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Mathematical Models for Predicting Covid-19 Pandemic: A Review

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Abstract. The catastrophic outbreak of the Novel Corona virus (Covid-19) has brought to light, the significance of reliable predictive mathematical models. The results from such models greatly affect the use of non-pharmaceutical intervention measures, management of medical resources and understanding risk factors. This paper compares popular mathematical models based on their predictive capabilities, practical validity, presumptions and drawbacks. The paper focuses on popular techniques in use for the predictive modeling of the Covid-19 epidemic. The paper covers the Gaussian Model, SIRD, SEIRD and the latest θ -SEIHRD techniques used for predictive modeling of epidemics.

Keywords: Covid-19, Mathematical Modeling, Epidemic, Mechanistic State Space, Gaussian Models, Predictive Modeling, SIR, SIRD, SEIRD, Non-Pharmaceutical Interventions.

1. Introduction

For over a decade, Machine Learning (ML) and Artificial Intelligence (AI) have provided unique solutions in the form of predictive modeling algorithms for complex social problems. These include medical diagnosis, predictive maintenance, Finance and Banking. However, this is not the case with Covid-19. The corona virus pandemic has been described as “the kryptonite of modern Artificial intelligence” [1]. The forecasts of the spread of Coronavirus by AI are neither accurate nor reliable [2]. The search for potential AI models has concluded that “very few of the reviewed systems have operational maturity at this stage” [3]. The failure of AI can be attributed to a range of factors, as demonstrated by [2]. Most prominent among them is the lack of sufficient data to build forecasting models. This is not only because of the lack of historical training data but also due to problems with big data, collected from unreliable sources such as social media. This pitfall has been explicitly demonstrated in the fabled Google Flu trends [4]. One of the first surveys on AI in accurately predicting the impact of Covid-19 has aptly concluded that “AI systems are still at a preliminary stage, and it will take time before the results of such AI measures are visible” [3]. The failure on the part of AI towards forecasting led to the consideration of simple and traditional mathematical models.

Epidemiological models need to predict disease progress, identify potential causes of transmission and suggest optimal intervention measures. The first successful modeling and containment of epidemic was that of cholera which tormented London in 1854. A physician, John Snow collected spatio-temporal data and visualized it on a map. He found transmission



patterns which centered around the Broad Street water pump, the zero point of transmission. The earliest publication addressing mathematical models in epidemiology dates back to 1766 by Daniel Bernoulli. It approximated death rate in London due to Chickenpox. However, a more structured approach was created by W. O. Kermack and A. G. McKendrick in 1927 titled “A Contribution to Mathematical Theory of Epidemics”. This approach introduced the use of deterministic compartmental models in epidemiology and acted as a cornerstone for mathematical transmission models. In this context it is important to mention the work of Enko, who in 1889 published a ground breaking probabilistic model in discrete time which was used to analyze the measles epidemic. Enko’s work can be considered as a forerunner to the renowned Reed-Frost chain binomial model introduced in 1928 at John Hopkins University. This model is based on the assumption that the disease spreads by discrete time Markov chain events.

Mathematical models for disease epidemic are either deterministic or stochastic, where the first is considered as a thermodynamic limit of the other. Mathematical modeling of epidemics broadly consists of three types, Statistical methods for epidemic surveillance, Mechanistic State-Space model and Empirical Learning models. Mechanistic State-Space models have outperformed the other two in describing respiratory diseases such as MERS and SARS. Mechanistic State-Space Models are classified (see Figure 1) as “Continuum” models, “Markov Chain” models, “Complex Network” models and “Agent Based Simulations”.

