CDC/IDSA COVID-19 Clinician Call

December 18, 2021

Welcome & Introductions

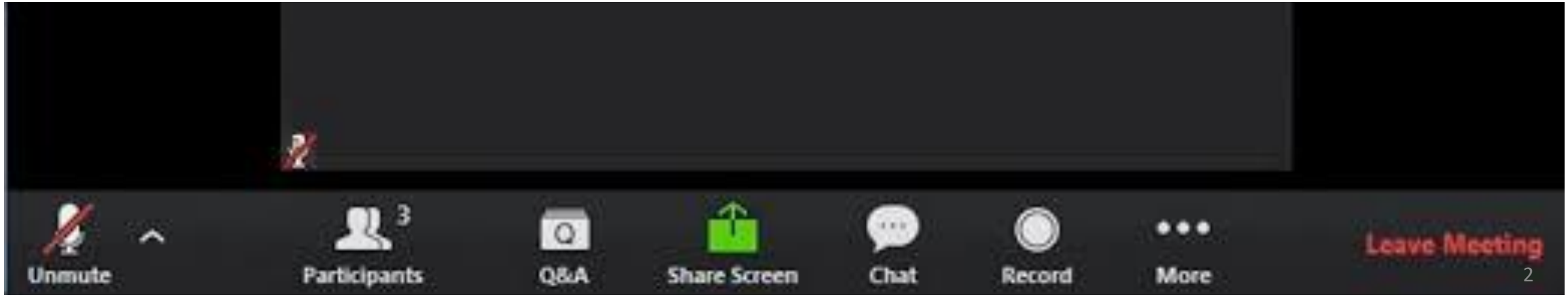
Dana Wollins, DrPH, MGC
Vice President, Clinical Affairs & Guidelines IDSA

- 81st in a series of weekly calls, initiated by CDC as a forum for information sharing among frontline clinicians caring for patients with COVID-19
- The views and opinions expressed here are those of the presenters and do not necessarily reflect the official policy or position of the CDC or IDSA. Involvement of CDC and IDSA should not be viewed as endorsement of any entity or individual involved.
- This webinar is being recorded and can be found online at www.idsociety.org/cliniciancalls.

COVID-19 Real-Time Learning Network
Brought to you by CDC and IDSA

Question?
Use the “Q&A” Button

Comment?
Use the “Chat” Button



TODAY'S CALL:

Omicron – Continued: Plus Monoclonal Antibody Therapy Updates

Johnson & Johnson Vaccine Update
Sara Oliver, MD, MSPH
LCDR, U.S. Public Health Service
Co-Lead, COVID-19 Work Group, Advisory Committee on Immunization Practices (ACIP
Centers for Disease Control and Prevention

Update on Current Situation with Omicron
John T. Brooks, MD
Chief Medical Officer, COVID-19 Response
U.S. Centers for Disease Control and Prevention

Re-infection and Omicron
Juliet Pulliam, PhD
Director
South African Center of Excellence in Epidemiological Modelling and Analysis

Evusheld for Pre-Exposure Prophylaxis in Adults & Children: Update & Clinical Considerations for Use
Cameron R. Wolfe, MBBS (Hons), MPH, FIDSA
Infectious Disease Specialist and Associate Professor of Medicine
Duke University

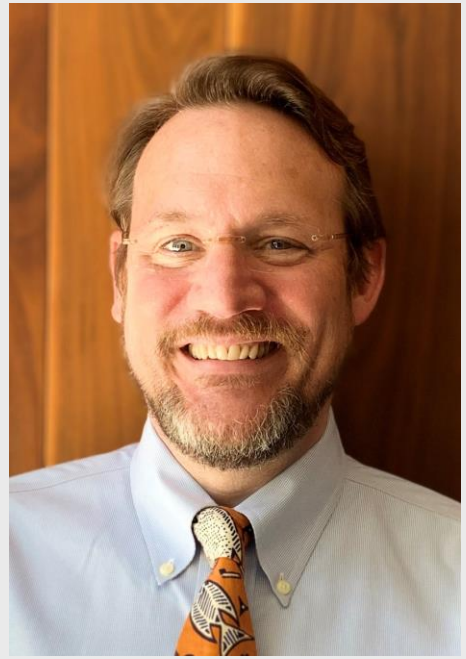
Bamlanivimab & Etesivimab for Treatment and Post-Exposure Prophylaxis In Pediatric Patients
Sameer J. Patel, MD
Attending Physician, Infectious Disease and Associate Professor of Pediatrics
Northwestern University Feinberg School of Medicine

Johnson & Johnson Vaccine Update

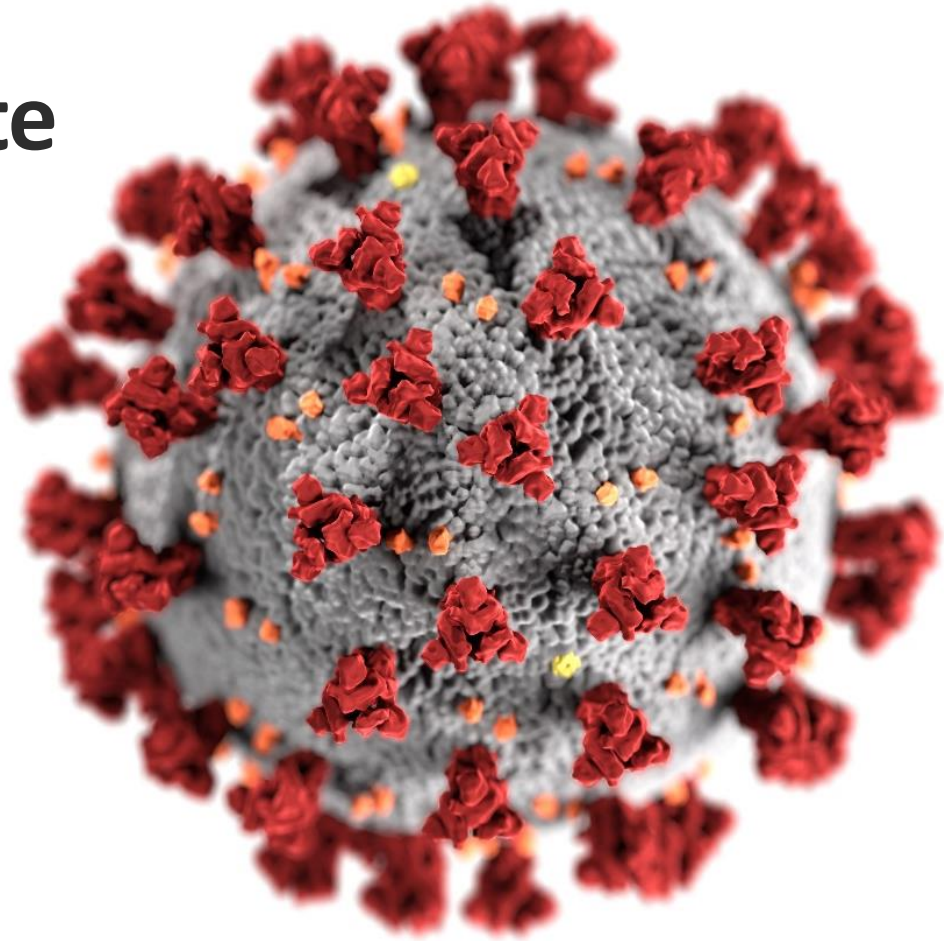
Sara Oliver, MD, MSPH

Update on Current Situation with Omicron

John T. Brooks, MD



B.1.1.529 – Omicron Variant Update



CDC COVID-19 Emergency Response
IDSA Clinician Call
December 18, 2021

cdc.gov/coronavirus

Four Key Questions

1. How transmissible is Omicron?
2. How virulent is Omicron compared to other variants?
3. How well do vaccines and prior infection protect against infection, transmission, clinical disease and death with Omicron?
4. How do populations understand these dynamics, perceive risk and follow control measures, including public health and social measures.

https://www.who.int/publications/m/item/enhancing-readiness-for-omicron-(b.1.1.529)-technical-brief-and-priority-actions-for-member-states

Four Key Questions

1. **How transmissible is Omicron?**
2. **How virulent is Omicron compared to other variants?**
3. **How well do vaccines and prior infection protect against infection, transmission, clinical disease and death with Omicron?**
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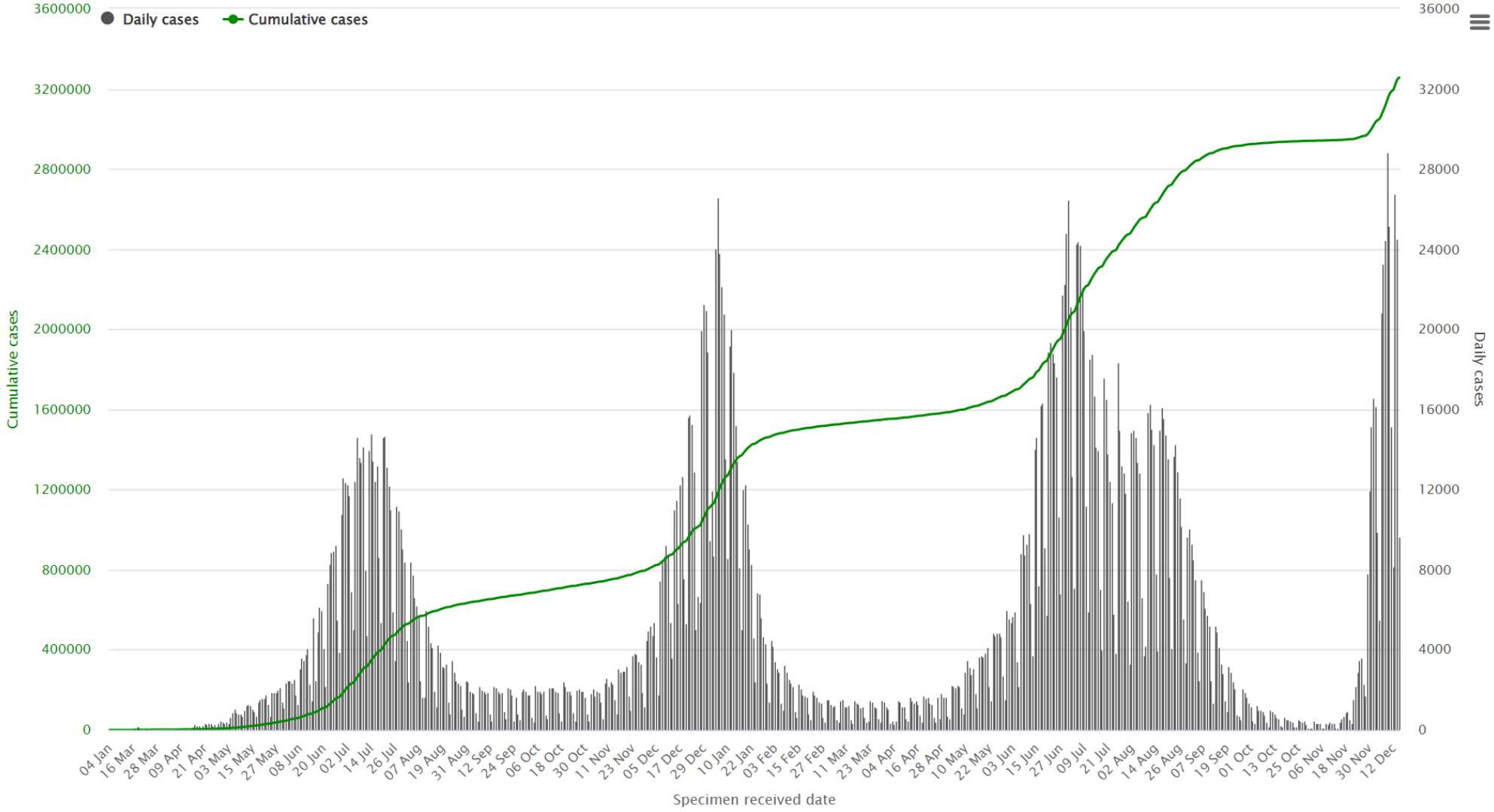
https://www.who.int/publications/m/item/enhancing-readiness-for-omicron-(b.1.1.529)-technical-brief-and-priority-actions-for-member-states

Number and cumulative number of laboratory-confirmed cases of COVID-19, South Africa, 3 March 2020 –15 December (n=3,255,814)



https://www.nicd.ac.za/diseases-a-z-index/disease-index-covid-19/surveillance-reports/national-covid-19-daily-report/

