Combining COVID-19 death data and serological survey results to estimate COVID-19 attack rate

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Webinar series in epidemics between France/Europe and China/Asia

Outline

- Background
- Two waves of COVID-19 in Manaus
- Revisit blood donor data in Manaus
- Fitting a two-strain model to data
- Summary

Collaborators: Lewi Stone, Yael Artzy, Salihu S Musa, Guihong Fan, Zhihang Peng, Xueying Wang, Yineke Li, Shi Zhao, and my PhD students.

Some rules from my experience

- Regarding data, before we develop a model for a set of data, we need to question whether the dataset is of good quality? can we trust the data? can we check the quality from a different source? how the data were collected? Are they biased or what is the range of reporting ratio? You do not want to build a model on unreliable data.
- Regarding model, we prefer simple model and as less as possible assumptions, try to use Information Criterion, which is the tradeoff of the goodness of fit and the model complexity, to remove all unnecessary components unless we have a strong reason to include it.
- Consider more realistic assumptions…

Science

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

Lewis F. Buss, Carlos A. Prete Jr., Claudia M. M. Abrahim, Alfredo Mendrone Jr., Tassila Salomon, Cesar de Almeida-Neto, Rafael F. O. França, Maria C. Belotti, Maria P. S. S. Carvalho, Allyson G. Costa, Myuki A. E. Crispim, Suzete C. Ferreira, Nelson A. Fraiji, Susie Gurzenda, Charles Whittaker, Leonardo T. Kamaura, Pedro L. Takecian, Pedro da Silva Peixoto, Marcio K. Oikawa, Anna S. Nishiya, Vanderson Rocha, Nanci A. Salles, Andreza Aruska de Souza Santos, Martirene A. da Silva, Brian Custer, Kris V. Parag, Manoel Barral-Netto, Moritz U. G. Kraemer, Rafael H. M. Pereira, Oliver G. Pybus, Michael P. Busch, Márcia C. Castro, Christopher Dye, Vítor H. Nascimento, Nuno R. Faria and Ester C. Sabino

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Attack rate in Manaus

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) incidence peaked in Manaus, Brazil, in May 2020 with a devastating toll on the city's inhabitants, leaving its health services shattered and cemeteries overwhelmed. Buss *et al.* collected data from blood donors from Manaus and São Paulo, noted when transmission began to fall, and estimated the final attack rates in October 2020 (see the Perspective by Sridhar and Gurdasani). Heterogeneities in immune protection, population structure, poverty, modes of public transport, and uneven adoption of nonpharmaceutical interventions mean that despite a high attack rate, herd immunity may not have been achieved. This unfortunate city has become a sentinel for how natural population immunity could influence future transmission. Events in Manaus reveal what tragedy and harm to society can unfold if this virus is left to run its course.

Science, this issue p. 288; see also p. 230

Science

REPORTS

Cite as: N. R. Faria *et al.*, *Science* 10.1126/science.abh2644 (2021).

Genomics and epidemiology of the P.1 SARS-CoV-2 lineage in Manaus, Brazil

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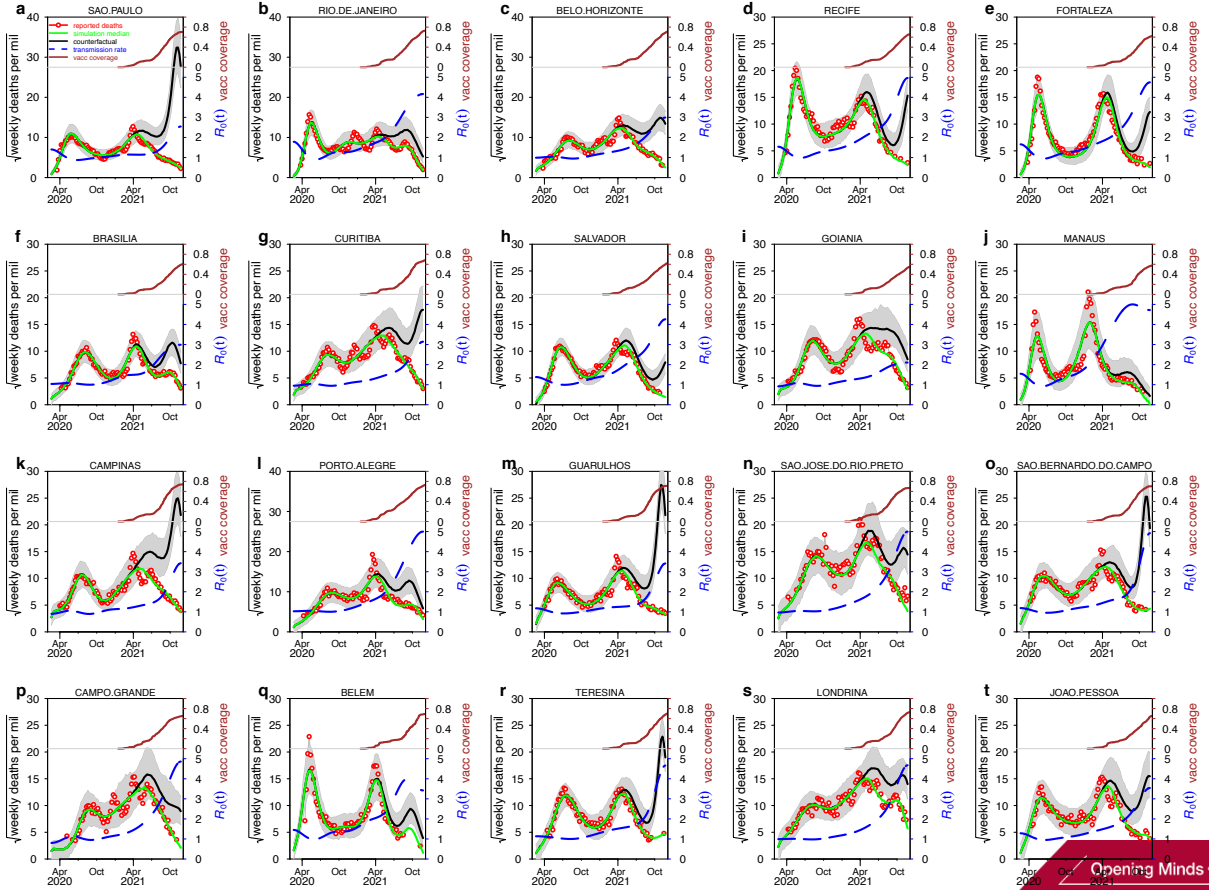
Two-waves of COVID-19 hit Manaus, Brazil



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http://dx.doi.org/10.1136/bmj.n394
Published: 12 February 2021

Covid-19: Is Manaus the final nail in the coffin for natural herd immunity?

Many thought a second wave was impossible in Brazil's Amazon because of the severity of the first. A second crisis has stunned the city of Manaus, reports Luke Taylor, and raises questions around a new variant and the likelihood of natural herd immunity

Luke Taylor *freelance journalist*

Hospitals in the Brazilian Amazon collapsed for the second time in mid-January.

A surge in patients with covid-19 exhausted hospital supplies of oxygen in the region's capital of Manaus, forcing friends and families of patients to race to private suppliers. Queuing for hours in the heat and torrential downpours, they are desperate to buy a $70 (£51; €58) cylinder that could turn out to be a lifesaver. Some patients are being airlifted to other states where beds are available. But, again, capacity is limited, so many in Manaus—where the crisis extends well beyond the hospital walls—are dying of asphyxiation.