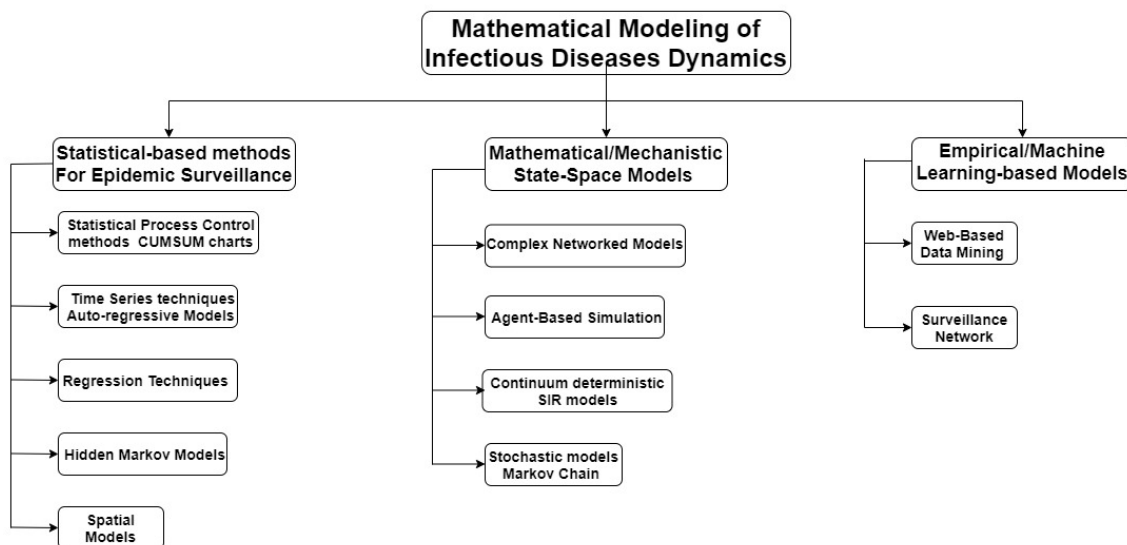


Figure 1. Classification of Mathematical Models in Epidemiology

The most significant functions of epidemic models are monitoring, forecasting major outbreaks and detection of patterns, disease characteristics that might suggest suitable measures for controlling the spread of disease. Mathematical simulations have allowed rapid situation assessments for proper resource allocation. In situations where cost of testing restricts collection of fresh data, mathematical simulations can be game changing. The Covid-19 pandemic has exemplified the centrality of dynamic mathematical models in predicting and containing outbreaks, response logistics and policy making on Non Pharmaceutical Intervention(NPI) measures.

2. Gaussian Models

Statistical Regression models detect dynamics of epidemic outbreak by monitoring the time-series statistics of reported infected cases. One of the early works on this was published by Serfling which was incepted to analyze the deaths caused by pneumonia and influenza. Gaussian Model(GM) is one such statistical model that has outperformed its peers in reliably predicting Covid-19 outbreaks. Gaussian models are based on the Central Limit theorem of Statistics [5], where the proposition consists of multiple independent and random variables, their suitably normalized sum tends towards a Gaussian distribution even if the original variables themselves aren't distributed normally.

In the Gaussian model, the bell shaped Gaussian function is fitted to existing data of cumulative deaths or detected infections and extrapolate the numbers to future times. Although Gaussian Model appears to be too simple and primitive, its applicability can be substantially justified. Firstly, GM appears to be a special case of Continuum models as suggested by[6]. Secondly, GM is know to be compatible with an agent based epidemiological model as showcased by[7].

A model was developed using Gaussian error function and Monte Carlo simulation[8] to predict the outbreak of corona virus in Italy. Based upon distribution observed in study of seasonal influenza[9], the cumulative numbers of detected cases and deaths in china were fitted with a Gaussian error function containing four parameters (see Figure 2).The Gaussian function used has been represented by Equation 1. Where erf represents Gaussian error function depicted by Equation 2.

