28/11/2024

How prior immunity impacted the deadly second wave of SARS-CoV-2 in Manaus

By: Jan Paul van Meenen

Who am I?

Master's: currently a 2nd-year Master's student in Bioinformatics and Biocomplexity at Utrecht University

Bachelor's: Molecular and Biophysical Life Sciences (MBLS, formerly MLS) at Utrecht University

Took the Biological Modeling course in 2021: one of my favorite courses! (*unbiased opinion*)

- Especially enjoyed the disease spread modeling (Chapter 6)

Jan Paul van Meenen

Who am I?

Research Interests: Exploring immunology and epidemiology through computational methods

Goal this lecture:

- Explaining our research
- Walking you through the ideas and concepts behind it
- Show how material covered in Chapter 6 has real-world application

The story of Manaus

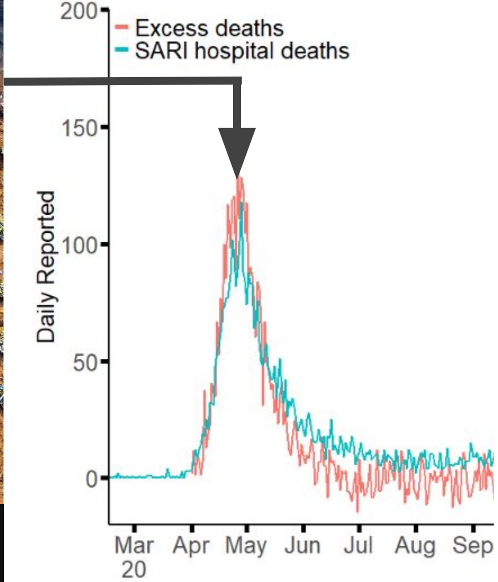
The case of Manaus

Population: 2.2 million

More than the population of Amsterdam, Rotterdam, The Hague and Utrecht combined!

The case of Manaus: devastating initial wave of COVID-19 deaths …

B.1.195 strain



SARI: Severe Acute Respiratory Infection

Nelson, B. W. (2021). *Excess deaths manaus*. Instituto Nacional de Pesquisas da Amazônia (INPA). Available from https://t.co/6g4HHEAuNY
SRAG 2020 - Banco de Dados de Síndrome Respiratória Aguda Grave; 2020. Available from: https://opendatasus.saude.gov.br/dataset/bd-srag-2020
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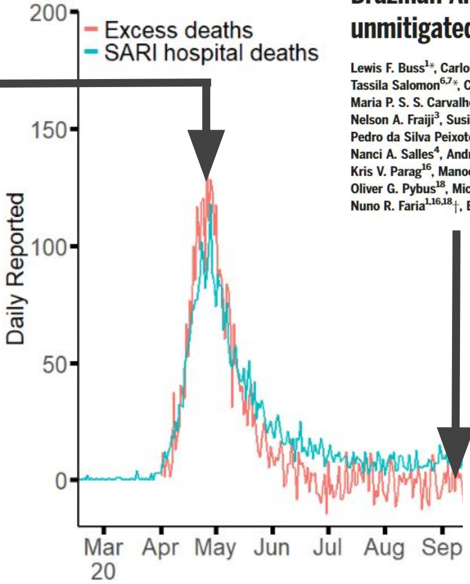

RESEARCH

CORONAVIRUS

Three-quarters attack rate of SARS-CoV-2 in the Brazilian Amazon during a largely unmitigated epidemic

Lewis F. Buss[1]*, Carlos A. Prete Jr.[2]*, Claudia M. M. Abrahim[3]*, Alfredo Mendrone Jr.[4,5]*, Tassila Salomon[6,7]*, Cesar de Almeida-Neto[4,5], Rafael F. O. França[8], Maria C. Belotti[2], Maria P. S. S. Carvalho[3], Allyson G. Costa[3], Myuki A. E. Crispim[3], Suzete C. Ferreira[4,5], Nelson A. Fraiji[3], Susie Gurzenda[9], Charles Whittaker[10], Leonardo T. Kamaura[11], Pedro L. Takecian[11], Pedro da Silva Peixoto[11], Marcio K. Oikawa[12], Anna S. Nishiya[4,5], Vanderson Rocha[4,5], Nanci A. Salles[4], Andreza Aruska de Souza Santos[13], Martirene A. da Silva[3], Brian Custer[14,15], Kris V. Parag[16], Manoel Barral-Netto[17], Moritz U. G. Kraemer[18], Rafael H. M. Pereira[19], Oliver G. Pybus[18], Michael P. Busch[14,15], Márcia C. Castro[9], Christopher Dye[18], Vítor H. Nascimento[2], Nuno R. Faria[1,16,18]†, Ester C. Sabino[1]†

76% of the population infected

Herd-immunity?

Nelson, B. W. (2021). *Excess deaths manaus*. Instituto Nacional de Pesquisas da Amazônia (INPA). Available from https://t.co/6g4HHEAuNY
SRAG 2020 - Banco de Dados de Síndrome Respiratória Aguda Grave; 2020. Available from: https://opendatasus.saude.gov.br/dataset/bd-srag-2020
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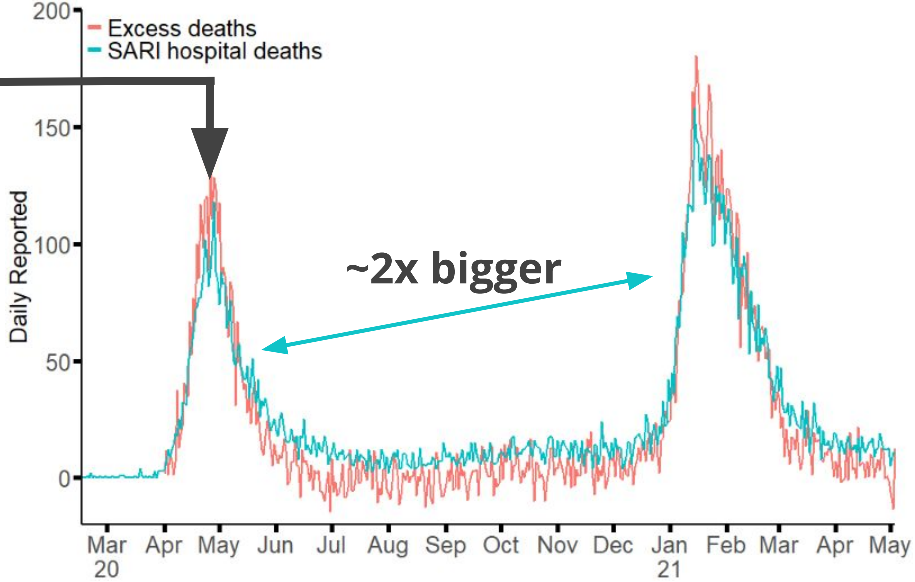
The case of Manaus: devastating initial wave of COVID-19 deaths followed by an even larger secondary wave

B.1.195 strain

Gamma P.1 strain



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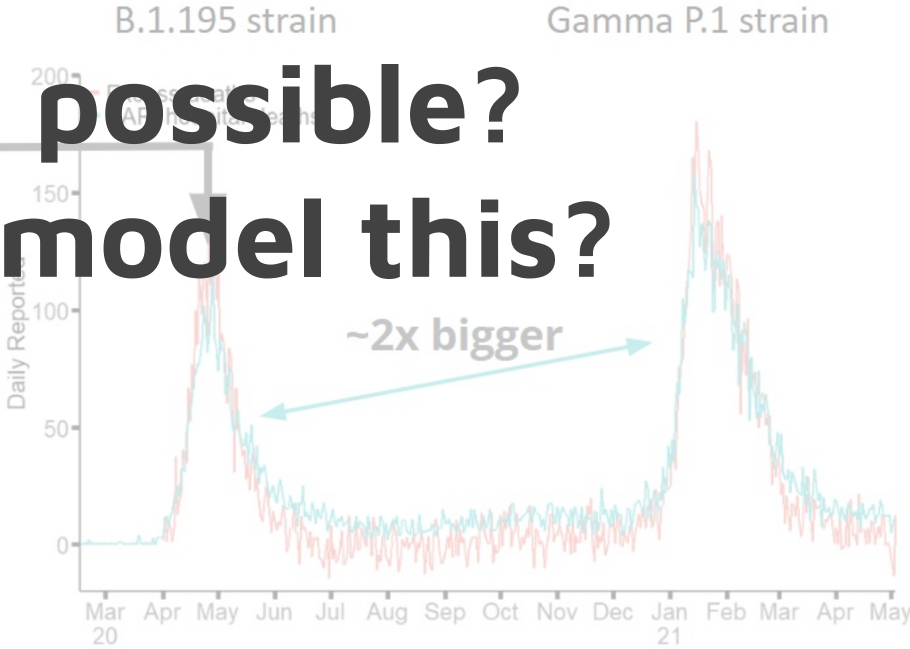
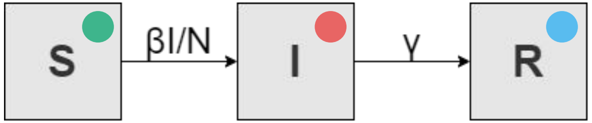


How is this possible?
How can we model this?

