**Supplementary file**

Title: The National COVID-19 Vaccine Model (NCVM): Estimating the impact of variants and vaccines on hospital admissions and deaths in South Africa

Authors: Sheetal Prakash Silal[1,2*], Juliet RC Pulliam[3], Gesine Meyer-Rath[4,5], Lise Jamieson[4] and Harry Moultrie[9]

[1] Modelling and Simulation Hub, Africa (MASHA), Department of Statistical Sciences, University of Cape Town, Cape Town, South Africa
[2] Centre for Tropical Medicine and Global Health, Nuffield Department of Medicine, University of Oxford, Oxford, UK
[3] South African DSI-NRF Centre of Excellence in Epidemiological Modelling and Analysis (SACEMA), Stellenbosch University, Stellenbosch, South Africa
[4] Health Economics and Epidemiology Research Office, Department of Internal Medicine, School of Clinical Medicine, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa
[5] National Institute for Communicable Diseases (NICD), a division of the National Health Laboratory Service, Johannesburg, South Africa

*Corresponding author: Sheetal Prakash Silal (Sheetal.Silal@uct.ac.za)

# NCVM Provincial Model – Technical Overview

This document provides a technical overview of the National COVID-19 Vaccine Model (NCVM) model. The model described in this document is the age-structured, provincial-level NCVM model, created by the South African COVID-19 Modelling Consortium. There is also a separate document, the NCEM Provincial Model Code Guide, that gives an overview of the structure of the model code for a previously published Provincial Model. The NCVM code structure follows a similar design. If there are any queries regarding the model or the code, please contact us on: info@sacovid19mc.co.za.

## Model description

The NCVM is a multi-strain, age-structured, risk-structured, compartmental model of COVID-19 transmission. The model follows a generalised Susceptible-Exposed-Infectious-Removed (SEIR) structure accounting for disease severity (asymptomatic, mild, severe and critical cases), treatment pathways (outpatient services, inpatient non-ICU and ICU beds), non-pharmaceutical intervention impact, vaccination (coverage, effectiveness and waning) and variant emergence and spread (beta, delta and omicron) among age and risk groups in the nine provinces of South Africa. The mechanistic modelling system is depicted in Figure S1.

Key features of the model include:

- Age structure: The population has been subdivided into age classes accounting for age-related differences in susceptibility to and severity of COVID-19 and to allow for age-related disease characteristics and age-targeted vaccination.
- Multi-strain: The wild type SARS-CoV-2 infection and the Beta, Delta and Omicron variants dominating transmission in South Africa's second, third and fourth wave of infections, respectively between 2020 and 2022, have been incorporated. The model structure assumes no co-infection with multiple strains, but allows for levels of reinfection with other variants. Likewise, imperfect natural immunity allows reinfection with the same lineage, with a lower

