid and cheap they can be used for mass testing in affected countries. In China, the Cellex test (rapid diagnostic tests (RDT) had a specificity of 95.6% and a sensitivity of 93.8%. A confusion matrix will help analyze these figures (assuming the total number of tests done were 100):-



93.8	4.4
6.2	95.6

<u>Positive predictive value</u> gives the probability of a true positive test and here it equals: $\frac{93.8}{93.8+4.4} = 0.955$

<u>Negative predictive value</u> gives the probability of a true negative test and here it equals: $\frac{95.6}{95.6+6.2} = 0.939$

- ❖ Although the Cellex tests give good accuracy rates, these figures cannot validate all the testing kits being manufactured by other companies around the world.

3. **<u>Medical imaging:</u>**
Chest CT scans are done to identify certain features typical to an infected person.

A study analyzed 1014 hospitalized patients with suspected COVID-19 in Wuhan, China—with patients undergoing both serial RT-PCR testing and chest CT scan. Of 1014 patients, 59% (601/1014) had positive RT-PCR results, and 88% (888/1014) had positive chest CT scans. Using RT-PCR results as reference standard, the sensitivity, specificity, and accuracy of chest CT in diagnosing COVID-19 were found to be 97% (n = 580), 25% (n = 105), and 68% (n = 685), respectively.
Thus,
Total patients tested positive for the disease were 888(126 tested negative).

Positive predictive value: $\frac{580}{580+308} = 0.6531$

Negative predictive value: $\frac{105}{105+21} = 0.8333$

Since this data was taken from Wuhan which is the origin of the pandemic, the radiologists may be suspecting higher rates of spread of the infection. This may have led to high numbers of positive results being depicted from the CT scans.
Initial RT-PCR pharyngeal swab sensitivity ranged from 66%-80% depending on assumptions made about patients with conflicting diagnostic data, these results cannot be considered optimal either.

The inaccuracy of these tests can result into a huge cost burden on the government of the different nations. This is because a false negative result will lead to an infected person going untreated and spreading the virus. A false positive test result, on the other hand, will lead to occupation of limited medical resources by an uninfected person.

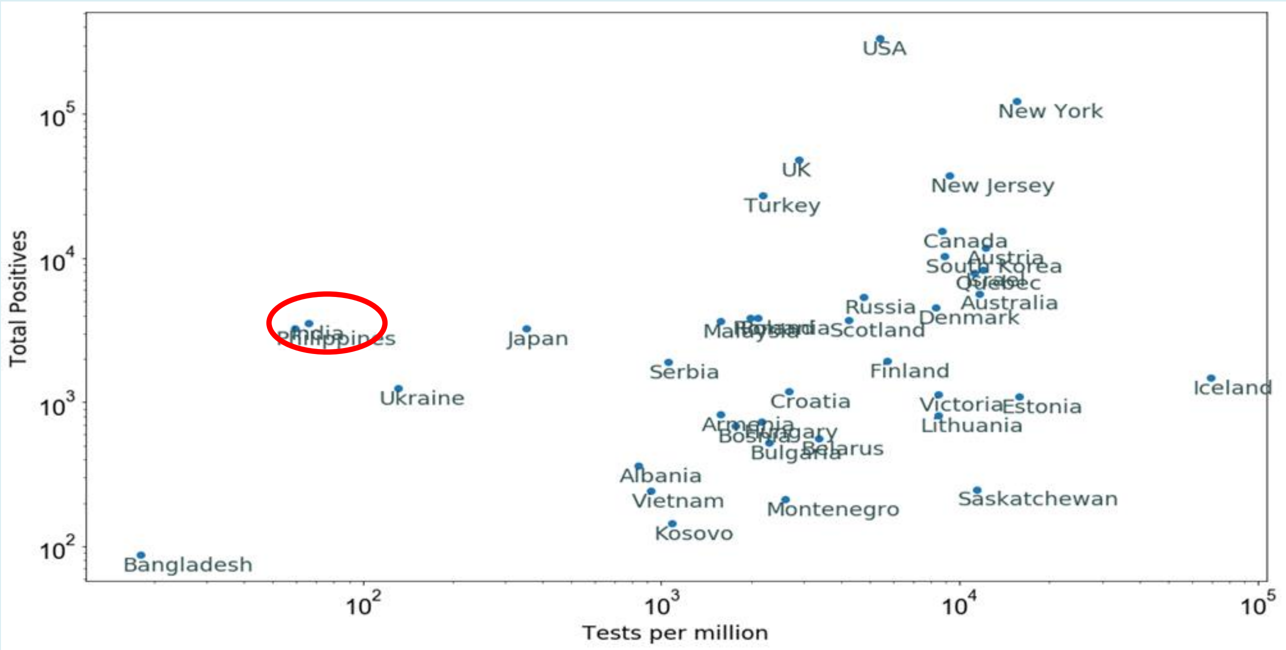
ESTIMATING POSSIBLY UNDETECTED COVID-19 CASES

