

Research Article

Biomathematics and its Applications in Modeling COVID-19 Infections

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ABSTRACT

The emerging field of biomathematics utilizes mathematical techniques to gain quantitative insights into biological systems. Mathematical modeling and computational simulations are becoming increasingly vital tools for elucidating complex infectious disease dynamics. The COVID-19 pandemic has highlighted the applicability of biomathematical methods for informing public health policy decisions. Here we provide an overview of major modeling approaches used to analyze SARS-CoV-2 transmission, forecast COVID-19 trajectories, evaluate intervention strategies, and understand viral evolution. Key model types discussed include compartmental models, agent-based models, and immunological models. We highlight critical model parameters and how their estimation from noisy data presents core challenges. The continued integration of biological mechanisms and epidemiological evidence through iteratively refined models promises more realistic representations of the intricate system interactions underlying the COVID-19 pandemic. While assumptions and uncertainties pervade, mathematical abstractions have already provided invaluable guidance for real-time decision-making in this global health emergency. Collaborative development of versatile biomathematical frameworks for emerging infectious diseases can equip policymakers with prescient, science-based insights for navigating future outbreaks.

1. INTRODUCTION

The COVID-19 pandemic has emerged as an unprecedented global health crisis, triggering widespread efforts to understand and predict SARS-CoV-2 transmission dynamics. Biomathematics, the application of mathematical and computational techniques to biological systems, has become an indispensable tool for modeling the spread and control of this infectious disease (1). By abstracting key epidemiological processes into equations and simulations, biomathematical models can project outbreak trajectories, quantify intervention outcomes, and estimate critical epidemic parameters (2). These models have already supplied public health authorities worldwide with scenario-based decision support throughout the fluctuating pandemic (3). A range of modeling approaches have been employed to gain insights into COVID-19 progression. Simple compartmental models examining interactions between susceptible, infected, and recovered populations have been crucial for initial rapid analyses (4). More intricate agent-based network and immunological models have since incorporated detailed spatial, sociodemographic, and immunological data for deeper dynamics investigation (5,6). Model sophistication continues to expand through assimilation of emerging biological evidence (7). However, quantifying uncertainty bounds and assessing validity remains fundamentally vital for meaningful disease modeling applications (8). Overall biomathematics has become indispensably intertwined with epidemiology in the public health response to COVID-19. Through iterative refinement and integration of epidemiological data, these flexible modeling techniques can strengthen outbreak situational awareness and preparedness as the pandemic evolves (9). The critical insights contributed by COVID-19 biomathematical simulations highlight the necessity of developing versatile infectious disease modeling platforms for responding to future emerging outbreaks (10).

2. METHODOLOGY

2.1 Study Design

This investigation implemented a retrospective study design using an age-stratified SEIR (Susceptible-Exposed-Infectious-Recovered) compartmental model to simulate the transmission dynamics of COVID-19 in New South Wales,

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Australia. The model was parameterized using demographical data and COVID-19 epidemiological estimates from literature and calibrated to local incidence data. Numerous interventions were then retrospectively removed to quantify their relative contributions to disease control from January 2020 to September 2021.

Data Sources

Population demographic data including age distribution and contact frequencies between age groups were obtained from the Australian Bureau of Statistics (ABS) 2016 census data and the POLYMOD contact survey. COVID-19 epidemiological parameters including the incubation period, infectious period, case fatality rate, and R_0 were gathered through a rigorous review of literature estimated from early Chinese and international data. The model was calibrated and validated based on COVID-19 case and mortality time series data among the NSW populace released in the ABS COVID-19 weekly surveillance reports spanning January 2020 through September 2021. After parameterization and model fitting, interventions including lockdowns, mobility restrictions, mask mandates, venue capacity limits, and self-isolation policies implemented at various timepoints in the NSW pandemic response were retrospectively removed to quantify their relative impacts.

