

## Model Variables

Variable	Definition	Units	Initial condition
$V$	Spike proteins on the vaccine	A.U.	45
$Th1$	$T_H1$ cytokines	A.U.	0
$Th2$	$T_H2$ cytokines	A.U.	0
$F$	Interferon $\gamma$ , IFN $\gamma$	A.U.	0
$I4$	Interleukin-4, IL4	A.U.	0
$CTL$	Cytotoxic T-cell, CD8+	Cell numbers	25000
$A$	Neutralizing antibodies	Antibodies Geometric mean MN $_{50}$	10
$B$	Ig-multiplex	ELISA	0

Table 1: Model variables and units, Arbitrary units (A.U.).

Ig-multiplex (IgG-S1, IgG-S2, IgG-SCLAMP, IgG-RBD, IgG1-S1, IgG1-S2, IgG1-SCLAMP, IgG1-RBD, IgG2-S1, IgG2-S2, IgG2-SCLAMP, IgG2-RBD, IgG3-S1, IgG3-S2, IgG3-SCLAMP, IgG3-RBD, IgG4-S1, IgG4-S2, IgG4-SCLAMP, IgG4-RBD, IgM-S1, IgM-S2, IgM-SCLAMP, IgM-RBD),  $T_H1$  cytokines (IFN $\gamma$ , TNF $\beta$  and IL-2),  $T_H2$  cytokines (IL-4 and IL-13)

## Supplementary Plots

We note that for all cytokine responses, the y-axes are in arbitrary units (A.U.) and depend on the methodology employed in [1].

The population fit values are determined through a fit to all individual data for the two-dose 45  $\mu$ g MF59-adjuvanted spike glycoprotein-clamp vaccine in Monolix. We simultaneously fit to all features in the data set. Predictive simulations based on the determined fit parameters were completed in R using the deSolve library.