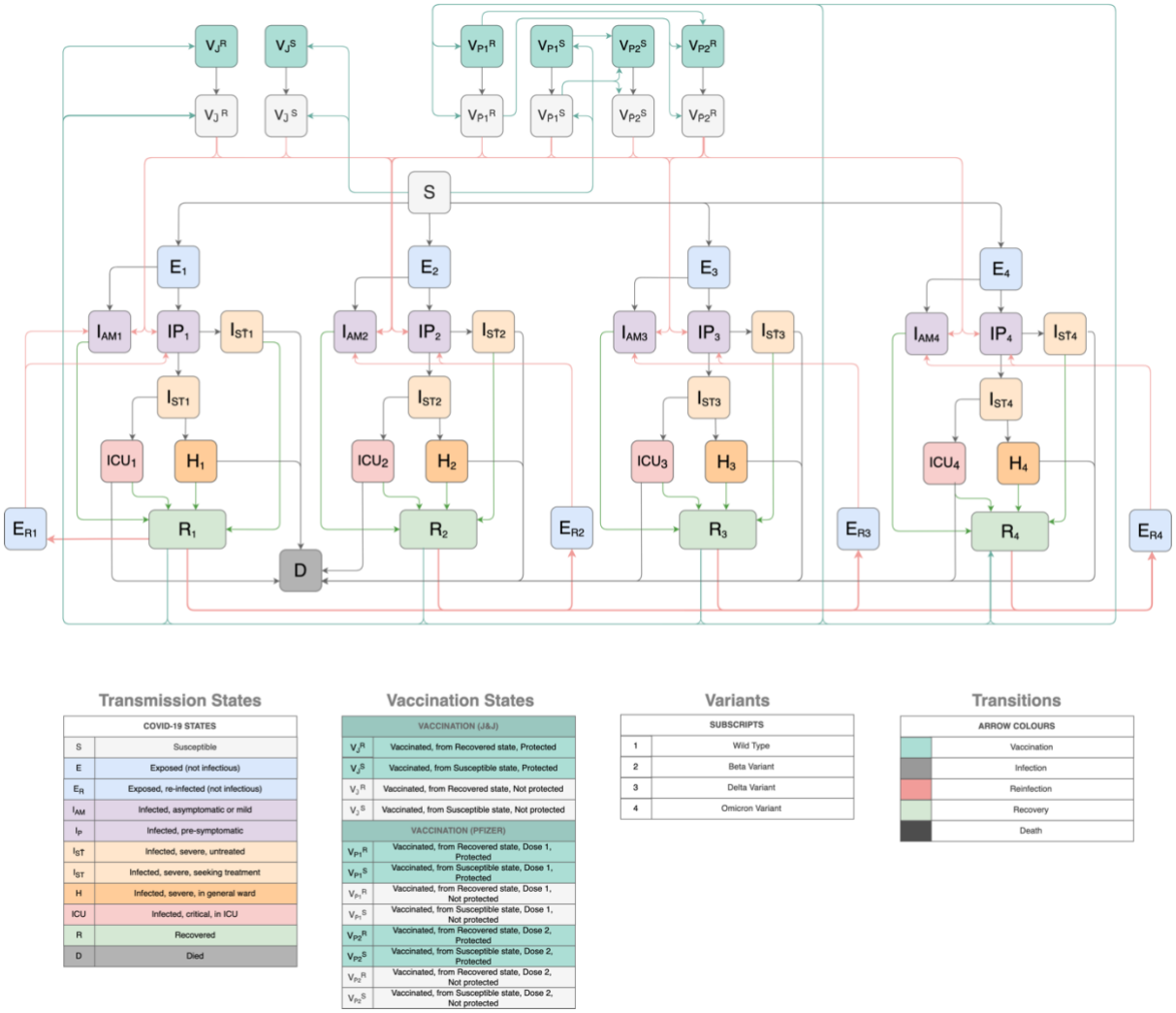
transmissibility. Where relevant, variants are simulated to have immune escape characteristics, reducing protection against infection and severe disease.

- Behavioural response: Change in population contact behaviour and response is incorporated as a driver of transmission. Factors that influence contact rates include holiday travel, large events such as religious and political gatherings, changes in adherence to NPIs such as mask wearing, and changes to government-imposed restriction levels. Given the lack of representative data on the impact of behaviour change, the model incorporates the substantial uncertainty in the timing and the rate of change in both nationally directed and individual behaviour, in particular reduced NPI adherence due to fatigue, as a responsive mechanism to mortality where susceptibility to infection reduces as mortality increases above a threshold.

- Vaccination: The model has been developed to account for vaccination of the susceptible and naturally immune populations with multiple vaccines of 1 or 2 doses (primary series) and a booster dose, allowing for age targeting, vaccine waning, imperfect protection, and the ability to provide distinct levels of protection against infection and severe disease.

