

Modeling COVID-19 in South Africa using a Vaccine Structured Model with Time-Varying Transmission Rates

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Abstract: Since the beginning of COVID-19 in December 2019, the whole world has been under a myriad of public health challenges. South Africa was one of the affected countries in this predicament. Due to the unique characteristics of this virus, including its evolution into new strains, popularly known as variants of concern (VOCs), COVID-19 posed significant challenges to governmental containment efforts. These efforts consisted of mainly non-pharmaceutical interventions (NPIs) and vaccination which essentially must be quantified to inform future pandemic responses. This research uses a stratified compartmental epidemiological model consisting of eight classes that divide the population into vaccinated and non-vaccinated individuals. With the help of ordinary differential equations (ODEs) and time-varying transition rates, the COVID-19 outbreak in South Africa is simulated. By examining data from the post-vaccination phase to the end of the state of emergency, the changes in the transmission rate to government policies and vaccination drives is correlated. Simulations demonstrate that the national vaccination campaign significantly alleviated the impact of Delta and Omicron variants. Hypothetical scenarios show that doubling the vaccination rate would have further reduced the disease burden. The baseline effective reproduction numbers at the four interval starts were 1.2654, 0.74376, 1.4761 and 0.56624, respectively. Compared with the baseline total of 2.1373 million predicted cases, the no-vaccination scenario produced 6.3375 million predicted cases, whereas enhanced vaccination reduced predicted cases to 1.1024 million. This study substantiates that NPIs and vaccination were critical interventions that significantly reduced the spread of COVID-19 and its variants in South Africa.

Keywords: Variants of Concern; Time-varying Transmission Rate; Stratified Compartmental Model; Reproduction Rate; Ordinary Differential Equations

1 Introduction

1.1 Overview

Coronavirus disease 2019 (COVID-19) emerged in December 2019 in China and was declared a pandemic by the World Health Organization (WHO) on March 11, 2020 [1]. Following the declaration, countries in all regions of the world rose to the occasion by initiating various containment efforts such as lockdowns, social distancing, masking and hand-cleaning, which are called non-pharmaceutical interventions (NPIs) [2]. These initiatives were instrumental in controlling the spread of the disease while awaiting the development of a safe and effective vaccine [3].

The impact of the pandemic presented a serious challenge to the progress of Africa toward the 2030 Agenda for Sustainable Development, extending far beyond a public health emergency. The United Nations recorded that socio-economic issues across the continent were sparked, with many years of progress halting or reversing [4]. To manage the pandemic, important targets in the education sector were neglected [5]. Employment rates reduced and infrastructure development stopped [5]. Reports from 2020 indicated that about 26 to 40 million people fell into extreme poverty [5,6]. Sustainable Development Goals (SDGs) such as 'No Poverty', which falls under SDG 1, were severely undermined [6]. Furthermore, economic activity was disrupted resulting in a decline in gross domestic product (GDP) per capita [7]. Progress towards 'Decent Work and Economic Progress' which is SDG 8, was hindered [7,6]. Although studies imply that all SDGs were affected, SDG 2, SDG4 and SDG 8 analogous for 'Zero Hunger', 'Quality Education' and 'Decent Work and Economic Growth' respectively, were the most impacted [8]. These observations highlight the

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importance of COVID-19 containment in ensuring that the development trajectory of Africa was sustained. Key targets like ‘Good Health and Well Being’ which reflects SDG 3 could only be achieved by building resilient systems that result from studying effective public health systems [8].

Due to the urgent nature of this worldwide crisis, scientists from every corner of the globe quickly developed different vaccines. mRNA-based vaccines were developed by pharmaceutical companies like Pfizer-BioNTech [9] and Moderna [10] while viral-vector vaccines were produced by companies such as Johnson & Johnson and AstraZeneca [11]. The clinical trials demonstrated high efficacy in preventing severe disease, hospitalization and death [9,10,12]. Furthermore, the vaccines were reported to reduce susceptibility and infectiousness [12]. What followed was a roll-out of vaccination campaigns from the beginning of 2021. In addition to the already implemented NPIs, vaccination played an important and complementary role in mitigating the impact of the virus. Consequently, a pathway was illuminated which provided a public life and economic activity restoration, hence socio-economic development goals which were on pause resumed progress.

Despite all these, COVID-19 had a complicated epidemiological profile. The evolutionary dynamics of the virus led to the emergence of new variants such as Alpha, Beta, Delta and Omicron [13]. The Omicron variant manifested greater transmissibility, immune evasion potential and increased disease severity. Such variants like the Omicron were referred to as variants of concern (VOCs) [13,14]. Because of these VOCs, COVID-19 produced successive wave-like infection numbers [15]. Additionally, studies showed that patients exhibited waning immunity from both vaccinated and naturally acquired immunity, hence the potential for reinfection remained probable [16]. The need for ongoing surveillance and adaptive public health strategies was therefore still very necessary. This study is based within this context of evolving viral characteristics, vaccination programmes and public health policy. The aim of this study is to analyze the transmission dynamics of COVID-19 in South Africa during the vaccination era by developing a mathematical model that takes into consideration the aforementioned factors.

1.2 Literature review

Compartmental models, deterministic ones in particular, are an essential field of infectious disease epidemiology [17]. Through such, understanding the dynamics of pathogen spread in a population as well as predictive analytics of the same is made possible. Based on the susceptible-infectious-recovered (SIR) framework structure, these models partition a population into distinct classes and use a system of ordinary differential equations (ODEs) to describe the rate of movement between them [18]. During the COVID-19 pandemic their usefulness became more visible as they were used to assess the potential impact of NPIs and vaccination campaigns, predict healthcare demand, evaluate control strategies, to mention but a few [19].

The highest burden of COVID-19 in Africa was experienced by South Africa, this was reported by numerous studies including Edholm et al. [3]. Having contributed significantly to the cumulative cases of the continent, it became a focal point of numerous modeling studies. Modeling experts like Musa et al. [20,21] focused on estimating initial growth rate, basic reproduction numbers and understanding continental heterogeneity. Taboe et al. [22] explored the impact of various response strategies. These early research studies provided initial information on how the pandemic might unfold in various African settings.

For the particular case of South Africa, initial mathematical models explored the initial wave and quantified NPI impacts like social distancing [23]. Early transmission dynamics and preliminary scenarios of vaccine efficacy were considered by researchers such as Mukandavire et al. [24]. More recently, Edholm et al. [3] introduced a sophisticated methodology for the Gauteng province, where they used a data-driven strategy to identify inflection points in case data and correlated them with policy changes. Through these, modeling transmission and testing rates as time-varying parameters was made possible, hence enabling them to effectively demonstrate how to quantitatively link government interventions with changes in the trajectory of the epidemic for a specific and densely populated region.

Beyond transmission modeling, an important line of research has focused on capturing the effects of vaccination by explicitly modeling vaccine efficacy within compartmental structures. In this case multiple vaccinated classes are incorporated thereby allowing the representation of different levels of protection such as partial immunity, waning immunity and natural immunity [25]. It is through these models that researchers were able to evaluate different vaccination strategies and their impact in how the epidemic transpired [26]. In the same way researchers were able to quantify the potential benefits of booster campaigns [26]. Additionally, models that take the vaccine status of individuals into consideration have been used in assessing how efficacy differs against variants of concerns in their variety, through

these evidence that informs policy was acquired [27].

Despite the fact that these studies laid an important foundation, a research gap remains and it is especially apparent towards the later stages of the pandemic in South Africa. While methodologically robust, the analysis by Edhold et al. [3] is geographically limited to the Gauteng province. A national-level analysis is necessary to understand the overall dynamics of the country, which result from the interplay of its nine distinct provinces. Secondly, previous models were largely parameterized on data from the initial waves, a period characterized primarily by NPIs and the circulation of earlier variants [3]. The epidemiological landscape shifted fundamentally with the initiation of mass vaccination in February 2021 and the subsequent arrival of the highly transmissible Delta and Omicron variants, which introduced complex dynamics of waning immunity and reinfection [28,29].

The aim of this study is to address this gap by taking the entire nation of South Africa into consideration. This will be fulfilled by: (1) applying the analysis to the data that spans the whole of South Africa; (2) using a vaccine-structured model that also covers waning immunity and infection; (3) and looking at the period from February 2021 onward in which the Delta and Omicron waves were in effect. In doing so, this work provides novel insights into the management of a pandemic in a population where NPIs, vaccination and viral evolution are significant concurrent factors. The rest of the paper is organized as follows: Section 2 describes the materials and methods, whereas the results are given in Section 3. Section 4 presents a discussion of the results. The conclusion of the study is discussed in Section 5.

2 Materials and Methods

2.1 Data Acquisition and Processing

The data used in this study were obtained from the Coronavirus COVID-19 (2019-nCoV) Data Repository for South Africa, a publicly available dataset maintained by the Data Science for Social Impact (DSFSI) research group at the University of Pretoria [30]. The national daily time series of cumulative COVID-19 cases from March 5, 2020, to April 22, 2022 was used. This was during the time of active vaccination campaigns [28]. The rise of the Delta and Omicron variants also occurred during this period [31,29]. To align with the reporting cycles and smooth out daily fluctuations, daily cumulative case data were aggregated into a weekly time series. This was achieved by selecting the last recorded cumulative value for each week. Any missing data points within the resulting weekly series were addressed using linear interpolation via the 'na.approx' function in R. These processed weekly data, shown in Figure 1, formed the basis for both the parameter estimation of the model and the identification of significant changes in the trajectory of the epidemic. Thus, the calibration data stream consisted of national weekly cumulative confirmed cases only. Hospitalization and death time series were not used for fitting; these outcomes are discussed only qualitatively because the model does not include explicit hospitalization compartments.

Following the approach of change-point analysis, a smoothing spline was fitted to the weekly cumulative case data to obtain a twice-differentiable approximation of the epidemic trajectory. The spline was obtained by minimizing a penalized least-squares criterion in which the smoothing parameter λ controls the trade-off between fidelity to the observed data and the roughness of the fitted function. Using the `smooth.spline()` algorithm with 16 effective degrees of freedom yielded an estimated smoothing parameter of $\lambda = 3.35 \times 10^{-5}$. The relatively small value of λ reflects a preference for preserving the underlying epidemic structure while applying sufficient regularization to suppress noise-induced fluctuations. Inflection points were then identified as locations where the second derivative of the fitted spline changed sign, indicating transitions between periods of epidemic acceleration and deceleration. This process yielded the specific change-point dates used to define the time intervals for the time-varying parameter estimation (shown by red dots in Figure 1).

The analysis in this study focused on the period following the beginning of the national vaccination program of South Africa. To identify the distinct epidemiological phases caused by new variants and changing public health responses, four time intervals for the model were defined, starting on March 28, 2021. These inflection points corresponds to the peaks and troughs of the epidemic waves, as shown in the weekly new cases data in Figure 2. The time-varying parameters of the model, particularly the transmission coefficients ($\beta_i(t)$), were held constant within each interval but allowed to change between them.