Classic epidemiological models

Simple SIR model



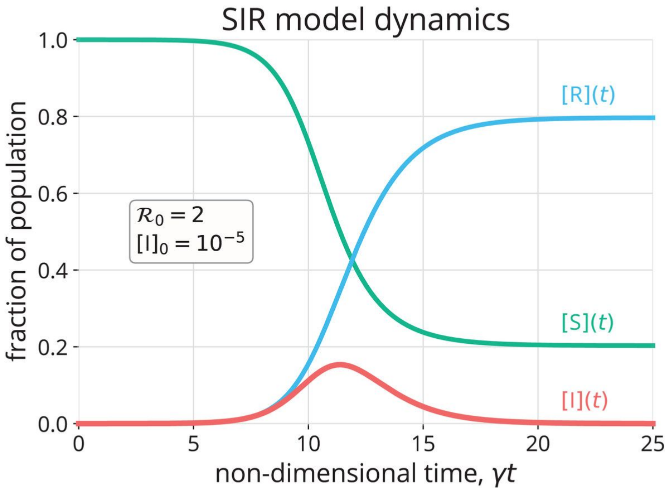
Three states:

- **S**usceptible
- **I**nfected
- **R**ecovered

N = S + I + R

Transition rates:

- Force of infection, β**I/N**
- Removal rate, γ

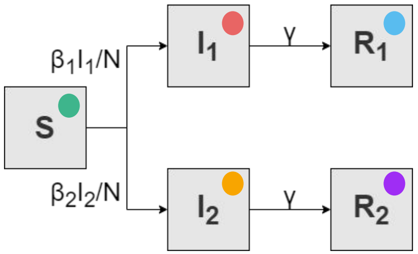


Ordinary Differential Equations (ODE's)

$$\frac{dS}{dt} = -\beta \frac{I}{N} S$$
$$\frac{dI}{dt} = \beta \frac{I}{N} S - \gamma I$$
$$\frac{dR}{dt} = \gamma I$$

Classic epidemiological models: multiple waves

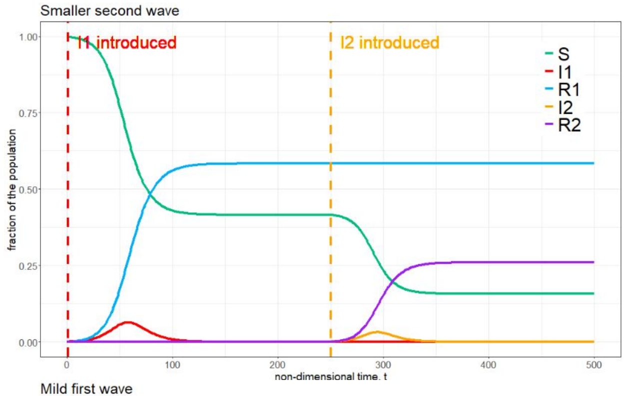
Simple two strain model

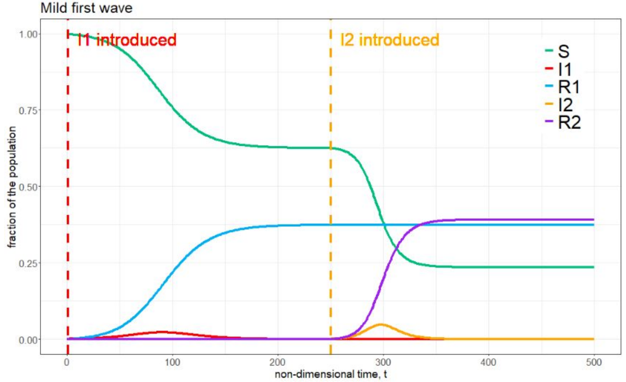


$R_{0,1} < R_{0,2}$

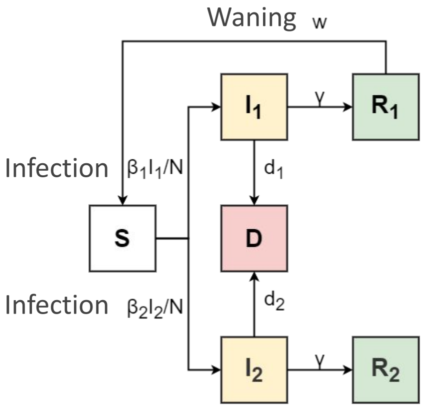
When sequentially introducing strains:
- Secondary waves are generally smaller
- Larger secondary waves are preceded by milder first waves

How can we generate large secondary waves following large primary waves?



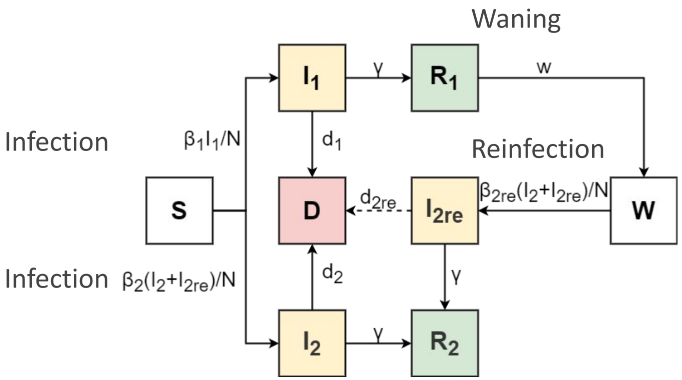


Idea: waned and reinfected individuals may have (very) different properties



SIRS-like model (He et al., 2023)

- Become naive after waning ($R_1 \rightarrow S$)
- Reinfections behave equally to primary infections



Our model (pilot version)

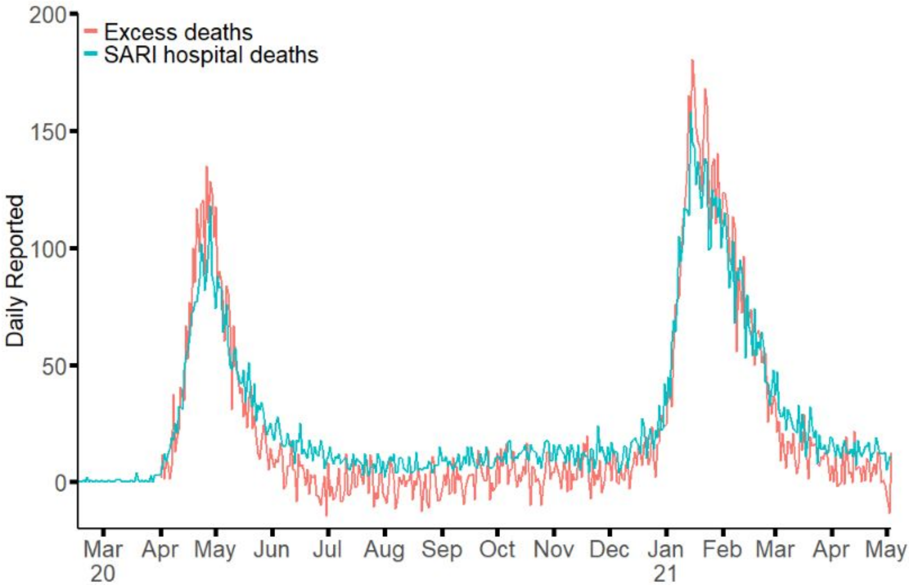
- Second susceptible class (W)
- Reinfection class (I_{2re})
- Waning precedes reinfection:
  - Waning ($R \rightarrow W$)
  - Reinfection ($W_1 \rightarrow I_{2re}$)

To what data can we fit our model?

Available data: disease burden

Disease burden:

- Nelson, 2021:
  - Reported burials & cremations
  - Excess deaths
- SIVEP-Gripe database:
  - Severe acute respiratory infection (SARI) admissions
  - Reporting mandatory in Brazil
  - SARI deaths:
    - Confirmed COVID-19 deaths
    - Excluding known other etiologies



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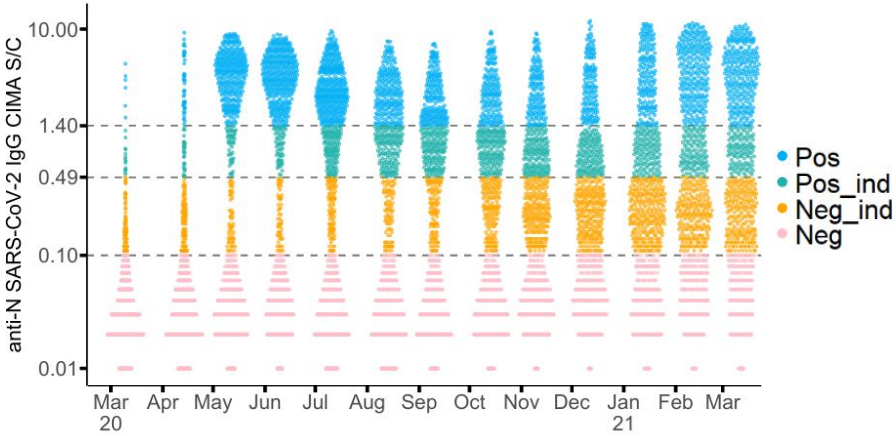
Available data: Antibody levels ...

Prete et al., 2022

Antibody data:

- HEMOAM Blood bank in Manaus
- Serial cross-sectional anti-nucleocapsid (anti-N) antibody levels



Prete, J., Carlos A, Buss, L. F., Whittaker, C., Salomon, T., Oikawa, M. K., Pereira, R. H. M., . . . Sabino, E. C. (2022). SARS-CoV-2 antibody dynamics in blood donors and COVID-19 epidemiology in eight brazilian state capitals: A serial cross-sectional study. eLife, 11 doi:10.7554/eLife.78233

Available data: Antibody levels and seroprevalence

Prete et al., 2022

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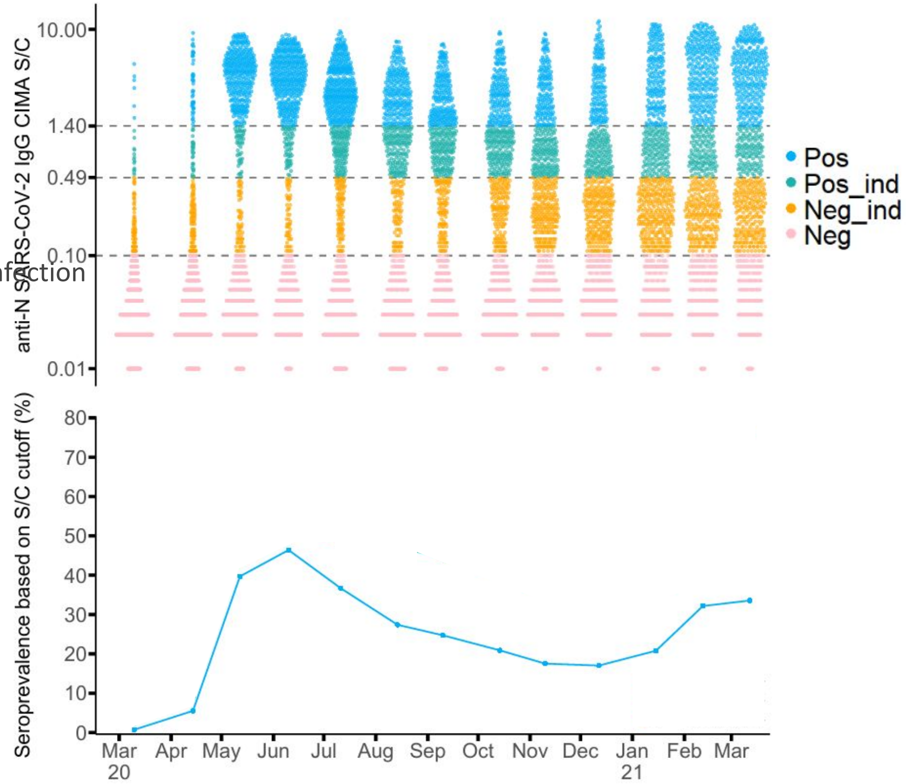
Pos/total

Infection



Seroprevalence:

- Fraction of sampled individuals with positive antibody results
- Proxy of fraction Recovered

R

Prete, J., Carlos A, Buss, L. F., Whittaker, C., Salomon, T., Oikawa, M. K., Pereira, R. H. M., . . . Sabino, E. C. (2022). SARS-CoV-2 antibody dynamics in blood donors and COVID-19 epidemiology in eight brazilian state capitals: A serial cross-sectional study. eLife, 11 doi:10.7554/eLife.78233