- Priority populations: Age-stratified priority populations are defined as Healthcare Workers, Population with Comorbidities, and Everyone Else with the ability for vaccine distribution to be tailored to these populations with respect to the type of vaccine, the timing of vaccination, and population age. The specific contact patterns and disease characteristics of these priority populations are additionally captured.

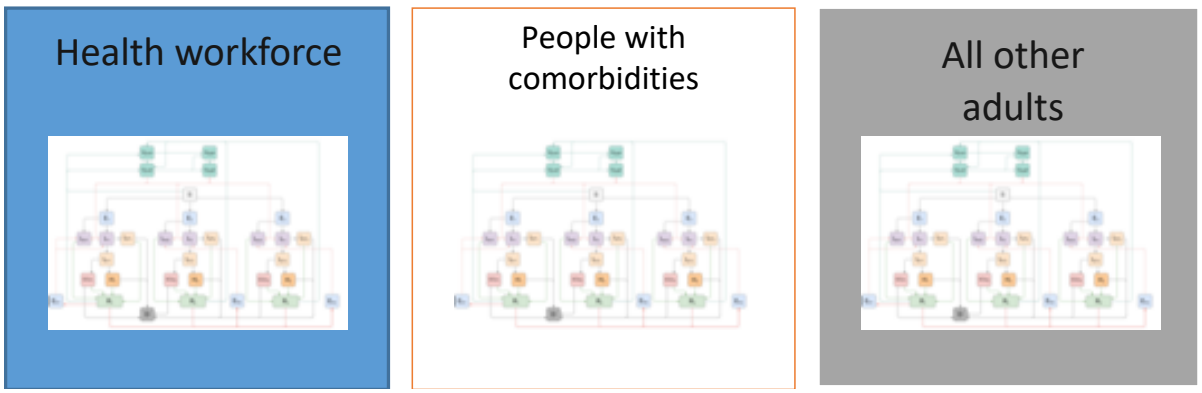
A)




B)

| Age groups (years) | | | | | | |
|---|---|---|---|---|---|---|
| 0-14 | 15-34 | 35-59 | 60-64 | 65-69 | 70-74 | 75+ |

C)




D)

| Province | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| EC | FS | GP | KZN | LP | MP | NC | NW | WC |

Figure S1. The age and risk-structured National COVID-19 Vaccine Model. A) The transmission dynamics for four variants of COVID-19. B) The transmission dynamics in (A) are replicated for each of 7 age bands, and C) each of 3 risk groups (Healthcare workforce, population with co-morbidities, general population). The model encompassing A, B and C is then calibrated to each of the nine provinces of South Africa listed in D).

The model describes the temporal evolution of the following state variables. These state variables represent a single subpopulation amongst all age groups and risk groups.

Table S1: NCVM State variable list and description

| State | Description |
|---|---|
| *S* | Uninfected non-immune |
| *E1* | Wild:infected & exposed |
| *Iam1* | Wild:asymptomatic or mild and infectious |
| *Ip1* | Wild:pre-symptomatic and infectious |
| *IsnotT1* | Wild:severe, destined to be untreated and infectious |
| *Ist1* | Wild:severe, destined to be treated and infectious |
| *H1* | Wild:severe treated in general bed |
| *ICU1* | Wild:severe entry in ICU bed |
| *1* | Wild:removed from infectious stage |
| *Er1* | Wild:infected & exposed with natural immunity |
| *D* | Dead |
| *E2* | New:infected & exposed |
| *Iam2* | New:asymptomatic or mild and infectious |
| *Ip2* | New:pre-symptomatic and infectious |
| *IsnotT2* | New:severe, destined to be untreated and infectious |
| *Ist2* | New:severe, destined to be treated and infectious |
| *H2* | New:severe treated in general bed |
| *ICU2* | New:severe entry in ICU bed |
| *2* | New:removed from infectious stage |
| *Er2* | New:infected & exposed with natural immunity |
| *VP1_S* | Pfizer: 1st dose on Susceptible (Protected) |
| *VPnot1_S* | Pfizer: 1st dose on Susceptible (Not Protected) |
| *VP1_R* | Pfizer: 1st dose on Recovered (Protected) |
| *VPnot1_R* | Pfizer: 1st dose on Recovered (Not Protected) |
| *VP2_S* | Pfizer: 2nd dose on Susceptible (Protected) |
| *VPnot2_S* | Pfizer: 2nd dose on Susceptible (Not Protected) |
| *VP2_R* | Pfizer: 2nd dose on Recovered (Protected) |
| *VPnot2_R* | Pfizer: 2nd dose on Recovered (Not Protected) |
| *VJ_S* | JnJ: on Susceptible (Protected) |
| *VJnot_S* | JnJ: on Susceptible (Not Protected) |
| *VJ_R* | JnJ: on Recovered (Protected) |
| *VJnot_R* | JnJ: on Recovered (Not Protected) |
| *VP3_S* | Pfizer: 3rd dose on Susceptible (Protected) |