The four intervals are defined as follows:

Interval 1: The Delta Wave Ascent (March 28, 2021 - July 10, 2021) This period represents the emergence and strong increase of the third wave, which was driven by the highly transmissible Delta variant [32]. The South African government responded to the increasing number of cases by moving the country to adjusted Alert Level 2 on May 31,

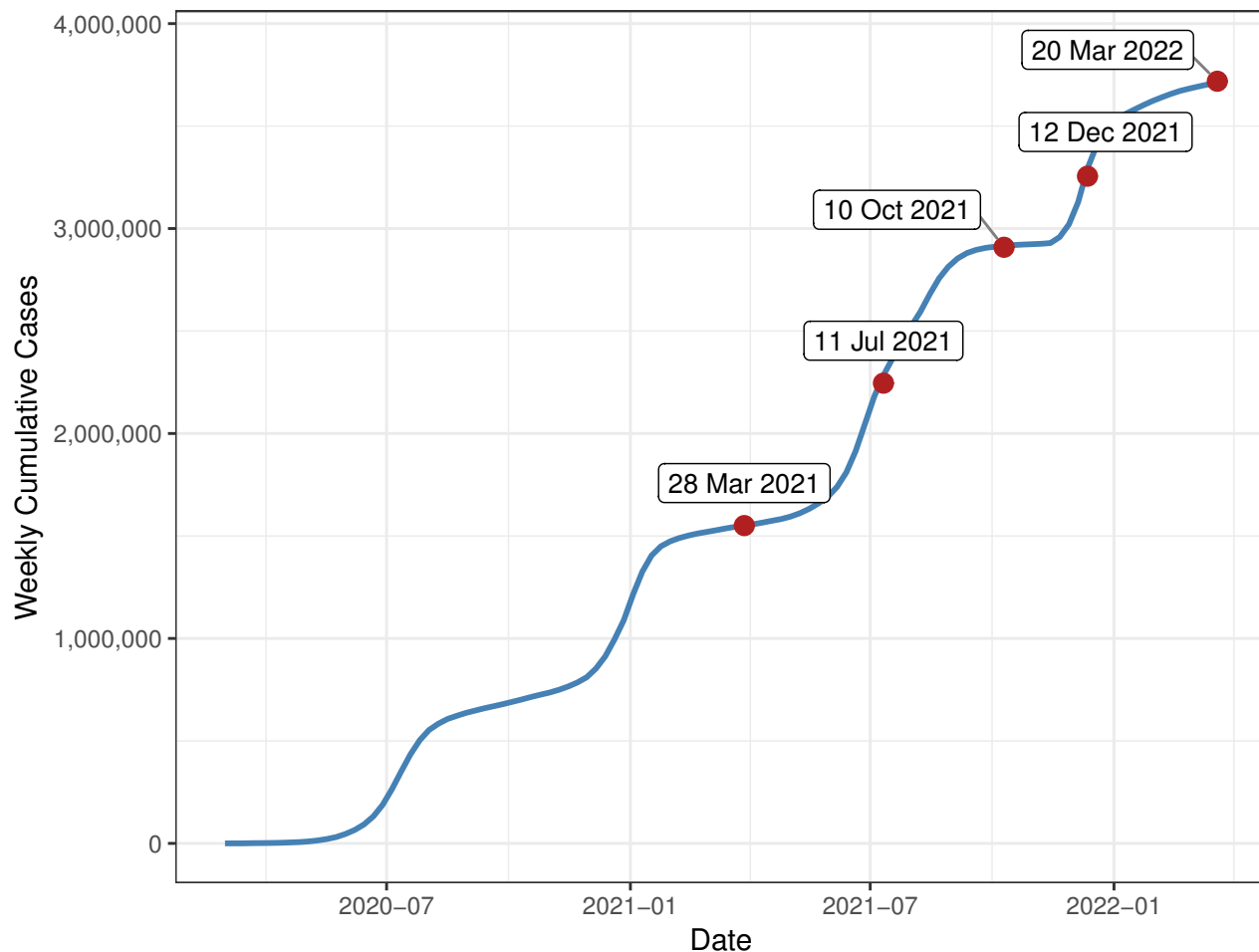


Fig. 1: Weekly Cumulative COVID-19 Cases with Inflection Points - South Africa

2021, followed by Level 3 on June 15 and a restrictive Level 4 on June 28 [31]. The interval concludes at the empirically-determined inflection point of July 11, 2021, which marks the peak acceleration of this wave.

Interval 2: The Delta Wave Decline (July 11, 2021 - October 9, 2021) Characterized by a sustained decline in infections following the peak of the Delta wave, this interval saw a corresponding easing of NPIs. The country was lowered to an adjusted Alert Level 3 on July 25, 2021, and further to Level 2 on September 13 [29]. This phase of decreasing transmission and relaxed public health measures concludes at the inflection point of October 10, 2021, where the rate of decline began to stabilize at a low level.

Interval 3: The Omicron Wave Explosion (October 10, 2021 - December 11, 2021) This interval began during a period of minimal restrictions under Alert Level 1. The detection and quick spread of the Omicron variant was the defining event of this period which was first reported to the WHO by South Africa on November 24, 2021 [33]. Due to the extreme transmissibility of this variant, the fourth wave was happened quickly and became very large. The inflection point on December 12, 2021, precisely identifies the point of maximum rise of this wave, where the cumulative case curve became nearly vertical.

Interval 4: Omicron Decline and Normalization (December 12, 2021 - March 20, 2022) Following this peak that has never been experienced before, this final interval covers the sharp decline of the Omicron wave and the subsequent transition toward the normalization of policies. This period saw a continued decrease in cases leading to the final easing of restrictions on March 23, 2022. The official termination of the National State of Disaster happened on April 4, 2022 [34]. This interval represents a new phase of the pandemic characterized by a lot of people having acquired immunity and the management of COVID-19 without emergency measures.

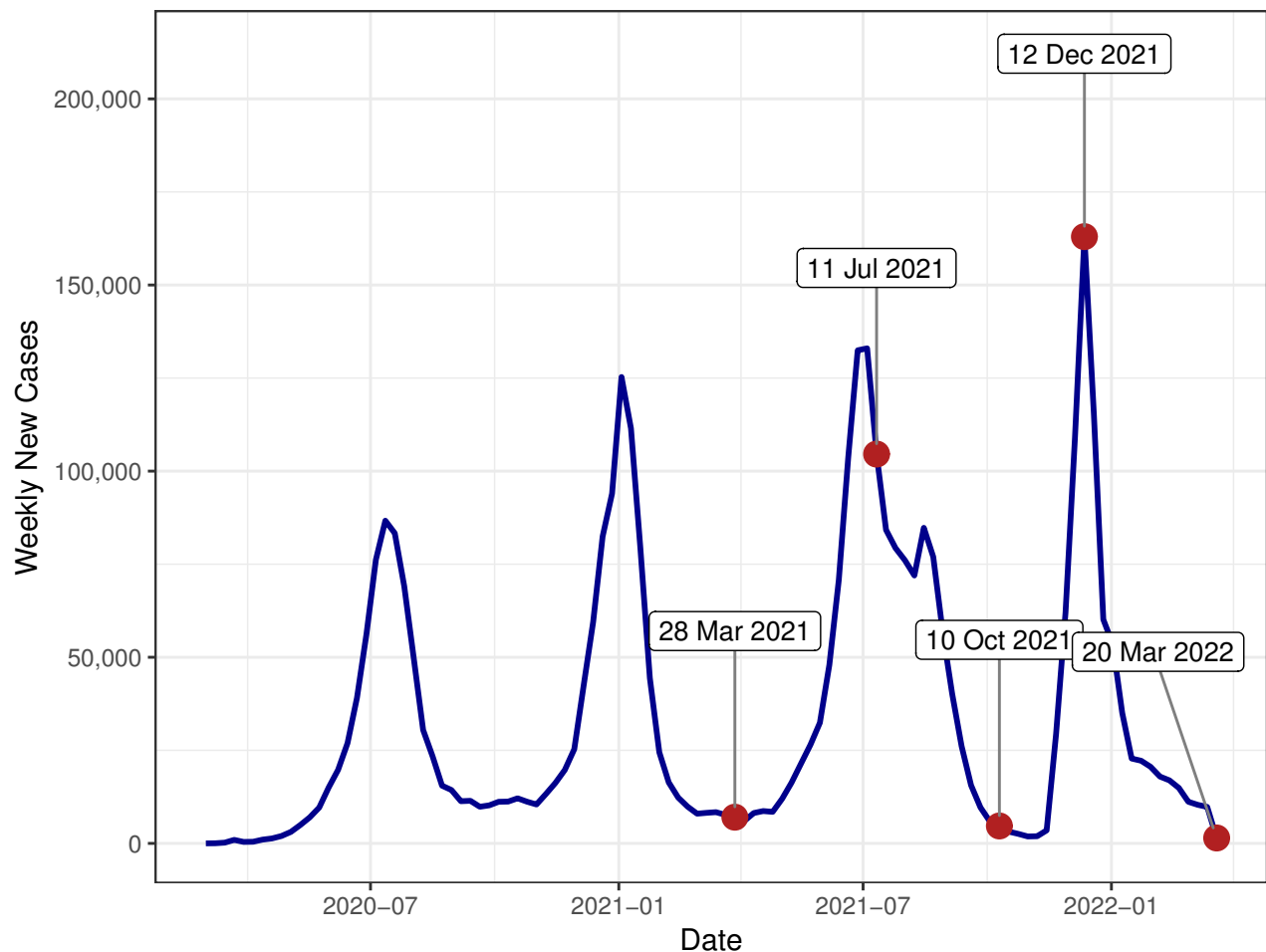


Fig. 2: Weekly New COVID-19 Cases with Inflection Points - South Africa

2.2 Model Formulation

To investigate the transmission dynamics of COVID-19 in South Africa during the vaccination era, a deterministic compartmental model was developed. The model stratifies the total population, $N(t)$, into eight mutually exclusive compartments based on vaccination and disease status. The compartments represent non-vaccinated susceptible (S_n), vaccinated susceptible (S_v), non-vaccinated exposed (E_n), vaccinated exposed (E_v), non-vaccinated infectious (I_n), vaccinated infectious (I_v), non-vaccinated recovered (R_n) and vaccinated recovered (R_v) individuals.

The total population is subdivided into two distinct groups: the non-vaccinated population, $N_n(t)$ and the vaccinated population, $N_v(t)$, such that $N(t) = N_n(t) + N_v(t)$. These sub-populations are defined as the sum of their respective compartments:

$$N_n(t) = S_n(t) + E_n(t) + I_n(t) + R_n(t) \quad \text{and} \quad N_v(t) = S_v(t) + E_v(t) + I_v(t) + R_v(t). \quad (1)$$

The model assumes no vertical transmission; therefore, all new births enter the non-vaccinated susceptible class at a constant recruitment rate, κ . Non-vaccinated individuals are vaccinated at a rate of ϕ . It is assumed that immunity is not permanent; vaccine-derived immunity wanes at rates ω_{sv} and ω_{rv} , while natural immunity wanes at a rate ω_m . This inclusion is based on extensive evidence documenting declining antibody levels following both vaccination and natural infection [35].

The vaccinated compartments represent individuals who have moved into the vaccinated stratum through the national campaign and are modeled as an aggregate vaccinated group. The model does not distinguish vaccine product, first dose, second dose or booster dose; instead, the average protective effect of vaccination is captured through reduced susceptibility and reduced infectiousness in the scaling factors below. Waning immunity returns individuals from vaccinated or recovered states to susceptible states, allowing reinfection in the vaccination era. Regarding mortality, the

model incorporates a natural death rate, μ , applicable to all classes [36]. Additionally, acknowledging that vaccination reduces disease severity [37], the COVID-19 induced mortality rates between the non-vaccinated (δ_n) and vaccinated (δ_v) infectious populations is differentiated. Taking these birth and death rates into account, the rate of change of the total population is obtained by summing the differential equations in System (3):

$$\frac{dN(t)}{dt} = \kappa - \mu N(t) - \delta_n I_n(t) - \delta_v I_v(t). \quad (2)$$

The transmission pathways and rates between compartments are visually illustrated in Figure 3 and all variables and parameters are detailed in Table 1.