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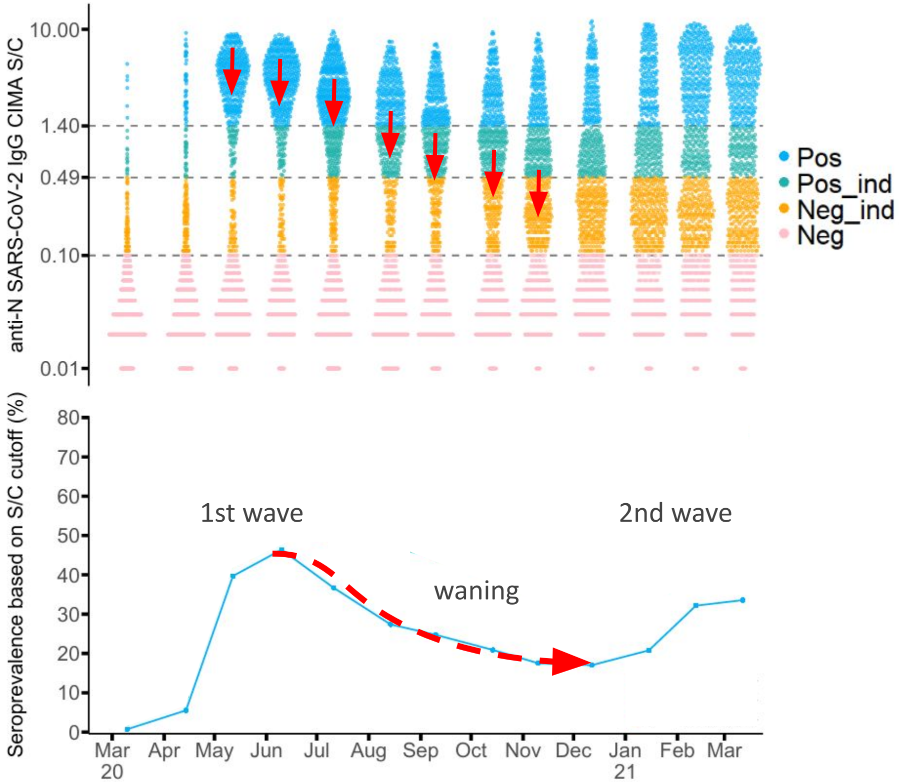
R

Declining antibody levels indicative could indicate waning immunity



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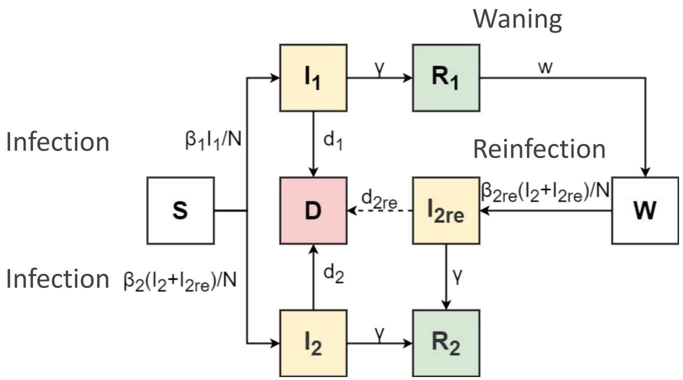
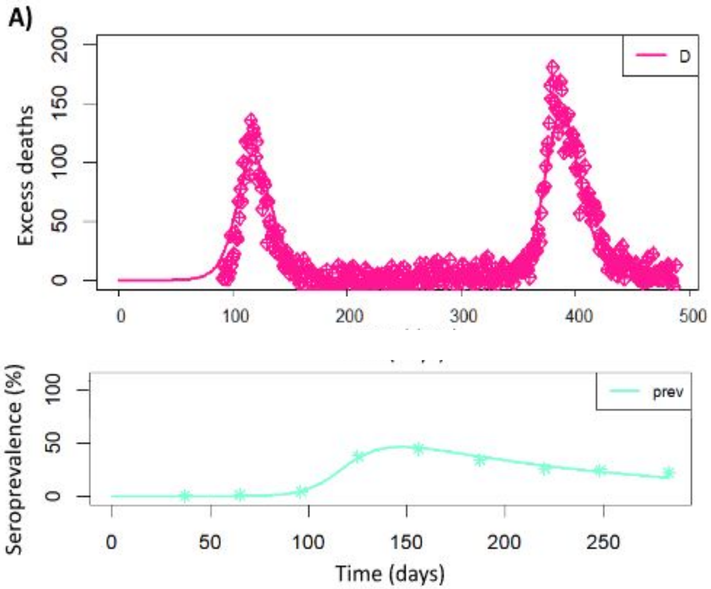
Our model: fits excess deaths and seroprevalence data better than SIRS-like models





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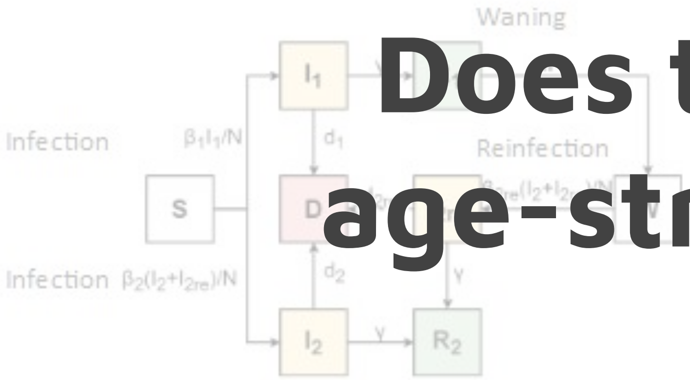

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- Second susceptible class (W)
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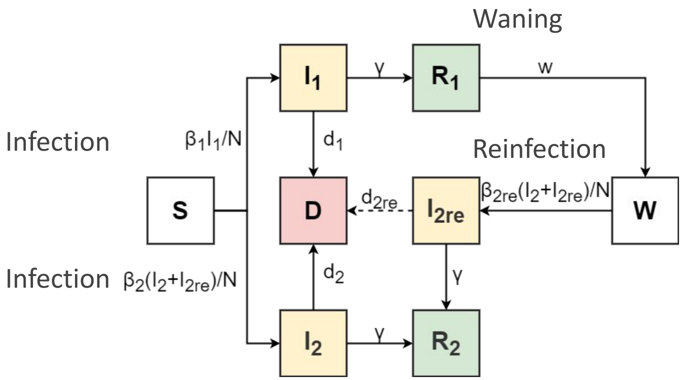
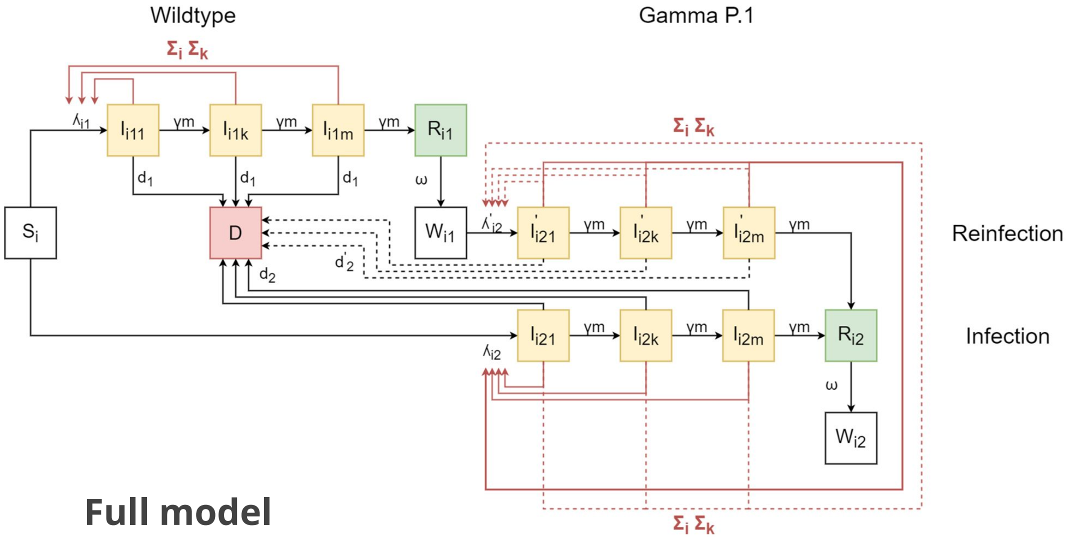
  - Reinfection ($W_1 \to I_{2re}$)

Does this hold in an age-stratified model?

Our model: waning immunity preceding reinfection





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Full model

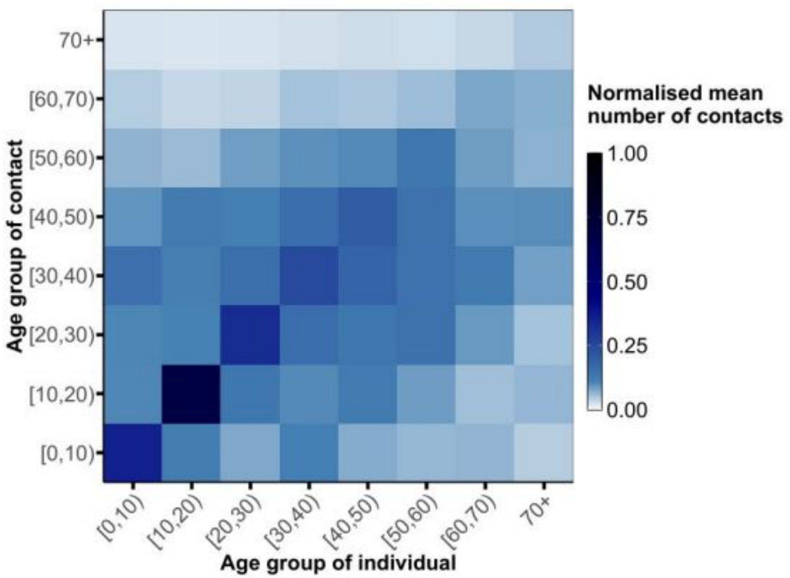
- \+ Stratified by age (8 age groups)
- \+ Erlang-distributed infectious period (J infection stages)
- \+ Contact matrix

Our model: including demography with age stratification, contact-matrices and age-dependent infection fatality rate

Age-specific contact matrix with entries $\{c_{ij}\}$

Describing contact pattern from a person in group j to persons in age group i

Older persons have fewer contacts than younger persons (loneliness epidemic among older adults)