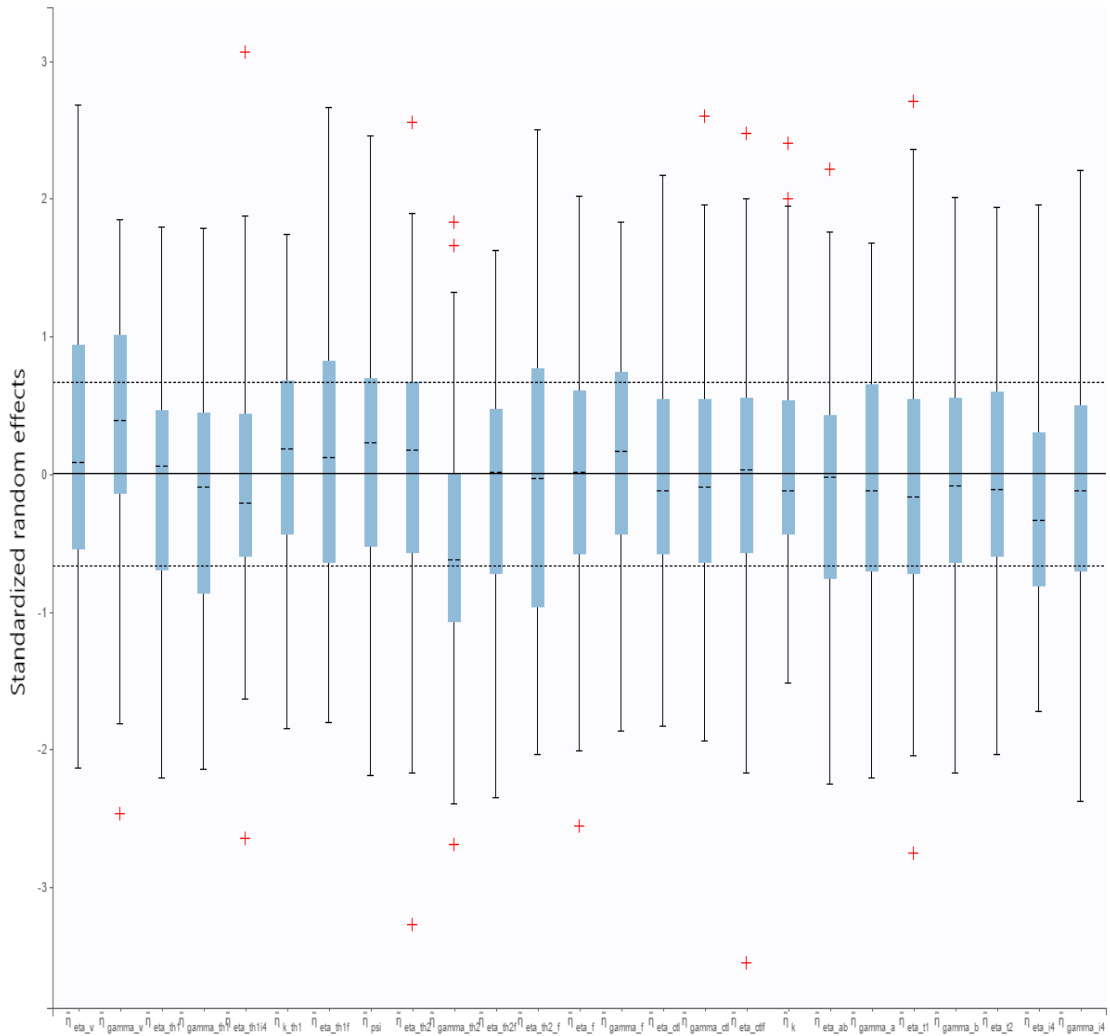


Figure 1: Standardized random effects for all fitted parameters

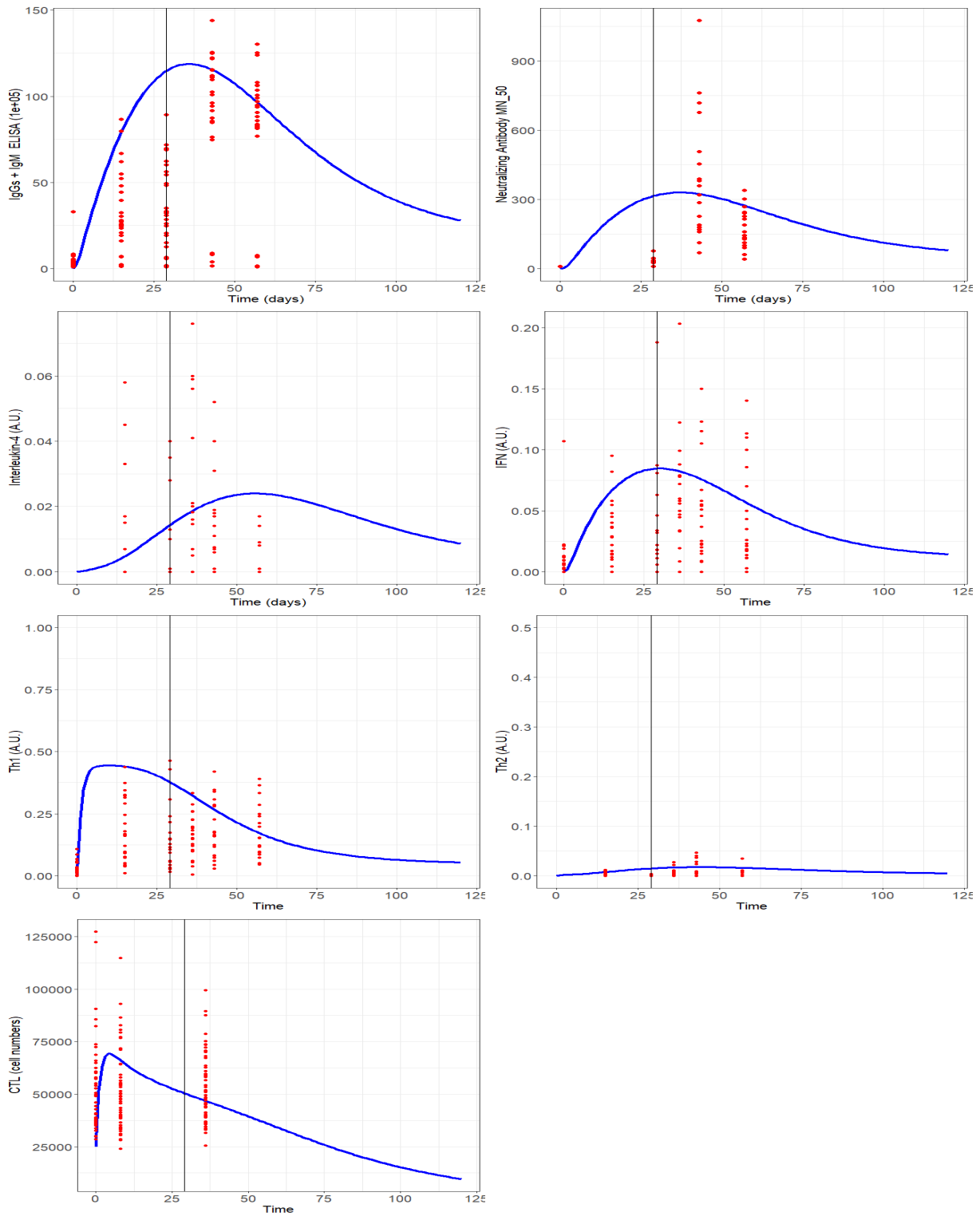


Figure 2: Population fits to the two-dose 45  $\mu\text{g}$  MF59-adjuvanted spike glycoprotein-clamp vaccine for the Ig-multiplex, neutralizing antibodies, IL-4, IFN $_{\gamma}$ , T $_H$ 1 cytokines, T $_H$ 2 cytokines, and cytotoxic T-lymphocytes. Red dots: Observed data [1], Blue curve: Population fits, Vertical line: Dosing times, at days 0 and 28.