Many countries such as China, Italy, the United States, the United Kingdom, Spain and others show sudden explosion in cases after a long period of few cases, indicating the possibility of many undetected cases.

We will use Bayes theorem to estimate undetected cases:

The quantity of interest for us is P(infected|notTested) i.e. the probability of infections that are not tested. This is equivalent to the percentage of the population infected by Covid-19 but not tested.

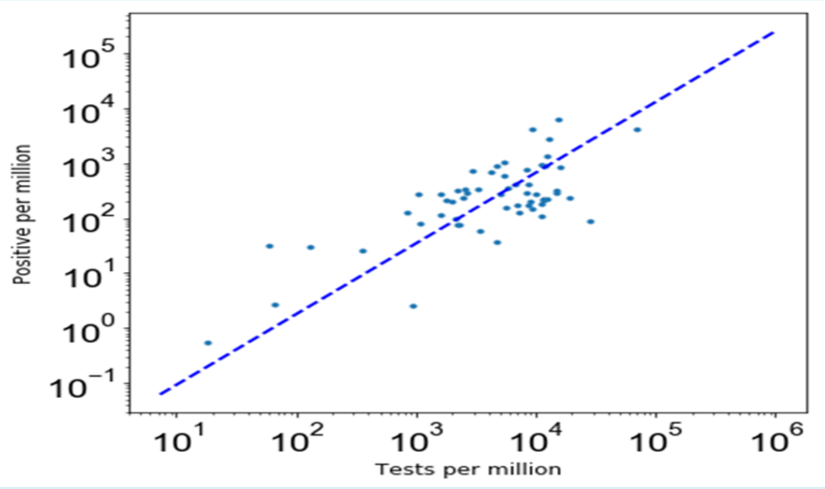
P(infected|notTested) = P(undetected|infected) × P(infected)/P(notTested)



Considering India we estimate the undetected infection cases by applying Baye's theorem.

where, P(infected) = (7*10^3)/10^6 ----1

P(not tested) = (10^6-100)/10^6 ----2



To estimate P(undetected|infected), We used the relation between the Covid-19 tests and confirmed cases as in the above graph. This is done by fitting a power law of the form: y = a * x**b, where 'a' is normalization and 'b' is the slope of this power law. The following plot shows a fit to the data points from the above plot, where the best fit a = 0.060±0.008 and b = 1.281±0.009.

Therefore,

$$P(\text{undetected}|\text{infected})=(10^6 - 100)/10^6 \, / \, (a * (10^6 - 100)^{**}b)/10^6 \qquad \text{----} 3$$

The estimate comes to be .34

When we apply the probabilities 1, 2 and 3 P(infected|notTested) comes out to be 0.00240 % of the population in India . On multiplying this by the actual population of India , it indicates a possibility of 33,58,990 infected but undetected cases in India. Now these infected persons can be symptomatic, asymptomatic or may be immune to the virus.

