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Mathematical Models Used to Assess the COVID-19 Outbreak and Preventive Measures

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Abstract

Background: Mathematical modelling is one of the most powerful methods for exploring the diverse range of intervention strategies, determining the fundamental reproduction rate, and forecasting disease spread. This paper reviews the mathematical models that were utilized to investigate coronavirus disease 2019 (COVID-19) transmission dynamics.

Methods: We looked through four electronic databases for research that evaluated the transmission dynamics of COVID-19 using a mathematical modeling strategy based on compartmental models. Research describing COVID-19 transmission utilizing compartmental models and published in English in preprints and peer-reviewed publications between December 30, 2019 and May 25, 2020 was eligible for inclusion. This limitation period of time was chosen because it's when the disease emerged and peaked in many countries worldwide.

Results: A total of 46 studies that used compartmental models to explain COVID-19 transmission were included in the review. Six studies employed the age-structured SEIR model, making up the majority of studies' (37/46) use of the Susceptible-Exposed-Infected-Recovered (SEIR) framework. In one of the eight investigations that used SIR, an age-structured model was used. One study evaluated COVID-19 transmission using the generalized SIRS model. To anticipate the onset of the disease, 36 of the 46 studies calculated the basic reproduction number, and 5 estimated the effective reproduction number.

Conclusion: Modelling studies applied generalised and age-structure models to assess the transmission and control of the COVID-19, suggesting that combined mitigations have a substantial impact on disease transmission.

Introduction

Coronavirus disease 2019 (COVID-19) is spread from person to person by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) through respiratory droplets or contacting surfaces with droplets from an infected individual [1,2]. Fever, coughing, and shortness of breath are the major signs of COVID-19 [3-5]. According to data, people over 50 and those with weakened immune systems or comorbid conditions may be more susceptible to COVID-19-related severe illness or mortality [5,6].

Many measures have been taken to stop COVID-19 from spreading around the globe. Every country has a different intervention strategy and level of rigor, but common tactics include social isolation, contact tracing, and the use of non-pharmaceutical therapies like masks. It's still debatable how well we understand the effectiveness of prospective therapies.

Mathematical models have been used in several countries to help determine the optimal combination and timing of interventions. Mathematical modelling is a powerful tool for exploring the complex landscape of intervention strategies, quantifying the basic and effective reproduction numbers, understanding disease dynamics, and forecasting the trajectory of outbreaks [4,7,24]. As an emerging infectious disease, there is much still unknown about COVID-19. Given the importance of expanding the knowledge base on COVID-19 and guiding time-sensitive

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decision making, a wide range of mathematical models have been developed for COVID-19. In this study, we reviewed studies that have used a mathematical modelling approach based on compartmental models to explore the transmission of COVID-19 and potential interventions.

Methods

Search Strategy and Inclusion Criteria

We searched four electronic databases (Pubmed, Web of Science, Scopus, and EBSCOHost) for studies that used mathematical models based on compartmental models to assess the transmission dynamics of COVID-19. In the database, we searched using the keywords "compartmental model" and "coronavirus disease 2019," or "COVID-19," and "transmission." All preprint papers and published articles in international peer-reviewed journals in English between December 30, 2019 and May 25, 2020 describing COVID-19 transmission using compartmental models were eligible for inclusion. We chose this limitation period because it's the time when the disease emerged and peaked in many countries worldwide. Our review included publications with primary data or parameter values to predict disease transmission but excluded reviews or theoretical papers without data or parameter values. Publications that met our review criteria were imported into Mendeley for citations.

Results

Model Structure

We reviewed studies that used a mathematical modelling approach based on compartmental models to assess the transmission dynamics of COVID-19. Based on our review of search terms and inclusion criteria, 46 articles were identified from the four electronic databases searched. Most reviewed studies (36/46) used the Susceptible-Exposed-Infected-Recovered (SEIR) compartmental model, of which six studies [9-14] applied the age-structured model. An SIR model was used in eight studies [2,16-21], with one study [21] using an age-structured model. One study [17] compared SIR and SEIR models to predict COVID-19 transmission and suggested that an SIR structure performs better than SEIR, and that predicting disease transmission using complex models may not be more reliable compared to using a simpler model. Although it is not well known if recovered individuals from COVID-19 acquire immunity and how long it takes for acquired immunity to wane, one study [29] applied an SIRS model to investigate COVID-19 transmission, suggesting that considering the impact of waning immunity is crucial in disease epidemiology. The study suggested that it is plausible to consider an SIRS model when assessing COVID-19 transmission, and that the impact of waning immunity should not be overlooked.

