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Article

Application of Mathematical Modelings in Prediction of COVID-19 Transmission Dynamics

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Abstract: Human civilizations are under enormous threats due to the outbreak of novel coronavirus (COVID-19) originated from Wuhan, China. The asymptomatic carriers are the potential spreads of this novel virus. Since, guaranteed antiviral treatments have not been available in the market so far, it is really challenging to fight against this contagious disease. To save the living mankind, it is urgent to know more about how the virus transmits itself from one to another quite rapidly and how we can predict future infections. Scientists and Researchers are working hard in investigating to understand its high infection rate and transmission process. One possible way to know is to use our existing COVID-19 infection data and prepare a useful model to predict the future trend. Mathematical modelling is very useful to understand the basic principle of COVID-19 transmission and provide necessary guidelines for future prediction. Here, we have reviewed 9 distinct commonly used models based on Mathematical implementations for COVID-19 transmission and dig into the deep head to head comparison of each model. Finally, we have discussed interesting key behaviour of each model, relevant upcoming important issues, challenges and future directions.

Keywords: Coronavirus, ODE, SIR, SEIR, transmission dynamic, prediction, SARS-CoV-2

1. Introduction

A large family of the virus (Coronaviruses) that can be a source of disease transmission in humans, starts with a typical cold to SARS (Severe Acute Respiratory Syndrome). The MERS-coronavirus (Middle East Respiratory Syndrome) was reported in 2012, in the Kingdom of Saudi Arabia (KSA), which generally originated from camel flu and spread as severe respiratory disorder to humans through various channels ([1][2][3]). With the symptoms of respiratory infections lead to acute form of pneumonia. The current ongoing novel coronavirus disease (COVID-19) outbreaks originated in December 2019 in Wuhan of Hubei province, China and have some link to Huanan Wholesale Seafood Market ([4][5][6]). Presently people and the community are suffering due to the disease (COVID-19) epidemic. Despite the fact that the World Health Organization (WHO) declared officially the pandemic has been spreading already not only in Asia, but also in Africa, South America, the Middle East, and Europe. The panic among people and the community of the virus (COVID-19) outbreaks recall the history of the London influenza pandemic in 1918. Besides, its mild symptoms characteristics in most of the cases and short sequential interval (4-5 days) are identical to influenza pandemic, rather than SARS-CoV or MERS-CoV ([7]). As of 28th September 2020, there have been 33,393,311 confirmed cases worldwide with 1,003,567 deaths and 24,701,429 recovered (https://www.worldometers.info/coronavirus/). These numbers are exponentially growing day by day.

At present, the people and community are under massive threats due to the coronavirus (COVID-19) disease. Since, there are still no recommended vaccines' or treatments available in the market, it is a really challenging issue for the decision-makers to fight against this contagious disease. To save human civilization, it is urgent to know more about how the virus transmits itself from one to another quite rapidly and how we can predict and to take the control measures for future spread of the infections. There are several different epidemiological factors including reproduction number is still unknown of the SARS-CoV-2, as this is a contemporary infectious virus. And the basic reproduction number/ratio is one of the crucial epidemiological factors to identify the current status of the disease outbreaks. At this end, a number of distinguished researchers are investigating high infection rate and transmission patterns considering the different characteristics of the SARS-CoV-2. Scientists, Doctors and Researchers are all working together investigating to understand its high infection rate and transmission process. However, in this pandemic situation there is one possible way to understand the basic principle of COVID-19 transmissible as well as transmission dynamics and to provide further necessary guidelines for the measures of disease mitigation is to develop a useful mathematical model.

Mathematical modelling is useful and applicable to assess the sizes, peak and transmission dynamics of the contagious disease such as novel SARS-CoV-2. For any pandemic of a contagious disease, it is essential to run its affecting parameters into a mathematical testing model to be able to take any further measures. There are a number of mathematical models for infectious diseases; as for compartmental models, starting from the very classical SIR to more sophisticated models. Such models play an important role in helping to quantify possible infectious disease control and mitigation strategies ([8]). Mathematical modelling showed a tremendous ability of analyzing multiple characteristics of the disease as well as providing the tools to predict the trends of transmission dynamics of any contagious disease such as COVID-19. Mathematical models estimate disease progress that can be helpful for public health interventions and able to inspect the momentum of disease outbreaks.

Following the studies reported in the literature which have been made available via leading databases (e..g, PubMed (https://pubmed.ncbi.nlm.nih.gov/), IEEEXplore (http://ieeexplore.ieee.org/), Web of Science (https://apps.webofknowledge.com/), and Scopus (https://www.scopus.com/)), our effort in this review is to study 9 most commonly used models (Figure 1) based on mathematical implementations and review critically to guide how those mathematical models play a vital role to investigate the transmission dynamic by analyzing the characteristics of the contagious disease (COVID-19). To this aim, the contributions made in the work can be summarized below:

- A detailed account of all the available mathematical models used in pandemic modeling and prediction;
- A comprehensive survey of the state-of-the-art application of available mathematical models in modeling and prediction of COVID-19 infection transmission;
- A Comparative analysis of the different mathematical models on the basis of their usage in COVID-19 infection transmission modeling and prediction;
- An elaborated discussion on the open challenges and required future research to fight against the COVID-19 pandemic situation using mathematical modeling.

The rest of the paper is organized as: section 1 provides an account of the available mathematical models, section 2 contains the application details of the mathematical models within the context of COVID-19 including Advantages and disadvantages of each model, section 3 points out some key observable behaviour for each of the models within the context of other Models, applied methods and results prediction, section 4 describes about the upcoming challenges and future research directions and section 5 presents the conclusion.

Overview of Mathematical Models used in Pandemic Modeling

To carefully select the available mathematical models used in pandemic modeling and prediction, we searched the leading databases of academic literature with specific search strings containing keywords: ‘mathematical modeling’, ‘COVID-19’, ‘Coronavirus’, ‘Corona’, ‘SARS-CoV-2’,

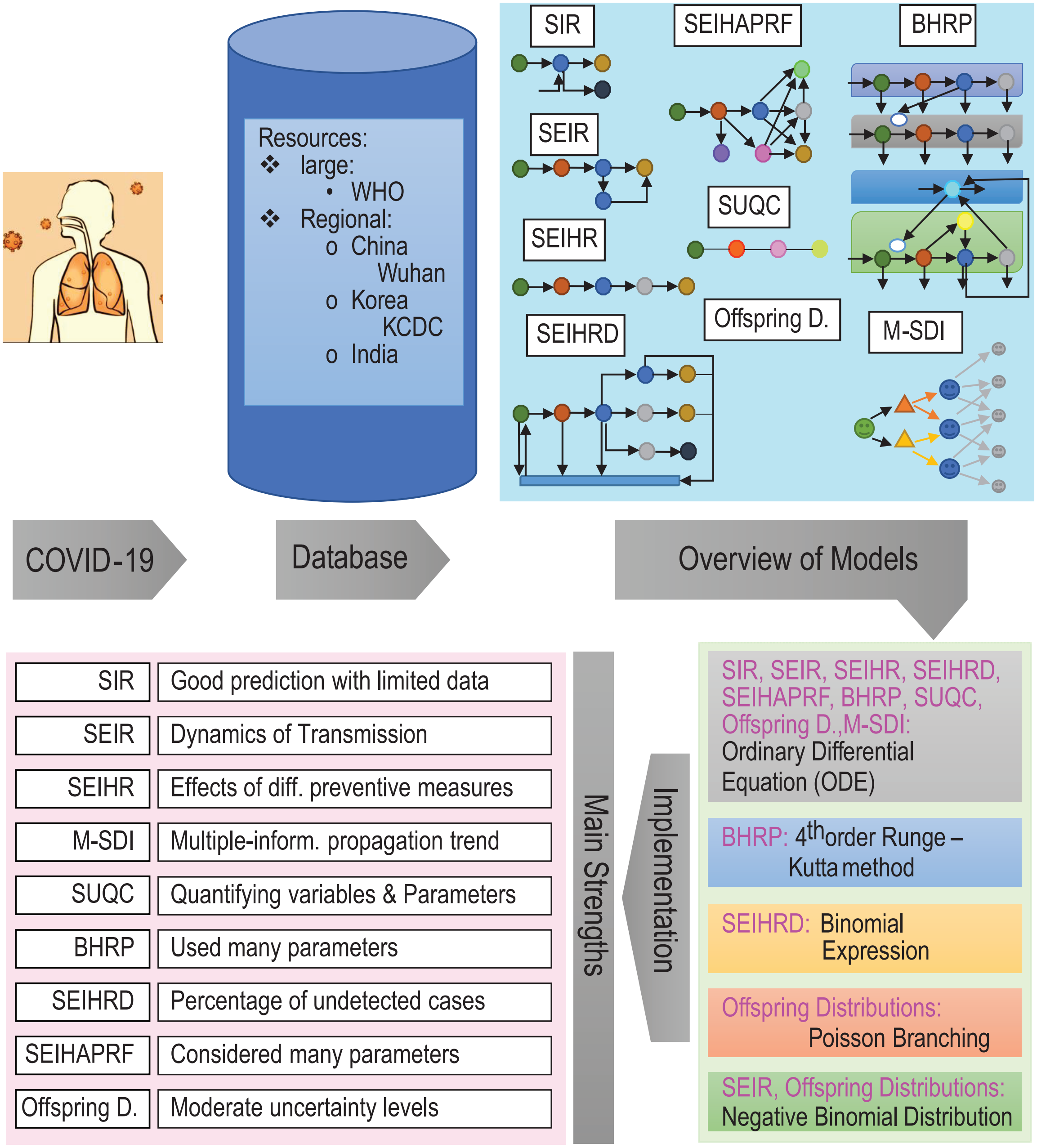


Figure 1. The main diagram which includes a cartoon of COVID-19 infection, data source for research, representative flow chart of each model, computational Mathematics behind it and main strengths of each model.

'transmission dynamics', and 'infection transmission dynamics'. The databases used were PubMed, IEEEXplore, Web of Science, and Scopus. The search generated a total of 193 articles (PubMed: 20, IEEEXplore: 35, Scopus: 34, Web of Science: 104) which were then manually scrutinized by removing the duplicates, checking for relevance to COVID-19 and being published after the onset of the disease. This resulted in 21 articles which used 9 different mathematical models to model and predict COVID-19 infection transmission dynamics.