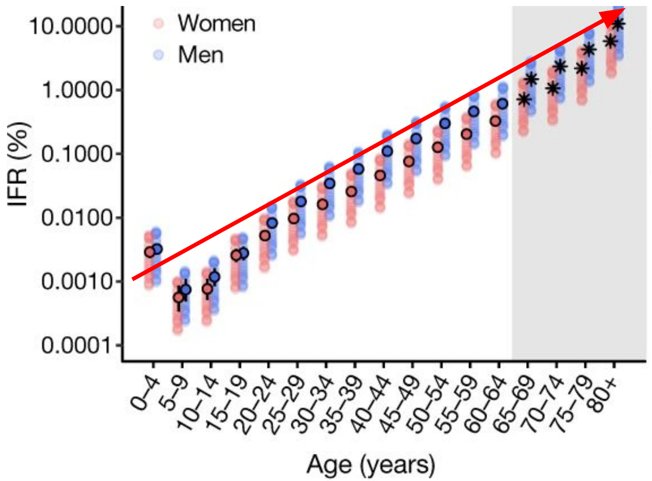


O'Driscoll, M., Ribeiro Dos Santos, G., Wang, L. et al. Age-specific mortality and immunity patterns of SARS-CoV-2. Nature 590, 140–145 (2021). https://doi.org/10.1038/s41586-020-2918-0

Our model: including demography with age stratification, contact-matrices and age-dependent infection fatality rate

Infection fatality rate (IFR) increases log-linearly with age

O'Driscoll et al., 2021



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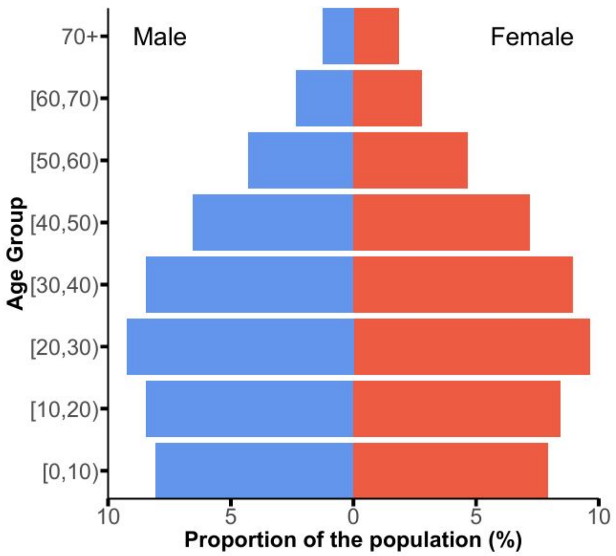
Infection fatality rate (IFR) increases log-linearly with age

~90% IFR variation across geographical locations due to age composition (Levin et al. 2020)

- 82.8% is under 50

Freire et al., 2019



Levin, A. T., Hanage, W. P., Owusu-Boaitey, N., Cochran, K. B., Walsh, S. P., & Meyerowitz-Katz, G. (2020). Assessing the age specificity of infection fatality rates for COVID-19: systematic review, meta-analysis, and public policy implications. European journal of epidemiology, 35(12), 1123–1138. https://doi.org/10.1007/s10654-020-00698-1

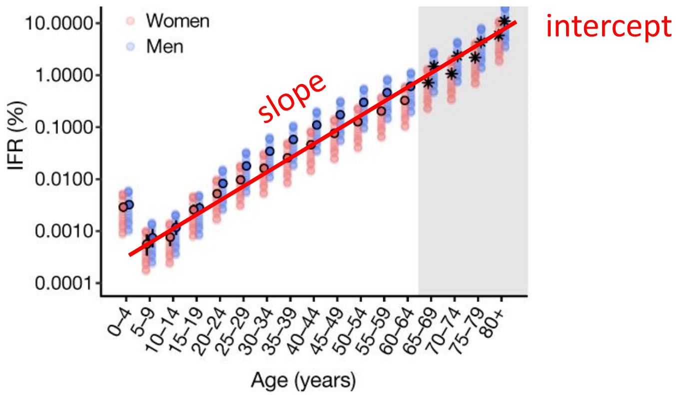
Freire, F. H. M. d. A., Gonzaga, M. R. & Queiroz, B. L. (2019, Projeção populacional municipal com estimadores bayesianos, Brasil 2010 - 2030. In: Sawyer, D.O (coord.). Seguridade Social Municipais. Projeto Brasil 3 Tempos. Secretaria Especial de Assuntos Estratégicos da Presidência da República (SAE/SG/PR) , United Nations Development Programme, Brazil (UNDP) and International Policy Centre for Inclusive Growth. Brasília (IPC-IG).

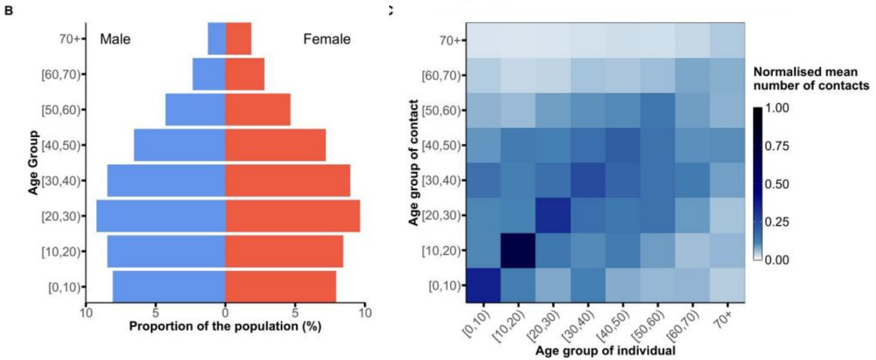
Our model: estimate 12 parameters

Fit model to seroprevalence and hospital deaths data, estimate:

- Infectious period: $1/\gamma$
- Infection rates: $\beta_1, \beta_2, \beta'_2$
- Waning time, $1/\omega$
- Intercepts and slopes of both IFR
  - Scalar for reduction of IFR

Incorporates the population structure for the starting state and uses a fixed age-dependent contact rate





Bob Carpenter, Andrew Gelman, Matthew D. Hoffman, Daniel Lee, Ben Goodrich, Michael Betancourt, Marcus Brubaker, Jiqiang Guo, Peter Li, & Allen Riddell. (2017). Stan: A Probabilistic Programming Language. Journal of Statistical Software, 76(1), 1. https://10.18637/jss.v076.i01

Our model: fit the data with MCMC methods using Stan

Coded using C++

Bayesian inference using Markov chain Monte Carlo (MCMC) with Hamiltonian Monte Carlo (HMC) sampling

- Similar to gradient descent

Relies on assumptions about how observations (data) are generated

Stan

Carpenter et al., 2017

#daily deaths ~ $\mathrm{Poisson}\left(d_{i1}\sum_{k=1}^{m} I_{i1k} + d_{i2}\sum_{k=1}^{m} I_{i2k} + d'_{i1}\sum_{k=1}^{m} I'_{i2k}\right)$

daily positive samples ~ $\mathrm{Binom}\left(Y_i, \frac{R_{i1}(\tau) + R_{i2}(\tau)}{N_i(\tau)}\right), \quad i \in [2, 7]$

Bob Carpenter, Andrew Gelman, Matthew D. Hoffman, Daniel Lee, Ben Goodrich, Michael Betancourt, Marcus Brubaker, Jiqiang Guo, Peter Li, & Allen Riddell. (2017). Stan: A Probabilistic Programming Language. Journal of Statistical Software, 76(1), 1. https://10.18637/jss.v076.i01

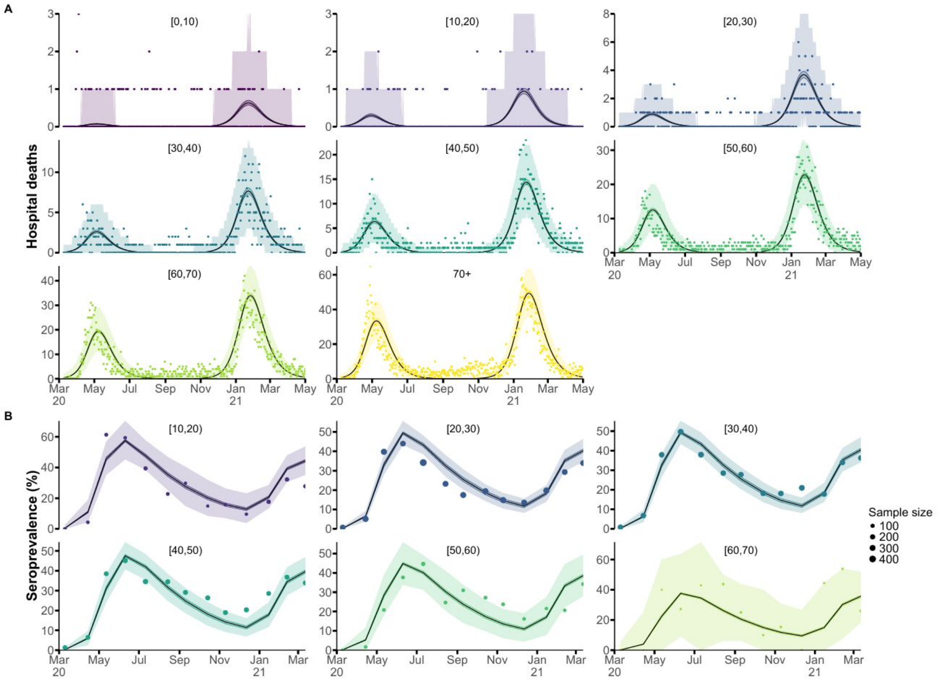
How well does our full model describe the available data?

