Can infectious modelling be applicable globally – lessons from COVID 19

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Can infectious modelling be applicable globally – lessons from COVID 19

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Abstract

Contagious diseases are needed to be monitored to prevent spreading within communities. Timely advice and predictions are necessary to overcome the consequences of those epidemics. Currently, emphasis has been placed on computer modelling to achieve the needed forecasts, the best example being the COVID-19 pandemic. Scientists used various models to determine how diverse sociodemographic factors correlated and influenced COVID-19 Global transmission and demonstrated the utility of computer models as tools in disease management. However, as modelling is done with assumptions with set rules, calculating uncertainty quantification is essential in infectious modelling when reporting the results and trustfully describing the limitations. This article summarizes the infectious disease modelling strategies, challenges, and global applicability by focusing on the COVID-19 pandemic.

Keywords

COVID-19, infectious diseases, infectious modelling, basic reproduction number, prediction

Introduction

A comprehensive understanding of the functional changes associated with an infection and its spread is essential for controlling and preventing an infectious disease [1]. In the current era, computer modelling has been widely used in the health sector in making policy decisions. When modelling is used from an epidemiologic standpoint, many factors must be considered as parameters for an accurate prediction. If one to model the magnitude of the infection spread, among many factors to be considered involves the transmission, number of infected and recovered, extra parameters such as different age groups, and other associated selections [2]. In accomplishing the maximum results in modelling, the data must be appropriate, precise, novel, and used in an organized and timely manner [3]. Ultimately, with its assumptions, the model should be able to predict real-world situations with a certain level of accuracy.

The etiological agent for the deadly COVID pandemic is SARS-CoV- 2. The first official record was in 2019 December, from the city of Wuhan, in the province of Hubei in China [4]. The virus has evolved from Bats and causes fever and serious pulmonary health conditions in humans; World Health Organization (WHO) termed it COVID-19 [5, 6]. According to the Worldometer estimation, as of 28th May 2022, 228 countries and territories worldwide have reported that a total of 531,054,349 people were officially confirmed as infected with COVID-19. The deaths due to COVID were 6,309,991. About 501,689,286 individuals have recovered, while 23,055,072 are currently infected, and 0.2% are in critical condition. After two and half years, do we know the facts about this pandemic? Many feel that the number of casualties and infections is more from COVID-19 than the documented official records worldwide. As we are still struggling to understand this deadly virus, to a certain extent, computer modelling has helped us to familiarize ourselves with the new pandemic.

Contagious diseases are needed to be monitored to prevent spreading within communities. Timely advice and predictions are necessary to overcome the consequences of those epidemics. Currently, emphasis has been placed on computer modelling to achieve the needed forecasts, the best example being the COVID-19 pandemic. Researchers are using various models to determine how diverse sociodemographic factors [7] correlated and influenced the transmission of the COVID-19 pandemic in different locations worldwide [8] and demonstrated the utility of computer models as tools in disease management. However, as modelling is done with assumptions and set rules, calculating uncertainty quantification is essential in infectious modeling when reporting the results accurately and in a trustworthy manner describing the limitations. This article summarizes the infectious disease modelling strategies, challenges, and global applicability by focusing on the COVID-19 pandemic.

History of mathematical modelling in infectious diseases

Mathematical modelling has been used to determine the transmission dynamics and managing numerous communicable diseases with records of severe pandemics. The most commonly researched diseases include acquired immunodeficiency syndrome, commonly known as AIDS, coronavirus, influenza or flu that attacks the lung, and malaria [1]. But as shown in figure 1, COVID-19 gets the top slot in the most published area in infectious modeling in the past two years. The first user of mathematical modelling for infectious diseases was Daniel Bernoulli in 1760 for Smallpox in England, while the pioneer for modern mathematical modelling was Ross R. The latter worked on the dynamics of malaria transmission [1]. Kermack and McKendrick [9] are the creators of deterministic compartmental epidemic modelling. The model assumes that a person's chance of being vulnerable to infection is equivalent to the number of infected individuals the person had associated with [9]. There are several models in practice for infection predictions and warnings. A forecast is generally made for a time series model while the linear regression model, a statistical model, is used in epidemiology to analyze one or many variables [10, 11]. Artificial neural networks are mostly used in nonlinear analysis, and various Markov models are useful in DNA alignments, uncertainty measurements with Bayesian modeling, and Complex networks [12, 13]. The model grey dynamics can be used to forecast peaks [14]. The basic reproduction number/rate in epidemiology is termed R_0 and calculates infectious agents' transmission capability within populations [15]. R_0 is defined as the average number of secondary infections an infected individual can cause in a population where everybody is considered susceptible. Epidemiologists can estimate R_0 using contact-tracing data, cumulative incidence data, or mathematical models with ordinary differential equations [15].