Table 1: Variables and Parameters in the Epidemiological Model

Notation	Description
<i>State Variables</i>	
S_n, S_v	Susceptible individuals (non-vaccinated, vaccinated)
E_n, E_v	Exposed individuals (non-vaccinated, vaccinated)
I_n, I_v	Infectious individuals (non-vaccinated, vaccinated)
R_n, R_v	Recovered individuals (non-vaccinated, vaccinated)
<i>Parameters</i>	
κ	Recruitment rate into S_n (births)
μ	Natural death rate
ϕ	Vaccination rate
σ_n, σ_v	Progression rate from exposed to infectious
γ_n, γ_v	Recovery rates for infectious (I_n, I_v)
δ_n, δ_v	COVID-19 induced death rates for infectious (I_n, I_v)
$\omega_{sv}, \omega_{rn}, \omega_{rv}$	Rates of waning immunity
$\beta_i(t)$	Time-varying baseline transmission rate
c_{nv}, c_{vv}, c_{vn}	Scaling factors for transmission involving vaccinated individuals
λ_n, λ_v	Forces of infection

The main modeling assumptions are as follows: mixing is homogeneous at the national level; transmission is frequency-dependent; demographic recruitment balances natural mortality in the absence of disease; vaccination moves individuals between vaccination strata at the average observed rollout rate; and confirmed cases are used as a proxy for infection burden. Under-reporting, reporting delays, regional heterogeneity and age-specific contact patterns are not modeled explicitly; their aggregate effects are absorbed partly through the fitted transmission rates.

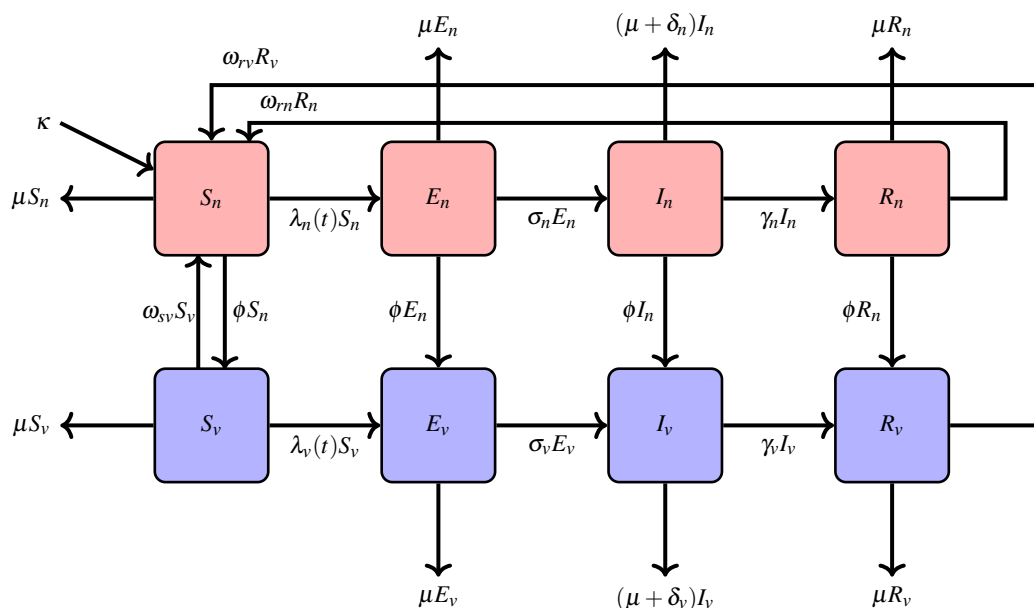


Fig. 3: Schematic Diagram of the Time-varying Epidemiological Model

The resulting system of Ordinary Differential Equations describing these dynamics is given by:

$$\frac{dS_n(t)}{dt} = \kappa + \omega_{sv}S_v + \omega_{rn}R_n + \omega_{rv}R_v - (\lambda_n(t) + \phi + \mu)S_n, \quad (3a)$$

$$\frac{dS_v(t)}{dt} = \phi S_n - (\lambda_v(t) + \omega_{sv} + \mu)S_v, \quad (3b)$$

$$\frac{dE_n(t)}{dt} = \lambda_n(t)S_n - (\sigma_n + \phi + \mu)E_n, \quad (3c)$$

$$\frac{dE_v(t)}{dt} = \lambda_v(t)S_v - (\sigma_v + \mu)E_v + \phi E_n, \quad (3d)$$

$$\frac{dI_n(t)}{dt} = \sigma_n E_n - (\gamma_n + \delta_n + \phi + \mu)I_n, \quad (3e)$$

$$\frac{dI_v(t)}{dt} = \sigma_v E_v - (\gamma_v + \delta_v + \mu)I_v + \phi I_n, \quad (3f)$$

$$\frac{dR_n(t)}{dt} = \gamma_n I_n - (\omega_{rn} + \phi + \mu)R_n, \quad (3g)$$

$$\frac{dR_v(t)}{dt} = \gamma_v I_v + \phi R_n - (\omega_{rv} + \mu)R_v. \quad (3h)$$

2.2.1 Forces of Infection

The transmission dynamics are driven by the forces of infection, $\lambda_n(t)$ and $\lambda_v(t)$, which quantify the instantaneous risk of infection for non-vaccinated and vaccinated susceptible individuals, respectively. Following the framework of frequency-dependent transmission [18,38], these forces are defined as:

$$\lambda_n(t) = \frac{\beta_i(t)}{N(t)} (I_n(t) + c_{nv}I_v(t)), \quad (4)$$

$$\lambda_v(t) = \frac{\beta_i(t)}{N(t)} (c_{vn}I_n(t) + c_{vv}I_v(t)). \quad (5)$$

Here, $\beta_i(t)$ represents the time-varying transmission rate, and $N(t)$ is the total active population. The coefficients c_{nv} , c_{vn} and c_{vv} are scaling factors that modify the baseline transmission probability based on the vaccination status of the interacting pair.

Time-Varying Transmission Rate $\beta_i(t)$

To capture the non-monotonic wave-like dynamics of the epidemic, the transmission rate $\beta_i(t)$ is modeled as a piecewise constant function (a step function). This approach aligns with the change point analysis employed by Edholm et al. [3], which demonstrated that spreading rates change discretely in response to specific government interventions. Similarly, Piccolomini and Zama [39] utilized time-dependent infection rate functions to construct a forced compartmental model (fSEIRD) that accurately fits multi-wave epidemic data.

A set of five distinct time points, as presented in Figure 2 are defined, denoted by $\tau_1 < \tau_2 < \tau_3 < \tau_4 < \tau_5$, which partition the simulation timeline into 4 disjoint epidemiological intervals T_i . The intervals are defined as $T_i = [\tau_i, \tau_{i+1})$ for $i = 1, 2, 3, 4$. The transmission rate function is given by:

$$\beta_i(t) = \sum_{i=1}^4 \beta_i \cdot \chi_{T_i}(t), \quad (6)$$

where β_i is the transmission rate during interval T_i , and $\chi_{T_i}(t)$ is the indicator function defined as:

$$\chi_{T_i}(t) = \begin{cases} 1 & \text{if } t \in [\tau_i, \tau_{i+1}), \\ 0 & \text{otherwise.} \end{cases}$$

In this piece-wise function, τ_1 represents the start of the simulation (initial time), τ_2, τ_3, τ_4 represent intermediate change points triggered by external factors (e.g., policy implementation, variant emergence) and τ_5 represents the end of the simulation horizon. This structure allows the model to switch between 4 distinct transmission periods [39].

Mathematically, NPIs and variant-driven changes enter the model through shifts in the interval-specific transmission coefficient rather than through separate policy-state variables. A reduction in social contact, masking or mobility is represented by a lower fitted transmission coefficient for the relevant interval, whereas relaxation of restrictions or circulation of a more transmissible variant is represented by a higher fitted transmission coefficient. This choice preserves a parsimonious ODE system while still allowing observed policy and variant events to alter the force of infection.

Scaling Factors and Vaccine Efficacy

The scaling factors c_{nv} , c_{vn} and c_{vv} provide a link between clinical vaccine efficacy and population-level transmission. They are defined as follows [40]:

1. Susceptibility Reduction (c_{vn}): Describes the interaction $I_n \rightarrow S_v$. The recipient is vaccinated, so the transmission probability is reduced by:

$$c_{vn} \in [0, 1]$$

2. Infectiousness Reduction (c_{nv}): Describes the interaction $I_v \rightarrow S_n$. The donor is vaccinated, so the transmission probability is reduced by (e.g., due to lower viral load):

$$c_{nv} \in [0, 1]$$

3. Combined Reduction (c_{vv}): Describes the interaction $I_v \rightarrow S_v$. Both donor and recipient vaccination effects apply:

$$c_{vv} \in [0, 1]$$

This parameterization allows the model to distinguish between vaccines that prevent infection and those that primarily prevent forward transmission.

2.3 Reproduction Number

To assess the epidemic potential in each time interval, the time-varying reproduction number is derived, $\mathcal{R}_i(t)$, for each interval T_i using the next-generation matrix (NGM) method [17]. The value of $\mathcal{R}_i(t)$ represents the average number of new secondary infections generated by a single infectious individual at a specific point in time [17,3]. The derivation is performed at the disease-free equilibrium (DFE), $Y^0 = (S_n^*, S_v^*, 0, 0, 0, 0, 0, 0)$.

The infected compartments are ordered as a vector $\mathbf{X} = (E_n, E_v, I_n, I_v)'$. The matrices for new infections, $\mathcal{F}_i(t)$, and for transitions between infected compartments, $\mathcal{V}$, are given by:

$$\mathcal{F}_i(t) = \begin{pmatrix} \lambda_n(t)S_n \\ \lambda_v(t)S_v \\ 0 \\ 0 \end{pmatrix} \quad \text{and} \quad \mathcal{V} = \begin{pmatrix} (\sigma_n + \phi + \mu)E_n & & & \\ -\phi E_n + (\sigma_v + \mu)E_v & & & \\ -\sigma_n E_n + (\gamma_n + \delta_n + \phi + \mu)I_n & & & \\ -\sigma_v E_v - \phi I_n + (\gamma_v + \delta_v + \mu)I_v & & & \end{pmatrix} \quad (7)$$

Let $F_i(t)$ and V be the Jacobians of $\mathcal{F}_i(t)$ and $\mathcal{V}$ evaluated at the DFE during interval T_i . From equations 4, 5 and 7, the matrix of new infections is:

$$F_i(t) = \begin{pmatrix} 0 & 0 & \beta_i(t)\frac{S_n^*}{N} & c_{nv}\beta_i(t)\frac{S_n^*}{N} \\ 0 & 0 & c_{vn}\beta_i(t)\frac{S_v^*}{N} & c_{vv}\beta_i(t)\frac{S_v^*}{N} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix} \quad (8)$$

From equation 7 the transition matrix V is given by:

$$V = \begin{pmatrix} \sigma_n + \phi + \mu & 0 & 0 & 0 \\ -\phi & \sigma_v + \mu & 0 & 0 \\ -\sigma_n & 0 & \gamma_n + \delta_n + \phi + \mu & 0 \\ 0 & -\sigma_v & -\phi & \gamma_v + \delta_v + \mu \end{pmatrix} \quad (9)$$

The inverse of the of the Jacobian matrix V is given by:

$$V^{-1} = \begin{pmatrix} \frac{1}{(\sigma_n + \phi + \mu)} & 0 & 0 & 0 \\ \frac{\phi}{(\sigma_n + \phi + \mu)(\sigma_v + \mu)} & \frac{1}{(\sigma_v + \mu)} & 0 & 0 \\ \frac{\sigma_n}{(\sigma_n + \phi + \mu)(\gamma_n + \delta_n + \phi + \mu)} & 0 & \frac{1}{(\gamma_n + \delta_n + \phi + \mu)} & 0 \\ \frac{\frac{\phi \sigma_n}{(\sigma_n + \phi + \mu)(\gamma_n + \delta_n + \phi + \mu)} + \frac{\phi \sigma_v}{(\sigma_n + \phi + \mu)(\sigma_v + \mu)}}{\gamma_v + \delta_v + \mu} & \frac{\sigma_v}{(\sigma_v + \mu)(\gamma_v + \delta_v + \mu)} & \frac{\phi}{(\gamma_n + \delta_n + \phi + \mu)(\gamma_v + \delta_v + \mu)} & \frac{1}{(\gamma_v + \delta_v + \mu)} \end{pmatrix} \quad (10)$$