This section focuses on nine available contagious disease models, mathematical implementation as well as models diagrams in the context of infection transmission dynamics of novel SARS-CoV-2 disease.

Model 1: SIR

The simplest compartmental model SIR ('Susceptible-Infectious-Removed') with S, I and R represent the susceptible, infectious (can infect others) and removed (recovered or dead) ([9]) populations. A flowchart of this model is presented in Figure 2. There exist many models in the literature to investigate transmission dynamics of viruses and those models are somehow derivatives of the basic SIR model. In the present corona pandemic circumstances many researchers developed SIR based mathematical models. Therefore the model is formulated by a set of nonlinear Ordinary Differential Equations (ODEs) and then solved numerically. The simplest form of the non-linear ODEs can be expressed as in Equation 1.

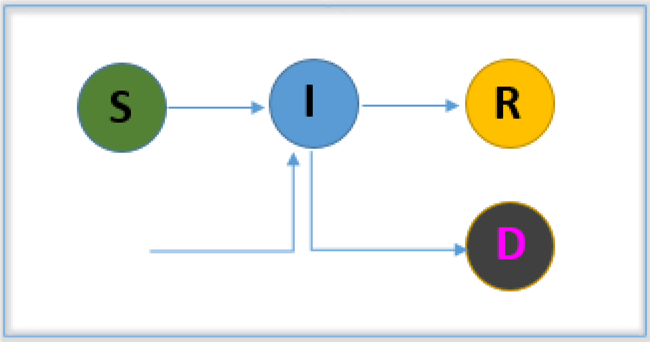
$$\begin{aligned}\frac{d}{dt}(S) &= -\beta SI \\ \frac{d}{dt}(I) &= \beta SI - \alpha I \\ \frac{d}{dt}(R) &= \alpha I\end{aligned} \tag{1}$$

(Parameters: α -removal rate, β -infection rate)

In a study [10], presented an age structured SIR mathematical model considering social connection matrices based on surveys and Bayesian imputation to inspect the momentum of the SARS-CoV-2 pandemic in India. This study accentuates the importance of both social contact and age structures in appraising the country specific impacts of widely used strategy social distancing for controlling and mitigating the virus. A flowchart of this model is presented in Figure 2. [11] proposed a simplified SIR mathematical model to predict the peak of the disease infection and also suggested that the health care system could significantly shorten the outbreak period and reduce one-half of the transmission. In another study, [12], used a SIR model to predict disease (COVID-19) trends and effect of the quarantine in decreasing the infection.

Model 2: SEIR

A compartmental model SEIR ('Susceptible-Exposed-Infectious-Removed') with S, E, I and R represent the Susceptible, Exposed (infected, but not infectious), Infectious (can infect others) and Removed (recovered or dead) populations. A flowchart of this model is presented in Figure 3.This model simplifies significantly the mathematical modelling of different infectious diseases such as the novel SARS-CoV-2. Thus the model is formulated by a set of nonlinear Ordinary Differential Equations (ODEs) and therefore solved numerically. Therefore the simplest form of a set ODEs for SEIR-based model is as follows:



2- Flow Chart of SIR Model.PNG

Figure 2. A flowchart representation of SIR model; [Susceptible(S)-Infectious(I)-Removed(R)-Dead(D)]

3- Flow Chart of SEIR Model.PNG

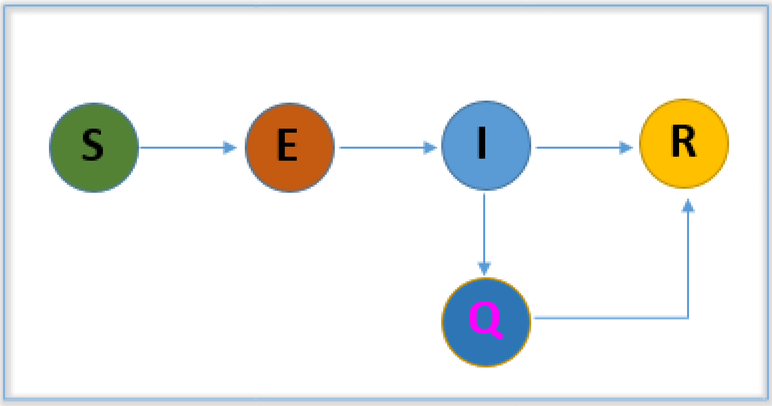


Figure 3. A flowchart representation of SEIR model;[Susceptible(S)-Exposed(E)-Infectious(I)- Removed(R)]

$$\begin{aligned}
\frac{d}{dt}(S) &= -\beta\frac{I}{N}S - \beta_F(1-e^{-\tau C})S \\
\frac{d}{dt}(E) &= \beta\frac{I}{N}S + \delta\beta\frac{I}{N}S - \kappa E \\
\frac{d}{dt}(I) &= \kappa E - \alpha I \\
\frac{d}{dt}(R) &= \gamma C
\end{aligned} \tag{2}$$

(Parameters and Notations: β_F-Behavior change transmission rate, β- Transmission rate between two groups, τ- Scaling factor, δ-Transmission reduction component, κ-Progression rate, α-Confirmation rate, γ-removal rate, C-Confirmed and isolated, N-Population)

In the current pandemic situation many researchers are trying to adopt the SEIR model to find the transmission dynamics of the COVID-19 disease. Accordingly using the SEIR model, [13], described transmission dynamics by quantifying the school closure potential effect on the disease and mainly investigated infection transmission of child-to-child. In their other work, [14] they predicted the pattern of local transmission dynamics based on changes of individuals' behavior in Korea and they found per-capita infection transmissions rate 8.9 times higher in the local area (Daegu/Gyeongbuk) than nationwide (average). Likewise [15][16][17][7][18] [19] [20][21][22] proposed and formulated the model with a set ODEs considering different transmission pathways and symptoms, they have identified transmission dynamics of the virus and suggested different control measures. Earlier [23], formulated a SEIRS model for avian influenza that includes birds to human interaction by investigating the essential transmission dynamics of the disease based on equilibrium analysis.

Model 3: M-SDI

The M-SDI (multiple-information susceptible-discussing-immune) dynamic model proposed by [15], to understand the types of significant information propagation on the social media based on the public discussions quantities and considering the frequent behavior change (search/comment) of users. A sample flowchart of this model is presented in Figure 4. They estimated the reproduction ratio decreases from 1.7769 to around 0.97, which reflects the public discussion peak has passed but still it will progress for a period of time. And the model is illustrated mathematically as follows:

4- Flowchart of M-SDI model.PNG

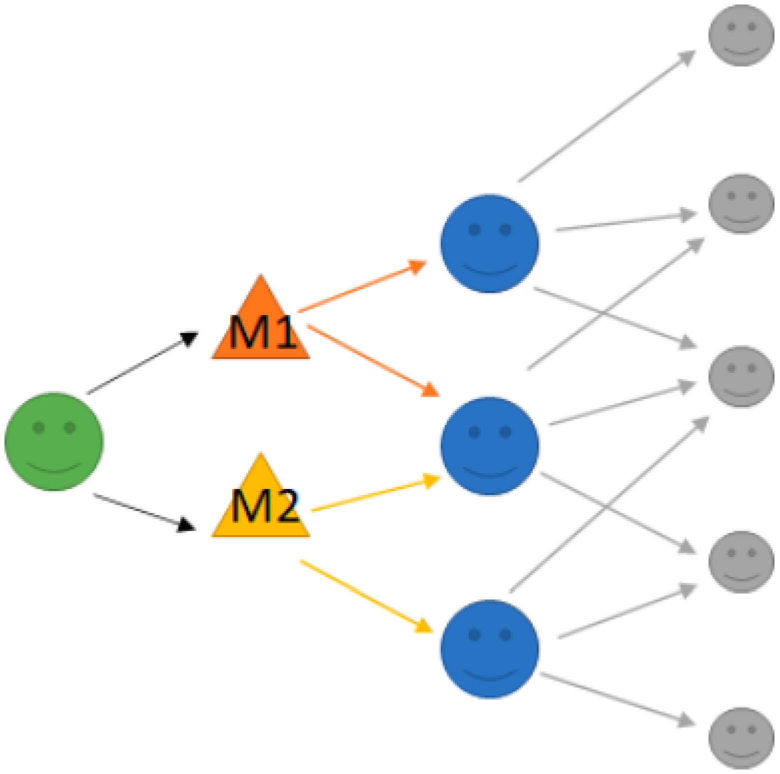


Figure 4. A Flowchart representation of M-SDI model;[multiple(M)-information-susceptible(S)-discussing(D)-immune(I)]

$$\begin{aligned}
\frac{d}{dt}(S) &= -\beta SD + (1-p-q)\,\beta SD + \theta\alpha D \\
\frac{d}{dt}(D) &= p\beta SD - \alpha D \\
\frac{d}{dt}(I) &= q\beta SD + (1-\theta)\alpha D
\end{aligned} \tag{3}$$

To explore some characteristics of qualitative nature for prediction in the M-SDI model, they have used the LS method for estimating parameters and primary susceptible population. Accordingly they estimated parameters in their model with the data of at least 3–4 days' to predict public discussion trends at different phases earlier.

Model 4: SUQC

SUQC ('susceptible - unquarantined infected - quarantine infected-confirmed infected) is a compartmental model with S, U, Q and C represent the susceptible (S is similar as in the existing infectious virus transmission models SIR and SEIR.), un-quarantined infected (infected and un-quarantined cases different from E in the existing SEIR model), quarantine infected (quarantine infected cases), and confirmed infected population. A flowchart of this model is presented in Figure 5. Essentially, [24], developed SUQC model to describe the transmission dynamics of novel SARS-CoV-2 and especially parameters the interference effects of control measures by analyzing the disease outbreak. And the method is formulated with a set of ODEs as follows:

5- Flow Chart of SUQC Model.PNG

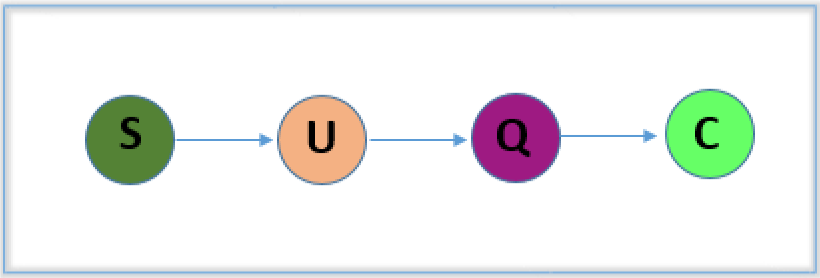


Figure 5. A flowchart prepresentation of SUQC model;[susceptible(S)-unquarantined(U)-infected quarantine(Q)-infected-confirmed(C)-infected]

$$\begin{aligned}
\frac{d}{dt}(S) &= -\alpha\frac{S}{N}U \\
\frac{d}{dt}(U) &= \alpha\frac{S}{N}U - U(\gamma + (1-\gamma)\delta) \\
\frac{d}{dt}(Q) &= \gamma U - \beta Q \\
\frac{d}{dt}(C) &= \beta Q + (1-\gamma)\delta U
\end{aligned} \tag{4}$$

(Parameters: α-Infection rate, γ-Quarantine rate, and β-Total confirmation rate)

This model is adapted to the data of daily released confirmed cases to analyze the outbreaks of the diseases in Hubei, Wuhan, and four other first-tier cities in China. Authors have demonstrated authentic prediction of the transmission trends considering multiple characteristics which includes high infectivity, time delay, interventions effects etc. However SUQC can quantify variables and parameters regarding the intervention effects of the outbreaks. According to the simulation results the method is further providing the guidance to control the disease spread.