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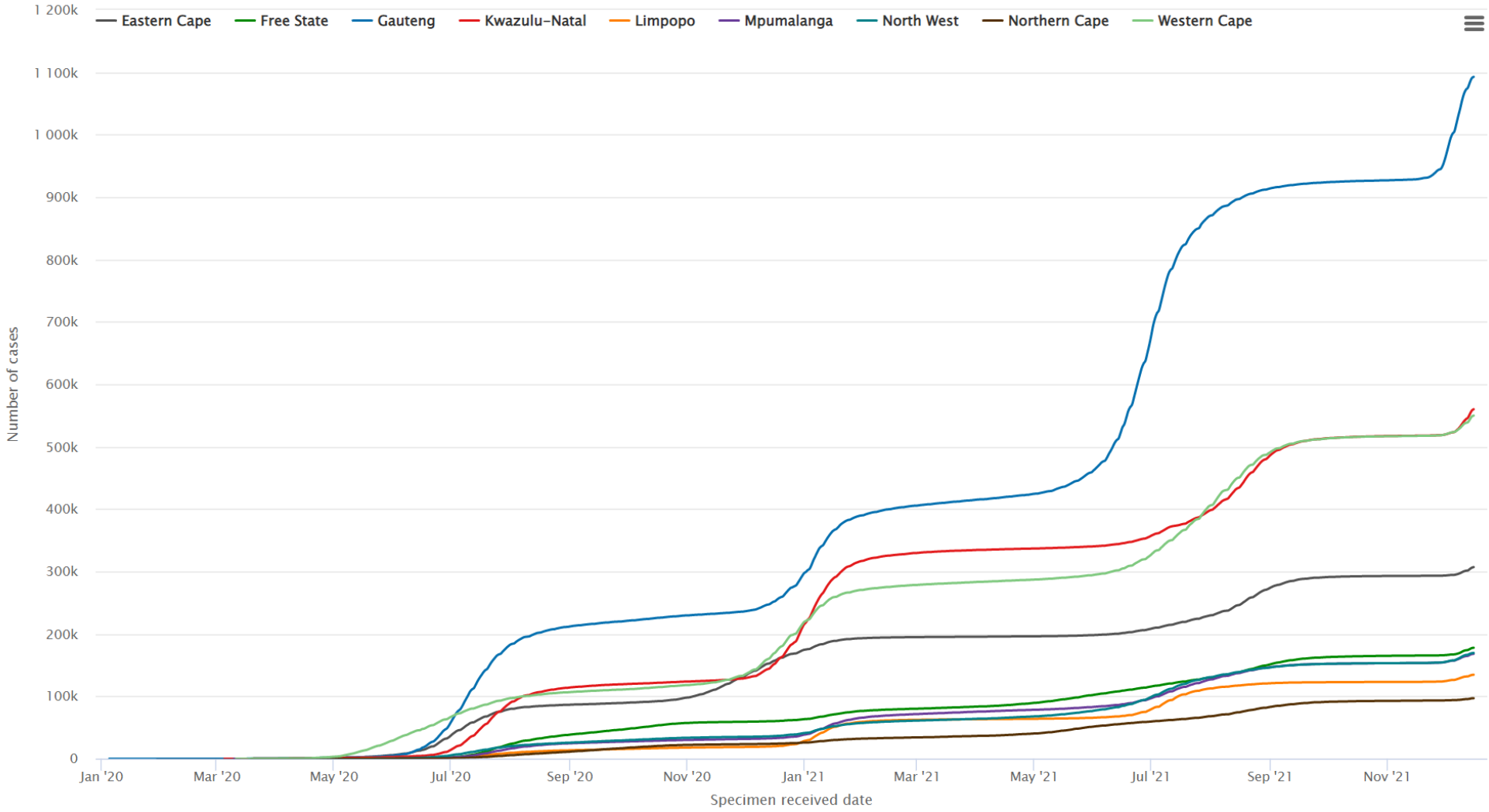

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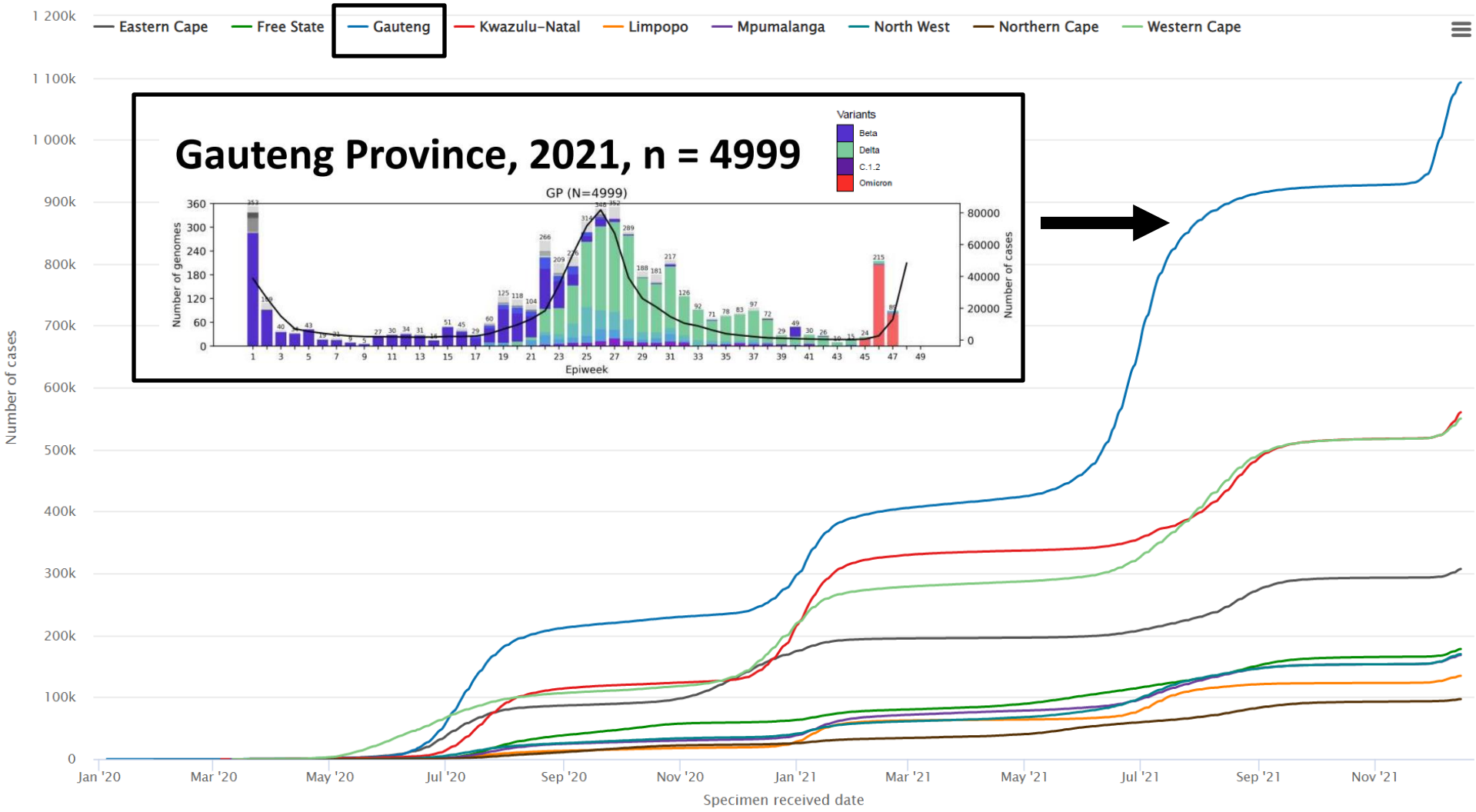
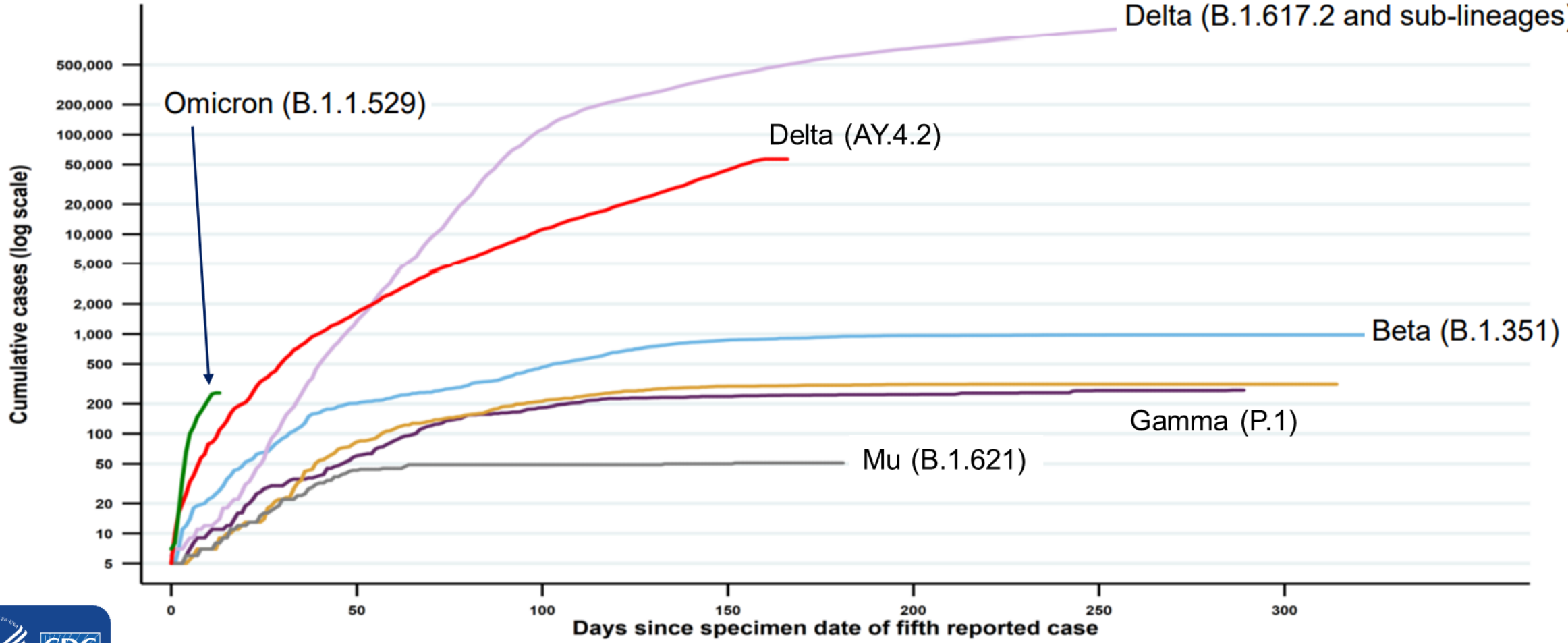


https://www.nicd.ac.za/diseases-a-z-index/disease-index-covid-19/surveillance-reports/national-covid-19-daily-report/

In U.K., Omicron cases growing rapidly, despite Delta

With growth rate of 0.35 per day, Omicron predicted to surpass Delta by mid-December



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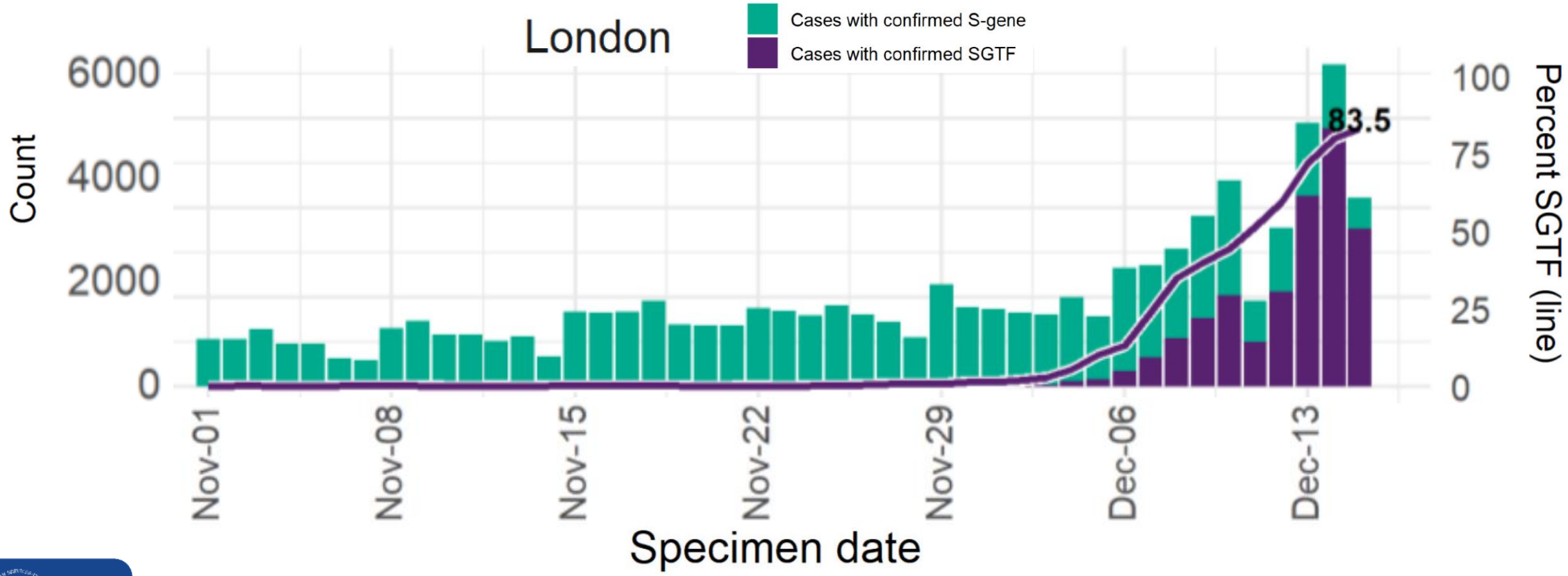
In U.K., Omicron cases growing rapidly, despite Delta