Interventions

In the model simulations, the majority of reviewed studies (36/46) considered interventions, such as quarantine, isolation, facemasks, and social distancing. Many of these studies (23 studies) applied generalized SEIR models, and seven studies applied generalized SIR models (not age-structured models) to assess the impact of interventions for disease control. Six studies [9,10,12-14,21] used age-structured models to assess the impact of interventions for disease control in different age groups. [9], for example, used an age-structured SEIR model to assess COVID-19 transmission and control in China and proposed that removing interventions quickly could result in an earlier secondary peak. Using an age-structured SEIR model to explore COVID-19 transmission and control in Canada, Tuite et al [10] suggested that without a substantial combination of interventions, Intensive Care Unit (ICU) resources could be overwhelmed. Additionally, Davies et al [11] applied an age-structured SEIR model to investigate the COVID-19 outbreak and control in China and suggested that without the implementation of effective control measures, the number of clinical cases may increase in regions with older populations. One study [13] suggested that interventions reduced contacts for adults above 60 years of age, adults 20–59 years of age, and children less than 19 years of age for 6 weeks.

Age-Stratification

Six studies [9-14] used age-structured SEIR model, and one [21] applied an age-structured SIR model to assess COVID-19 transmission. Of seven age structured models, four studies [9-11,13] observed the impact of symptomatic and asymptomatic in disease transmission, suggesting that asymptomatic individuals have a low ability to transmit disease. One study [21] suggested that children aged between 0 and 14 years are less susceptible to COVID-19 infection than adults aged between 15 and 64 years, and that individuals over 65 years are more susceptible to infection. However, based on the fact that the number of confirmed cases and deaths due to COVID-19 are highly associated with age globally, observations in some of these studies were based more on interventions, and they could not clearly quantify the exact age groups at high risk of acquiring infection and developing disease.

Basic and Effective Reproduction Number

The basic reproduction number (R0) is the expected number of secondary cases generated by a case in a naive population [22]. The effective reproduction number (Re) is a measure of the number of secondary cases generated by one primary case in a population with partial immunity or where intervention measures have been implemented [23]. The "basic reproduction number" is a central concept in infectious disease epidemiology that predicts the risk of an infectious agent with respect to epidemic spread. R0>1 indicates that the number of infected individuals is likely to increase, and R0<1 means that transmission is likely to die out [22].

Estimation of the basic reproduction number by means of mathematical modelling can therefore help to determine the potential severity of an outbreak and provide critical information to inform disease interventions [24]. Of 46 reviewed studies, 36 estimated the basic reproduction number, and 5 studies [8,17,23,24,26] estimated effective reproduction number using a range of approaches, such as the next generation matrix, Markov Chain Monte Carlo and model parameters to assess the transmission of COVID-19. Two studies [13,27] estimated both the basic and effective reproduction numbers. Two studies [9,10] estimated the basic reproduction number from literature to simulate age-structured models to assess COVID-19 transmission in China and Canada, respectively. Of the 46 reviewed studies, five could not be estimated or assumed to have a basic or effective reproduction number.

Estimated basic reproduction numbers from reviewed studies ranged from approximately 1.2 to 5.5 and effective reproduction numbers from 0.5 to 2, suggesting that the spread of the disease was increasing.

Discussion

We have reviewed studies that used a mathematical modeling approach based on compartmental models to explore the transmission dynamics of COVID-19. A mathematical model can successfully capture the COVID-19 outbreak and shed light on understanding the trends of disease transmission and control [46]. The majority of the studies reviewed (37/46 studies) used SEIR models to assess COVID-19 transmission using surveillance data from several countries with high disease prevalence, including Wuhan, China, where the outbreak began. Epidemiological data from these studies suggest that 40–50% of infections were not identified as infected cases, including asymptomatic infections, mild disease, and under-assessed individuals [48].