"A lot of people have died at the hospital entrance and outside in the ambulance, but most have died and are still dying at home while their families search

certain, and not just down to overly optimistic assumptions.

For one thing, using blood donors as a sample may have skewed the results. "Donors are a special subset of the population," says Paulo Lotufo, an epidemiologist at the University of São Paulo. They are more likely to spend time outside the home and work in jobs that put them at higher risk of contracting covid-19, he says. Lotufo believes the proportion of residents who have antibodies was likely lower, and that false confidence created by the first study played a role in causing the second surge in cases.

But several leading epidemiologists, while acknowledging the study's limitations, believe significant inaccuracies are unlikely.

MATTER

Virus Variant in Brazil Infected Many Who Had Already Recovered From Covid-19

The first detailed studies of the so-called P.1 variant show how it devastated a Brazilian city. Now scientists want to know what it will do elsewhere.

"25-60% reinfection rate!"

30

Kermack and McKendrick (1927)
Susceptible-Infectious-Recovered model

$$\frac{dS}{dt} = -\frac{\beta}{N} SI$$

$$\frac{dI}{dt} = \frac{\beta}{N} SI - \gamma I$$

$$\frac{dR}{dt} = \gamma I$$

$$N = S + I + R$$

$$\mathcal{R}_0 = \frac{\beta}{\gamma} = \beta \cdot \gamma^{-1}$$

β Transmission rate

γ^{-1} Mean Infectious Period

Herd Protection Threshold / Critical Vaccination Threshold

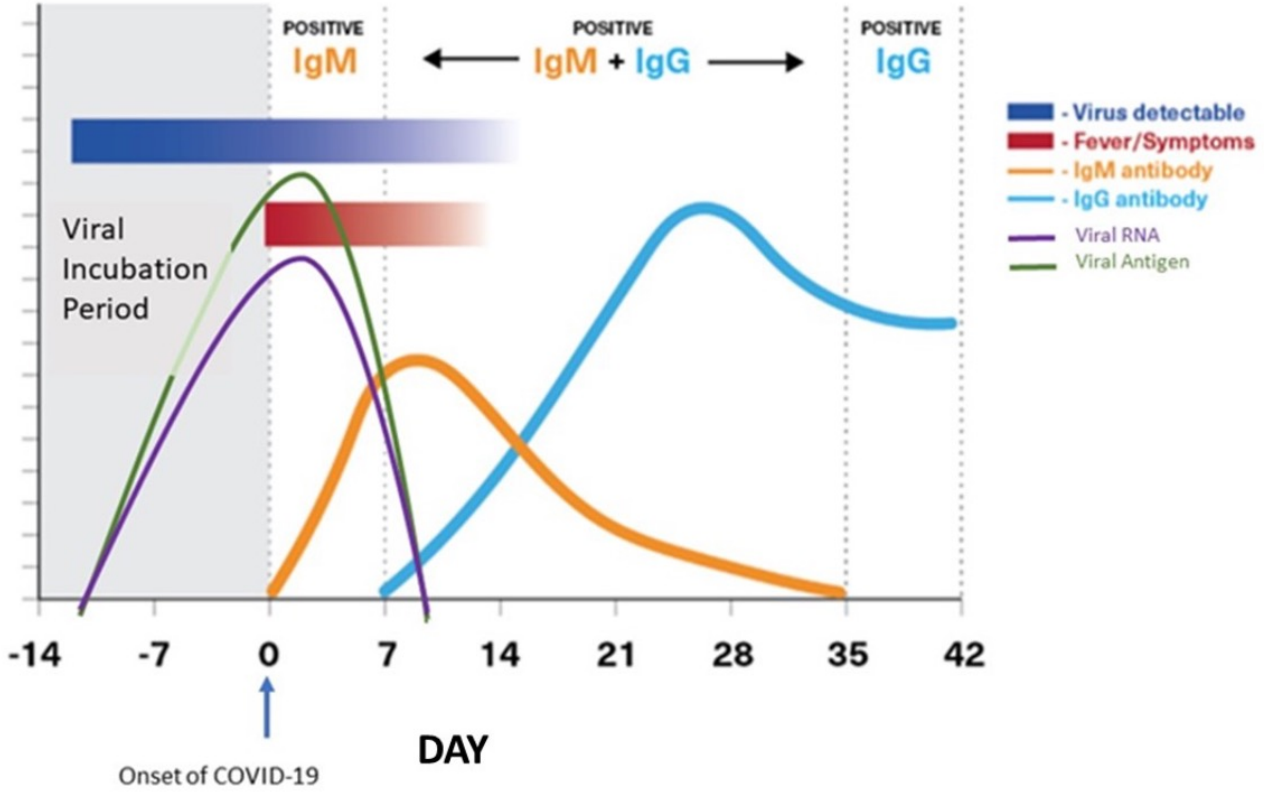
$$\frac{dI}{dt} = \left(\frac{\beta}{N} S - \gamma \right) I \qquad \varepsilon = \exp\left[\left(\mathcal{R}_0 \frac{S}{N} - 1 \right) \gamma t + C \right]$$

$$\mathcal{R}_0 \frac{S_0}{N} < 1 \qquad \frac{S_0}{N} < \frac{1}{\mathcal{R}_0}$$

$$V_c > 1 - \frac{1}{\mathcal{R}_0}$$

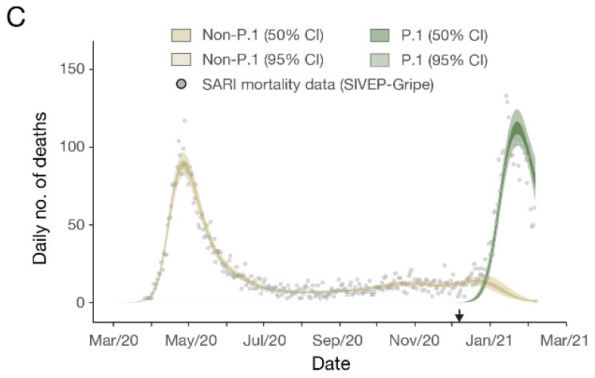
Here we assume 100% vaccine efficacy Ve=100%.
If Ve<100%, then HPT=Vc/Ve.