$$a + b \operatorname{erf}(cx + d) \tag{1}$$

$$\operatorname{erf}(z) = \frac{2}{\sqrt{\pi}} \int_0^z e^{-t^2} dt \tag{2}$$

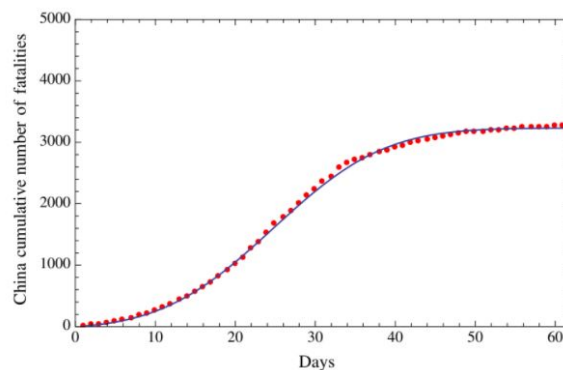


Figure 2. Gaussian Error Function fitted to cumulative number of deaths caused by COVID-19 in China (red dots) from January 22, 2020 [8]

The day of the Flex(i.e., the day the number of daily positive cases start decelerating) in Italy is predicted to lie between March 23rd and March 27th. However it was actually observed on 3rd April,2020. Additionally, the day with substantial reduction in the number of daily positive cases (decrease in number of new cases by more than 100) was predicted to lie between April 17th and April 27th. This substantial reduction was observed on 5th and 6th April,2020.

Similar model[10] was developed by IHME COVID-19 health services utilization forecasting team. This model forecasts the impact of Covid-19 on hospital beds and demand for ventilators in

the United States. Findings from this study have been crucial in developing lockdown strategies and justifying the use of Non-Pharmaceutical Interventions.

Another model similar to IHME COVID-19 was developed to predict the spread of the virus in Germany[11] and Europe[7]. It differs from the earlier mentioned work [8] by suggesting the use of monitored doubling times to approximate the total duration of the first wave and the point of time with peak deaths. This paper has concluded that higher order co-efficients tend to fit noise better than the signal itself. Therefore, second order polynomial (GM) is used to fit logarithmic daily deaths. Daily fatalities as a function of time denoted by $d(t)$ and cumulative deaths denoted by $D(t)$. The Gaussian model used can be described by equations mentioned below. Here, ω_d is the width of the Gaussian, d_{max} is the maximum value of deaths and $t_{d,max}$ is the instant of time with maximum deaths. And c_0 , c_1 and c_2 are coefficients of polynomial function of degree 2.

$$d(t) = d_{max} \exp \left\{ \frac{(t - t_{d,max})^2}{\omega_d^2} \right\} \tag{3}$$

$$d_m(t) = \frac{dD_m(t)}{dt} \tag{4}$$

$$\ln (d_m(t)) = \ln \left(d_{max} - \left(\frac{t - t_{d,max}}{\omega_d} \right)^2 \right) = c_0 + c_1 t + c_2 t^2 \tag{5}$$

$$c_0 = \ln d_{max} - \frac{t_{d,max}^2}{\omega_d^2}, c_1 = \frac{2t_{d,max}}{\omega_d^2}, c_2 = \frac{1}{\omega_d^2} \tag{6}$$

The applicability of such model can be confirmed using a holistic agent model[12]. It is also observed that the width of GM is within 10 and 15 days, and the peak in fatalities approximately occurs below 20 deaths per million.

The GM for Germany[11] predicted the first wave of Covid-19 pandemic to reach its maximum on April 11th^{+5.4days}_{-3.4days} with 90% confidence. Predictions made on the time of maximum deaths $t_{d(max)}$, maximum deaths per day d_{max} and cumulative deaths at the time maximum deaths D_{total} , for various European countries by [7], have been compared with values recorded by [13] [14] (see Table 1).

The major drawbacks of mathematical models involving sigmoidal functions are: (i) their tendency of over-fitting the data, (ii) high sensitivity to initial conditions and (iii) requiring large number of parameters. However, sigmoidal functions have been acknowledged for automatically accounting for exponential growth phase and the subsequent flattening phase that are observed in epidemic curves. Most exponential models rely on doubling times, which demands extensive pre-processing of the data. It is important to note that GM is able to accurately fit and model data produced by agent-based approach, given that the degree of social distancing remains unchanged. Gaussian models are so simple that comprehensive understanding of neither statistics nor epidemiology is required for its implementation.