The time-varying reproduction number is the spectral radius of the next-generation matrix, $\mathcal{R}_i(t) = \rho(F_i(t)V^{-1})$. The non-zero eigenvalues of $F_i(t)V^{-1}$ are determined by the eigenvalues of the matrix $K_i(t)$,

$$K_i(t) = \begin{pmatrix} K_{11} & K_{12} & K_{13} & K_{14} \\ K_{21} & K_{22} & K_{23} & K_{24} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix} \quad (11)$$

where

$$\begin{aligned} K_{11} &= \beta_i(t) \frac{S_n^*}{N^*} \frac{\sigma_n}{(\sigma_n + \phi + \mu)(\gamma_n + \delta_n + \phi + \mu)} \\ &\quad + C_{nv} \beta_i(t) \frac{S_n^*}{N^*} \frac{\frac{\phi \sigma_n}{(\sigma_n + \phi + \mu)(\gamma_n + \delta_n + \phi + \mu)} + \frac{\phi \sigma_v}{(\sigma_n + \phi + \mu)(\sigma_v + \mu)}}{(\gamma_n + \delta_v + \mu)}, \\ K_{12} &= C_{mv} \beta_i(t) \frac{S_n^*}{N^*} \frac{\sigma_v}{(\sigma_v + \mu)(\gamma_v + \delta_v + \mu)}, \\ K_{13} &= \beta_i(t) \frac{S_n^*}{N^*} \frac{1}{(\gamma_n + \delta_n + \phi + \mu)} + C_{nv} \beta_i(t) \frac{S_n^*}{N^*} \frac{\phi}{(\gamma_n + \delta_n + \phi + \mu)(\gamma_v + \delta_v + \mu)}, \\ K_{14} &= C_{mv} \beta_i(t) \frac{S_n^*}{N^*} \frac{1}{(\gamma_v + \delta_v + \mu)}, \\ K_{21} &= C_{vn} \beta_i(t) \frac{S^*}{N^*} \frac{\sigma_n}{(\sigma_n + \phi + \mu)(\gamma_n + \delta_n + \phi + \mu)} \\ &\quad + C_{vv} \beta_i(t) \frac{S^*}{N^*} \frac{\frac{\phi \sigma_n}{(\sigma_n + \phi + \mu)(\gamma_n + \delta_n + \phi + \mu)} + \frac{\phi \sigma_v}{(\sigma_n + \phi + \mu)(\sigma_v + \mu)}}{(\gamma_n + \delta_v + \mu)}, \\ K_{22} &= C_{vv} \beta_i(t) \frac{S_v^*}{N^*} \frac{\sigma_v}{(\sigma_v + \mu)(\gamma_v + \delta_v + \mu)}, \\ K_{23} &= C_{vn} \cdot \beta_i(t) \frac{S_v^*}{N^*} \frac{1}{(\gamma_n + \delta_n + \phi + \mu)} + C_{vv} \frac{S_v^*}{N^*} \cdot \frac{\phi}{(\gamma_n + \delta_v + \phi + \mu)(\gamma_v + \delta_v + \mu)}, \\ K_{24} &= C_{vv} \beta_i(t) \frac{S_v^*}{N^*} \frac{1}{(\gamma_v + \delta_v + \mu)}. \end{aligned}$$

The reproduction number for interval T_i is then the largest eigenvalue of the matrix K_i , which is given by:

$$\mathcal{R}_i(t) = \frac{(K_{11} + K_{22}) + \sqrt{(K_{11} - K_{22})^2 + 4K_{12}K_{21}}}{2}$$

This allows for the direct calculation of the reproduction number for each distinct epidemiological period by substituting the corresponding estimated value of $\beta_i(t)$.

3 Results

3.1 Parameter Estimation

The model parameters were categorized into two groups: fixed parameters, derived from literature and demographic data and unknown parameters, which were estimated by fitting the model to epidemiological data. The estimation of the unknown parameter set, denoted as vector Θ , was performed by minimizing the sum of squared differences (SSE) between the weekly cumulative case output of the model and the weekly cumulative cases observed for South Africa.

This optimization problem was solved using the Trust-Region-Reflective algorithm implemented in the MATLAB function `lsqcurvefit` [23]. The objective function $J(\Theta)$ seeks to minimize the residual sum of squares between the observed data $C_{obs}(t_i)$ and the model simulation $C_{model}(t_i, \Theta)$ over T time points [38,41]:

$$\min_{\Theta} J(\Theta) = \sum_{i=1}^T (C_{obs}(t_i) - C_{model}(t_i, \Theta))^2 \quad (12)$$

subject to the bound constraints:

$$\Theta_{lb} \leq \Theta \leq \Theta_{ub} \quad (13)$$

where Θ_{lb} and Θ_{ub} represent the lower and upper bounds of the parameter space, respectively. To ensure the estimated parameters remained within biologically plausible ranges, these bounds were derived from a review of literature regarding COVID-19 transmission dynamics, vaccine efficacy and waning immunity profiles specific to the Delta and Omicron variants. The specific bounds imposed on the optimization process are detailed in Table 2. The values are scaled to match the weekly time-step of the fitting procedure. The fitted vector consisted of the four interval-specific transmission coefficients, the three vaccination transmission modifiers, the recovery and disease-induced mortality parameters and the three waning-immunity parameters reported as estimated quantities in the parameter table. All demographic quantities and initial conditions were fixed before optimization. The criterion is a deterministic least-squares criterion so the reported estimates should be interpreted as point estimates [3].

Uncertainty intervals were not computed in the present analysis because the available fitting source was a single case series. This creates some limitations: interval-specific transmission and vaccine-effect modifiers can partly compensate for each other when only cumulative cases are fitted. To reduce this confounding, change-point dates were fixed from the inflection-point analysis and parameter bounds were restricted to ranges that biologically make sense taken from the literature. As a structured sensitivity interpretation, the conclusions are strongest for directions of change that are consistent across the imposed parameter bounds: higher transmission or lower vaccine protection increases projected cases, whereas higher vaccination flow decreases susceptible individuals and suppresses peaks. However, precise numerical magnitudes should be read as scenario estimates conditional on the fitted parameter set, not as formal confidence intervals.

Table 2: Bounds Imposed on the Parameters in the Optimization Problem.

Parameter	Bounds	Notes / Source	Scaled to Weekly
$\beta(t)$	0.19 – 2.14	Derived from $R_0 \in [1.9, 6.5]$ and $\gamma \in [0.10, 0.33]$; see [15] for R_0 meta-analysis.	1.33 - 14.98
c_{nn}, c_{vn}, c_{vv}	$\beta(t) \times [0.17-0.78]$	Multiplier = $(1 - \text{Vaccine Efficacy(VE)}_{\text{infection}})$; VE against infection range 22%–83%. [42]	0.2261 - 11.6844
ω_{sv}	0.0020 – 0.0200	Corresponds to immunity duration $\approx 50 - 500$ days ($1/\omega$); Vaccine-induced immunity wanes substantially by 3–6 months for infection. [43]	0.014 - 0.14
ω_{rn}	0.0010 – 0.0100	Natural immunity after infection may last 100 – 1000 days before significant waning. [44]	0.007 - 0.07
ω_{rv}	0.000004 – 0.0050	Hybrid immunity appears more durable; thus slower waning.	2.8×10^{-5} - 0.035
δ_n	$1 \times 10^{-6} - 5.5 \times 10^{-3}$	Infection Fatality Rate (IFR) $\approx 0.53\%-0.82\%$. [45]	$7 \times 10^{-6} - 3.85 \times 10^{-2}$
δ_v	$1 \times 10^{-7} - 5.5 \times 10^{-4}$	Assume vaccinated severe outcome reduction $\approx 50-95\%$.	$7 \times 10^{-7} - 3.85 \times 10^{-3}$
γ_n, γ_v	0.10 – 0.36	Infectious period $\approx 3-10$ days so $\gamma = 1/\text{infectious period}$.	0.70 - 2.52

The total population of South Africa was set at $N = 60.14$ million based on the mid-year population estimates for 2021 of Statistics South Africa (Stats SA) [46]. From the same source, using pre-pandemic (2020) life expectancy data, the daily natural death rate was calculated as $\mu = 1/(65.4 \times 365.25)$. Assuming a stable population, the daily recruitment rate was set to balance natural deaths, $\kappa = \mu \times N$. The average daily vaccination rate, ϕ , was calculated from official national data aggregated by Our World in Data throughout the study period [47]. The progression rate from exposed to infectious (σ_n, σ_v) was set to 1/4 per day, corresponding to a 4-day latent period, which reflects the shorter incubation times of the Delta and Omicron variants [48].

The initial conditions for the start date of the simulation which is March 28, 2021 were derived from public data. The number of recovered unvaccinated individuals which $R_n(0) = 1,545,431$ was taken directly from cumulative case data [30]. The initial vaccinated population, $S_v(0) = 231,605$, corresponds to official figures from the South African Department of Health [28]. The active infectious population ($I_n(0), I_v(0)$) was estimated by multiplying the 7-day moving average of new daily cases ($\approx 1,150$) by a 14-day infectious period, a duration suggested by some studies [49]. The exposed population ($E_n(0), E_v(0)$) was assumed to be twice the size of the infectious population, a standard assumption to account for unobserved infections that will drive future transmission [50]. The remaining population was assigned to the susceptible unvaccinated compartment, $S_n(0)$. All fixed parameters were converted to weekly rates for the fitting procedure.

Table 3: Model initial conditions and parameter values with associated units.

Symbol	Value	Unit	Source or Deduction Logic
Initial Conditions (for March 28, 2021)			
$S_n(0)$	58,314,706	Individuals	Remainder of the total population N
$S_v(0)$	231,605	Individuals	SA Dept. of Health data [28]
$E_n(0)$	14,000	Individuals	Assumed $2 \times I_n(0)$ based on literature [50]
$E_v(0)$	70	Individuals	Assumed $2 \times I_v(0)$
$I_n(0)$	7,000	Individuals	Deduced from 7-day avg. new cases $\times$ 14-day infectious period
$I_v(0)$	35	Individuals	Proportional to the vaccinated population at the time
$R_n(0)$	1,545,431	Individuals	Cumulative cases on start date from data [30]
$R_v(0)$	0	Individuals	Assumed no recovered vaccinated individuals at start date
Fixed Parameters			
N	60,140,000	Individuals	Stats SA 2021 mid-year population estimate [46]
μ	$1/(65.4 \times 365.25)$	day ⁻¹	Inverse of avg. life expectancy [46]
κ	$\mu \times N$	Indiv. $\cdot$ day ⁻¹	Assumes a stable population
ϕ	$51825/N$	day ⁻¹	Avg. daily vaccination rate [47]
σ_n, σ_v	1/4	day ⁻¹	4-day latent period [48, 51]
Estimated Parameters (Weekly Rates)			
β_1	1.9402	week ⁻¹	Fitted (Delta transmission)
β_2	1.4582	week ⁻¹	Fitted (Wave tail)
β_3	2.3625	week ⁻¹	Fitted (Omicron transmission)
β_4	1.3361	week ⁻¹	Fitted (Wave tail)
c_{nv}	0.3018	Dimensionless	Fitted (70% protection)
c_{vv}	0.0351	Dimensionless	Fitted (High protection)
c_{vn}	0.0735	Dimensionless	Fitted (Medium protection)
γ_n	1.5444	week ⁻¹	Fitted (Avg duration $\approx$ 4.5 days)
γ_v	1.1834	week ⁻¹	Fitted (Avg duration $\approx$ 5.9 days)
δ_n	0.0291	week ⁻¹	Fitted (High mortality risk)
δ_v	0.0018	week ⁻¹	Fitted (Low mortality risk)
ω_{sv}	0.0426	week ⁻¹	Fitted (Waning $\approx$ 5.5 months)
ω_{rn}	0.0128	week ⁻¹	Fitted (Waning $\approx$ 1.5 years)
ω_{rv}	0.0078	week ⁻¹	Fitted (Waning $\approx$ 2.5 years)

The model was fitted to weekly cumulative case data for South Africa for the period from March 28, 2021, to April 4, 2022. The estimated parameter values obtained from the `lsqcurvefit` optimization are presented in Table 3. The resulting simulation demonstrates a significant correspondence with the observed data, as shown in Figure 4. The output of the model (solid red line) closely tracks the trajectory of the actual cumulative cases (blue circles).