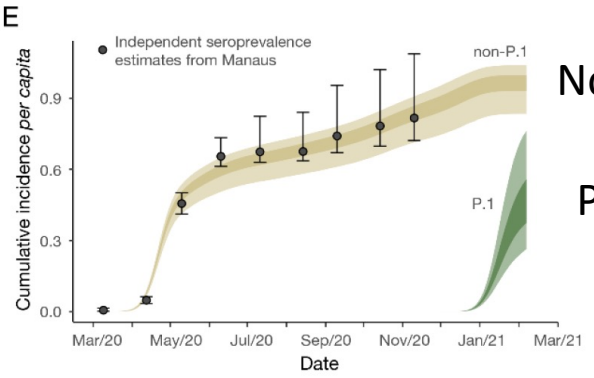
Typical Immune Response to Coronavirus Infection



https://www.flowmetric.com/cytometry-blog/serology-testing-for-sars-cov-2

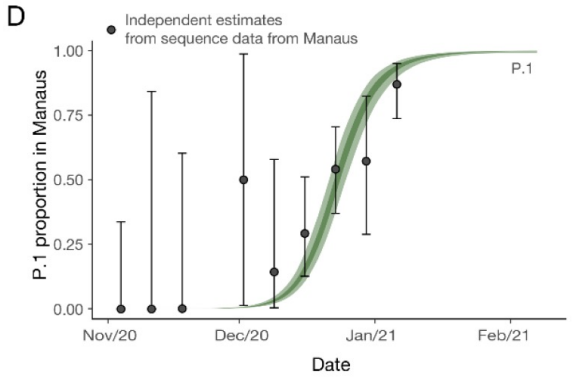
Emergence of P.1 Variant and the Second Wave

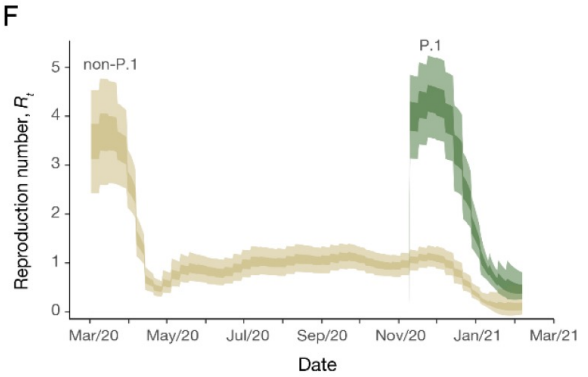




Non-P.1 IAR = 96%

P.1 IAR = 46%





N501Y, E484K and K417T.

Faria et al Science 2021

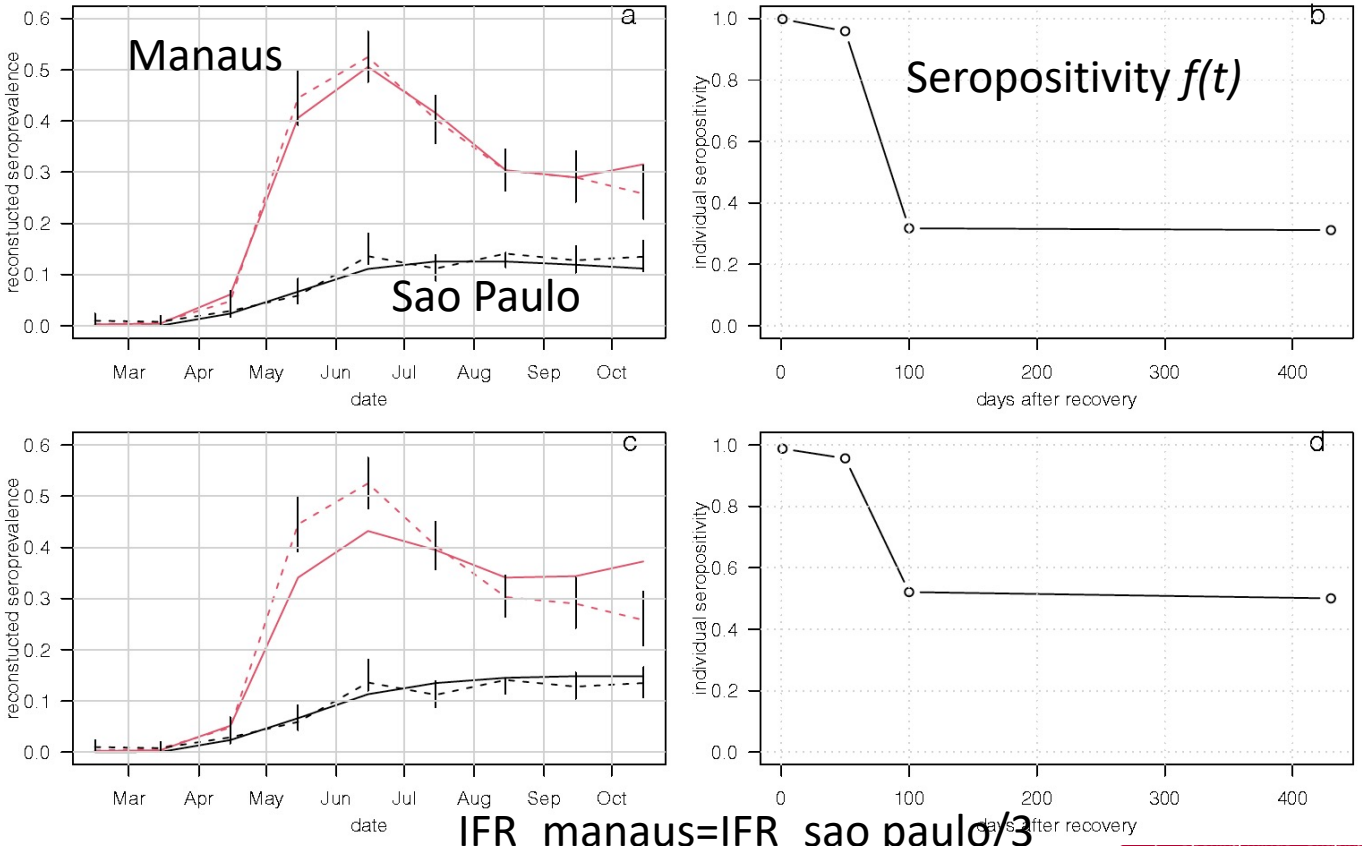
Seroprevalence as a Convolution of Deaths and Seroposivity

$$p(T) = \int_0^T r^{-1} d(t) f\,(T-t)/N\,dt\,.$$

where *d(t)* is daily COVID-19 deaths, *r* is infection fatality rate, thus *rd(t)* is daily infections (individuals infected and seroconverted), *f(t)* is the seropositivity, *i.e.* the probability of a seroconverted cases still be positive at time *t* after seroconversion.

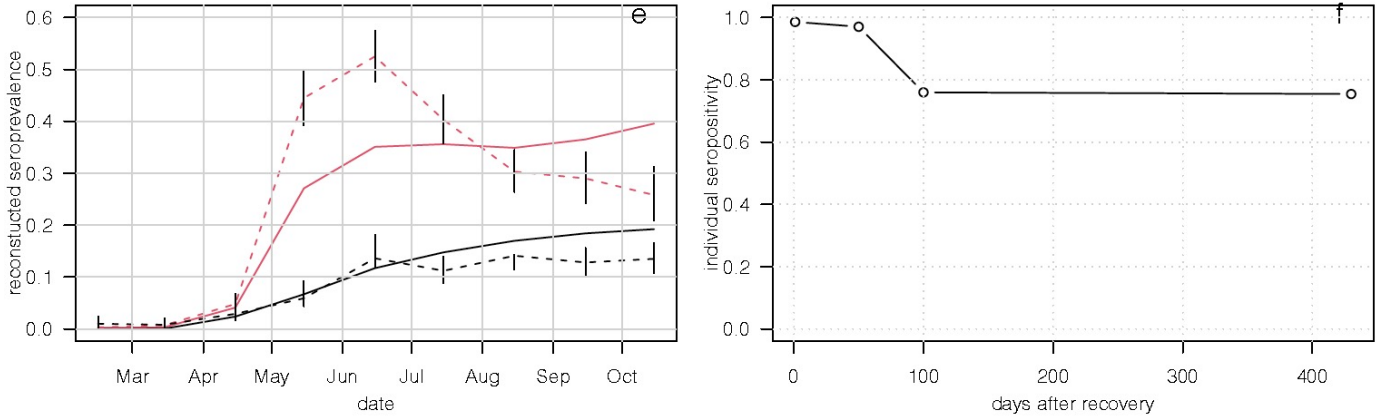
Individuals infected and seroconverted recently (or a long time ago) will have a major (or reduced) contribution to the current population seroprevalence.

