

Evolution of Donor Serosurveillance from Cross-Sectional to Longitudinal Approaches

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SARS-CoV-2 Serological Assays

Rapid point-of-care (POC) assays

- IgG +/- IgM Abs or Ag

High-throughput laboratory screening assays

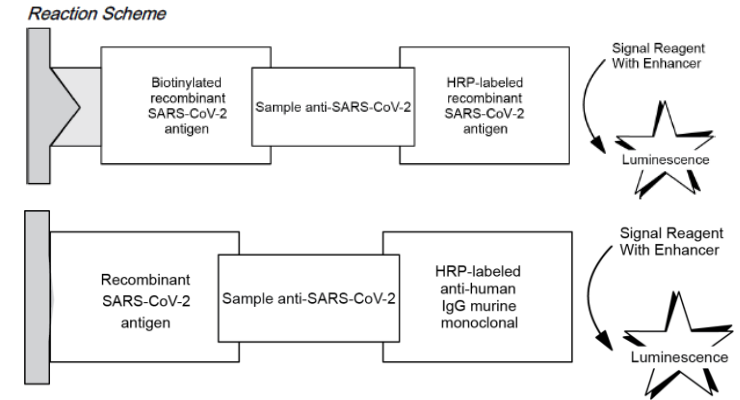
- Direct: double antigen sandwich Total Ig assays
- Indirect: IgG, IgM and IgG Ab assays
- Antigens:
 - Spike: S1/S2, **S1** or receptor binding domain (**RBD**);
 - Nucleocapsid (**N**), membrane (M), envelope (E), other ORFs
- Qualitative & quantitative/semiquantitative detection

Multiplex arrays and Luminex assays

- Multiple SARS-CoV-2 +/- other CoV and Acute Respiratory Virus (ARV) Ags

Neutralizing antibody quantitative assays

- Live virus plaque reduction neutralizing titer (PRNT) assays
- Pseudovirus reporter virus particle neutralizing titer (RVPNT) assays
- RBD/ACE-2 blocking or competitive “proxy” neutralization assays



Evaluation of Commercially Available High-Throughput SARS-CoV-2 Serologic Assays for Serosurveillance and Related Applications

[Emerg Infect Dis.](#) 2022 Mar; 28(3): 672–683.

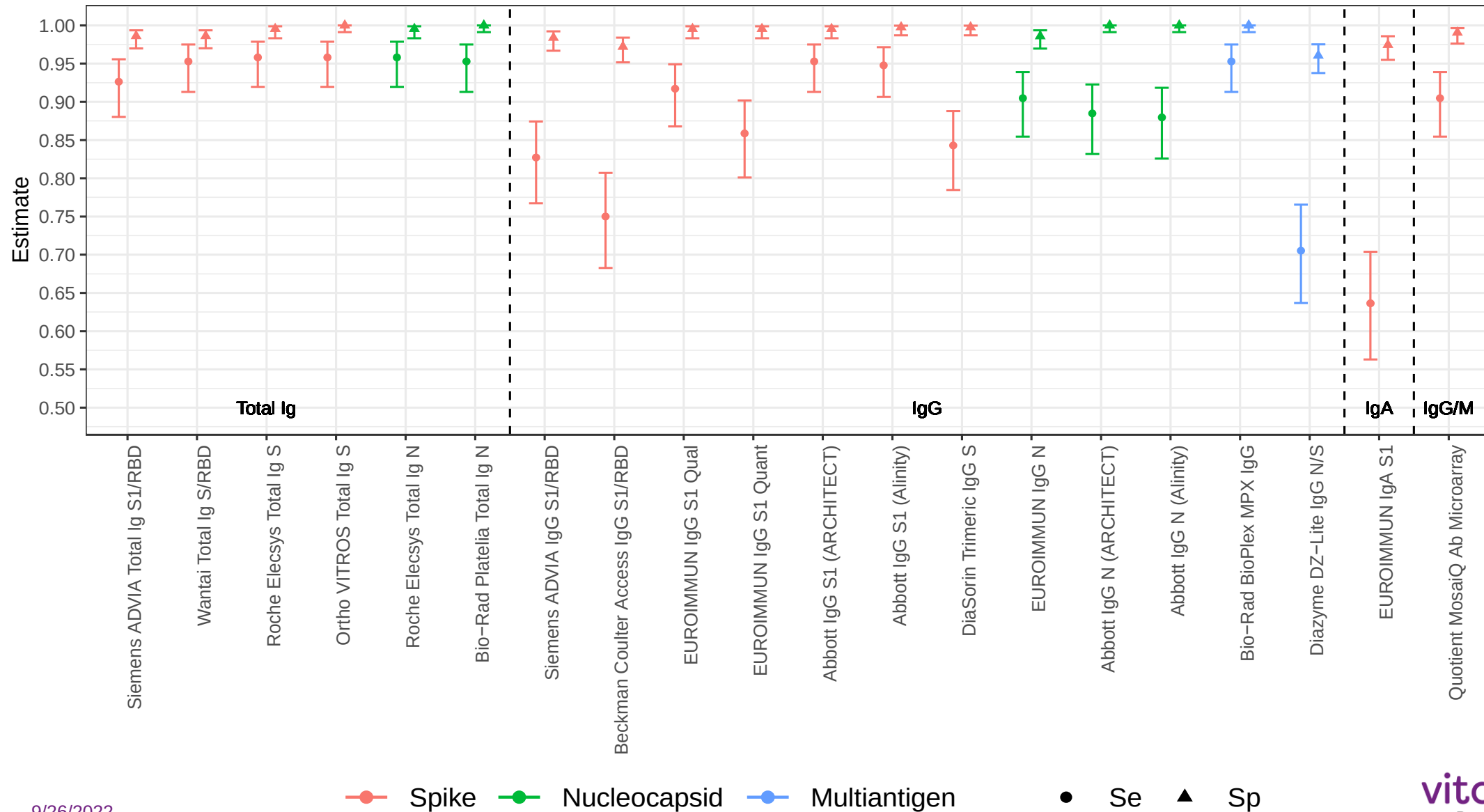
[Mars Stone](#),¹ [Eduard Grebe](#),¹ [Hasan Sulaeman](#), [Clara Di Germanio](#), [Honey Dave](#), [Kathleen Kelly](#), [Brad J. Biggerstaff](#), [Bridgit O. Crews](#), [Nam Tran](#), [Keith R. Jerome](#), [Thomas N. Denny](#), [Boris Hogema](#), [Mark Destree](#), [Jefferson M. Jones](#), [Natalie Thornburg](#), [Graham Simmons](#), [Mel Kraiden](#), [Steve Kleinman](#), [Larry J. Dumont](#), and [Michael P. Busch](#)

The primary objectives

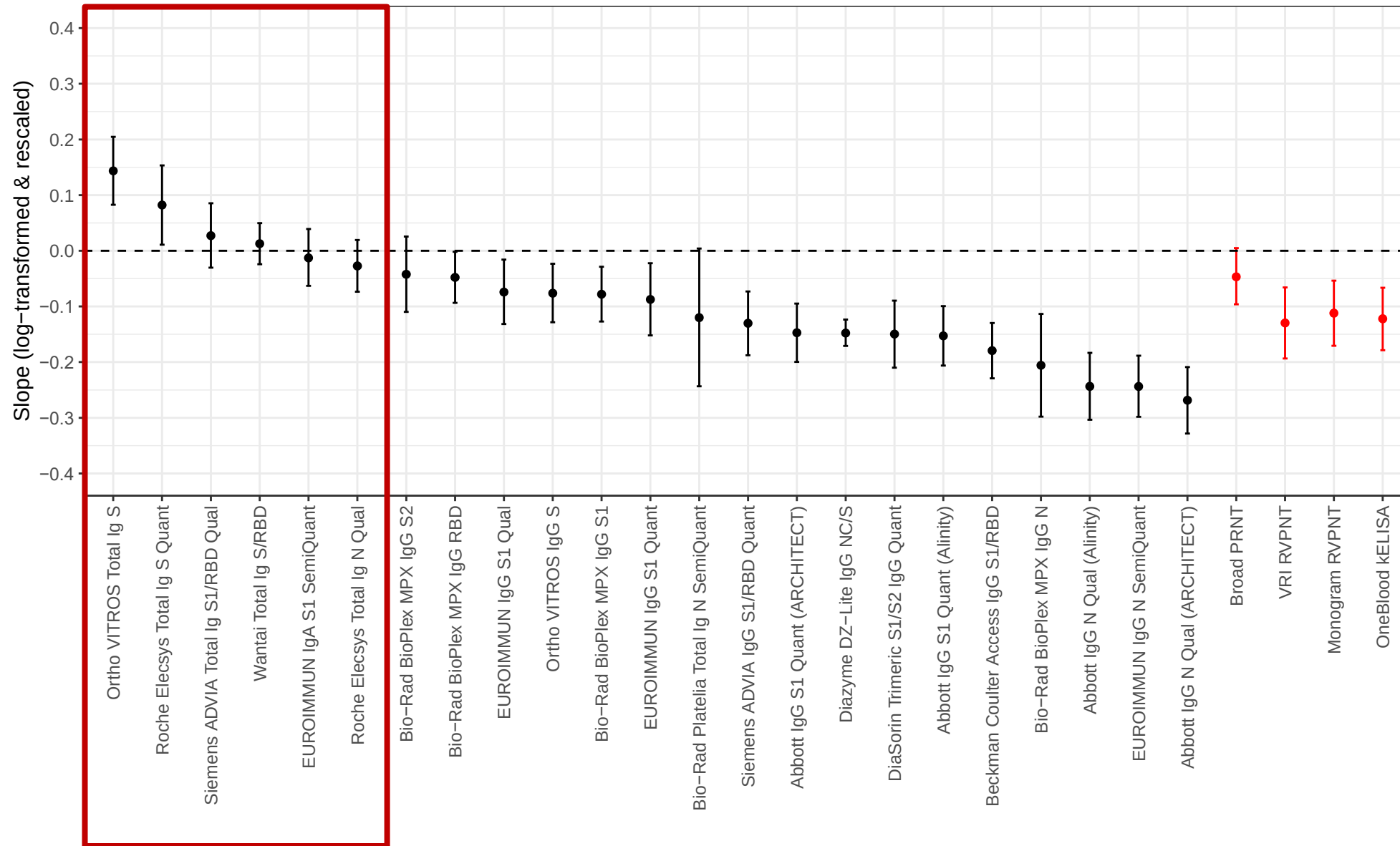
- establish and compare assay performance characteristics of *sensitivity* and *specificity* as well as positive and negative predictive values
- evaluate repeatability and dilutional performance
- determine and compare the performance of assays with respect to durability of antibody detection
- evaluate the relative timing of seroconversion
- evaluate the ability to detect antibodies in low titer samples and ‘serosilent’ cases
- establish and compare correlations between signal intensity and neutralizing antibody titers
 - evaluate the suitability of assays for COVID-19 Convalescent Plasma qualification and cutoffs that predict neutralizing titers relevant to protective immunity

Manufacturer	Assay	Ig Target	Antigen	Assay Format	Reported units	Testing Lab
Ortho	VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Ig	Total Ig	S1	Double-antigen sandwich CLIA	S/CO	Vitalant Research Institute
	VITROS Immunodiagnostic Products Anti-SARS-CoV-2 IgG	IgG	S1	Indirect CLIA	S/CO	CTS
EUROIMMUN	Anti-SARS-CoV-2 NCP ELISA	IgG	N	Indirect IgG EIA	S/CO	Advent Health
	Anti-SARS-CoV-2 ELISA	IgG	S1	Indirect IgG EIA	S/CO	
	Anti-SARS-CoV-2 QuantiVac ELISA	IgG	S1	Indirect IgG EIA	RU/ml	
	Anti-SARS-CoV-2 ELISA	IgA	S1	Indirect IgA EIA	S/CO	
Roche	Elecsys Anti-SARS-CoV-2 N on cobas	Total Ig	N	Double-antigen sandwich CLIA	S/CO	University of California, Davis
	Elecsys Anti-SARS-CoV-2 S on cobas	Total Ig	S1/S2/RBD	Double-antigen sandwich CLIA	S/CO	
DiaSorin	LIAISON SARS-CoV-2 TrimericS IgG	IgG	TrimericS	IgG magnetic particle CLIA	AU/ml	British Colombia Centers for Disease Control and Prevention
Siemens	ADVIA Centaur SARS-CoV-2 Total Ig	Total Ig	S1/RBD	Ag sandwich CLIA	S/CO	
	ADVIA Centaur SARS-CoV-2 IgG	IgG	S1/RBD	Ag sandwich CLIA	Index	
Abbott	SARS-CoV-2 IgG N on ARCHITECT	IgG	N	CMIA	AU/ml	Duke Human Vaccine institute
	SARS-CoV-2 IgG S1 on ARCHITECT	IgG	S1	CMIA	S/CO	
	SARS-CoV-2 IgG N on Alinity	IgG	N	CMIA	S/CO	Fred Hutchinson Cancer Research Center
	SARS-CoV-2 IgG S1 on Alinity	IgG	S1	CMIA	AU/ml	
Bio-Rad	Platelia SARS-CoV-2 Total Ab (Evolis)	Total Ig	N	One-step antigen capture	S/CO	BloodWorks NorthWest
	BioPlex 2200 SARS-CoV-2 IgG Panel	IgG	RBD, S1, S2, N	Multiplexed microbeads two-step assay	S/CO	
Quotient	MosaiQ™ COVID-19 Antibody Microarray	IgM/IgG	S1/S2	Array	Qual only	
Diazyme	DZ-Lite SARS CoV-2	IgG	N & S1/S2	IgG microbead CLIA	S/CO	University of California, Irvine
Beckman Coulter	Access SARS-CoV-2 IgG	IgG	S1 RBD	IgG 2-step paramagnetic particle CLIA	S/CO	
Wantai	SARS-CoV-2 Total Ig	Total Ig	S1 RBD	Total Ig sandwich ELISA	S/CO	Sanquin

