SARS-CoV-2 seroprevalence study among blood donor in Brazil

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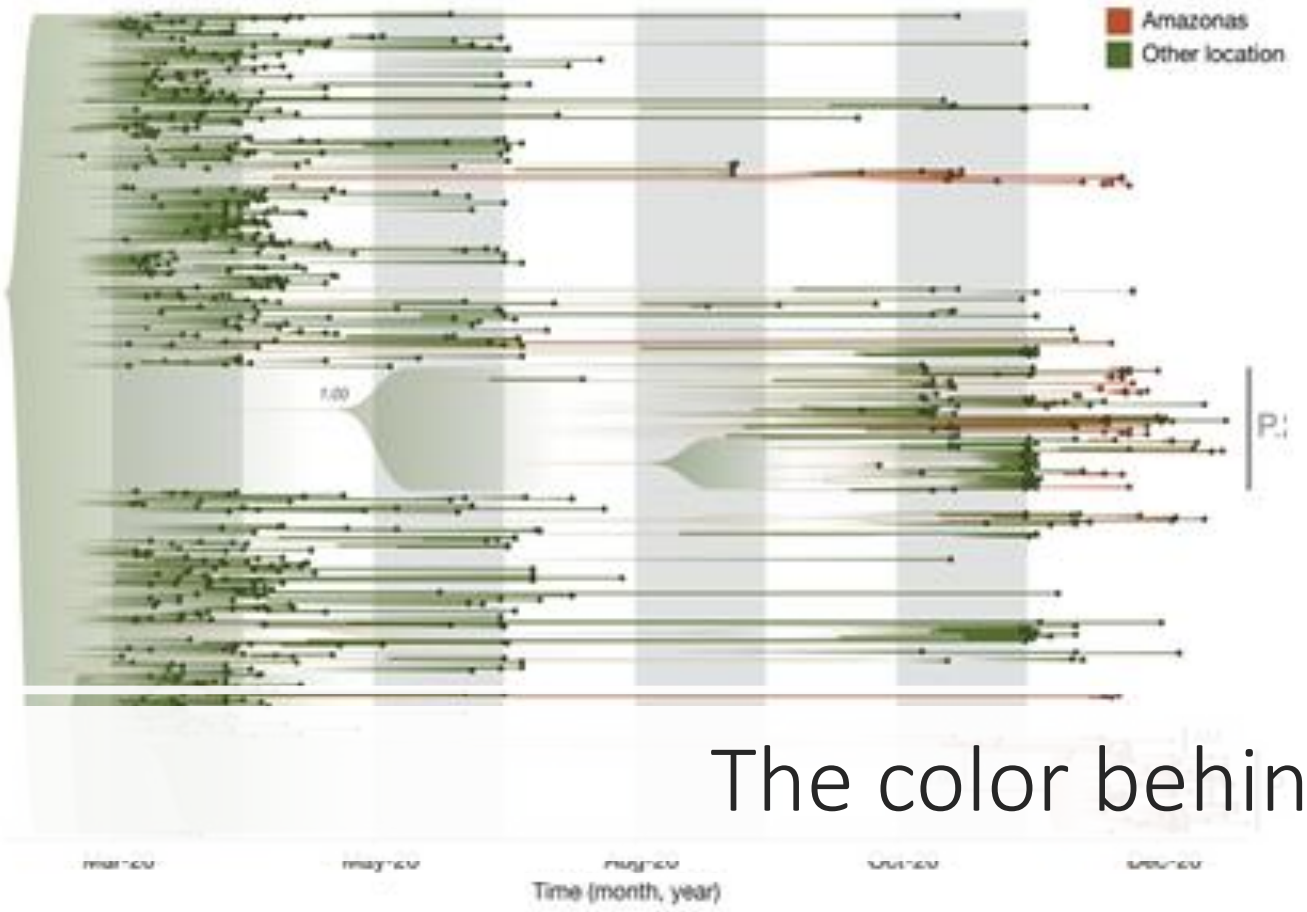
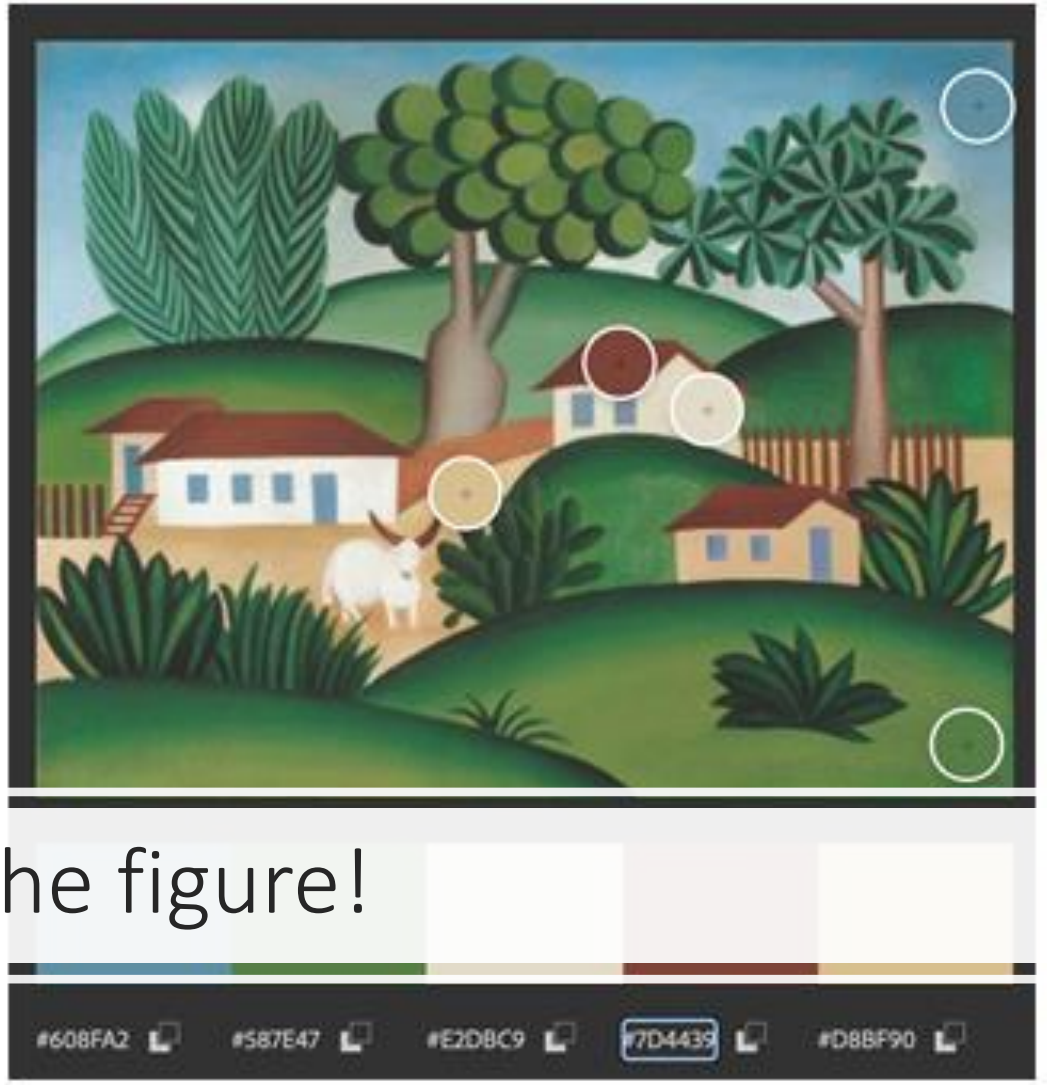
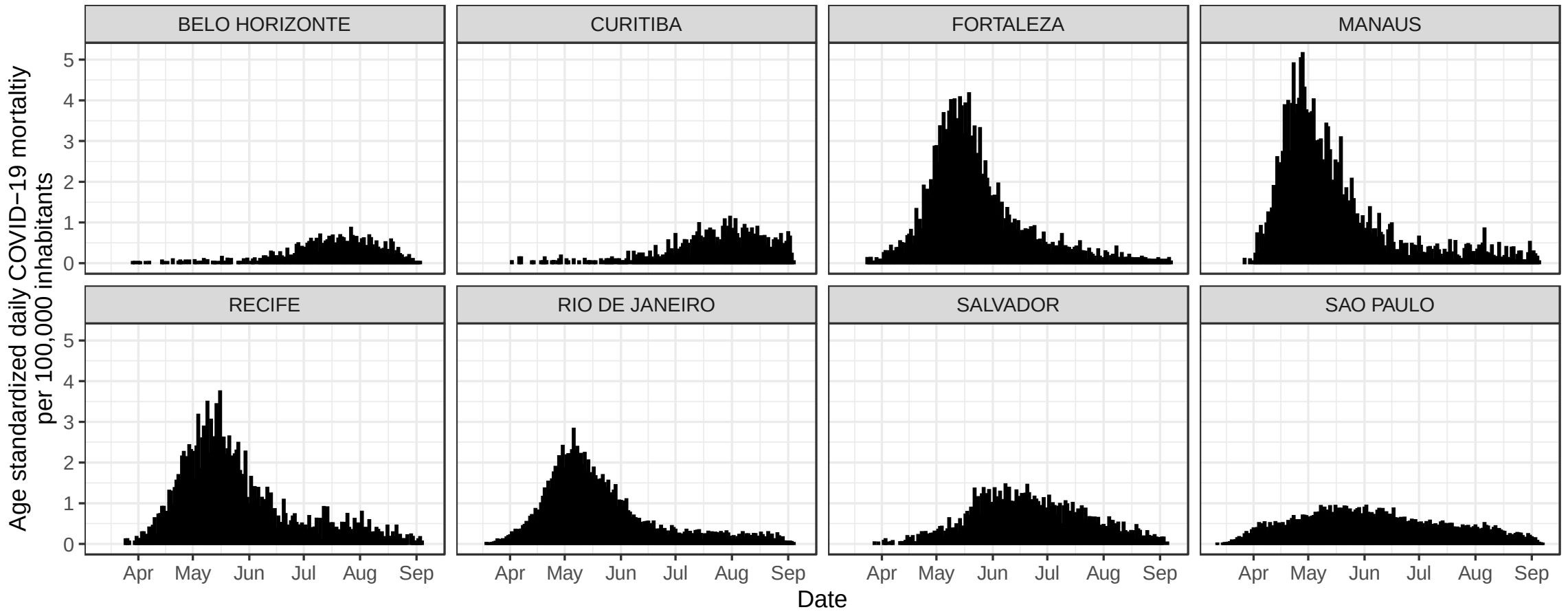
Instituto Todos pela Saúde





The color behind the figure!

Centre for Arbovirus
cadde
Discovery, Diagnostics, Genomics & Epidemiology

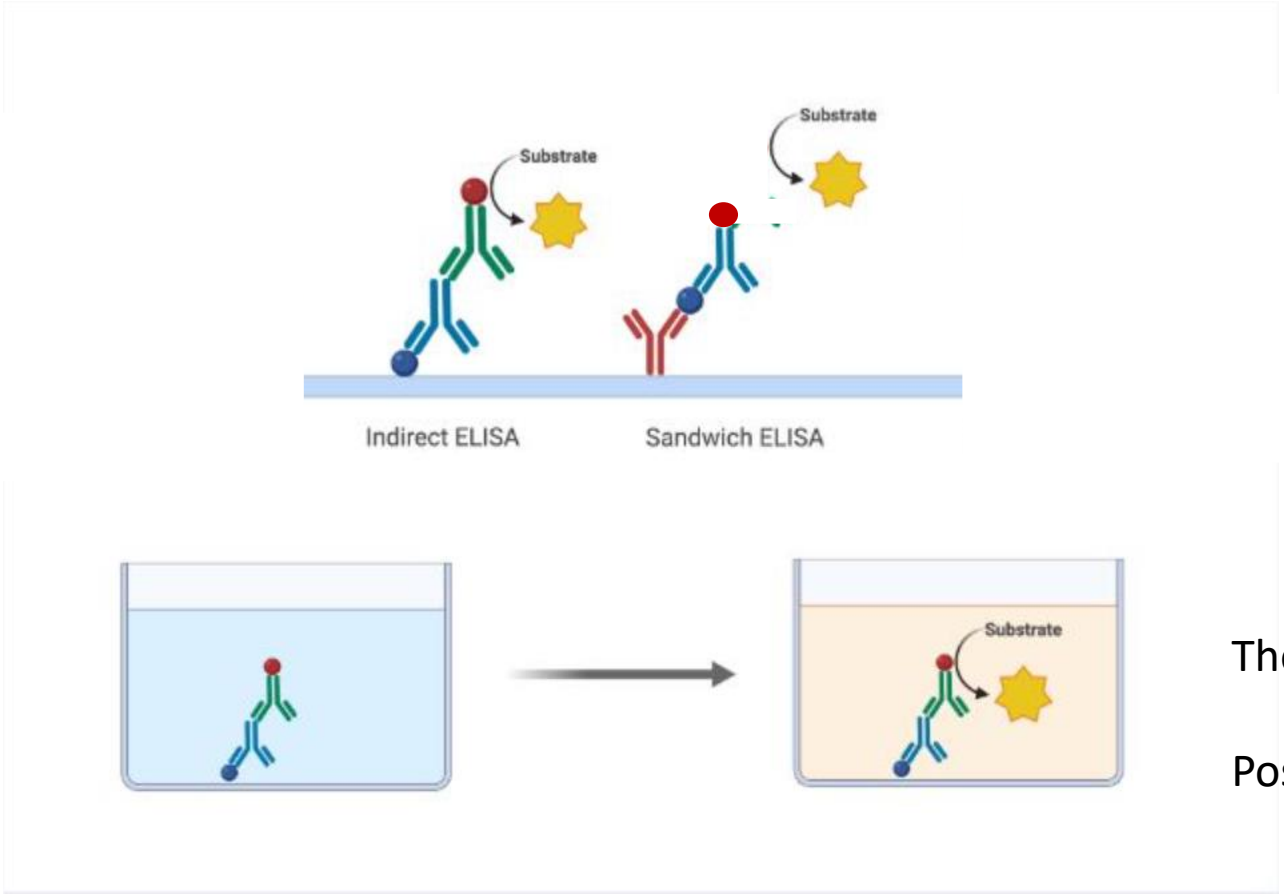


Why do we need serological studies

- Key questions:
  - how many people were infected
  - may also indicate how many people are protected

- How do you develop and validate a test?
  - Producing the protein: the DNA sequence is enough
  - Defining the cut off and analytical sensitivity: samples from patients
  - Defining sensitivity and specificity