The model was first fitted to the weekly cumulative case data. The resulting fit was statistically strong, explaining 99.59 % of the variance ($R^2 = 0.9928$). Notably, the adjusted R-squared ($R^2_{adj} = 0.9898$) remained high, indicating the 14-

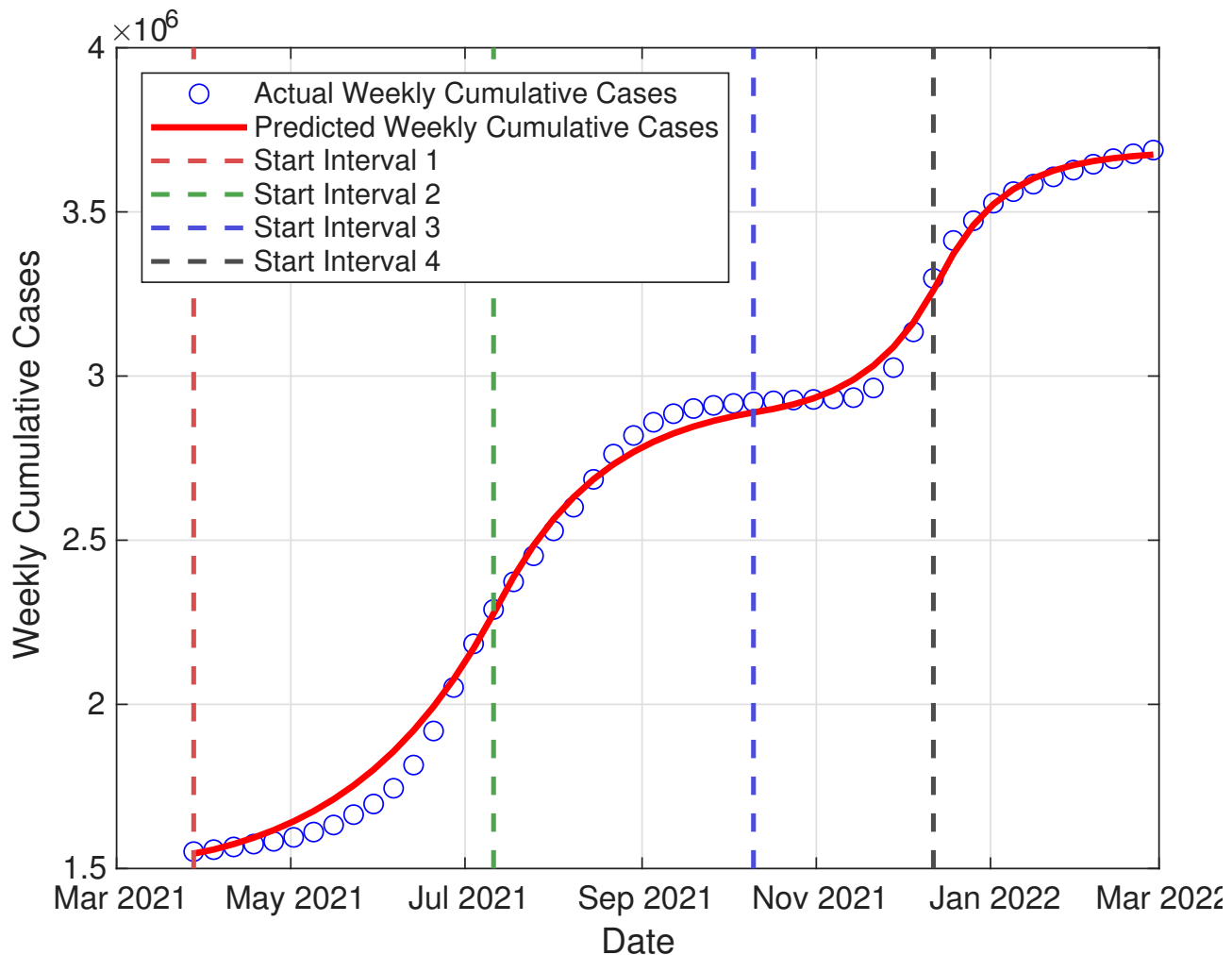


Fig. 4: Simulation Output Using Fitted Parameters on the Weekly Cumulative Cases - South Africa

parameter model is not over-fitted. The Root Mean Squared Error (RMSE) was 61,016, which represents a low relative error given the cumulative totals. While these metrics validate the fit, the true test of an epidemiological model is its ability to reproduce the dynamics of the epidemic (the ‘waves’), not just the cumulative total. Therefore, to further validate the performance of the model, the estimated parameters were used to simulate the weekly new cases, which were then compared against the actual weekly incidence data. This comparison, shown in Figure 5, confirms the ability of the model to reproduce the wave-like behavior of the epidemic. The model accurately captures the timing and magnitude of the two main waves in the study period. The first peak in the simulation corresponds to the third wave in South Africa, driven by the Delta variant. The second peak, which is both steeper and higher represents the fast and aggressive transmission dynamics of the Omicron variant, acknowledged for its notably increased transmissibility [33]. The ability of the model to reproduce these distinct wave structures provides to a certain extent validation for the estimated parameters and the overall model framework.

3.2 Impact of National Vaccination Initiation

To assess whether the national vaccination initiative worked or not, the validated model was used to simulate two counterfactual scenarios: one with no vaccination ($\phi = 0$) and another with double the increase in the vaccination rate. The outcomes of these simulations, contrasted with the baseline model (reflecting the actual vaccination rate) and observed data, are presented in Figure 6. In the equations, the no-vaccination scenario sets the vaccination flow to zero for the entire simulation horizon. The enhanced scenario replaces the baseline vaccination flow by twice the estimated average vaccination rate over the same calendar period, so the flows from non-vaccinated to vaccinated susceptible, exposed, infectious and recovered classes are doubled simultaneously. All other fitted parameters, vaccine-effect modifiers, waning rates and change-point dates are held fixed; therefore, the counterfactual isolates the effect of faster

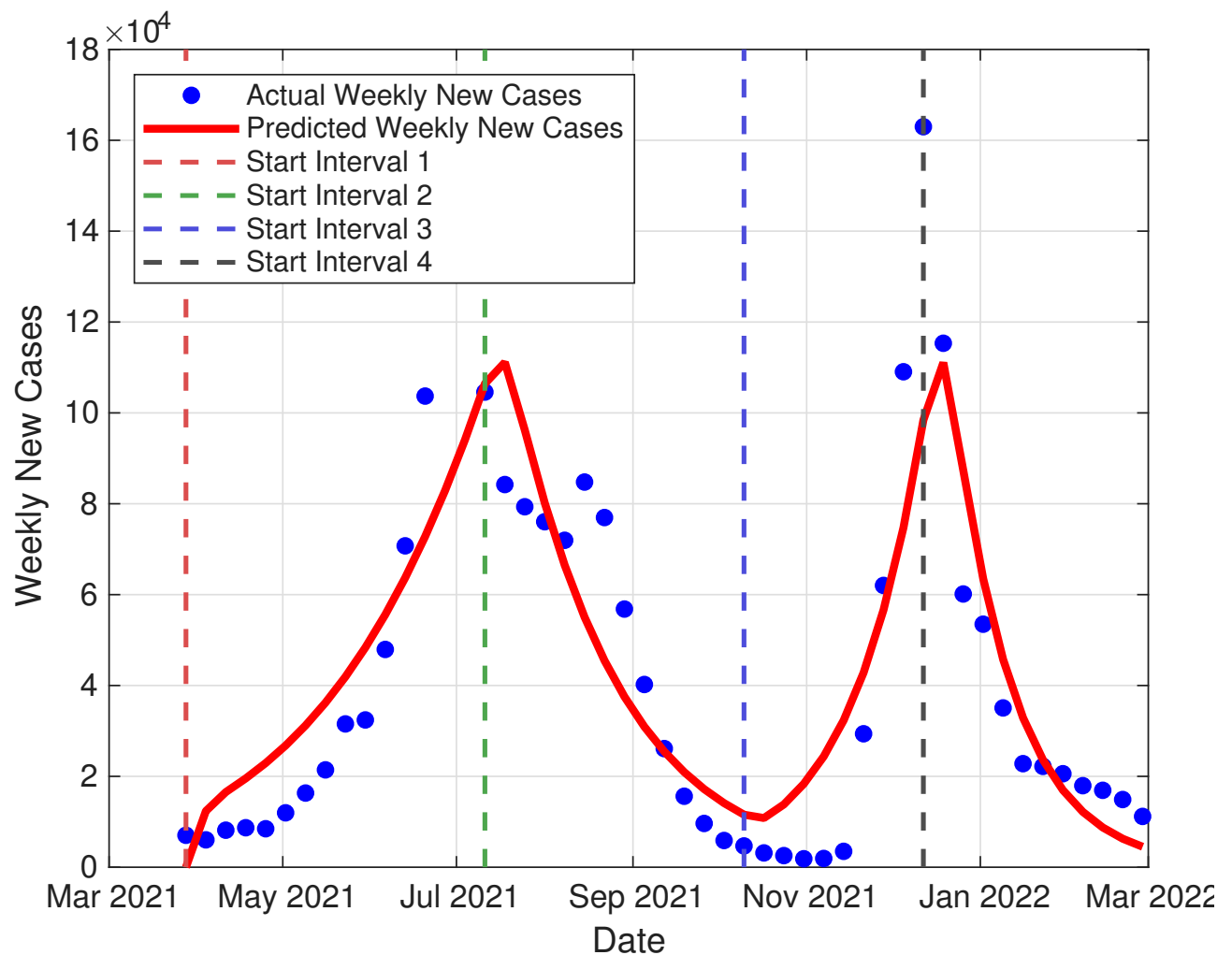


Fig. 5: Simulation Output Using Fitted Parameters on the Weekly New Cases - South Africa

uptake under the same vaccine effectiveness and epidemic timing assumptions. The primary outcomes emphasized are peak weekly incidence, cumulative infections, and the susceptible, exposed and infectious trajectories; hospital burden is not reported because no hospitalization compartment is included. The reproduction-number expression in Section 2.3 is used to interpret interval-level transmissibility after substituting fitted parameters, but the scenario comparison is reported primarily in cases.

The calculated baseline reproduction numbers at the starts of Intervals 1–4 were 1.2654, 0.74376, 1.4761 and 0.56624, respectively, indicating growth during the Delta ascent and Omicron expansion intervals and decline during the corresponding wave-tail intervals. Table 4 summarizes these.

Table 4: Baseline reproduction numbers at interval starts.