Sensitivity and specificity of SARS-CoV-2 serological assays



Standardized slopes of bAb signal intensity and nAb titers



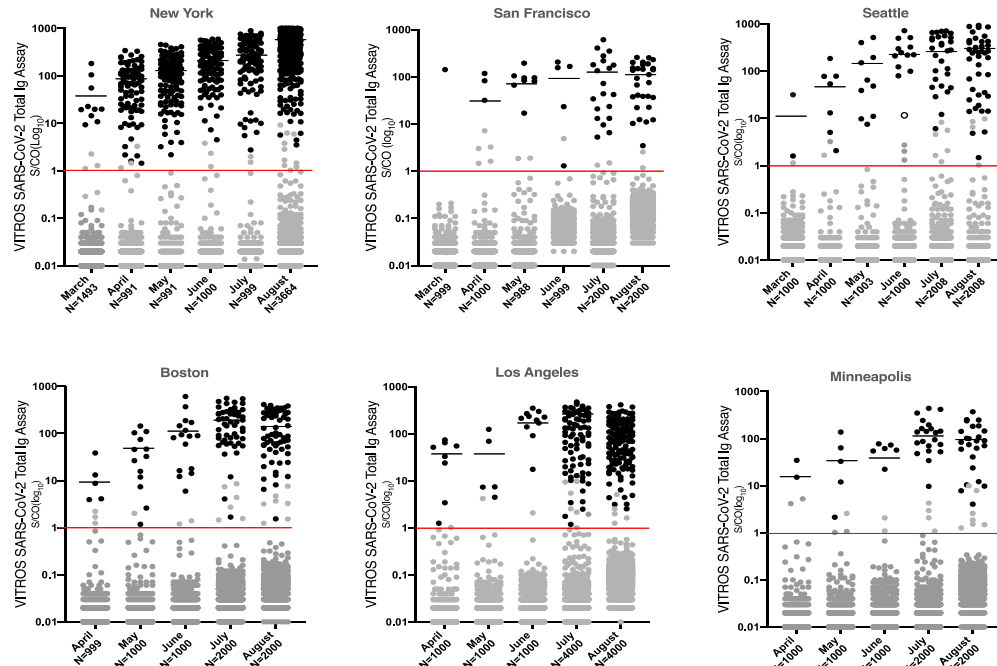
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REDS-IV-P RESPONSE Aim 2: Perform serosurveillance of blood donors and determine dynamics of seroreactivity

Clinical Infectious Diseases

Use of U.S. Blood Donors for National Serosurveillance of SARS-CoV-2 Antibodies: Basis for an Expanded National Donor Serosurveillance Program

Program FREE *Clinical Infectious Diseases*, ciab537, <https://doi.org/10.1093/cid/ciab537>
 Published: 10 June 2021 Article history ▾
 Mars Stone, Clara Di Germanio, David J Wright, Hasan Sulaeman, Honey Dave, Rebecca V Fink, Edward P Notari, Valerie Green, Donna Strauss, Debbie Kessler, Mark Destree, Paula Saa, Phillip C Williamson, Graham Simmons, Susan L Stramer, Jean Opsomer, Jefferson M Jones, Steven Kleinman, Michael P Busch ✉, NHLBI Recipient Epidemiology and Donor Evaluation Study-IV-Pediatric (REDS-IV-P)



- Ortho Vitros SARS-CoV-2 S total Ig
- Well validated testing algorithm

Region and Month	Infections per Reported Case, Estimated No. ^a (95% CI)
New York, NY	
March	3.7 (1.4–9.6)
April	6.9 (4.8–9.6)
May	6.4 (5.0–8.2)
June	5.8 (4.3–7.7)
July	5.3 (4.0–7.0)
August	5.6 (4.9–6.4)
San Francisco, CA	
March	13.6 (1.2–101.7)
April	1.9 (1.4–9.7)
May	3.8 (1.6–8.7)
June	5.5 (1.8–17.1)
July	1.8 (1.0–3.2)
August	1.8 (1.8–3.7)
Seattle, WA	
March	33.7 (7.5–144.1)
April	7.7 (3.0–19.9)
May	3.8 (1.7–8.4)
June	5.7 (2.3–14.2)
July	2.9 (1.8–4.4)
August	2.6 (1.7–4.0)
Boston, MA	
April	4.3 (1.2–15.2)
May	1.4 (1.7–2.6)
June	1.4 (1.7–2.8)
July	2.2 (1.6–3.1)
August	2.3 (1.6–3.2)
Los Angeles, CA	
April	20.2 (7.7–52.3)
May	2.5 (1.9–6.8)
June	3.4 (1.7–7.0)
July	2.1 (1.5–2.9)
August	2.4 (2.1–2.9)
Minneapolis, MN	
April	41.8 (7.5–233.4)
May	2.4 (1.7–7.8)
June	1.5 (1.5–4.6)
July	2.4 (1.1–5.1)
August	2.5 (1.7–3.8)

- 6 months serial cross sectional serology testing
- Collect routine donor demographics
- Overall and weighted cumulative incidence
- Impute rates in general population
- Regional infections to reported case rates

Characteristic	Odds Ratio (95%CI)	p-value
Gender		0.22
Female	1 (reference)	
Male	0.93 (0.82, 1.05)	
Age		<0.0001
16-29	1.31 (1.11, 1.55)	
30-49	1.12 (0.97, 1.30)	
50-64*	1 (reference)	
65+	0.66 (0.53, 0.83)	
Race/Ethnicity		<0.0001
White	1 (reference)	
Black	2.16 (1.64, 2.85)	
Hispanic	2.57 (2.17, 3.05)	
Other	1.16 (0.96, 1.41)	
Blood Type		0.29
A	1.11 (0.97, 1.26)	
AB	1.21 (0.91, 1.61)	
B	1.00 (0.82, 1.21)	
O	1 (reference)	
Rh type		0.69
Rh negative	1.03 (0.88, 1.22)	
Rh positive	1 (reference)	
Donation Type		<0.0001
First time	2.24 (1.58, 3.16)	
Repeat	1 (reference)	



REDS-IV-P
Optimizing Transfusion Across the Lifespan

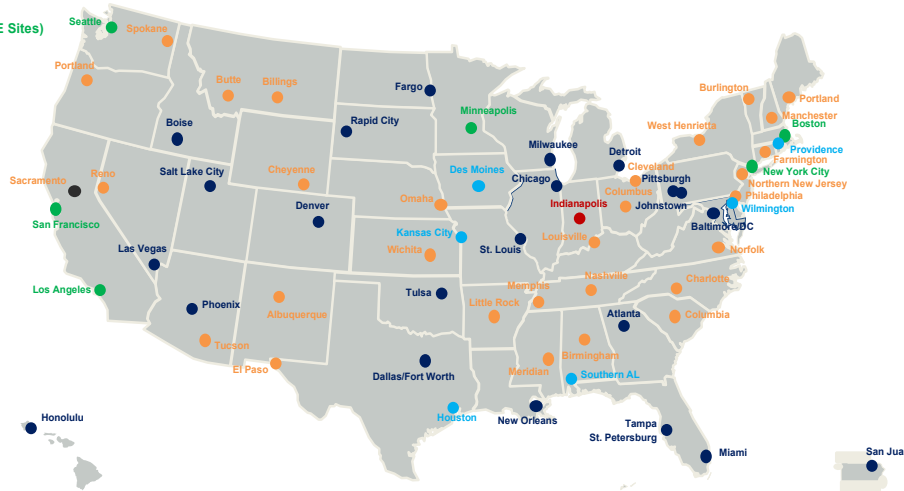
vitalant
Research Institute

CDC MULTISTATE ASSESSMENT OF SARS-CoV-2 SEROPREVALENCE IN BLOOD DONORS (MASS-BD)

60+ U.S. Metropolitan Areas, all 50 states

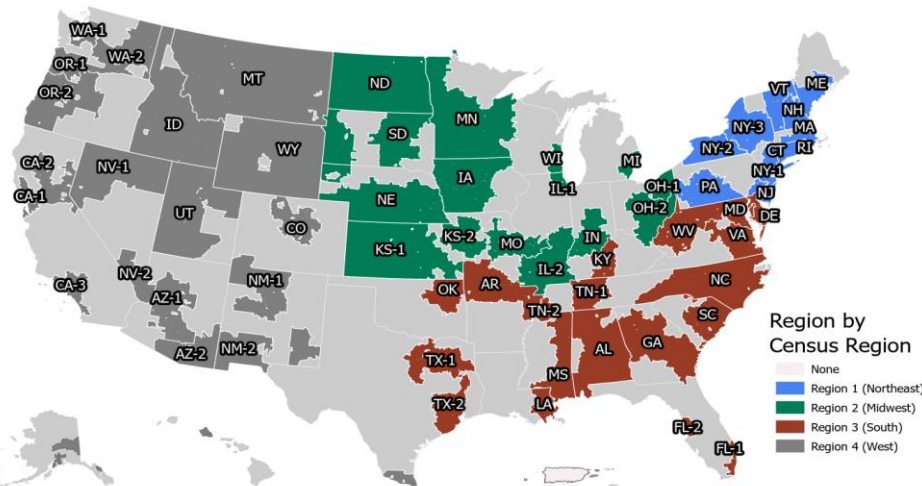
Data Collection Start

- April/March (RESPONSE Sites)
- July
- August
- September
- October



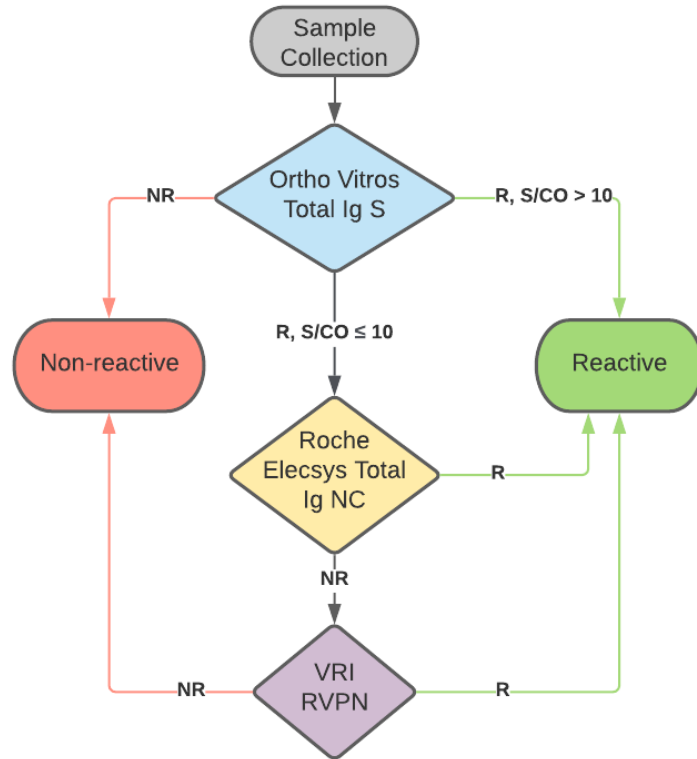
Expansion of NHLBI RESPONSE 6 region study by adding 55 more metropolitan areas

- Selection criteria:
 - Broad geographical distribution
 - Mix of high and low COVID-19 case incidence
 - Racial and ethnic diversity
- Identify the percentage of the population that has been infected with SARS-CoV-2 by testing 2,000-6,000 residual blood donation samples for anti-SARS-CoV-2 antibody monthly from each of 62 metropolitan areas from July 2020 through Dec 2021
- Generate “weighted” overall, geographic-, age group-, sex-, and racial/ethnic-specific seroprevalence of SARS-CoV-2 in blood donation populations
- Extended scope and timeline will allow assessment of increasing penetrance of SARS-CoV-2 infection into distinct U.S. communities and determine overall seroprevalence over time
- Correlate cumulative incidence from donor serosurveillance with clinical case and death rates

