

A mechanistic model describing SARS-CoV-2 viral load and antibody response

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Background

- The **Omicron variant** shows increased immune escape but reduced virulence, compared to earlier strains¹.
- Public health efforts is shifting towards protecting **high-risk groups**, such as the elderly and immunocompromised.
- **Widespread vaccination**, including boosters, has provided protection against severe COVID-19
- Elevated antibody levels from boosters enhance virus clearance, making **antiviral effects less apparent**.
- **Models of viral load and antibody dynamics** can help with reassessment of antiviral therapy²

Aim: To develop a mathematical model that integrates viral load and antibody kinetics to elucidate their dynamic relationship during SARS-CoV-2 infection.

Method

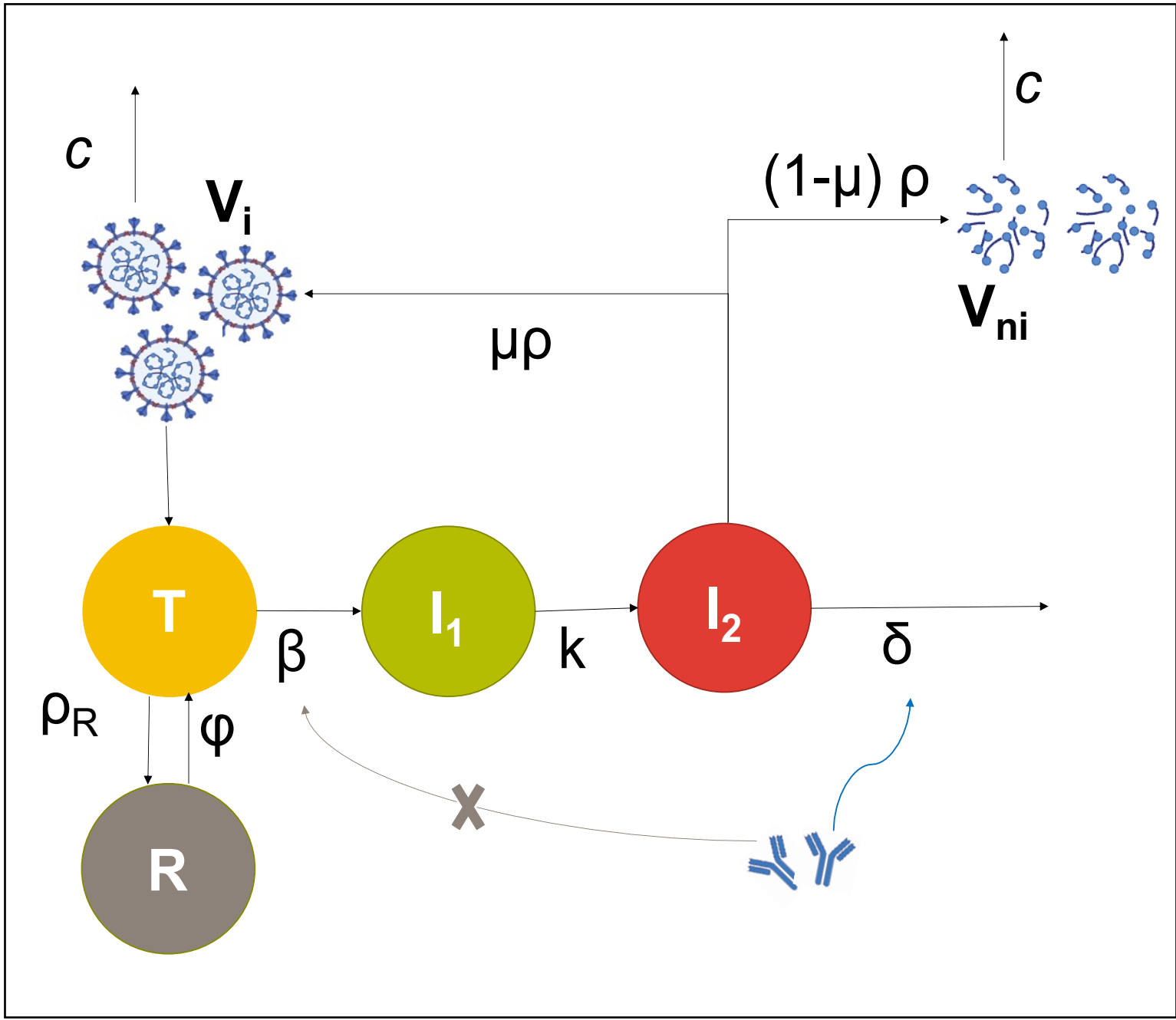
Data

- **PANORAMIC** virology substudy³

Day	1	2	3	4	5	6	7	14
Treatment								
Viral load - intensive group								
Viral load - non-intensive group								
Spike antibody level								
Viral genetic whole genome sequence								

- Outpatient **aged 50 years** or aged 18 - 49 years with **high-risk chronic condition**
- 636 patients from **Usual care group**, 79 allocated to the **intensive sampling group**
- Infected by **Omicron** variant
- Received **0-6 vaccines** (median = 3)

Model



- **Viral dynamic model:** TCLE model + Refractory cell
- **Ab model:** Gompertz model
- **Nlmixr2** (version 3.0.1) - FOCEi