Interval	Start date	Baseline $\mathcal{R}$
1	March 28, 2021	1.2654
2	July 11, 2021	0.74376
3	October 10, 2021	1.4761
4	December 12, 2021	0.56624

In the baseline scenario, the predicted peak was 146,200 weekly cases on Dec 05, 2021, with 2.1373 million total predicted cases over the simulation horizon. In the no-vaccination scenario, the peak increased to 838,310 weekly cases on Dec 05, 2021 and total predicted cases increased to 6.3375 million, which is 4.2003 million cases or 196.52 percent above baseline. This finding illustrates the important role vaccination played in mitigating the impact of the variant. Conversely, the enhanced vaccination scenario reduced the peak to 83,053 weekly cases on Jul 04, 2021 and lowered total predicted

cases to 1.1024 million, corresponding to 1.0349 million fewer cases and a 48.421 percent reduction relative to baseline. Table 5 summarizes the exact scenario outcomes used for these comparisons.

Table 5: Predicted case outcomes under vaccination scenarios.

Scenario	Peak weekly cases	Peak date	Total cases	Difference from baseline
Baseline	146,200	December 05, 2021	2,137,300	0
No Vaccination	838,310	December 05, 2021	6,337,500	+4,200,300
Enhanced Vaccination	83,053	July 04, 2021	1,102,400	-1,034,900

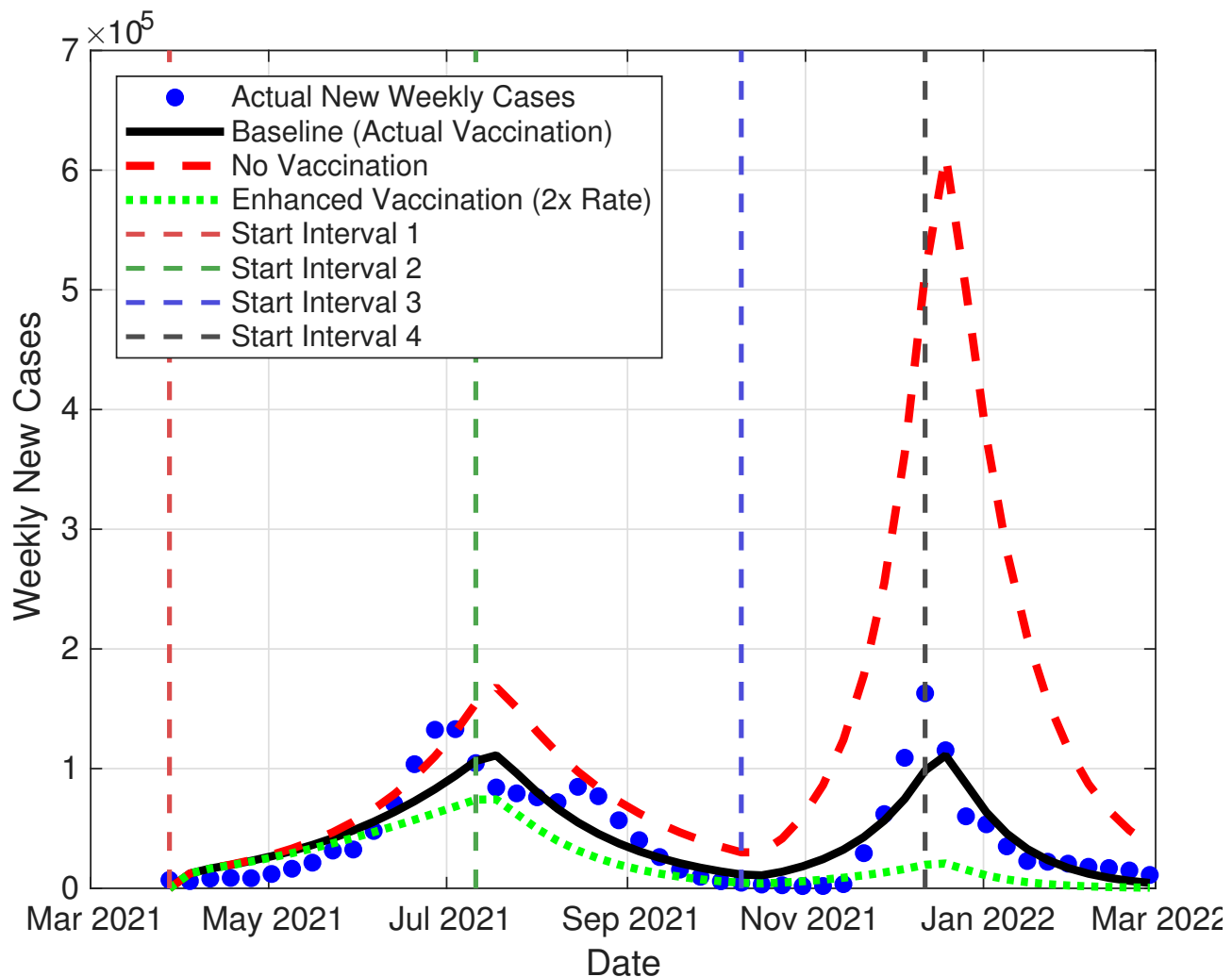


Fig. 6: Comparison of predicted weekly new cases under three vaccination scenarios: Baseline (actual vaccination rate), No Vaccination, and an Enhanced (2x) rate. Actual weekly case data is shown for comparison.

The underlying drivers of these outcomes are revealed in the compartmental dynamics shown in Figure 7. In the ‘No Vaccination’ scenario, the Omicron wave causes a rapid depletion of the susceptible population through widespread infection, not immunization (Figure 7A). This uncontrolled transmission precipitates a subsequent enormous spike in exposed and infectious populations (Figures 7B and 7C), far exceeding the baseline peaks. In contrast, the ‘Enhanced (2x) Vax’ scenario preserves a larger susceptible pool by moving individuals into a protected state via vaccination. This, in turn, significantly blunts the peaks in the exposed and infectious compartments.

4 Discussion

This study aimed to quantify the impact of the COVID-19 vaccination program on the trajectory of the pandemic in South Africa. The results provide substantial quantitative evidence that the vaccination campaign was instrumental in mitigating the severity of this wave. The counterfactual no-vaccination scenario projected a peak of 838,310 weekly

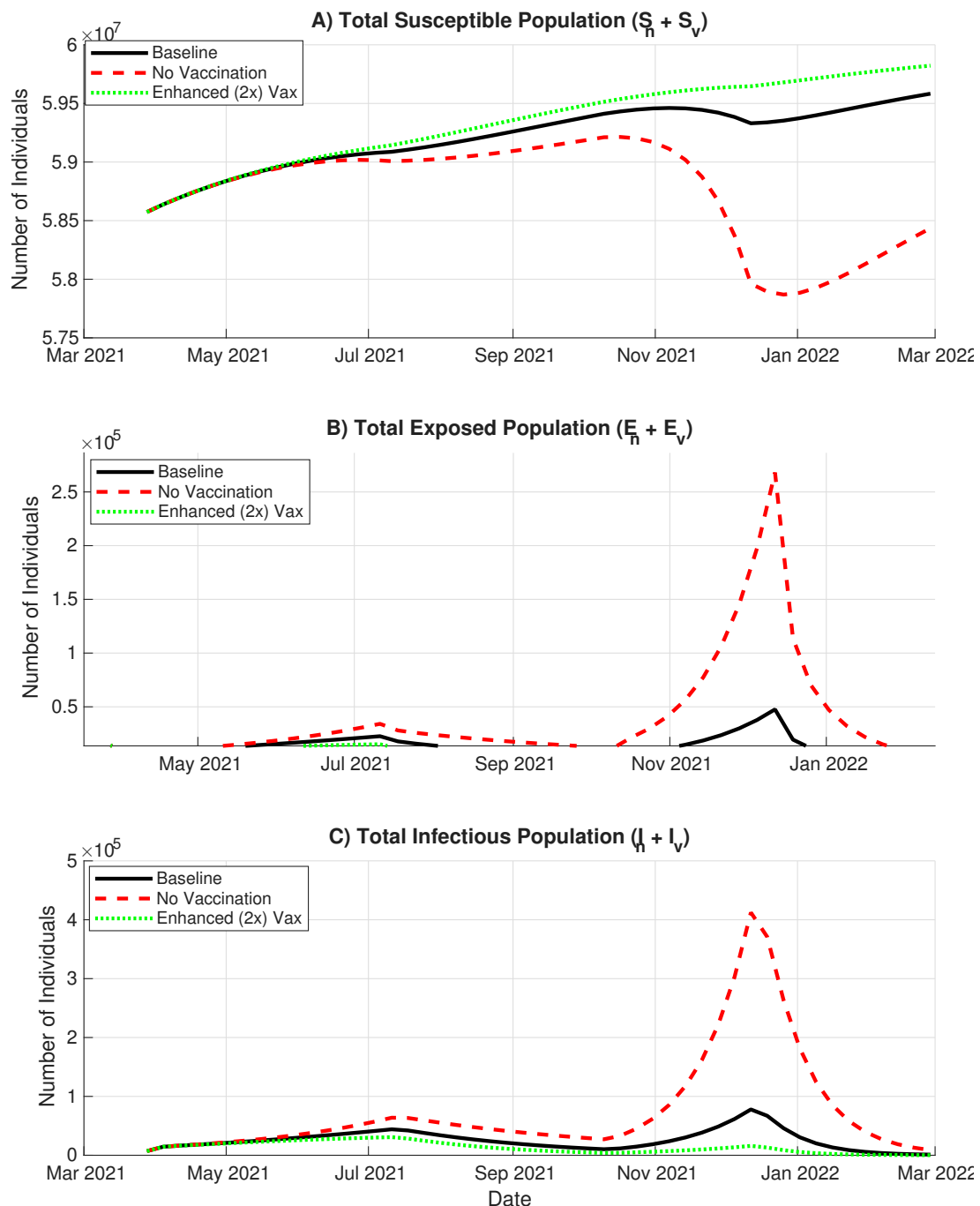


Fig. 7: Dynamics of the (A) Total Susceptible, (B) Total Exposed and (C) Total Infectious populations for the Baseline, No Vaccination, and Enhanced Vaccination scenarios.

cases, compared with 146,200 weekly cases under baseline vaccination and increased total predicted cases from 2.1373 million to 6.3375 million. In contrast, the enhanced vaccination strategy reduced total predicted cases to 1.1024 million, averting 1.0349 million cases relative to baseline and reducing the total burden by 48.421 percent. These findings highlight the immense public health value of mass vaccination as a primary pandemic control measure.

These conclusions are consistent with the wider body of literature on COVID-19 modeling. For example, studies conducted in other regions using similar compartmental models have also demonstrated the effect of vaccines on reducing transmission and disease burden during the Omicron wave [52]. A study focusing on the South African context by Pratama et al. [12] similarly concluded that vaccination, despite the immune-evasive properties of Omicron, was the

critical factor in preventing the collapse of the healthcare system. The model formulated in this study contributes to this consensus by providing an estimate of the cases averted and the potential scale of the crisis that was avoided.

A primary strength of model proposed here is its direct calibration to weekly case data from South Africa, which grounds scenario analyses in observed reality. The structure of the model, which stratifies the population into vaccinated and non-vaccinated compartments, allows for a direct investigation of the intervention in question. However, the model is not without limitations. Chief among these is the assumption of homogeneous mixing, which implies that all individuals in the population have an equal chance of interacting. This simplification does not capture the complex contact patterns in society, which can be better represented by network models or age-structured contact matrices. Furthermore, the model does not explicitly stratify the population by age, which matters determining disease severity. The use of piecewise-constant parameters for different time intervals is an approximation of the continuous changes in behavior and viral characteristics that occur in reality. Another limitation is the absence of formal confidence intervals, so the reported counterfactual differences should be interpreted as deterministic scenario contrasts rather than fully probabilistic forecasts. The main conclusion is therefore strongest in qualitative direction, namely that removing vaccination increases peak incidence while faster uptake reduces infections, whereas exact magnitudes require future uncertainty quantification.