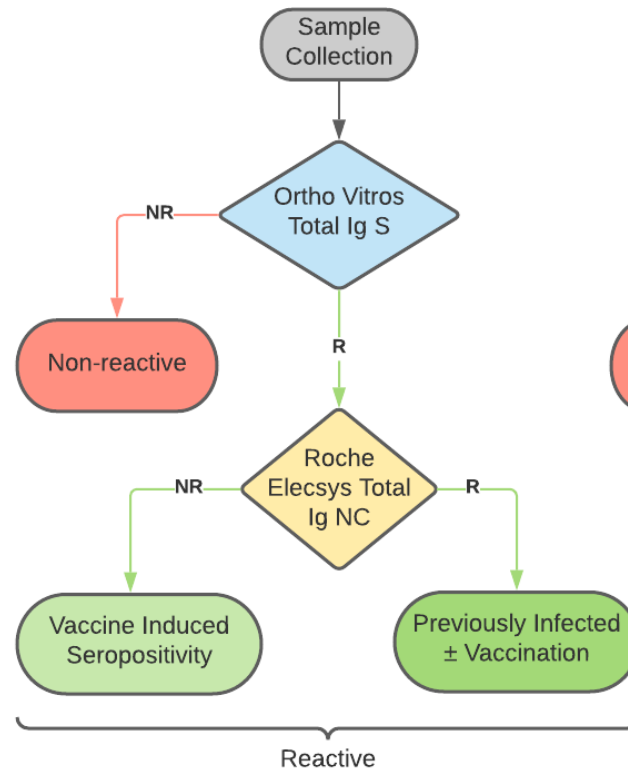


Evolving Testing Algorithms for CDC MASS-BD Program

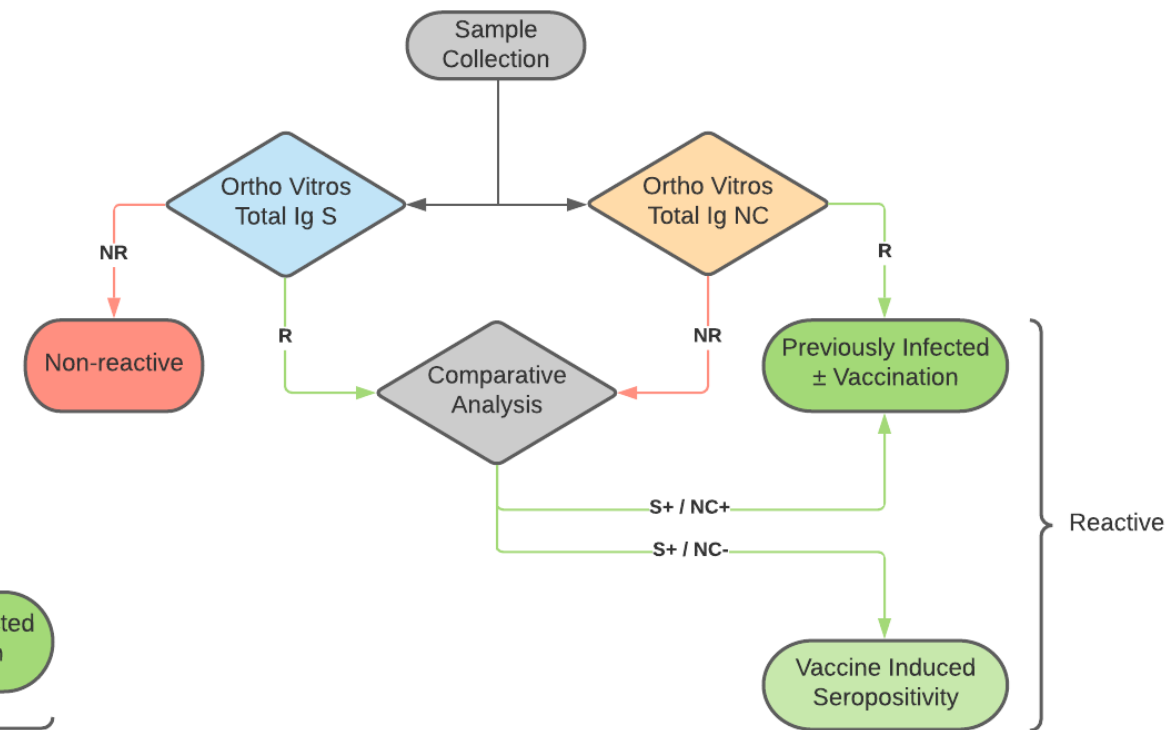
2020 Testing Algorithm



2021 Testing Algorithm

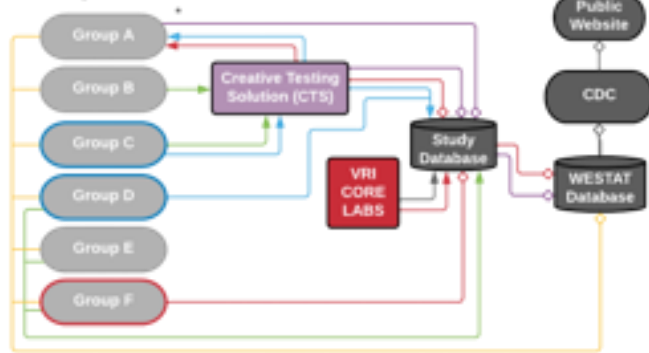


2021 Parallel Testing

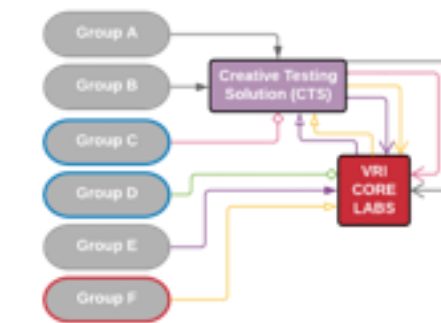


MASS-BD Serosurveillance Specimen and Data Flow

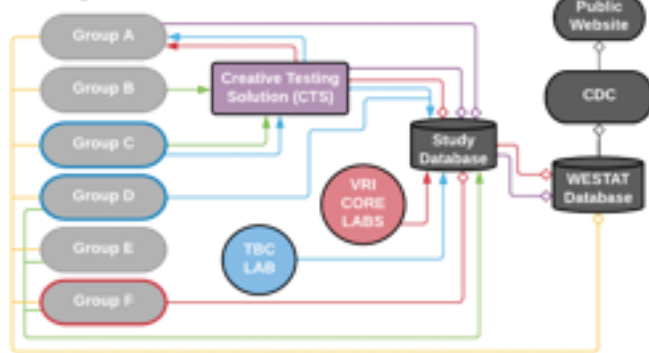
2020 Algorithm: Data Flow



2020 Algorithm: Specimen Flow



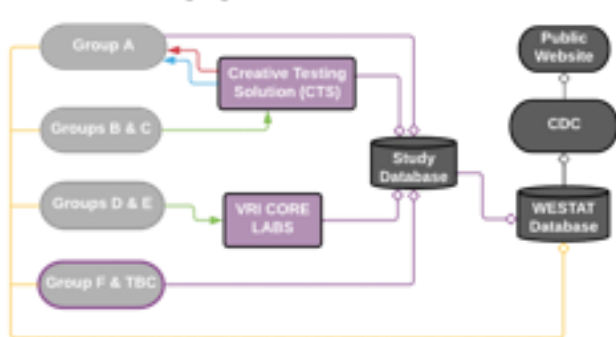
2021 Algorithm: Data Flow



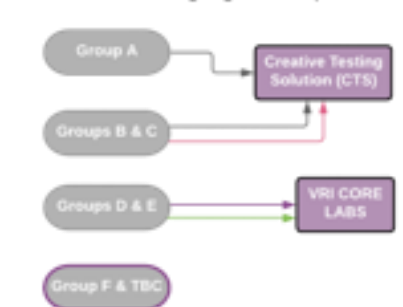
2021 Algorithm: Specimen Flow



2021 Parallel Testing Algorithm: Data Flow



2021 Parallel Testing Algorithm: Specimen Flow



Building the plane as we fly it!



HOW DO I?

TRANSFUSION

How do we...form and coordinate a national serosurvey of SARS-CoV-2 within the blood collection industry?

Rebecca V. Fink¹ | Lois Fisher² | Hasan Sulaeman² | Honey Dave² |
 Matthew E. Levy¹ | Lily McCann² | Clara Di Germanio² |
 Edward P. Notari IV³ | Valerie Green⁴ | Sherri Cyrus⁴ | Phillip Williamson⁴ |
 Paula Saa⁵ | James M. Haynes³ | Jamel Groves⁵ | Sunitha Mathew¹ |
 Zhanna Kaidarova² | Roberta Bruhn^{2,6} | Eduard Grebe^{2,6,7} | Jean Opsomer¹ |
 Jefferson M. Jones⁸ | Maureen J. Miller⁸ | Michael P. Busch^{2,6} | Mars Stone^{2,6}

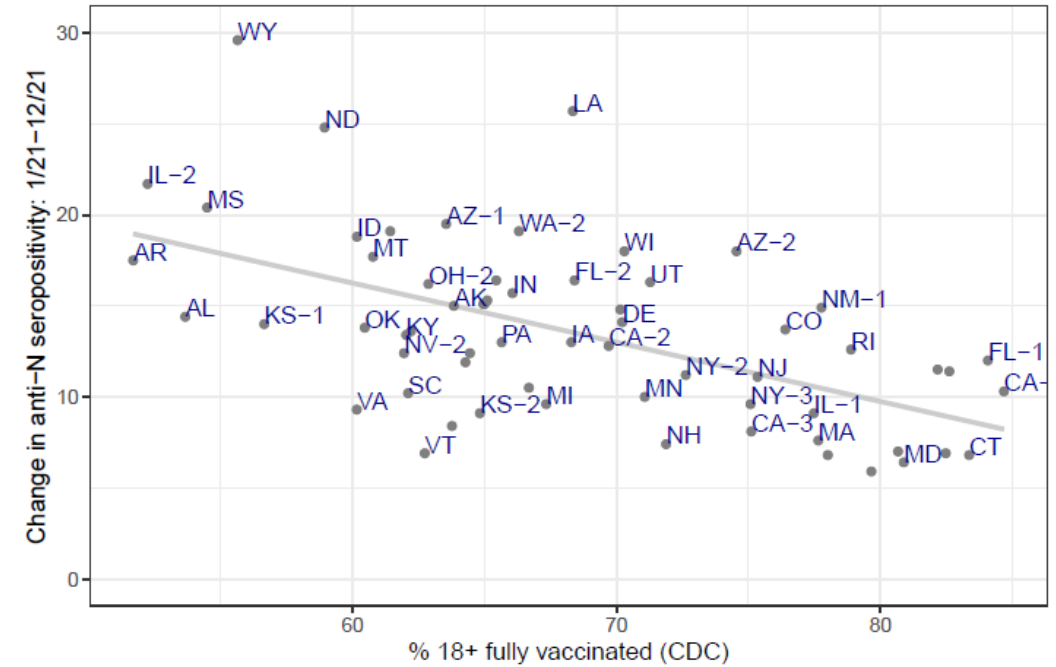
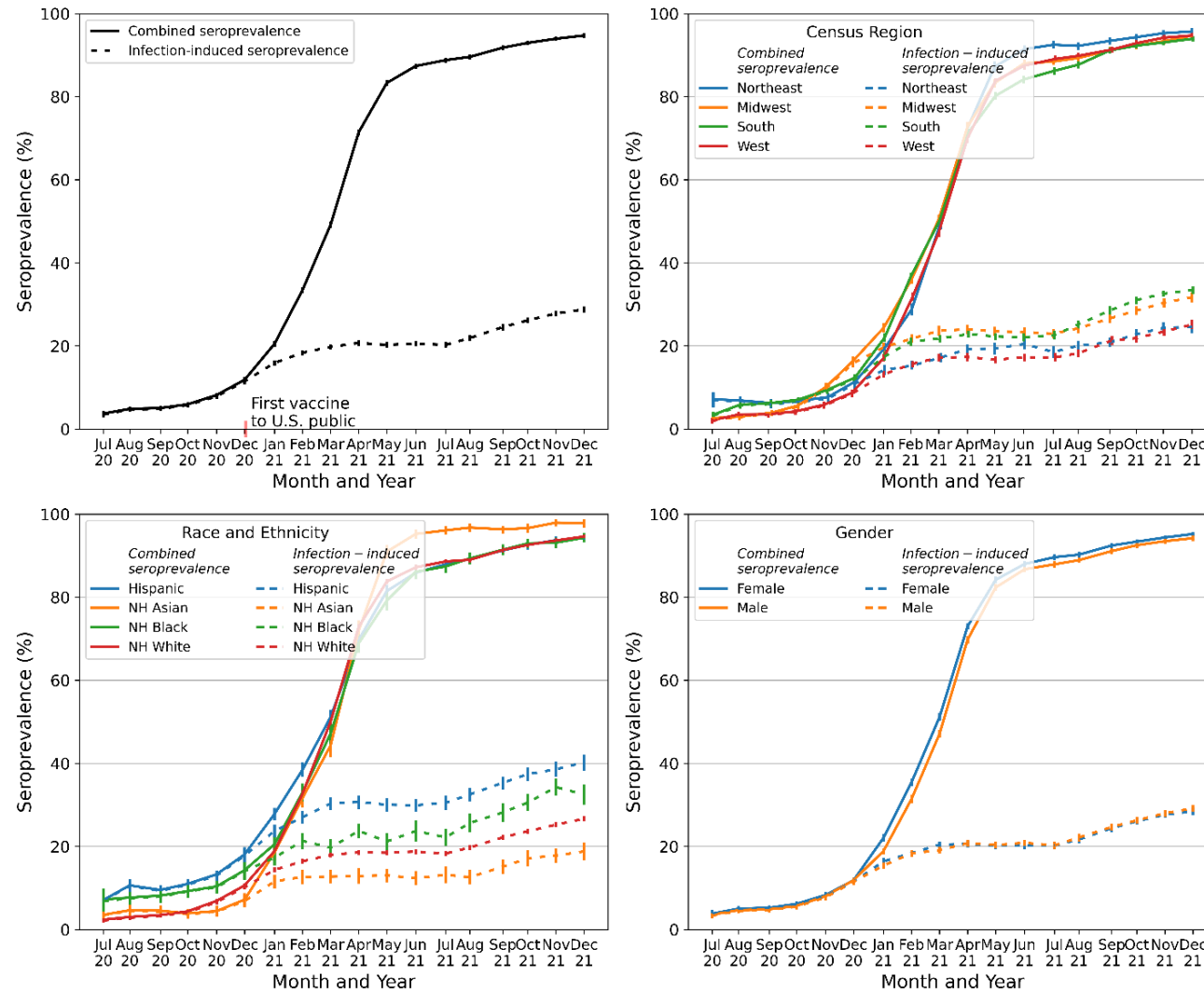
Estimated US Infection- and Vaccine-Induced SARS-CoV-2 Seroprevalence Based on Blood Donations, July 2020-May 2021

Jefferson M. Jones, MD, MPH; Mars Stone, PhD; Hasan Sulaeman, MS; Rebecca V. Fink, MPH; Honey Dave, MS; Matthew E. Levy, PhD; Clara Di Germanio, PhD; Valerie Green, MS; Edward Notari, MPH; Paula Saa, PhD; Brad J. Biggerstaff, PhD; Donna Strauss, MS; Debra Kessler, MS; Ralph Vassallo, MD; Rita Reik, MS; Susan Rossmann, MD, PhD; Mark Destree, MBA, MS; Kim-Anh Nguyen, MD, PhD; Merlyn Sayers, MBBCh, PhD; Chris Lough, MD; Daniel W. Bougie, PhD; Megan Ritter, MD; Gerardo Latoni, MD; Billy Weales; Stacy Sime, MS; Jed Gorlin, MD, MBA; Nicole E. Brown, PhD; Carolyn V. Gould, MD, MSCR; Kevin Berney, BA; Tina J. Benoit, MPH; Maureen J. Miller, MD, MPH; Dane Freeman, PhD; Deeksha Kartik; Alicia M. Fry, MD, MPH; Eduardo Azziz-Baumgartner, MD; Aron J. Hall, DVM, MSPH; Adam MacNeil, PhD; Adi V. Gundlapalli, MD, PhD; Sridhar V. Basavaraju, MD; Susan I. Gerber, MD; Monica E. Patton, MD; Brian Custer, PhD, MPH; Phillip Williamson, PhD; Graham Simmons, PhD; Natalie J. Thornburg, PhD; Steven Kleinman, MD; Susan L. Stramer, PhD, MS; Jean Opsomer, PhD, MBA; Michael P. Busch, MD, PhD

RESULTS Among 1 443 519 specimens included, 733 052 (50.8%) were from women, 174 842 (12.1%) were from persons aged 16 to 29 years, 292 258 (20.2%) were from persons aged 65 years and older, 36 654 (2.5%) were from non-Hispanic Black persons, and 88 773 (6.1%) were from Hispanic persons. The overall infection-induced SARS-CoV-2 seroprevalence estimate increased from 3.5% (95% CI, 3.2%-3.8%) in July 2020 to 20.2% (95% CI, 19.9%-20.6%) in May 2021; the combined infection- and vaccination-induced seroprevalence estimate in May 2021 was 83.3% (95% CI, 82.9%-83.7%). By May 2021, 2.1 SARS-CoV-2 infections (95% CI, 2.0-2.1) per reported COVID-19 case were estimated to have occurred.