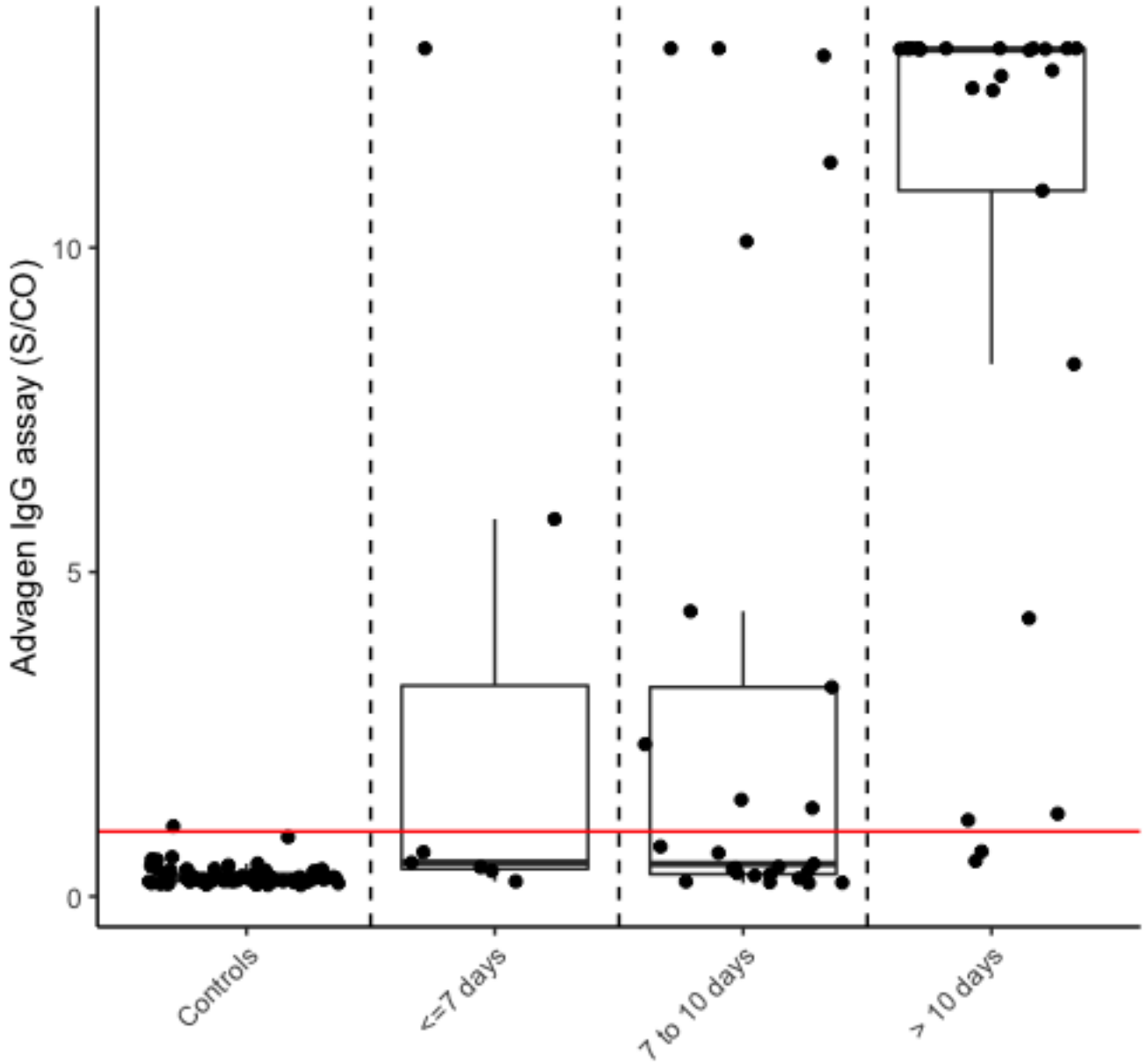
How we detect antigen and antibody



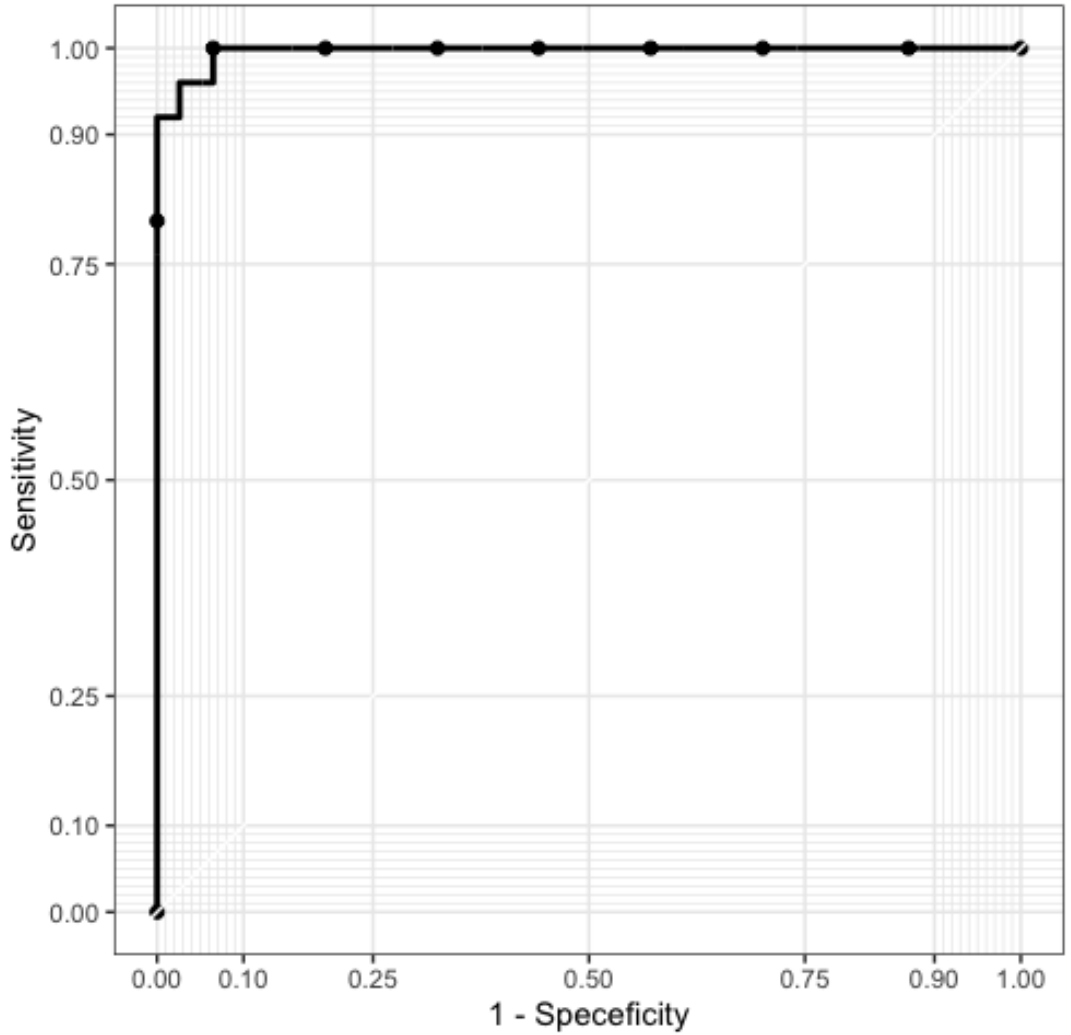
The amount of color = signal

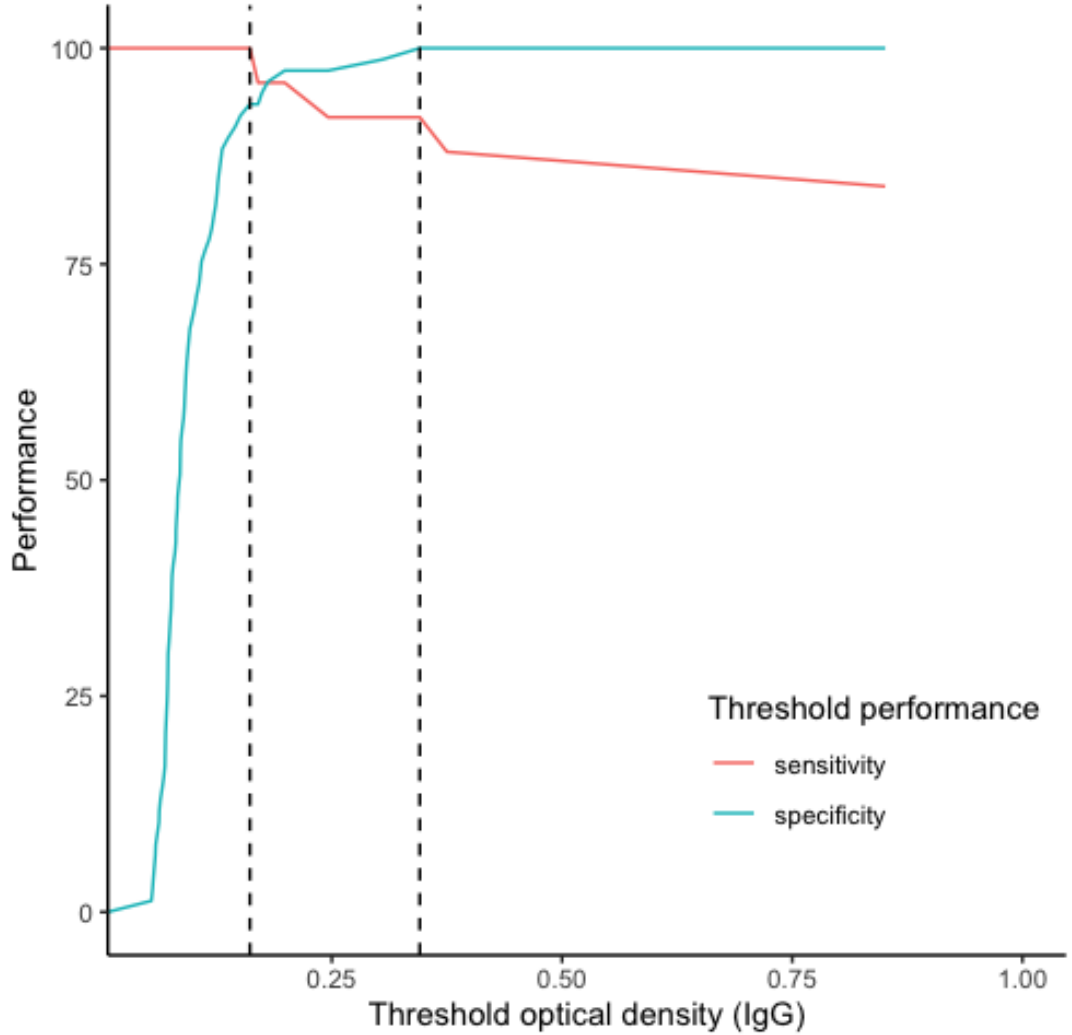
Positive: Signal > cut of value

Reactivity of Advagen IgG assay in cases at different time points after symptom onset and among controls – S/CO calculated using Manufacturer's threshold of 0.306



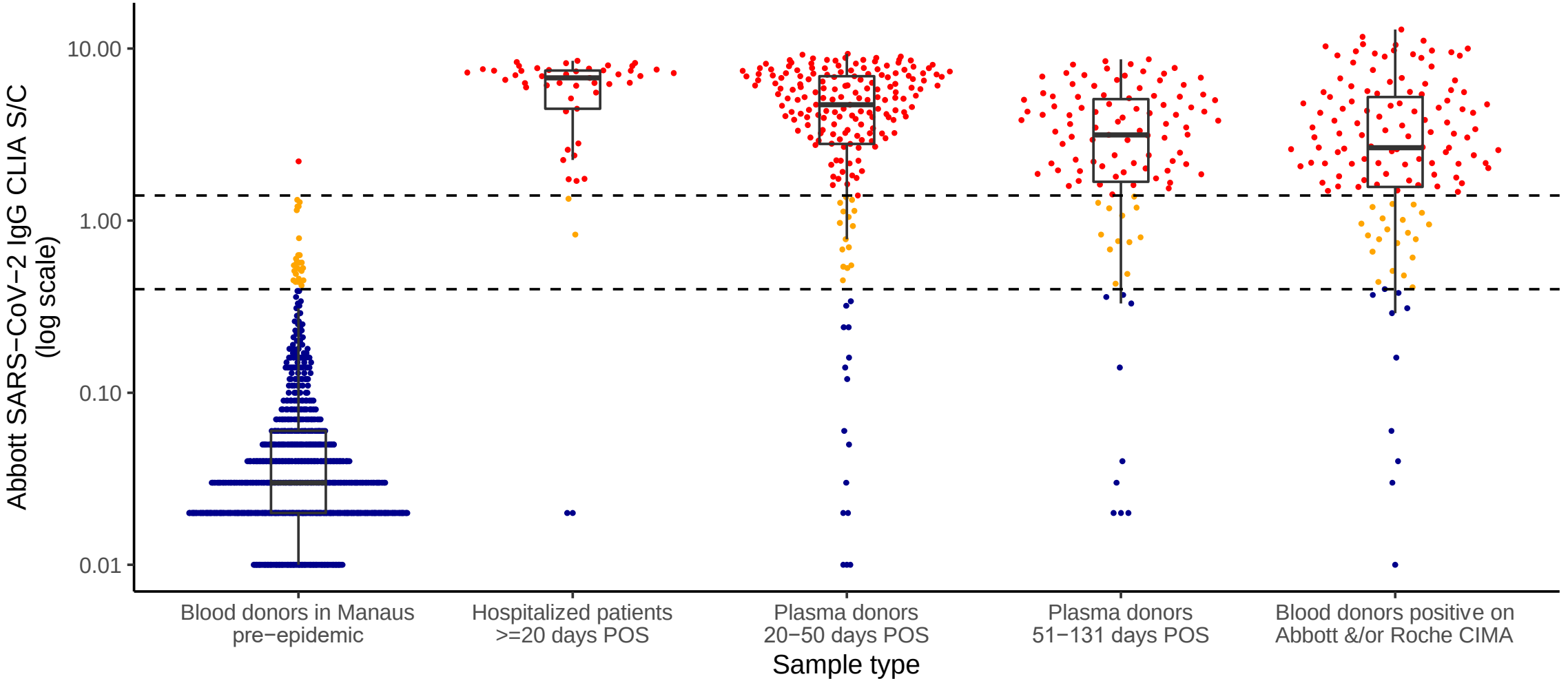
Performance of Advagen IgG assay at different thresholds – comparing cases with serology performed > 10 days from symptom onset against healthy controls