Model 5: BHRP

BHRP (Bats-Hosts-Reservoir-People) is a network model for simulating the transmission of the virus with B, H, R and P represent the bats (probable infection source), hosts (unknown but probably wild animals), reservoir (seafood market) and people (exposed) population developed by [25]. A flowchart of this model is presented in Figure 6. In this method finally they ignored Bats-Host transmission network and presented the BHRP model in a simplified form as RP (Reservoir-People) model. In this case they have divided People into five different compartments such as susceptible, exposed, symptomatic infected, asymptomatic infected, and removed. Therefore the simplified model is illustrated mathematically as follows:

6- Flow Chart of BHRP Model.PNG

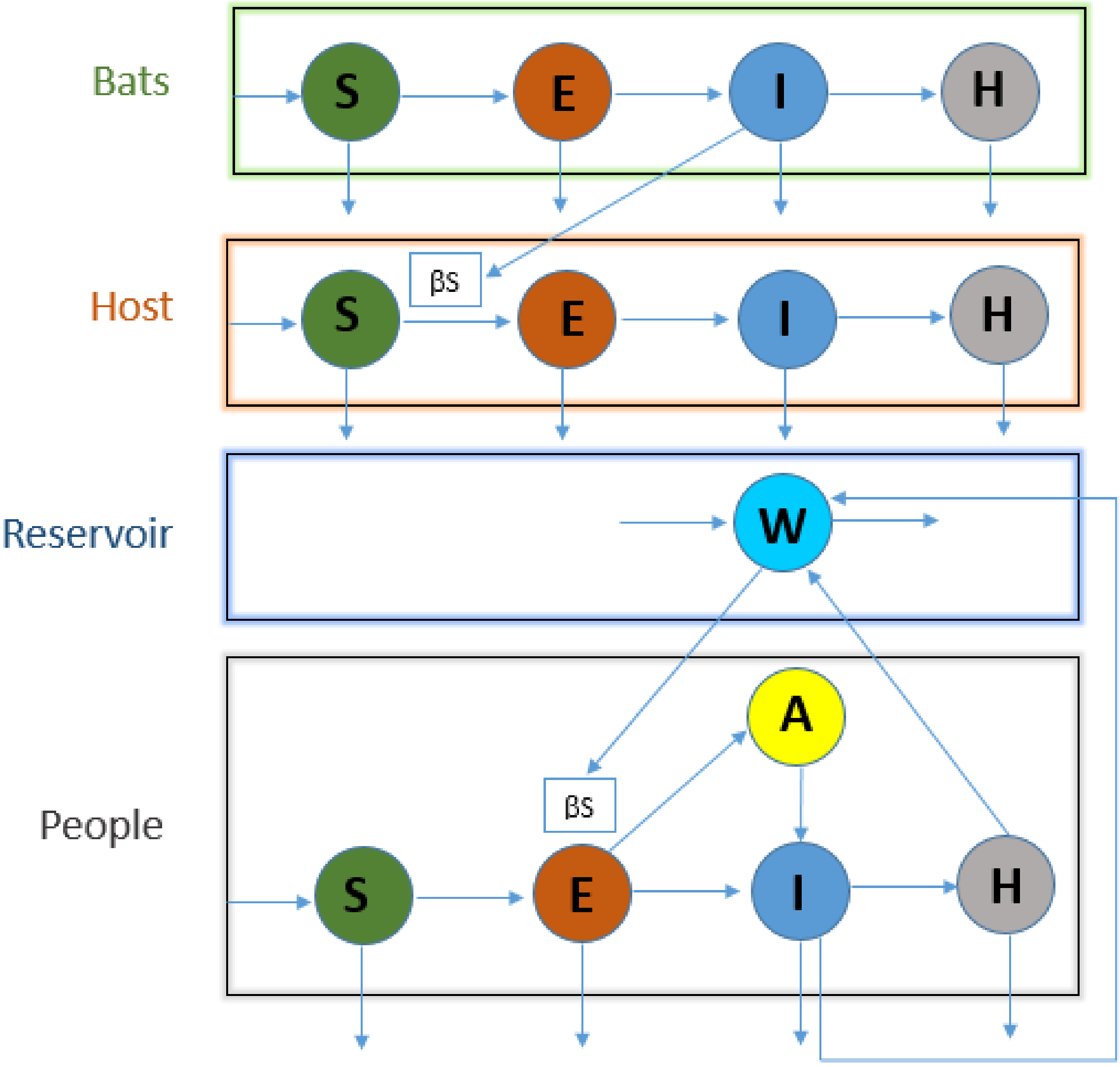


Figure 6. A flowchart representation of BHRP model;[Bats(B)-Hosts(H)-Reservoir(R)-People(P);Susceptible(S) -Exposed(E)-Infectious(I)- Removed(R)]

$$
\begin{aligned}
\frac{d}{dt}(S_p) &= \mu_p - (I_p + \sigma A_p) y_p S_p - \beta_p S_p X \qquad (5)\\
\frac{d}{dt}(S_p) &= (I_p + \sigma A_p)\beta_p S_p + \beta_x S_p X - (1 - S_p)\omega_p E_p - S_p \omega_p^{'} E_p - y_p E_p\\
\frac{d}{dt}(I_p) &= (1 - \delta_p)\omega_p E_p - (\gamma_p + y_p) I_p\\
\frac{d}{dt}(A_p) &= S_p \omega_p^{'} E_p - (\gamma_p^{'} + y_p) R_p\\
\frac{d}{dt}(R_p) &= \gamma_p I_p - \gamma_p^{'} A_p - y_p R_p\\
\frac{d}{dt}(X) &= \rho_p I_p + \rho_p^{'} A_p - \varepsilon X
\end{aligned}
$$

7- Flow Chart of SEIHR Model.PNG

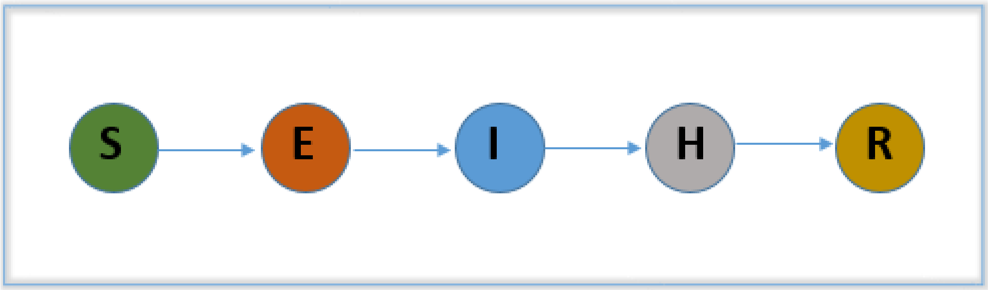


Figure 7. A flowchart representation of SEIHR model;[Susceptible(S)-Exposed(E)-Symptomatic infectious(I)-Hospitalized(H)- Removed(R)]

(y_p-death rate (people), σ-multiple of transmissibility (A_p to I_p), δ_p- infection rate (asymptomatic people), β_p-transmission rate (I_p to S_p))

They have estimated the basic reproduction number according to their numerical illustration by assessing the transmissibility of the virus based on a simplified RP model and they found the value is 2.30 (from reservoir-person), 3.58 (from person-person). The results showed transmissibility of SARS-CoV-2 is comparatively higher than MERS in the Middle East, and is similar to serious respiratory syndrome. They also found that the transmissibility is smaller than MERS in Korea.

Model 6: SEIHR

SEIHR (Susceptible-Exposed-Symptomatic infectious-Hospitalized-Removed) is a virus transmission deterministic model with S, E, I, H and R represent the susceptible, exposed, symptomatic infectious, hospitalized and removed (recovered or death) populations. A flowchart of this model is presented in Figure 7. In this model, [26], estimated the size of the outbreak and the reproduction number and they found if the rate of transmission decreases, then the outbreak of the disease ends early as well as the size of the virus infection cases also will decrease. The mathematical implementation of the model is illustrated with the system of nonlinear ODEs as follows:

$$\begin{aligned}\frac{d}{dt}(S) &= -\beta\frac{SI}{N}\\ \frac{d}{dt}(E) &= \beta\frac{SI}{N} - \sigma E\\ \frac{d}{dt}(I) &= \sigma E - \alpha I\\ \frac{d}{dt}(H) &= \alpha I - \gamma H\\ \frac{d}{dt}(R) &= \gamma H\end{aligned} \tag{6}$$

(β- Transmission rate, σ-Progression rate, α-Isolation rate, γ-Removal rate)

In the study they did not consider natural deaths and births, infections during latency and asymptomatic infections, and re-infected cases. But according to their simulation results they have suggested different social awareness activities such as wearing masks and as social distancing to reduce the fast transmission of the virus.