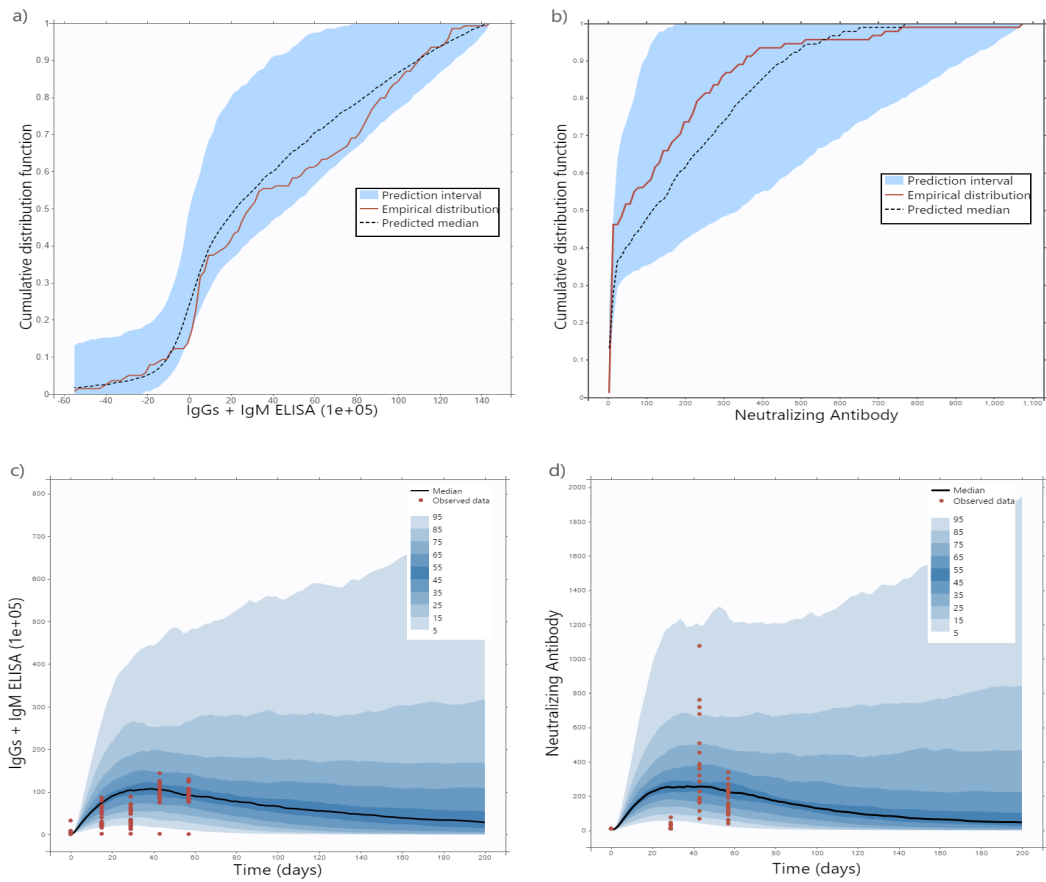


Figure 3: Predictive checks for the two-dose 45 µg MF59-adjuvanted spike glycoprotein-clamp vaccine [1] to fit the Model 1. a) Numerical predictive checks for IgGs + IgM, b) Numerical predictive checks for neutralizing antibody. c) Prediction distributions for Ig-multiplex d) Prediction distributions for neutralizing antibody

Parameter	Definition	Value of 45 $\mu\text{g}$	Confidence Interval	Value of 15 $\mu\text{g}$	Comment
$\psi$	Adjuvant	0.0948	[0 , 0.388]	0.0948	Fitted
$\eta_v$	Vaccine and antibody binding rate	1e-6	NA	1e-6	[2]
$\gamma_v$	Vaccine clearance rate	0.75	[0.603 , 1.463]	0.06	Fitted
$\eta_{th1}$	$T_H1$ cytokines activation rate by vaccine	0.00678	[0.001 , 0.013]	0.0052	Fitted
$\eta_{th1_f}$	$T_H1$ cytokines activation rate by interferon- $\gamma$	0.044	[0.039, 0.066]	0.00023	Fitted
$\beta_{th1,i4}$	$T_H1$ cytokines inhibition rate by interleukin-4	0.85	[0.739 , 0.869]	0.66	Fitted
$k_{th1}$	$T_H1$ duplication threshold due to Interleukin-4	0.426	NA	0.42	Chosen
$\gamma_{th1}$	$T_H1$ cytokines clearance rate	0.000956	[0, 0.001]	0.00069	Fitted
$\eta_{th2}$	$T_H2$ cytokines activation rate by vaccine	2.78e-5	[2.1e-05, 4.2e-05]	3.2e-6	Fitted
$\eta_{th2_f}$	$T_H2$ cytokines activation rate by interferon- $\gamma$	0.017	[0.013 , 0.017]	0.017	Fitted
$\beta_{th2_f}$	$T_H2$ cytokines inhibition rate by interferon- $\gamma$	0.059	[0.002, 0.071]	0.0059	Fitted
$\gamma_{th2}$	$T_H2$ cytokines clearance rate	0.07	[0, 0.152]	0.033	Fitted
$\eta_f$	Interferon- $\gamma$ activation rate by $T_H1$	0.0181	[0.016 , 0.022]	0.018	Fitted
$\gamma_f$	Interferon- $\gamma$ clearance rate	0.0796	[0.066 , 0.083]	0.07	Fitted
$\eta_{i4}$	Interleukin-4 activation rate by $T_H2$	0.138	[0.122 , 0.16]	0.1	Fitted
$\gamma_{i4}$	Interleukin-4 clearance rate	0.0913	[0.076 , 0.878]	0.02	Fitted
$\eta_{ctl}$	Cytotoxic T-cell activation rate by vaccine	800	[263.891 , 1503.92]	73.27	Fitted
$\eta_{ctl_f}$	Cytotoxic T-cell stimulation rate by Interferon- $\gamma$	110	[21.105 , 464.489]	3.82	Fitted
$k_{ctl}$	Cytotoxic T-cell duplication threshold rate due to interferon- $\gamma$	600	NA	600	[3]
$\gamma_{ctl}$	Cytotoxic T-cell clearance rate	0.026	[0.011 , 0.027]	0.0055	Fitted
$\eta_a$	neutralizing antibody activation rate by Ig-multiplex	2.5	[1.049 , 2.985]	1.83	Fitted
$\gamma_a$	Neutralizing antibody clearance rate	0.90	[0.90 , 0.932]	0.35	Fitted
$\eta_{b_{th1}}$	Ig-multiplex activation rate by $T_H1$ cytokines	18	[16.118 , 21.935]	0.64	Fitted
$\eta_{b_{th2}}$	Ig-multiplex activation rate by $T_H2$ cytokines	6	[4.553 , 6.908]	0.31	Fitted
$\gamma_b$	Ig-multiplex clearance rate	0.05	[0.013 , 0.06]	0.047	Fitted

Table 2: Population fitted values of the model parameters for the two-dose MF59-adjuvanted spike glycoprotein-clamp vaccine.