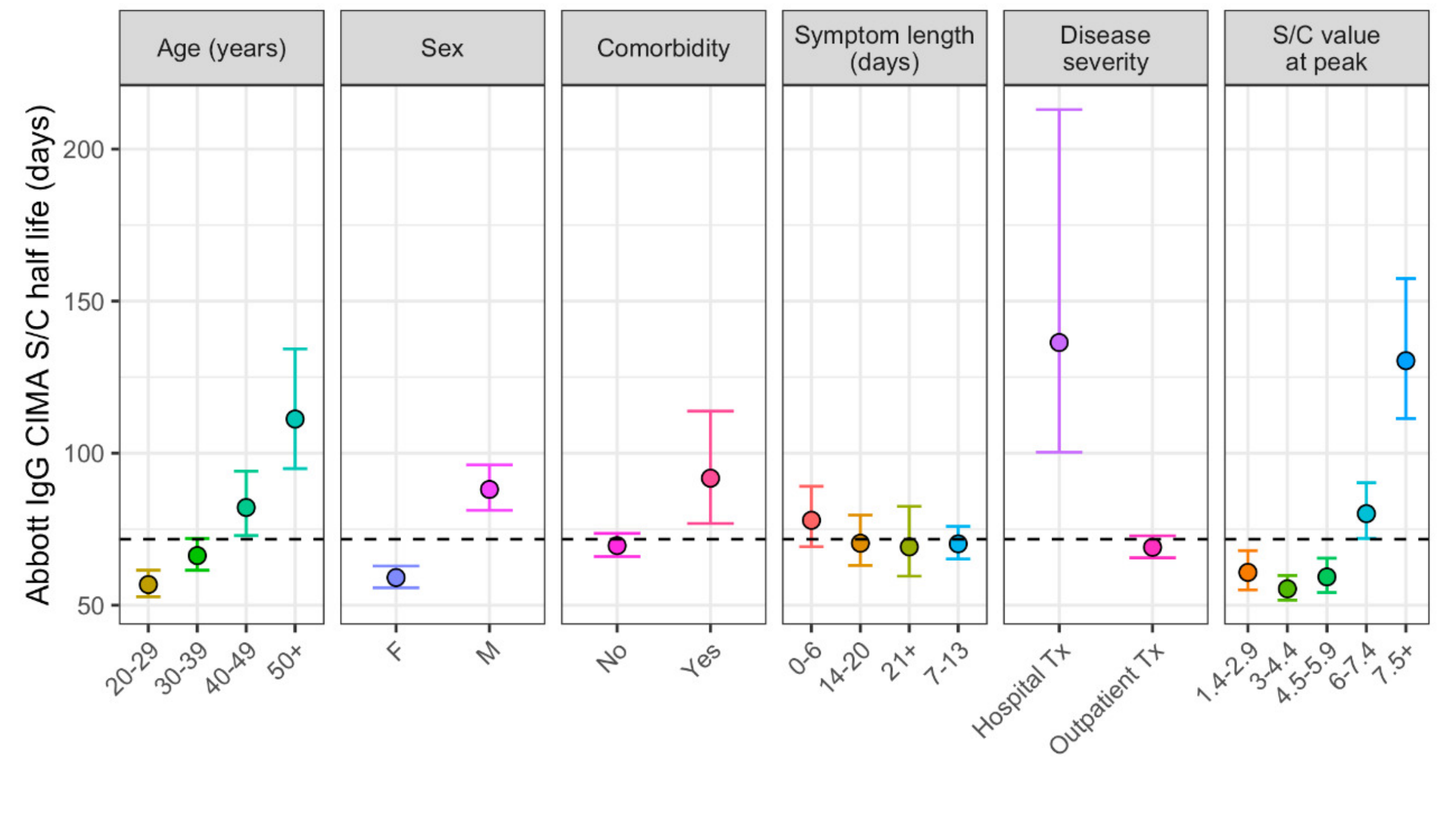


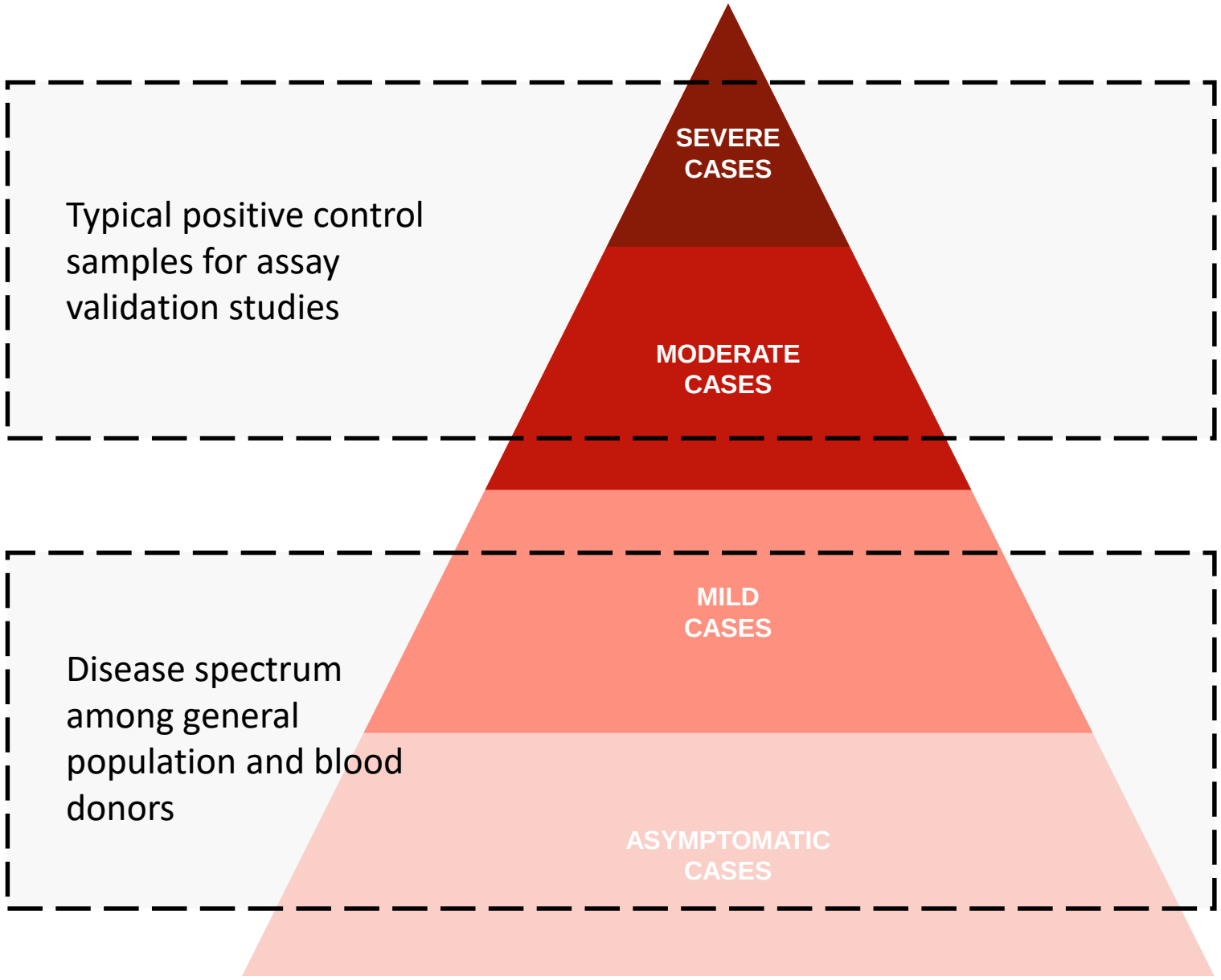


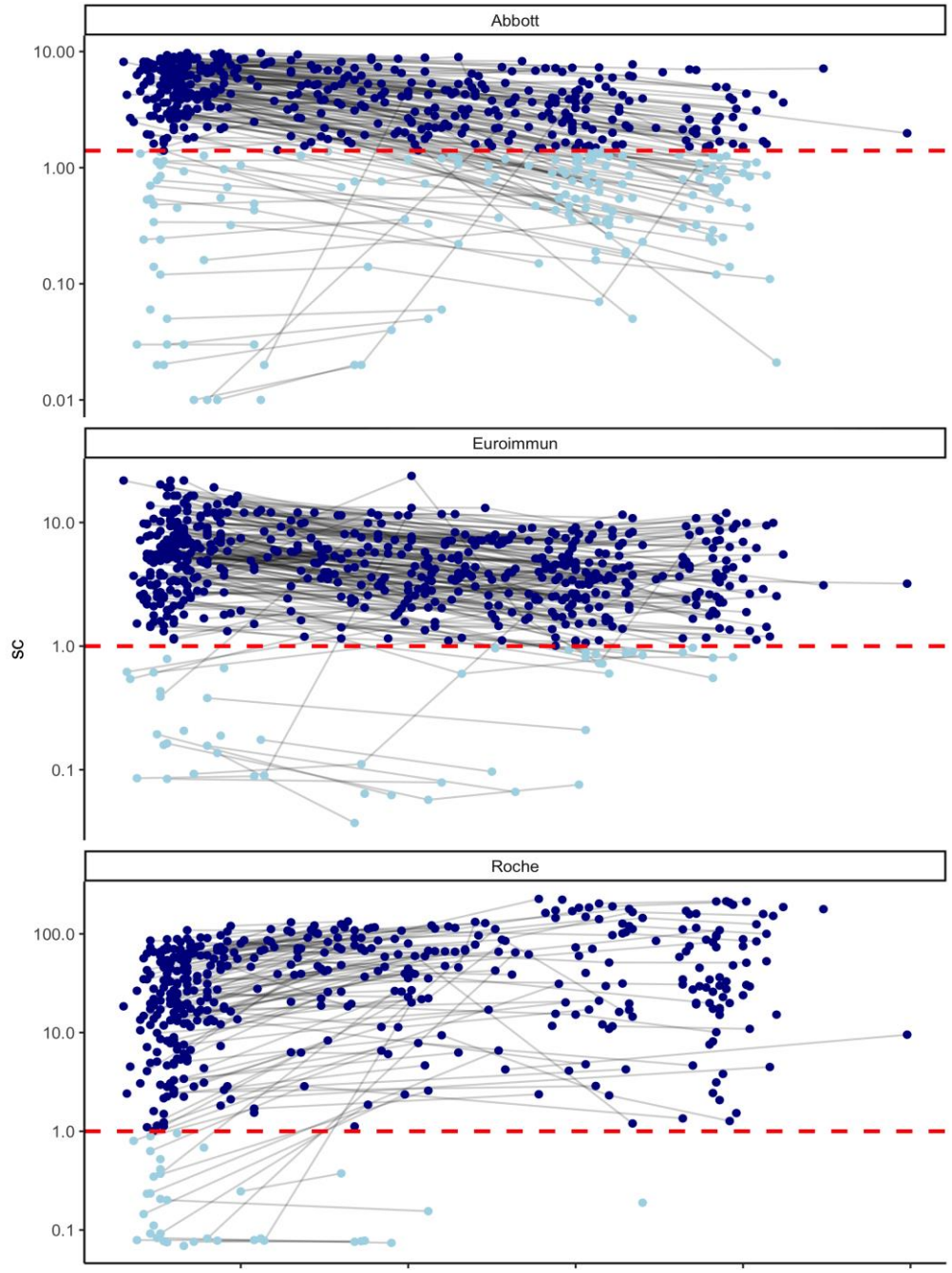
Methodological questions

Serology test characteristics and Abbot anti-N Ab dynamics



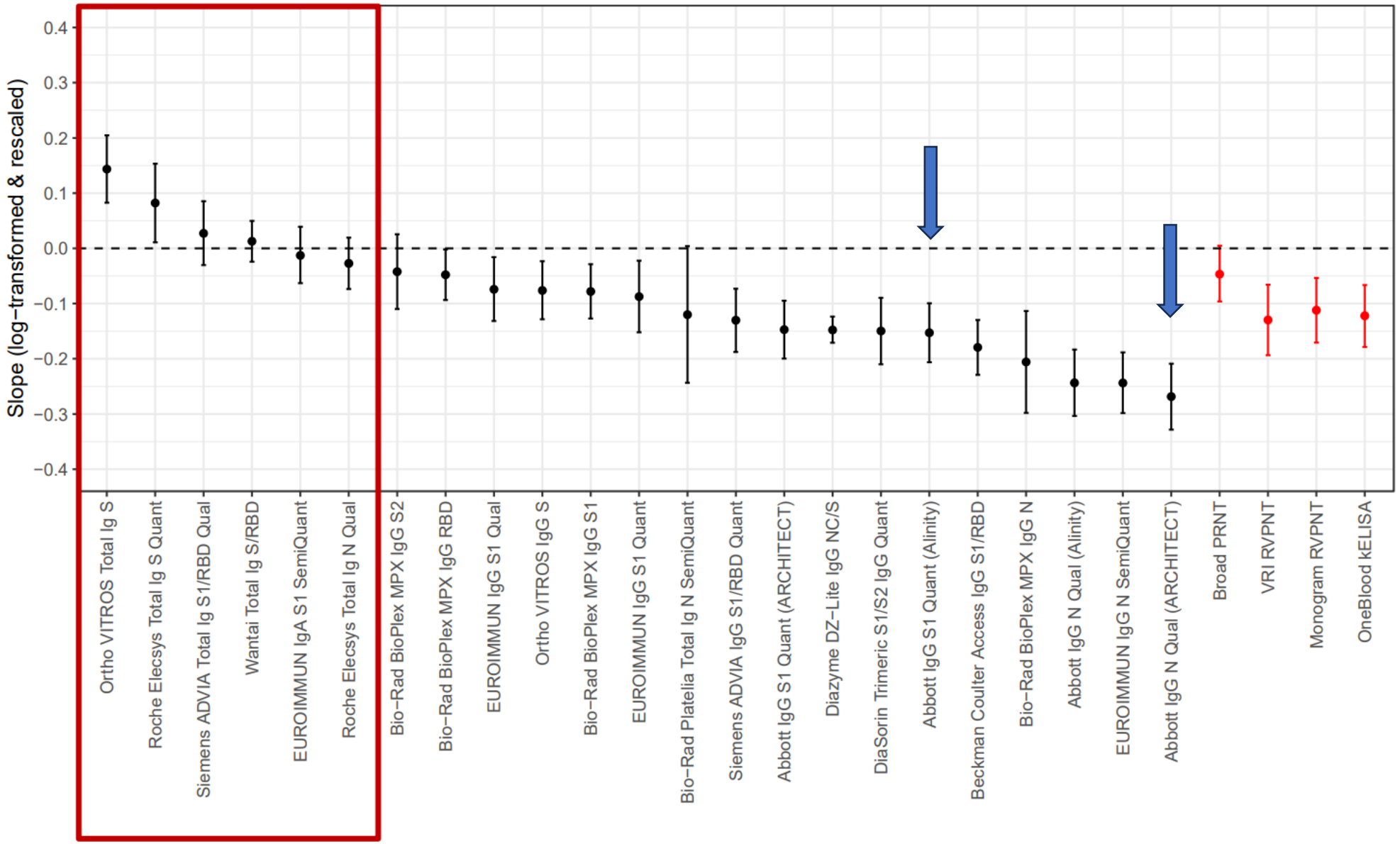

Age (years)
Sex
Comorbidity
Symptom length (days)
Disease severity
S/C value at peak
Abbott IgG CIMA S/C half life (days)
200
150
100
50
20-29
30-39
40-49
50+
F
M
No
Yes
0-6
14-20
21+
7-13
Hospital Tx
Outpatient Tx
1.4-2.9
3-4.4
4.5-5.9
6-7.4
7.5+


Typical positive control samples for assay validation studies
SEVERE CASES
MODERATE CASES
Disease spectrum among general population and blood donors
MILD CASES
ASYMPTOMATIC CASES



Tests had different decline rate

Standardized slopes of bAb signal intensity and nAb titers



Show half lives slide

vitalant Research Institute

Methodological questions
Blood donors as proxy for population sample

Advantages

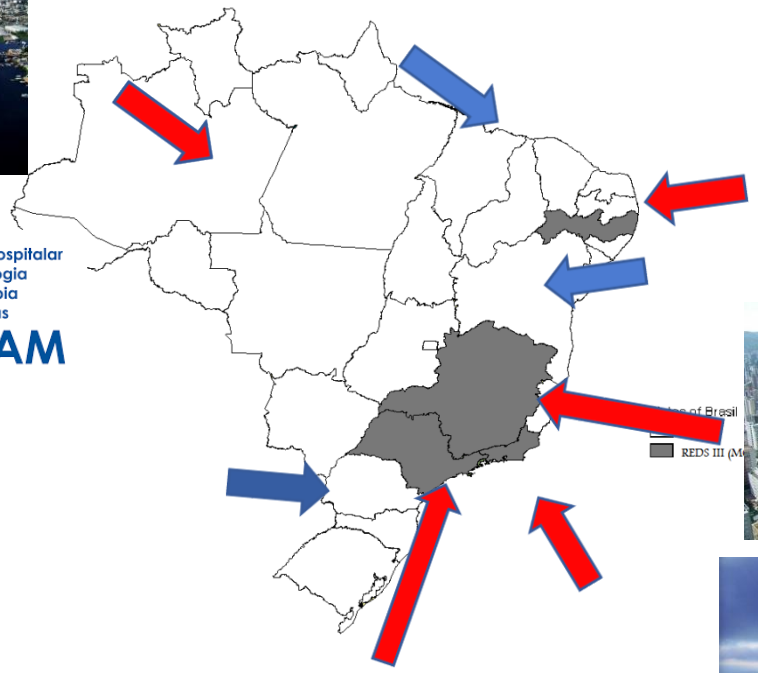
- Fast
- Relatively inexpensive
- Access to state-of-the-art testing infrastructure
- Stored historical samples for 6m in Brazil

Disadvantages

- Selection bias
  - age group
  - socioeconomic
  - spatial distribution
  - deferral criteria
  - behavioral differences

REDS II- IV program – NHLBI/NIH (2007 – 2025)

Belo Horizonte, Manaus, Recife, Rio de Janeiro, Sao Paulo



Fundação Hospitalar de Hematologia e Hemoterapia do Amazonas
HEMOAM

HEMOPE

FUNDAÇÃO HEMOMINAS

vitalant
Blood Donation

FUNDAÇÃO PRÓ-SANGUE
HEMOCENTRO DE SÃO PAULO

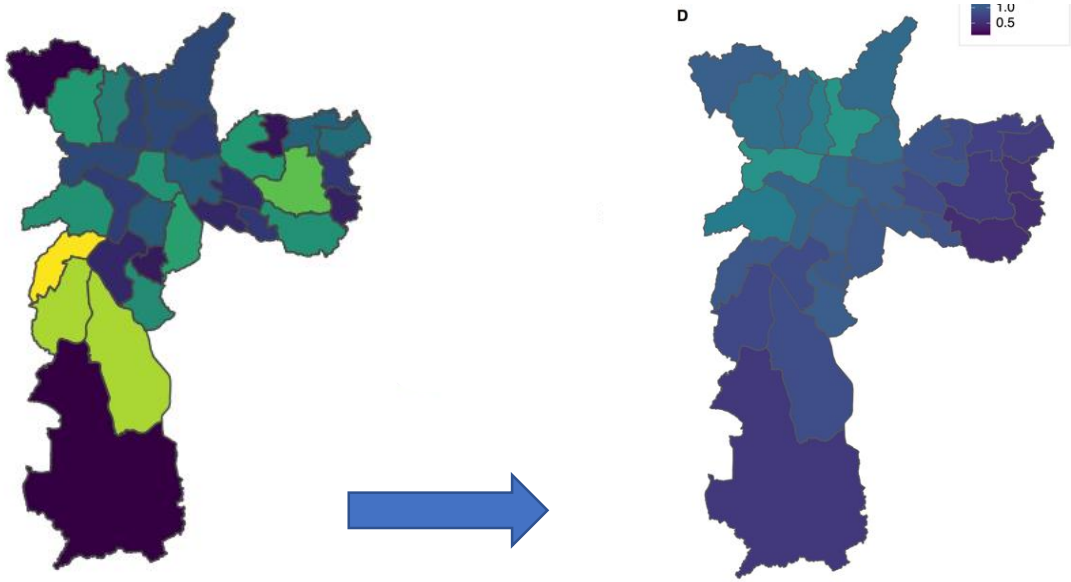
HEMORIO

todos pela saúde

Blood donor study in Brazil

- Total of 8 capitals (most populated)
- Retrospectively – Mar-Jul/20 – Abbott anti-N
- Prospectively Aug /20 – Apr/21 Abbot anti-N
- Apr-Nov 21 Abbott anti-S (7 cities)

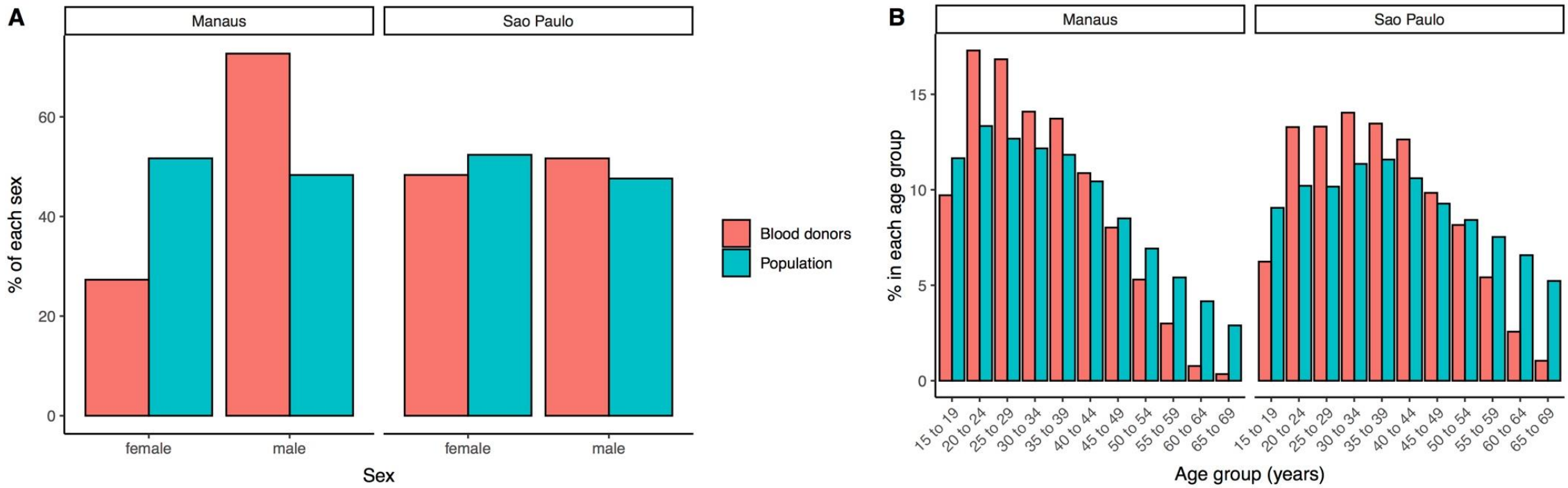
- ~800- 1000 samples per month.
- Samples were geographically stratified using donor zip code (except Manaus)
- System to control sample testing



Blood donors

Study participant

Methodological questions
Blood donors as proxy for population sample



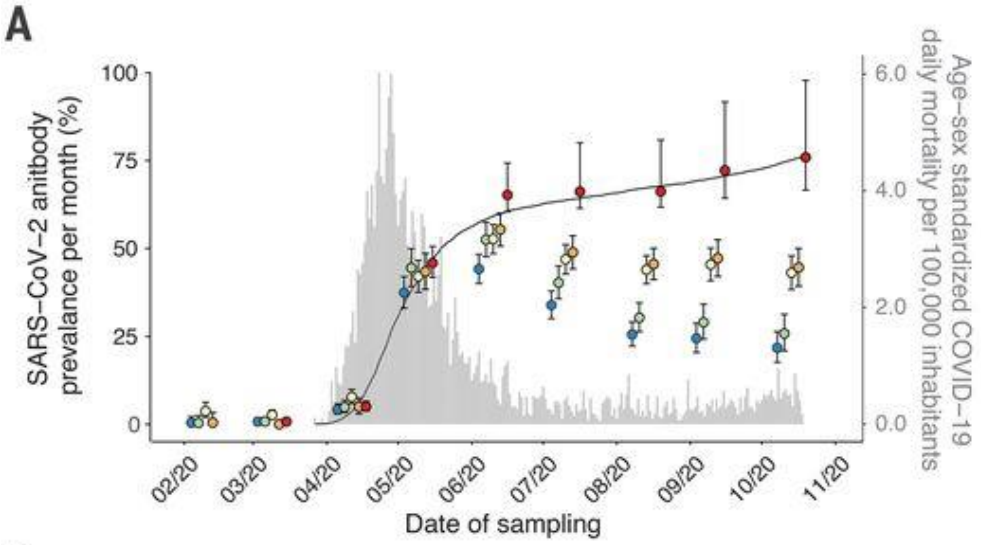
Lewis et al
www.medrxiv.org/content/10.1101/2020.09.16.20194787v1