8- Flow Chart of ThetaSEIHRD Model.PNG

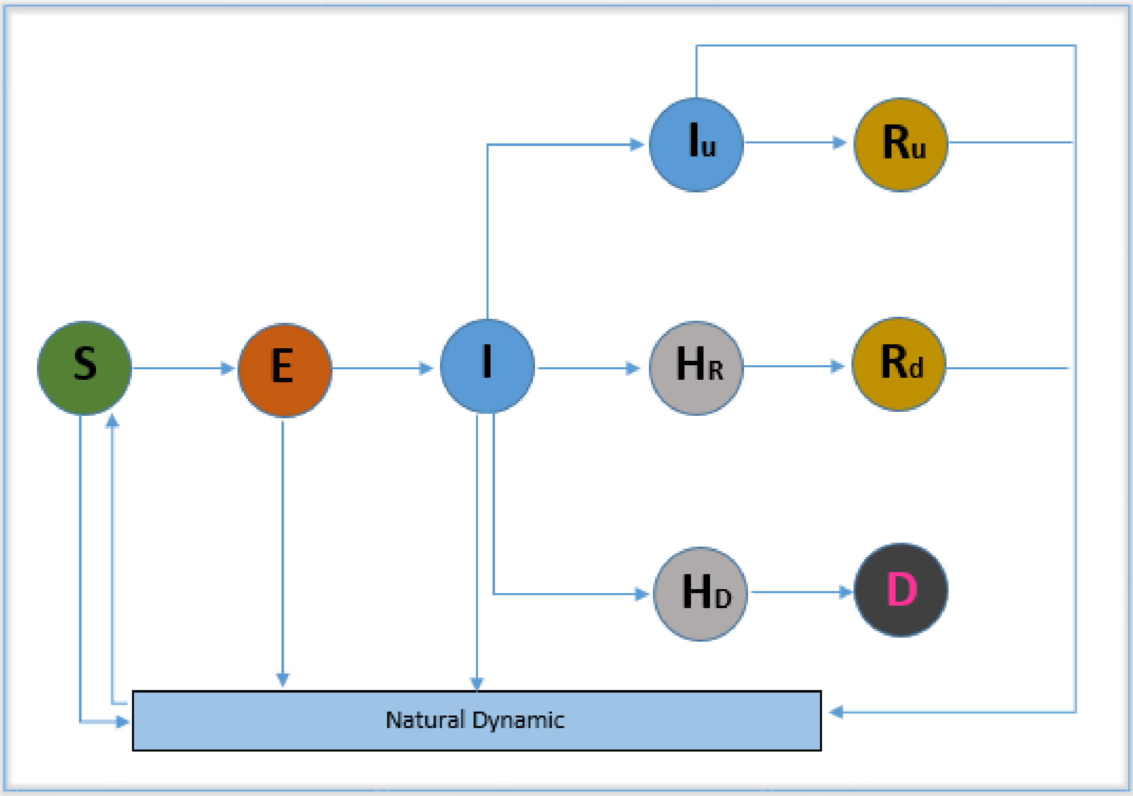


Figure 8. A flowchart representation of *Theta*-SEIHRD model;[Susceptible(S)-Exposed(E)-Symptomatic infectious(I)-Hospitalized(H)- Removed(R)-Dead(D)]

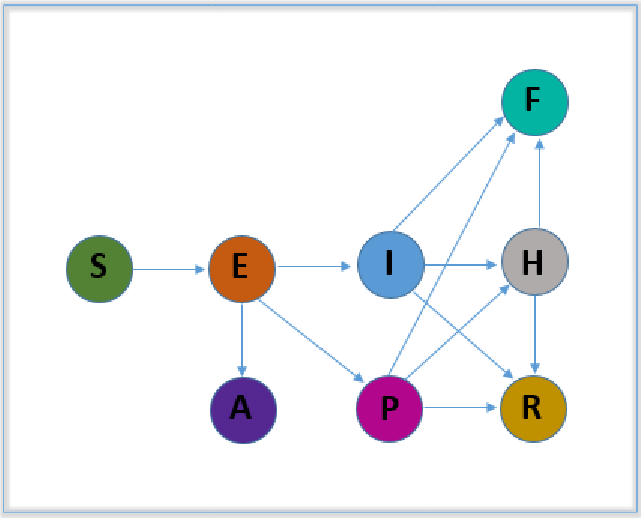
Model 7: Theta-SEIHRD

An extended compartmental model *Theta*-SEIHRD (Susceptible-Exposed-Infectious-Hospitalized-Recovered-Dead) with S, E, I, H, R and D represent the susceptible, exposed (incubation period), infectious (undetected but still can infect others), hospitalized (recovered or dead), recovered (previously detected and previously undetected but infectious) and dead populations developed by [27]. A flowchart of this model is presented in Figure 8. The model is illustrated mathematically as follows (presented concisely here for simplicity):

$$\begin{aligned}
&\frac{d}{dt}(S) = -\frac{S}{N}(m_{\varepsilon}\beta_{\varepsilon}E + m_i\beta_i I + m_{iu}\beta_{iu}\theta I_u) - \frac{S}{N}(m_{hr}\beta_{hr}H_r + m_{hd}\beta_{hd}) \qquad (7)\\
&\frac{d}{dt}(E) = \frac{S}{N}(m_{\varepsilon}\beta_{\varepsilon}E + m_i\beta_i I + m_{iu}\beta_{iu}\theta I_u) + (m_{hr}\beta_{hr}H_r + m_{hd}\beta_{hd}) - \gamma_e E\\
&\frac{d}{dt}(I) = \gamma E - \gamma I\\
&\frac{d}{dt}(H) = \gamma I - \gamma H\\
&\frac{d}{dt}(R) = \gamma H(infectious\ detected\ and\ infectious\ undetected)\\
&\frac{d}{dt}(D) = \gamma H(Dead\ Compartment)
\end{aligned}$$

(Parameters: γ-Transition rate for different compartment, β-disease contact rate for different compartment θ-fraction of infected people)

This model investigates transmission dynamics of the disease considering the known major characteristics of the disease as the presence of infectious undiscovered as well as detected cases and the distinct sanitary and infectiousness conditions of hospitalized individuals. This model is able to estimate the required number of beds needed in hospitals as well as it can calculate basic reproduction number.



9- Flow Chart of SEIPAHRF Model.PNG

Figure 9. A flowchart of SEIPAHRF model;[susceptible(S) - exposed(E)- symptomatic and infectious(I) - super spreaders(P)- infectious but asymptomatic(A)- hospitalized(H)- recovery(R) - fatality(F)]

Model 8: SEIPAHRF

A compartmental model SEIPAHRF (susceptible class - exposed class- symptomatic and infectious class - super spreaders class- infectious but asymptomatic class - hospitalized class - recovery class - fatality class) divided into eight epidemiological compartment with S, E, I, P, H, R, and F represent the susceptible individuals, exposed, symptomatic and infectious, super-spreaders, infectious but asymptomatic, hospitalized, recovery, and fatality population developed by [8]. A flowchart of this model is presented in Figure 9.The model is illustrated mathematically with the system of nonlinear ODEs as follows:

$$\begin{aligned}
&\frac{d}{dt}(S) = -\beta\frac{SI}{N} - m\beta\frac{SH}{N} - \beta' P\frac{S}{N}; && \frac{d}{dt}(E) = \beta\frac{SI}{N} + m\beta\frac{SH}{N} + \beta' P\frac{S}{N} - \sigma E\\
&\frac{d}{dt}(I) = \sigma\rho_1 E - (\gamma_a + \gamma_b)I - \delta_b I; && \frac{d}{dt}(P) = \sigma\rho_2 E - (\gamma_a + \gamma_b)P - \delta_p P\\
&\frac{d}{dt}(A) = \sigma(1-\rho_1-\rho_2)E; && \frac{d}{dt}(H) = \gamma_a(I+P) - \gamma_c H - \delta_h H\\
&\frac{d}{dt}(R) = \gamma_b(I+P) + \gamma_c H; && \frac{d}{dt}(F) = \delta_b I + \delta_p P + \delta_h H
\end{aligned}$$

(β-Ttransmission coefficient (infected individuals), β'- Transmission coefficient (super-spreaders), m- Relative transmissibility (hospitalized patients), σ-infectious rate (from exposed people), ρ_1- Rate (exposed individual become infected I) ρ_2-Rate (exposed individual become super-spreaders), γ_a- Rate (hospitalized), γ_b- Recovery rate (without hospitalized), γ_c- Recovery rate (hospitalized patients), δ_b-

Death rate (infected class), δ_p- Death rate (super-spreaders class), δ_h- Death rate (hospitalized class))

[8], studied the stability of the epidemic free equilibrium of basic reproduction number as well as they investigated the sensitivity by considering the variation of its parameters. Authors (F Ndaïrou and his colleagues) have analyzed and simulated the current outbreak considering some important aspects of the virus transmission and give an acceptable approximation based on the data in Wuhan, China. They also have fitted the model with the daily confirmed cases real data. According to their findings, the numerical results reflect the real scenario of the Wuhan outbreak.

1.1. Model 9: Offspring distribution

To quantify the individual human to human level variation for COVID-19 transmission and observe the outbreak sizes in affected countries, [28], has proposed an interesting mathematical model applying a branching process model where the number of secondary transmission was assumed to follow a negative-binomial distribution.

By assuming that the distribution of number of secondary transmissions (offspring distributions) for COVID-19 cases are independently- and identically-distributed negative-binomial distributions. They constructed a likelihood following a previous study [29]. They have computed the probability mass function for the final cluster size resulting from s initial cases following the formula below:

$$c(x;s) = P(X = x;s) = \frac{ks}{kx + x - s}\binom{kx + x - s}{x - s}\frac{(\frac{R_0}{k})^{x-s}}{(1 + \frac{R_0}{k})^{kx+x-s}} \tag{8}$$

To adjust the future growing issue for cluster size, the research team has introduced a corresponding likelihood functions presented below:

$$c_0(x;s) = P(X \geq x;s) = 1 - \sum_{m=0}^{x-1} c(m;s) \tag{9}$$

To compute total likelihood, the research group has applied final likelihood cluster size of those countries with the other ongoing outbreak countries following the formula below:

$$L(R_0, K) = \prod_{i \epsilon A} P(X = x_i; s_i) \prod_{i \epsilon B} P(X \geqslant x_i; s_i) \tag{10}$$

For statistical analysis, they have used the Markov-chain Monte Carlo (MCMC) method with 95% credible intervals (CrIs). To investigate the best method, they compared our negative-binomial branching process model with a Poisson branching process model. However, they have used simulations to investigate potential bias caused by under reporting (fail to report fully), one of the major limitations of their study.