The practice has proved that what is essential is that when a health crisis occurs in a community, models used for forecasting should be capable of delivering active measures for halting the infections from spreading than taking part in passive prevention. The hybrid stochastic model can include many parameters such as interactions within the public, diverse patterns in an infection spreading, the number of participants in screening, sensitivity, and testing frequency, delays in getting the test result, and adherence to quarantine processes [16].

Mathematical models used in the COVID-19 pandemic

The purpose of a screening test is to detect individuals who neither present any symptoms associated with the infection nor a known or suspected contact history with the particular disease. Regarding the COVID-19 pandemic, many communities were subjected to mass screening as a precautionary measure to isolate undetected cases and prevent further transmission. Mathematical models and numerical simulations are extensively used to study the value of screening in managing epidemics [16]. During COVID-19 pandemic, many higher education institutes worldwide used the compartmental model [17], and Liège University used the Hybrid stochastic model [16] to determine their screening efficacies. According to Liège University's study, community participation and regular screening were the key features in reducing transmission [16].

Drew et al. [18] compared the actual progression of COVID-19 among ten countries hugely affected by the disease. Data recorded up to November 2020 were considered for "re-forecasts" with the aid of two models. One is the SIR or Susceptible–Infected-Recovered/Removed model, a compartment-type model widely used in evolving epidemics. The other is the *Holt-Winters time series model*, a statistical approach [18]. Bertozzi et al. [2] demonstrated the convenience of parsimonious models in delivering early-time data providing manageable outlines to generate policy decisions. Their study showed the effectiveness of modelling by linking time-series data to a specific area. Additionally, these can access and predict how effective isolation is as a control measure.

Further, the researchers underlined the risks of reducing nonpharmaceutical public health interventions (NPHI) due to the lack of vaccines and antiviral therapies [2]. Imperial College used an agent-based method, modelling people getting infected and recovering from interacting with other persons within the community. But the Bertozzi study used three macroscopic models, the SIR, a model for exponential or rapid growth rate, and the self-exciting or Hawkes process due to uncomplicatedness, usage of few parameters, and the capability of describing the pandemic on a zonal scale [2].

Computer modelling helped prepare rules and guidelines at the national level within a country or globally for the cross-border closure during COVID-19, to prevent the virus from spreading [19]. Further, during the crisis, mathematical modelling assisted in developing strategies regarding social distancing, wearing masks, and hand hygiene [20- 22]. Table 1 summarizes the selective COVID-19 modelling studies reported from different countries.

The study by Gao and Wang [34] discusses the likelihood of an epidemic's occurrence with the IDD model. At the same time, for the situation assessments in public health emergencies (PHEs), it was a dynamic Bayesian network (DBN). According to analysis data in solitary confinements, the confirmed patients from China for COVID was 1.503, and in the city of Wuhan, it was 1.729, similar to real figures. By the 21st day, and with self-isolation in practice, the confirmed COVID infected number was 24495, and the model estimation was 24085 with a 95% CI of 23988 - 25056 [34]. They demonstrated that forecasts about the situation assessments for the COVID-19 created with DBN were consistent with the epidemic's real ground situation and the progression of the infection. They highlight the competence of the two models, IDD and the scenario deduction model of DBN, validating the likelihood and wisdom in using these models in combating COVID -19 pandemic [34].

WHO assessed the R_0 of COVID-19 and initially predicted it as between 1.4 to 2.4. The forecast was vital as it helped the governments to have an estimate as well as manage the pandemic. The value for R_0 can be a decisive factor in how the strategies should be implemented to address the pandemic while considering both the generation time (Tg) and R_0 can finalize the time existing to execute the appropriate control strategies. In a comparative study on 12 research findings conducted from 1st January to 7th February, Liu *et al.* [35] projected an R_0 value for COVID-19 in the range of 1.5- 6.68 [35], which exceeded the predictive value of WHO. The value of Re (effective reproduction number) is defined as the average number of secondary infections caused by an infected individual, assuming that the population comprises both susceptible and non-susceptible persons. Re will fluctuate when people develop immunity either by vaccination or immunity gained due to infection and death [15].