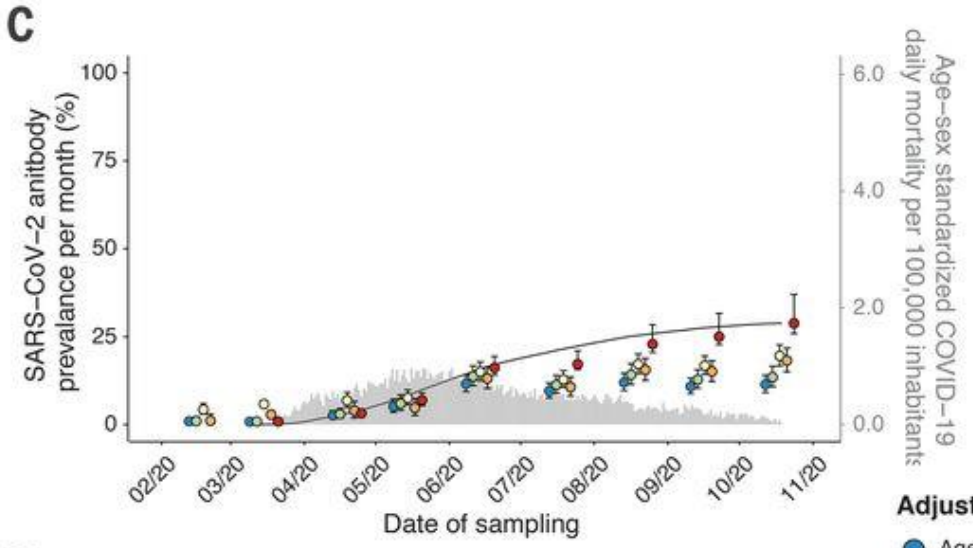
Are blood donors reactivity different than the general population

Results EIA	Ever donated %		Donated last year %	
SARS-COV-2	YES	NO	YES	NO
Positive	10.7	9.4	9.7	10.8
Negative	88.4	89.3	89.7	88.2
Inconclusive	1.0	1.4	0.6	1.0

Cesar Victora personal communication

First results from Manaus and Sao Paulo





Lewis Buss

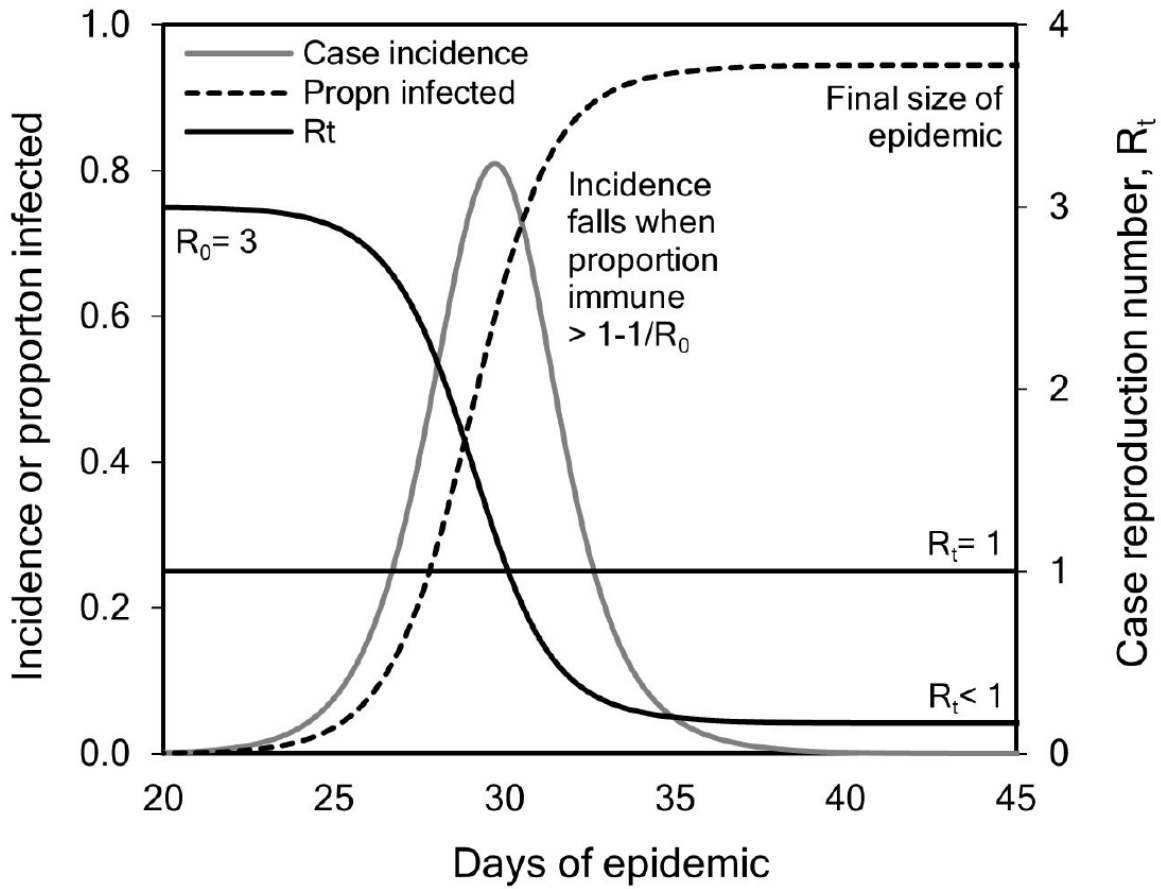
Adjustment method (S/C threshold):

- Age-sex weighted (1.4)
- Age-sex weighted and sens/spec-adjusted (1.4)
- Age-sex weighted (0.4)
- Age-sex weighted and sens/spec-adjusted (0.4)
- Seroreversion corrected (1.4)

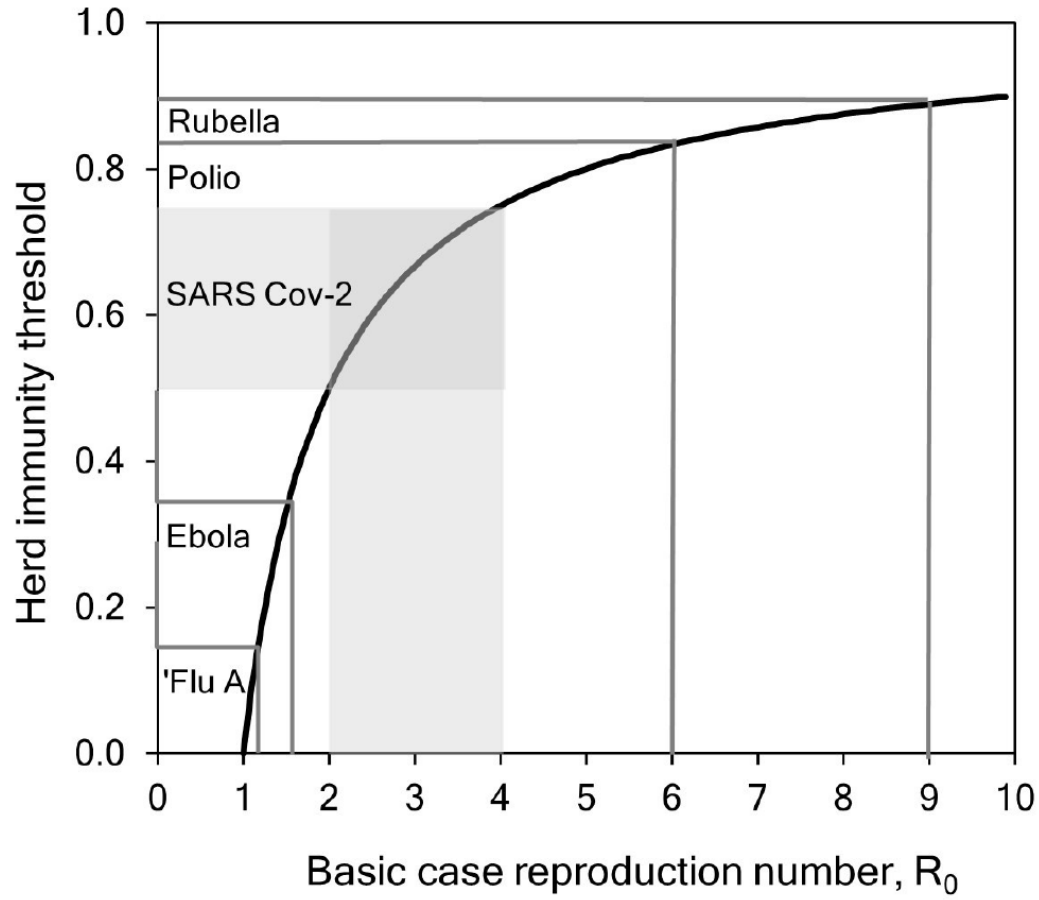
Carlos Prete

Lewis F. Buss et al. Science 2021;371:288-292

a) Build-up of herd immunity during a model epidemic of SARS CoV-2.



b) Herd immunity threshold in relation to R_0, comparing SARS CoV-2 with influenza A, Ebola virus disease, poliomyelitis and rubella



BIOTECHNOLOGY

A city in Brazil where covid-19 ran amok may be a 'sentinel' for the rest of the world

So many people have gotten sick in Manaus that researchers say the virus is running out of people to infect.

By Antonio Regalado September 22, 2020

In a report posted to the preprint server medRxiv, a group led by Ester Sabino, of the Institute of Tropical Medicine at the University of São Paulo, says it tested banked blood for antibodies to the virus and estimates that between 44 and 66% of the population of Manaus has been infected since the city detected its first case in March.

"From what we learned this is probably the highest prevalence in the world," Sabino said in a phone interview. "Deaths have dropped very rapidly, and what we're saying is that it's related."

REPORT

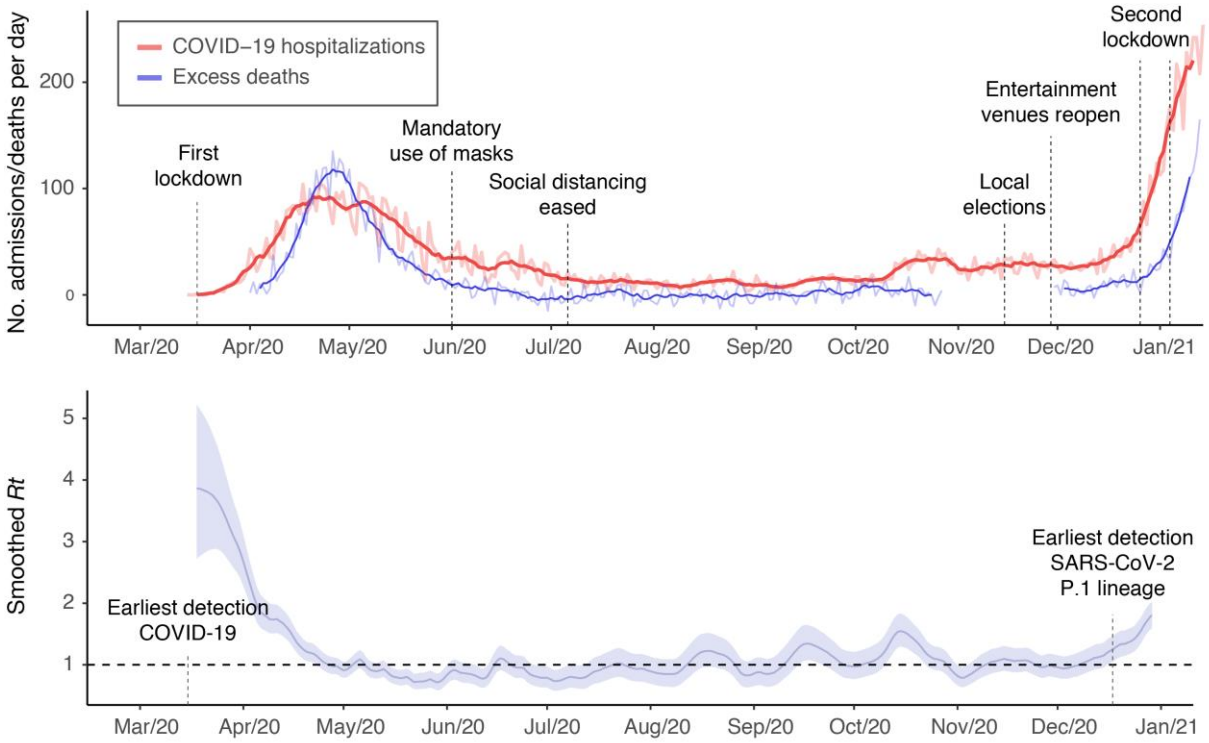
Three-quarters attack rate of SARS-CoV-2 in the Brazilian Amazon during a largely unmitigated epidemic

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, [...], AND ESTER C. SABINO +26 authors Authors Info & Affiliations

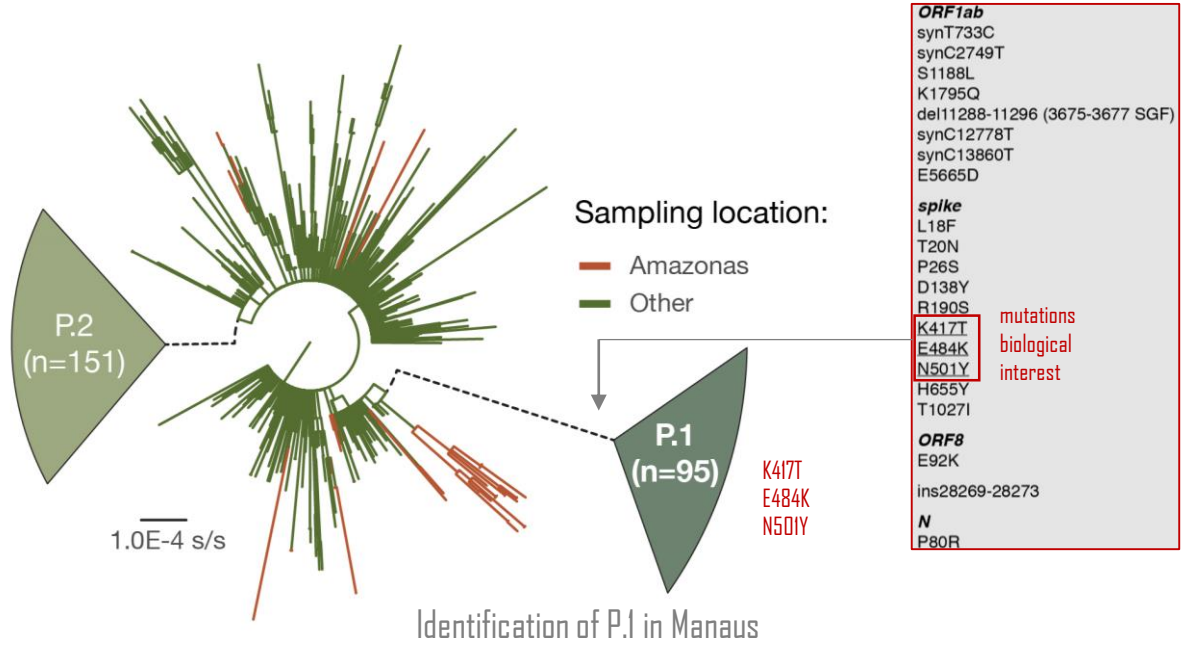
SCIENCE · 8 Dec 2020 · Vol 371, Issue 6526 · pp. 288-292 · DOI: 10.1126/science.abe9728

Our data show that >70% of the population had been infected in Manaus about 7 months after the virus first arrived in the city. This is above the theoretical herd immunity threshold. However, prior infection may not confer long-lasting immunity (*30*, *31*). Indeed, we observed rapid antibody waning in Manaus, consistent with other reports that have shown signal waning on the Abbott IgG assay (*14*, *32*). However, other commercial assays, with different designs or targeting different antigens, have more stable signal (*14*), and there is evidence for a robust neutralizing antibody response several months out from infection (*33*). Rare reports of reinfection have been confirmed (*34*), but the frequency of its occurrence remains an open question (*35*). Manaus represents a "sentinel" population, giving us a data-based indication of what may happen if SARS-CoV-2 is allowed to spread largely unmitigated. Further seroepidemiological, molecular, and genomic surveillance studies in the region are required urgently to determine the longevity of population immunity, the correlation with the observed antibody waning, and the diversity of circulating lineages.