2. The State-of-the-Art Application of Mathematical Modeling: A COVID-19 Case Study

2.1. Model 1: SIR

To estimate the epidemic size, predict disease transmission trends as well as to forecast the advancement of the disease, the basic SIR model (Figure 2) has been applied. In the present pandemic (COVID-19), to understand the interventions' effect such as quarantine, social distancing etc. on the disease outspread and to control and mitigate the virus outbreaks with the models researchers present their ideas. We have found three different scientific research works ([27][11][10]) based on the basic SIR mathematical model. [27], used a SIR model to predict disease (COVID-19) trends and effect of the quarantine in decreasing the infection. [11], proposed a simplified SIR mathematical model to predict the peak of the disease (COVID-19) infection. And also in a study [10], presented an age structured SIR mathematical model considering social connection matrices based on surveys and

Bayesian imputation to inspect the momentum of the SARS-CoV-2 pandemic in India. According to the simulation results based on their studies they accentuates the importance of the strategy of social distancing, improvement of health care system, age-structuring and different interventions measures for controlling and mitigating the disease (COVID-19) outbreaks. To prevent the rise of the disease infection they have evaluated the mentioned different policy in the well-defined contexts of COVID-19. In the presented models some of the parameters and variables are estimated and also some of are composed from the references of published articles. To formulate the models and for numerical illustrations they have used a set of nonlinear Ordinary Differential Equations (ODEs) (for more details see overview section). In mathematical simulation the challenging issue is reasonable data availability for better estimation and prediction. In most of the cases they have used short and limited epidemiological data, in some cases unreasonable released data. As their main objectives are to identify lockdown/quarantines, infection rate, social distancing impact through parameter estimation; these models have been suggested disease mitigation policies according to their numerical illustrations.

2.2. Model 2: SEIR

The SEIR is a simple compartmental model and difference between the models SIR and SEIR; in the SEIR model (Figure 3) the exposed compartment as well as a parameter (denote the movement from exposed compartment to infected compartment) is additionally adopted to describe the transmission dynamics of the exposed individuals. This framework significantly simplifies the mathematical modelling of different infectious diseases for example the present novel SARS-CoV-2 pandemic. Recently several researches focused on mathematical modelling and adopted the SEIR model with mathematical implementation (for more details see overview section) to estimate the transmission and to predict the trends of the disease (COVID-19) outbreaks. In their studies they have considered multiple transmission pathways-mechanism including environment-to-human and human-to-human routes in the infection dynamics emphasizing the role of the environmental source in the transmission and growth. These researches have applied nonlinear ODEs and MCMC methods to calculate the important parameter, the basic reproduction number. This parameter thus provides valuable observations of the current COVID-19 outbreaks.

2.3. Model 3: M-SDI

The M-SDI(Figure 4) is developed to understand the types of significant information propagation on the social media based on the public discussions quantities and considering the frequent behavior change (search/comment) of users. In this work, they focused on the characteristic that users are choosing and re-entering the other related information considering different topics when they finished one discussion of certain information. By analyzing and according to model simulation multiple-information generation mechanism regarding COVID-19; this model distinctly can predict evolution of the public opinion. They have estimated the reproduction ratio decreases from 1.7769 to around 0.97, which reflects the public discussion peak has passed but still it will progress for a period of time. To explore some characteristics of qualitative nature for prediction in the M-SDI model (Figure 4), they have used the LS method for estimating parameters and primary susceptible population. Accordingly they also have estimated parameters in their model with the data of at least 3–4 days' to predict public discussion trends at different phases earlier. M-SDI model can predict the multiple-information development trend during a large-scale community health emergency. They have used limited data for the estimation of parameters from the most popular Chinese Sina-microblog.

2.4. Model 4: SUQC

The SUQC model (Figure 5) is developed to characterize the transmission dynamics of novel SARS-CoV-2 and especially parameterize the effects of interventions for controlling measures. SUQC is not the same as SEIR, as infected people are classified into confirmed, quarantined, and un-quarantined in SUQC. And in this case un-quarantined people are able to infect susceptible people only but in

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SEIR, infected individuals are infectious. Additionally the parameter quarantine rate in SUQC to especially model the influence of quarantine as well as control measures. According to the author's explanation the model is more effective than other available epidemic models for analyzing dynamics of the disease. This model is fitted with the daily released confirmed cases data to analyze the outbreaks patterns of the diseases in Hubei, Wuhan, and four other first-tier cities in China. This model is illustrated with deterministic ODEs and in this case it is needed to interpret some uncertainties. Authors have demonstrated authentic prediction of the transmission trends considering multiple characteristics which includes high infectivity, time delay, interventions effects etc. However SUQC can quantify variables and parameters regarding the intervention effects of the outbreaks. According to the simulation results they found reproduction number>1 before Jan 30, 2020, in Hubei, Wuhan, and other first-tier cities in China except Beijing, and after Jan 30, 2020, the reproduction number<1, in all regions which is indicating the effectiveness of control measures. Subsequently the method is further providing the guidance to control the disease (COVID-19) spread.

2.5. Model 5: BHRP

Reservoir-People (RP) transmission model (Figure 6) has been developed in this study,[25], considering the routes from reservoir (market) to person and from person to person for severe acute respiratory syndrome SARS-CoV-2 respectively. Published data of Wuhan City, China were used to fit this model. The simulation results found by this study with basic reproduction numbers for SARS-CoV-2 was 3.58 from person to person and 2.30 from reservoir to person respectively. This model might predict interesting transmission chains applying limited data involving a number of important parameters. However, these predictions might not reflect the actual situation of the early stage virus transmission. Because, some parameters were not taken from the accurate database or applied through assumption. Overall, the objective of this study was to provide an effective mathematical model to estimate virus transmission as accurately as possible with limited data using more parameters.

2.6. Model 6: SEIHR

The SEIHR (Figure 7) is a deterministic ODEs model developed by [26], to estimate the size of the outbreak and the reproduction number. As well as they evaluated the effects of different preventive measures. In this study they have used daily data of confirmed cases in the area Daegu and North Gyeongsang (NGP), the main outbreak regions in Korea. According to the mathematical illustrations they found if the rate of transmission decreases, then the outbreak of the disease ends early as well as the size of the virus infection cases also will decrease. Also they have suggested different social awareness activities such as wearing masks, social distancing and other intervention measures to reduce the fast transmission of the virus. In this study they did not consider natural deaths and births, infections during latency and asymptomatic infections, and re-infected cases. So far as we observed in most of the research they were not considering demographic factors but basically demographic factors (birth, death, emigration, and immigration) are significantly needed to add to any compartmental models to generate it more realistically.

2.7. Model 7: Theta-SEIHRD

[27], proposed an extended compartmental model Theta-SEIHRD (Figure 8) to investigate transmission dynamics of the disease (COVID-19) considering the known major characteristics of the virus. They have studied the specific case of China including Hong-Kong, Macao, Taiwan, and Chinese Mainland considering reported data to fit the parameters of the model that can be also useful to estimate the spread of the disease (COVID-19) in some other countries. The presented model is adapted to the disease and capable of estimating the progression of the distinct number of undetected and detected cases, deaths as well as the required number of beds needed in hospitals where the health problem is severe due to the outbreaks in territories, considering several different scenarios. In addition they have calculated the basic reproduction number of COVID-19 which is 4.2250 but it

reached to less than 1 after first Feb, 2020, due to control measures. Also they have included in their model a new approach taking into account 'Theta' the fraction of total detected cases (infected) to study the importance of this fraction on the influence of the disease (COVID-19).

2.8. Model 8: SEIPAHRF

SEIPAHRF model (Figure 9), developed by [8], gives feasible approximation based on the data in Wuhan, China by studying some important aspects of the virus (COVID-19) transmission. They have divided their model into eight important epidemiological compartments and also illustrated the model mathematically with nonlinear ODEs. Authors have investigated the sensitivity by considering the variations of its parameters. They also have fitted the model with the real data of daily confirmed cases and found actual scenarios of the Wuhan outbreak. Interestingly they considered many parameters to quantify transmissible and computed the basic reproduction number, a measure of virus spread based on Jacobian matrices. Limited data accessibility was one of the major limitations of this study.

2.9. Model 9: Offspring distribution

To estimate the level of over-dispersion in COVID-19 transmission and characterize the sustained transmission chains of human-to-human transmission, this model has been introduced. Although, one research publication ([28]) has been found so far, the Mathematical implementation (See overview section for more details) and statistical analysis of Offspring distribution looks powerful and should have the computational ability for better estimation of moderate uncertainty levels with limited data resources. This was proven by widely-applicable Bayesian information criterion (WBIC) that this model was better estimated than Poisson branching process model in this study. However, this model can only provide information about the lower boundary of basic reproduction number RO(95% CrIs: R0 1.4–12) because of marginal negative binomial distribution in this study. Overall, the majority of model consistency and certainty is relying on available homogeneous real data resources and imputed parameters by avoiding stochastic simulation.

Table 1. Mathematical Models and Their Details

Basic Model	**Reference**	**Main Findings**	**Strengths**	**Limitations**
SIR	Vega 2020	• Provides an overview to enhance awareness of covid-19 disease trends • Effect of the quarantine in decreasing the infection • Proposed extended lockdown	• Investigated the effectiveness of social distancing considering both social contact and age structuring	• Emphasizes only on quarantines
	Zhong et al 2020	• Health care system could significantly shorten the outbreak period • It could reduce one-half of the disease transmission.	• Good ability to predict by the historical data such as SARS 2003 • It can also give a good prediction of the limited covid-19 data	• Used short period data (two weeks)
	Singh & Adhikari 2020	• Accentuates the importance of both social contact and age structures • Social distancing is effective for controlling and mitigating the virus	• Estimates the contact structures • Large-scale social distancing is effective	• Insufficient data used in the case asymptomatic • The model is not resolved spatially
SEIR	Kim et al 2020a	• Quantifying the school closure potential effect on the disease • Considered isolation and behavior-changed susceptible individuals	• Found school opening delay is effective • The rate of child-to-child transmission decreases	• They did not consider cross-population infection rise
	Lin et al 2020	• Captured the course of coronavirus (COVID-19) outbreaks • Computed the reported ratio and future trends • The method is applicable to other cities or other countries	• Considered: government actions • Individual behavioral responses • Emigration of large portion of the people • Zoonotic transmission	• Considers small number of asymptotically infected transmission confirmed cases