These limitations point to several avenues for future research. An immediate improvement would be the incorporation of an age-structured model to explore the differential impact of vaccination across various age ranges. Second, developing a more sophisticated framework that includes continuous functions for waning immunity would provide a more realistic portrayal of population-level susceptibility over time. Future work could also integrate mobility data to better approximate contact patterns or expand the model to include compartments for hospitalizations and deaths, thereby allowing an analysis of the impact on severe disease outcomes, not just infections.

5 Conclusion

In conclusion, this modeling study demonstrates that South Africa's national vaccination campaign was an effective public health intervention. It substantially curtailed the trajectory of the COVID-19 pandemic. The findings show that vaccination dramatically reduced the number of infections that would have otherwise occurred during the Omicron-driven fourth wave. The key quantitative findings are that the no-vaccination counterfactual generated a peak of 838,310 weekly cases and 6.3375 million total predicted cases, whereas the baseline produced 146,200 peak weekly cases and 2.1373 million total predicted cases. The enhanced uptake scenario reduced total predicted cases to 1.1024 million, averting 1.0349 million cases relative to baseline under the model assumptions. This outcome is particularly significant given the context of the Omicron variant, which was first identified in South Africa and posed a global challenge due to its high transmissibility and immune escape properties [33].

During the counterfactual analysis stage, it was revealed that in the absence of vaccination, South Africa would have likely faced a catastrophic surge in infections, potentially overwhelming its healthcare system. This aligns with other research which concluded that vaccination was the critical factor in preventing the collapse of healthcare services during this period [12]. Despite challenges such as vaccine hesitancy and logistical hurdles in a country with significant socio-economic disparities [53], the rollout achieved a level of coverage that averted a worst-case scenario. The policy implications for South Africa are clear: continued investment in vaccination programs and public health infrastructure is not merely a preventative measure but a vital component of national resilience against future pandemics. This study provides strong evidence to support policies that prioritize vaccination strategies to safeguard public health and mitigate the impact of evolving viral threats.

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Author Contributions:

Aubrey Ndovie contributed to the conceptualization, methodology, data analysis and visualization, and writing of the original draft. Claris Shoko participated in the supervision, conceptualization, methodology and writing review. Sivasamy Ramasamy contributed to supervision, validation, and writing review. Olusegun S. Ewemooje participated in supervision, validation and writing review.

Abbreviations

The following abbreviations are used in this manuscript:

COVID-19 : Coronavirus Disease 2019

DFE: Disease Free Equilibrium.

DSFSI: Data science for Social Impact Research Group.

NGM: Next Generation Matrix.

NPIs : Non-Pharmaceutical Interventions

ODEs: Ordinary Differential Equations

SEIR: : susceptible-exposed-infections-recovered

WHO : World Health Organization

References

- [1] World Health Organization, "WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020," 2020. <https://www.who.int/news-room/speeches/item/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020>. Accessed: 14 July 2025.
- [2] T. Hale, N. Angrist, R. Goldszmidt, B. Kira, A. Petherick, T. Phillips, S. Webster, E. Cameron-Blake, L. Hallas, S. Majumdar, and H. Tatlow, "A global panel database of pandemic policies (oxford covid-19 government response tracker)," *Nature Human Behaviour*, vol. 5, no. 4, pp. 529–538, 2021. DOI: <https://doi.org/10.1038/s41562-021-01079-8>.
- [3] C. J. Edholm, B. Levy, L. Spence, F. B. Agosto, F. Chirove, C. W. Chukwu, D. Goldsman, M. Kgosimore, I. Maposa, K. A. J. White, and S. Lenhart, "A vaccination model for covid-19 in gauteng, south africa," *Infectious Disease Modelling*, vol. 7, pp. 333–345, 2022. DOI: <https://doi.org/10.1016/j.idm.2022.06.002>.
- [4] United Nations, Africa Renewal, "How COVID-19 has impacted the SDGs in Africa," 2021. <https://africarenewal.un.org/en/magazine/how-covid-19-has-impacted-sdgs-africa>, Accessed: 14 July 2025.
- [5] F. Fagbemi, "COVID-19 and Sustainable Development Goals (SDGs): An Appraisal of the Emanating Effects in Nigeria," AGDI Working Paper WP/21/026, African Governance and Development Institute, 2021. Available at: <https://www.econstor.eu/bitstream/10419/244201/1/agdi-wp-21-026.pdf>.
- [6] United Nations Development Programme, "2020 Africa Sustainable Development Report," tech. rep., UNDP, New York, NY, 2022. Available at: <https://files.acquia.undp.org/public/migration/africa/RBA---ASDR-2020---updated---03032022.pdf>.
- [7] United Nations Economic Commission for Africa and African Union and African Development Bank and United Nations Development Programme, "2024 Africa Sustainable Development Report," tech. rep., UNECA, Addis Ababa, Ethiopia, 2024. Available at: https://www.undp.org/sites/g/files/zskgke326/files/2024-07/asdr_2024_-_en.pdf.
- [8] G. Nhamo, B. Ndlela, C. Nhemachena, and S. Mubvuma, "Impacts of COVID-19 on SDGs implementation and service delivery in South Africa's Limpopo Province," *Frontiers in Sustainability*, vol. 5, 2024. DOI: <https://doi.org/10.3389/frsus.2024.1477474>. Available at: <https://www.frontiersin.org/articles/10.3389/frsus.2024.1477474/full>.
- [9] F. P. Polack, S. J. Thomas, N. Kitchin, J. Absalon, A. Gurtman, S. Lockhart, J. L. Perez, G. P. Marc, E. D. Moreira, C. Zerbini, R. Bailey, K. A. Swanson, S. Roychoudhury, K. Koury, P. Li, W. V. Kalina, D. Cooper, R. W. F. Jr., L. L. Hammitt, Ö. Türeci, H. Nell, A. Schaefer, S. Ünal, D. B. Tresnan, S. Mather, P. R. Dormitzer, U. Şahin, K. U. Jansen, W. C. Gruber, and for the C4591001 Clinical Trial Group, "Safety and efficacy of the bnt162b2 mrna covid-19 vaccine," *The New England Journal of Medicine*, vol. 383, no. 27, pp. 2603–2615, 2020. DOI: <https://doi.org/10.1056/NEJMoa2034577>.
- [10] L. R. Baden, H. M. E. Sahly, B. Essink, K. Kotloff, S. Frey, R. Novak, D. Diemert, S. A. Spector, N. Rouphael, C. B. Creech, J. McGettigan, S. Khetan, N. Segall, J. Solis, A. Brosz, C. Fierro, H. Schwartz, K. Neuzil, C. L. Robertson, P. Cárdenas, W. Buchanan, M. J. McElrath, J. M. Miller, T. Smith, F. J. Dutko, W. Deng, H. Bennett, B. D. Girard, M. Koch, D. Montefiori, A. B. McDermott, J. R. Mascola, B. S. Graham, R. Pajon, B. Leav, H. Janes, and for the COVE Study Group, "Efficacy and

- safety of the mRNA-1273 SARS-CoV-2 vaccine,” *The New England Journal of Medicine*, vol. 384, no. 5, pp. 403–416, 2021. DOI: <https://doi.org/10.1056/NEJMoa2035389>.
- [11] J. Sadoff, G. Gray, A. Vandebosch, V. Carrryn, G. Shukarev, D. Grinsztejn, P. A. Goepfert, C. Truysers, H. Schuitemaker, J. V. Hoof, M. Douoguih, H. Fennema, and for the ENSEMBLE Study Group, “Safety and efficacy of single-dose mRNA-1273 vaccine against COVID-19,” *The New England Journal of Medicine*, vol. 384, no. 23, pp. 2187–2201, 2021. DOI: <https://doi.org/10.1056/NEJMoa2101544>.
 - [12] N. R. Pratama, I. A. Wafa, D. S. Budi, H. Sutanto, T. P. Asmarawati, G. Barlian Effendi, and C. D. K. Wungu, “Effectiveness of COVID-19 Vaccines against SARS-CoV-2 Omicron Variant (B.1.1.529): A Systematic Review with Meta-Analysis and Meta-Regression,” *Vaccines*, vol. 10, no. 12, p. 2180, 2022. DOI: <https://doi.org/10.3390/vaccines10122180>.
 - [13] World Health Organization, “Tracking SARS-CoV-2 variants,” 2021. <https://www.who.int/activities/tracking-SARS-CoV-2-variants>. Accessed: 14 July 2025.
 - [14] T. Harder, J. Koch, A. Vygen-Bonnel, “Duration of protection after vaccination against SARS-CoV-2 infection, symptomatic and severe COVID-19,” *The Lancet Infectious Diseases*, vol. 22, no. 10, pp. 1533–1546, 2022. DOI: [https://doi.org/10.1016/S1473-3099\(22\)00311-0](https://doi.org/10.1016/S1473-3099(22)00311-0).
 - [15] M. A. Billah, M. M. Miah, and M. N. Khan, “Reproductive number of coronavirus: A systematic review and meta-analysis based on global level evidence,” *PLoS ONE*, vol. 15, no. 11, p. e0242128, 2020. DOI: <https://doi.org/10.1371/journal.pone.0242128>.
 - [16] H. N. Altarawneh, H. Chemaitelly, M. R. Hasan, H. H. Ayoub, S. Qassim, S. AlMukdad, P. Coyle, H. M. Yassine, H. A. Al-Khatib, F. M. Benslimane, Z. Al-Kanaani, E. Al-Kuwari, A. Jeremijenko, A. H. Kaleeckal, A. N. Latif, R. M. Shaik, H. F. Abdul-Rahim, G. K. Nasrallah, M. G. Al-Kuwari, A. A. Butt, H. E. Al-Romaihi, M. H. Al-Thani, A. Al-Khal, R. Bertollini, P. Tang, and L. J. Abu-Raddad, “Protection against the omicron variant from previous SARS-CoV-2 infection,” *New England Journal of Medicine*, vol. 386, no. 13, pp. 1288–1290, 2022.
 - [17] P. van den Driessche and J. Watmough, “Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission,” *Mathematical Biosciences*, vol. 180, no. 1–2, pp. 29–48, 2002. DOI: [https://doi.org/10.1016/S0025-5564\(02\)00108-6](https://doi.org/10.1016/S0025-5564(02)00108-6).
 - [18] M. J. Keeling and P. Rohani, *Modeling Infectious Diseases in Humans and Animals*. Princeton, NJ: Princeton University Press, 2011.
 - [19] S. M. Garba, J. M.-S. Lubuma, and B. Tsanou, “Modeling the transmission dynamics of the COVID-19 pandemic in South Africa,” *Mathematical Biosciences*, vol. 328, p. 108441, 2020. DOI: <https://doi.org/10.1016/j.mbs.2020.108441>.
 - [20] S. S. Musa, S.-F. Zhao, M.-W. He, A. G. Habib, U. T. Mustapha, and D.-H. He, “Estimation of exponential growth rate and basic reproduction number of the coronavirus disease 2019 (COVID-19) in Africa,” *Infectious Diseases of Poverty*, vol. 9, no. 1, p. 96, 2020. DOI: <https://doi.org/10.1186/s40249-020-00718-y>.
 - [21] S. S. Musa, X.-C. Wang, S.-F. Zhao, S.-L. Li, N. Hussaini, W. Wang, and D.-H. He, “The heterogeneous severity of COVID-19 in African countries: a modeling approach,” *Bulletin of Mathematical Biology*, vol. 84, no. 3, p. 37, 2022. DOI: <https://doi.org/10.1007/s11538-022-01000-0>.
 - [22] H. B. Taboe, K. V. Salako, J. M. Tison, C. N. Ngonghala, and R. G. Kakai, “Predicting COVID-19 spread in the face of control measures in West Africa,” *Mathematical Biosciences*, vol. 328, p. 108431, 2020. DOI: <https://doi.org/10.1016/j.mbs.2020.108431>.
 - [23] F. Nyabadza, F. Chirove, C. W. Chukwu, and M. V. Visaya, “Modelling the potential impact of social distancing on the COVID-19 epidemic in South Africa,” *Computational and Mathematical Methods in Medicine*, vol. 2020, p. 8379685, 2020. DOI: <https://doi.org/10.1155/2020/8379685>.
 - [24] Z. Mukandavire, F. Nyabadza, N. J. Malunguza, D. F. Cuadros, T. Shiri, and G. Musuka, “Quantifying early COVID-19 outbreak transmission in South Africa and exploring vaccine efficacy scenarios,” *PLoS ONE*, vol. 15, no. 7, p. e0236003, 2020. DOI: <https://doi.org/10.1371/journal.pone.0236003>.
 - [25] D. S. Khoury, D. Cromer, A. Reynaldi, T. E. Schlub, A. K. Wheatley, J. A. Juno, K. Subbarao, S. J. Kent, J. A. Triccas, and M. P. Davenport, “Neutralizing antibody levels are highly predictive of immune protection from symptomatic SARS-CoV-2 infection,” *Nature Medicine*, vol. 27, no. 7, pp. 1205–1211, 2021.
 - [26] L. Matrajt, J. Eaton, T. Leung, and E. R. Brown, “Optimizing vaccine allocation for COVID-19 vaccines: critical role of single-dose vaccination,” *Nature Communications*, vol. 12, no. 1, p. 3449, 2021.
 - [27] D. Lin, Y. Gu, B. Wheeler, Y. Weng, A. Iwasaki, C. B. Wilen, E. F. Foxman, N. D. Grubaugh, and S. B. Omer, “Vaccine effectiveness against SARS-CoV-2 variants of concern,” *medRxiv*, 2021. DOI: <https://doi.org/10.1101/2021.07.20.21260872>.
 - [28] E. Mathieu, H. Ritchie, L. Rod  s-Guirao, “Coronavirus pandemic (COVID-19) vaccinations,” 2022. <https://ourworldindata.org/covid-vaccinations>. Our World in Data. Accessed: 14 July 2025.
 - [29] South African Government, “President Cyril Ramaphosa: South Africa’s response to latest COVID-19 developments,” 2021. <https://www.gov.za/speeches/president-cyril-ramaphosa-south-africas-response-latest-covid-19-developments-12-sep-2021>. Accessed: 10 October 2025.
 - [30] Data Science for Social Impact Research Group @ University of Pretoria, “Coronavirus COVID-19 (2019-nCoV) data repository for South Africa,” 2021. Available at: <https://github.com/dsfsi/covid19za>.
 - [31] South African Government, “President Cyril Ramaphosa: South Africa’s response to a third wave of COVID-19 infections,” 2021. <https://www.gov.za/speeches/president-cyril-ramaphosa-south-africas-response-third-wave-covid-19-infections-27-jun-2021>. Accessed: 10 October 2025.
 - [32] S. S. A. Karim and Q. A. Karim, “COVID-19 in South Africa: the double-edged sword of variants of concern,” *The Lancet*, vol. 398, no. 10317, pp. 2123–2125, 2021. DOI: [https://doi.org/10.1016/S0140-6736\(21\)02598-6](https://doi.org/10.1016/S0140-6736(21)02598-6).