Results

Table 1. Parameter estimation

Parameter	Description	Estimation	RSE(%)	IIV
β	Viral infection rate (copy ⁻¹ mLd ⁻¹)	0.001	1.49	1.4
δ	Loss rate of infected cells(d ⁻¹)	1.11	8.97	0.05
ρ	Production rate of viruses (copies.mL ⁻¹ cells ⁻¹ d ⁻¹)	4450	0.92	0.29
c	Viral clearance rate(d ⁻¹)	10	Fixed	-
k	Conversion rate from eclipse phase to productive cells(d ⁻¹)	4	Fixed	-
μ	Proportion of infectious virus	1×10 ⁻⁴	Fixed	-
ϕ	Conversion rate from target cells to refractory cells (cell ⁻¹ .d ⁻¹)	2.77×10 ⁻⁷	0.19	0.10
ρ_{-R}	Conversion rate from refractory cells to target cells (d ⁻¹)	0.01	1.66	0.10
A_{max}	Maximum spike antibodies (IU.mL ⁻¹)	14800	0.25	0.30
α_1	Asymptote coefficient	0.67	2.86	0.14
α_2	Inherent production rate	0.1	0.97	0.35
t_A	Time of inflexion from infection(d)	2.22	3.34	-
Ea	Maximal antibody effect on infected cell elimination	0.31	1.37	0.20
A_{90}	Spike antibodies producing 90% maximal effect (IU.mL ⁻¹)	1.8 10 5	1.33	0.70
Add.err.vl	Viral load additive error	1.2	-	-
Add.err.ab	Antibody additive error	0.2	-	-

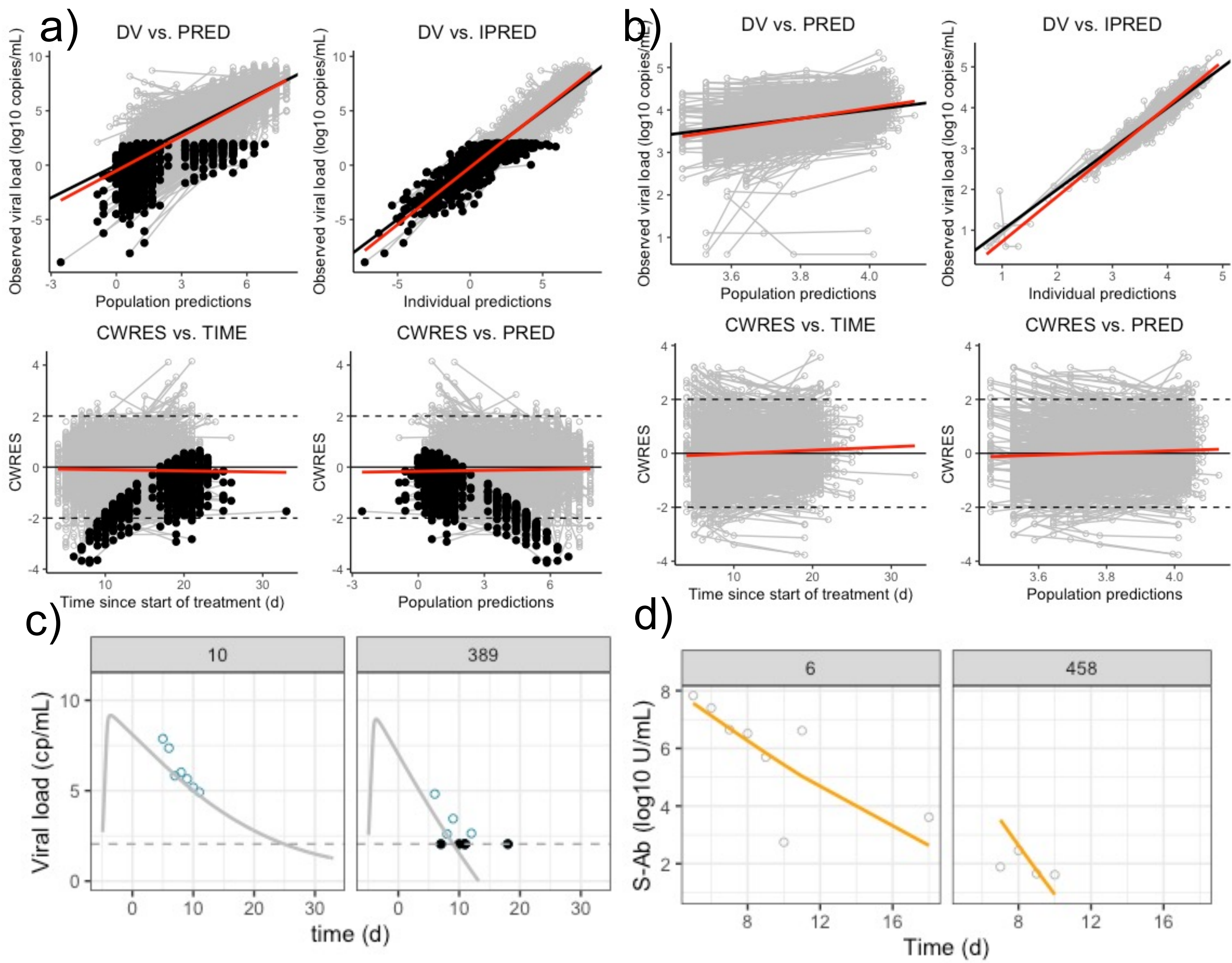


Table 2. Model fit of viral load and antibody levels

- The model well described the viral load and antibody change after infection

Future plan

- Add antiviral PK models to the joint model
- Test covariates, such as age, sex, lung disease etc

Araf Y, Akter F, Tang Y dong, et al. Omicron variant of SARS-CoV-2: Genomics, transmissibility, and responses to current COVID-19 vaccines. *Journal of Medical Virology*. 2022;94(5):1825-1832. doi:10.1002/jmv.27588

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Nguyen BT, Bertrand J, Agyeman AA, et al. A Viroimmunologic Model to Characterize the Antiviral Effect of Molnupiravir in Outpatients Infected With SARS-CoV-2: Implication for Treatment Duration. *The Journal of Infectious Diseases*. Published online April 1, 2025;jiaf158. doi:10.1093/infdis/jiaf158