83.5% of sequenced isolates have S-gene dropout



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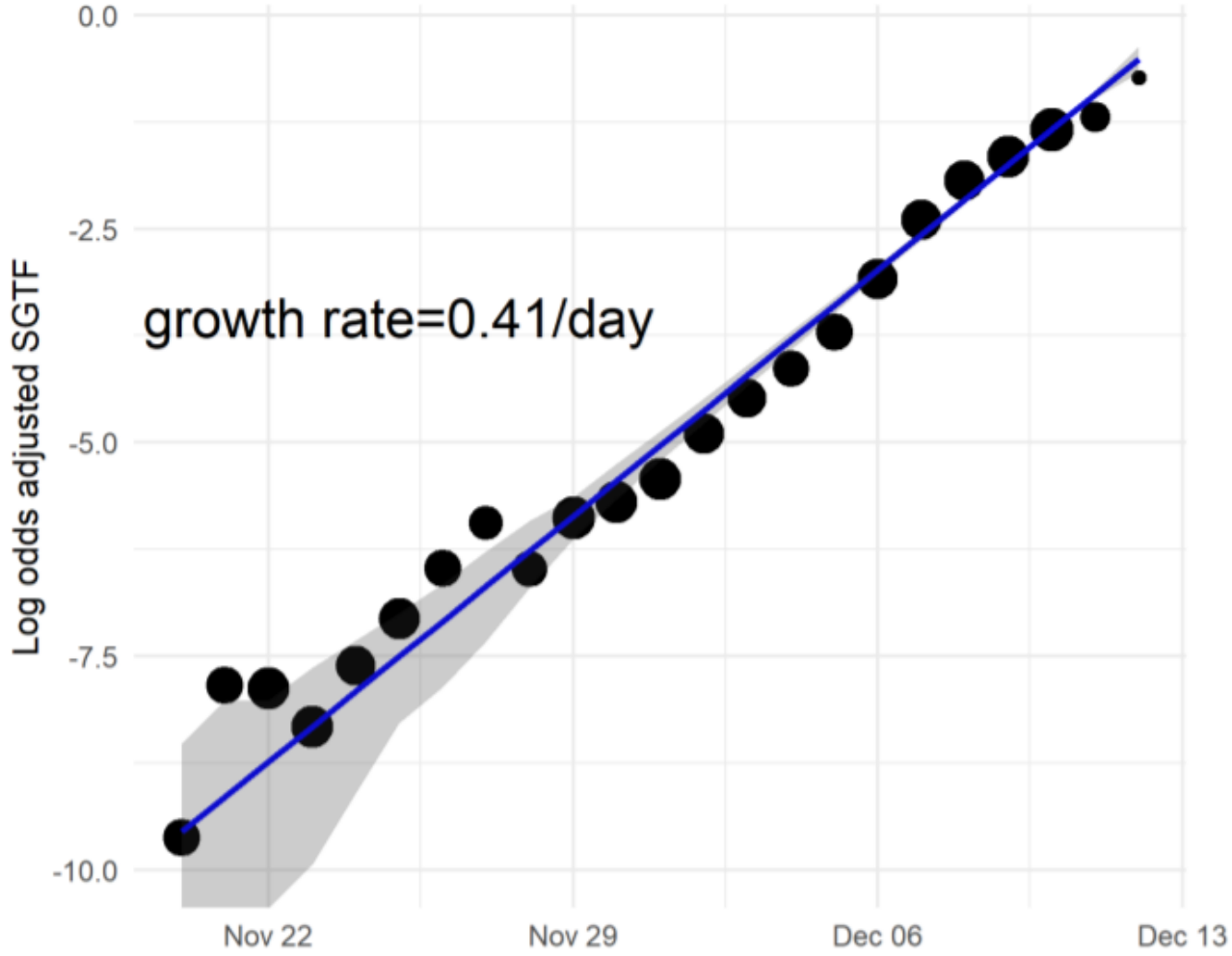
In U.K., Omicron cases growing rapidly, despite Delta



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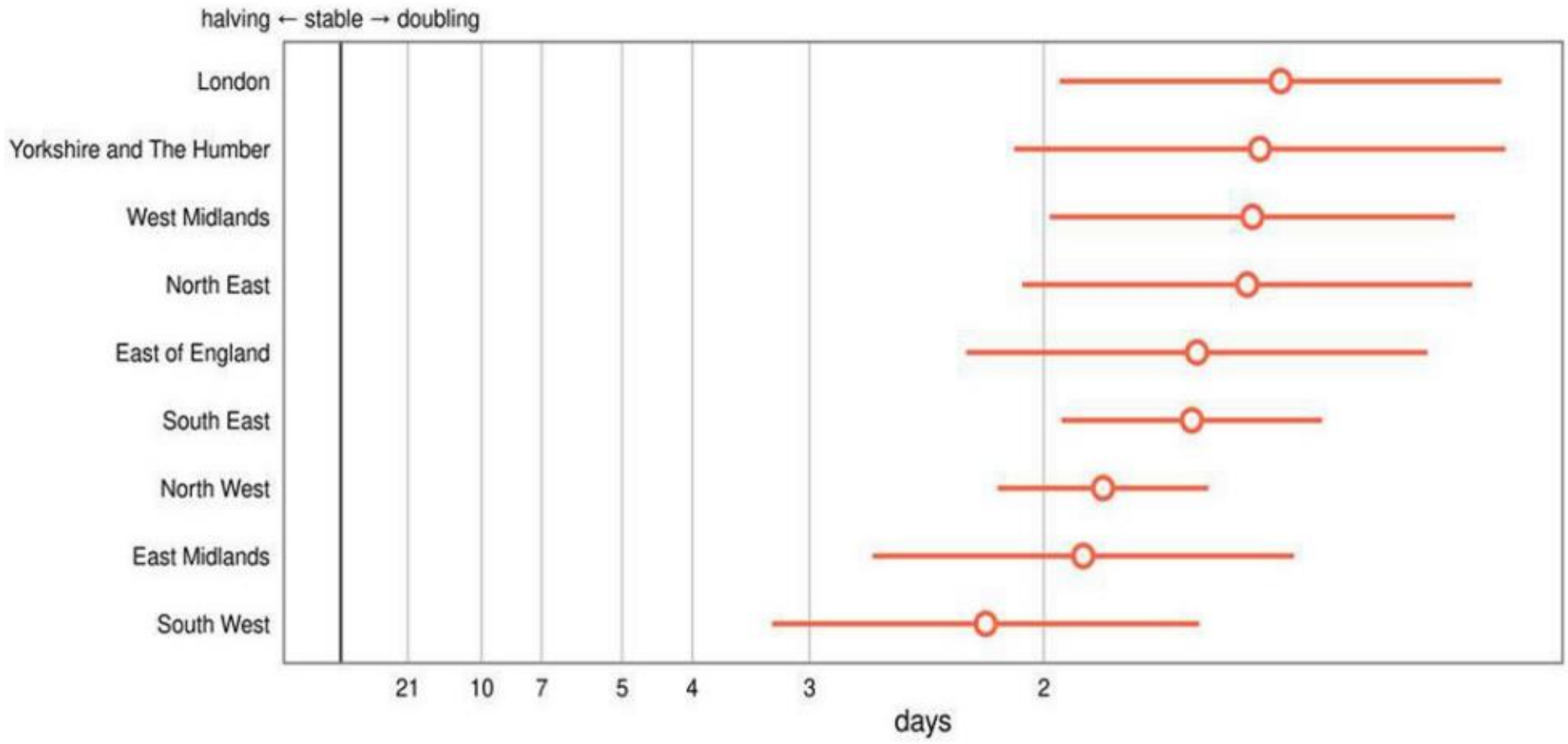
In U.K., Omicron cases growing rapidly, despite Delta

Doubling time <2.0 days

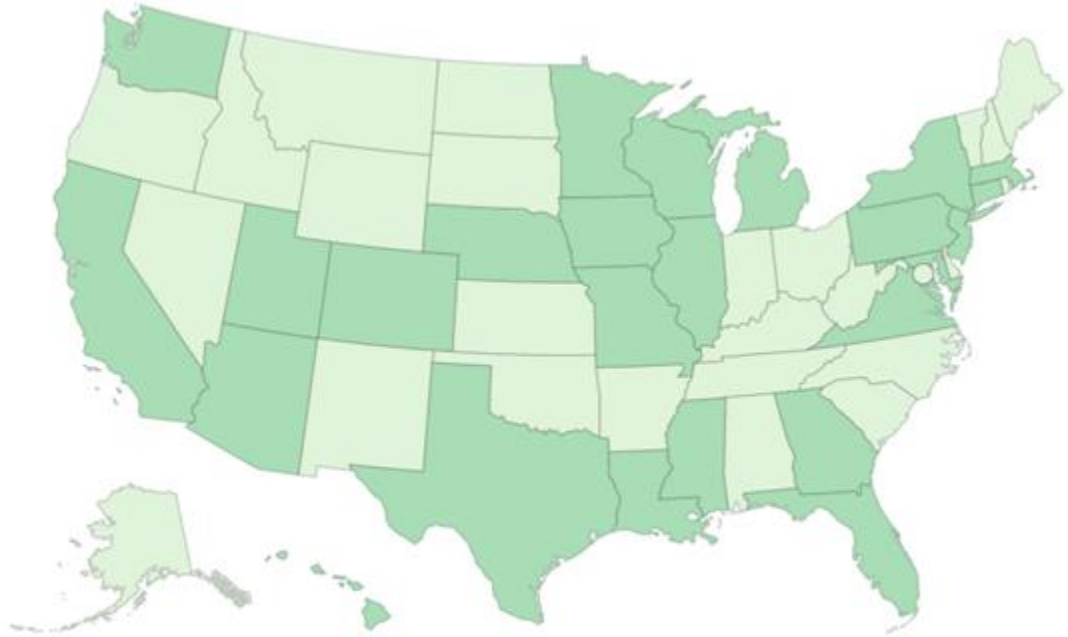


https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1040076/Technical_Briefing_31.pdf

U.S. States and Territories Reporting Omicron Detections

December 11, 2021 (N = 25)

25 states and DC, 0 Territories

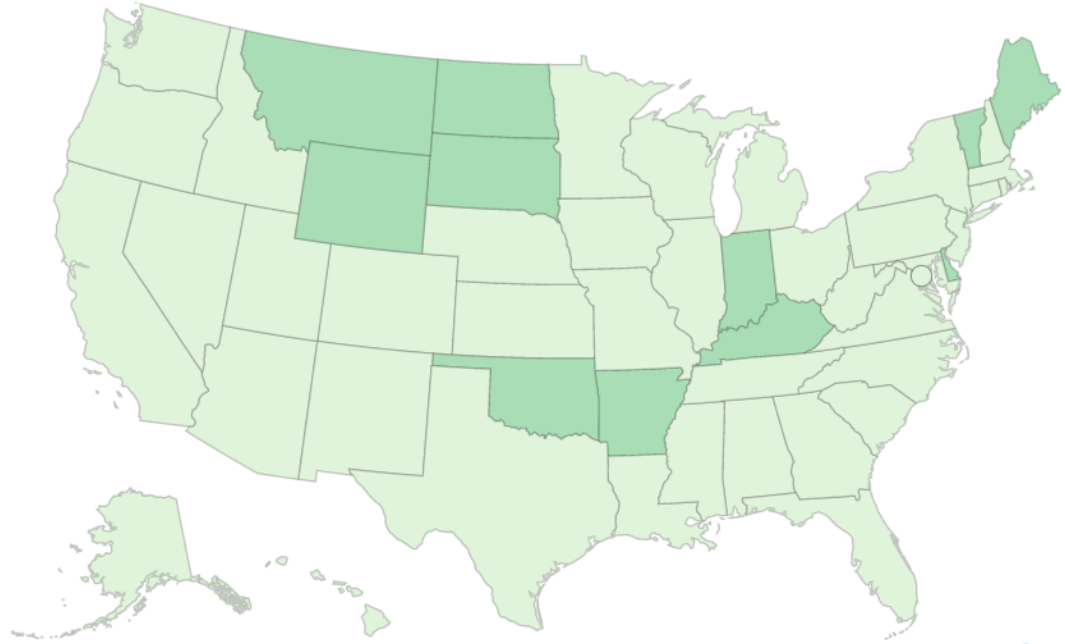


Yes
No

Territories AS GU PR VI MP FM PW MH

December 18, 2021 (N = 48)