Result: model cofits death and seroprevalence very well

Our model can describe both waves:

A. Mortality data
- all 8 age groups

B. Seroprevalence data
- 6 available age groups

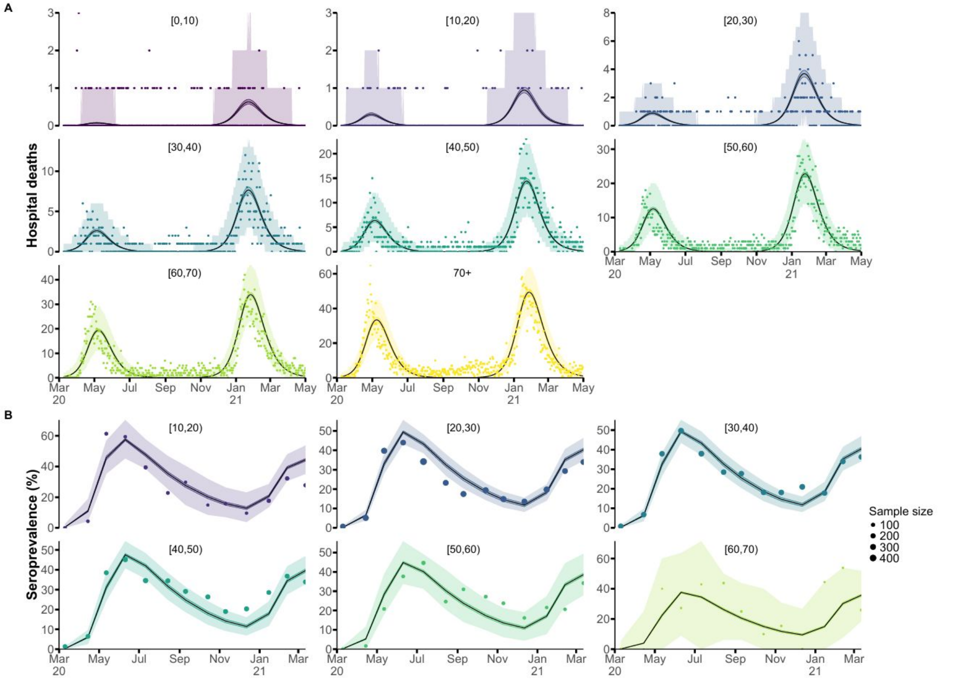


Our model vs. SIRS-like: SIRS-like fails to fit the seroprevalence of the second wave

SIRS-like:

A. Fits mortality data equally well

B. Fails to fit seroprevalence data of the second wave.



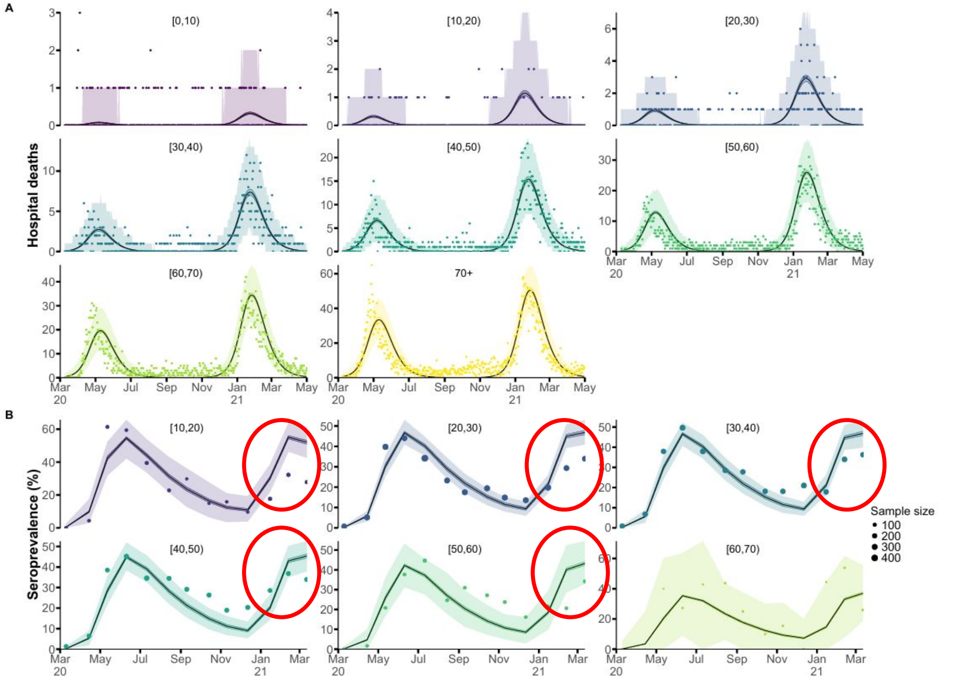
Our model vs. SIRS-like: SIRS-like fails to fit the seroprevalence of the second wave

SIRS-like:

A. Fits mortality data equally well

B. Fails to fit seroprevalence data of the second wave..

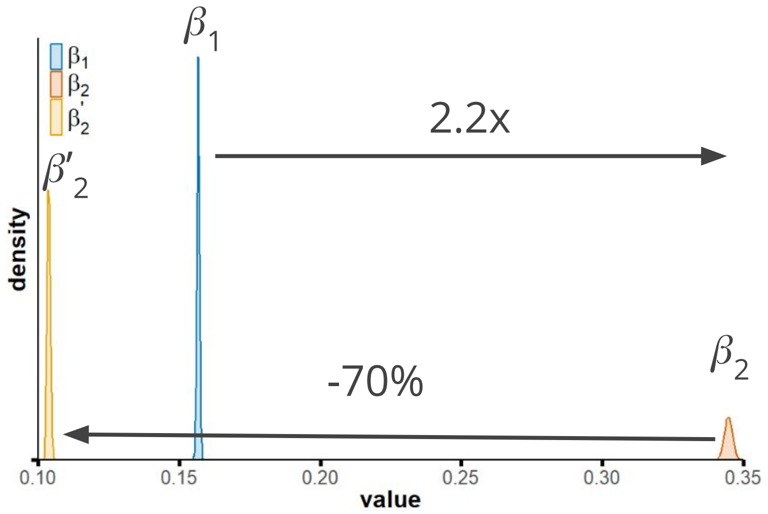
Seroprevalence is important as different assumptions about immunity can result in the similar mortality fits.



Result: Gamma P.1 more transmissible, previous infection reduces susceptibility

- Gamma P.1 ~2.2 times more transmissible than the
- First strain

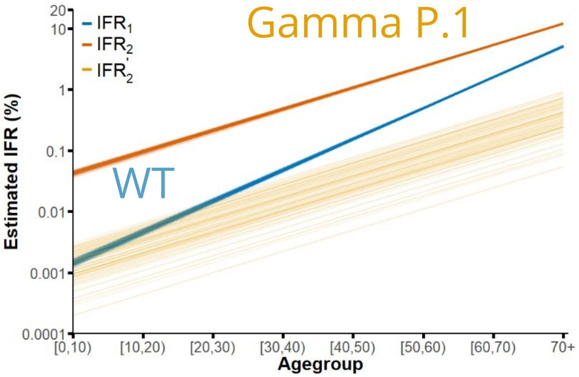
- Cross-immunity reduces Gamma P.1 susceptibility by 70%



Result: Gamma P.1 has increased mortality rates, notably in younger age groups

- First strain IFR:
  - 0.0014% [0,10)
  - 5.1% 70+
- Second strain IFR: (Gamma P.1)
  - 0.037% [0,10)
  - 12.1% 70+

  Notably affects younger age groups



de Souza et al., 2021 Freitas et al., 2021

Nonaka et al., 2021

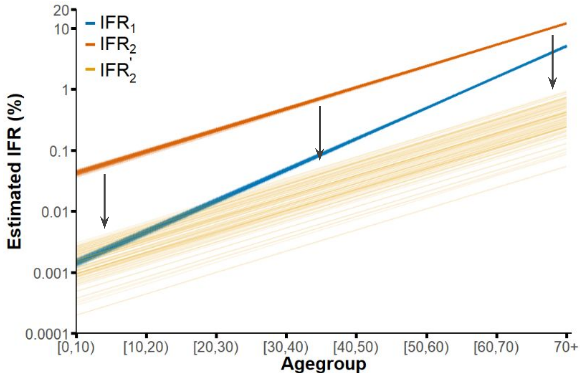
Banho et al., 2022

Sauré et al., 2023

Result: Previous immunity reduces IFR by **100-fold**

- First strain IFR:
  - 0.0014% [0,10)
  - 5.1% 70+
- Second strain IFR: (Gamma P.1)
  - 0.037% [0,10)
  - 12.1% 70+

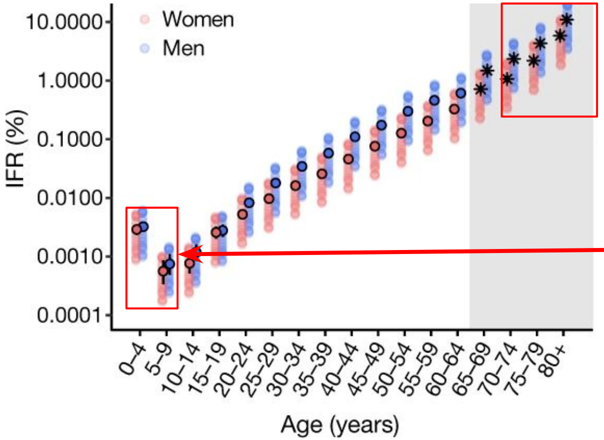
  Notably affects younger age groups
- Previous immunity reduces Gamma P.1 IFR by **93.4 to 99.7%**



Meta-analysis: 90.2% (69.7-97.5%)
(COVID-19 Forecasting Team, 2023)

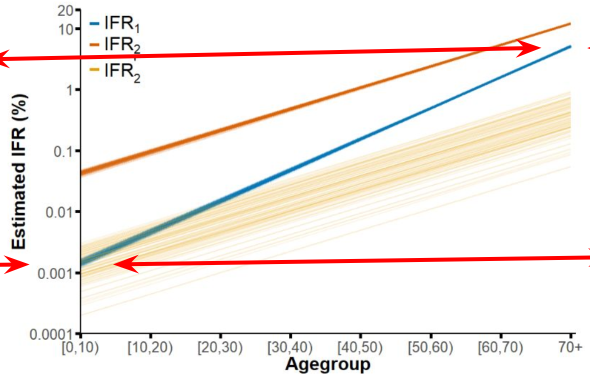
COVID-19 Forecasting Team. Past SARS-CoV-2 infection protection against re-infection: a systematic review and meta-analysis. Lancet. 2023 Mar 11;401(10379):833-842. doi: 10.1016/S0140-6736(22)02465-5. Epub 2023 Feb 16. PMID: 36930674; PMCID: PMC9998097.