*VPnot3_S* Pfizer: 3rd dose on Susceptible (Not Protected)
*VP3_R* Pfizer: 3rd dose on Recovered (Protected)
*VPnot3_R* Pfizer: 3rd dose on Recovered (Not Protected)
*VJ2_S* JnJ: 2nd dose on Susceptible (Protected)
*VJnot2_S* JnJ: 2nd dose on Susceptible (Not Protected)
*VJ2_R* JnJ: 2nd dose on Recovered (Protected)
*VJnot2_R* JnJ: 2nd dose on Recovered (Not Protected)
*IPam1* Wild:asymptomatic or mild and infectious for Pfizer Vaccinated
*IPp1* Wild:pre-symptomatic and infectious for Pfizer Vaccinated
*IPam2* New:asymptomatic or mild and infectious for Pfizer Vaccinated
*IPp2* New:pre-symptomatic and infectious for Pfizer Vaccinated
*IJam1* Wild:asymptomatic or mild and infectious for JnJ Vaccinated
*IJp1* Wild:pre-symptomatic and infectious for JnJ Vaccinated
*IJam2* New:asymptomatic or mild and infectious for JnJ Vaccinated
*IJp2* New:pre-symptomatic and infectious for JnJ Vaccinated

## Key parameter values

Table 2 and 3 below show the values of key parameters used to inform the model. Parameter values have been selected for use by an expert panel of clinicians on the SA COVID-19 Modelling Consortium and updated with inputs from recent South African data where indicated. Parameter values that are provided as ranges only differ by province.

Table S2. Key model parameters

| Parameter | Description | Value | Lower bound | Upper bound | Source |
|---|---|---|---|---|---|
| *Vaccination parameters* | | | | | |
| vstartJ | Day since start of simulation of Vaccination Sisonke Trial (Jansen) | 138 | - | - | https://sacoronavirus.co.za/latest-vaccine-statistics/ |
| vstartP | Day since start of simulation of Vaccination Dose 2 (Pfizer) | 229 | - | - | https://sacoronavirus.co.za/latest-vaccine-statistics/ |
| vdelay | rate of delay after vaccination till protection against severe infection develops (days) | 1/14 days | | | Polack et al (2020) |
| epsP_S | Pfizer: effectiveness of protection against infection for 1 dose in naïve population | 0.57 | 0.50 | 0.63 | Pouwels et al (2021) |
| epsP_R | Pfizer: effectiveness of protection against infection for 1 dose in previously infected population | 0.91 | 0.84 | 0.95 | Pouwels et al (2021) |
| epsJ_S | JJ: effectiveness of protection against infection for 1 dose in naïve population | 0.35 | 0.31 | 0.39 | unpublished |
| epsJ_R | JJ: effectiveness of protection against infection for 1 dose in previously infected population | 0.91 | 0.84 | 0.95 | Assumption; same as epsP_R |
| epsJ_S2 | JJ: effectiveness of protection against infection for 2 dose in naïve population | 0.05 | | | Gray et al (2021) |