In the design and simulation of the model, many of the reviewed studies (36/46 studies) considered interventions, such as hospital isolation, physical distancing, facemasks, and quarantine for disease control. These studies suggested that application of social distancing to the entire population would have a greater impact, and in combination with other interventions such as home or hospital isolation of confirmed cases and home quarantine of contact traced individuals, they have the potential to suppress transmission below the basic reproduction threshold of 1 required to rapidly reduce case incidence [48]. On the other hand, it shows that the effectiveness of any one intervention in isolation is likely to be limited, and that multiple interventions should be combined to have a substantial impact on disease transmission.

To predict the transmission dynamics of COVID-19, reviewed studies used various approaches to estimate the basic and effective reproduction numbers, such as the next-generation matrix and Markov Chain Monte Carlo [7,28]. Many studies estimated the basic reproduction number of COVID-19 to be higher than that of SARS-CoV and MERS-CoV and suggested that the high reproduction number implies that the outbreak may be more serious than what has been reported, given the particular season of increasing social contacts [8].

Of the 46 studies reviewed, six studies [9-14], applied age-structured SEIR, and one study [21] used an age-structured SIR model to investigate COVID-19 transmission. One study [9] suggested that lifting control measures quickly might result in the emergence of new secondary cases. Tuite et al [10] suggested that without a substantial combination of interventions, ICU resources could be overwhelmed, and Davies et al suggested that more clinical cases may be seen in regions with older populations if no effective control measures. Zhang et al [21] found that children aged between 0 and 14 years are less susceptible to COVID-19 infection than adults aged between 15 and 64 years, and that individuals over 65 years are more susceptible to infection. These studies suggested that the risk of acquiring and dying from COVID-19 increases with age and that an increasing number of new cases could be seen in older populations. However, based on the fact that COVID-19 transmission is associated with age, some of these age-structured studies could not quantify the exact vulnerable age groups at high risk.

Table 1: Studies that used compartmental models to assess the COVID-19 transmission. Studies are arranged based on the model structure as follows: 1-7 generalised SIR, 8 age-structured SIR, 9 generalised SIRS, 10-40 generalised SEIR model, and 41-46 age-structured SEIR model.

Study	Model type	Intervention	Ro or Re	Conclusion
[1]	Susceptible-exposed-infected-quarantine-diagnosed-recovered (SEIQDR) compartmental model.	Quaranrine and treatment	R=4.01 main land China and 4.3 in Wuhan	Intervention measures in the early stage of the epidemic are crucial for disease control
[2]	Susceptible-infected-recovered (SIR) compartmental model	Not considered	R0=2.6 (estimated using model parameters)	The COVID-19 outbreak is not well understood
[7]	Susceptible-exposed-infected-recovered (SEIR) compartmental model.	Quarantine	R0=2.68 (estimated using Markov Chain Monte Carlo)	The Outbreak was inevitable because of substantial exportation of pre-symptomatic cases globally
[8]	Susceptible-exposed-infected-recovered (SEIR) model with additional intervention compartments for quarantined and hospitalized individuals.	Quarantine, isolation and treatment	Re=6.47 (estimated using next generation matrix)	High reproduction number suggests that the outbreak may be more serious than what has been reported so far
[9]	Age-structured susceptible-exposed-infected-recovered (SEIR) compartmental model.	Physical distancing	R=2.2 (estimated from literature)	Lifting of interventions quikly could lead to an earlier secondary peak
[10]	Age-structured susceptible-exposed-infectious-recovered (SEIR) compartmental model with additional of intervention compartments	Testing, isolation and quarantine	R0=2.3 (estimated from literature)	Without substantial combination of interventions ICU resources could be overwhelmed
[11]	Age-structured Susceptible-exposed-infected-recovered (SEIR) model with addition of preclinical and subclinical infectious states	Not considered	R0=2.4 (estimated using next generation matrix)	Regions with older populations may see more clinical cases if no effective control measures
[12]	Age-structured susceptible-exposed-infected-recovered (SEIR) model compartmental model.	Social distancing	R=3 (estimated using next generation matrix)	Social distancing together with testing and contact tracing will potentially mitigate virus transmission
[13]	Age-structured susceptible-exposed-infected-recovered (SEIR) model compartmental model.	Universal testing, contact tracing and facemask	R0=2.56 (estimated using next genration matrix) Re=0.73	Combination of interventions while under lockdown would minimize deaths and infections
[14]	Age-structured susceptible-exposed-infected-recovered (SEIR) compartmental model.	Isolation	Not stated	Although transmission in child hood is low, group transmission is possible
[14]	Generalised Susceptible-exposed-infected-recovered (SEIR) model compartmental model.	Quarantine	Not stated	Sustained non-pharmaceutical interventions are required to reduce the outbreak