3. Continuum Models

State-Space models, have been used to infuse our mechanistic understanding of disease transmission with a statistical framework by associating observed incidence disease dynamics with underlying population disease burden and susceptibility. The field of study in mechanistic modeling is described by a set of differential equations. These differential equations can be discretized to give simpler difference equations. The differential equations symbolize the general

Table 1. Comparison between Predictions[7] and Observations[13]

Country	$t_{d(max)}$	d_{max}	D_{total}	Time of Max Deaths	Max Deaths	Total Death
Austria	April 7 ± 21	21.6 ± 4.7	500 ± 170	April 8	30	273
Belgium	April 14 ± 18	430 ± 26	10,200 ± 1100	April 10	496	3019
Switzerland	April 5 ± 17	63 ± 12	1300 ± 300	April 4	75	666
China	February 17 ± 3	95 ± 3	2600 ± 100	April 15	1290	17169
Germany	April 12 ± 10	340 ± 6	7900 ± 400	April 15	510	3804
Spain	April 1 ± 6	960 ± 70	17,500 ± 1600	June 19	1179	28315
France	April 11 ± 8	980 ± 320	26,600 ± 9000	April 15	1438	17169
Greece	March 27 ± 9	3.8 ± 1.3	47 ± 17	April 3	10	63
Indonesia	March 19 ± 22	5.3 ± 4.7	111 ± 91	July 22	139	4459
Iran	March 25 ± 2	150 ± 14	4100 ± 400	July 28	235	16147
Italy	March 27 ± 1.8	832 ± 60	18,300 ± 1400	March 27	919	9134
Netherlands	April 2 ± 4	144 ± 23	2500 ± 400	April 17	1290	4636
Portugal	March 29 ± 4	24 ± 4	260 ± 40	April 3	37	246
Sweden	April 15 ± 35	162 ± 12	3600 ± 600	April 21	185	1765

state space where as the difference equations define the various states. Owing to the uncertainty related to measurement and process states, random abrupt peaks it is critical to remove measurement noise and on-line estimation of the process states for the real-time deployment of this mechanistic model.

Continuum models can describe the rough dynamics of the disease in the population. Continuum models can project the severity of epidemics as a function of age distributions or the evolution of disease transmission under Non-Pharmaceutical Interventions. The classical SIR model divides the population into 3 groups: susceptible individuals(**S**), infected individuals(**I**), and recovered individuals(**R**). Successive models SIRD, SEIRD also include dead individuals(**D**) and exposed but asymptomatic individuals (**E**). The compartmental action-mass model introduced by Kermack and McKendrick in 1922, can be considered as the basis of such models. The idea behind Continuum model scan be summed up in following set of equations,

$$\frac{dP_t(S)}{dt} = -p_{s \rightarrow 1} \sum_{N(S)} P_t(S, I), \quad \frac{P_t(I)}{dt} = -p_{I \rightarrow R} P_t(I), \quad \frac{P_t(R)}{dt} = -p_{I \rightarrow R} P_t(I) \quad (7)$$

$$\frac{dS}{dt} = -\alpha SI, \quad \frac{dI}{dt} = \alpha SI - \beta I, \quad \frac{dR}{dt} = \beta I \quad (8)$$

$$\frac{dS}{dt} = -\alpha SI + \gamma R, \quad \frac{dI}{dt} = \alpha SI - \beta I, \quad \frac{dR}{dt} = \beta I - \gamma R \quad (9)$$

Equations 7 denote probabilities of population moving from one compartment to the other. The symbols α and $(1/\beta)$ denote average values of the probability of disease transmission and the mean time period during which an infected person can spread the disease before completely recovering respectively.