Table 1 continued from previous page

Basic Model	Reference	Main Findings	Strengths	Limitations
	Chang et al 2020	• Estimated epidemic peak: In Wuhan and Hubei Province in the end of February 2020 • Other regions in China on February 13, 2020 • Outbreaks would decrease in March and April in China	• To estimate epidemic trend, they applied phase-adjusted and region-adjusted mathematical model	• Assumed diseases transmission evenly across homogeneous population • Total cases might be underestimated as existence of asymptomatic, and super-spreaders infectors • Data lag might exist
	Kim et al 2020b	• Investigated pattern of local transmission dynamics • Found per-capita infection transmissions rate 8.9 times higher in local area (Daegu/Gyeongbuk) than nationwide (average).	• Predicted the time of end of corona outbreaks	• Mortality rate was not included
	Modnak & Wang 2019	• The effects of infection latency and human vaccination	• Virus can spread birds to humans • Human hosts	• Consider bi-linear incidence
	Tang et al 2020a	• Reproduction rate quantification for the evolution of interventions	• Time-dependent contact and diagnose rates	• Highly sensitive & depend upon available period data
	Prem et al 2020	• Physical distancing is effective physical distancing can reduce and delay the peak of the disease	• Changes of transmission patterns decrease the number of cases in Wuhan	• Individuals' level heterogeneity is not captured in contacts • Climatic factor does not include • Large uncertainties over estimation of reproduction and infectiousness duration
	Mandal et al 2020	• Found basic reproduction rate 1.5 in an optimistic case, it reduces 62% cumulative incidence • In pessimistic case basic reproduction rate is 4	• Described rational interference to control the outbreaks • Found potential impact of port entry screening • A mitigation strategy of symptomatic cases	• Used data only of airport entry individuals from China • Ignored travellers from other countries • It may affect infection duration; period of incubation, and fatality rate

Table 1 continued from previous page

Basic Model	**Reference**	**Main Findings**	**Strengths**	**Limitations**
	Kucharski et al 2020	• Estimated day-to-day reproduction number • Reproduction number declined from 2·35 (95% CI 1·15–4·77) to 1·05 (0·41–2·39) within one week • Found SARS-like variations	• Dynamics of transmission in Wuhan & risk of infections	• Simple model • Transmission more homogeneous
	Tang et al 2020b	• calculated the effective daily ratio of reproduction • Re-estimated disease transmission risk • Evaluated the outbreaks trend • Estimated disease peak phase	• Used current revised data and information to estimates outbreaks trend	• Needed to update parameters
	Yang and Wang 2020	• Found infection transmission remain endemic • Long-term disease prevention and intervention programs should be needed	• Evaluated the reproduction rate is 4.25 • Predicted the epidemic peak of the virus infection	• Ecological, pathological, and epidemiological aspects not clearly considered
M-SDI	Yin et al 2020	• Reproduction ratio decreases from 1.7769 to around 0.97 • Public discussion peak has passed	• Predicted the multiple-information propagation trend	• Used a limited data for the estimation of parameters
SUQC	Zhao & Chen 2020	• Predicted trends of transmission dynamics • Effects of quarantine or confirmation procedures on the diseases	• Quantifying variables and parameters • Able to provide guidance for other countries to control the outbreaks	• Not considered demographic factors such as death
BHRP	Chen et al 2020	• Reproduction estimated from reservoir to person and it is lower than from person to person	• Used many parameters to quantify transmissibility	• Used limited data • Parameter assumptions • Not reflect the real results
SEIHR	Choi & Ki et al 2020	• Estimated the size of the outbreak the reproduction number	• Evaluated the effects of different preventive measures	• Not considered natural deaths and births • Latency and asymptomatic infections, and re-infected cases were not considered

Table 1 continued from previous page

Basic Model	Reference	Main Findings	Strengths	Limitations
SEIHRD	Ivorra et al 2020	• Calculated basic reproduction number • Found the effective reproduction decreases due to taken different control measures	• Estimated basic reproduction rate and percentage of undetected cases	• Spatial distribution within the territory is omitted • Between-country transmission has not been considered • Officially released data was not in quality due to several uncertainties.
SEIPAHRF	Ndairou et al 2020	• Investigated the sensitivity by considering the variations of its parameters	• Considered many parameters to quantify transmissibility and computed the basic reproduction number	• Limited data were studied
Offspring distributions	Endo et al 2020	• Better estimation of moderate uncertainty levels with limited data resources • Provide lower boundary of basic reproduction number	• Moderate uncertainty levels	• Highly over dispersed due to a very small fraction of individuals

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Table 2. Head-to-head comparison between the models: the first column indicates the specific model and first column illustrates the model to be compared with respect of models presented in the first row. In other words, this is an antisymmetric information matrix other than first row and column. [**E**-exposed class, **I**-infectious, **Isi**-symptomatic infectious, **U**-unquarantined infected class, **Q**- quarantine infected class, **C**- confirmed infected class, **D**-discussing class, **Im**-immune class, **SI**-symptomatic infected, **AI**-asymptomatic infected, **H**-hospitalized, **SS**-super spreaders class, **F**-fatality class, **Stm**- secondary transmission]

	SIR	**SEIR**	**M-SDI**	**SUQC**	**BHRP**	**SEIHR**	**Theta-SEIHRD**	**SEIPAHRF**	**Offspring distributions**
SIR		• E absent • Less parameter	• D, and I absent • Different parameter	• U, Q and C are absent • Different parameters	• E, SI, and AI are absent • Differently parametarize	• E and H absent • Less parameter	• *Theta as fraction and E, H absent* • *Less parameter*	• E,SI, AI,SS,H, and F absent • Less parameter	• Different Approach
SEIR	• E added • More parameter appended		• E, I, and R are different • Different parameter approximation	• E, I, and R are different from U, Q, and C	• I is different from SI and AI • Simple than RP	• I is different from SI and H • Parameters estimations different	• H is absent • Parameter approximation different	• H absent • I in simplest form • Parameter representation different	• Different Approach
M-SDI	• I, R absent • Public opinion based	• E, I, and R absent • Parameterize public opinion		• U, Q and C are absent • Multiple-information based	• Different approach • Public opinion data		• Different approach	• Analyzed users propagation	• Different Approach
SUQC	• U, Q, and C are different • R absent	• U different from E • R absent	• Different approach		• E and R absent • U, Q and C appended	• E, H, and R absent • U, Q and C appended	• E, H, R, D absent • U, Q, C appended	• E, I, P, A, H, R, F are different and absent • U, Q, C appended	• Different Approach
BHRP	• E appended • SI, AI different from I	• SI, AI different from I	• Different approach	• E and R appended • SI and AI different from U and Q		• SI, and AI are different from I • H absent	• SI, and AI are different from I • H absent • Fraction Theta absent	• SI, and AI are different • H absent	• Different Model

Table 2 continued from previous page

	SIR	SEIR	M-SDI	SUQC	BHRP	SEIHR	Theta-SEIHRD	SEIPAHRF	Offspring distributions
SEIHR	• E and H appended	• H appended	• Different model	• E,H, and R appended • I not same as U, Q, and C	• H appended • Isi different from SI and AI		• Fraction Theta is absent	• Isi(=I) is same as SI(=I) • P, A absent	• Different Model
Theta-SEIHRD	• H, R, D appended • SI(=I) is different	• H appended • SI(=I) is different	• Different model	• I different • H, R, D appended	• I different • H appended	• I different from Isi		• I different • P, A absent	• Different Model
SEIPAHRF	• Isi(=I) different from I • E, P, A, H appended	• Isi(=I) different from I • P, A, H appended	• Different model	• E, I, P, A, H differently appended	• P, A appended	• P, A appended	• Fraction Theta absent • P A appended		• Different Model
Offspring distributions	• Different model Assumed Stm	• Different model Assumed Stm	• Different model • Assumed Stm	• Different model • Assumed Stm	• Different model • Assumed Stm	• Different model • Assumed Stm	• Different model • Assumed Stm	• Different model • Assumed Stm	

3. Observable Behaviour of the Different Models

Next, we are interested to address few interesting key observable behaviours of different models within the context of COVID-19 mathematical modeling, data source, applied methods, used parameters, and results prediction. The base principle of this subsection is to give an overall effectiveness of the specific model in the context of COVID-19 Pandemic. Also, we describe these behaviours in Table1. In addition, Table2 highlights the important comparisons between the models.

3.1. Model 1: SIR

- SIR is the basic compartmental model to assess the pandemic sizes, transmission peak and predict the trends of the current 2019 n-COV disease.
- Identified effectiveness of lockdown/quarantines, different social distancing measures through parameter estimation.
- This model has been suggested disease mitigation policies according to their numerical illustrations in the context of 2019 n-COV.

3.2. Model 2: SEIR

- SEIR model is also applicable to assess the transmission dynamics of contagious disease such as 2019 n-COV.
- In SEIR the exposed compartment as well as a parameter (denote the movement from exposed compartment to infected compartment) additionally adopted to describe the transmission dynamics of the exposed individuals in the context of 2019 n-COV.

3.3. Model 3: M-SDI

- This approach is different from the studied models in this research as the model is developed based on information propagation on social media especially on the topic of public discussions in the context of 2019 n-COV. • In this study, they focused on the characteristics that users are choosing and re-entering to discuss certain topics of current pandemic (COVID-19). • To predict public discussion trends they have approximated parameters using LS method and estimated the public discussion peak by calculating the reproduction ratio.

3.4. Model 4: SUQC

- This model is developed by [24] to describe the COVID-19 transmission dynamics.
- Especially parameterize the interference effects of control measures by analyzing the disease outbreak.
- This model is adapted to the data of daily released confirmed cases to analyze the outbreaks of the diseases in Hubei, Wuhan, and four other first-tier cities in China.
- In this study, they have considered multiple characteristics to predict the transmission trends.

Model 5: BHRP

- BHRP model might be an advanced version of both SIR and SEIR models.
- BHRP mathematical computational part involves many differential equations.
- Most challenging part is to estimate many parameters.
- More data are needed for better understanding of the transmission dynamics in the context of 2019 n-COV.

3.5. Model 6: SEIHR

- SEIHR model estimates the size of the outbreak, the reproduction number as well as they evaluated the effects of different preventive measures.
- Results demonstrated that wearing masks, maintaining social distance and other intervention measures can reduce the fast transmission of the virus COVID-19.

- In this study, they did not consider natural deaths and births, infections during latency and asymptomatic infections, and re-infected cases.