Result: First strain IFR estimates in line with meta-analysis IFR estimates



O'Driscoll et al., 2021

● First strain IFR



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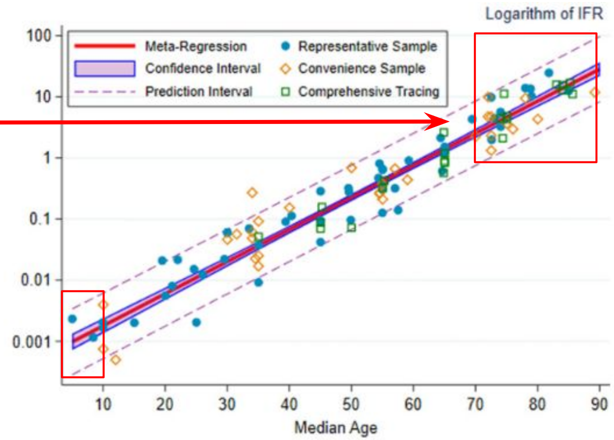


Levin et al., 2020

O'Driscoll, M., Ribeiro Dos Santos, G., Wang, L. et al. Age-specific mortality and immunity patterns of SARS-CoV-2. Nature 590, 140–145 (2021). https://doi.org/10.1038/s41586-020-2918-0

Levin, A. T., Hanage, W. P., Owusu-Boaitey, N., Cochran, K. B., Walsh, S. P., & Meyerowitz-Katz, G. (2020). Assessing the age specificity of infection fatality rates for COVID-19: systematic review, meta-analysis, and public policy implications. European journal of epidemiology, 35(12), 1123–1138. https://doi.org/10.1007/s10654-020-00698-1

How prior immunity impacted the deadly second wave of SARS-CoV-2 in Manaus

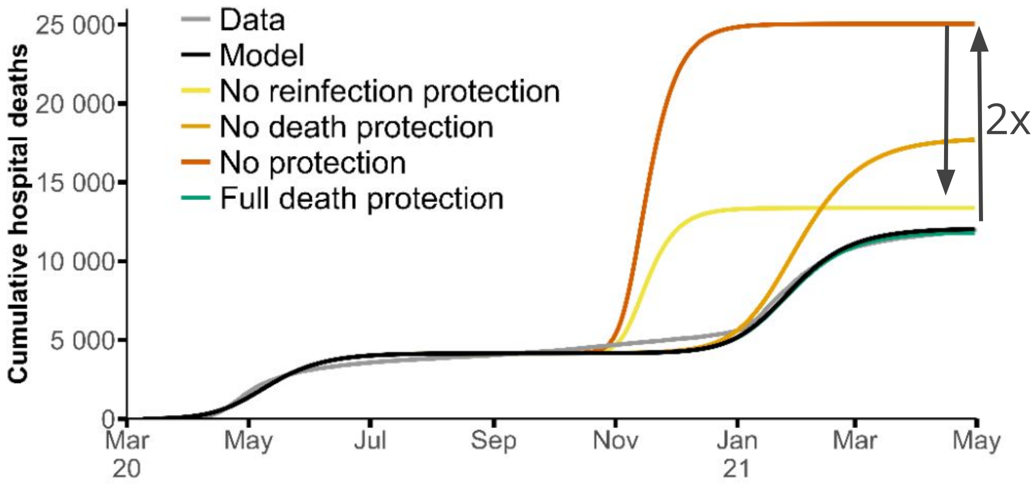
Counterfactual: First wave protected against an even deadlier second wave by reducing the infect

What if previous immunity does not provide protection against reinfection and/or deaths

Three scenarios:

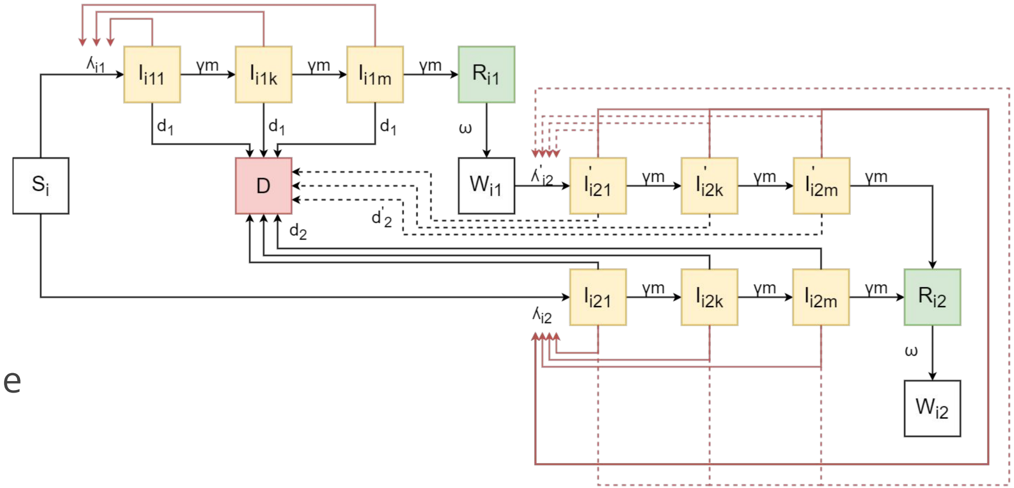
- No protection
- No protection against death
- No protection against reinfection

Without any protection, the cumulative number of deaths would have **doubled**, with about **13 000** additional deaths.



Conclusions

- Adding waning compartment greatly improves the fit:
  - mortality data
  - seroprevalence data
- Model reproduces IFR1 estimates in line in line with literature:
- Gamma P.1 variant:
  - more infectious
  - higher infection fatality rate,
  - affected younger age groups
- Long lasting protective cross-immunity mitigated an even deadlier second wave by greatly reducing the infection fatality rate
  - Even if cross-immunity does not prevent reinfection itself



Carpenter et al., 2017

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Utrecht University

Dr. M. (Michiel) van Boven

UMC Utrecht

Dr. C.H. (Christiaan H.) van Dorp

COLUMBIA
COLUMBIA UNIVERSITY
IRVING MEDICAL CENTER

Questions?

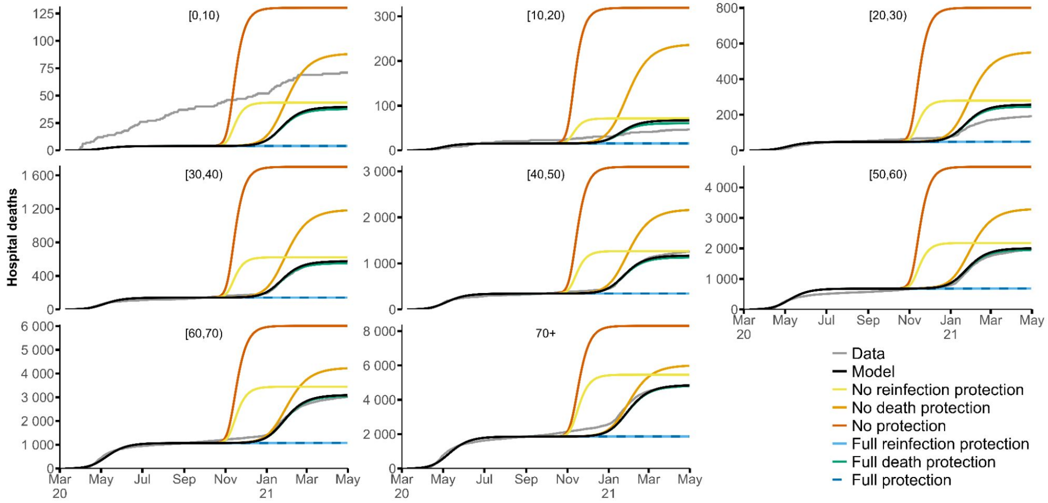
Counterfactual: First wave protected against an even deadlier second wave

What if previous immunity does not provide protection against reinfection and/or deaths

Three scenarios:

- No protection
- No protection against death
- No protection against reinfection

Increased deaths are not equally distributed over the age groups



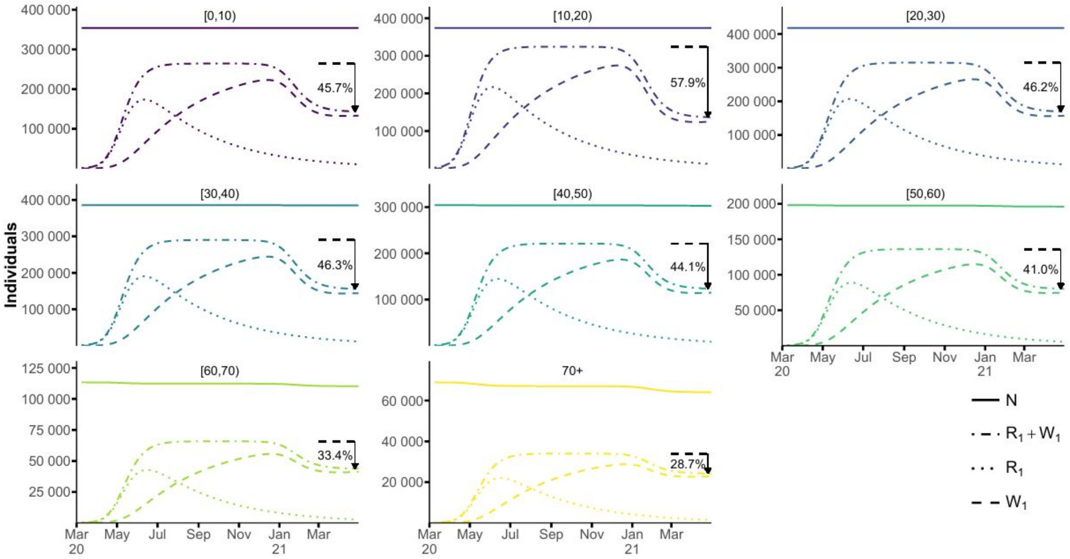
Result: High attack rate after the first wave

First wave attack rate:

- Model: 74.7%
- Buss et al., 2021: 76.0%

Attack rate depends on age group

After first wave: sizeable number of susceptible individuals in older age group



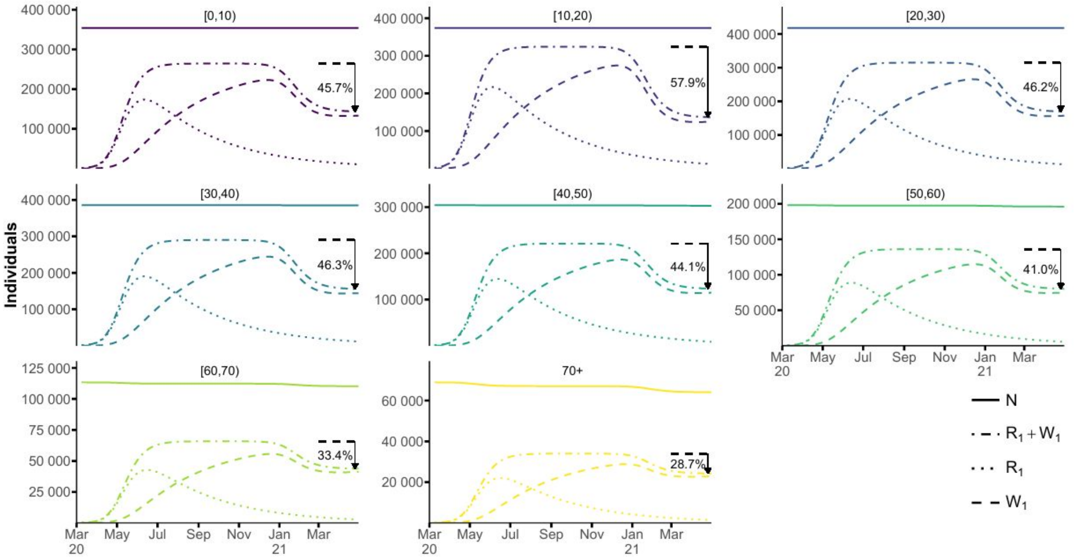
Belotti, M. C., Carvalho, M. P. S. S., Costa, A. G., Crispim, M. A. E., Ferreira, S. C., Fraiji, N. A., Gurzenda, S., Whittaker, C., Kamaura, L. T., Takecian, P. L., da Silva Peixoto, P., Oikawa, M. K., Nishiya, A. S., … Sabino, E. C. (2021). Three-quarters attack rate of SARS-CoV-2 in the Brazilian Amazon during a largely unmitigated epidemic.