41 states and DC, 7 Territories



Territories AS GU PR VI MP FM PW MH

https://www.cdc.gov/coronavirus/2019-ncov/variants/omicron-variant.html

U.S. States and Territories Reporting Omicron Detections

December 8 , 2021
Houston Methodist Hospital

HEALTH & SCIENCE

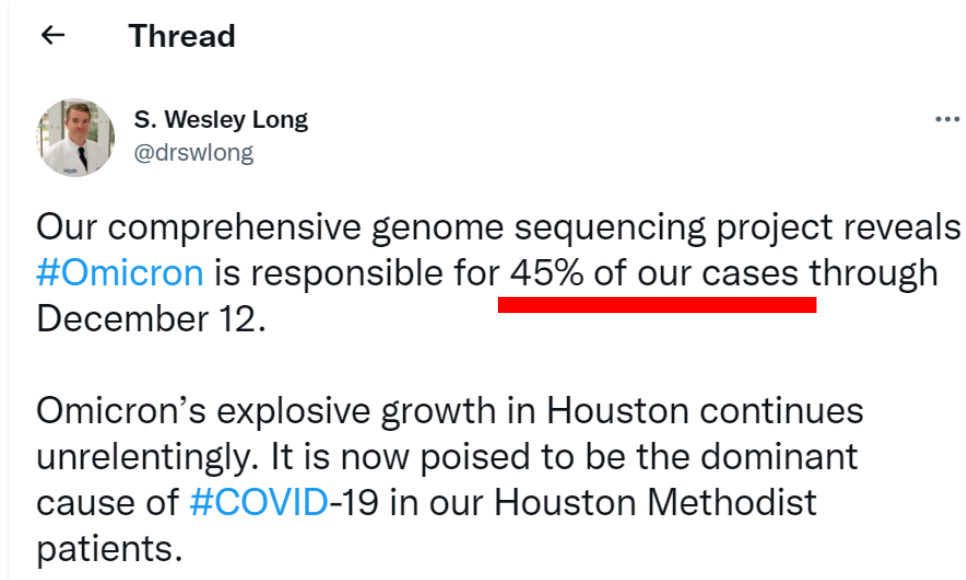
Houston Methodist has identified 8 new cases of the COVID-19 omicron variant

Methodist researchers identified the cases through its genome sequencing surveillance project.

MATT HARAB | DECEMBER 9, 2021, 8:07 AM (LAST UPDATED: DECEMBER 9, 2021, 8:31 AM)

https://www.houstonpublicmedia.org/articles/news/health-science/2021/12/09/415133/houston-methodist-has-identified-8-new-cases-of-the-covid-19-omicron-variant/

December 12 , 2021
Houston Methodist Hospital



← Thread

S. Wesley Long
@drswlong

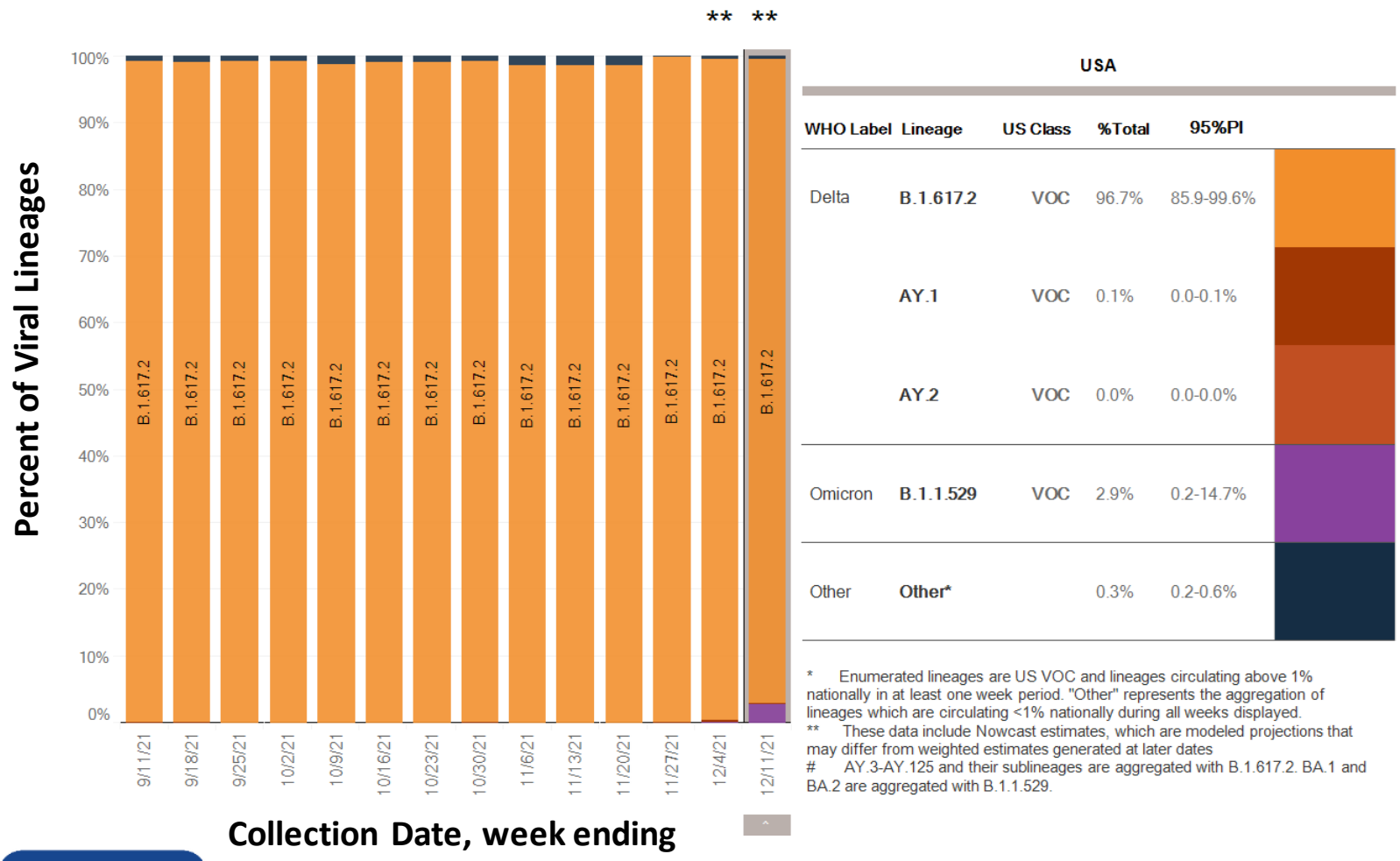
Our comprehensive genome sequencing project reveals #Omicron is responsible for 45% of our cases through December 12.

Omicron's explosive growth in Houston continues unrelentingly. It is now poised to be the dominant cause of #COVID-19 in our Houston Methodist patients.

https://twitter.com/drswlong/status/1471948374681309188?ref_src=twsrc%5Etfw%7Ctwcamp%5Etweetembed%7Ctwterm%5E1471948374681309188%7Ctwgr%5E%7Ctwcon%5Es1_&ref_url=https%3A%2F%2Fwww.houstonpublicmedia.org%2Farticles%2Fnews%2Fhealth-science%2F2021%2F12%2F17%2F415844%2Fomicron-variant-is-now-responsible-for-nearly-half-of-houston-methodists-covid-19-cases%2F

Estimated Proportions of SARS-CoV-2 lineages in the US

September 11 – December 11, 2021 with NOWCAST



USA

WHO Label	Lineage	US Class	%Total	95%PI
Delta	B.1.617.2	VOC	96.7%	85.9-99.6%
	AY.1	VOC	0.1%	0.0-0.1%
	AY.2	VOC	0.0%	0.0-0.0%
Omicron	B.1.1.529	VOC	2.9%	0.2-14.7%
Other	Other*		0.3%	0.2-0.6%

* Enumerated lineages are US VOC and lineages circulating above 1% nationally in at least one week period. "Other" represents the aggregation of lineages which are circulating <1% nationally during all weeks displayed.
** These data include Nowcast estimates, which are modeled projections that may differ from weighted estimates generated at later dates
# AY.3-AY.125 and their sublineages are aggregated with B.1.617.2. BA.1 and BA.2 are aggregated with B.1.1.529.

Variants of Concern

Delta (B.1.617.2, AY lineages) 96.7%

AY.1 ≤0.1%

AY.2 ≤0.1%

Omicron (B.1.1.529, BA lineages) 2.9%

CDC COVID Data Tracker As of 12/14/21; VOC = variant of concern; VOI = variant of interest

Confirmed and Presumptive B.1.1.529 Infections 04-Dec-2021 @13:00 (N = 38 countries)

Confirmed by sequencing

Presumptive by PCR SGTF

Courtesy of BNO News: https://newsnodes.com/nu_tracker

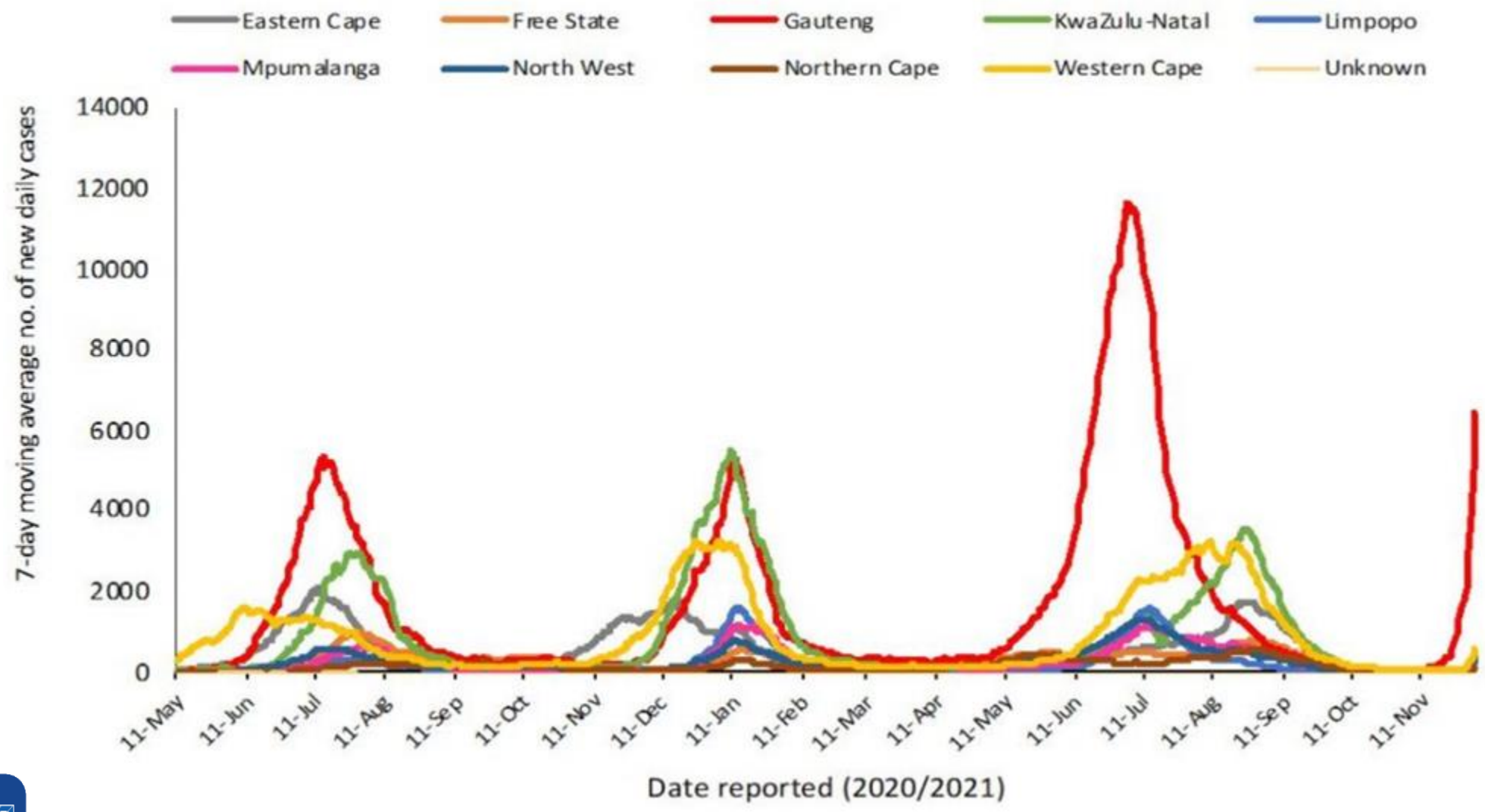
Confirmed and Presumptive B.1.1.529 Infections 18-Dec-2021 @09:00 (N = 95 countries)