Updated U.S. Infection- and Vaccine-Induced SARS-CoV-2 Seroprevalence Estimates Based on Blood Donations, July 2020–December 2021

Jefferson M. Jones, Jean D. Opsomer, Mars Stone, Tina Benoit, Robyn A. Ferg, Susan L. Stramer, Michael P Busch



Association between December 2021 vaccination rate and increase in infection-induced seroprevalence during 2021 by Study Region, US, January – December 2021

Population-weighted percentages of seropositivity from previous SARS-CoV-2 infection and/or COVID-19 vaccination status, including “hybrid immunity”, stratified by Census divisions

Internal use

Clinical Infectious Diseases

MAJOR ARTICLE

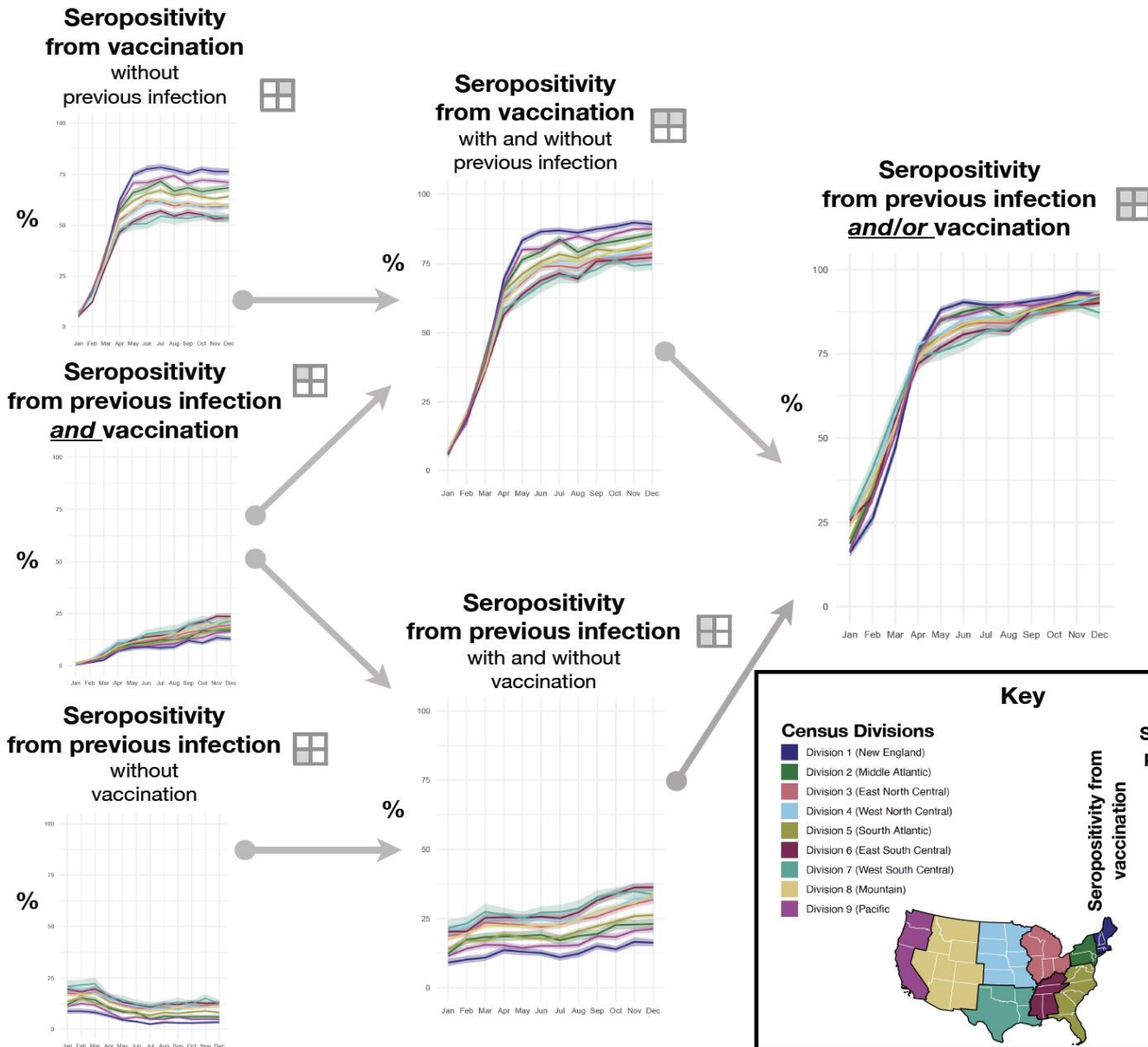
Supplement Article

Population-Weighted Seroprevalence from Severe Acute Respiratory Syndrome Coronavirus 2 Infection, Vaccination, and Hybrid Immunity among US Blood Donations from January to December 2021

Verso running head : Busch et al

Recto running head : SARS-CoV-2 Seroprevalence

Michael P. Busch^{1,2}, Susan L. Stramer³, Mars Stone^{1,2}, Elaine A. Yu^{1,2}, Eduard Grebe^{1,2}, Edward Notari³, Paula Saa³, Robyn Ferg⁴, Irene Molina Manrique⁴, Natalia Weil⁴, Rebecca V. Fink⁴, Matt Levy⁴, Valerie Green⁵, Sherri Cyrus⁵, Phillip C. Williamson⁵, James Haynes³, Jamel Groves³, David Kryzstof³, Brian Custer^{1,2}, Steve Kleinman¹, Brad J. Biggerstaff⁶, Jean D. Opsomer^{4,a}, Jefferson M. Jones^{7,a} [AQ1]



Repeat Blood Donor Longitudinal Study to Characterize Waning Immunity, Identify Breakthrough and Reinfections, and Correlates of Protection

Collaborative studies by largest U.S. blood collection organizations/research teams

- Vitalant/Vitalant Research Institute (VRI)
- American Red Cross/ARC Scientific Support Office (SSO)

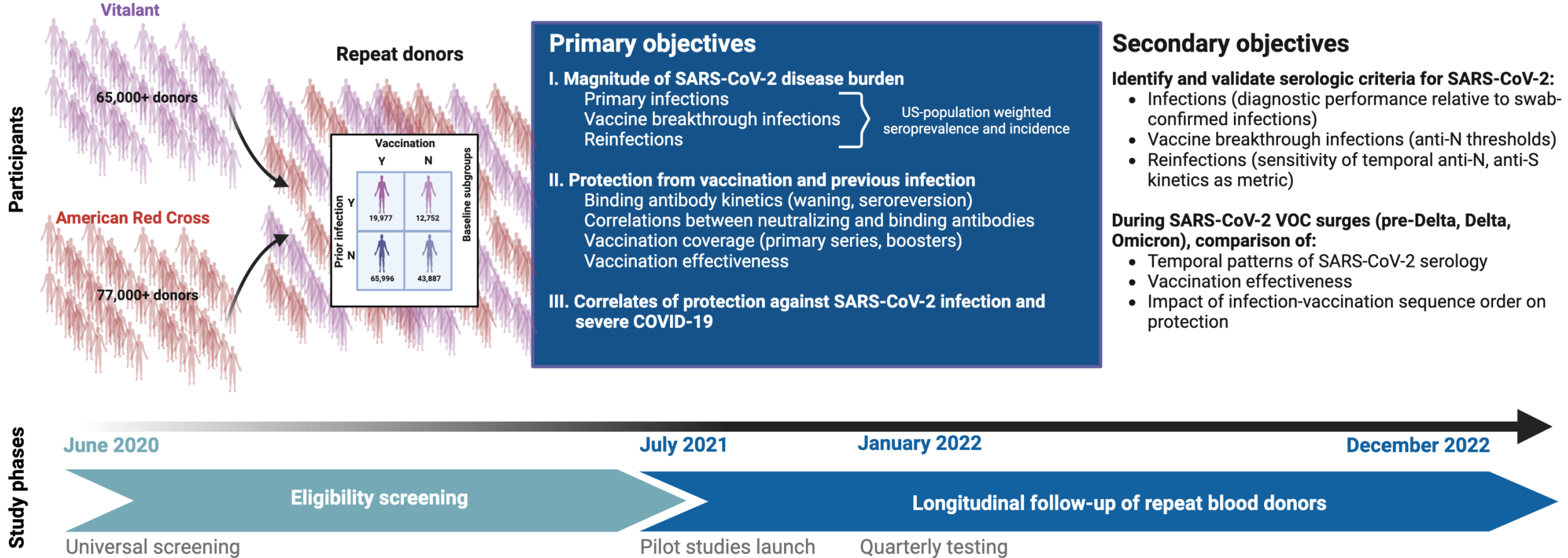
Retrospective SARS-CoV-2 Ab data and samples captured from universal screening of donations for SARS-CoV-2 Abs using Ortho S1 Total Ig and Roche NC Total Ig assays from June 1, 2020-June 30, 2021

Prospective donation samples being captured from repeat donor “cohorts” selected based on retrospective universal screening data with Ab reactivity from **previous infections, vaccinations or both**

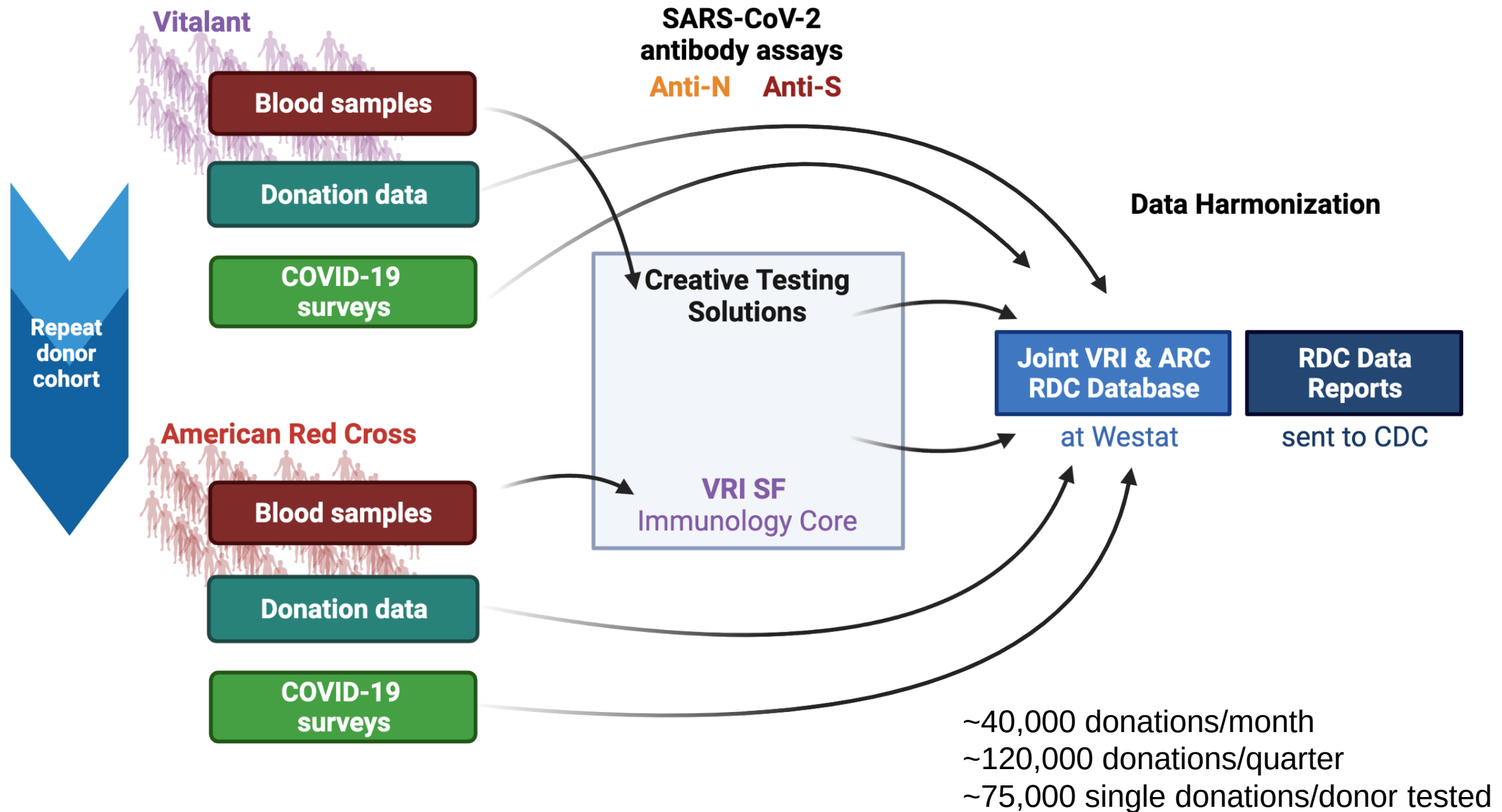
All donors are being surveyed to collect details on their known infection and vaccination history

Cohort	Not-infected, Vaccinated	Not-infected, Not vaccinated	Infected, Vaccinated	Infected, Not Vaccinated
	Yes to Vx DHQ	No to Vx DHQ	Yes to Vx DHQ	No to Vx DHQ
	S+/ NC-	S-/NC-	S+/NC+	S+/NC+
	NIV	NINV	IV	INV
Vitalant	29,407	24,937	7,290	3,889
ARC	36,589	18,950	12,687	8,863
Total	65,996	43,887	19,977	12,752

Vitalant and ARC Repeat Donor Cohorts: Overview of primary and secondary objectives