INCUBATION PERIOD

Models suggest household quarantine as a key intervention to mitigate against increased infection. Researchers defined a home-based quarantine in response to following identification of a symptomatic case in the household, where all household members remain at home for 14 days. The assumption suggested household contact rates would double during the quarantine period, but contacts in the community would reduce by **75%, if 50%** of each household comply with the policy.

A 14 day incubation period was announced by World Health organization for those individuals that were exposed to the virus. However, several cases of detection of the infection after the 14-day period have been reported worldwide.

Pooled analysis of 181 confirmed COVID-19 cases reported between 4 January 2020 and 24 February 2020 outside the Hubei province in China.97.5% of those infected developed symptoms within 11.5 days (CI, 8.2 to 15.6 days) of infection. These estimates imply that, under conservative assumptions, 101 out of every 10 000 cases (99th percentile, 482) will develop symptoms after 14 days of active monitoring or quarantine. It is uncertain by how much, however these numbers must have increased now that more and more asymptomatic patients are coming forward worldwide.

SYMPTOMATIC AND ASYMPTOMATIC PATIENTS

How to understand and react to your symptoms?

Let us find out the chances of a person being infected based on his/her symptoms. For this purpose we took a dataset that contains the symptoms shown by 500 individuals and their coronavirus test report(infect/not infected). The following things were deduced:

	Infected	Not Infected
Total number of people	254	246
Have fever	200	194
Have body pain	119	153
Have runny nose	129	126
Have difficulty in breathing	175	165

It can be inferred from these results that one symptom alone cannot indicate whether or not an individual has coronavirus.

It was however found that people suffering from both fever and running nose had a 59.84% chance of being diagnosed with the infection. Similarly people suffering from a combination of any 2 or all amongst fever, difficulty in breathing and running nose saw a 30-54.72% probability of being infected. This makes us believe that a person suffering from a combination of these illnesses should get tested a 100% if they have had a history of foreign travel in the recent past or have been in contact to an infected person. In case any of these two scenarios don't exist then the person must immediately contact a doctor who based on the patient's age and co-morbid conditions must prescribe proper treatment.

WHO report found that "**80%** of infections are mild or asymptomatic, **15%** are severe infections and **5%** are critical infections". Though we don't know what proportion of that **80%** were purely asymptomatic but it points to the large majority of undetected cases.

We will estimate the asymptomatic ratio by using information on Japanese nationals that were evacuated from Wuhan, China.

As of 6th Feb'20 a total of N=565 citizens were evacuated. Among them, pN=63 (11.2%) were considered symptomatic upon arrival based on (1) temperature screening before disembarkation, and (2) face-to-face interviews eliciting information on symptom. All passengers additionally undertook RT-PCR test, and m=4 asymptomatic and n=9 symptomatic passengers tested positive for COVID-19.Employing a Bayes theorem, the asymptomatic ratio is defined as:

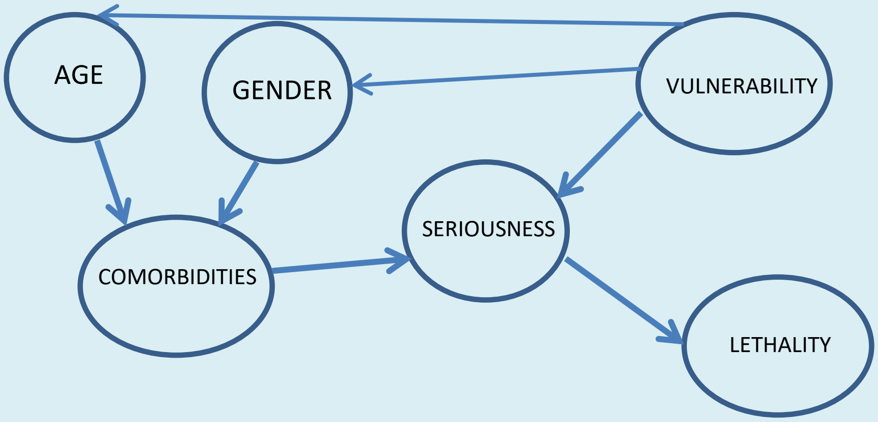
Pr(asymptomatic|infection)=Pr(infection|asymptomatic)XPr(asymptomatic)/Pr(infection)

Which can be calculated as m/(n+m). Using a binomial distribution, the asymptomatic ratio is thus estimated at 30.8% among evacuees.