Interesting research [15] was carried out incorporating three variants of classical SIR model, a time dependent SIR model, a discrete time time-dependent SIR model and a SIR model considering undetected infected persons. Discrete time time-dependent model can be represented as the following difference equations:

$$S(t + 1) - S(t) = \frac{-\beta(t)S(t)X(t)}{n} \quad (10)$$

Table 2. List of Notations Used

Notation	Description
β	Disease transmission rate(stationary)
$\beta(t)$	Disease transmission rate as function of time
β_1	Disease transmission rate of detectable cases
β_2	Disease transmission rate of undetectable cases
γ	Rate of recovery(stationary)
$\gamma(t)$	Rate of recovery as function of time
γ_1	Rate of recovery for detectable cases
γ_2	Rate of recovery for undetectable cases
n	The total population
R_0	The basic reproduction number
$R_0(t)$	The basic reproduction number as function of time
$R(t)$	Number of recovered persons at time t
$S(t)$	Number of susceptible persons at time t
ω_1	Probability that an infected person is detectable
ω_2	Probability that an infected person is undetectable
$X(t)$	Number of infected person at time t

$$X(t + 1) - X(t) = \frac{\beta(t)S(t)X(t)}{n} - \gamma(t)X(t) \tag{11}$$

$$R(t + 1) - R(t) = \gamma(t)X(t) \tag{12}$$

According to reports from WHO[16], only 87.9% of Covid-19 patients have fever and only about 67.7% of them develop dry cough. Other studies[17][18] on the characteristics of the virus have also given similar conclusions. Therefore, it is essential to consider undetected infected persons while developing mathematical models. The SIR model designed to consider undetected infected persons with w_1 being probability of detectable cases and w_2 being probability of undetectable cases. See Table 2 for complete list of notations used in Equations 10-16.

$$w_1 + w_2 = 1 \tag{13}$$

$$X_1(t + 1) - X_1(t) = \beta_1 X_1(t)\omega_1 + \beta_2 X_2(t)\omega_1 - \gamma_1 X_1(t) \tag{14}$$

$$X_2(t + 1) - X_2(t) = \beta_1 X_1(t)\omega_2 + \beta_2 X_2(t)\omega_2 - \gamma_2 X_2(t) \tag{15}$$

$$R(t + 1) - R(t) = \gamma_1 X_1(t) + \gamma_2 X_2(t) \tag{16}$$

A study[6] similar in nature carried out employing a slightly modified SIR model has yielded accurate predictions with an errors less than 3% (see Table 3). Since Gaussian evolution observed from China-driven Gaussian model, a standard SIR model was developed additionally which has derived similar dependence. The Gaussian function used is mentioned below. Here, α and μ are infection and recovery rates respectively. While β and γ are respective constants such that they satisfy equation.

$$I(t) = I_c e^{-\frac{\alpha\beta}{2} + (\alpha\gamma - \mu)t} \tag{17}$$

Table 3. Total number of cases reported of april 4 [6]

Country	Reported cases	Predicted cases	Error(%)	Predicted peak date	Horizon (4σ)	Total cases
Greece	1673	1621	3.0	04/03	05/18	2811
Netherlands	16,627	16,862	1.4	03/31	05/05	23,713
Germany	91,622	90,460	1.3	04/02	05/08	140,003
Italy	124,632	129,180	3.6	03/26	05/08	156,975
Spain	124,736	129,628	3.9	03/31	05/02	173,535
France	68,605	69,330	1.1	04/05	05/21	141,973
UK	41,903	42,888	2.4	04/12	05/26	165,443
USA	312,273	315,677	1.1	04/05	05/10	654,207

Intuitive research [19] was conducted based on deaths reported in New York city, Madrid and Stockholm to estimate standard epidemiological model of Covid-19. A simple SIRD Model was developed to include parameters for representing social distancing. Seven-day simulations of the spread in various cities across the globe was considered. It is important to note that the model fits appropriately to the mortality rates between 0.5% and 1.2% and thus emphasizes the uncertainty about this number. Relative to classical time varying SIRD, this model has included time-varying β , and therefore time-varying R_o to fit the death data.