Resurgence of SARS-CoV-2 in Manaus, despite seroprevalence



E484K



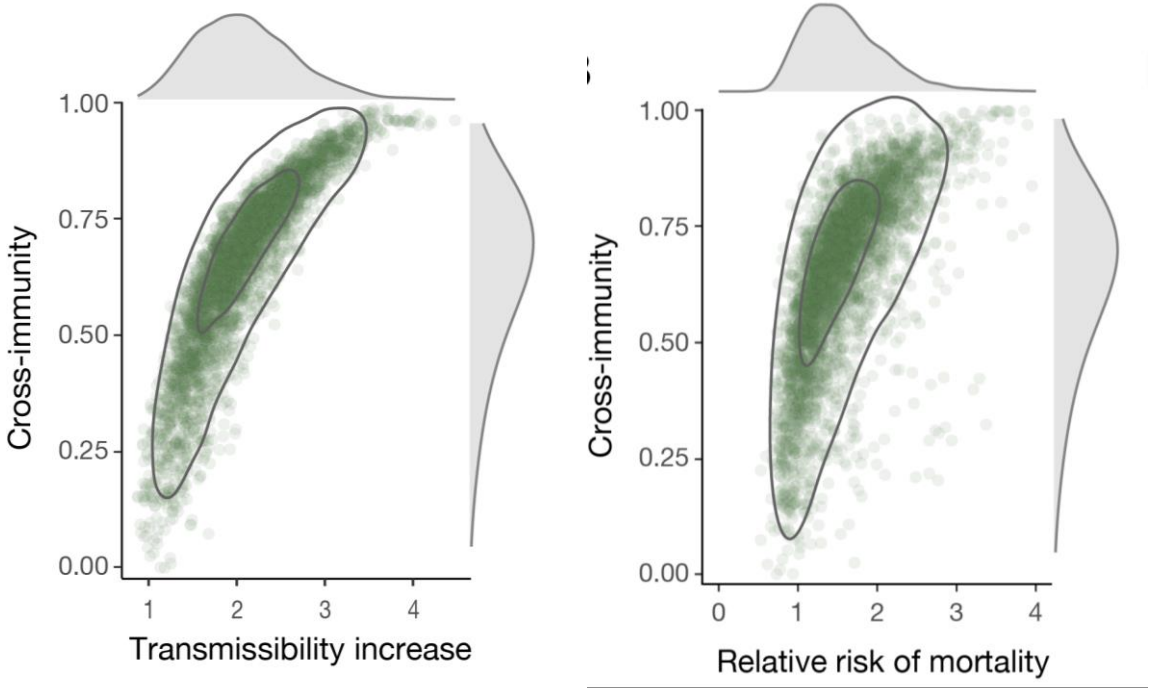
Identification of P.1 in Manaus

Darlan Candido & Ingra Claro

Altered epidemiological characteristics of the P.1/Gamma VOC in Manaus

Two-category mathematical model to investigate transmissibility, immune evasion and disease severity of P.1 lineage in Manaus:

- P.1 is 1.7–2.4 (50% BCI) more transmissible compared to non-P1 lineages in Manaus
- P.1 can evade 21-46% (50% BCI) of protective immunity elicited by previous infection with non-P1 lineages
- 1.2–1.9 (50% BCI) times more likely to result in mortality: strained healthcare systems?
- Validated by subsequent studies on reinfection, disease severity and transmissibility



Faria et al. *Science* 2021;

Prete Jr et al. BMC Infectious Diseases (2022) 22:127
https://doi.org/10.1186/s12879-022-07094-y

RESEARCH Open Access

Reinfection by the SARS-CoV-2 Gamma variant in blood donors in Manaus, Brazil

Carlos A. Prete Jr[1], Lewis F. Buss[2], Renata Buccheri[3], Claudia M. M. Abrahim[4], Tassila Salomon[5], Myuki A. E. Crispim[4], Marcio K. Oikawa[6], Eduard Grebe[3,7,8], Allyson G. da Costa[4], Nelson A. Fraiji[4], Maria do P. S. S. Carvalho[4], Charles Whittaker[9], Neal Alexander[10], Nuno R. Faria[2,9,11], Christopher Dye[11], Vítor H. Nascimento[1], Michael P. Busch[3,7] and Ester Cerdeira Sabino[2*]

Proportion of reinfection cases in 2021:

- V curve 13.6%, (95% CI [7.0%, 24.5%])
- +Probable 22.7% (95% CI [14.3%, 34.2%])
- +Possible 39.3% (95% CI [29.5%, 50.0%])

Rates of reinfection in individuals positive in 2020

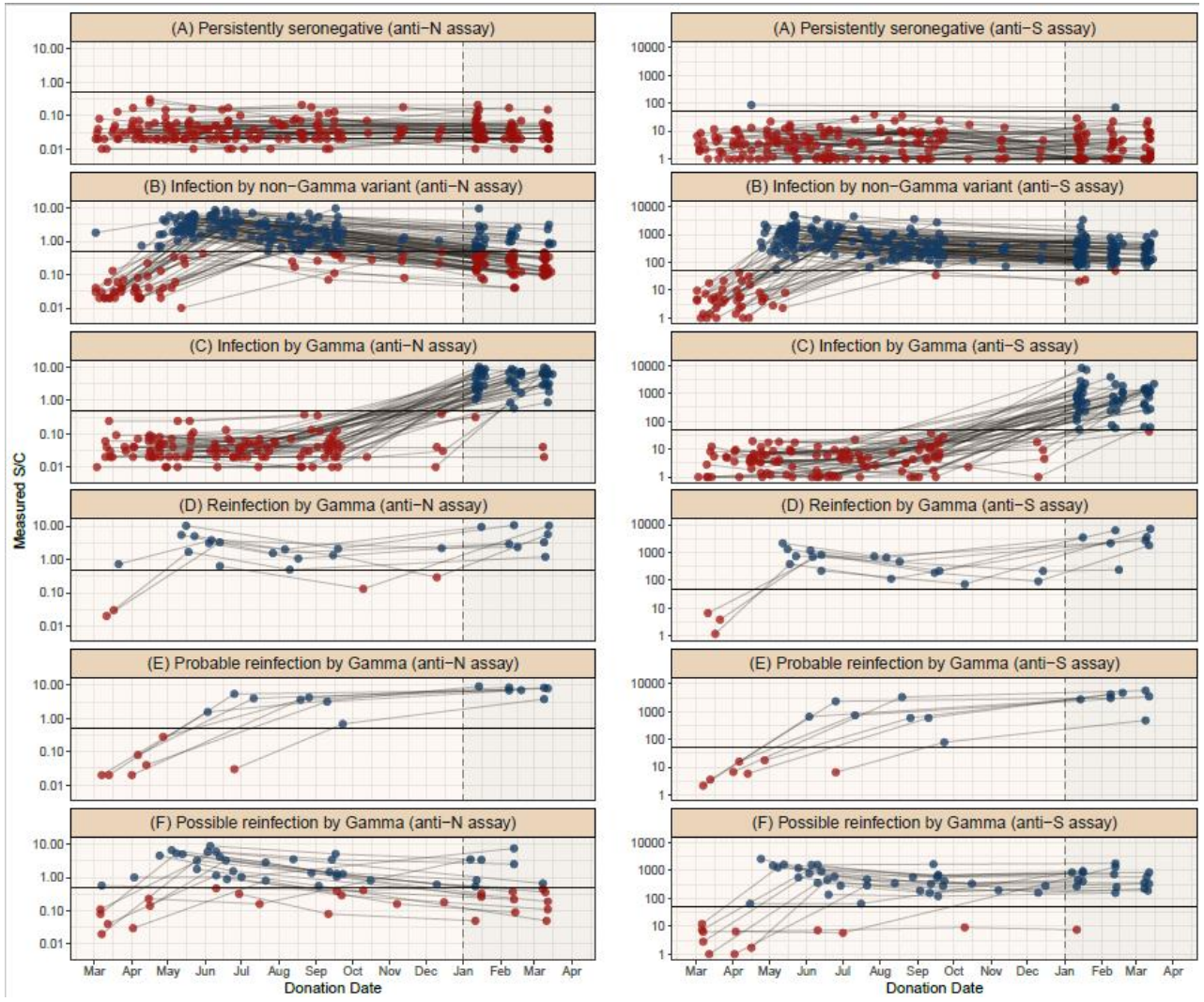
- V curve 6.5% (95% CI [3.3%, 12.3%])
- +Probably 12.2% (95% CI [7.5%, 19.1%])
- +Possible 26.8% (95% CI [19.8%, 35.3%])

Rates of gamma infection in negative samples

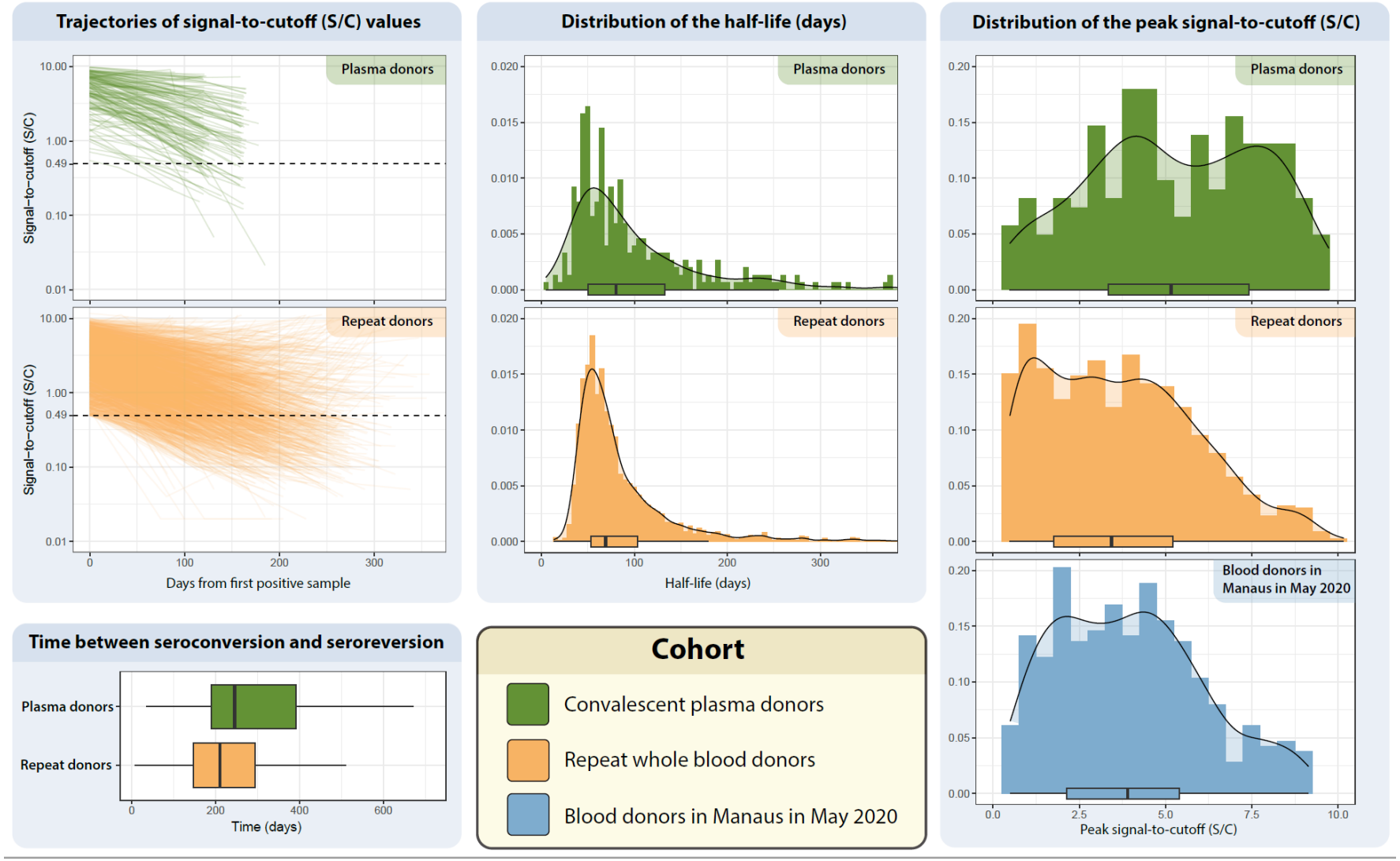
- 115 negative in 2020: 51 infected in 2021 (44.3%, 95% CI [35.6%, 53.5%]).

The protection against reinfection conferred by previous infection

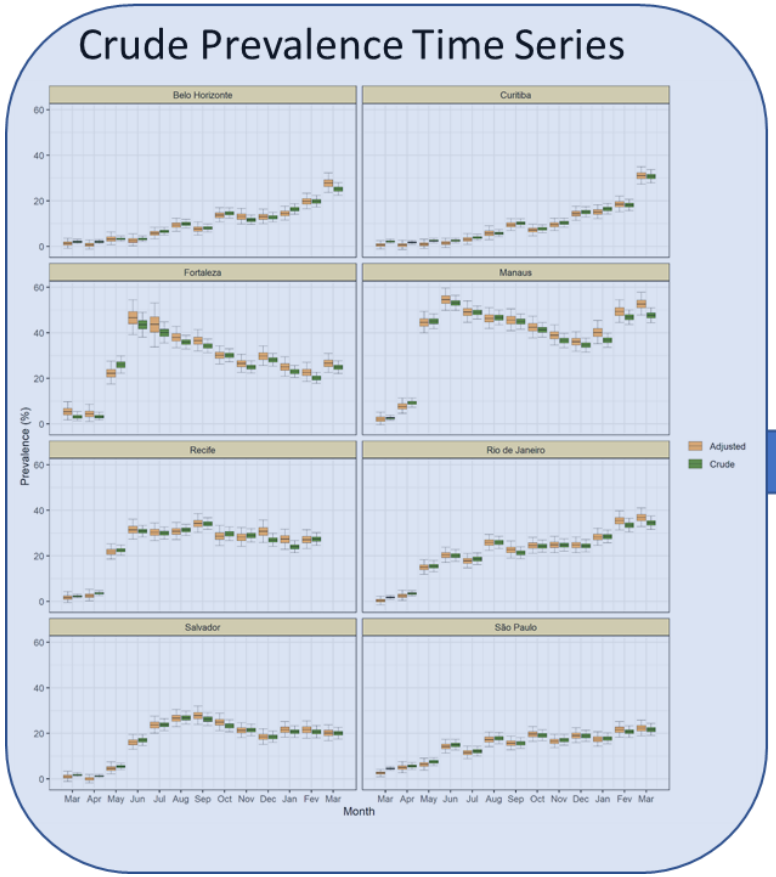
- V curve 85.3% (95% CI [71.3%, 92.7%]),
- + probably 72.5% (95% CI [54.7%, 83.6%])
- + possible 39.5% (95% CI [14.1%, 57.8%])



Antibody waning and disease spectrum



Prete CA Jr. & al. SARS-CoV-2 antibody dynamics in blood donors and COVID-19 epidemiology in eight Brazilian state capitals: A serial cross-sectional study. Elife. 2022 Sep 22;11:e78233.



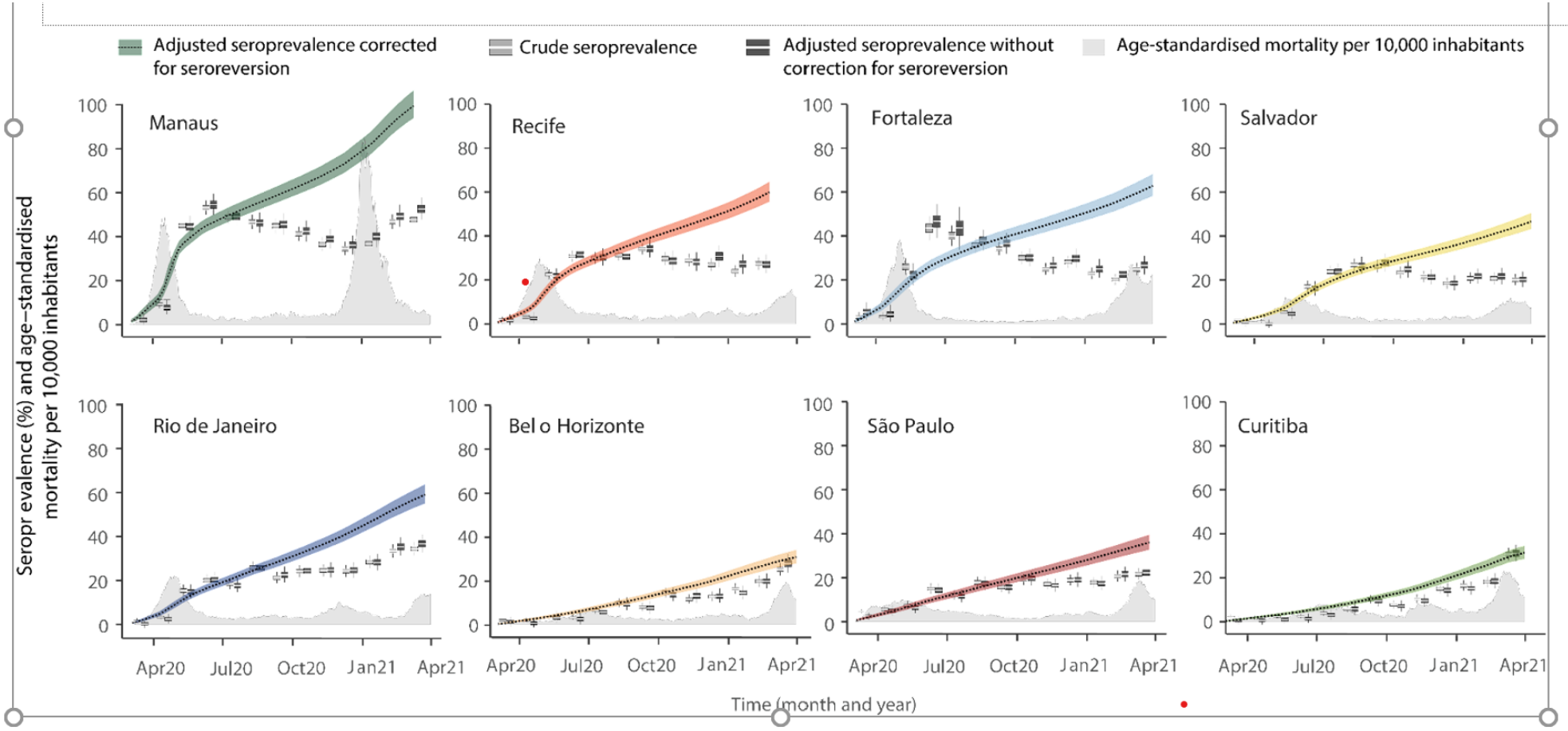
Distribution of the delay between seroconversion and seroreversion