How many asymptomatic cases become pre-symptomatic?
From the Diamond Princess Cruise ship about 50% of the patients who were tested turned out to be positive without having symptoms. They were asymptomatic at the time of the test but over a period of time, almost 75% of those turn out to have symptoms. So only 25% remained asymptomatic and 75% became symptomatic after a little while.
Why do asymptomatic patients not have symptoms? That's a sign that the body's immune response is working. The viral load was either low, so it did not mount a strong immune challenge or the people have a good immune system that blocked the virus and did not cause any symptoms.
Asymptomatic people can however spread the virus even though the probability is relatively lower.

ROLE OF COMORBIDITIES and PROGNOSTIC FACTORS

For a person infected with Covid-19 predictors of mortality can be dependent like:



The data we collected from an online survival rate calculator gave an insight into a few trends.

- Females have better survival rates as compared to males (not drastically different though). It is uncertain why this trend exists but it could be because of excessive indulgence in smoking and related practices, difference in immune responses etc.
- People with no comorbidities had very low chances of suffering from fatal medical conditions if infected with the virus **(the probability is less than 15%)**. Not to say that older age groups would absolutely not face any dire symptoms if infected and hence should take extra precautions.
- The prospects of survival of young individuals even with comorbidities are more favorable. Individuals suffering from cardiovascular diseases and/or diabetes are more likely to face severe consequences of the disease.
- People older than 40 years of age with comorbidities can be said to be at risk with those older than 60 years being at higher risk. Such individuals(with 2 or more comorbidities) if exposed and/or found symptomatic should be given highest medical priority and extensive treatment. These individuals have lesser chances of recovery from the disease and their comorbidities might result into complications at a later stage that cannot be foretold.

Can there be a relapse? 14% people in the world have reported a recurrence of the disease. However these people have not been re-infected, instead the virus present in the body just multiplied manifold again (called *"bouncing back"*) as the immune system of the person did not fully develop to fight the virus at all times. The chances of this happening are obviously higher in old aged people and very young children.

MEASURES USED WORLWIDE TO COMBAT THE DISEASE

Herd Immunity-> a situation that allowing the majority of the population to be infected to develop an immune system.
Mitigation-> normally known as "flattening the curve" to make the pandemic less intense, via means including massive testing, contact tracking, isolating cases, quarantining.
Suppression-> shutting down the city, closing public events, schools, universities to cut the spread.

HERD IMMUNITY

Base population 'N'

P , Immune

1-P , Not Immune

Take an R0 rate, the virus can only infect to the non-immune group. **R0(1-P)**
If we manage to get the **[R0 (1-P)] < 1**, the disease will go away in a short period of time. To satisfy this, we need to have **P >1-1/R0**
Taking the COVID-19 **R0 = 2.5** in this equation, we will have a **P> 60 %.**This means **2/3** of the person in this group need to be infected and recover with immunity to stop the virus.
Britain had proposed the Herd Immunity approach to contain the disease. So taking its example, let's say if the British government goes ahead and implement this approach, **66.4 M**(population of Britain) *** 60 % ≈40 M** people will be infected. Furthermore, the current case fatality rate (CFR) of Covid-19 is **4% and 8%** in China and Italy prospectively, and let's assume Britain has the best health care system in the world that could bring down this rate to just 1%, there will still be **about 40 M * 1% =400 K** deaths.
In 2018, the total death toll in the UK is just over 500K. And with the herd immunity strategy, Covid-19 will take almost the same amount of people's lives in just a few months. And as a comparison, World War Two only cost over 450K

lives in Britain including soldiers, nurses, citizens, etc. This implies Covid-19 will potentially have a larger impact in the UK than WWII.
However, to combat a pandemic with an R0>=2.5 and CER of 1%, would people willing to get infected in order to gain public herd immunity?
Mitigation cost too many lives and suppression may be economically unsustainable, herd immunity? Are we able to put a price tag on people's lives?