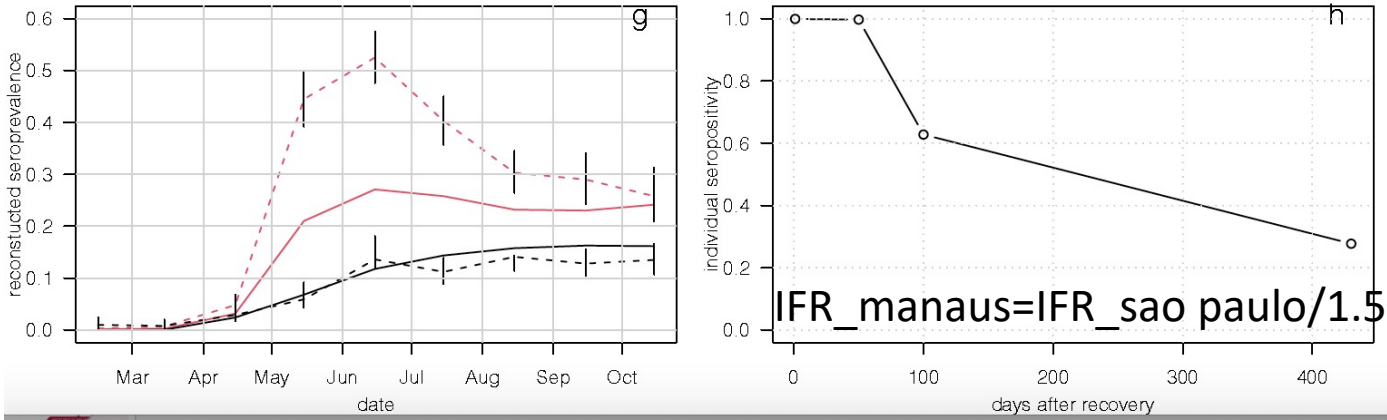
Seroprevalence among Blood Donors in Manaus



IFR_manaus=IFR_sao paulo/3

Seroprevalence among Blood Donors in Manaus





IFR_manaus=IFR_sao paulo/1.5

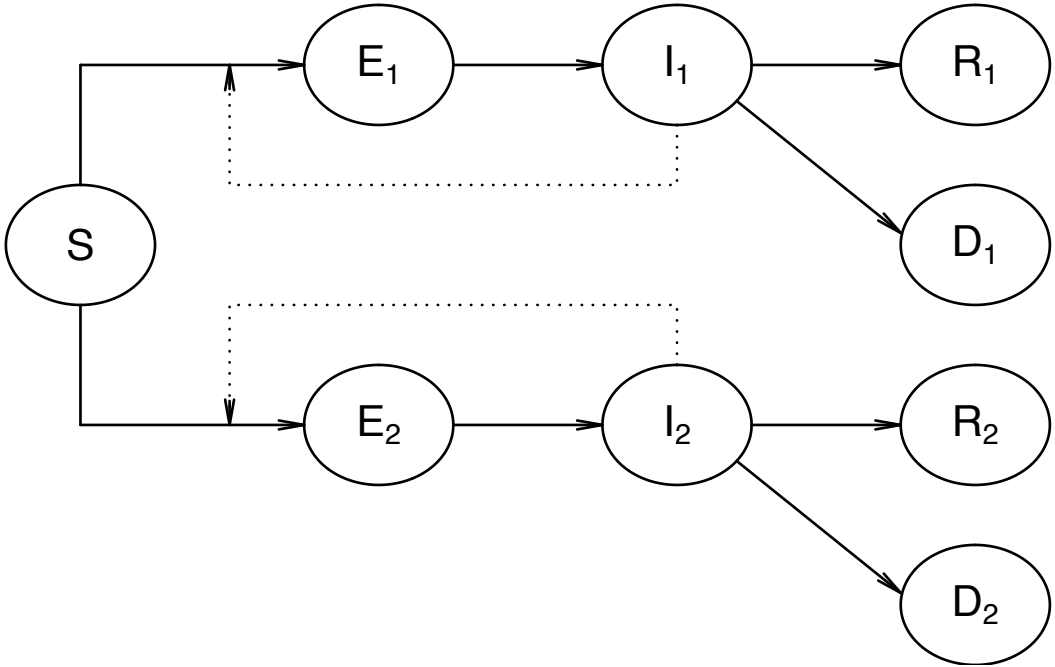
Blood donor data during peak of pandemic could be biased

“Jesem Orellana, an epidemiologist from Manaus who works at the Fundação Oswaldo Cruz, a public research institution, notes the prospect of a free COVID-19 test upon donating blood may have prompted specific groups of people to contribute.”

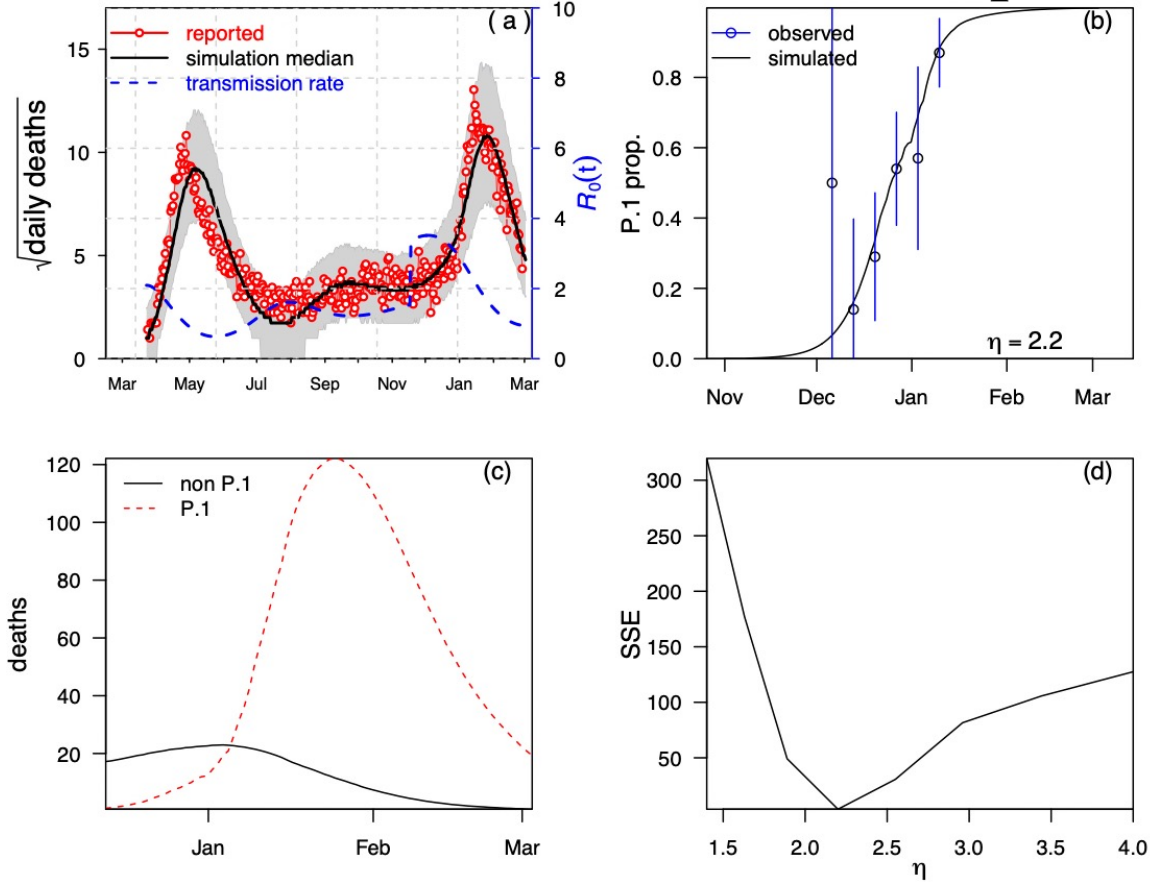
“Many people may have donated blood to know their serological status, especially those who suspected they had been infected and with less financial resources,” Orellana says. He adds that the blood center even partnered with Uber to offer a discount to donors heading to the facility. All of this might have influenced the outcome of the study.”