Our proposed Bayesian model

Seroprevalence corrected for seroreversion

Prete CA Jr. & al. SARS-CoV-2 antibody dynamics in blood donors and COVID-19 epidemiology in eight Brazilian state capitals: A serial cross-sectional study. Elife. 2022 Sep 22:11:e78233

Adjusted seroprevalence in eight Brazilian capitals



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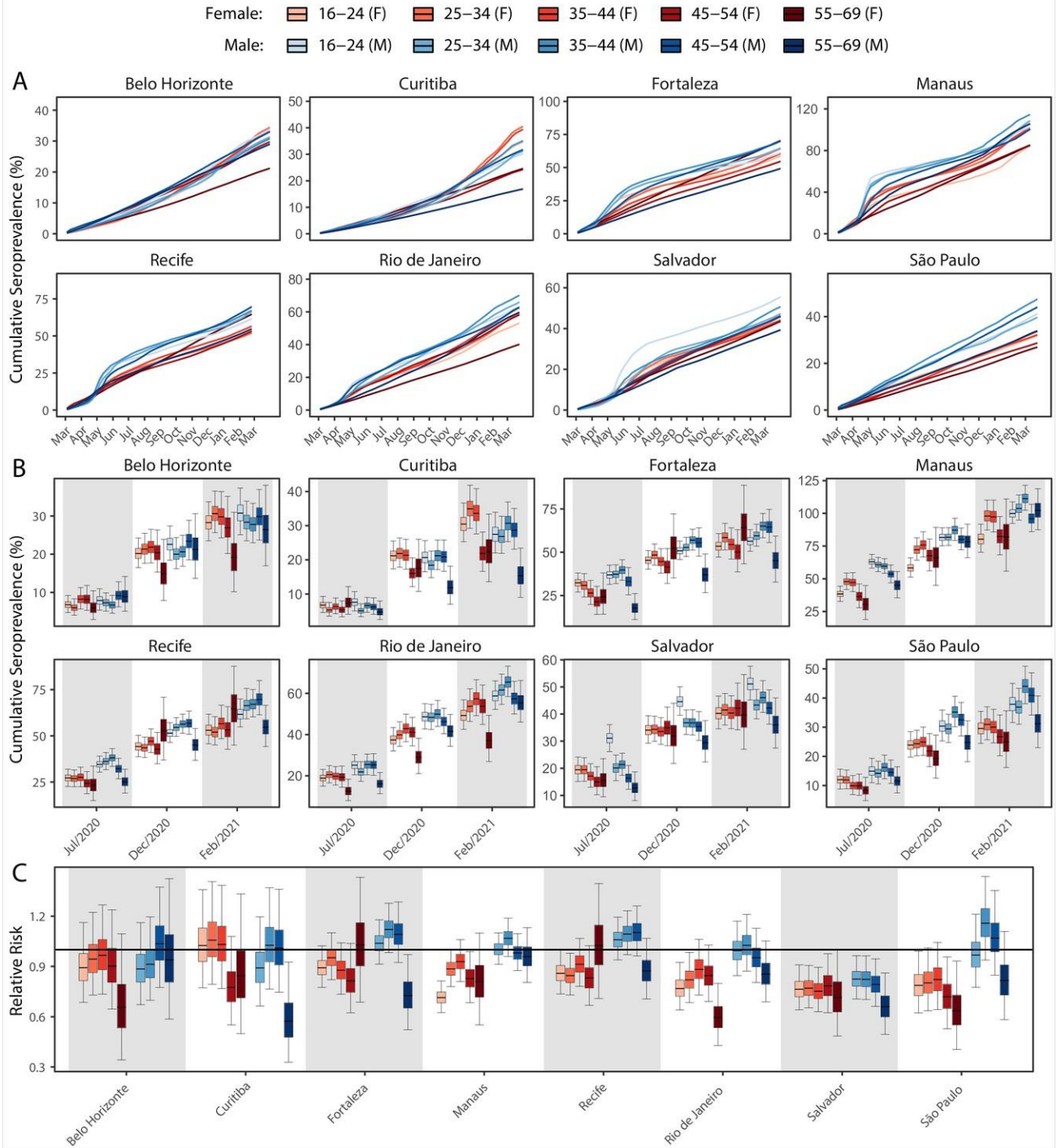
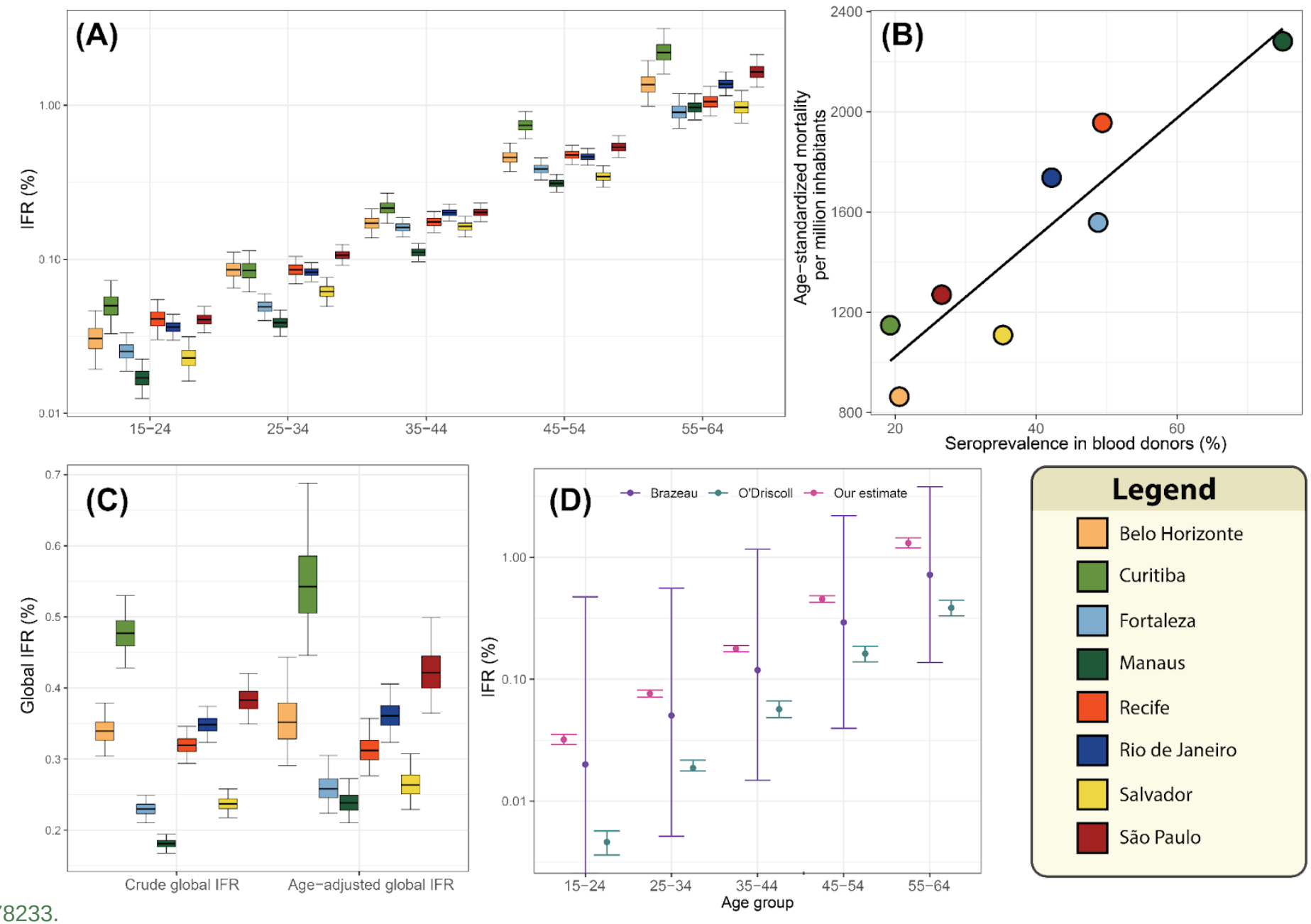
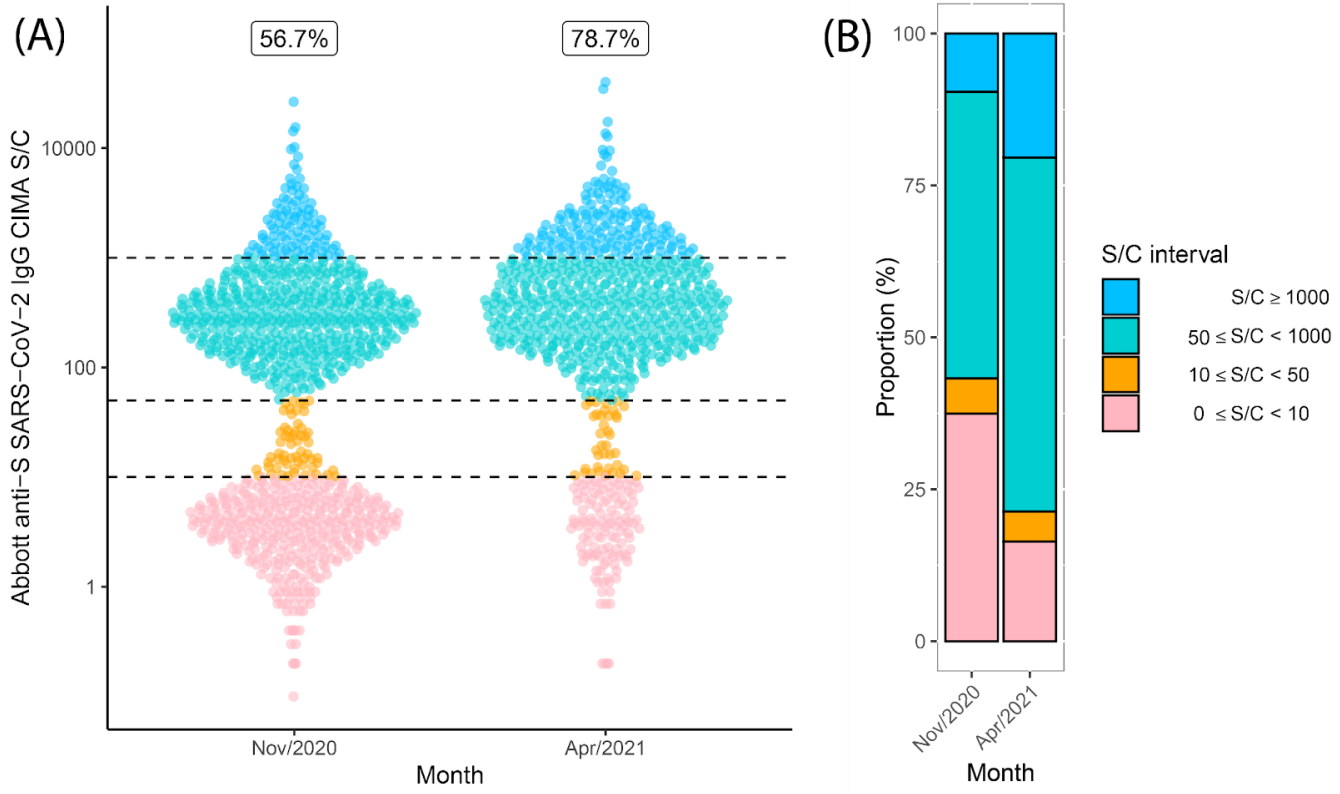

Female: 16–24 (F) 25–34 (F) 35–44 (F) 45–54 (F) 55–69 (F)
Male: 16–24 (M) 25–34 (M) 35–44 (M) 45–54 (M) 55–69 (M)
A
Belo Horizonte
Curitiba
Fortaleza
Manaus
Recife
Rio de Janeiro
Salvador
São Paulo
Cumulative Seroprevalence (%)
Mar Apr May Jun Jul Aug Sep Oct Nov Dec Jan Feb Mar
B
Belo Horizonte
Curitiba
Fortaleza
Manaus
Recife
Rio de Janeiro
Salvador
São Paulo
Cumulative Seroprevalence (%)
Jul/2020 Dec/2020 Feb/2021
C
Relative Risk
Belo Horizonte Curitiba Fortaleza Manaus Recife Rio de Janeiro Salvador São Paulo

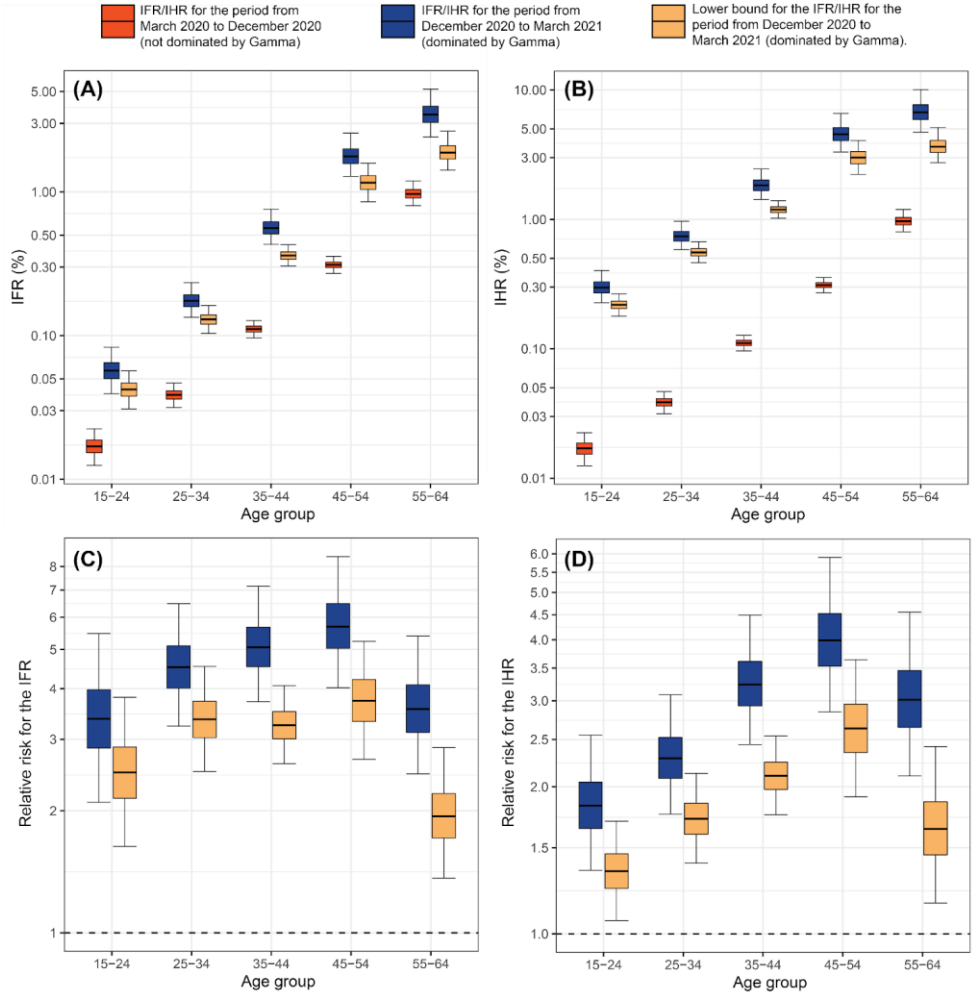
IFR according to age and location



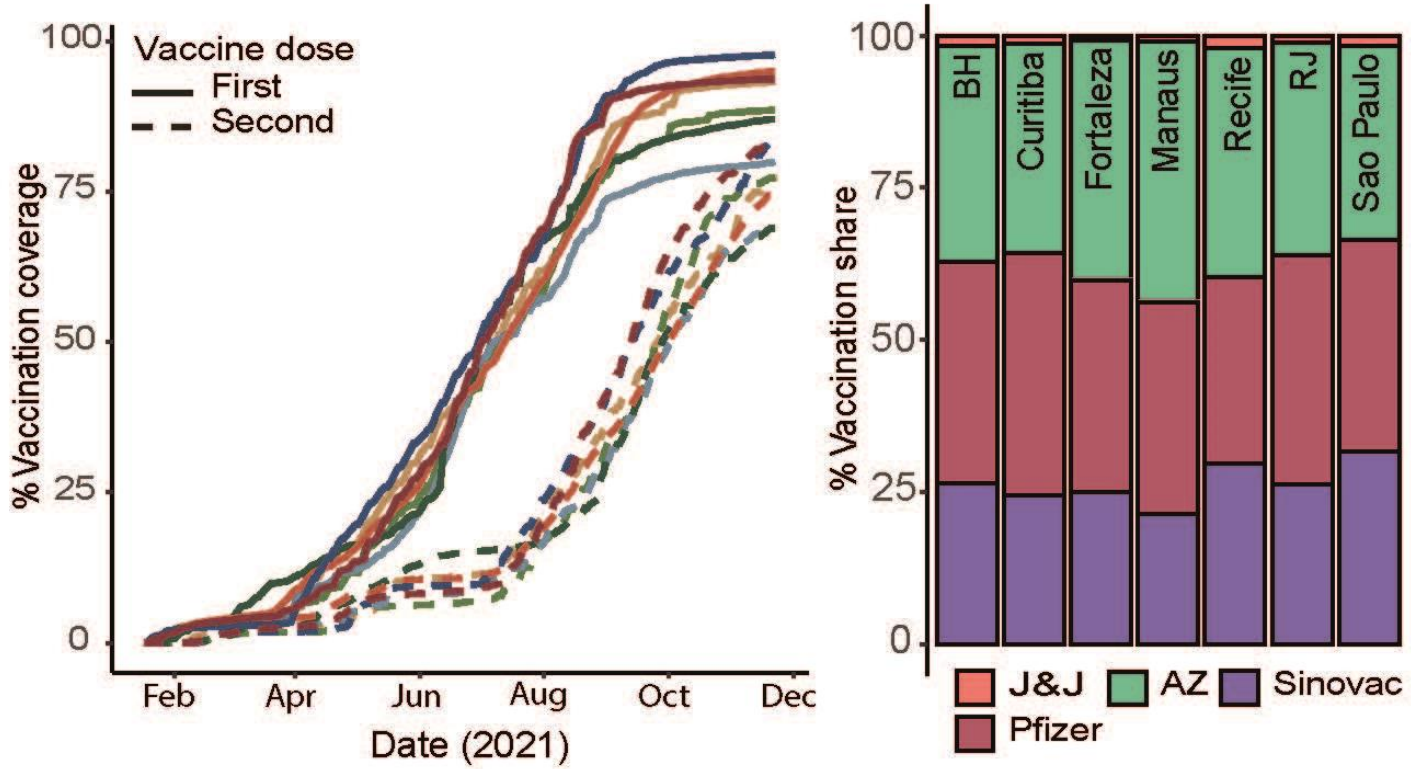
Prete CA Jr. & al. Elife. 2022 Sep 22;11:e78233.