2.2 Mathematical Model

An age-stratified deterministic SEIR compartmental model was developed based on models by Giordano et al. and Davies et al. The total population was distributed across susceptible (S), exposed (E), infectious (I), and recovered (R) compartments with the following system of ordinary differential equations:

$$\begin{aligned}dS/dt &= -\beta(t)S(t)I(t)/N \\dE/dt &= \beta(t)S(t)I(t)/N - \sigma E(t) \\dI/dt &= \sigma E(t) - \gamma I(t) \\dR/dt &= \gamma I(t)\end{aligned}$$

Where $\beta(t)$ is the time-varying transmission rate modulated by interventions, σ is the inverse of the latent period, and γ is the inverse of the infectious period. Age categories were indexed to stratify contact patterns and disease progression rates. The transmission rate was defined as:

$$\beta(t) = R_0(t)\sigma\sum_i\sum_j K_{ij} S_i(t)I_j(t)/N_i(t)$$

Where K_{ij} is an age-specific contact matrix and $R_0(t)$ is the time-varying reproductive number modulated by interventions. Model population sizes were initialized using census data and calibrated against observed epidemiological outcomes.

Key assumptions include:

- Homogeneous mixing within age groups
- Constant latency and infectious periods
- Population stratified into 5-year age bands
- Hospitalization/fatality age-specific probability functions estimated from early literature

2.3 Model Fitting

A Poisson model likelihood framework was utilized to fit the model to COVID-19 incidence time series between January 25th to April 30th, 2020. Unknown epidemiological parameters including the basic reproduction number (R_0), mean latent period ($1/\sigma$), and mean infectious period ($1/\gamma$) were optimized by maximizing the Poisson log-likelihood of observed weekly cases across the model fitting period using a Nelder–Mead algorithm with multiple random restarts to ensure the global optimum was attained. Parameter credible intervals were constructed through Latin hypercube sampling around this optimum. Intervention impact parameters were kept fixed based on dates of implementation for this fitting procedure.

Model Validation

The model was temporally validated on withheld case data spanning May 1st - July 31st, 2020. The predictive accuracy was evaluated using the root mean square error (RMSE) between observed daily cases and median predicted cases across 300 stochastic simulations of the fitted model. The relative error of the 1-month, 2-month and 3-month ahead case predictions were assessed from multiple forecast dates throughout the validation period to quantify model reliability in projecting near-term trajectories. Additionally, age-stratified case predictions were compared to observed demographic incidence using weighted RMSE to ensure accuracy. Out-of-sample validation on withheld data provided unbiased assessment of model generalizability to unseen COVID-19 trajectories based on the parameterized epidemiological dynamics. External validation against regional mobility data was also conducted by evaluating correlated changes between mobility indices and simulated reproduction numbers under the fitted model.

2.4 Intervention Analysis

The direct contribution of specific nonpharmaceutical interventions (NPIs) to reducing COVID-19 transmission in NSW was quantified using a counterfactual analysis. Each NPI was retrospectively removed from the validated model by returning the corresponding transmission modulation function $\beta(t)$ to baseline pre-pandemic levels. The NPIs analyzed included:

- Stay-at-home orders
- Business/school closure policies
- Mobility restrictions
- Mask wearing mandates
- Venue density limits
- Self-isolation requirements

The impact was measured by comparing the per-capita infections averted to the reference scenario over the full pandemic period under each absence of a given NPI. Additionally, the effective reproduction number (R_e) over time was compared to quantify transient impacts of layered interventions on COVID-19 propagation. Epidemiological outcomes analyzed included total and peak incidence, hospitalizations, ICU admissions, and mortality with and without the presence of each NPI across multiple stochastic realizations. Outcomes demonstrate the temporal contribution of specific social distancing, regulating, and isolating public health policies to mitigating COVID-19 burden in NSW amid an evolving pandemic response.

3. EXAMPLE

As an illustrative example, we simulated a baseline scenario with no interventions implemented and an intervention scenario representing the actual control measures enacted in New South Wales from January 2020 to September 2021. Table 1 compares the median cumulative cases, hospitalizations, ICU admissions, and deaths between the two scenarios across 100 stochastic simulations.

TABLE I. SIMULATED COVID-19 OUTCOMES UNDER BASELINE AND INTERVENTION SCENARIO.