Model 7: Theta-SEIHRD

- Theta-SEIHRD is developed to assess the dynamics of the virus (COVID-19) considering the major known characteristics of the disease.
- In this method they have added a new approach 'Theta' the fraction of total detected cases (infected) to study the importance of this fraction on the influence of the disease (COVID-19).
- They fitted and estimated many parameters with the reported data in the model that could be useful to estimate the spread of the disease (COVID-19) in some other countries.
- Reported data that they have used was homogeneously distributed and weak in quality (uncertainty in both undetected infections and a number of characteristics of the virus).

3.6. Model 8: SEIPAHRF

- SEIPAHRF model gives feasible approximation by studying different important aspects of the disease (COVID-19) transmission.
- The model is illustrated mathematically with nonlinear ODEs and investigated the sensitivity by considering the variations of its parameters.
- They also have fitted the model with the real data of daily confirmed cases and considered many parameters to quantify transmissibility.
- According to the theoretical findings as well as numerical illustrations the model was well adapted to the actual data and it reflected the real scenarios in Wuhan, China.

Model 9: Offspring distribution

- Offspring Distribution performs better for uniform and homogeneous data.
- Computationally, this model is powerful.
- It might be challenging to include additional parameters and distinguish stages which are quite easily applicable and identifiable respectively in other mentioned models.

Most of the study did not consider natural deaths and births although demographic factors (birth, death, emigration, and immigration) are significantly needed to add to any compartmental models for making it more realistic. Moreover in M-SDI model they have used public opinion data which is different from other models. And Theta-SEIHRD model used a new approach 'Theta' the fraction of total detected cases (infected) to assess the significance of this fraction on the influence of the disease (COVID-19). In the model SUQC they have parameterized the interference effects of control measures by characterizing multiple aspects to predict the transmission trends. Besides, SEIHR model demonstrated that wearing masks, maintaining social distances and other intervention measures can reduce the fast transmission of the virus by calculating the effects of different preventive measures. Furthermore it is noted that Offspring Distribution model perform better for uniform and homogeneous data as well. SEIPAHRF have fitted the model by considering many parameters to quantify transmissibility. Subsequently, more data are needed for better understanding of the transmission dynamics in the context of 2019 n-COV in BHRP model.

Accordingly, applying more parameters and adding more stages make the model more complex and computationally challenging. Using original values and data collected from the field work certainly move the model towards the real prediction of the near future. More complex models and methods might come in the future to handle the upcoming challenges. However, applying different models and methods under the same investigation might reflect the model variability and provide a boundary signature about the future situation.

4. Challenges and Future Research Directions

Symptoms of COVID-19 may vary in different areas, age groups and even person to person because of mutations. Therefore, it will be extremely challenging to predict the future research directions. Here, we are presenting a list of challenges to be faced by the existing models and possible ways to mitigate them.

4.1. Data size:

COVID-19 information data are increasing multiplicative day-by-day and the data storage system is becoming rich. It increases the possibility to predict the true model for the near future. In addition, these large data encourages researchers to think about more complex models by digging and including inside available information. However, these are extremely challenging to handle such a huge amount of data as well as to select the right model for accurate future prediction regarding COVID-19 virus transmission. More computational power(ex. Supercomputer) will be required for the analysis.

4.2. Parameter estimation:

How good a model will be depends upon the used parameters of the model. Since a large data-set invites researchers to implement more complex models, there is always an important issue regarding those parameter estimation. Complex models often use simulated data for unknown parameter estimation moving towards the opposite direction of the reality. In other words, it is always expected to use real data for parameter estimation to predict the real virus transmission rate in the near future. Less complex models should be chosen in case of limited data.

4.3. Survival & Lost dynamics:

Majority of the studies computed the transmission model of COVID-19 following only the nature of survival dynamics. However, lost dynamics (where,when and how people die) might also be valuable information for future prediction. Just computing the results of death might not help us to understand the true dynamics. In combination of survival & lost dynamics might provide us the true picture towards the reality.

Undetected/self Quarantine:

Although the COVID-19 data storage system is getting rich day-by-day, many people around the world are afraid of testing COVID-19 and move to self Quarantine with or without having symptoms([27][30]). Therefore the actual number of the Quarantine people might never be detected unless a safe and remote personal testing kit is discovered and encourage Quarantine people not to hide this information to the proper authority. For the computation of Mathematical modeling, Quarantine might be a challenging stage regarding parameter estimation which might make an impact in the final transmission rate for COVID-19.

4.4. COVID-19 infect twice:

Scientists can't guarantee that one person can't catch COVID-19 twice even though increased immunity was observed in the patient after COVID-19 recovery. An online portal news reported that a Chinese group found evidence of being caught twice by monkey study. So, the possibility of reinfection might not be excluded. Therefore, the model researchers might not be able to separate the already infected people from the upcoming analysis.

4.5. Mutations:

Human civilization may face enormous challenge near future new mutations, specifically in glycoproteins ([31]). Scientists have already spotted thousands of generic material changes in the corona-virus or mutations all around the world. However, not all of the mutations infect everywhere. For country or region specific mathematical modelling, it is also important to include the number of mutations of this virus (if possible). This information can be investigated for weather/area/temperature based virus transmission.

4.6. Multiple Model Implementation:

Which model fits well depending on the available data and the goal of the analysis. So far, it has been observed that researchers' goal is to implement a specific model or an improved version of the model to investigate virus transmission. However, applying different models (e.g., SIR & SEIR) in the same study might provide the range and center of true expected virus transmission. In addition, limitations on parameters between different models might be overcome or minimized.

4.7. Second wave:

Human civilization has learnt a big lesson from this COVID-19 pandemic and is now preparing for the second attack (often called second wave) specially in Europe and North American countries ([32]). These countries have already announced mandatory wearing mask restrictions on all indoor public areas. People might still be infected and the data will be stored. For mathematical modeling, researchers should consider this issue and add a new stage of the COVID-19 transmission with new parameters based on the data information.

Next we are going to address some of the possible future directions of mathematical modelling.

4.8. Decision support system (DSS):

So far no guaranteed antiviral treatment has been recommended regarding COVID-19 ([33]). The only way to fight against this contagious disease is to emphasize preventive healthcare guidelines and implement necessary rules and regulations depending on the spreading nature of the virus transmission. Here, Decision Support System (DSS) ([34]) can play a very important role by providing priority guidelines (Eg. Social distancing or lock down) to the national as well as international authorities in an effective and efficient way. The outcome of mathematical modelling can be plugged into this DSS system. However, the necessary supporting information can be collected from the corresponding authority.

4.9. Artificial intelligence(AI):

Majority of the AI implementations on COVID-19 analysis are relying on Convolutional Neural Network following X-ray and CT images. However data-sets are also available for aggregated case reports, management strategies, healthcare workforce, demography, and mobility during the outbreak. Interestingly, both Mathematical modeling and AI have shown their ability as reliable tools to fight against this COVID-19 pandemic [35]. These tools altogether might discover the new insights of this pandemic.

4.10. Other Implementable Mathematical methods:

The field of Mathematics is expanding over time with new methods and implementations. Majority of the study for COVID-19 applied Ordinary differential equations (ODEs) by adding suitable parameters. However, Partial differential equations (PDEs) can also be useful to apply in similar studies when the rest of the parameters do not change with respect to a specific parament. To solve the equations (eg. ODEs) with higher numbers of unknown variables (Known as Parameters for COVID-19 study), Galois theory [36]) can be used. However, to investigate the specific effect of similarities between different areas or countries of COVID-19, Pólya's Theorem ([37] can be applied. Also fuzzy logic can be used as it is able to handle some uncertainties by considering several membership functions based on the transmission dynamic trend data of contagious disease such as (COVID-19).

5. Conclusion

How useful a model/method will be depends mostly upon the availability of the sufficient real data and the usage of specific parameters reflecting the real value. Importantly, more elaborate data set (containing more information) might provide valuable information for the model prediction. So far, text based spreed sheet and medical imaging data[38] are available. Surprisingly, A COVID-19 mouse is also already available for research [39]. It might be able to discover the new insights of COVID-19 by rodent behavioural experiment[40], brain imaging[41][42],advanced computational image analysis[43] and cellular level gene expression [44]. These imaging and gene data can be helpful for mathematical analysis as additional parameters to investigate long term future effect, prediction and prevention.

Only continuing research on COVID-19 disease might not be able to save human civilization unless proposed rules and regulations are implemented strictly considering the stage of the Pandemic of that area/region. DSS might help the local authority by providing necessary guideline following the mathematical modeling transmission dynamics [34]. Everyone in the locality must follow the directions as best as possible. However, some people are already at high risk due to job condition (e.g. nurse,doctors), medical condition (e.g. Heart disease, Lung disease, Diabetes Cancer) and age condition [45] (e.g. High risk for the Older (65+)). Special monitoring system as well as better facilities are in demand to protect them. In the bigger context, the world is united against COVID-19 to stop its transmission.

The only good news under this major crisis is that Russia has already produced the first batch of coronavirus vaccine called "Sputnik V". This might be the first world approved vaccine which is still in clinical trial. It is expected that the vaccine will be effective and will be available in the market for general people soon.

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Supplementary Materials: We do not have any supplementary materials, data-set or supporting information available anywhere else other than this manuscript.