2nd wave had a lower attack rate and a higher morbility/mortality

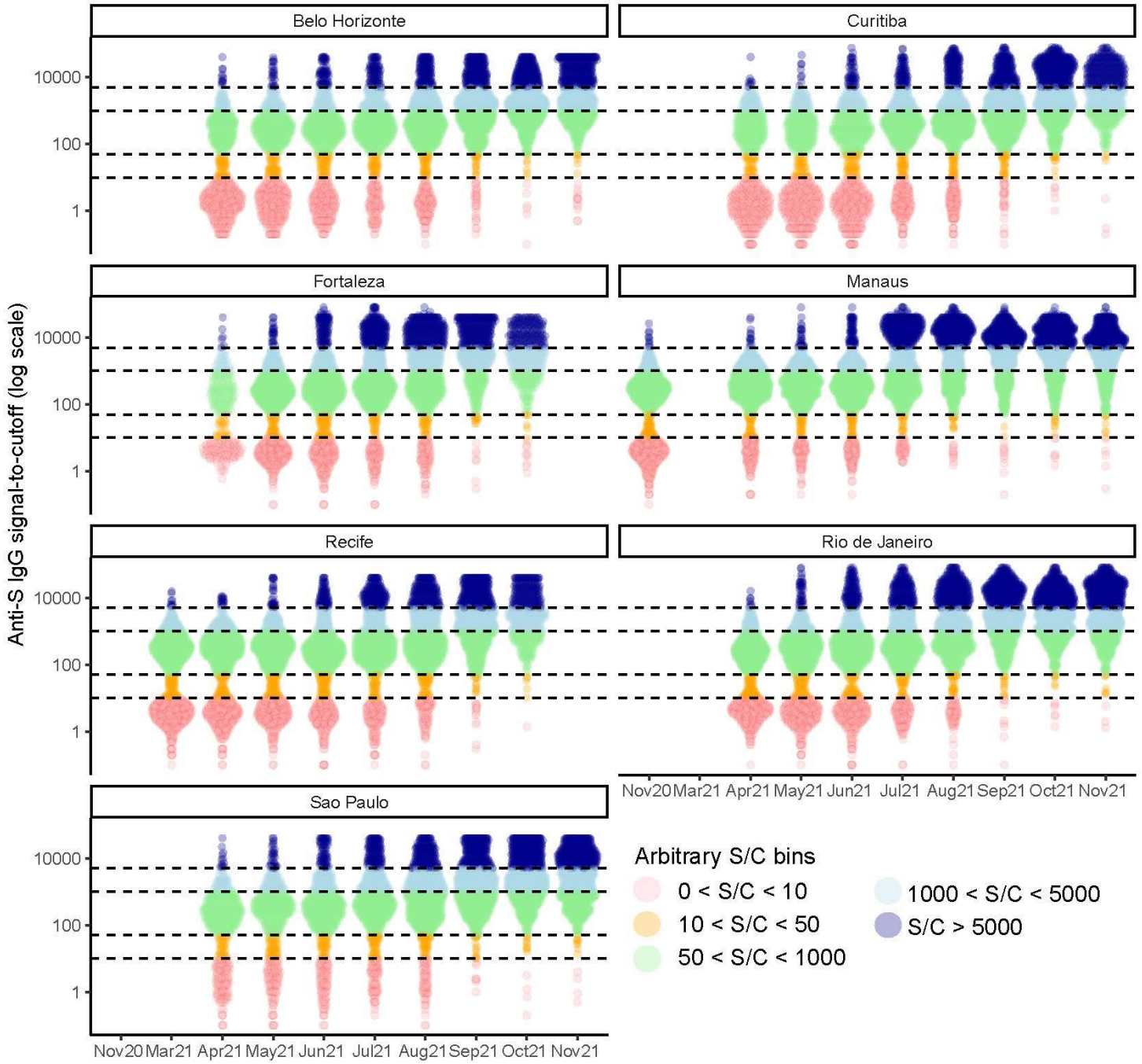




Vaccination coverage in blood donor eligible age range



Buss et al Vaccines (Basel). 2022 Aug 31;10(9):1437

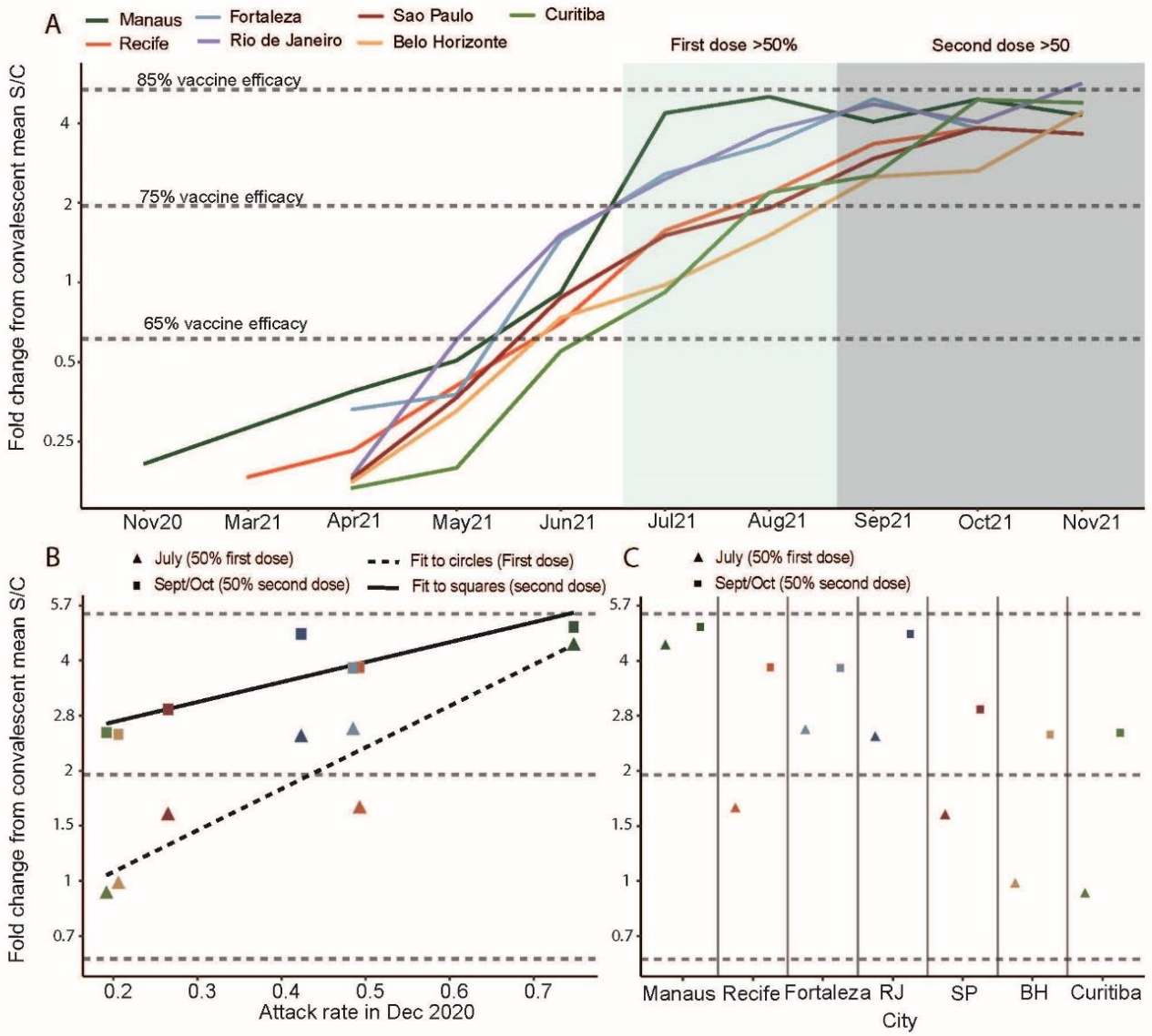


Buss et al Vaccines (Basel). 2022 Aug 31;10(9):1437

Predicting SARS-CoV-2 variant spread in a completely seropositive population using semi-quantitative antibody measurements in blood donors

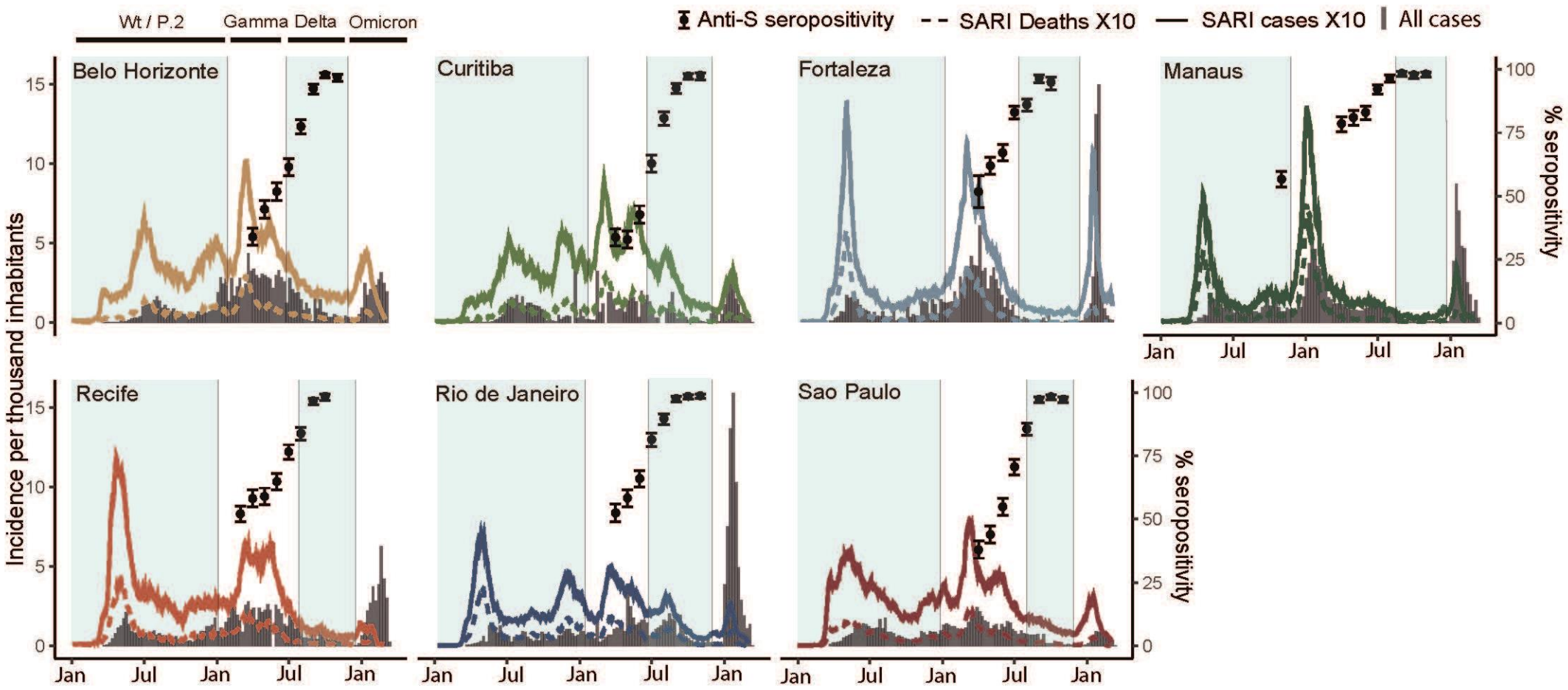
Lewis F Buss, Carlos A Prete Jr., Charles Whittaker, Tassila Salomon, Marcio K. Oikawa, Rafael H. M. Pereira, Isabel C. G. Moura, Lucas Delerino, Rafael F. O. Franca, Fabio Miyajima, Alfredo Mendrone-Junior, César de Almeida Neto, Nanci A. Salles, Suzete C. Ferreira, Karine A. Fladzinski, Luana M. de Souza, Luciane K. Schier, Patricia M. Inoue, Lilyane A. Xabregas, Myuki A. E. Crispim, Nelson Fraiji, Luciana M. B. Carlos, Veridiana Pessoa, Maisa A. Ribeiro, Rosenvaldo E. de Souza, Anna F. Cavalcante, Maria I. B. Valença, Maria V. da Silva, Esther Lopes, Luiz A. Filho, Sheila O. G. Mateos, Gabrielle T. Nunes, David Schlesinger, Sônia Mara Nunes da Silva, Alexander L. Silva-Junior, Marcia C Castro, Vítor H. Nascimento, Christopher Dye, Michael P Busch, Nuno R Faria, Ester C Sabino