https://www.the-scientist.com/news-opinion/study-estimates-76-percent-of-brazilian-city-exposed-to-sars-cov-2-68272

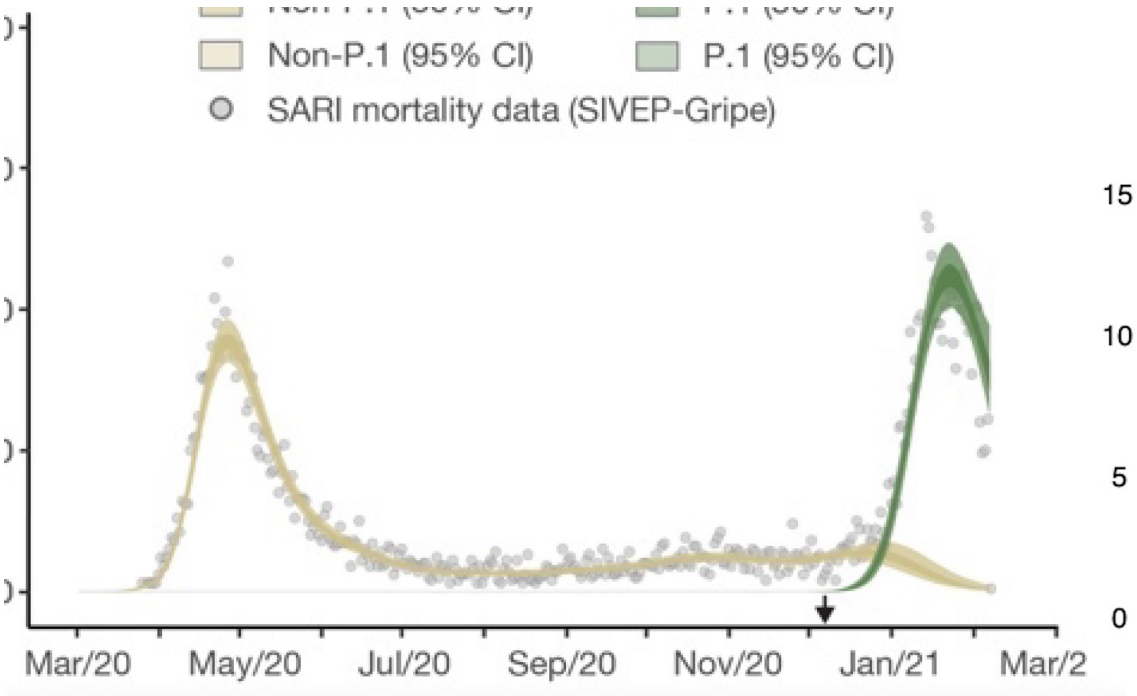
Two-strain SEIR Model without reinfection



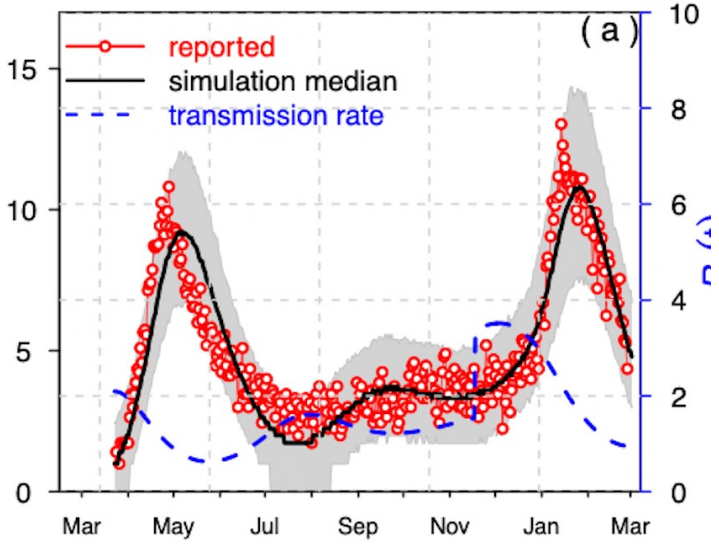
Fitting two-strain model to deaths and sequence proportions