Result: Reinfection is common and a driving force in the epidemic of Manaus

Reinfection levels depend on age group

Gamma P.1 reinfection:
- Model: 46.9%
- Prete et al., 2021: 14-50%

Reinfections need not be symptomatic:
- Asymptomatic individuals have similar viral loads
- Gamma P.1 reinfections display viral loads comparable to primary infections (Naveca et al., 2023)

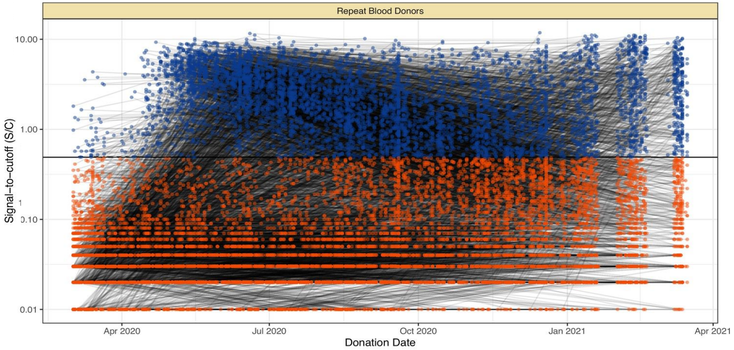


Prete, J., Carlos A, Buss, L. F., Buccheri, R., Abrahim, C. M. M., Salomon, T., Crispim, M. A. E., Oikawa, M. K., Grebe, E., da Costa, A. G., Fraiji, N. A., do P S S Carvalho, M., Whittaker, C., Alexander, N., Faria, N. R., Dye, C., Nascimento, V. H., Busch, M. P., & Sabino, E. C. (2022). Reinfection by the SARS-CoV-2 Gamma variant in blood donors in Manaus, Brazil. BMC Infectious Diseases, 22(1), 127. https://10.1186/s12879-022-07094-y

Naveca FG, Nascimento VA, Nascimento F, Ogrzewalska M, Pauvolid-Corrêa A, Araújo MF, Arantes I, Batista ÉR, Magalhães AÁ, Vinhal F, Mattos TP, Riediger I, Debur MDC, Grinsztejn B, Veloso VG, Brasil P, Rodrigues RR, Rovaris DB, Fernandes SB, Fernandes C, Santos JHA, Abdalla LF, Costa-Filho R, Silva M, Souza V, Costa ÁA, Mejía M, Brandão MJ, Gonçalves LF, Silva GA, de Jesus MS,

Experimental data: Reinfection results in v-shaped antibody curves

Longitudinal signal-to-cutoff (S/C) antibody levels (Prete et al. 2022a)



Prete, J., Carlos A, Buss, L. F., Whittaker, C., Salomon, T., Oikawa, M. K., Pereira, R. H. M., . . . Sabino, E. C. (2022a). SARS-CoV-2 antibody dynamics in blood donors and COVID-19 epidemiology in eight brazilian state capitals: A serial cross-sectional study. eLife, 11 doi:10.7554/eLife.78233

Prete CA Jr, Buss LF, Buccheri R, Abrahim CMM, Salomon T, Crispim MAE, Oikawa MK, Grebe E, da Costa AG, Fraiji NA, do P S S Carvalho M, Whittaker C, Alexander N, Faria NR, Dye C, Nascimento VH, Busch MP, Sabino EC. Reinfection by the SARS-CoV-2 Gamma variant in blood donors in Manaus, Brazil. BMC Infect Dis. 2022 Feb 5;22(1):127. doi: 10.1186/s12879-022-07094-y. PMID: 35123418; PMCID: PMC8817641.

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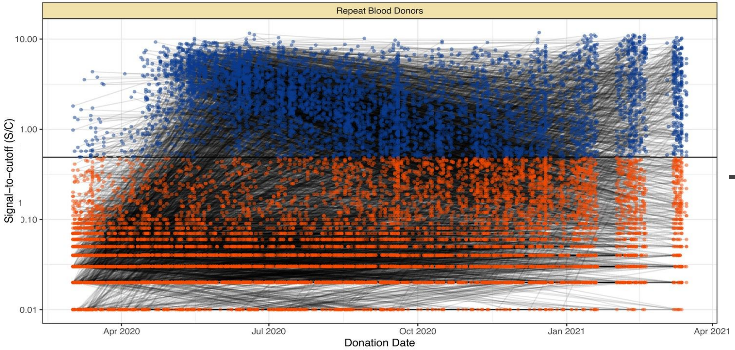
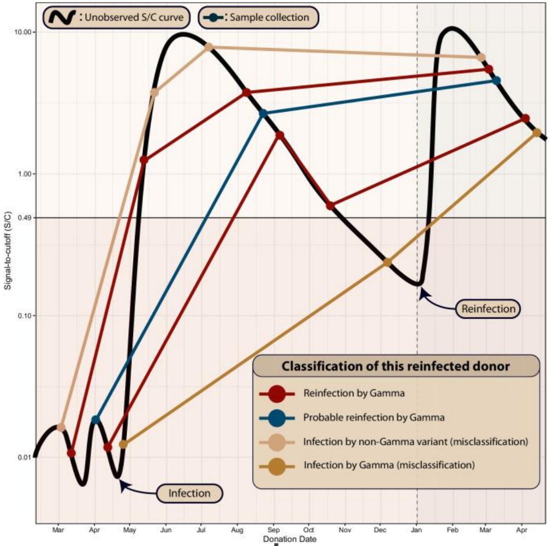
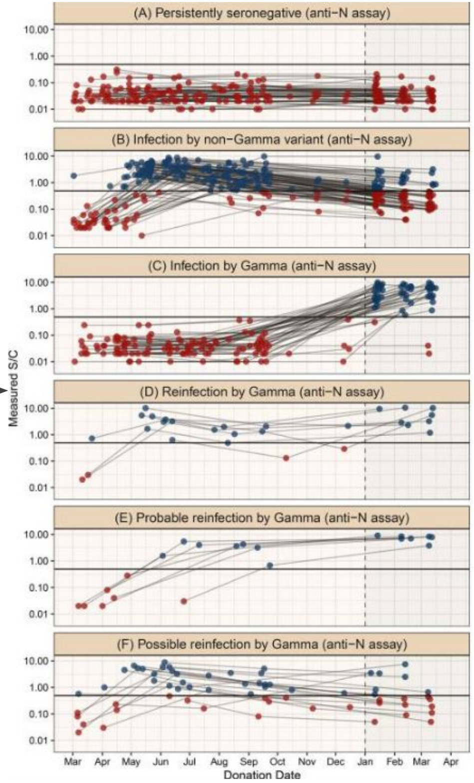






Repeat blood donor classification (Prete et al. 2022b)

Prete, J., Carlos A, Buss, L. F., Whittaker, C., Salomon, T., Oikawa, M. K., Pereira, R. H. M., . . . Sabino, E. C. (2022a). SARS-CoV-2 antibody dynamics in blood donors and COVID-19 epidemiology in eight brazilian state capitals: A serial cross-sectional study. eLife, 11 doi:10.7554/eLife.78233

Prete CA Jr, Buss LF, Buccheri R, Abrahim CMM, Salomon T, Crispim MAE, Oikawa MK, Grebe E, da Costa AG, Fraiji NA, do P S S Carvalho M, Whittaker C, Alexander N, Faria NR, Dye C, Nascimento VH, Busch MP, Sabino EC. Reinfection by the SARS-CoV-2 Gamma variant in blood donors in Manaus, Brazil. BMC Infect Dis. 2022 Feb 5;22(1):127. doi: 10.1186/s12879-022-07094-y. PMID: 35123418; PMCID: PMC8817641.

Experimental data: cellular response remains strong and protects against severe outcomes

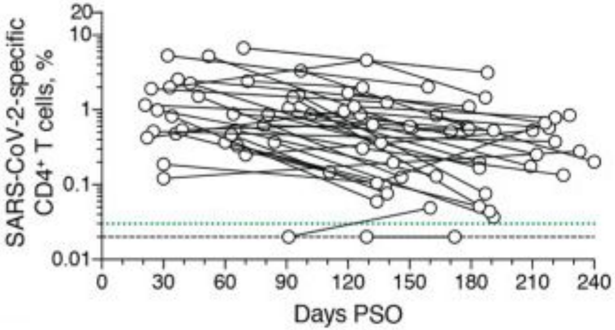
92% still positive for SARS-CoV-2 memory **CD4$^+$ T** cells up to 8 months (Dan et al., 2021)

Similarly, **CD8$^+$ T** cell responses remain robust 8 months after infection (Dan et al., 2021)

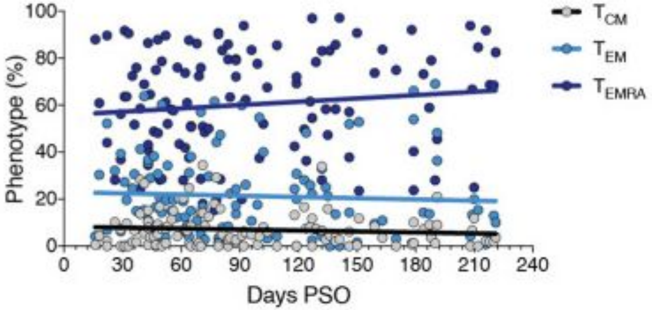
- CD8$^+$ T_{EMRA} cells associated with protection against severe disease in humans increase in proportion

In ~45% with CD4$^+$ and CD8$^+$ T cell responses, antibody levels decline to pre-pandemic levels in 8 months (Vo et al., 2022)

Longitudinal CD4$^+$ T-cell analysis with paired samples



Crosssectional CD8$^+$ T-cell phenotype (%)



Dan, J. M., Mateus, J., Kato, Y., Hastie, K. M., Yu, E. D., Faliti, C. E., . . . Crotty, S. (2021). Immunological memory to SARS-CoV-2 assessed for up to 8 months after infection. Science, 381(6529), 587. doi:10.1126/science.abf4063