doi: https://doi.org/10.1101/2022.06.16.22276483

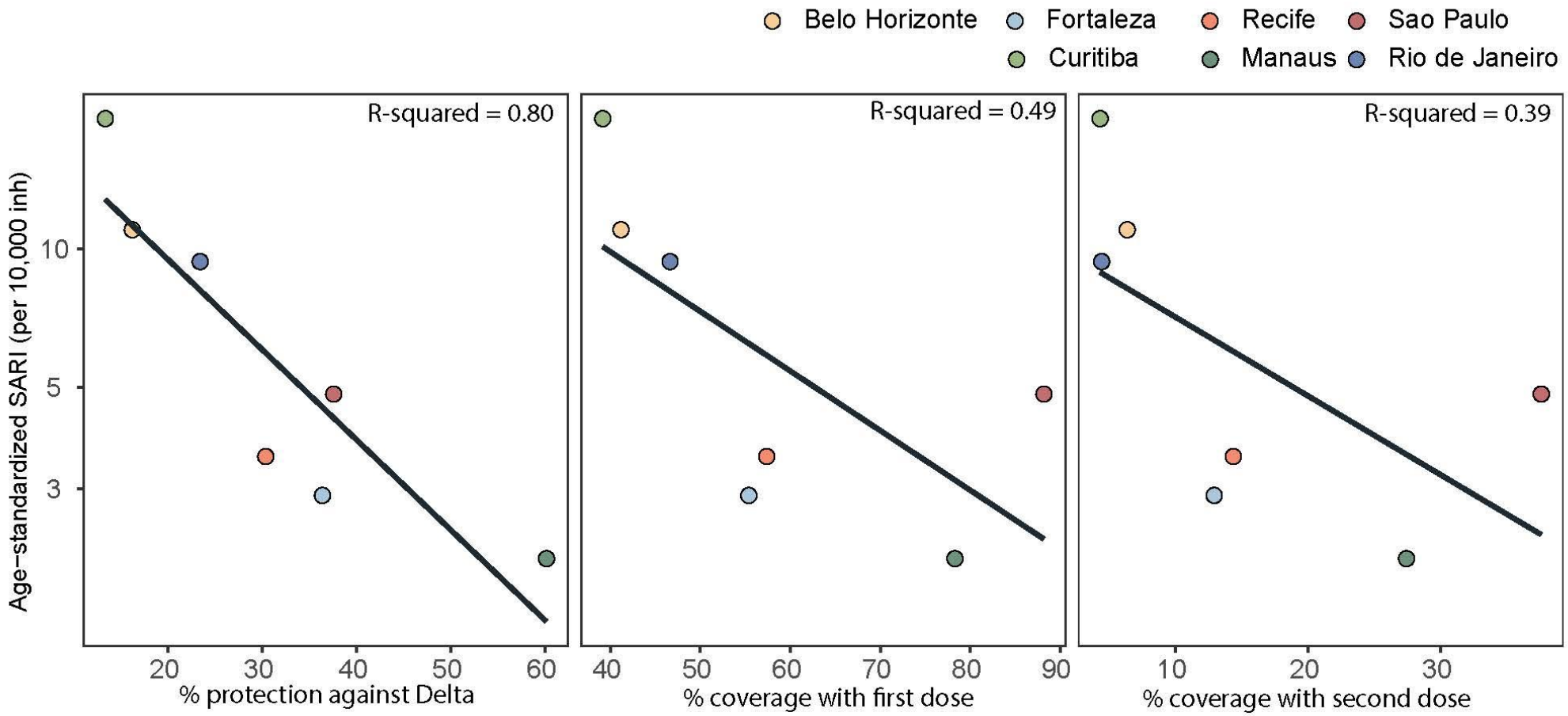


Results normalized by convalescent plasma donor S/C

Buss et al Vaccines (Basel). 2022 Aug 31;10(9):1437

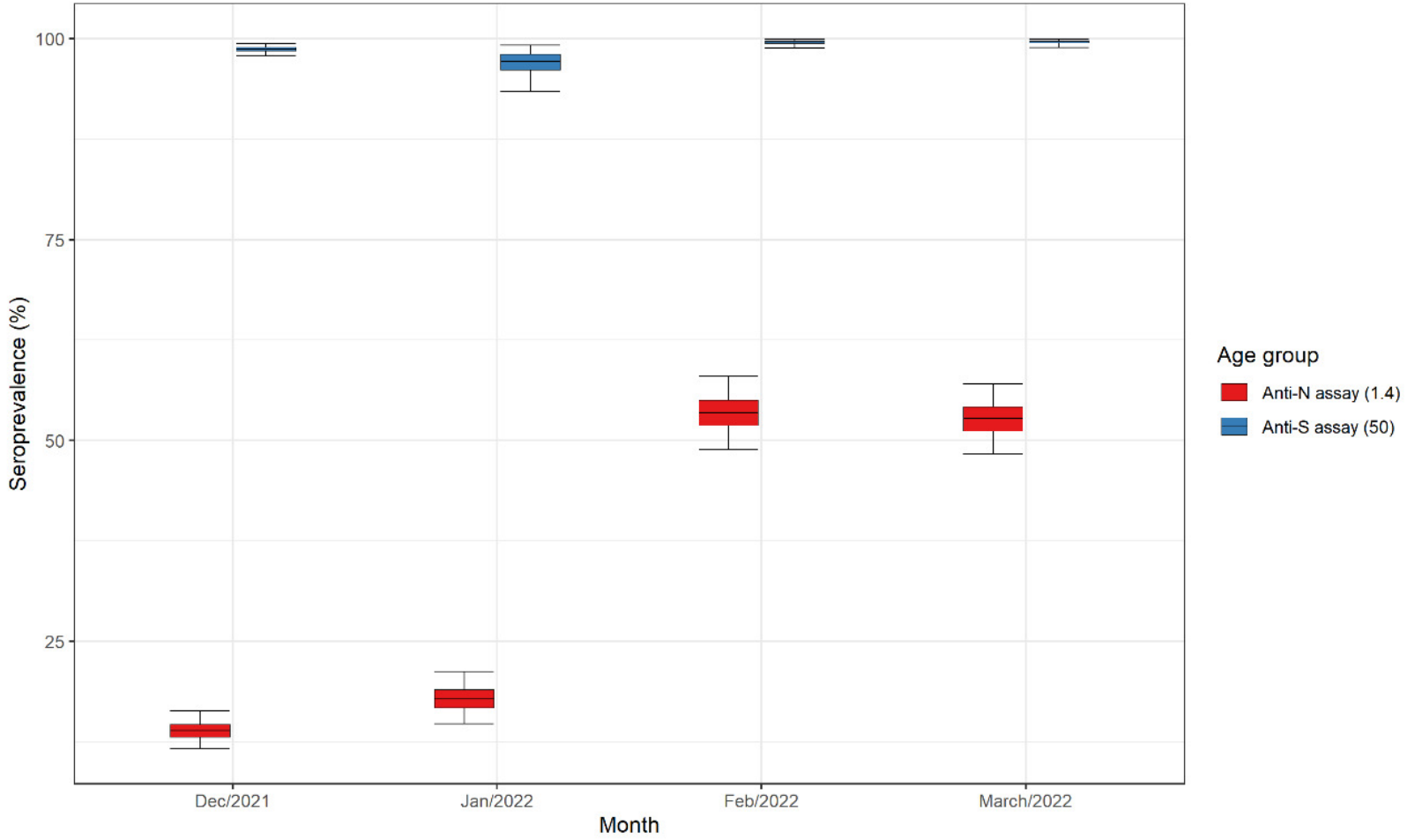

Wt / P.2
Gamma
Delta
Omicron
Anti-S seropositivity
SARI Deaths X10
SARI cases X10
All cases
Belo Horizonte
Curitiba
Fortaleza
Manaus
Recife
Rio de Janeiro
Sao Paulo
Incidence per thousand inhabitants
% seropositivity
0
5
10
15
0
25
50
75
100
Jan
Jul
Jan
Jul
Jan

Antibody level correlated better with protection against delta than vaccination coverage



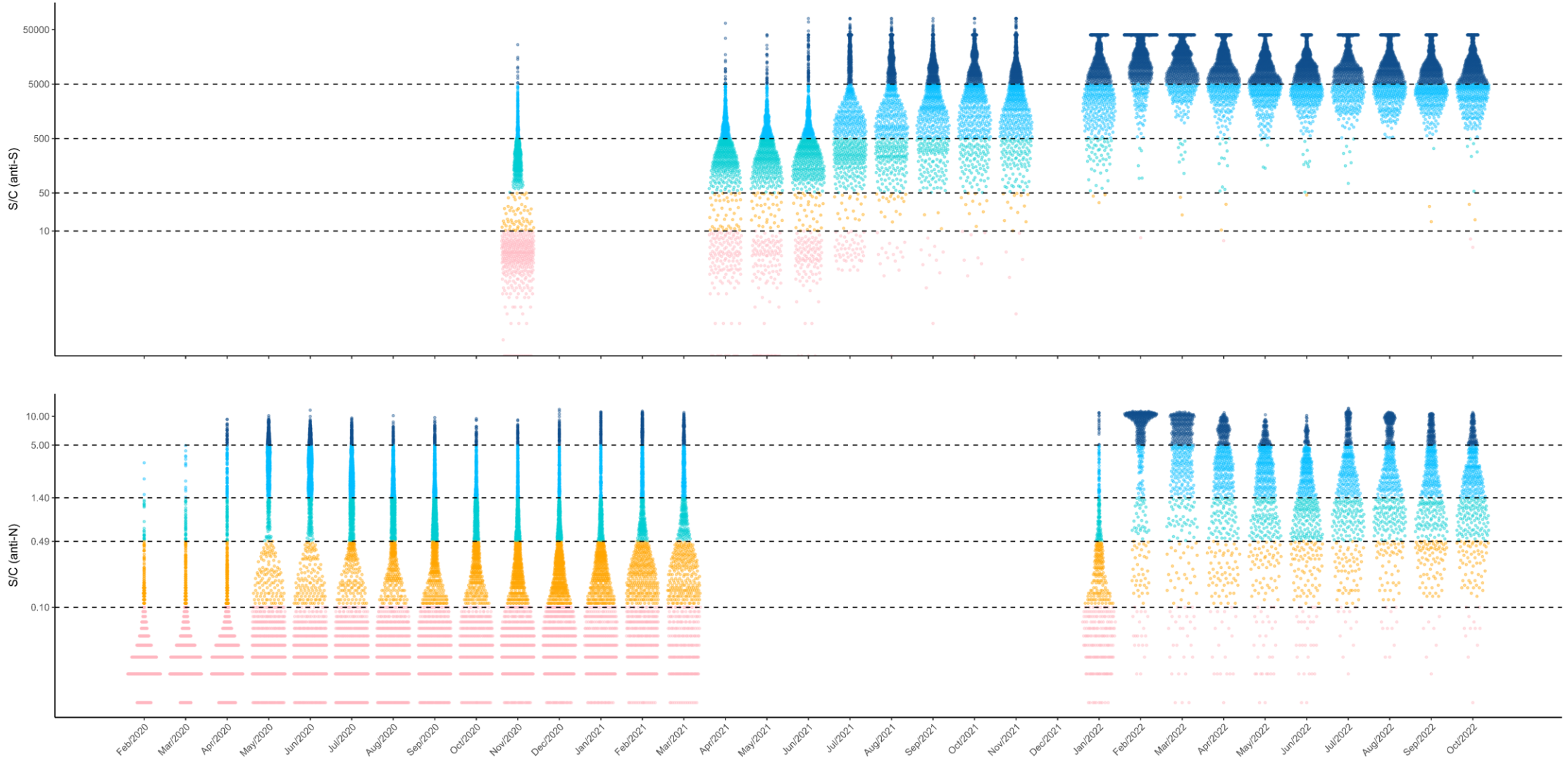
Buss et al Vaccines (Basel). 2022 Aug 31;10(9):1437

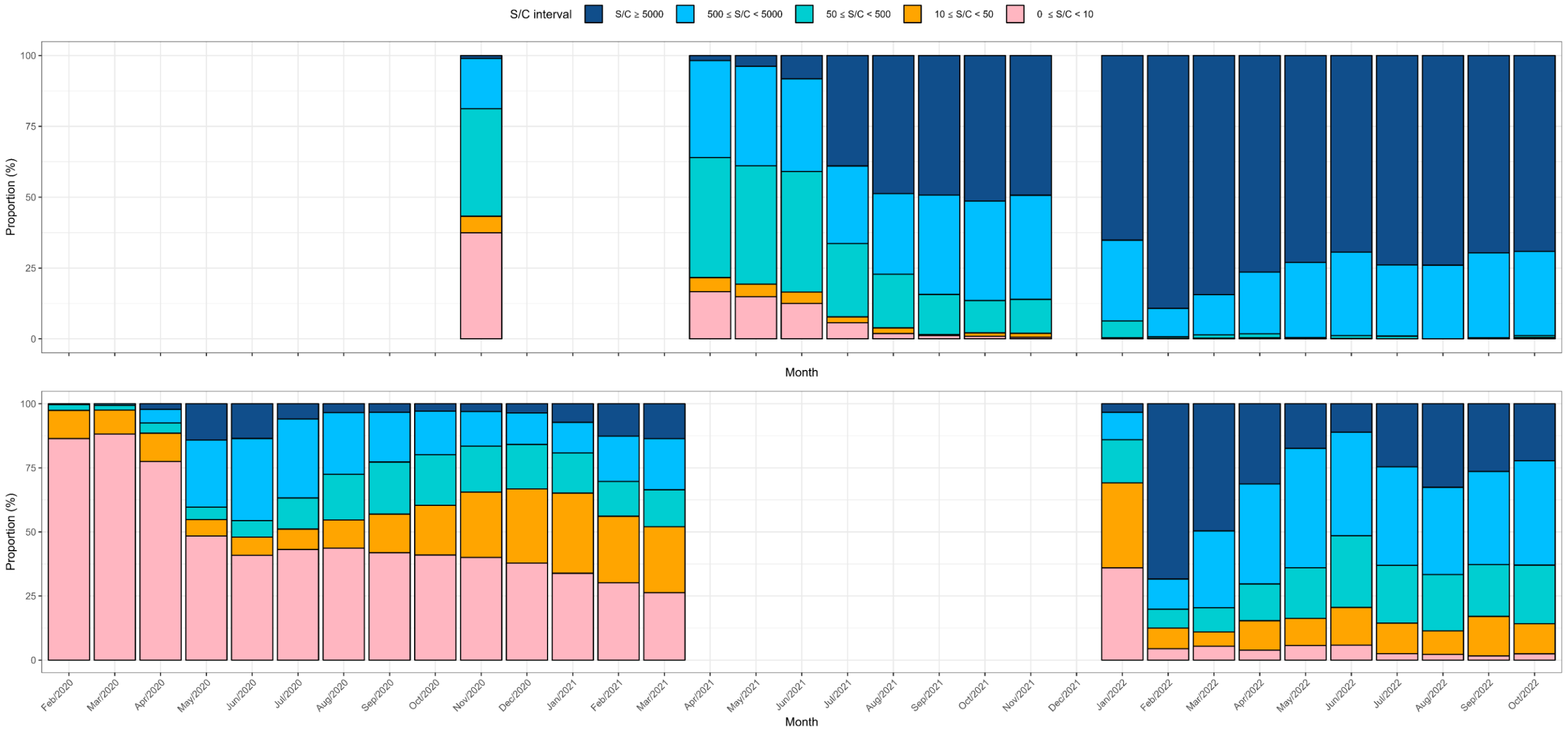
Crude prevalence of Abbott anti-N and anti-S before and after Omicron 1 wave in the city of Sao Paulo



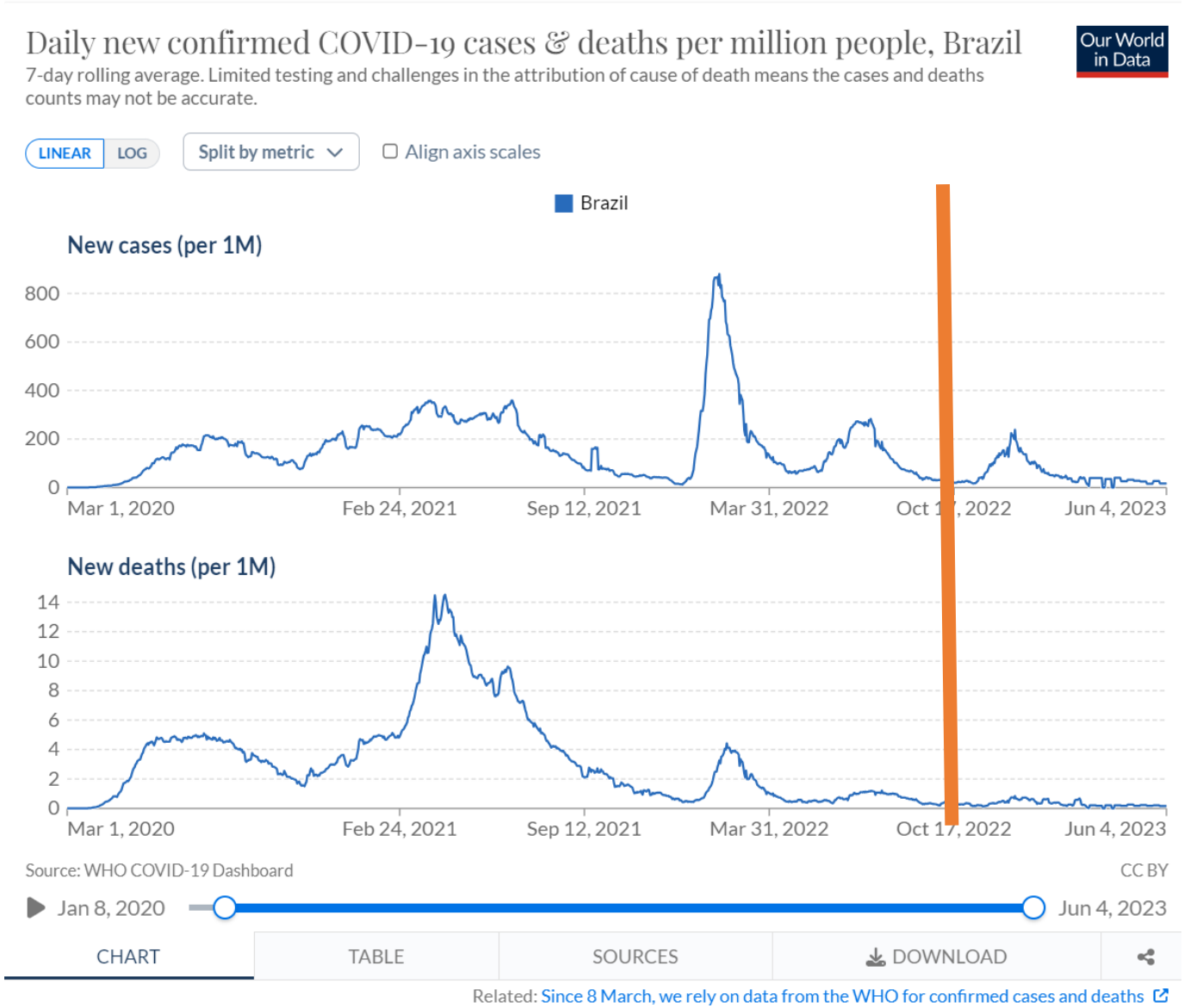
Anti-N Abbott as a proxy of recent infection?

Evolution of SARS CoV-2 Ab levels in Manaus




S/C interval
S/C ≥ 5000
500 ≤ S/C < 5000
50 ≤ S/C < 500
10 ≤ S/C < 50
0 ≤ S/C < 10
Proportion (%)
100
75
50
25
0
Month
Feb/2020
Mar/2020
Apr/2020
May/2020
Jun/2020
Jul/2020
Aug/2020
Sep/2020
Oct/2020
Nov/2020
Dec/2020
Jan/2021
Feb/2021
Mar/2021
Apr/2021
May/2021
Jun/2021
Jul/2021
Aug/2021
Sep/2021
Oct/2021
Nov/2021
Dec/2021
Jan/2022
Feb/2022
Mar/2022
Apr/2022
May/2022
Jun/2022
Jul/2022
Aug/2022
Sep/2022
Oct/2022

Deaths and cases in Brazil overtime



Conclusion

- Blood donors can provide important insights during an emergency.
- Studies are needed to compare rates of disease among donors and general population as a preparation for next crisis.
- Can serological data indicate population level of protection?

Acknowlegement

Poli USP
Carlos Prete Junior
Vitor Nascimento
USCS
Marcio Oikawa
IPEA
Rafael Pereira
UNICAMP
Jose LP Modena
Willian M de Souza
FPS/HSP
Alfredo Medrone Jr
Cesar Almeida Neto
Nanci Salles
Suzete Ferreira
HemoAm
Nelson Fraiji
Myuki Crispim
Lilyane Xabregas
Alexander Silva-Jr
HemoRio
Esther Lopes
Sheila Mateos
Luiz Amorim
Gabrielle Nunes
HemoBA
Fernando Araujo
Luciana Carlos
Veridiana Pessoa
HemoMinas
Maisa Ribeiro
Rosenvaldo de Souza
HEMOPE
Anna Cavalcante
Maria Valença
Maria da Silva
Hemepar
Karine Fladzinski
Luana de Souza
Luciane Schier
Patricia Inoue
FCMMG
Tassila Salomon
Isabel Moura
FioCruz
Lucas Delerino
Natalia Tavares
Rafael Franca
Viviane Boaventura
Fabio Miyajima
UFBA
Samara Santos
Imperial College
Nuno Faria
Charles Whittaker
Darlan Candido
Ingra Claro
Lewis Buss
Havard
Marcia Castro
Oxford University
Christopher Dye
Vitalant
Michael Busch
Brian Custer

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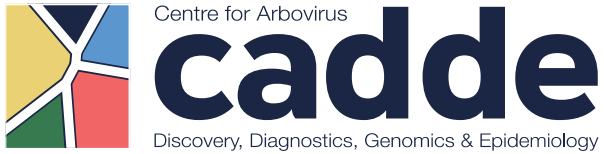
Acknowledgments