Fitting two-strain model to deaths and sequence proportions

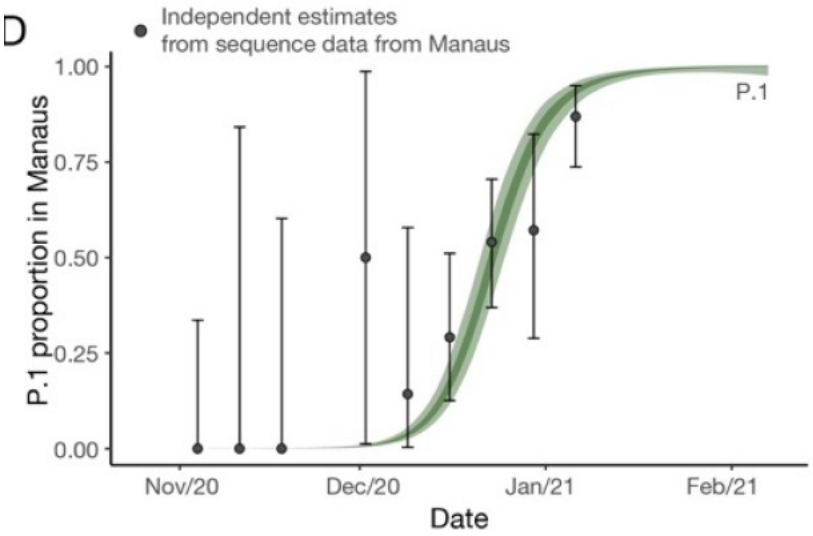


Allow 25-61% reinfection

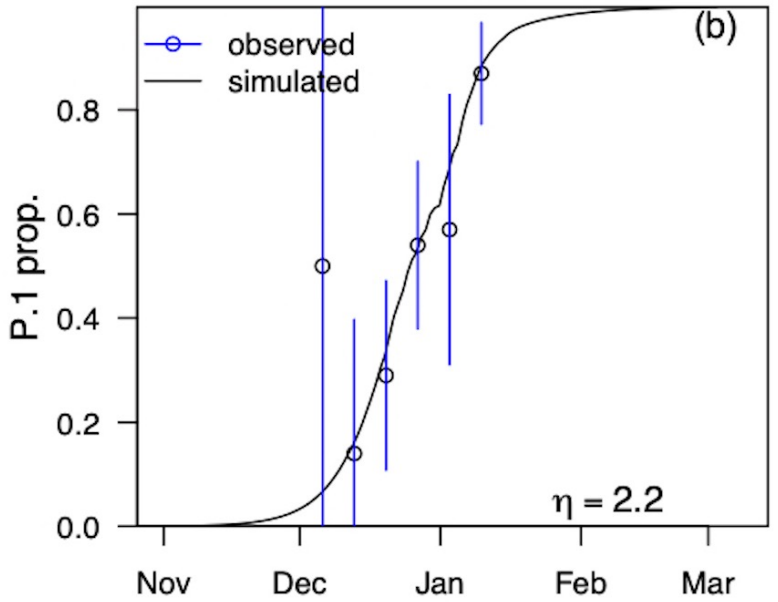


zero reinfection

Fitting two-strain model to deaths and sequence proportions



Allow 25-61% reinfection



zero reinfection

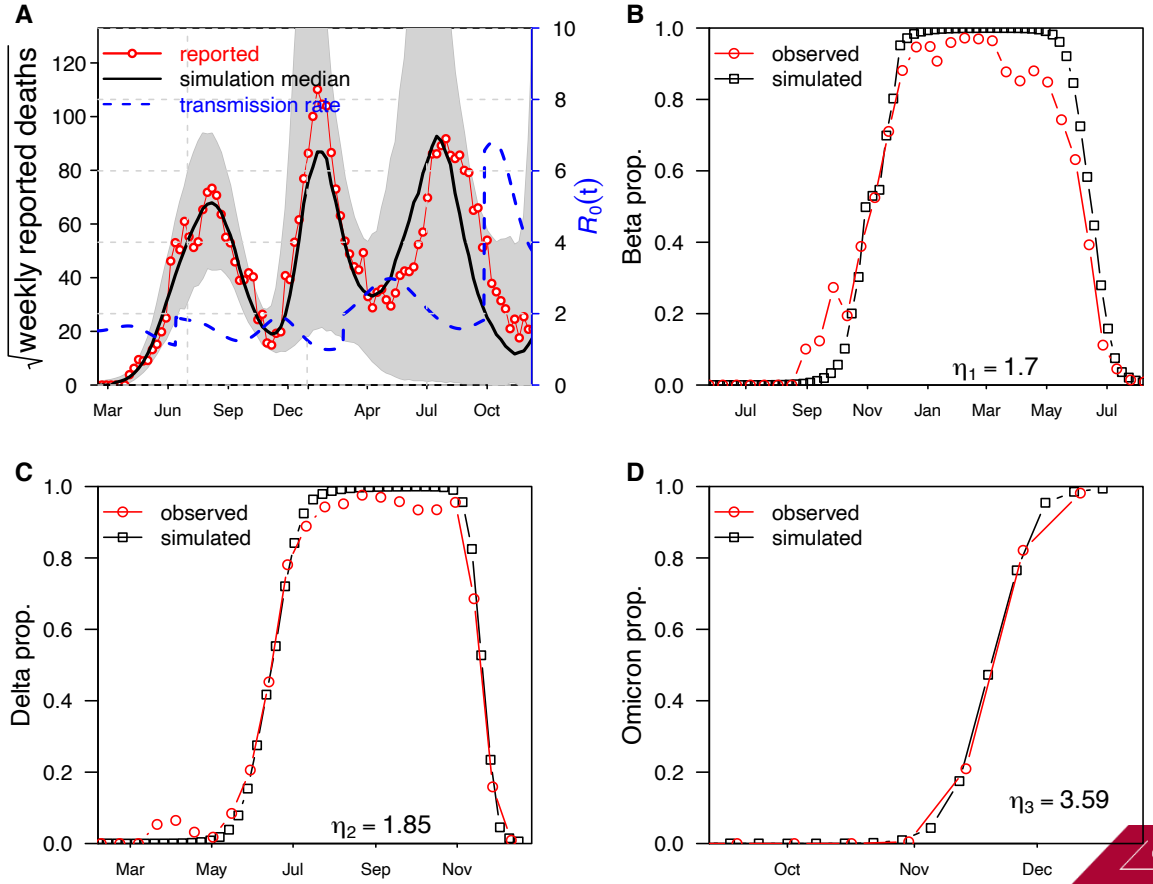
Confirmed reinfection in Brazil before Omicron

TABELA 5 Número de casos de reinfecção pela covid-19 registrados e notificados oficialmente ao Ministério da Saúde. Brasil, SE 50 - 2020 a SE 52, 2021

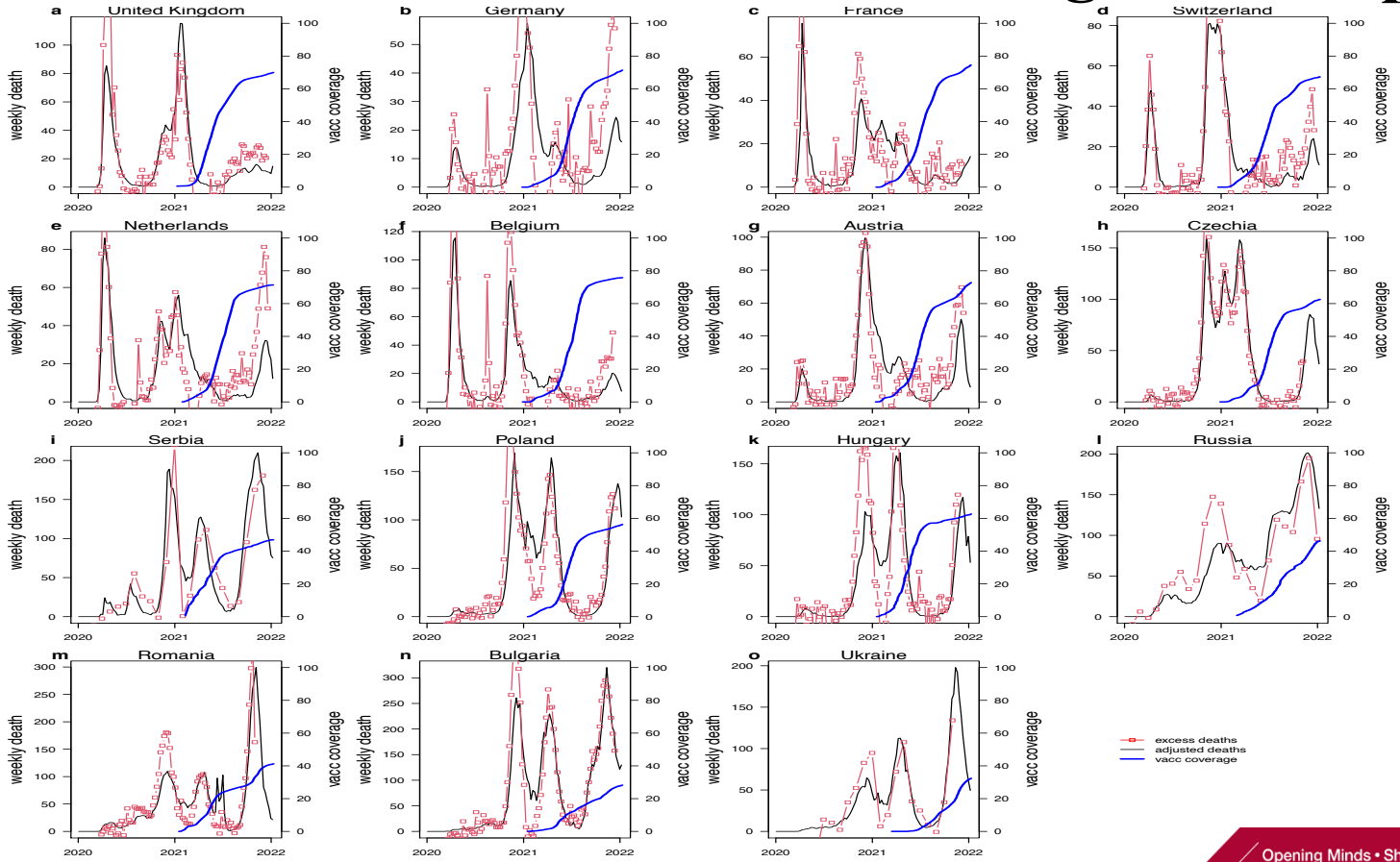
Unidade Federada*	Variantes Não Preocupação	VOC Gama	VOC Delta	VOC Ômicron	Total
Amazonas		3			3
Bahia	1				1
Distrito Federal		1	1		2
Espírito Santo		1			1
Goiás	4	11		2	17
Mato Grosso do Sul	3				3
Minas Gerais	1				1
Paraná	1	2			3
Pernambuco	1				1
Rio Grande do Norte	1				1
Rio de Janeiro		1			1
Santa Catarina	1	4	2		7
São Paulo	2	1			3
Brasil	15	24	3	2	44