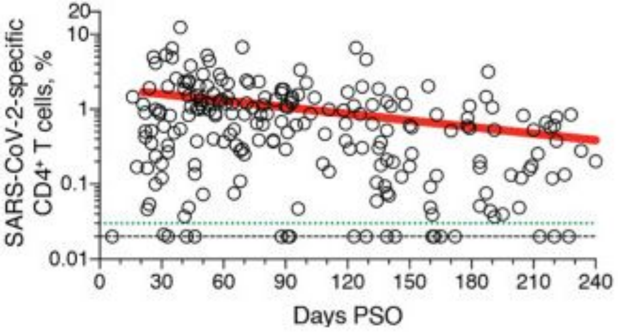
Vo, H. T. M., Maestri, A., Auerswald, H., Sorn, S., Lay, S., Seng, H., . . . Cantaert, T. (2022). Robust and functional immune memory up to 9 months after SARS-CoV-2 infection: A southeast asian longitudinal cohort. Frontiers in Immunology, 13, 817905. doi:10.3389/fimmu.2022.817905

Experimental data: cellular response remains strong and protects against severe outcomes

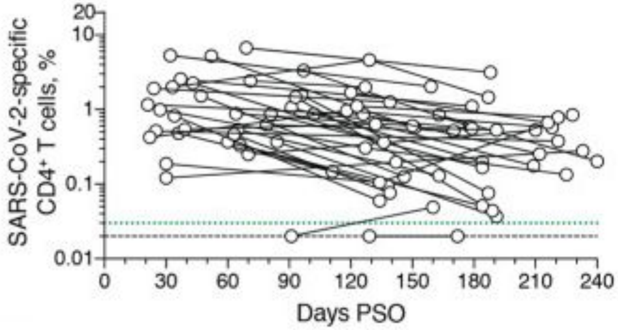
SARS-CoV-2 memory **CD4⁺ T** cell responses, up to 8 months after infection (Dan et al., 2021)

- half life of 94 days
- 92% still positive at ≥ 6 months post-symptom onset (PSO) for SARS-CoV-2 memory CD4⁺ T cells

Cross-sectional analysis



Longitudinal analysis with paired samples



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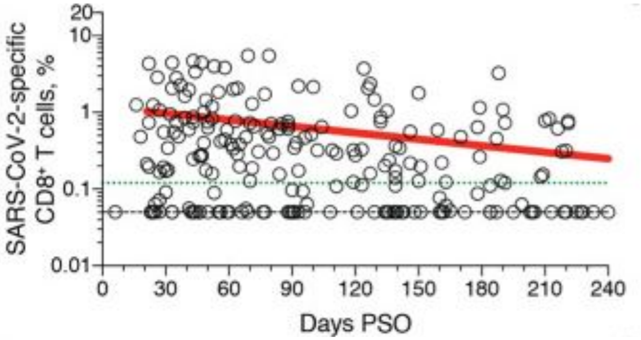
Experimental data: cellular response remains strong and protects against severe outcomes

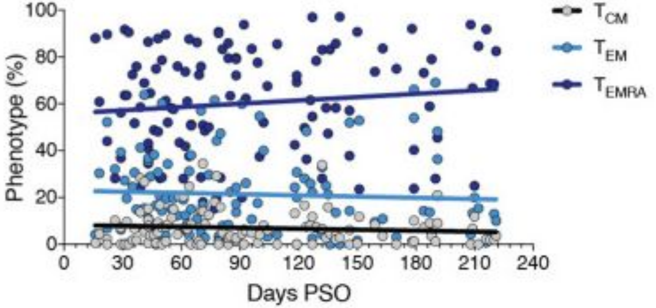
Similarly, **CD8^{+} T** cell responses remain robust 8 months after infection (Dan et al., 2021)

- half life of 125 days
- Proportion T_{EMRA} increases over time
- CD8^{+} T_{EMRA} cells associated with protection against severe disease in humans

Cross-sectional analysis



Distribution of central memory (T_{CM}), effector memory (T_{EM}), and terminally differentiated effector memory cells (T_{EMRA})



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Our model: including demography with age stratification, contact-matrices and age-dependent infection fatality rate

Infection fatality rate (IFR) increases log-linearly with age

~90% IFR variation across geographical locations due to age composition (Levin et al. 2020)

- 82.8% is under 50

Gamma (P.1) variant:

- Dominated second wave
- Emerged in Amazonas
- Higher mortality rate
- **Affected younger age groups**

de Souza, F. S. H., Hojo-Souza, N. S., da Silva, C. M., & Guidoni, D. L. (2021). Second wave of COVID-19 in Brazil: younger at higher risk. European Journal of Epidemiology, 36(4), 441–443. https://10.1007/s10654-021-00750-8

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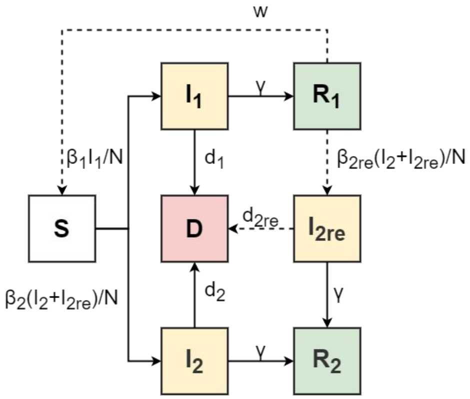
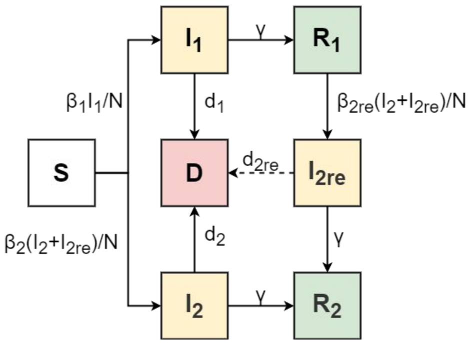
Epidemiological modeling: cannot describe both observed deaths and seroprevalence well



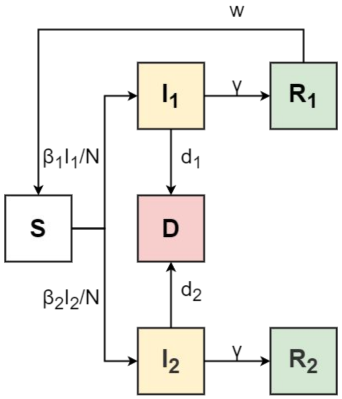
Previous Manaus models

- Waning and/or reinfection independent
- Waning (R→S)
- Reinfection (R→I)

Epidemiological modeling: cannot describe both observed deaths and seroprevalence well

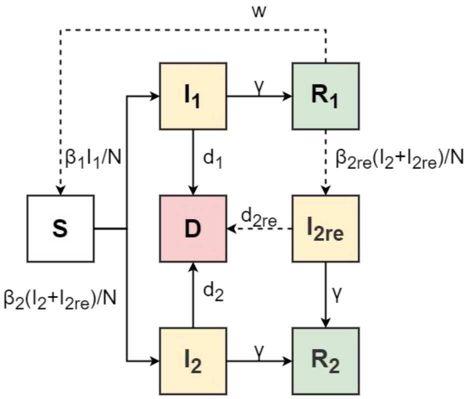


Direct reinfection (R→Ire)
(Coutinho et al., 2023)



Waning only (R→S)
(He et al., 2023)

Become naive after waning
Can't track reinfections



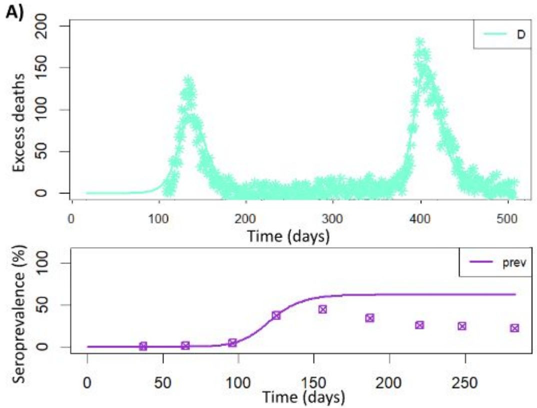
Both (R→S) & (R→I)
(Ferrante et al., 2022)

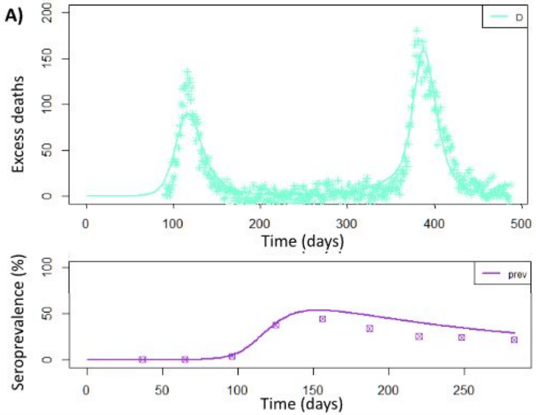
Only track direct reinfections

Coutinho, R. M., Marquitti, F. M. D., Ferreira, L. S., Borges, M. E., da Silva, R. L. P., Canton, O., . . . Prado, P. I. (2021). Model-based estimation of transmissibility and reinfection of SARS-CoV-2 P.1 variant. Communications Medicine, 1(1), 48. doi:10.1038/s43856-021-00048-6

He, D., Lin, L., Artzy-Randrup, Y., Demirhan, H., Cowling, B. J., & Stone, L. (2023). Resolving the enigma of iquitos and manaus: A modeling analysis of multiple COVID-19 epidemic waves in two amazonian cities. *Proceedings of the National Academy of Sciences - PNAS, 120*(10), e2211422120. doi:10.1073/pnas.2211422120

Epidemiological modeling: cannot describe both observed deaths and seroprevalence well





Direct reinfection (R→Ire)
(Coutinho et al., 2023)

Can't describe decline in seroprevalence

Waning only (R→S)
(He et al., 2023)

Become naive after waning
Can't track reinfections

Both (R→S) & (R→I)
(Ferrante et al., 2022)

Only track direct reinfections
Fit to seroprevalence not great

Coutinho, R. M., Marquitti, F. M. D., Ferreira, L. S., Borges, M. E., da Silva, R. L. P., Canton, O., . . . Prado, P. I. (2021). Model-based estimation of transmissibility and reinfection of SARS-CoV-2 P.1 variant. Communications Medicine, 1(1), 48. doi:10.1038/s43856-021-00048-6

He, D., Lin, L., Artzy-Randrup, Y., Demirhan, H., Cowling, B. J., & Stone, L. (2023). Resolving the enigma of iquitos and manaus: A modeling analysis of multiple COVID-19 epidemic waves in two amazonian cities. *Proceedings of the National Academy of Sciences - PNAS, 120*(10), e2211422120. doi:10.1073/pnas.2211422120

Result: Gamma P.1 more transmissible, previous infection reduces susceptibility

- Gamma P.1 ~1.6 times more transmissible than the first strain
- Previous immunity reduces Gamma P.1 susceptibility by 70%