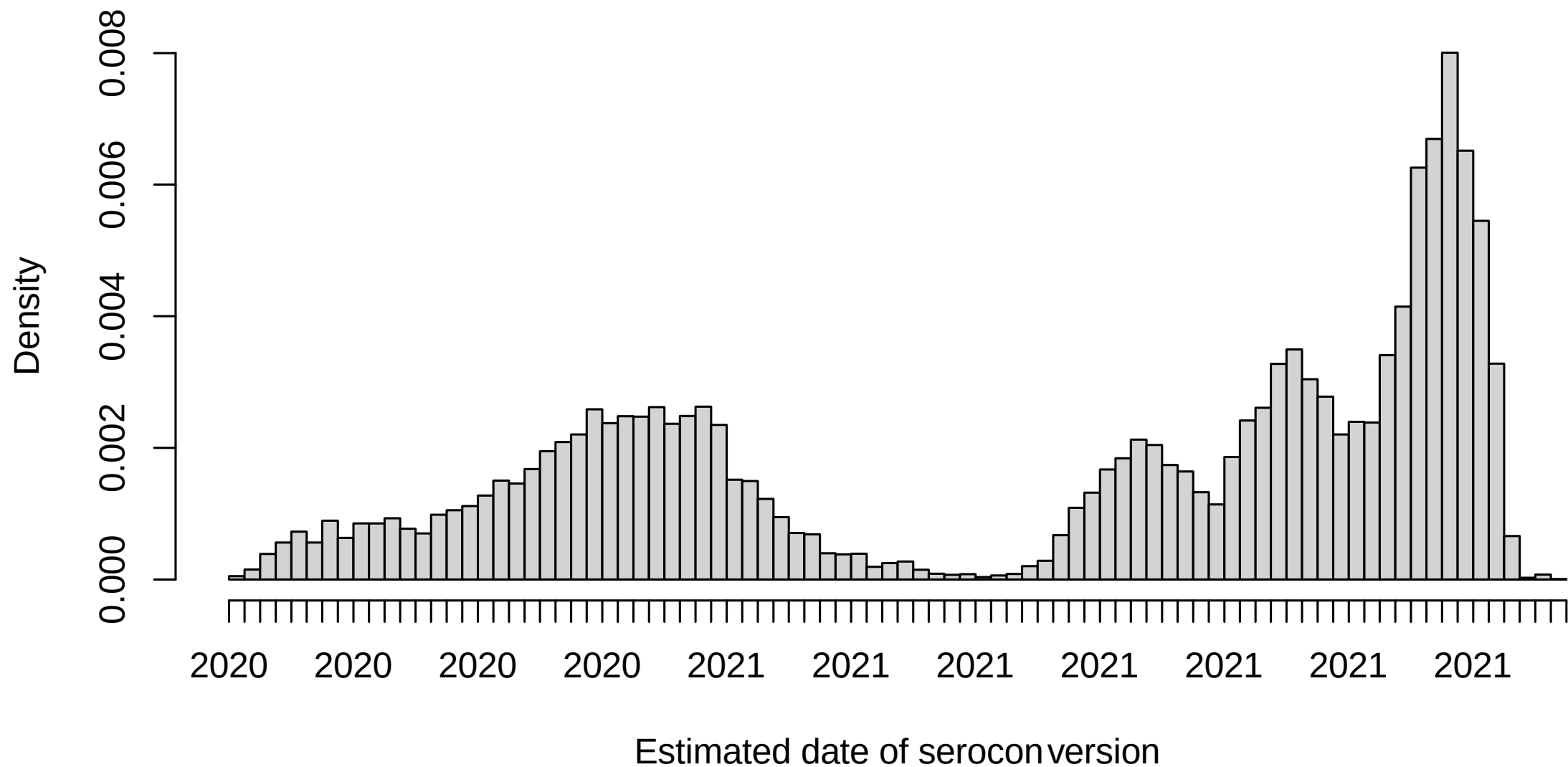
Created with BioRender.com



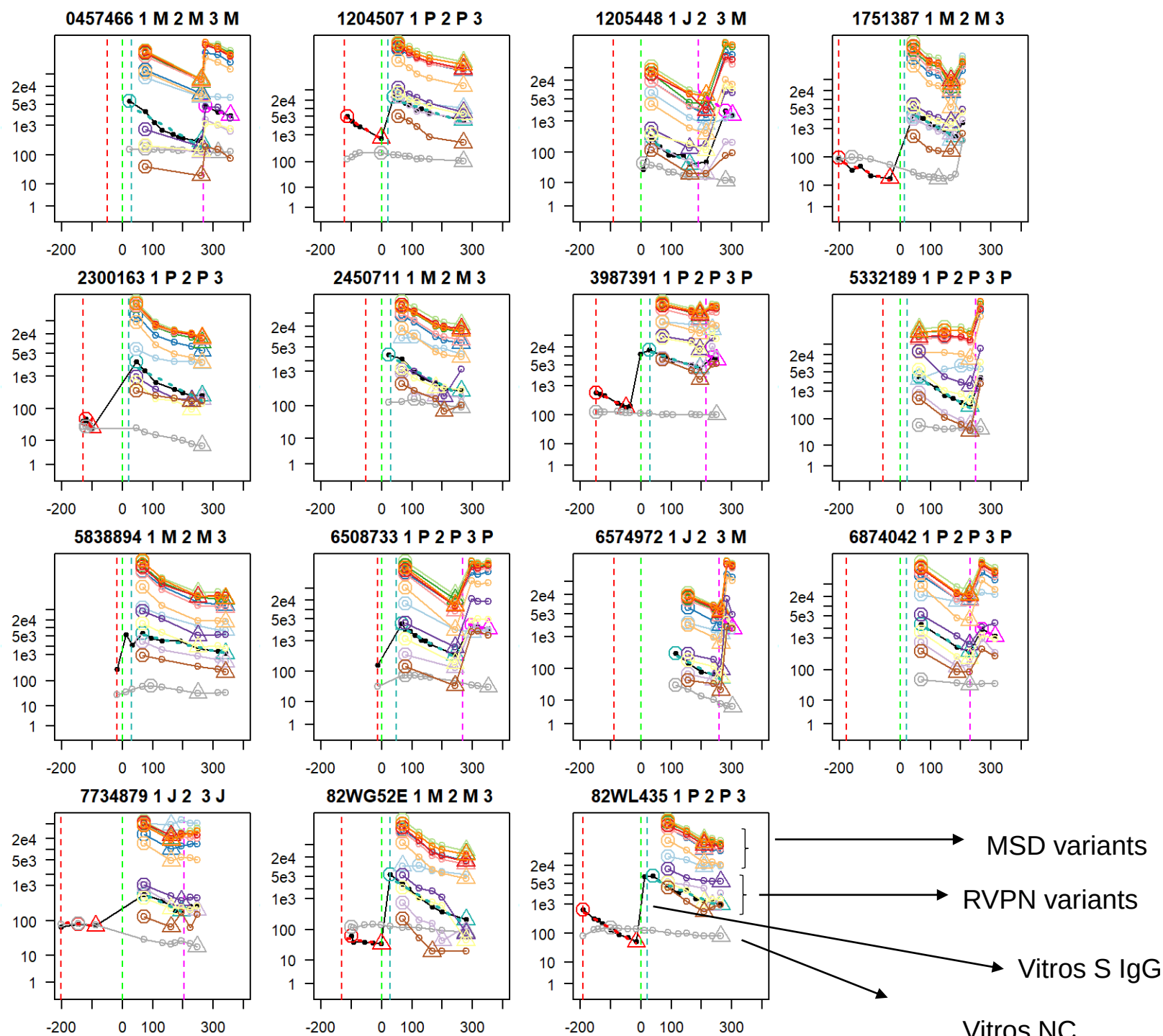
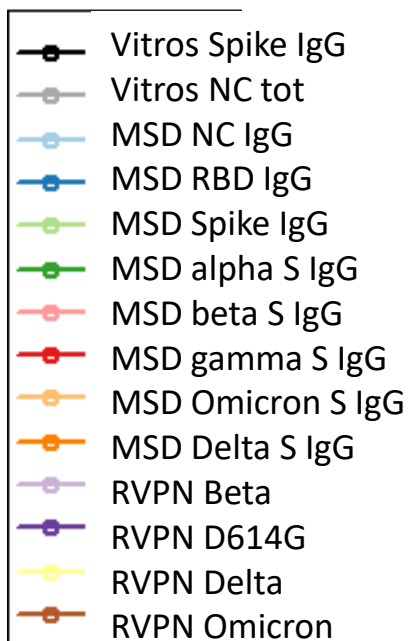
Studies of Ab dynamics, vaccine breakthrough infections & reinfections, vaccine effectiveness, correlates of protection relative to VoC waves

- **Dynamics of Ab reactivity associated with infection and vaccination**
 - Collaboration with Ortho to characterize impact of vaccination and infection on seroreactivity and analysis of CoP
- **Detection of Vx breakthrough infections**
 - samples from vaccinated/uninfected donors July-Oct 2021 and Q1/Q1 2022 tested for anti-NC Abs
 - Analysis in progress to establish lower cutoff given low NC Ab reactivity in Vx breakthrough infections
- **Detection of reinfections**
 - Patterns of reactivity including boosting of S and NC Abs
- **Incidence for Vx effectiveness analysis**
 - samples from unvaccinated donors from Sep-Oct 2021 and Q1/Q1 2022 tested for anti-NC Abs
- **Correlates of protection**
 - Serial donations from Vx breakthrough and uninfected vaccinated controls Ortho S quant IgG assay (with supplemental MSD and RVPNT)
 - Case:Control ratio (projected 500 breakthrough cases w/ ~5 serial samples)