Only three reinfections were confirmed in Amazonas by Jan 1, 2022 and one is a kidney transplant survivor.

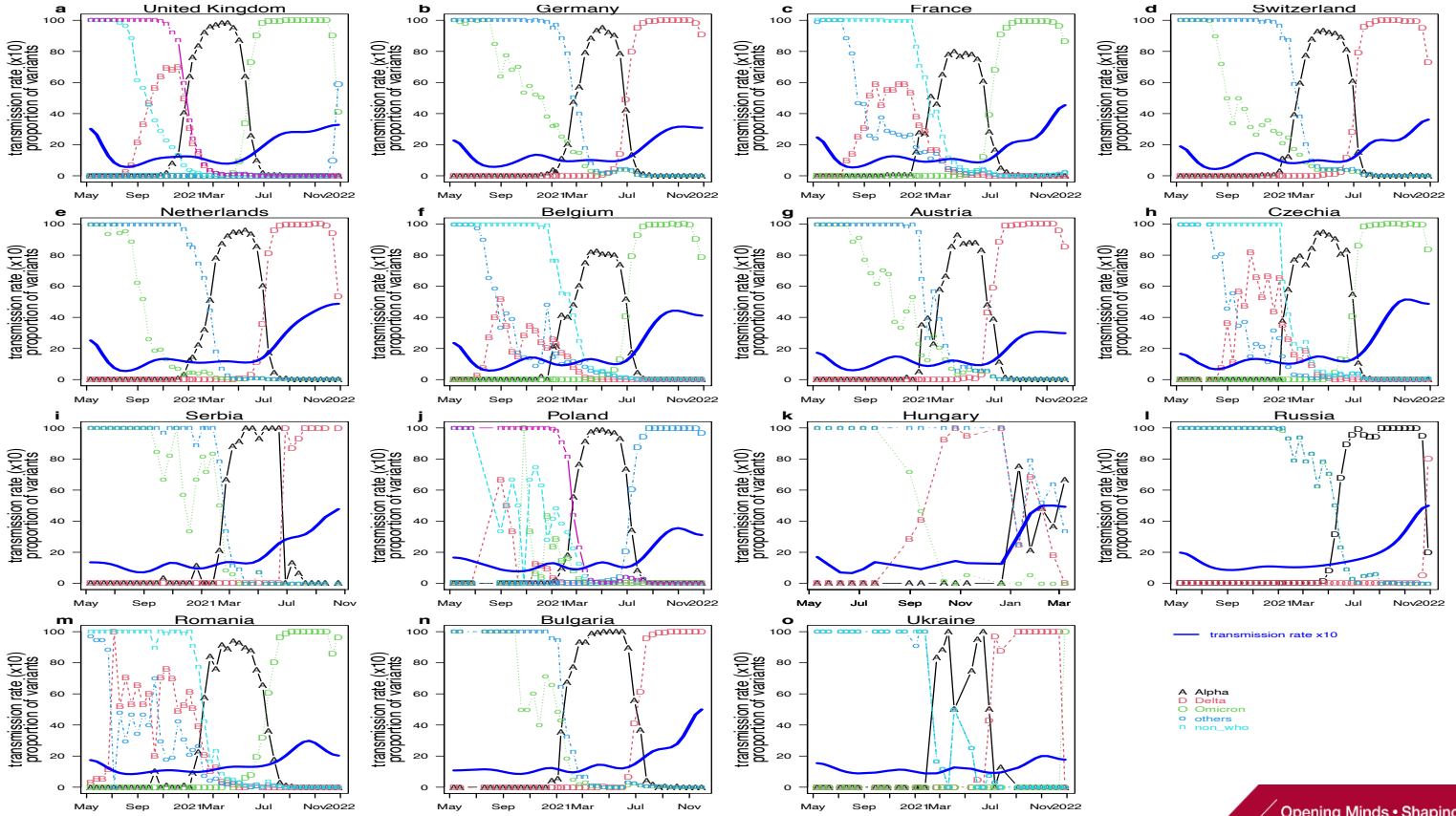
Fitting a two-strain model to three variant replacements in South Africa: Beta, Delta and Omicron