Additionally, another research[20] carried out reflected a comparative analysis of SIRD and SEIRD models. The study observed that there was no difference about the accuracy of the fit to data, and both models yielded very close values for epidemiological parameters. However, the average time taken for an infected person to die was slightly lower on SIERD model. The SEIRD models indicates slower growth rate, which can be attributed to the incubation period included in its design. When it comes to predicting the impact of the epidemic with age distributions, SEIRD model offers more precision. But even with better predictions, the proposed SEIRD model is far more complicated than the SIRD model and the use of the latter should not compromise data analysis. The paper concludes that the age division does not alter predictions drastically, implying that in the case of simple predictions or analysis, SIRD models are useful.

During the early days of the epidemic, it was observed that the primary agents in spreading the virus from its epicenter in Wuhan to other cities were passengers who traveled by air. To estimate the number of infected cases exported out of Wuhan to other parts of Mainland China as well as cities across the world, an alternate study[21] was rolled out comprising a novel SEIR model. Here, global and domestic air travel data was analyzed to map the spread of the virus. Using this information, the study predicted the potential risks of spread in all major cities of mainland China.

Taking into account, the known special characteristics of this virus, the existence of infected undetected cases[22], a novel θ -SEIHRD model[23] was developed to consider the fraction θ of undetected cases over the real number of total infected cases, which allows the examination of this ratio's impact on the epidemic. In this paper, both deterministic and stochastic versions of the model were proposed. However, the deterministic model was used considering various advantages that it offered over the later. Advantages such as (a) low computational complexity allowing for finer tuning of the model parameters or (b) possibility of using simpler ordinary differential equations for suitable analysis have made the deterministic model more viable. This study has concluded that about 52% of infected persons are undetected. This is in close proximity of other medical studies[24][25] which suggest between 40%-50%.

4. Non-Pharmaceutical Interventions

Non-Pharmaceutical Interventions(NPI) can be defined as measures(apart from vaccination and use of pharmaceutical drugs) that can be taken by people and communities to help slow the spread of diseases like influenza and Covid-19. These measures are also referred to as community mitigation strategies. NPIs can be broadly classified into four groups (a) Communication for behavioral impact, (b) Personal protective measures (for example, hand hygiene and face masks), (c) Environmental measures (for example, modifying humidity and increased ventilation), (d) Social Distancing measures and (d) travel related measures. Studies[26][27] have revealed confirmatory evidence of efficacy and overall effectiveness in an influenza pandemic. The flattening of curve is crucial because a more gradual uptick of the number of cases will overburden the healthcare systems (see Figure 3). The rationale behind **”flattening the curve”** is that the use of appropriate social intervention measures would stagger the growth in number of new cases over a long period of time. This would reduce the number of active cases at the peak of the epidemic and reduce pressure on public infrastructure. Resulting in increased access to the limited medical resources.

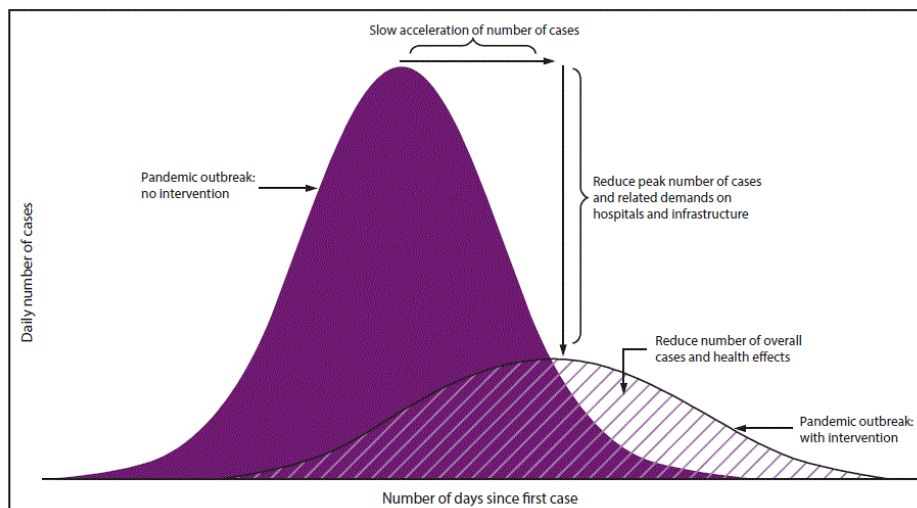


Figure 3. ”Flatten the Curve”