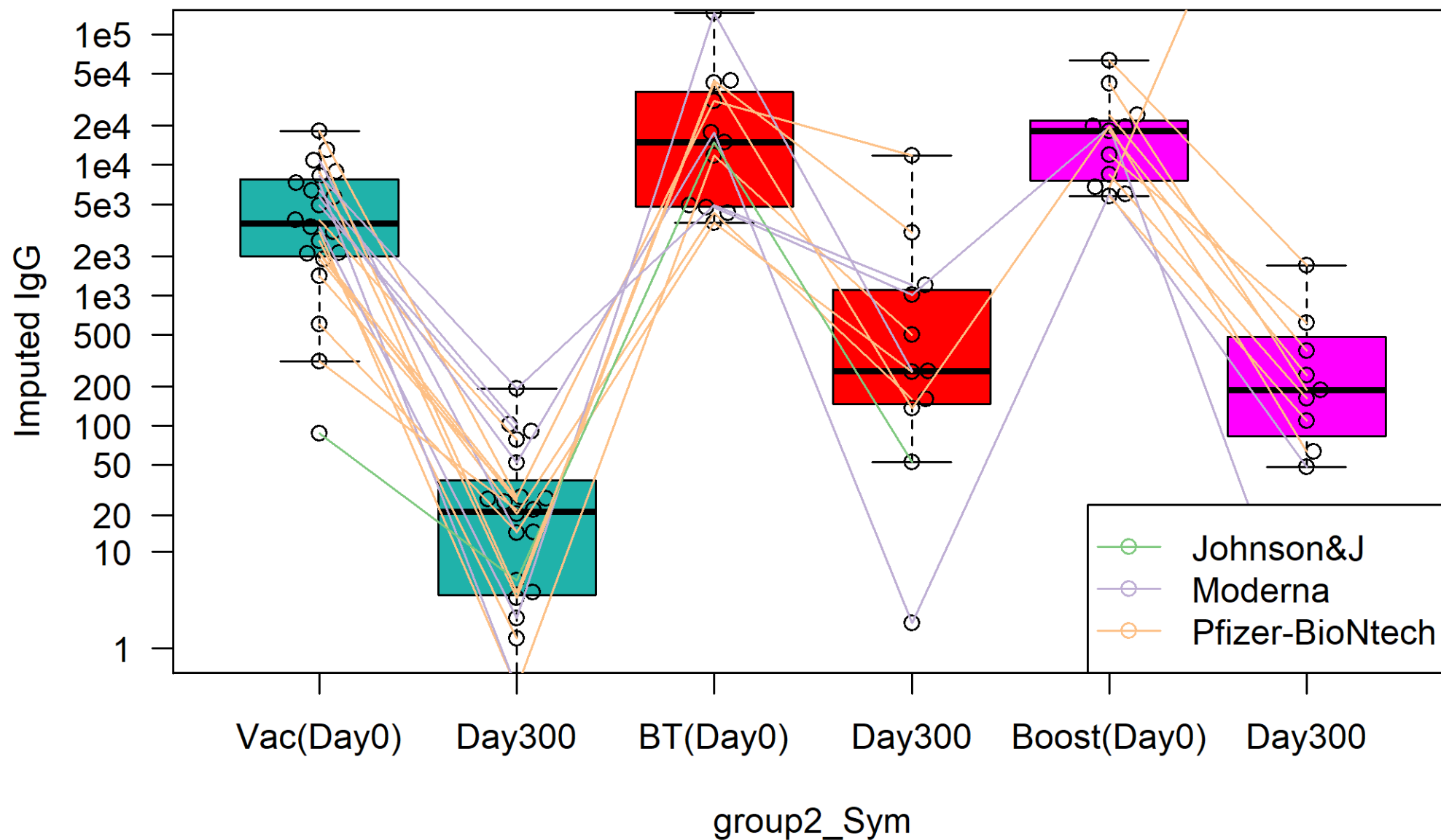
Vitalant RDC seroconverting donors



Infected then vaccinated Symptomatic

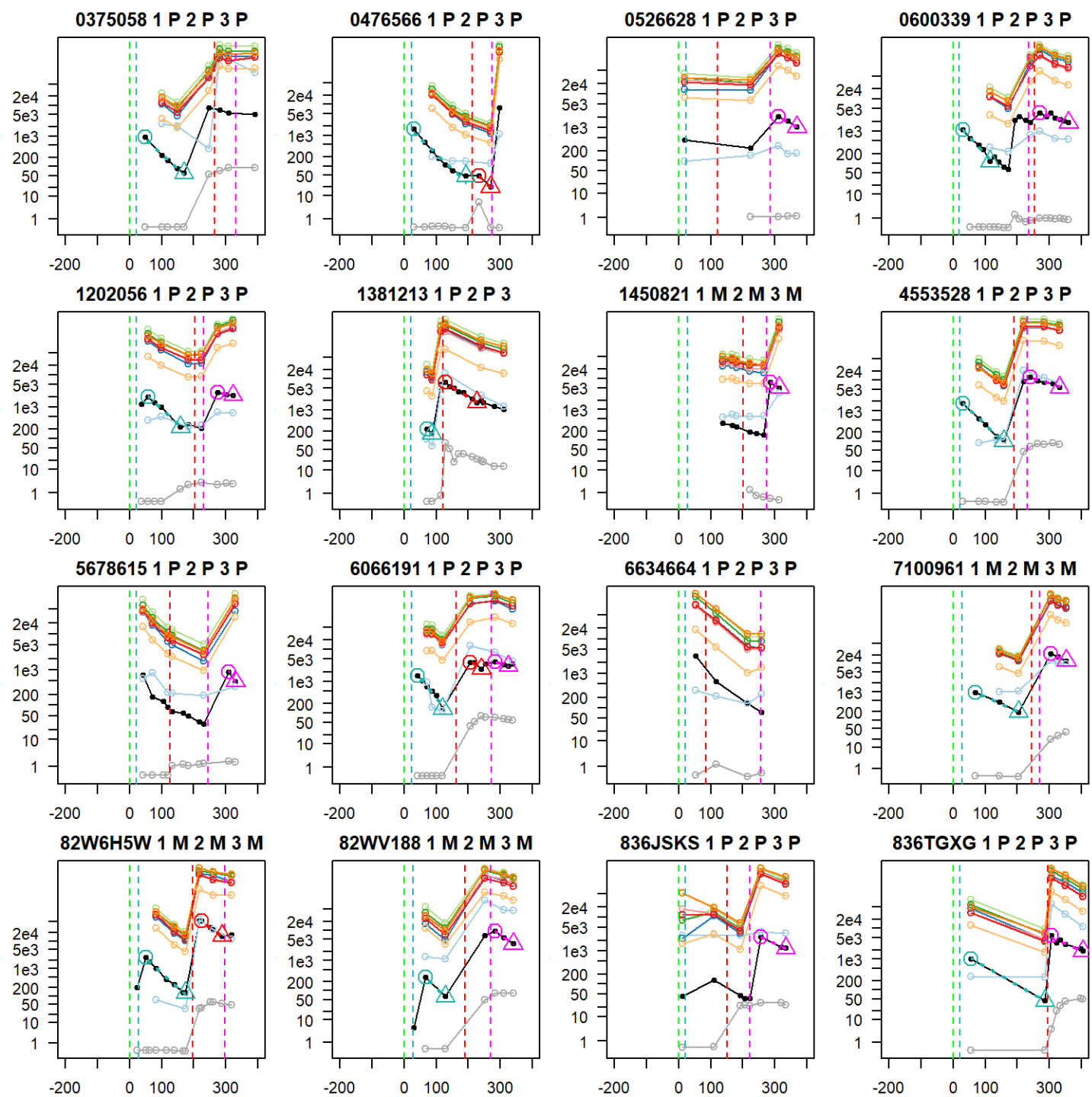


S1 IgG dynamics

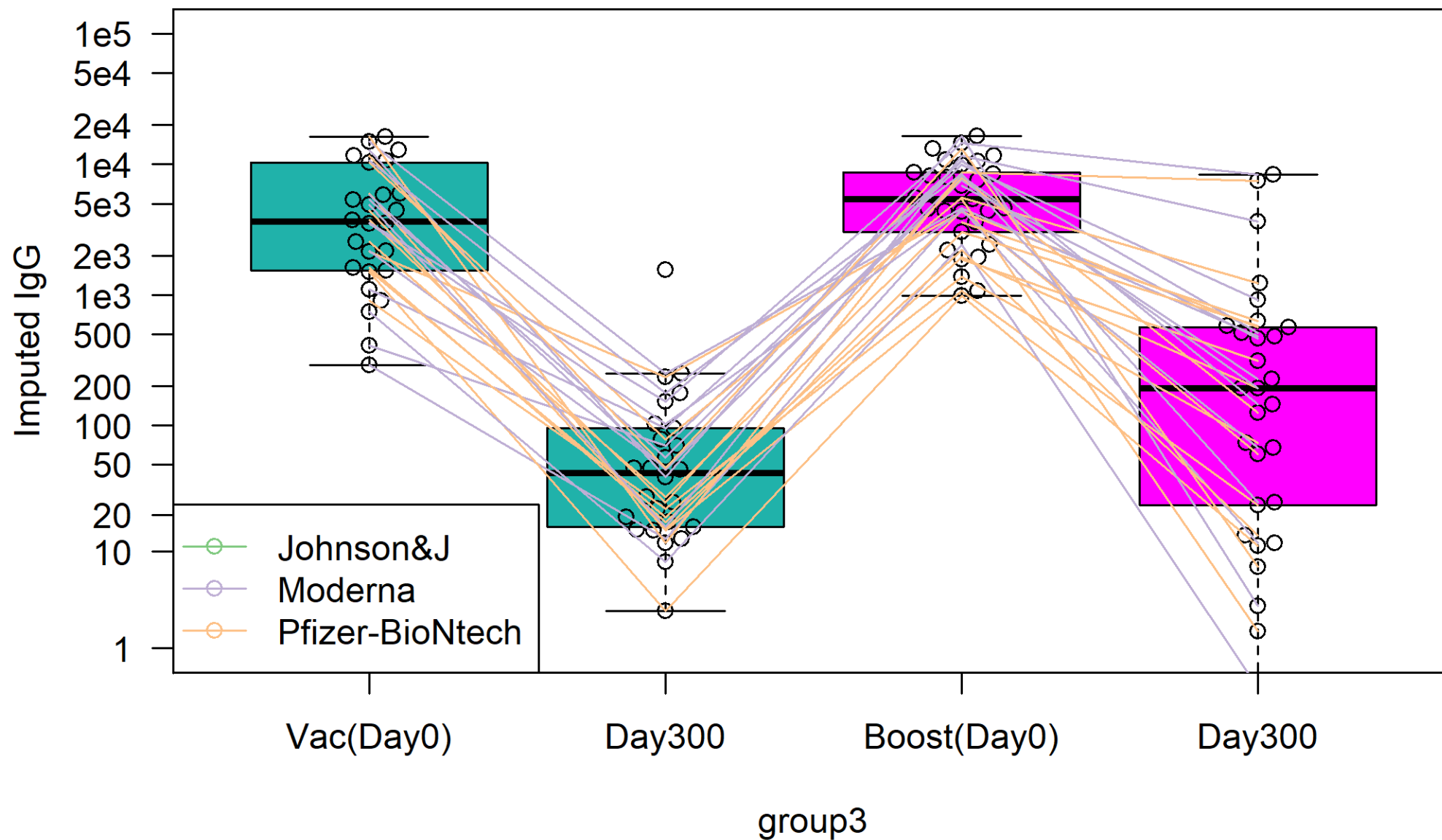


Vaccinated then Infected Asymptomatic

- Vitros Spike IgG
- Vitros NC tot
- MSD NC IgG
- MSD RBD IgG
- MSD Spike IgG
- MSD alpha S IgG
- MSD beta S IgG
- MSD gamma S IgG
- MSD Omicron S IgG
- MSD Delta S IgG
- RVPN Beta
- RVPN D614G
- RVPN Delta
- RVPN Omicron