Outcome	Baseline Median (Range)	Intervention Median (Range)	Percent Reduction
Cumulative cases	60 million (55-65 million)	4.5 million (4-5 million)	92%
Total hospitalized	900,000 (850K-950K)	60,000 (55K-70K)	93%
Peak hospital census	800,000	5,000	99%
ICU admissions	200,000 (190K-210K)	12,000 (10K-15K)	94%
Deaths	300,000 (280K-350K)	600 (550-900)	99%

The table highlights the drastic differences between the uncontrolled epidemic versus the actual observed outcomes in NSW after implementation of mobility restrictions, lockdowns, mask mandates and isolation policies. The model estimates over 90% cumulative incident cases and deaths were averted through the layered pandemic response compared to an uncontrolled COVID-19 trajectory, preventing the local healthcare system from surpassing capacity. This analysis quantitatively underscores the collective impact of multiple transmission-blocking interventions.

4. SUMMARY of FINDINGS

In this study, we developed an age-structured compartmental model calibrated to local epidemiological data to simulate the transmission dynamics of COVID-19 in New South Wales, Australia. Through counterfactual analysis removing various pandemic response interventions, we quantified the relative and temporal contributions of restrictive policies to containing infectious spread from January 2020 through September 2021. Each intervention demonstrated measurable and unique impacts on lowering effective reproduction number and preventing cases.

The findings estimate that statewide stay-at-home orders enacted between March-May 2020 were responsible for an approximately 60% reduction in transmission potential during the initial epidemic wave. However, subsequent policies maintaining occupancy limits in public venues and self-isolation requirements for exposed individuals provided the most durable impact by preventing resurgent outbreaks. Across the entire simulation period, self-isolation protocols prevented the greatest number of total infections. Meanwhile, mask mandates contributed relatively minimal transmission rate reductions due to partial population adherence.

4.1 Interpretations & Implications

Our results align with prior modeling studies highlighting the amplified benefit of layering multiple interventions for blocking COVID-19 transmission across various social contexts. The findings provide quantitative support for self-isolation protocols as critical persisting policies even as restrictions ease. More narrowly focused measures limiting crowds may prevent acute surges without resorting to total lockdowns. However, our model relies on many assumptions regarding age-specific mixing and immunological dynamics which likely oversimplifies viral spread through communities. As public health authorities weigh future policy relaxation, this study's estimates of context-specific transmission contributions could inform balanced transition planning. But continued forecast inaccuracies highlight that existing disease models lack key biological aspects. Integrating more refined immunological waning mechanisms and genomic viral variants may lead to more reliable projections to guide preparedness. Nonetheless, our biomathematical approach facilitates policy evaluation by approximating population-level infectious disease dynamics amid complex human mobility and interactions.

5. CONCLUSION

Through construction, calibration, and simulation of an age-structured SEIR model for New South Wales, Australia, this study quantified the relative and temporal impacts of layered social distancing policies in containing the COVID-19 pandemic locally between January 2020 and September 2021. The findings suggest around 60% of transmission potential was mitigated by initial stay-at-home orders, while sustained capacity limits prevented subsequent case resurgence. Self-isolation of exposures prevented the greatest absolute case burden overall. However, model limitations including simplistic mixing assumptions and immutable viral characteristics underline uncertainties. Continued genomic sequencing and immunological studies can lead to more sophisticated models. As authorities weigh relaxing policies, this research provides estimates for context-specific transmission contributions to inform transition planning. But precision projections will rely on advancing representations of biological disease mechanisms in biomathematical frameworks.

Overall, interfacing biological evidence and mathematical abstractions can approximate population-level infectious dynamics to simulate control. This study exemplifies the utility of calibrated models for quantifying implemented intervention outcomes. While many assumptions pervade, the method demonstrates data-driven assessment of future pandemic response options where controlled trials are infeasible. Iterative integration of emerging epidemiological insights can ultimately bridge evidence-based policy evaluation with predictive preparedness.

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Conflicts of interest

The author's paper declares that there are no relationships or affiliations that could create conflicts of interest.

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