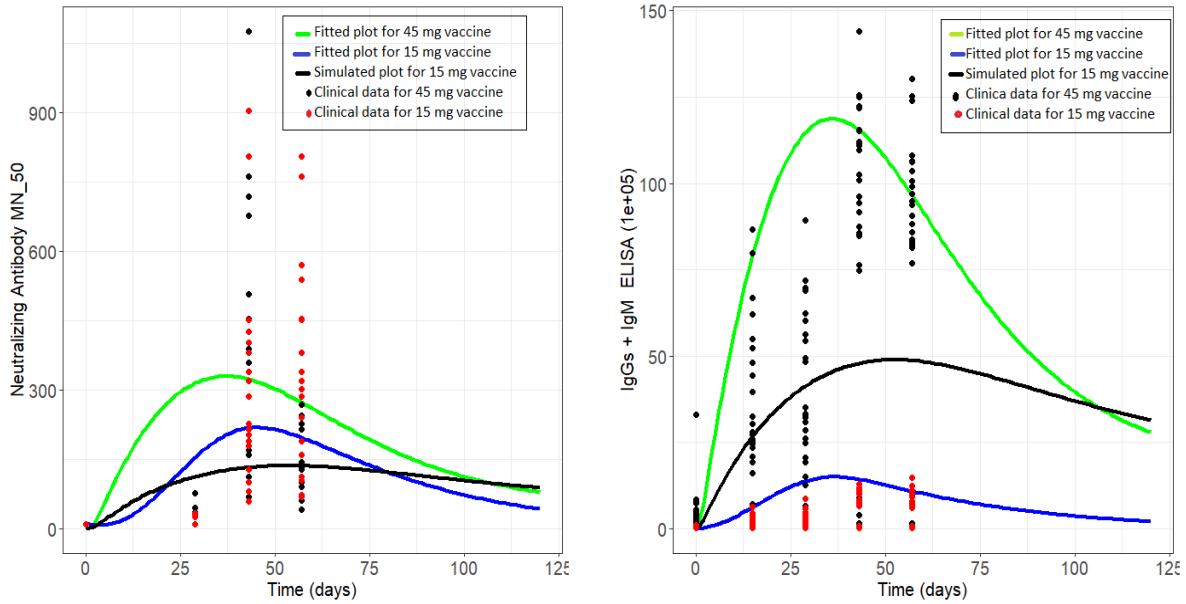


Figure 4: Population fits to the two-dose 15, 45  $\mu\text{g}$  MF59-adjuvanted spike glycoprotein-clamp vaccine for the Ig-multiplex, neutralizing antibodies. Red dots: Observed data [1], Blue curve: Population fits, Vertical line: Dosing times, at days 0 and 28. Black curve: simulated plot of 15 $\mu\text{g}$  with 45 $\mu\text{g}$ -vaccine model parameters

## References

- [1] Keith J Chappell, Francesca L Mordant, Zheyi Li, Danushka K Wijesundara, Paula Ellenberg, Julia A Lackenby, Stacey TM Cheung, Naphak Modhiran, Michael S Avumegah, Christina L Henderson, et al. Safety and immunogenicity of an mf59-adjuvanted spike glycoprotein-clamp vaccine for sars-cov-2: a randomised, double-blind, placebo-controlled, phase 1 trial. *The Lancet Infectious Diseases*, 2021.
- [2] Andreas Handel, Laura E Liao, and Catherine AA Beauchemin. Progress and trends in mathematical modelling of influenza a virus infections. *Current Opinion in Systems Biology*, 12:30–36, 2018.
- [3] Suzan Farhang-Sardroodi, Chapin S Korosec, Samaneh Gholami, Morgan Craig, Iain R Moyles, Mohammad Sajjad Ghaemi, Hsu Kiang Ooi, and Jane M Heffernan. Analysis of host immunological response of adenovirus-based covid-19 vaccines. *Vaccines*, 9(8):861, 2021.