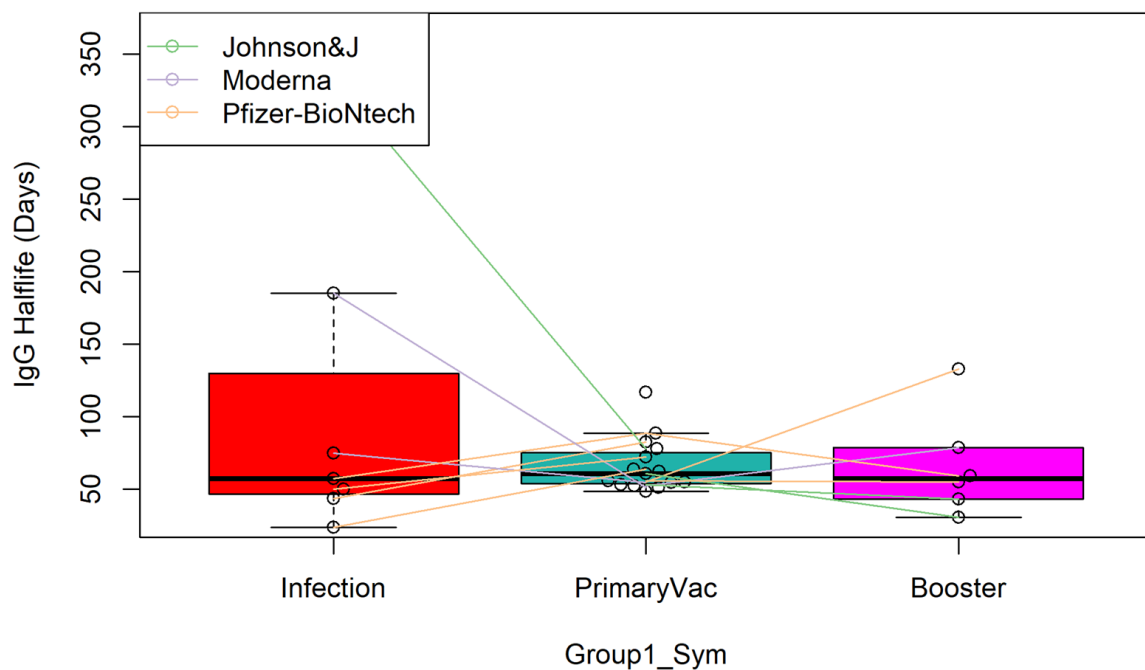


S1 IgG dynamics

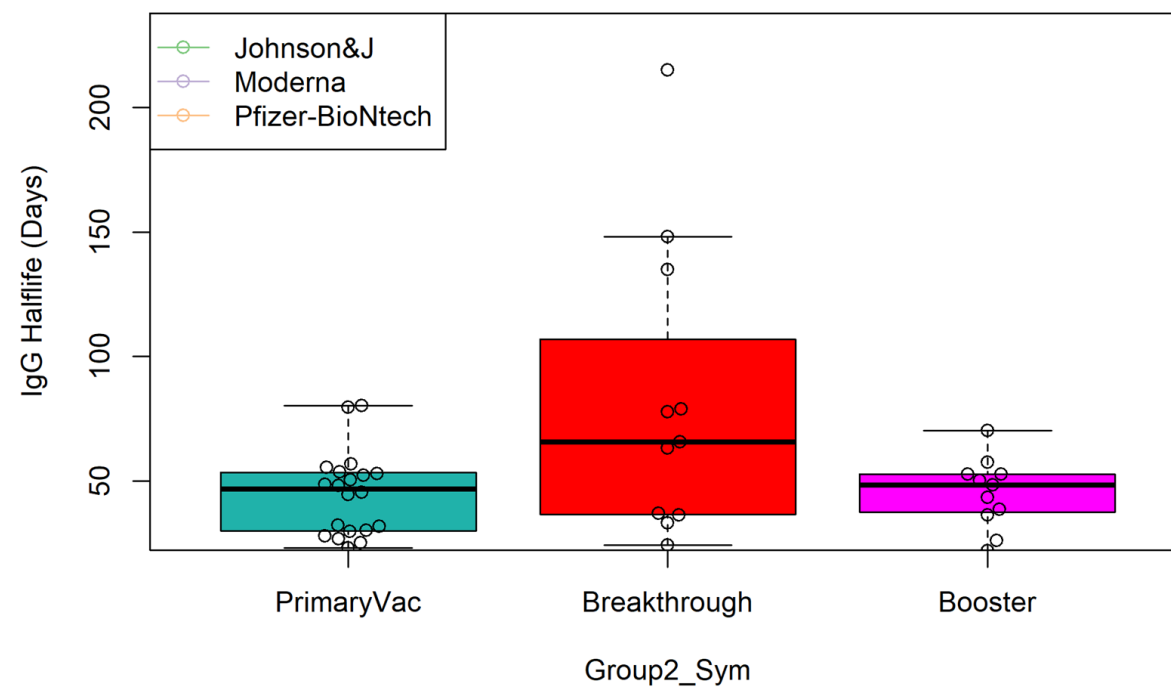


Spike IgG half-life

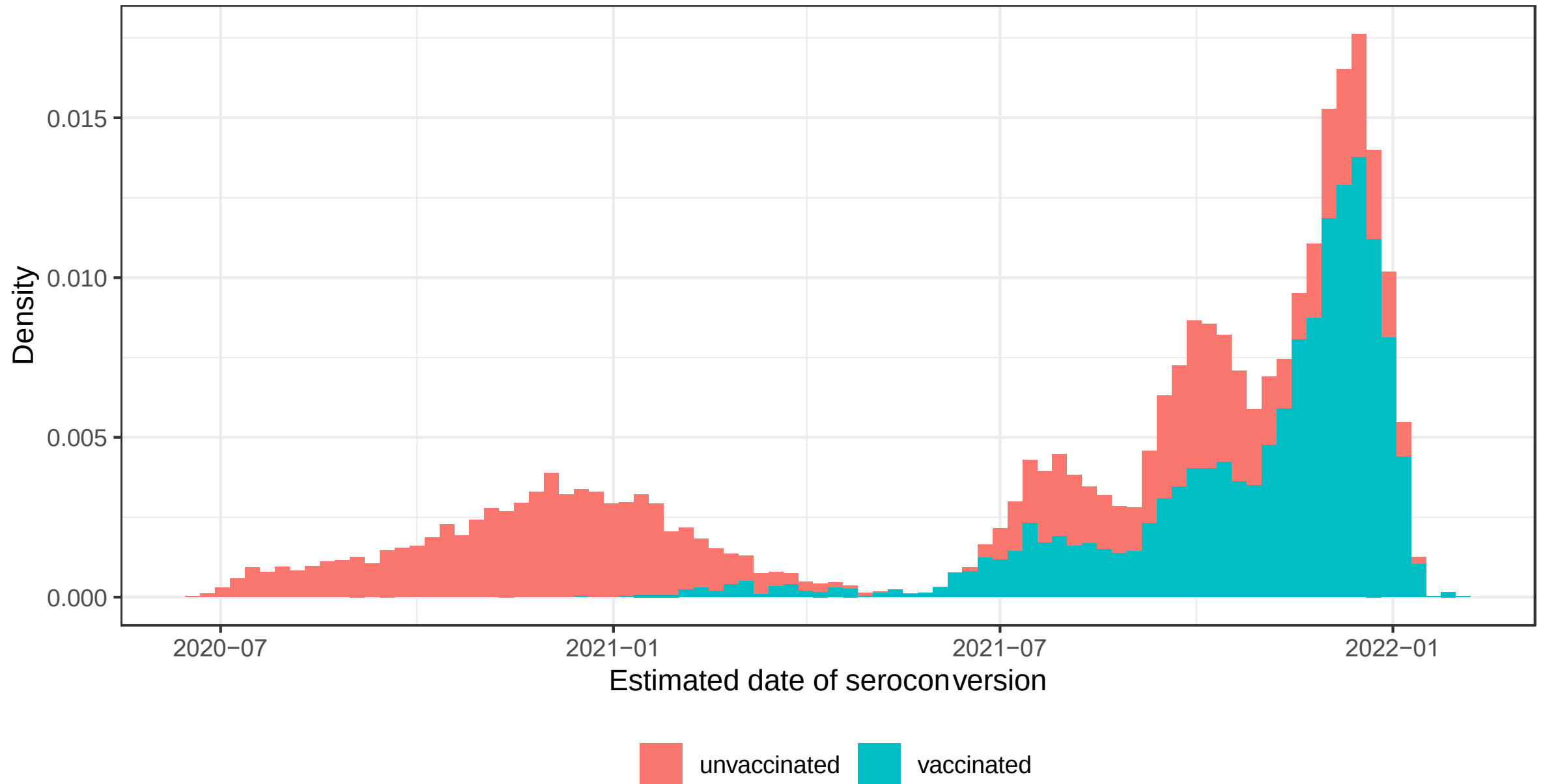
Infected then vaccinated



Vaccinated then infected

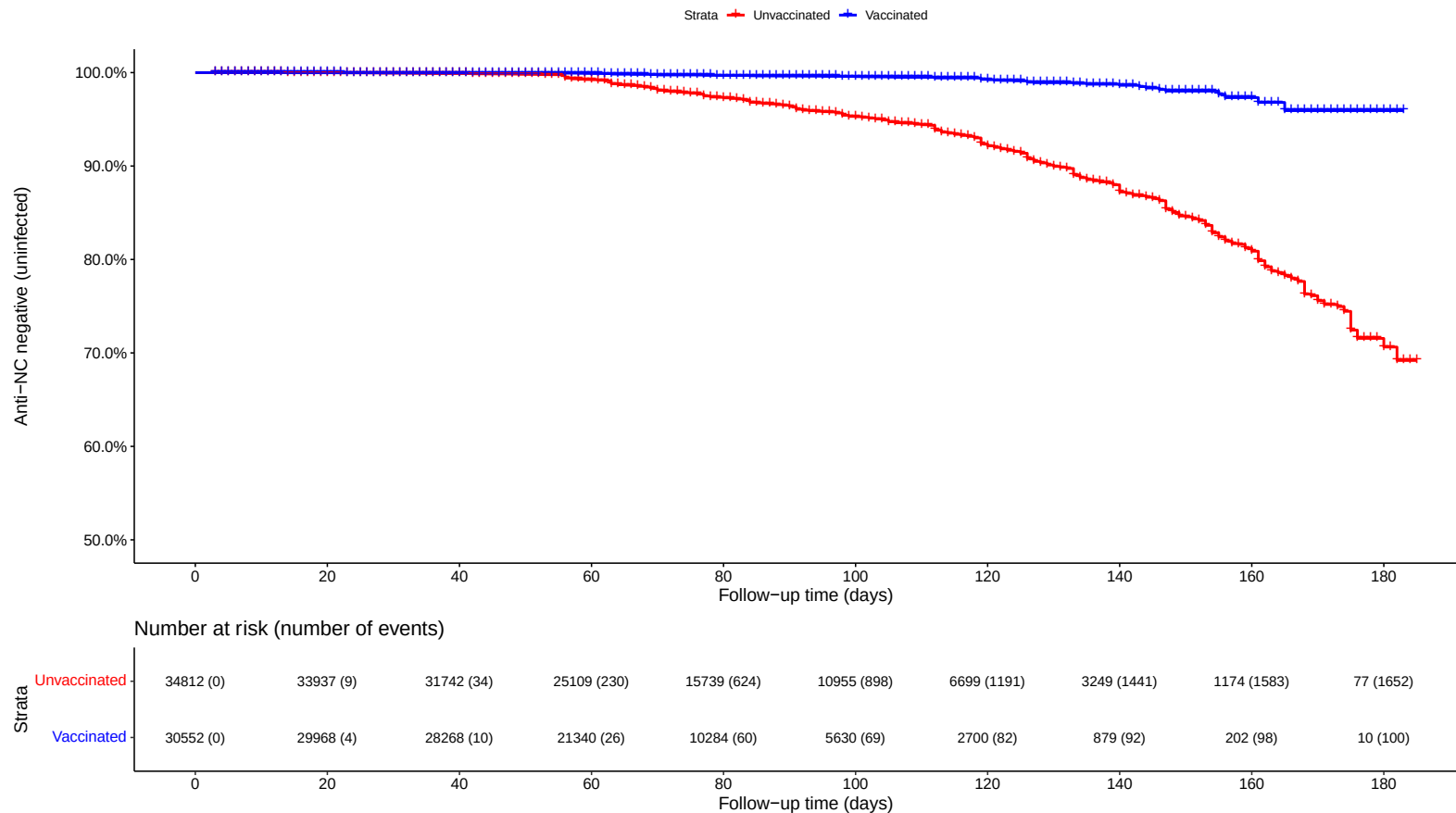


Seroconverting donors by vaccination status



Vaccine Effectiveness: January to June 2021

- Naïve estimate: 92.5% (90.8%–93.8%)
- Adjusted VE: 88.8% (86.2%–91.1%)



The Journal of Infectious Diseases

BRIEF REPORT

Coronavirus Disease 2019 Vaccine Effectiveness Against Severe Acute Respiratory Syndrome Coronavirus 2 Infection in the United States Before the Delta- and Omicron-Associated Surges: A Retrospective Cohort Study of Repeat Blood Donors

Eduard Grebe,^{1,2,3} Elaine A. Yu,¹ Marjorie D. Bravo,⁴ Alex Welte,³ Roberta L. Bruhn,^{1,2} Mars Stone,^{1,2} Valerie Green,⁵ Phillip C. Williamson,⁵ Leora R. Feldstein,⁶ Jefferson M. Jones,⁶ Michael P. Busch,^{1,2,a} and Brian Custer^{1,2,a}

Vaccine effectiveness: July 2021 to March 2022

74.6% (73.1%–76.1%)

- Vaccination status, age, sex, race, Hispanic ethnicity, and calendar time of follow-up are significant predictors of infection in multivariable model

Q1 2022 Vitalant RDC testing:

	Unvaccinated donors	Vaccinated donors
Tested	6,580	17,252
anti-N reactive	4,064	4,022
Proportion reactive	61.8% (60.5%–62.9%)	23.3% (22.7%–24.0%)
Incidence (cases/100 person-weeks)	4.01	1.16

Unadjusted VE Q1 2022: ~ 70%

Correlates of Protection

Vaccinated uninfected donors who donated during period July – October 2021 had all available donation samples tested with Ortho Total Ig anti-NC assay

- cases were defined as those who previously were anti-NC non-reactive and seroconverted, either overtly ($S/CO > 1.0$), or
- gray zone seroconversion ($S/CO > 0.37$)

Controls were matched to cases (1:4) on calendar time of observation, and similar time from prior observation to final observation

- *to account for variable incidence (i.e., risk of infection) over time*
- *no matching on potential confounders*

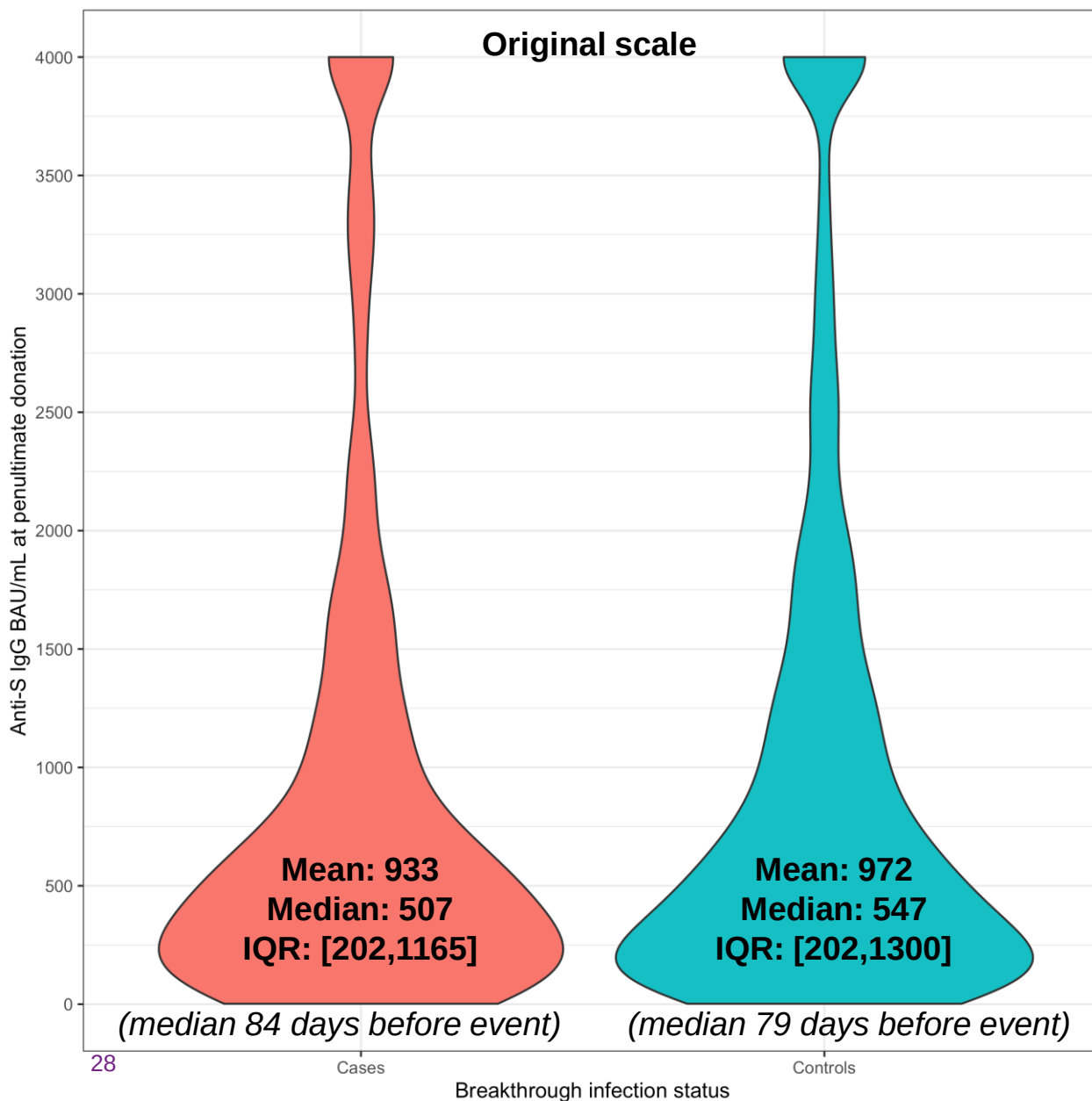
Cases and controls had longitudinal samples tested with the Ortho anti-S1 quantitative IgG assay

- *at 1:20 dilution (DR: 40–4000 BAU/mL) and reflexed to neat testing if below the LoQ (DR 2-200 BAU/mL)*

Anti-S IgG BAU/mL distributions in VBT cases and controls

Internal use

No association between anti-S IgG level and risk of vaccine breakthrough infection



- Conditional logistic regression, *controlling for age, sex, geographic region, and time since primary vaccination*:

Covariate	Coefficient	OR (95% CI)
$\log_{10}$ BAU/mL at penultimate donation	-0.06431	0.938 (0.787–1.117)

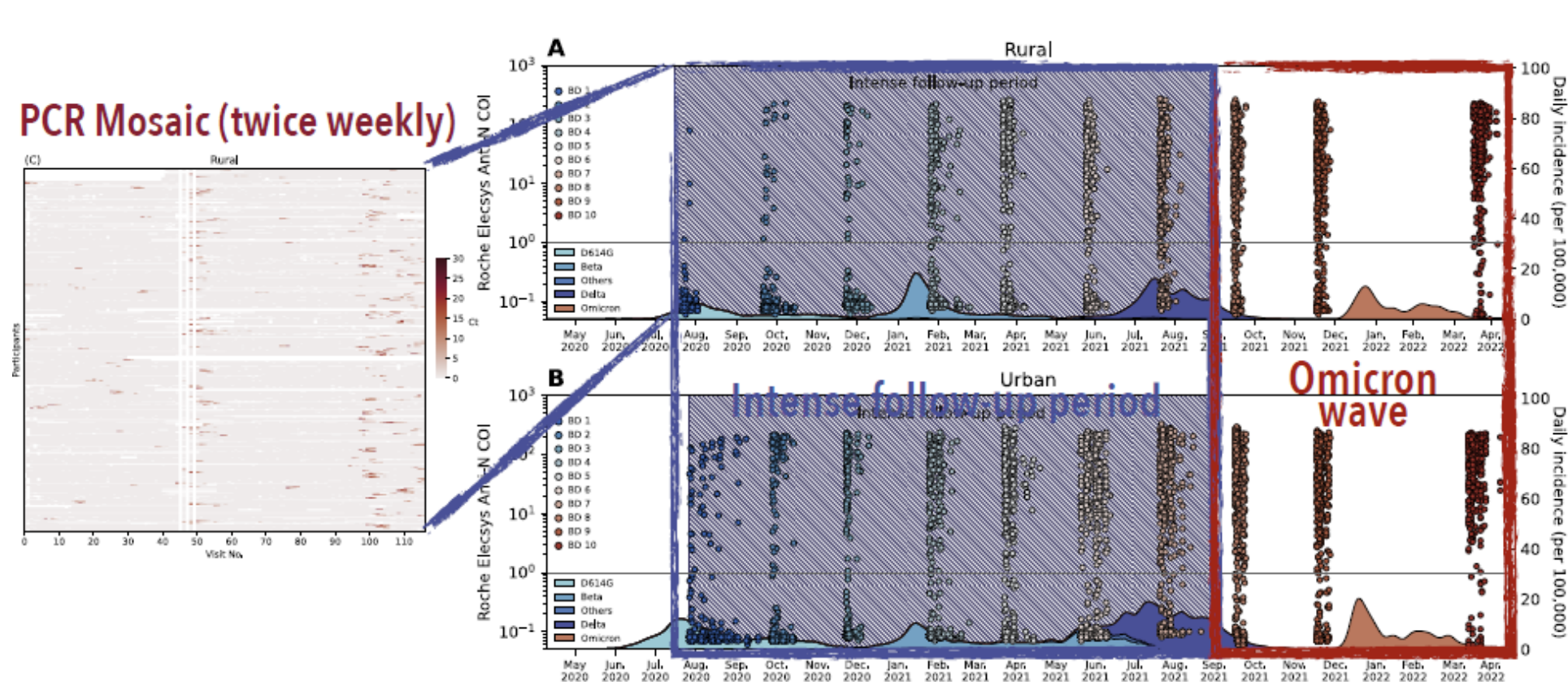
- Time-to-event analysis (Cox proportional hazards regression), treating Ab level as a time-varying covariate and controlling for age, sex, geographic region, and time since primary vaccination, also failed to show a statistically significant relationship.*

CORONAVIRUS

SARS-CoV-2 transmission, persistence of immunity, and estimates of Omicron's impact in South African population cohorts