Imperial College Covid-19 Response [28] has published the conclusions of epidemiological modeling which has influenced policy making in the UK and other western countries. Microsimulation model was applied to Great Britain and the USA. Five scenarios of NPIs are discussed and their potential in mitigating the virus are depicted. The expected demand of ICU beds and total deaths were also projected against the time period for which these NPIs would be in effect. The results of this simulation signify the importance of non-pharmaceutical intervention measure. It concludes that relatively short term (three month) mitigation policy might reduce deaths by half and peak demand on health care infrastructure by two-thirds.

Effectiveness of social distancing and intervention measures have been highlighted by a recent study [29] that examines data from early exponential growth period of the epidemic. Here, a Bayesian inference based on Markov chain Monte Carlo sampling is applied to a class of compartmental SIR model. Important parameters in this model are the spreading rate λ , recovery rate μ and reporting delay (D)(Equation 18). Here R_o is the basic reproduction number.

$$R_o = \lambda/\mu \tag{18}$$

Three major change points in the spread rate were assigned with respect to three governmental intervention measures, (i) ban on large events and gatherings of more than 1000 people, (ii) the closing down of schools, child care centers and departmental stores (iii) complete contact ban and closing of all non-essential businesses. This study has credited the first two intervention measures for substantial reduction in the growth rate λ from 30% to 12% and down to 2% respectively.

On May 8th 2020, UK government announced its plans towards a complete lock down. In this context, research[30] on the effects of lockdown had it been implemented one week earlier or one week later was undertaken. A two layered Gaussian process where upper layer uses a compartmental SEIR model as a prior mean function with country and policy specific parameters and lower layer parameters are shared across all countries. This study has concluded that had the lockdown been implemented one week earlier would have saved 13,827 lives. 22,405 more deaths would have occurred if it had been implemented one week later. Also under the current plans of the UK government to re-open the daily deaths would stabilize around 200. However if the lockdown was maintained it would lead to the daily deaths falling under 100 in August, which would save an additional 6,215 lives. Integrating epidemic models with health-care and economic models can provide a holistic framework that may assist predicting the social impacts of various policy decisions.

5. Conclusions

According to mathematical modelers, a good mathematical model reflects the data it uses. The major hurdle currently faced by Mathematical models is the lack of noiseless undelayed consistent data. The adulteration of data appears to be occurring primarily due to the variations in guidelines to register cases and the uncertainty of the symptoms of Covid-19. The Continuum (SIR) family of models seems to be rapidly growing with ever-increasing considerations and variables, subsequently increasing the complexity of differential equations involved. Challenges faced by mathematical modelers is summarized into:

(a)**Pathogen evolution**: Similar to most flu virus, Covid-19 has also undergone mutations, which disrupts the design of models and dynamically changes parameters.

(b)**Statistical uncertainties**: The impact of the epidemic in a particular region depends on unknown factors such as the underlying immunity of the general population. Such factors greatly experience temporal and spatial variations. Statistical techniques that extract parameters that describe the properties and transmission characteristics of the disease from incomplete and noisy surveillance data are yet to be developed.

(c)**Contact patterns**: Laws such as “mass action” are based on the assumption that infectious contacts between persons are purely random in nature. However, if the interaction between individuals is not random, it would result in localized saturation of infection and undermine these laws. Such mixing would cause complex epidemics that cannot be predicted using traditional modeling techniques.

”**One model fits to all**” is not applicable to devise a Mathematical model in epidemiology. The nature of the problem assists in identifying the suitable model. The key factor is not to cite which model is accurate but to identify the model that caters to the requirement and in addressing the problem. The models discussed in this paper cater to different requirements. Few models predict the number deaths accurately whereas few are good at describing the disease attributes while others are designed to explore and measure the effects of measures of intervention.

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