As modelling is done with assumptions and set rules, calculating uncertainty quantification is essential in infectious modeling when reporting the results and trustfully describing the limitations. Jensen et al. [36] used the generalized Polynomial Chaos (gPC) framework to propose the effect of total uncertainties in compartmental epidemic models. This model can be considered an improved version of the SIR model and data for the modelling were obtained from two case studies done in Denmark. The factors considered included the assessment of the peak time of the pandemic and the underlining forces between virus transmission and travel banning or imposing partial restrictions. Their outputs displayed the efficacy and practicability of the technique. Furthermore, the importance of quantifying the uncertainties in infectious modelling was highlighted [36].

Lessons from COVID -19 modelling

Modelling has been successful globally due to the easiness of forecasting compared to laboratory experiments. However, mathematical modelling and its application in medicine, specifically in infectious diseases, have to be performed precisely as outcomes will be used in decision-making that will determine the future of humanity. By applying infectious modelling to COVID-19, the scientists learned the challenges of using mathematical modelling on new or emerging infectious disease outbreaks. If contagious disease modelling is a reality in preventing future pandemics, research alliances among developing and developed nations are vital to overcoming the financial constraints and lack of resources in low-income countries.

Challenges associated with the COVID-19 modelling and associated uncertainties

A recent review of Menon and Mohapatra [37] summarizes the role of environmental factors on the transmission dynamics of the COVID-19 virus. It further defines the importance of considering diverse parameters when designing models to predict risk assessments with a particular disease. In addition to virus transmission, environmental parameters such as temperature, humidity, and climatic changes could significantly influence the virus genome, creating gene mutations. Initially, and up to now, the virus's nature keeps changing. Its properties have changed, and specific variants have become more virulent. Certain variants have the genetic ability to change the COVID-19 virus characteristics and are named Variants of Interest (VOIs). The variants such as Alpha, Beta, Delta, and Gamma are called Variants of Concern or VOCs. Omicron and the new sub-variant named Deltacron have become more transmissible than the rest.

The nature of the environment is a decisive factor in host immunity and will vary from person to person. Though COVID -19 is considered an airborne respiratory virus, viral RNA as well as COVID-19 has been detected in aquatic environments and also from fecal matter, which is a global concern [38, 39]. All these factors will influence the R_0 value. Therefore, modeling with a globally unknown virus, and uncertainties associated with all these diverse environmental and behavioral factors of the global communities [40] are the main challenges scientists faced in providing predictions to control this global pandemic.

Drawbacks in COVID-19 infectious modelling in disease predictions

As discussed in a recent review by Mohapatra and Menon [40] one of the shortcomings was the failure to identify the intermediate host, where the uncertainty lies in whether it is a single species, or many involved. Additionally, it has not yet been able to determine who was the first patient that was infected with the SARS-CoV-2 virus. It prevented forecasting the actual beginning of the pandemic and most countries would have been late in implementing their policy decisions [40].

The quality of data used in modelling is crucial, whether the country is developed or still developing with minimal resources. In COVID-19 disease containment, one major drawback was the quality of input data used for the predictions. Drew et al. [18] discussed that irrespective of the modelling complications, predictions on forthcoming diseases of COVID-19, fatalities, and hospital admissions are connected with substantial doubts and how the output will change with the quality of data used. The findings display the significant disparities in the assessing skills or the knowledge gap among the ten nations, demonstrating variations observed with the forecasts made with individual modeling and how the assumptions made for each parameter will change the precision [18]. Also, whether the data indicate factual status, the accuracy of the documented data for authorized infected numbers, actual figures on recovery, and the verified deaths due to COVID-19 either nationally or globally will influence the accuracy of the forecasts [18].

Recommendations for future

To maintain the selected model's repeatability and unambiguity, it is vital to use open-access datasets. Validation is essential for a model to be accepted. However, when researchers are unable to authenticate the process it is recommended to declare the causative factors liberally [41]. Furthermore, uncertainties arising from all the parameters must be considered when models are used to predict an infectious disease. A multidisciplinary approach with international research collaborations with expertise in different fields needs to be promoted in designing models for combating deadly pandemics such as COVID-19.

Conclusion

Predicting solutions to natural disasters or global pandemics with mathematical equations is not an easy task. Complications arise in modelling the emerging infections due to the non-existent data for model parameterization, authentication, and complexity in the methods used. Uncertainty quantification is indispensable in infectious modeling and the use of actual facts will yield accurate forecasts which could be useful in controlling a progression of a deadly pandemic.

Figure Caption

Figure 1: Comparison of number of modelling papers published for infectious diseases, SARS-CoV-2 and COVID-19

Declaration of competing interest

We, as authors declare that we do not have known competing financial interests.