Kaiyuan Sun^{1*}, Stefano Tempia^{2,3,4}, Jackie Kleynhans^{2,3}, Anne von Gottberg^{2,5}, Meredith L. McMorrow⁴, Nicole Wolter^{2,5}, Jinal N. Bhiman^{2,5}, Jocelyn Moyes^{2,3}, Mignon du Plessis^{2,5}, Maimuna Carrim^{2,5}, Amelia Buys², Neil A. Martinson^{6,7}, Kathleen Kahn⁸, Stephen Tollman⁸, Limakatso Lebina⁶, Floidy Wafawanaka⁸, Jacques D. du Toit⁸, Francesc Xavier Gómez-Olivé⁸, Thulisa Mkhencele², Cécile Viboud^{1†}, Cheryl Cohen^{2,3*†}

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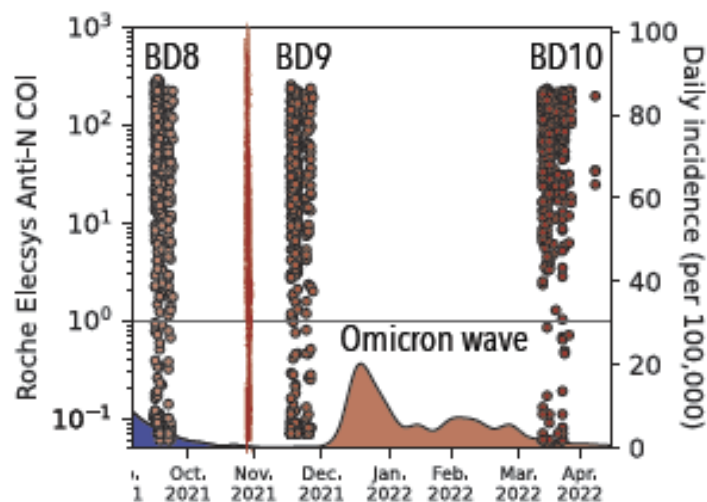
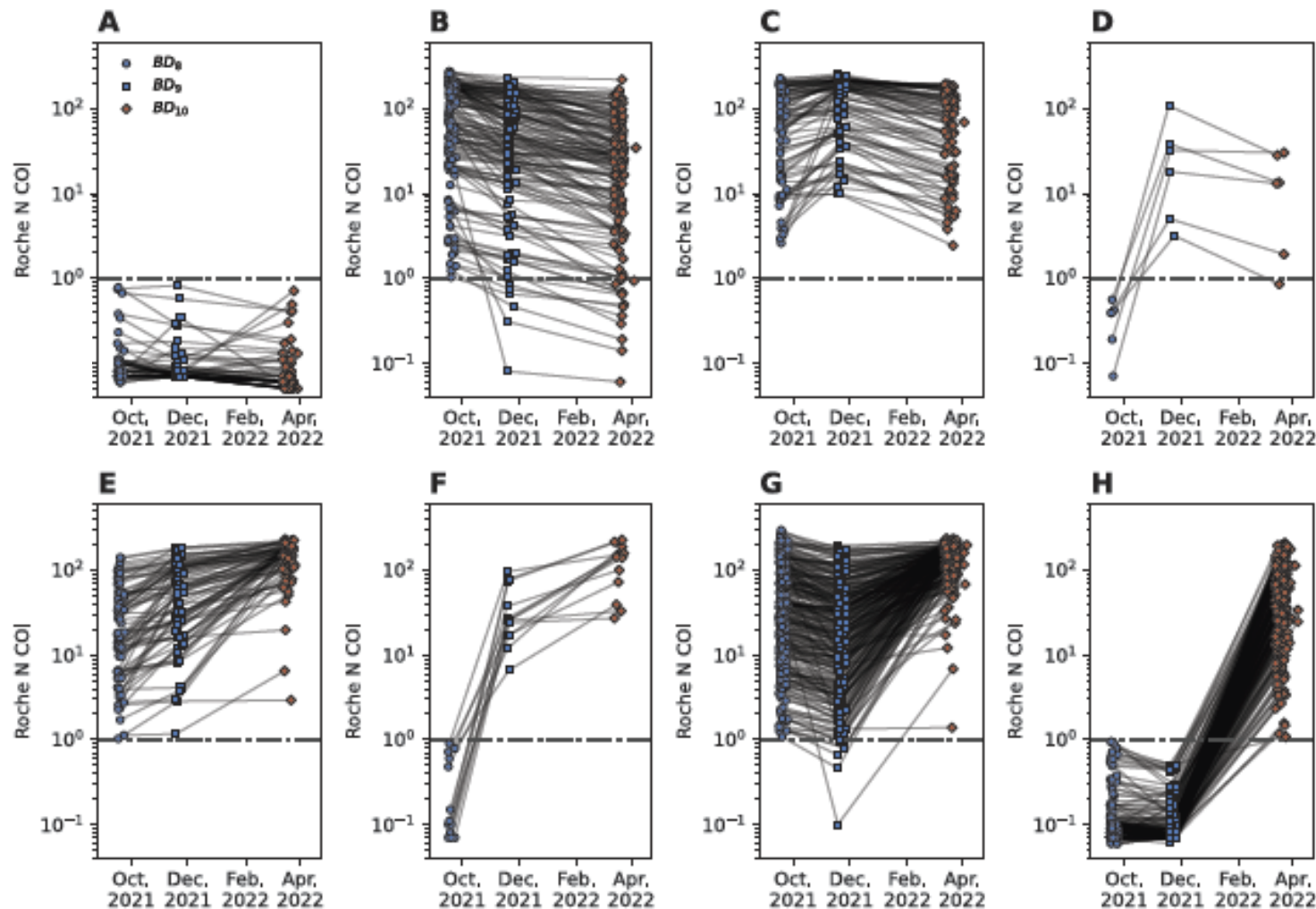
Which serologic patterns indicate Omicron infection?

RESEARCH

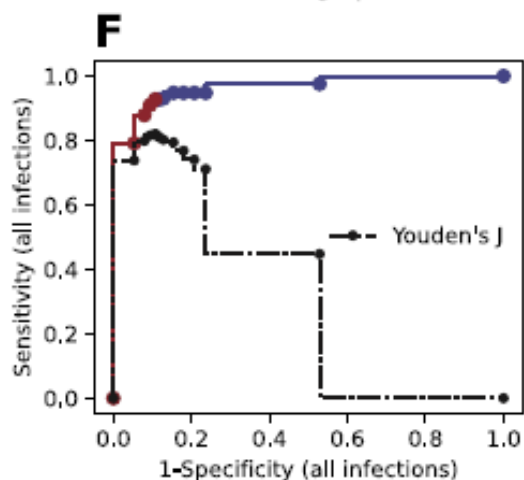
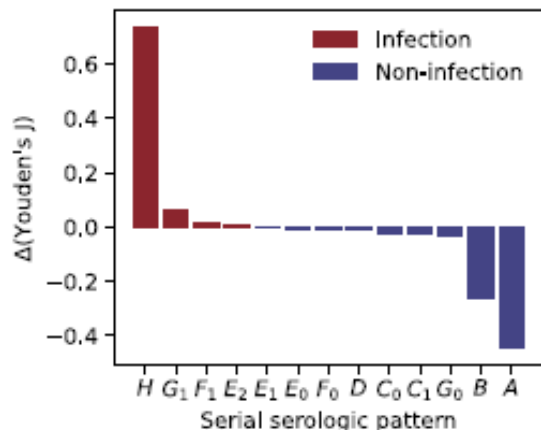
Open Access

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

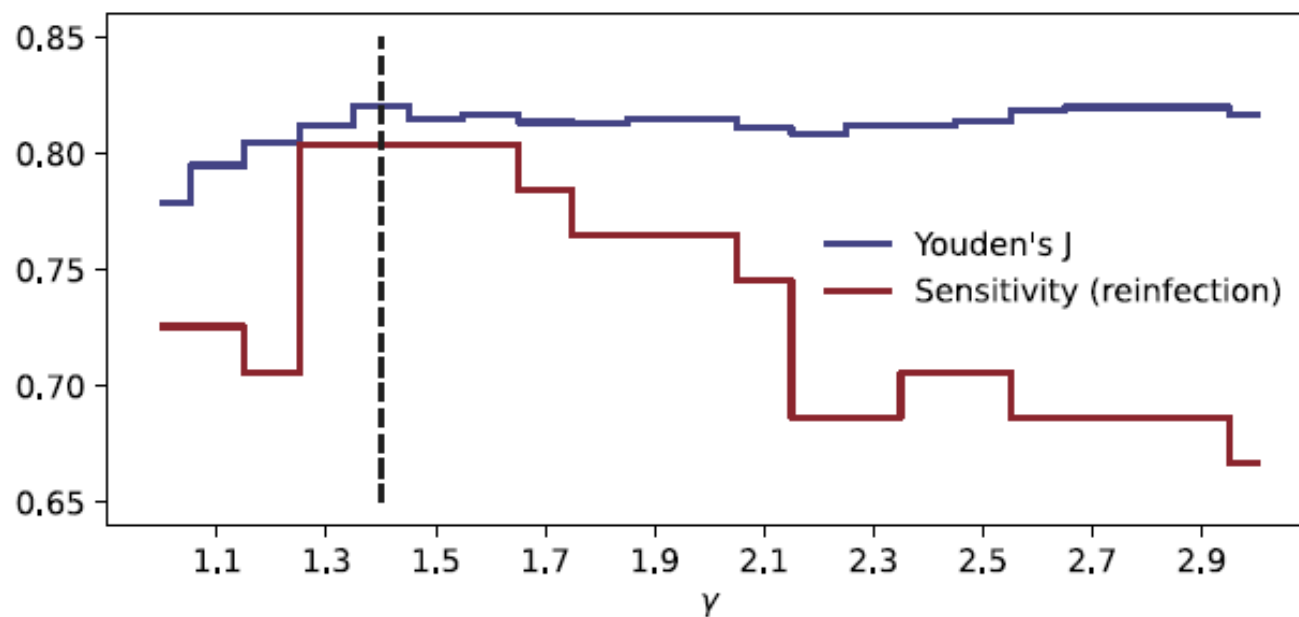
Carlos A. Prete Jr.¹, Lewis F. Buss², Renata Buzcheri¹, Claudia M. M. Abrahim³, Tassila Salomon³, Myuki A. E. Crispim⁴, Marcio K. Okawa⁵, Eduard Grebe^{1,2}, Allyson G. da Costa⁶, Nelson A. Fraij⁶, Maria do P. S. S. Carvalho⁴, Charles Whittaker⁸, Neal Alexander¹⁰, Nuno R. Faria^{10,11}, Christopher Dye¹¹, Victor H. Nascimento⁷, Michael P. Busch¹² and Ester Cordelia Sabino^{2*}



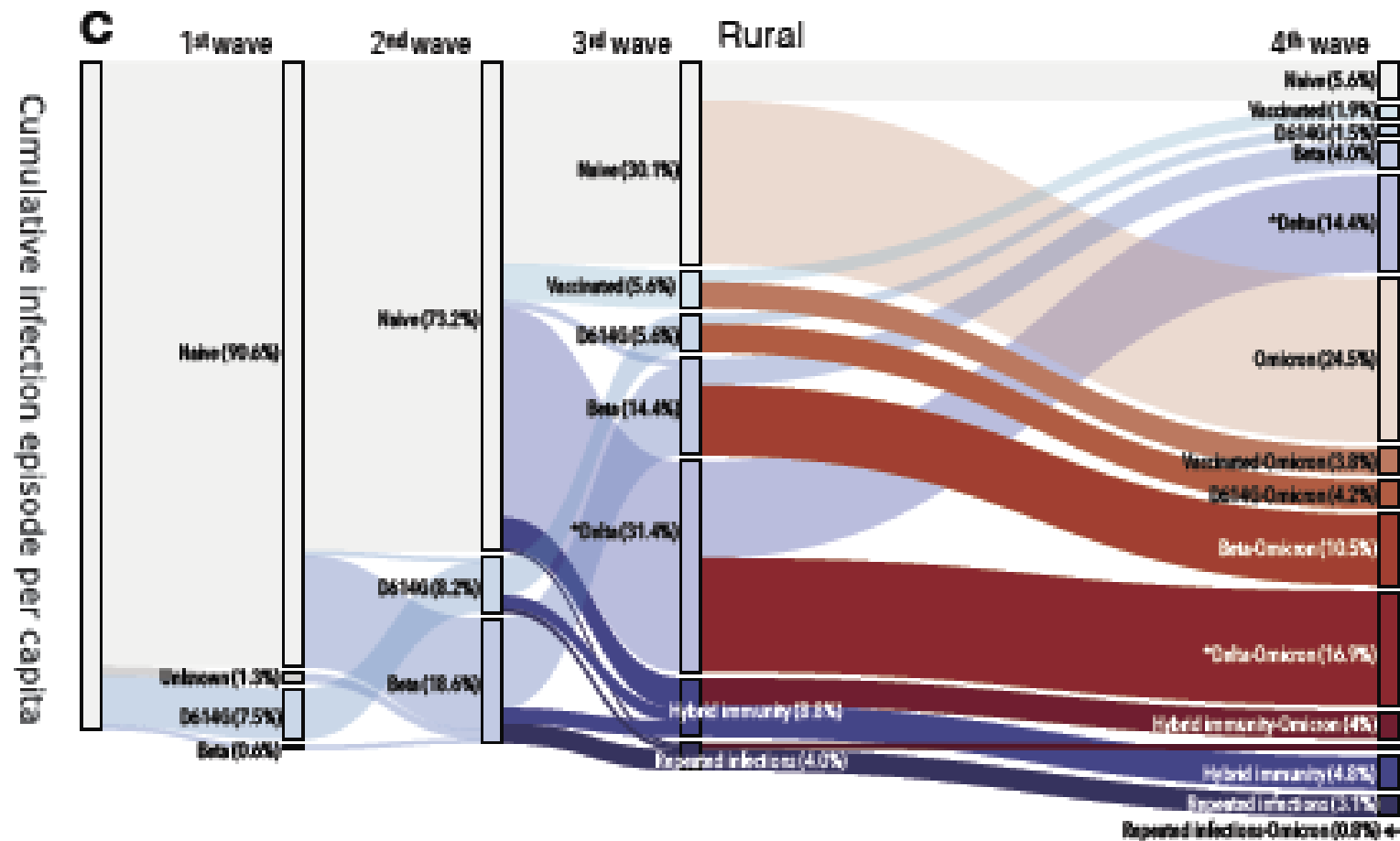
Optimizing boosting threshold γ



$$\text{Youden's } J = \text{Sensitivity} + \text{Specificity} - 1$$



Rapidly shifting immunological landscape and severity of SARS-COV-2 in the Omicron era in South Africa



Thank you