Sweden implemented the herd immunity strategy… can India do the same?
Sweden's 1,937 deaths are far higher in number compared to its neighbors Denmark and Finland. However India has been identified as suitable for this experiment pertaining to the relatively younger population. But it is also an over populated country. Lockdowns cannot be implemented for longer periods so at some stage herd immunization will have to be the approach. It should however come at a stage when the curve has been flattened to some extent so that it helps in controlling the outbreak without throwing the older population under the bus.

MITIGATION AND SUPPRESSION

India's Lockdown

Epidemiologic and mathematical models and the examples of other countries provide support for the effectiveness of a lockdown. Even if the disease isn't controlled completely it does buy the government some time to prepare and gather resources to fight it.

Psychological Impact of Disease and Lockdown

This study included **1210** respondents from **194 cities** in China. In total, **53.8%** of respondents rated the psychological impact of the outbreak as moderate or severe; **16.5%** reported moderate to severe depressive symptoms; **28.8%** reported moderate to severe anxiety symptoms; and **8.1%** reported moderate to severe stress levels. Most respondents spent 20–24 h per day at home **(84.7%);** were worried about their family members contracting COVID-19 **(75.2%);** and were satisfied with the amount of health information available **(75.1%).** Female gender, student status, specific physical symptoms (e.g., myalgia, dizziness, coryza), and poor self-rated health status were significantly associated with a greater psychological impact of the outbreak and higher levels of stress, anxiety, and depression **($p < 0.05$)**. Specific up-to-date and accurate health information (e.g., treatment, local outbreak situation) and particular precautionary measures (e.g., hand hygiene, wearing a mask) were associated with a lower psychological impact of the outbreak and lower levels of stress, anxiety, and depression **($p < 0.05$).**

It can be inferred that these strange times are extremely mentally taxing on many individuals. Loneliness, frustration and fear of the uncertainty must be very prevalent in most societies if not other severe mental illnesses. India has seen in a spike in cases of domestic violence owing to the lockdown. Migrant laborers, homeless and jobless people whose needs have been unaccounted for by the governments can be seen openly defying the stringent lockdown. There exists a high chance of more and more such cases coming forward as the lockdown extends. The policies of the governments around the world do not seem to have considered the impact that the pandemic can have on the mentality of the citizens that actually is common knowledge and not a revelation.

Economic Effects of the Lockdown

The projection of GDP growth done by IMF shows that the economy of all nations will take a massive hit due to this disease and the lockdowns instituted worldwide. For India the figures are:

	2019	2020	2021
India	4.2	1.9	7.4

What is surprising is how most world organizations predict that India will come out stronger as compared to superpower nations. Yes people are becoming jobless, companies are facing huge losses and the government hasn't been able to mitigate all the problems but these issues are not confined to India. They exist even in some of the most powerful nations. Thus although a major economic slowdown leading to a recession is in the cards for India, there exists a chance that India comes out of this disease shining.

CONCLUSION

The challenges that governments are facing across the world had been predicted in some form or the other from the outbreak in China. Therefore all nations should keep in mind all these scenarios when taking policy decisions. The demography of each country is different so the same approach for every population is unlikely to work. Open communication between affected people and the head of states should be encouraged. In such critical times dirty politics is highly unrequired. The uncertainty of the future course of events should not keep us from putting our best foot forward .If India has to come out a winner in this fight against the virus, the governments need to join forces, unite with the citizens and make decisions to support one and all. We are all moving towards a new world that will have a new normal.