- [33] R. Viana, S. Moyo, D. G. Amoako, H. Tegally, C. Scheepers, C. A. Scheepers, J. Everatt, A. Ismail, S. Pillay, Y.-P. Koofhethile, S. K. Singh, L. K. Tshiabula, D. M. Kgoadi, S. S. Mewa, M. Moshabela, M. A. van der Walt, M. Venter, K. Mlisana, A. von Gottberg, R. J. Lessells, J. N. Bhiman, C. Williamson, and T. de Oliveira, "Rapid epidemic expansion of the sars-cov-2 omicron variant in southern africa," *Nature*, vol. 603, no. 7902, pp. 679–686, 2022. DOI: <https://doi.org/10.1038/s41586-022-04411-y>.
- [34] South African Government, "President cyril ramaphosa: Termination of national state of disaster," 2022. <https://www.gov.za/speeches/president-cyril-ramaphosa-termination-national-state-disaster-4-apr-2022-0000>. Accessed: 10 October 2025.
- [35] F. Menegale, C. Ciavarella, V. Marziano, G. Guzzetta, S. Merler, and M. Ajelli, "Evaluation of Waning of SARS-CoV-2 Vaccine-Induced Immunity Against the Omicron and Delta Variants: A Systematic Review and Meta-analysis," *JAMA Network Open*, vol. 6, no. 4, p. e2310860, 2023. DOI: <https://doi.org/10.1001/jamanetworkopen.2023.10860>. Available at: <https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2804451>.
- [36] S. Ghosh, S. Samanta, and V. Volpert, "An Epidemic Model with Time-Distributed Recovery and Death Rates," *Journal of Mathematical Biology*, vol. 85, no. 1, p. 5, 2022. DOI: <https://doi.org/10.1007/s00285-022-01768-4>. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9243747/>.
- [37] B. de Gier, S. Andeweg, W. van der Hoek, H. E. de Melker, F. R. M. van der Klis, R. C.-. mortality, and vaccination study group, "Effect of COVID-19 vaccination on mortality by cause of death in the Netherlands, 1 January 2021 to 31 January 2022," *Eurosurveillance*, vol. 28, no. 23, p. 2200543, 2023. DOI: <https://doi.org/10.2807/1560-7917.ES.2023.28.23.2200543>. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10247887/>.
- [38] L. J. Allen and P. van den Driessche, "Relations between deterministic and stochastic thresholds for disease extinction in continuous-and discrete-time infectious disease models," *Mathematical biosciences*, vol. 243, no. 1, pp. 99–108, 2013.
- [39] E. L. Piccolomini and F. Zama, "Monitoring italian covid-19 spread by a forced seird model," *PLoS ONE*, vol. 15, no. 8, p. e0237417, 2020. DOI: <https://doi.org/10.1371/journal.pone.0237417>.
- [40] M. E. Halloran, I. M. Longini Jr, and C. J. Struchiner, *Design and Analysis of Vaccine Studies*. Statistics for Biology and Health, Springer Science & Business Media, 2010.
- [41] L. J. Allen, "Stochastic population and epidemic models," *Mathematical biosciences lecture series, stochastics in biological systems*, vol. 1, pp. 120–128, 2015.
- [42] P. Ssentongo, A. E. Ssentongo, E. S. Heilbrunn, D. M. Ba, and V. M. Chinchilli, "Sars-cov-2 vaccine effectiveness against infection, symptomatic and severe covid-19: a meta-analysis," *BMC Infectious Diseases*, vol. 22, no. 1, p. 439, 2022. DOI: <https://doi.org/10.1186/s12879-022-07418-y>.
- [43] D. R. Feikin, M. M. Higdon, L. J. Abu-Raddad, N. Andrews, R. Araos, Y. Goldberg, M. J. Groome, A. Huppert, K. L. O'Brien, P. G. Smith, A. Wilder-Smith, S. Zeger, M. Deloria Knoll, and M. K. Patel, "Duration of effectiveness of vaccines against sars-cov-2 infection and covid-19 disease: results of a systematic review and meta-regression," *The Lancet*, vol. 399, no. 10328, pp. 924–944, 2022. DOI: [https://doi.org/10.1016/S0140-6736\(22\)00152-0](https://doi.org/10.1016/S0140-6736(22)00152-0).
- [44] K. Talaat, A. Goldberg, A. Freedman, "Had covid recently? here's what to know about how long immunity lasts," *AAMC News*, 2023. Online article. Available at: <https://www.aamc.org/news/had-covid-recently-what-know-about-how-long-immunity-lasts-long-covid-and-more>.
- [45] G. Meyerowitz-Katz and L. Merone, "A systematic review and meta-analysis of published research data on covid-19 infection fatality rates," *International Journal of Infectious Diseases*, vol. 101, pp. 138–148, 2020. DOI: <https://doi.org/10.1016/j.ijid.2020.09.1464>.
- [46] Statistics South Africa, "Mid-year population estimates, 2021," July 2021. Available at: <https://www.statssa.gov.za/?p=14519>.
- [47] E. Mathieu, H. Ritchie, E. Ortiz-Ospina, M. Roser, J. Hasell, C. Appel, C. Giattino, and L. Rod s-Guirao, "A global database of COVID-19 vaccinations," *Nature Human Behaviour*, vol. 5, no. 7, pp. 947–953, 2021. DOI: <https://doi.org/10.1038/s41562-021-01122-8>.
- [48] B. Li, A. Deng, K. Li, Y. Hu, Z. Li, Y. Shi, Q. Xiong, Z. Liu, Q. Guo, L. Zou, H. Zhang, M. Zhang, F. Ouyang, J. Su, W. Su, J. Xu, H. Lin, J. Sun, J. Peng, H. Jiang, P. Zhou, T. Hu, M. Luo, Y. Zhang, H. Zheng, and J. Xiao, "Viral infection and transmission in a large, well-traced outbreak caused by the SARS-CoV-2 Delta variant," *Nature Communications*, vol. 13, no. 1, p. 460, 2022. DOI: <https://doi.org/10.1038/s41467-022-28089-y>.
- [49] A. W. Byrne, D. McEvoy, A. B. Collins, K. Hunt, M. Casey, A. Barber, F. Butler, J. Griffin, E. A. Lane, C. McAloon, K. O'Brien, P. Wall, K. A. Walsh, and S. J. More, "Inferred duration of infectious period of SARS-CoV-2: rapid scoping review and analysis of available evidence for asymptomatic and symptomatic COVID-19 cases," *BMJ Open*, vol. 10, no. 8, p. e039856, 2020. DOI: <https://doi.org/10.1136/bmjopen-2020-039856>.
- [50] M. Gatto, E. Bertuzzo, L. Mari, "Spread and dynamics of the covid-19 epidemic in italy: Effects of emergency containment measures," *Proceedings of the National Academy of Sciences*, vol. 117, no. 19, pp. 10484–10491, 2020. DOI: <https://doi.org/10.1073/pnas.2004978117>.
- [51] L. Jansen, B. Tegomoh, K. Lange, K. Showalter, J. Figliomeni, B. Abdalhamid, P. C. Iwen, J. Fauver, B. Buss, and M. Donahue, "Investigation of a sars-cov-2 b.1.1.529 (omicron) variant cluster—nebraska, november–december 2021," *Morbidity and Mortality Weekly Report*, vol. 70, no. 51–52, p. 1782, 2021. DOI: <https://doi.org/10.15585/mmwr.mm705152e3>.
- [52] J. Wang, Y. C. Chan, R. Niu, E. W. M. Wong, and M. A. van Wyk, "Modeling the Impact of Vaccination on COVID-19 and Its Delta and Omicron Variants," *Viruses*, vol. 14, no. 7, p. 1482, 2022. DOI: <https://doi.org/10.3390/v14071482>.
- [53] S. Cooper, C. Betsch, E. Z. Sambala, N. Mchiza, and C. S. Wiysonge, "Vaccine hesitancy - a potential threat to the achievements of vaccination programmes in Africa," *Human Vaccines & Immunotherapeutics*, vol. 14, no. 10, pp. 2355–2357, 2018. Epub 2018 May 22. DOI: <https://doi.org/10.1080/21645515.2018.1460987>.