[16]	Susceptible-infected-recovered (SIR) compartmental model	School closure, lockdown and facemasks	Not estimated	The COVID-19 cases appear to be considerable if no effective interventions implemented.
[17]	Susceptible-infected-recovered (SIR) compartmental model	Quarantine	Re=1.629 (estimated from the model)	Disease predictions using complex models may not be more reliable compared to using a simpler model
[18]	Susceptible-infected-recovered (SIR) compartmental model	Lockdown	R0=2.43 in Feb and 3.10 in March (estimated as using model parameters)	Interventions would help in reducing the R0 especially in countries with low outbreak
[19]	Susceptible-infected-recovered (SIR) compartmental model	None Vs Mass testing	R0=2.2 – 4.5 (estimated using model parameters)	Intervention is unlikely to be effective in for COVID-19 if Ro >2.7 within 49 days
[20]	Susceptible-exposed-infected-recovered (SIR) model with addition of diagnosed-ailing-recognized-threatened-extinct compartments	Testing, contact tracing and social distancing	R0=1.66-2.38 based on interventions. (Estimated using next generation matrix)	Combined mitigation will potentially end the ongoing COVID-19 pandemic
[22]	Susceptible-exposed-infected-recovered (SEIR) compartmental model.	Not considered	R=2.35 before travel restriction and 1.05 after.	Chains of transmission might lead to new outbreaks as more cases arrive in international locations
[23]	Susceptible-exposed-infected-hospitalized-recovered (SEIHR) Compartmental model	Hospital isolation	Re=0.47 (estimated using model parameters)	There is a possibility of future outbreaks if adequate protective measures are not implemented
[24]	Updated their previous SEIR compartmental model	Quarantine, isolation and treatment	Re <1 (estimated using next generation matrix)	The epidemics will continue to grow, and can peak soon depending on implemented interventions
[26]	Susceptible-exposed-infected-recovered-death-cumulative (SEIRDC) compartmental model.	Not considered	Re=4.08 (estimated using model parameters)	COVID-19 poses a major public health threat and it is important to evaluate the effectiveness of stringent measures
[27]	Susceptible-exposed-infected-hospitalized-recovered (SEIHR) compartmental model.	Hospital isolation	R0=4.71, Re=2.08 (estimated using model parameters)	A quick diagnosis that leads to quarantine and other interventions will have a major impact on disease control.
[28]	Susceptible-exposed-infected-recovered (SEIR) compartmental model.	Not considered	R0=3.58 (estimated using next generation matrix)	The transmissibility of COVID-19 was higher than the MERS in the Middle East, similar to SARS, but lower than MERS in Korea
[29]	Susceptible-infected-recovered- susceptible (SIRS) compartmental model	Not considered	R0=2.91 (estimated using model parameters)	Asymptomatic infectious may play an important role in disease transmission
[30]	Susceptible-exposed-infected-recovered (SEIR) compartmental model	Isolation and hospitalization	R=1.5 (estimated using model parameters)	The calculated R0 in the two states proved a reliable summary of the success of interventions
[31]	Susceptible-infected-recovered (SIR)	anti-epidemic measures, such as quarantine	Not stated	Anti-epidemic measures may reduce the number of cases by 40%-49%
[32]	Age-structured susceptible-infected-recovered (SIR) model	Social distancing and school closure	R0=1.5 - 2.5 based on interventions. (estimated using next generation matrix)	Social distancing is sufficient to control COVID-19 during the outbreak
[33]	Genralised susceptible-exposed-infected-recovered (SEIR) compartmental model.	Isolation, quarantine, and treatment	Not stated	Governments could control disease transmission by applying the proposed interventions
[34]	Susceptible-exposed-infected-recovered (SEIR) compartmental model.	Wuhan travel ban	R0=0.04 - 3.15 based on interventions. (estimated using model parameters	Implementation of interventions associated with reductions in case incidence
[35]	Generalised Susceptible-exposed-infected-recovered (SEIR) model compartmental model.	Quarantine	R0=1.5 optimistic and 4 Pessimistic scenario	Quarantine of symptomatics may have impact on disease outbreak
[36]	Susceptible-exposed-infected-recovered (SEIR) model compartmental model.	Isolation, social distancing, quarantine and travel restriction	R0=5.3 (estimated using model parameters)	Mathematical modeling can provide decision guidelines for disease control
[37]	Susceptible-exposed-infected-recovered (SEIR) model compartmental model.	Surveillance, contact tracing, quarantine and social distancing	R0=5.7 (derived by integrating uncertainties in parameter values)	Strong mitigations are needed to stop the virus trans-mission