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Table 1: Summary of the selective COVID 19 modelling studies reported from different countries

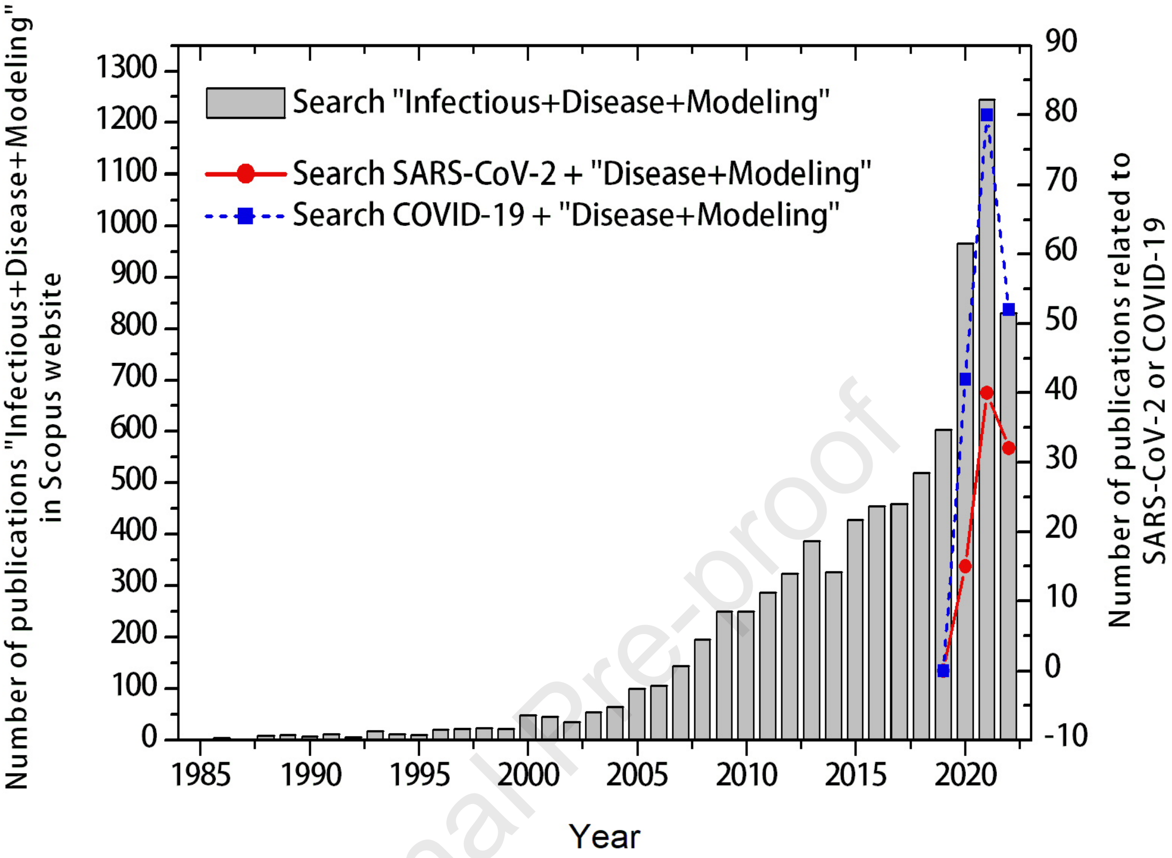
Country	Aim of the work	Simulation platform/ Model	Parameters considered in Modelling	Findings	Reference
Australia	To estimate the impact of global air travel limitations, patient isolation, home confinement, maintenance of physical distancing and school shutdowns	Agent-based modelling	χ_1: Time to reach to the infectivity peak χ_2: Recovery period χ_3: Possibility of spread for asymptomatic/presymptomatic agents χ_4: Fraction of symptomatic cases χ_5: Age	Combination of school shutdowns together with physical distancing resulted in significant control of COVID-19. Further, the disease could be controlled within 13–14 weeks by maintaining social physical distance along with case isolation and imposing boundaries to global air travel.	[23]
China	To recognize how national and international travel restrictions influence on spreading the COVID 19	Global metapopulation disease transmission model (GLEAM)	Latency period (mean) Infectious period (mean) Generation time (Tg) Starting dates considered in an interval Initial number of zoonotic cases	A notable reduction of case introductions was observed at the international level.	[24]
China	To forecast the rise of COVID 19 epidemic and short term spreading of the virus	Dynamics model of infectious diseases and time series model (SEIQDR model)	γ: Cure rate δ: Fatality rate d_{qd}: Quarantine intensity d_{id}: Rate of highly infectious people in the free environment transferred as confirmed cases δ_1: Rate of move out due to lack of timely treatment	This model is effective for the prediction of COVID 19 epidemic transmission in short term.	[25]