Confirmed by sequencing

Presumptive by PCR SGTF

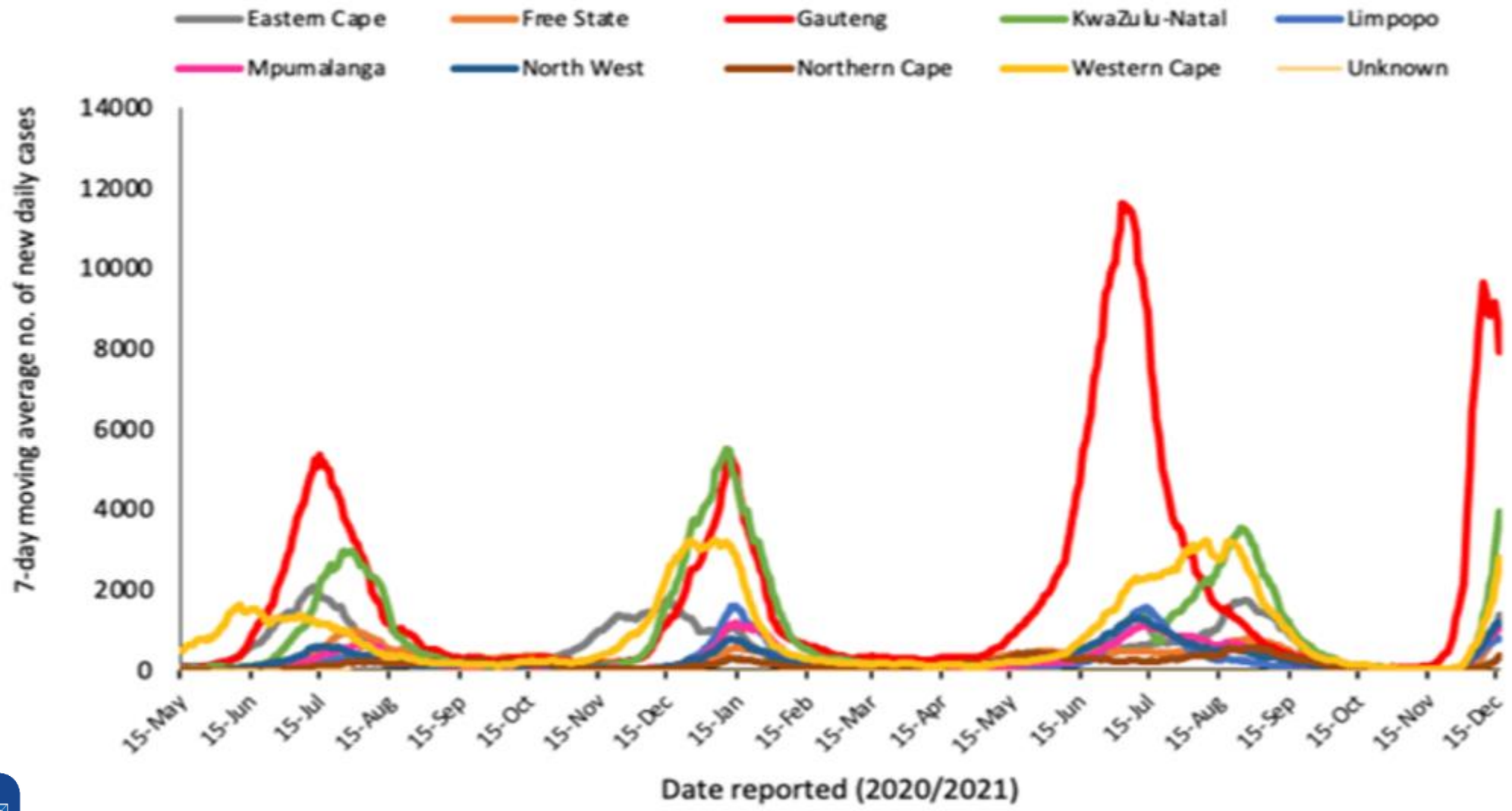
Courtesy of BNO News: https://newsnodes.com/nu_tracker

New cases by province – South Africa, 2020-2021
December 4, 2021



https://www.nicd.ac.za/latest-confirmed-cases-of-covid-19-in-south-africa-4-december-2021/

New cases by province – South Africa, 2020-2021
December 17, 2021



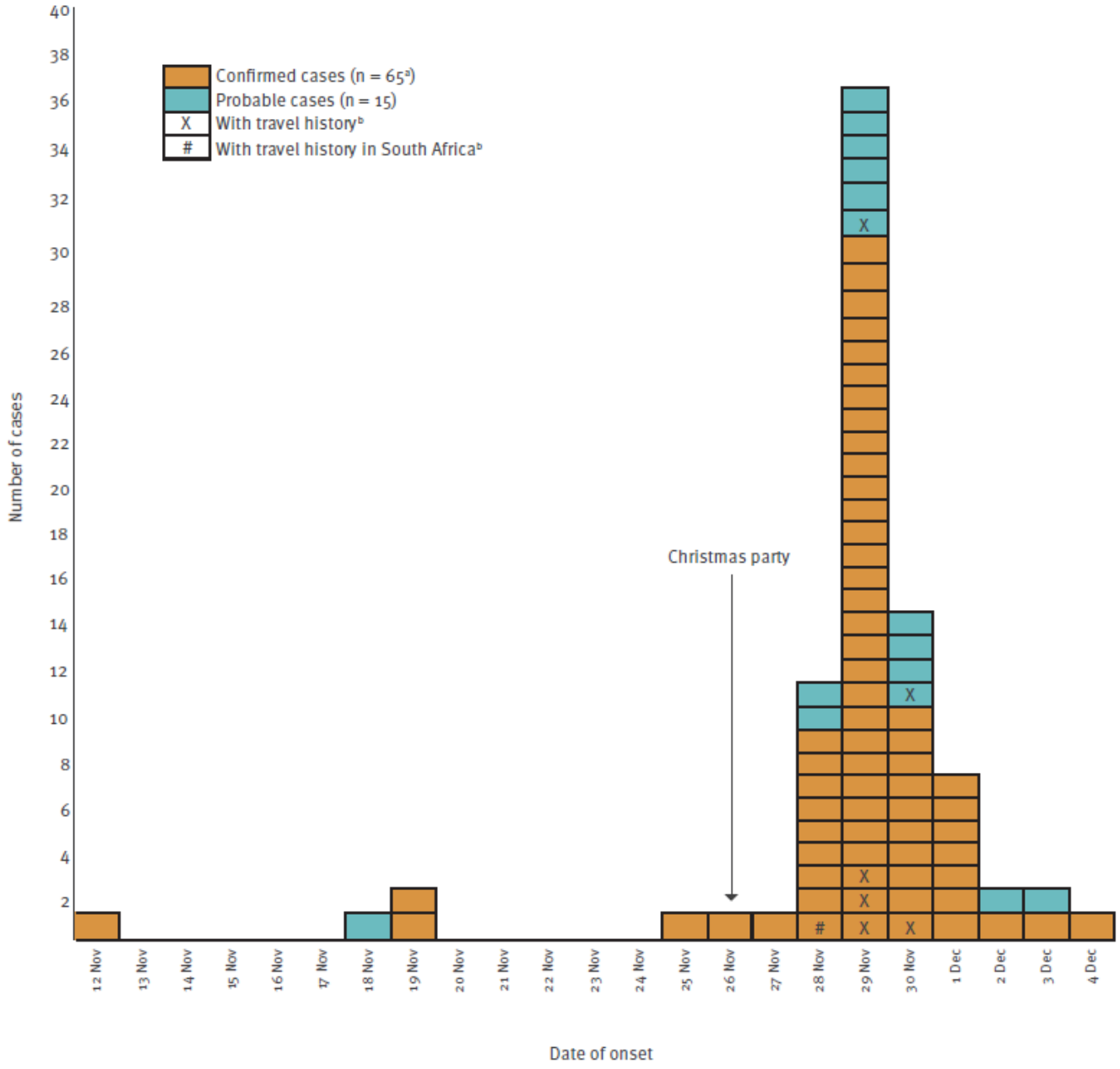
https://www.nicd.ac.za/latest-confirmed-cases-of-covid-19-in-south-africa-17-december-2021/

Findings on Omicron from other countries

Christmas Party Outbreak (Oslo Norway)

- Held at a restaurant in a separate room 145m^2 (1,560 ft^2)
- Among 117 guests, attack rate over 70%
  - 98% of cases fully vaccinated (median 79 days since last dose)
  - Median incubation period 3 days (IQR: 3-4)
- No facemask use required
- 70 other restaurant patrons diagnosed with COVID-19
  - 53 confirmed Omicron
- No hospitalizations
  - 77.5% fully and 3.4 % partially vaccinated as of 16-Dec-2021

https://www.fhi.no/en/news/2021/preliminary-findings-from-outbreak-investigation-after-christmas-party-in-o/
Brandal 2021, Euro Surveill;26(50):pii=2101147. https://doi.org/10.2807/1560-7917.ES.2021.26.50.2101147
https://ourworldindata.org/covid-vaccinations



Brandal 2021, Euro Surveill;26(50):pii=2101147. https://doi.org/10.2807/1560-7917.ES.2021.26.50.2101147

Findings on Omicron from other countries: Severity

Danish review of their first 785 Omicron infections

Characteristics of SARS-CoV-2 Delta and Omicron variant cases, Denmark, 22 November–7 December 2021

	Number of Delta[a] cases (n=19,137)	% of all Delta[a] cases	Number of Omicron cases (n=785)	% of all Omicron cases
Hospitalisation				
Yes	290	1.5	9	1.2
Intensive care treatment				
Yes	22	0.11	1	0.13
Death				
Yes	14	0.07	0	0

Imperial College report

Hospitalization and asymptomatic infection indicators were not significantly associated with Omicron infection, suggesting at most limited changes in severity compared with Delta.

Epidemiological characterisation of the first 785 SARS-CoV-2 Omicron variant cases in Denmark, December 2021. Espenhain *et al.* Eurosurveillance (December 16, 2021)
Ferguson et al. 2021, Growth, population distribution and immune escape of the Omicron in England. Imperial College London (16-12-2021), https://doi.org/10.25561/93038

Findings on Omicron from other countries: Reinfection

U.K household transmission study

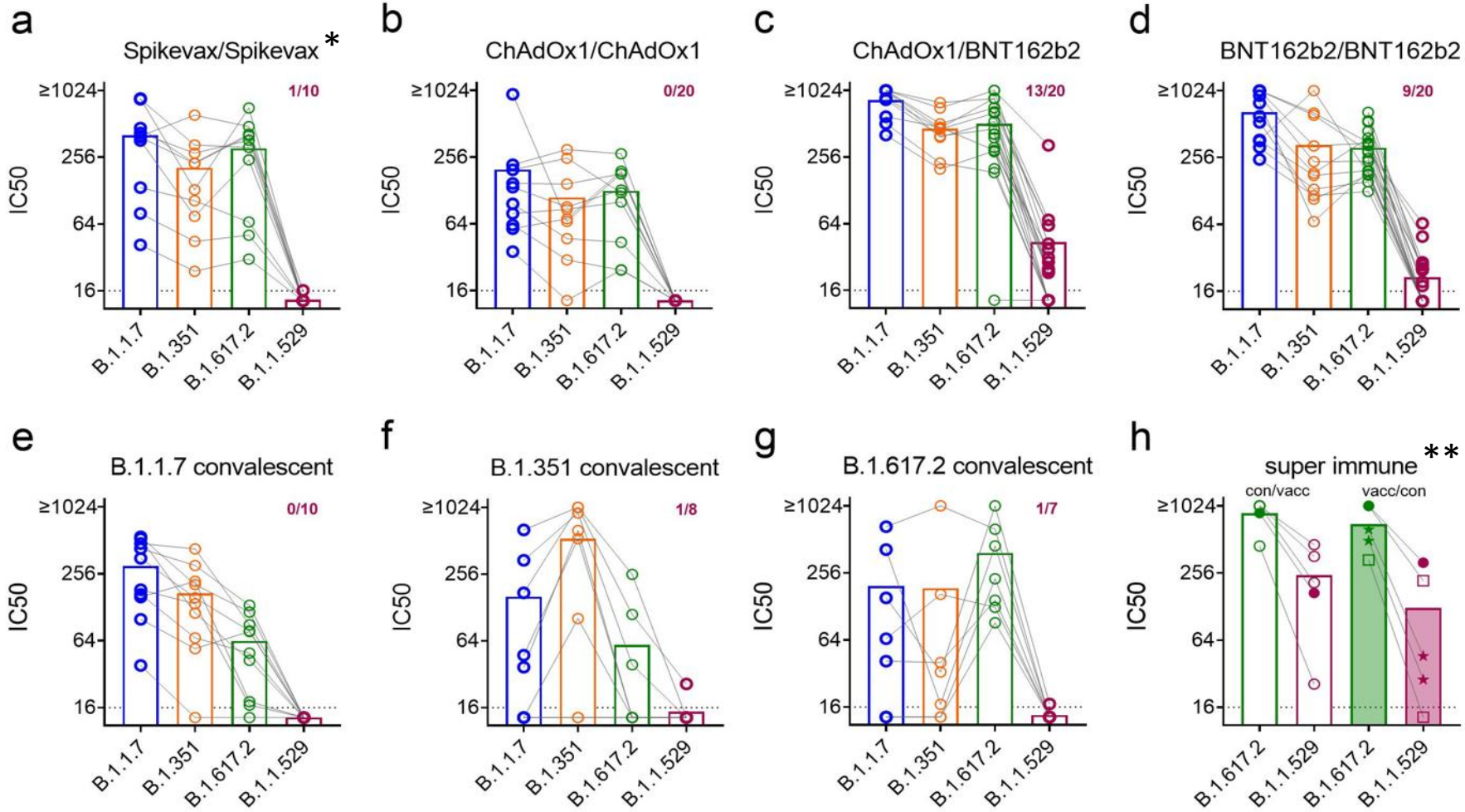
- Relative risk for reinfection with *Omicron vs. non-Omicron*
  - 3.3 (95% CI: 2.8–3.8)

Imperial College report

- Controlling for vaccine status, age, sex, ethnicity, asymptomatic status, region and specimen date and using conditional Poisson regression to predict reinfection status, relative risk for reinfection with *Omicron vs. Delta*
  - 5.41 (95% CI: 4.87-6.00)

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1042046/Technical_Briefing_32.pdf
Ferguson et al. 2021, Growth, population distribution and immune escape of the Omicron in England. Imperial College London (16-12-2021), https://doi.org/10.25561/93038.