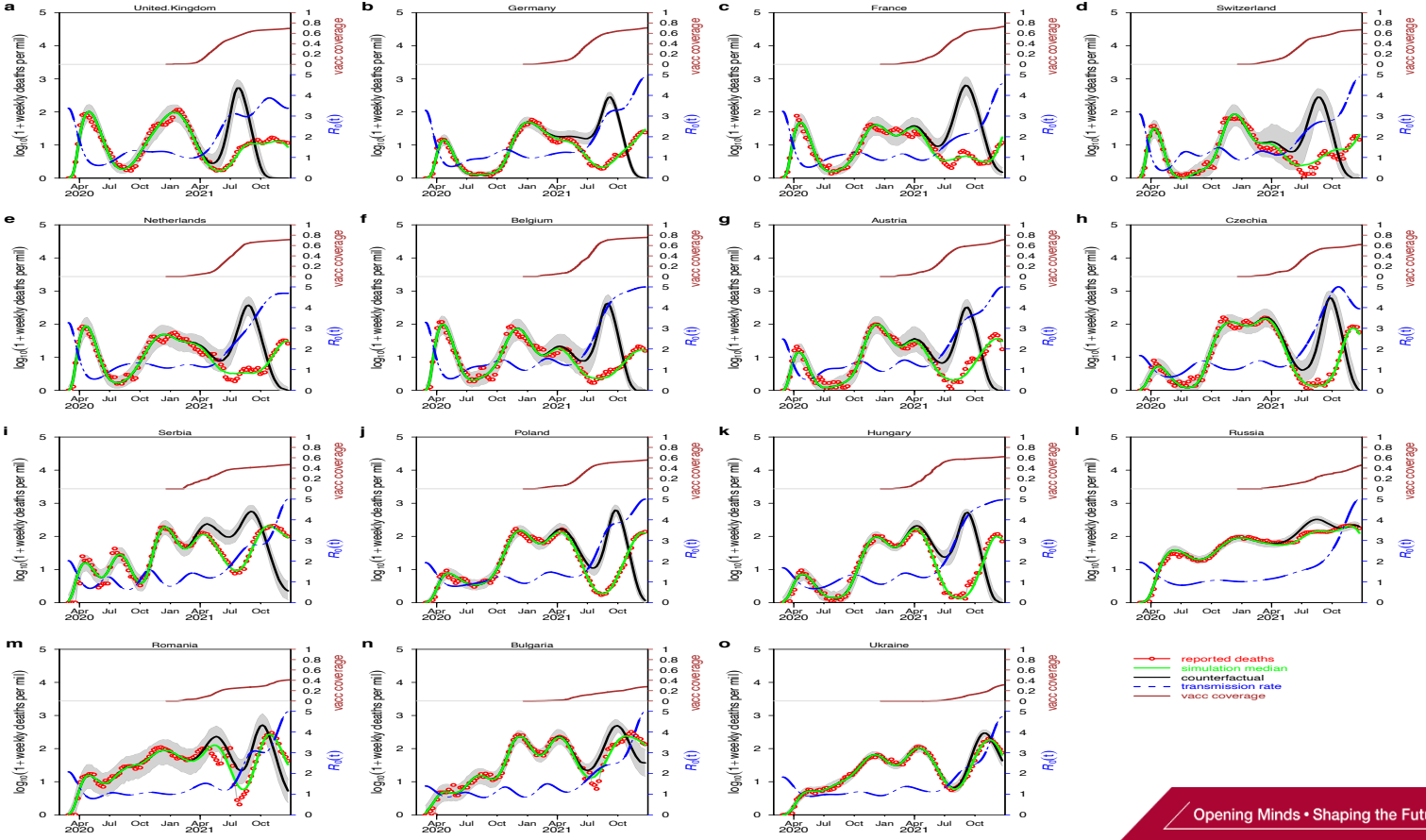
COVID-19 deaths and vaccine coverage in Europe



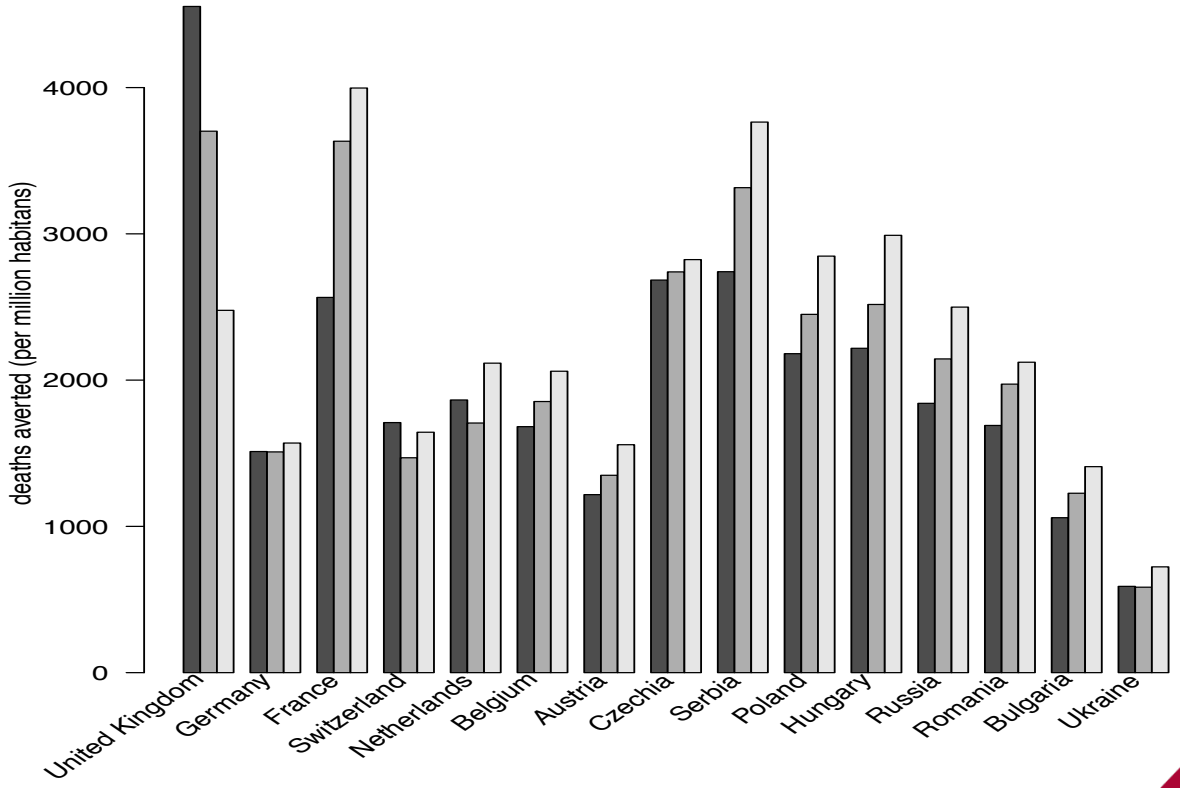
Dominant Variants and Transmission Rates in Europe



Fitting model to deaths with vaccine coverage in Europe



COVID-19 deaths averted due to vaccine in Europe



Summary

- High infection attack rate would imply high rate of reinfection, but so far only three confirmed reinfections in Amazonas (by Jan 12, 2022).
- Thus seroprevalence among blood donors in Manaus is most likely biased. The severe first wave could have changed the composition of the blood donors and driven some high risk group into blood donation.
- We fit two-age-group model to observed SARI deaths and two-strain model to both SARI deaths and sequence proportions, and get reasonable IAR (30% by Oct 2020 and ~70% by Feb 2021), which is far less than Buss et al claimed 75% by Oct 2020 and > 100% by Feb 2021 with 25-61% re-infections.
- Household or large-scale random sample serological study is needed to pin down the puzzle.
- Vaccination has save a substantial number of lives in Europe.

A Simple Model to Estimate the Transmissibility of SARS-COV-2 Beta, Delta and Omicron Variants in South Africa

https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3989919

Model analysis of vaccination effectiveness by state in the United States
https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3987537

Two Waves of COVID-19 in Brazilian Cities and Vaccination Impact

https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3977464

Further Discussion on the Attack Rate and Reinfections in Manaus, Brazil

https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3929140

The unexpected dynamics of COVID-19 in Manaus, Brazil: Herd immunity versus interventions

https://www.medrxiv.org/content/10.1101/2021.02.18.21251809v1

Modelling COVID-19 Vaccine Breakthrough Infections in Highly Vaccinated Israel - the effects of waning immunity and third vaccination dose

https://www.medrxiv.org/content/10.1101/2022.01.08.22268950v1

Thank You!