[38]	Generalised susceptible-exposed-infected-recovered (SEIR) model compartmental model.	Quarantine and social distancing	R0=0 (estimated using next generation matrix)	Death rate may be determined by the ratio of infection and recovery rates
[39]	Generalised susceptible-exposed-infected-recovered (SEIR) compartmental model.	Isolation, quarantine and public closure	Computed using next generation matrix but not qantified	Latently infected individuals play an
[40]	Generalised susceptible-exposed-infected-recovered (SEIR) compartmental model.	Quarantine	R0=1 (estimated using next genration matrix)	Reducing the contact is the most effective intervention in achieving disease control
[41]	Generalised susceptible-exposed-infected-recovered (SEIR) compartmental model.	Quarantine, social-distancing, isolation and face-masks	R0=1.95 for New york and 2.07 for entire USA (estimated using next generation matrix)	COVID-19 can be controlled by interventions, such as social-distancing and facemask
[42]	Generalised susceptible-exposed-infected-recovered (SEIR) compartmental model.	Facemask and hand-washing	R0=4.28 (estimated using model parameters)	Protection measures, such as facemasks and hand-washing control the COVID-19 pandemic
[43]	Susceptible-exposed-infected-recovered (SEIR) compartmental model.	Not stated	R0=2.5 under optimistic and 7 under pessimistic	Preventing the rapid spread of COVID-19 necessitates intervention measures
[44]	Generalised susceptible-exposed-infected-recovered (SEIR) compartmental model.	Quarantine and hospital isolation	R=3.6 (estimated using next generation matrix)	The plan for emergency measures should be supported for disease control
[45]	Generalised susceptible-exposed-infected-recovered (SEIR) compartmental model.	Facemask	Computed but not quantified	Face-masks should be used in conjunction with other non-pharmaceutical practices
[46]	Susceptible-exposed-infected-recovered (SEIR) compartmental model.	Not considered	R0=2.8 (estimated using next generation matrix)	The model predicted and highlighted understanding the trend of the COVID-19 outbreak.
[47]	Susceptible-exposed-infected-recovered (SEIR) model with addition of insusceptible, quarantined and death compartments	Quarantine	R0 <1 (estimated using model parameters)	The epidemics in Beijing and Shanghai will end soon, while for most part of China, the success of anti-epidemic may take long time.
[48]	Susceptible-exposed-infected-recovered (SEIR) with addition of intervention compatments	Quarantine and isolation	R0=2.4 (assumed)	Multiple interventions should be combined to have a substantial impact on transmission.
[49]	Susceptible-exposed-infected-recovered (SEIR) with addition of quarantined and hospitalized compartments	Quarantine and isolation	R0=5.3167 (estimated using next generation matrix)	Deterministic dynamical model was suitable to examine the interaction of the disease progression.
[50]	Susceptible-exposed-infected-recovered (SEIR) compartmental model	Not considered	R0=4.25 (estimated using next generation matrix)	COVID 19 would remain endemic, which necessitates long-term disease prevention and Intervention programs
[51]	Susceptible-exposed-infected-recovered (SEIR) compartmental model	Not considered	R0=2.6 (estimated using model parameters)	Reducing the risk of outbreaks is a further reduction in the importation number either by entry screening or travel restrictions
[52]	Susceptible-exposed-infected-recovered (SEIR) model with addition of hospitalized and fatality compartments	Hospital isolation	R=0.945 (estimated using next generation matrix)	The basic reprodction number suggests that COVID-19 transmission in Wuhan can be controlled

Author Statements

Competing Interests

The authors declare no competing interests.

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