Omicron has extensive but incomplete escape of other vaccine- and infection-elicited neutralization as well

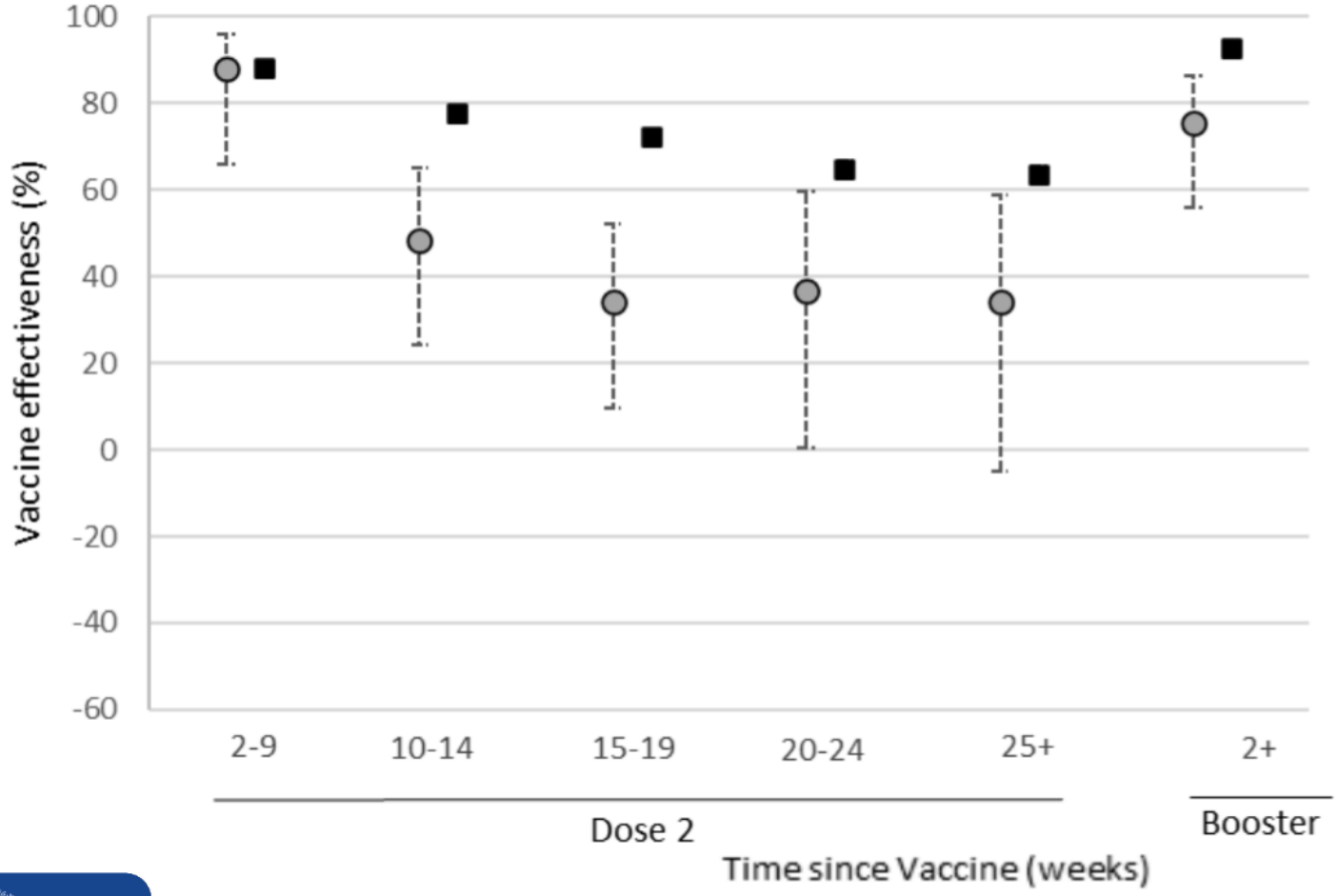


* Moderna mRNA-1273 vaccine

** convalescent/vaccinated or vaccinated/convalescent individuals

Source: Roessler et al. 2021, medRxiv; https://doi.org/10.1101/2021.12.08.21267491.

Pfizer BNT162b2 mRNA vaccine effectiveness (VE) against Delta and Omicron variant infections



Delta

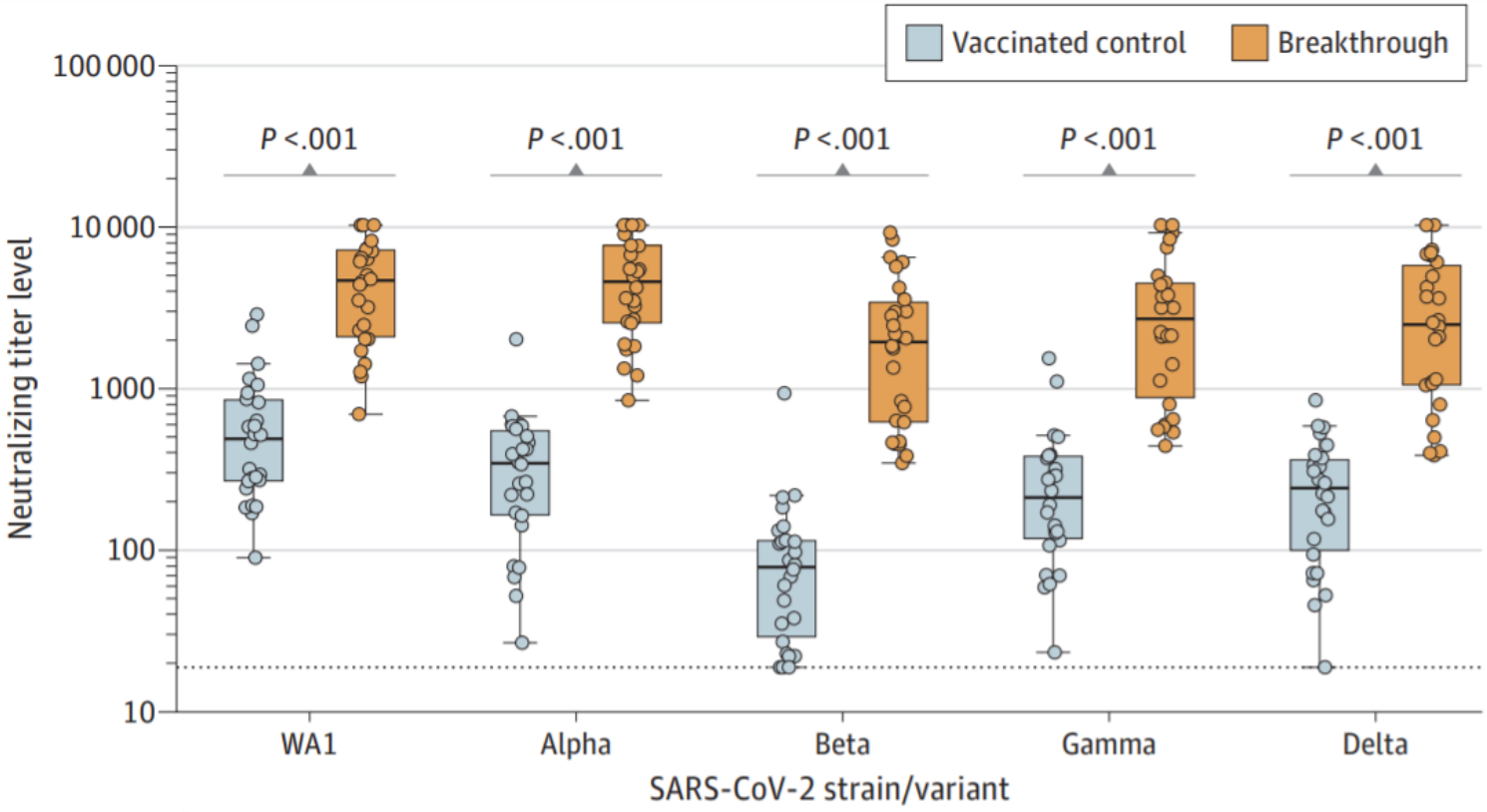
Omicron

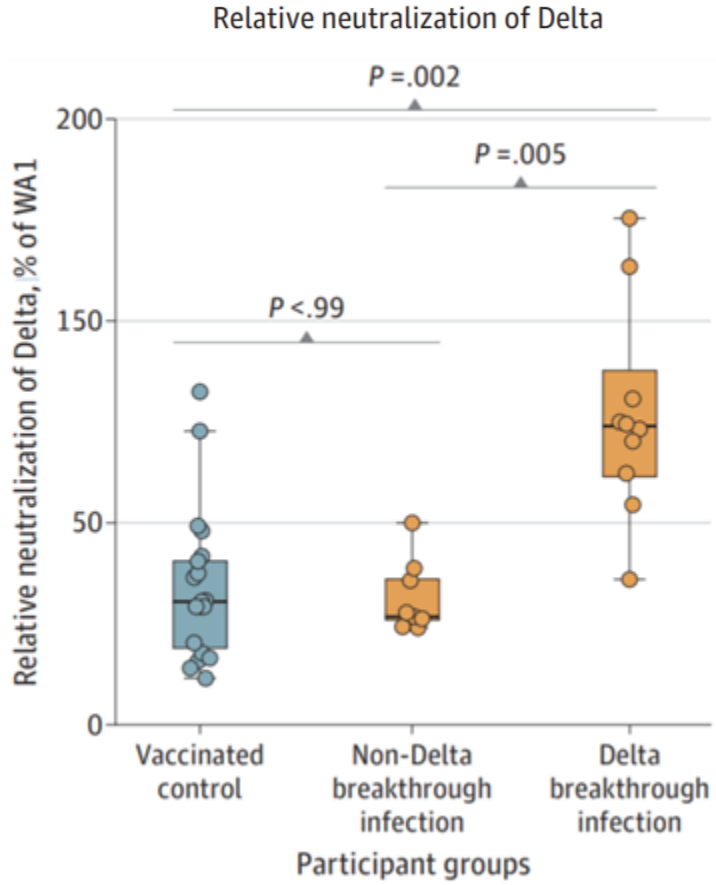
- Increased waning of VE for Omicron vs. Delta
  - 35% vs. 64% at 25+ weeks
- VE 2 after 3rd dose (booster) Omicron vs. Delta
  - 75% vs. 93% at 2+ weeks

Andrews 2021, medRxiv; https://www.medrxiv.org/content/10.1101/2021.12.14.21267615v1.full.pdf