| Parameter | Description | Value | Lower bound | Upper bound | Source |
|---|---|---|---|---|---|
| epsJ_R2 | JJ: effectiveness of protection against infection for 2 dose in previously infected population | 0.05 | | | Assumption; same as epsJ_S2 |
| epsP_S2 | Pfizer: effectiveness of protection against infection for 2 doses in naïve population | 0.85 | 0.79 | 0.90 | Pouwels et al (2021) |
| epsP_R2 | Pfizer: effectiveness of protection against infection for 2 doses in previously infected population | 0.93 | 0.87 | 0.96 | Pouwels et al (2021) |
| epsP_S3 | Pfizer: effectiveness of protection against infection for 3 doses in naïve population | 0.669 | 0.661 | 0.676 | Andrews et al (2022b) |
| epsP_R3 | Pfizer: effectiveness of protection against infection for 3 doses in previously infected population | 0.669 | 0.661 | 0.676 | Assumption; same as epsP_S3 |
| sevP_1 | Pfizer: VE against severe infection after 1 dose | 0.92 | 0.85 | 0.95 | Andrews et al (2022a) |
| sevP_2 | Pfizer: VE against severe infection after 2 dose | 0.97 | 0.92 | 0.99 | Andrews et al (2022a) |
| sevP_3 | Pfizer: VE against severe infection after 3 dose | 0.91 | 0.79 | 0.96 | Chemaitelly et al (2022) |
| sevJ | JJ: VE of 1 dose against severe infection | 0.83 | 0.80 | 0.87 | unpublished |
| sevJ2 | JJ: VE of 2 doses against severe infection | 0.70 | | | Gray et al 2022 (https://www.nejm.org/doi/full/10.1056/NEJMc2202061) |
| omega | Waning rate per dose across vaccines and immune history (p.a.) | 2 | | | Andrews et al (2022a) |

* A full list of parameters are available in the code.

**References**


1. Andrews, N., Tessier, E., Stowe, J., Gower, C., Kirsebom, F., Simmons, R., ... & Lopez Bernal, J. (2022). Duration of protection against mild and severe disease by Covid-19 vaccines. *New England Journal of Medicine*, *386*(4), 340-350.
2. Andrews, N., Stowe, J., Kirsebom, F., Toffa, S., Rickeard, T., Gallagher, E., ... & Lopez Bernal, J. (2022). Covid-19 vaccine effectiveness against the Omicron (B. 1.1. 529) variant. *New England Journal of Medicine*, *386*(16), 1532-1546.
3. Chemaitelly, H., Ayoub, H. H., AlMukdad, S., Coyle, P., Tang, P., Yassine, H. M., ... & Abu-Raddad, L. J. (2022). Duration of mRNA vaccine protection against SARS-CoV-2 Omicron BA. 1 and BA. 2 subvariants in Qatar. *Nature communications*, *13*(1), 3082.
4. Gray, G. E., Collie, S., Garrett, N., Goga, A., Champion, J., Zylstra, M., ... & Bekker, L. G. (2021). Vaccine effectiveness against hospital admission in South African health care workers who received a homologous booster of Ad26. COV2 during an Omicron COVID19 wave: Preliminary Results of the Sisonke 2 Study. *MedRxiv*, 2021-12.
5. Polack, F. P., Thomas, S. J., Kitchin, N., Absalon, J., Gurtman, A., Lockhart, S., ... & Gruber, W. C. (2020). Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. *New England journal of medicine*, *383*(27), 2603-2615.
6. Pouwels, K.B., Pritchard, E., Matthews, P.C. *et al.* Effect of Delta variant on viral burden and vaccine effectiveness against new SARS-CoV-2 infections in the UK. *Nat Med* **27**, 2127–2135 (2021). https://doi.org/10.1038/s41591-021-01548-7

## Calibration output (October 2020 to September 2023)