Abbreviations

The following abbreviations are used in this manuscript:

BHRP=Bats-Hosts-Reservoir-People
DSS=Decision support system
M-SDI=Multiple-information susceptible-discussing-immune
SIR=Susceptible-Infectious-Removed
SEIR=Susceptible-Exposed-Infectious-Removed
SUQC=Susceptible - unquarantined infected - quarantine infected-confirmed infected
SEIHR=Susceptible-Exposed-Symptomatic infectious-Hospitalized-Removed
Theta=SEIHRD-Susceptible- Exposed-Infectious-Hospitalized-Recovered-Dead
SEIPAHRF=Susceptible class - exposed class- symptomatic and infectious class - super spreaders class- infectious but asymptomatic class - hospitalized class - recovery class - fatality class

References

1. Organization, W.H.; others. Middle East respiratory syndrome coronavirus (MERS-CoV), 2019.
2. Tahir, M.; Shah, S.I.A.; Zaman, G.; Khan, T. Stability behaviour of mathematical model MERS corona virus spread in population. *Filomat* **2019**, *33*, 3947–3960.
3. Parry, R.L. Travel alert after eighth camel flu death. *The Times. Retrieved* **2015**, *11*.
4. Li, Q.; Guan, X.; Wu, P.; Wang, X.; Zhou, L.; Tong, Y.; Ren, R.; Leung, K.S.; Lau, E.H.; Wong, J.Y.; others. Early transmission dynamics in Wuhan, China, of novel coronavirus–infected pneumonia. *New England Journal of Medicine* **2020**.
5. Huang, C.; Wang, Y.; Li, X.; Ren, L.; Zhao, J.; Hu, Y.; Zhang, L.; Fan, G.; Xu, J.; Gu, X.; others. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The lancet* **2020**, *395*, 497–506.
6. Kucharski, A.J.; Russell, T.W.; Diamond, C.; Liu, Y.; Edmunds, J.; Funk, S.; Eggo, R.M.; Sun, F.; Jit, M.; Munday, J.D.; others. Early dynamics of transmission and control of COVID-19: a mathematical modelling study. *The lancet infectious diseases* **2020**.
7. Lin, Q.; Zhao, S.; Gao, D.; Lou, Y.; Yang, S.; Musa, S.S.; Wang, M.H.; Cai, Y.; Wang, W.; Yang, L.; others. A conceptual model for the outbreak of Coronavirus disease 2019 (COVID-19) in Wuhan, China with individual reaction and governmental action. *International journal of infectious diseases* **2020**.
8. Ndairou, F.; Area, I.; Nieto, J.J.; Torres, D.F. Mathematical modeling of COVID-19 transmission dynamics with a case study of Wuhan. *Chaos, Solitons & Fractals* **2020**, p. 109846.
9. Anderson, R.M. Discussion: the Kermack-McKendrick epidemic threshold theorem. *Bulletin of mathematical biology* **1991**, *53*, 1.
10. Singh, R.; Adhikari, R. Age-structured impact of social distancing on the COVID-19 epidemic in India. *arXiv preprint arXiv:2003.12055* **2020**.
11. Zhong, L.; Mu, L.; Li, J.; Wang, J.; Yin, Z.; Liu, D. Early prediction of the 2019 novel coronavirus outbreak in the mainland china based on simple mathematical model. *Ieee Access* **2020**, *8*, 51761–51769.
12. Vega, D.I. Lockdown, one, two, none, or smart. Modeling containing COVID-19 infection. A conceptual model. *Science of the Total Environment* **2020**, p. 138917.
13. Kim, S.; Kim, Y.J.; Peck, K.R.; Jung, E. School opening delay effect on transmission dynamics of Coronavirus disease 2019 in Korea: Based on mathematical modeling and simulation study. *Journal of Korean medical science* **2020**, *35*.
14. Kim, S.; Seo, Y.B.; Jung, E. Prediction of COVID-19 transmission dynamics using a mathematical model considering behavior changes in Korea. *Epidemiology and health* **2020**, *42*.
15. Yin, F.; Lv, J.; Zhang, X.; Xia, X.; Wu, J. COVID-19 information propagation dynamics in the Chinese Sina-microblog. *Mathematical biosciences and engineering: MBE* **2020**, *17*, 2676.
16. Aragón-Caqueo, D.; Fernández-Salinas, J.; Laroze, D. Optimization of group size in pool testing strategy for SARS-CoV-2: A simple mathematical model. *Journal of Medical Virology* **2020**, pp. 1–7. doi: 10.1002/jmv.25929.
17. Chang, R.; Wang, H.; Zhang, S.; Wang, Z.; Dong, Y.; Tsamlag, L.; Yu, X.; Xu, C.; Yu, Y.; Long, R.; others. Phase-and epidemic region-adjusted estimation of the number of coronavirus disease 2019 cases in China. *Frontiers of Medicine* **2020**, pp. 1–11.
18. Mandal, S.; Bhatnagar, T.; Arinaminpathy, N.; Agarwal, A.; Chowdhury, A.; Murhekar, M.; Gangakhedkar, R.R.; Sarkar, S. Prudent public health intervention strategies to control the coronavirus disease 2019 transmission in India: A mathematical model-based approach. *The Indian journal of medical research* **2020**, *151*, 190.
19. Cakir, Z.; Savas, H. A Mathematical Modelling Approach in the Spread of the Novel 2019 Coronavirus SARS-CoV-2 (COVID-19) Pandemic. Electron J Gen Med. 2020; 17 (4): em205, 2020.
20. Prem, K.; Liu, Y.; Russell, T.W.; Kucharski, A.J.; Eggo, R.M.; Davies, N.; Flasche, S.; Clifford, S.; Pearson, C.A.; Munday, J.D.; others. The effect of control strategies to reduce social mixing on outcomes of the COVID-19 epidemic in Wuhan, China: a modelling study. *The Lancet Public Health* **2020**.
21. Tang, B.; Wang, X.; Li, Q.; Bragazzi, N.L.; Tang, S.; Xiao, Y.; Wu, J. Estimation of the transmission risk of the 2019-nCoV and its implication for public health interventions. *Journal of clinical medicine* **2020**, *9*, 462.

22. Tang, B.; Bragazzi, N.L.; Li, Q.; Tang, S.; Xiao, Y.; Wu, J. An updated estimation of the risk of transmission of the novel coronavirus (2019-nCov). *Infectious disease modelling* **2020**, *5*, 248–255.
23. Modnak, C.; Wang, J. An avian influenza model with latency and vaccination. *Dynamical Systems* **2019**, *34*, 195–217.
24. Zhao, S.; Chen, H. Modeling the epidemic dynamics and control of COVID-19 outbreak in China. *Quantitative Biology* **2020**, pp. 1–9.
25. Chen, T.M.; Rui, J.; Wang, Q.P.; Zhao, Z.Y.; Cui, J.A.; Yin, L. A mathematical model for simulating the phase-based transmissibility of a novel coronavirus. *Infectious diseases of poverty* **2020**, *9*, 1–8.
26. Choi, S.; Ki, M. Estimating the reproductive number and the outbreak size of COVID-19 in Korea. *Epidemiology and health* **2020**, *42*.
27. Ivorra, B.; Ferrández, M.R.; Vela-Pérez, M.; Ramos, A. Mathematical modeling of the spread of the coronavirus disease 2019 (COVID-19) taking into account the undetected infections. The case of China. *Communications in nonlinear science and numerical simulation* **2020**, p. 105303.
28. Endo, A.; Abbott, S.; Kucharski, A.J.; Funk, S.; others. Estimating the overdispersion in COVID-19 transmission using outbreak sizes outside China. *Wellcome Open Research* **2020**, *5*, 67.
29. Blumberg, S.; Funk, S.; Pulliam, J.R. Detecting differential transmissibilities that affect the size of self-limited outbreaks. *PLoS Pathog* **2014**, *10*, e1004452.
30. Pedersen, M.G.; Meneghini, M. Quantifying undetected COVID-19 cases and effects of containment measures in Italy. *ResearchGate Preprint (online 21 March 2020) DOI* **2020**, *10*.
31. Dawood, A.A. Mutated COVID-19, may foretells mankind in a great risk in the future. *New Microbes and New Infections* **2020**, p. 100673.
32. Xu, S.; Li, Y. Beware of the second wave of COVID-19. *The Lancet* **2020**, *395*, 1321–1322.
33. Shereen, M.A.; Khan, S.; Kazmi, A.; Bashir, N.; Siddique, R. COVID-19 infection: Origin, transmission, and characteristics of human coronaviruses. *Journal of Advanced Research* **2020**.
34. Kaiser, M.S.; Lwin, K.T.; Mahmud, M.; Hajializadeh, D.; Chaipimonplin, T.; Sarhan, A.; Hossain, M.A. Advances in crowd analysis for urban applications through urban event detection. *IEEE Transactions on Intelligent Transportation Systems* **2017**, *19*, 3092–3112.
35. Mohamadou, Y.; Halidou, A.; Kapen, P.T. A review of mathematical modeling, artificial intelligence and datasets used in the study, prediction and management of COVID-19. *Applied Intelligence* **2020**, pp. 1–13.
36. Nasseef, M.T. Field Extension by Galois Theory. *General Letters in Mathematics* **2017**, *3*, 132–153.
37. Nasseef, M.T. Counting Symmetries with Burnside's Lemma and Polya's Theorem. *European Journal of Pure and Applied Mathematics* **2016**, *9*, 84–113.
38. Wang, K.; Kang, S.; Tian, R.; Zhang, X.; Wang, Y. Imaging manifestations and diagnostic value of chest CT of coronavirus disease 2019 (COVID-19) in the Xiaogan area. *Clinical radiology* **2020**.
39. Oliveira, G.M.d. Laboratory Mouse & COVID-19 Research. *Open Access Journal of Biomedical Science* **2020**, *2*, 338–340.
40. Boulos, L.J.; Nasseef, M.T.; McNicholas, M.; Mechling, A.; Harsan, L.A.; Darcq, E.; Hamida, S.B.; Kieffer, B.L. TouchScreen-based phenotyping: altered stimulus/reward association and lower perseveration to gain a reward in mu opioid receptor knockout mice. *Scientific reports* **2019**, *9*, 1–13.
41. Nasseef, M.T.; Devenyi, G.A.; Mechling, A.E.; Harsan, L.A.; Chakravarty, M.M.; Kieffer, B.L.; Darcq, E. Deformation-based morphometry MRI reveals brain structural modifications in living mu opioid receptor knockout mice. *Frontiers in psychiatry* **2018**, *9*, 643.
42. Nasseef, M.T.; Singh, J.P.; Ehrlich, A.T.; McNicholas, M.; Park, D.W.; Ma, W.; Kulkarni, P.; Kieffer, B.L.; Darcq, E. Oxycodone-mediated activation of the mu opioid receptor reduces whole brain functional connectivity in mice. *ACS Pharmacology & Translational Science* **2019**, *2*, 264–274.
43. Nasseef, M.T. Measuring directed functional connectivity in mouse fMRI networks using Granger Causality. PhD thesis, University of Trento, 2015.
44. Ehrlich, A.T.; Maroteaux, G.; Robe, A.; Venteo, L.; Nasseef, M.T.; van Kempen, L.C.; Mechawar, N.; Turecki, G.; Darcq, E.; Kieffer, B.L. Expression map of 78 brain-expressed mouse orphan GPCRs provides a translational resource for neuropsychiatric research. *Communications Biology* **2018**, *1*, 1–14.
45. Covid, C.; Team, R. Severe outcomes among patients with coronavirus disease 2019 (COVID-19)—United States, February 12–March 16, 2020. *MMWR Morb Mortal Wkly Rep* **2020**, *69*, 343–346.