Breakthrough infections boost neutralizing antibody titers

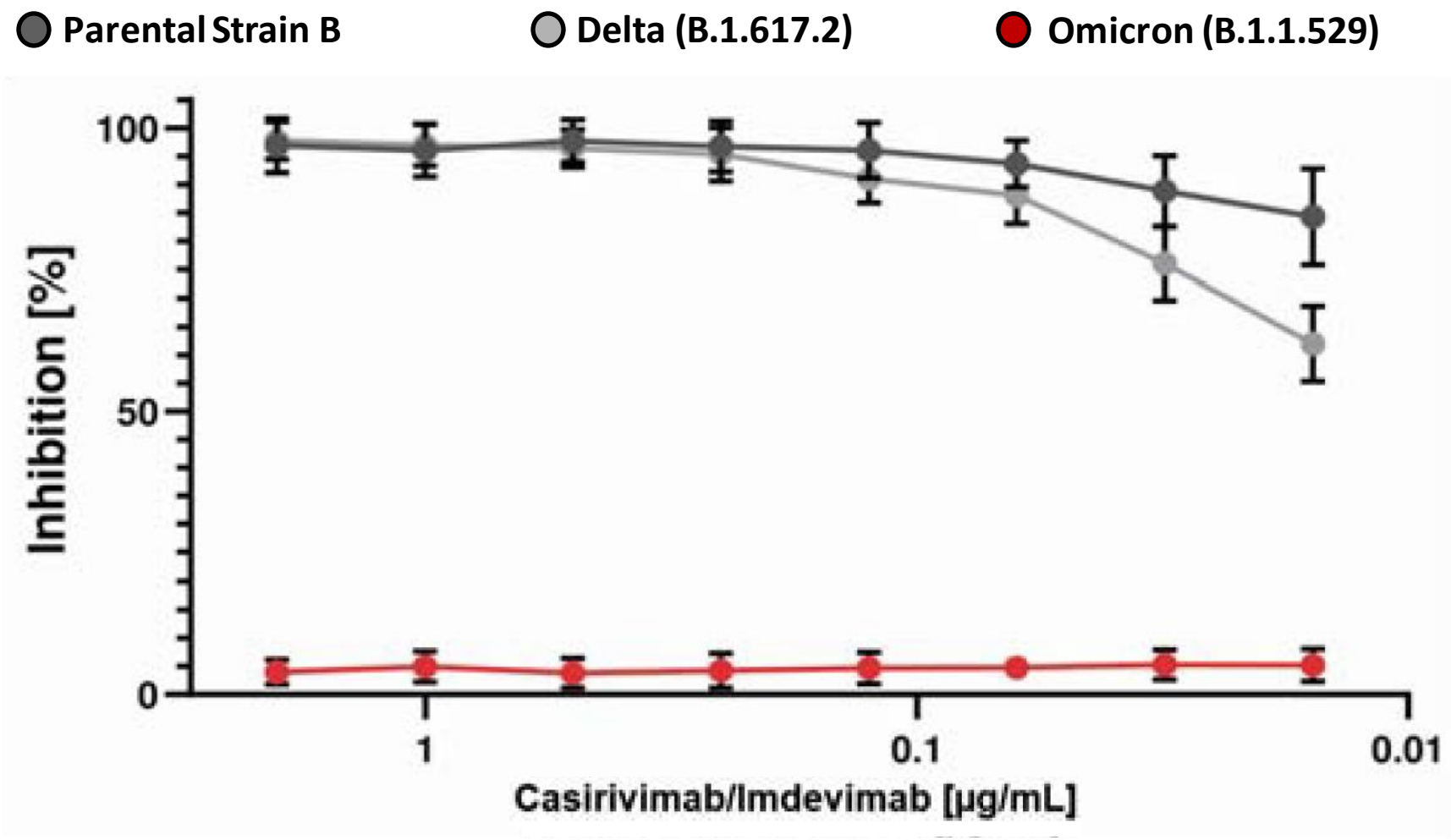
26 vaccinees with breakthrough infections compared to 26 non-breakthrough vaccinees. Of isolates available for sequencing: 10 Delta, 9 non-Delta.





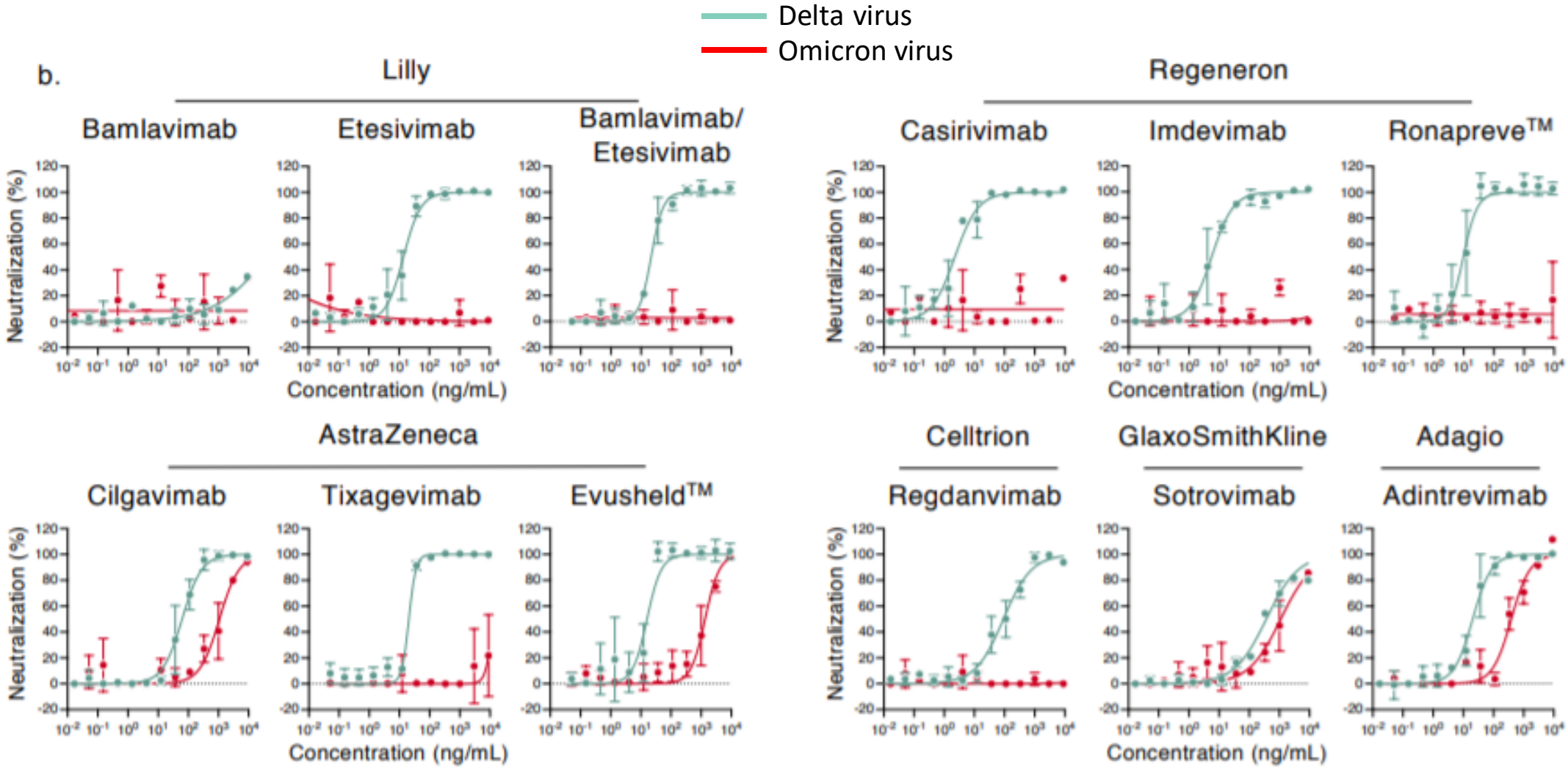
Source: Bates 2021, JAMA; : December 16, 2021. doi:10.1001/jama.2021.22898

Neutralization efficacy of monoclonal antibodies imdevimab and casirivimab against authentic SARS-CoV-2



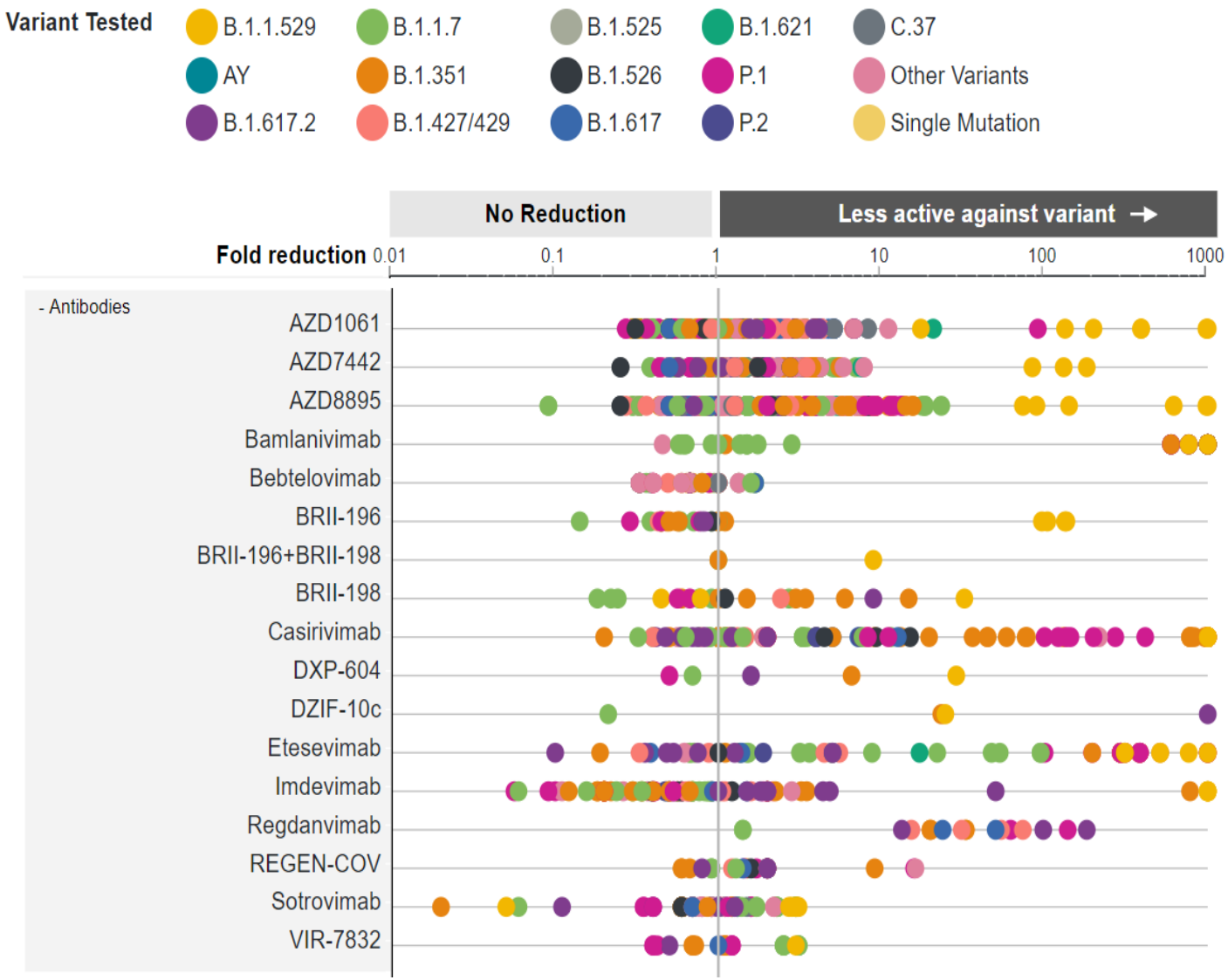
Source: Wilhelm 2021, medRxiv; https://www.medrxiv.org/content/10.1101/2021.12.07.21267432v4.full.pdf

Virus neutralization with additional monoclonals



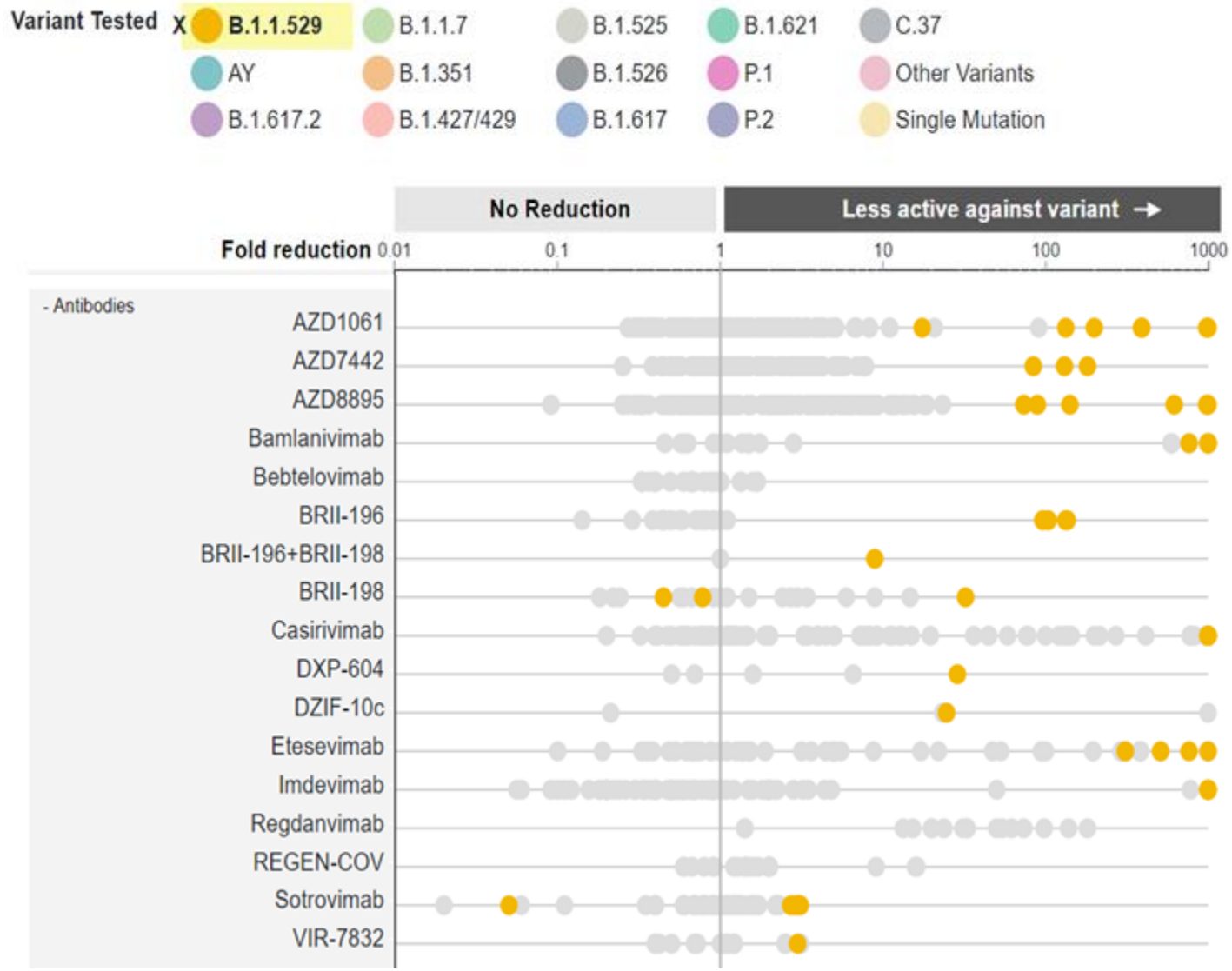
Source: Planas et al. Considerable escape of SARS-CoV-2 variant Omicron to antibody neutralization. bioRxiv (December 15, 2021)