China	To study COVID-19 dynamics and consequences of precautionary actions	Susceptible, Un-quarantined infected, Quarantined infected, Confirmed infected (SUQC) model	α: Infection rate γ_1: Quarantine rate γ_2: Confirmation rate of quarantined infected σ: Confirmation rate of those infected confirmed with other tests δ: Confirmation rate of the un-quarantined infected	Strict isolation and precautionary actions are needed to control the disease. Model is capable of determining the progression of disease and it could be utilized for other high-risk countries.	[26]
Germany	To develop COVID 19 prediction tool in Germany	Susceptible-Exposed-Infected-Recovered (SEIR) model	β: Infection rate Γ: The rate to become infectious δ: The rate with which one dies or recovers	Modeled short-term COVID-19 predictions for some regions of Germany. Accessibility was offered to policymakers via web applications.	[27]
India	To predict the prevalence of the COVID 19 disease	AutoRegressive Integrated Moving Average (ARIMA), Seasonal Autoregressive Integrated Moving Average (SARIMA) and Prophet	ARIMA Autoregressive (AR): Differencing & moving-average (MA) AR- (p); Impact of past values on Xt, $Xt=c+a_1x_{t-1}$----+ a_px_{t-p}+ ε_t t=1,2, ---T MA- (q); Past errors as explanatory variables ARMA (p, q)-Time series data stationary ARIMA (p, d, q)- generalized to non -stationary time series with differencing	For the prediction of COVID-19 occurrence, new and for total deaths, ARIMA & SARIMA can be used. SARIMA is considered better as it includes weather/seasonal variations. For the total number of cases Prophet	[28]

			SARIMA: (p, d, q) (P, D, Q) s Improvement to ARIMA by considering seasonal fluctuations Prophet model: Used past data to predict the future dt: Date of the day x: Accumulated values of a country (India)	model yields better accuracy	
Italy	To characterize dynamics and predicting the future prevalence	A five-dimensional COVID-19 epidemic model	r: Rate of getting infected a: Average rate of recovery & death α: Lockdown rate of susceptible μ: Isolation rate of infectious	Developed an optimal control model. Predictions were made on the disease control time and showed how effective imposing restrictions on movement in controlling the COVID 19 epidemic.	[29]
Sri Lanka	To investigate COVID 19 dynamics in Sri Lanka	SEIR model	β: Exposed rate to the novel coronavirus σ: Infected rate γ: Recovery rate γ_1: Recovery rate of patients who show mild symptoms γ_2: Recovery rate of severely ill patients who are treated in ICUs δ: Rate at which a patient's level becomes critical	COVID 19 could be controlled by strict control measures.	[30]
UK	To forecast the fluctuations to COVID 19 pandemic due to	SIR model	β: Infection rate 1/μ: Average infectious period	Immediate lockdowns showed significant control of COVID 19.	[31]

	nonpharmaceutical interferences				
UK	To study the effectiveness of two impending lockdown release approaches	SEIR model	β: Transmission rate c: Effectiveness of the self-isolation μ: Natural death rate α: Death rate due to SARS-CoV-2 σ: Incubation rate γ: Recovery rate and how long individuals remain infectious	Removal of quarantine for the whole community at once is a high-risk approach in comparison to the gradual re-integration approach.	[32]
United States	To investigate the COVID 19 transmission dynamics	A mathematical model based on differential equations	Λ: Population influx rate μ: Natural death rate for the human hosts, α^{-1}: Incubation period p: Portion of exposed individuals who become severely ill and hospitalized after the incubation period q: Rate of infected individuals (who initially show minor or moderate symptoms) getting hospitalized due to the worsening of their conditions w: Disease induced death rate σ: Removal rate of the coronavirus from the environment γ1, γ2, γ3: Rates of recovery	Environmental factors could contribute to the spread of the disease.	[33]

			ε1, ε2, ε3: Rates of contributing the coronavirus to the environment, from the exposed, infected (non-hospitalized), and hospitalized individuals, respectively.		
Ten high-risk countries including Argentina, Brazil, Colombia, France, India, Italy, Russia, Spain, United Kingdom and Unites States	A comparative study of COVID 19 spread in ten high-risk countries	SIR model and Holt-Winters time series model	β: Transition rate from the infected to susceptible individuals γ: Transition rate between infected individuals and individuals removed from the model	There's a significant difference in forecasting skills in ten countries.	[18]


Number of publications "Infectious+Disease+Modeling" in Scopus website
Number of publications related to SARS-CoV-2 or COVID-19
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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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