Resistance to monoclonal antibodies



https://opendata.ncats.nih.gov/variant/activity

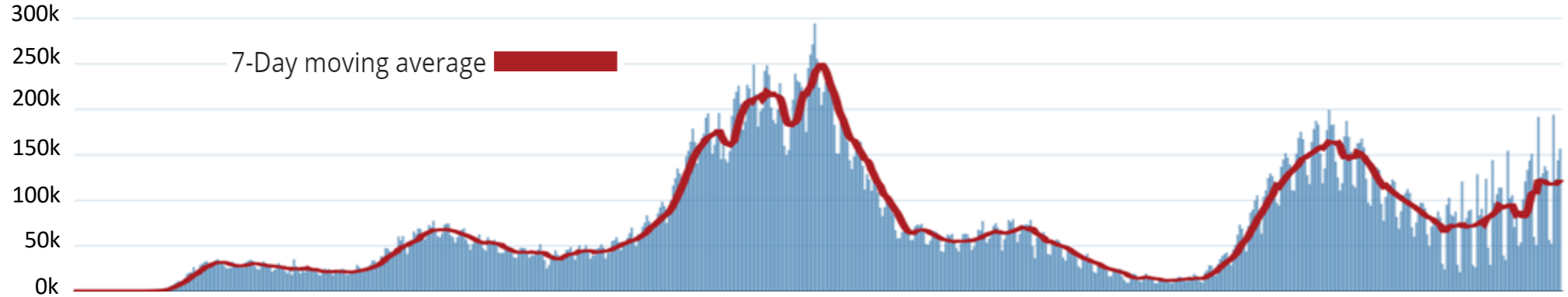
Resistance to monoclonal antibodies



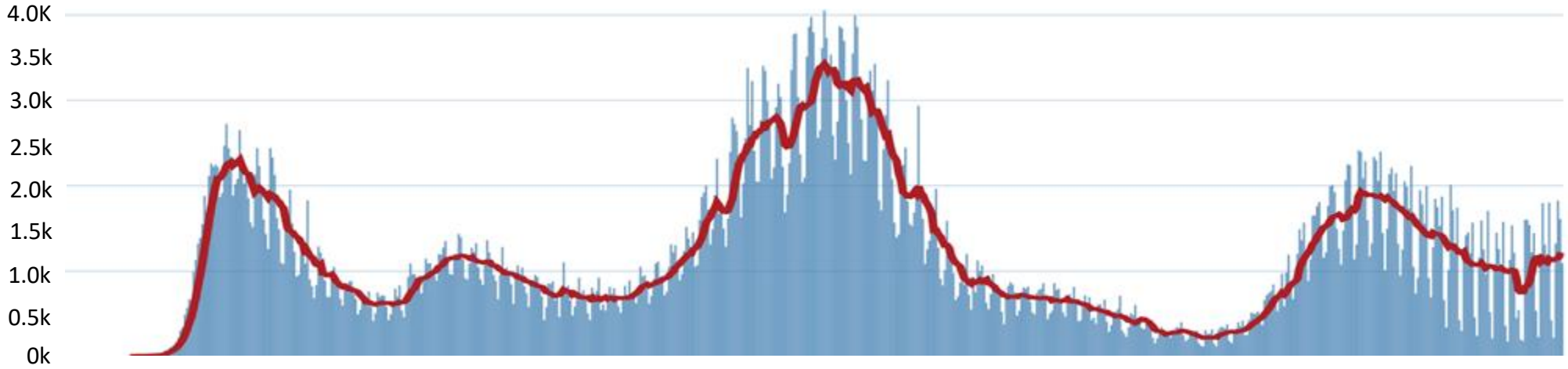
https://opendata.ncats.nih.gov/variant/activity

Daily Number of COVID-19 Cases and Deaths, U.S. January 23, 2021 - December 16, 2021 – CDC COVID Data Tracker

Cases



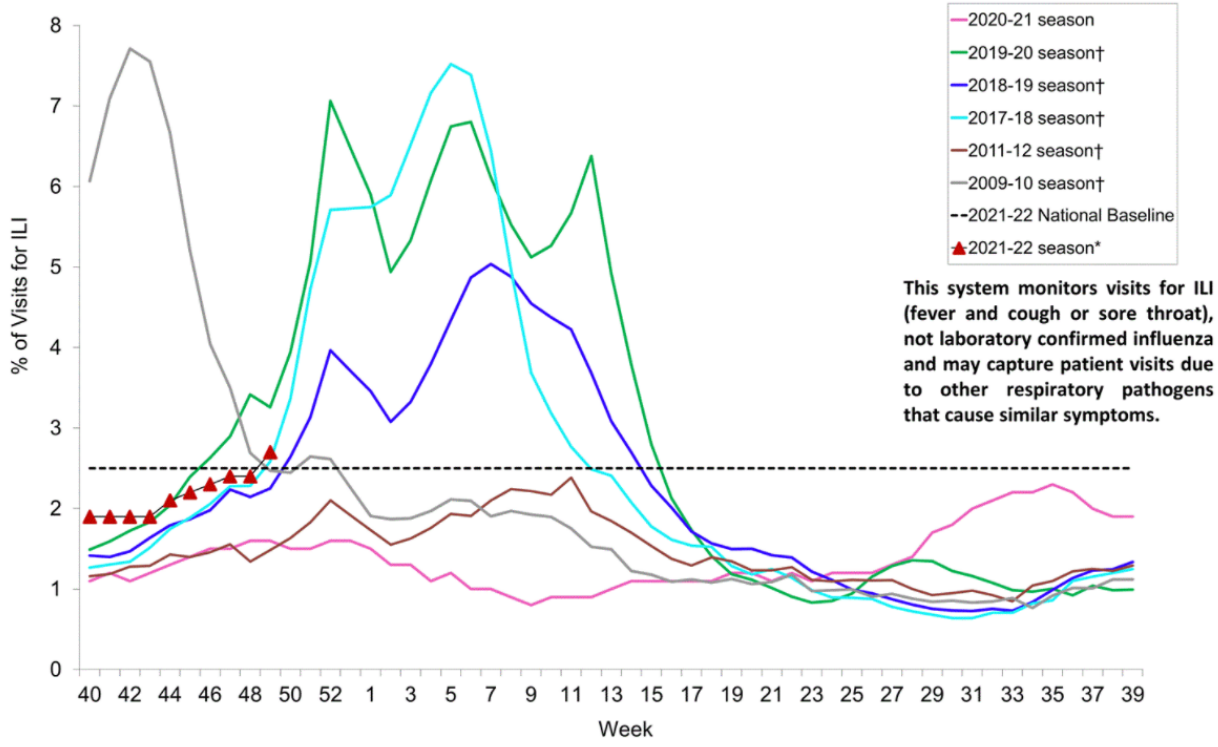
Deaths



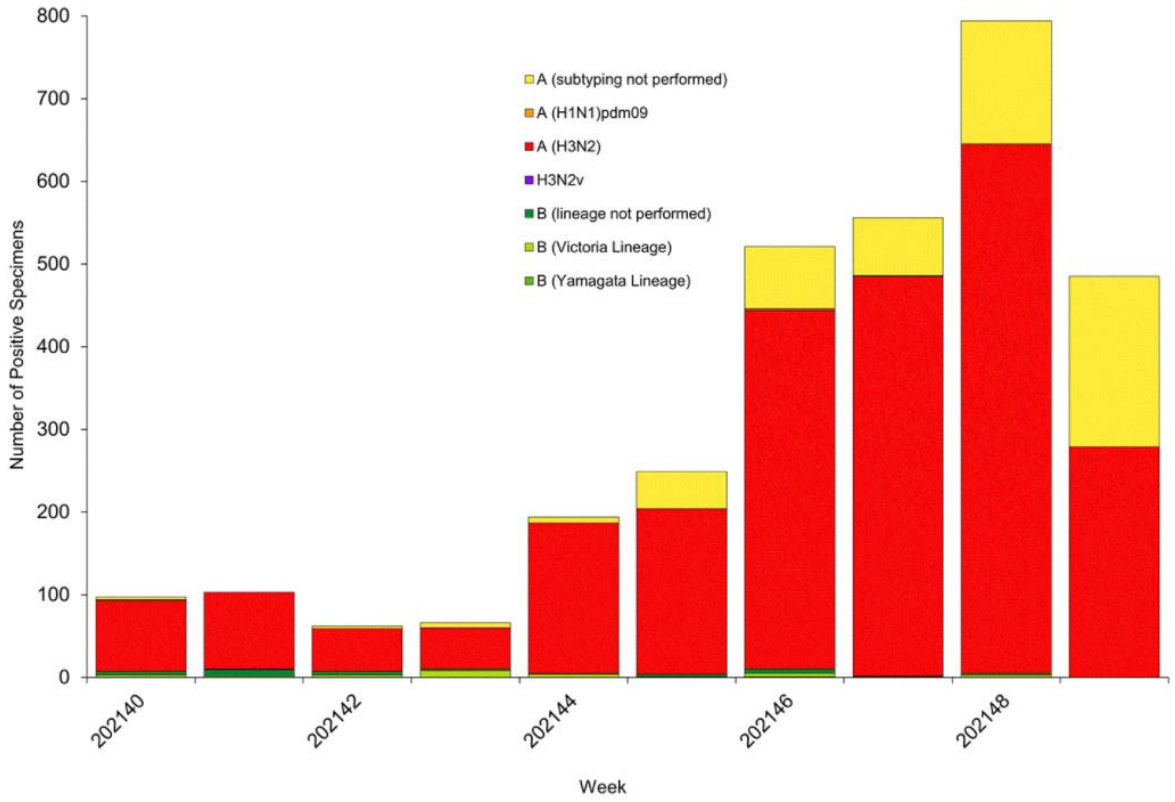
https://covid.cdc.gov/covid-data-tracker/#trends_dailytrends

Weekly U.S. Influenza Surveillance

Percentage of Outpatient Visits for Respiratory Illness Reported By The U.S. Outpatient Influenza-like Illness Surveillance Network (ILINet), Weekly National Summary, 2021-2022* and Selected Previous Seasons



Influenza Positive Tests Reported to CDC by U.S. Public Health Laboratories, National Summary, October 3, 2021 – December 11, 2021



https://www.cdc.gov/flu/weekly/index.htm

Four Key Questions

1. How transmissible is Omicron?
   - Highly infectious and moves quickly

2. How virulent is Omicron compared to other variants?
   - Not clearly less virulent, milder disease in persons immunized by vaccination and prior infection

3. How well do vaccines and prior infection protect against infection, transmission, clinical disease and death with Omicron?
   - Preliminary evidence suggest likely at least equally protective against severe illness and death from Omicron infection as from Delta infection but limited data for medically fragile, elderly and children

Four Key Questions

4. How do populations understand these dynamics, perceive risk and follow control measures, including public health and social measures.

https://www.who.int/publications/m/item/enhancing-readiness-for-omicron-(b.1.1.529)-technical-brief-and-priority-actions-for-member-states

Prevention strategies to slow US spread of Omicron variant

- Vaccination against COVID-19
  - Recommended for everyone aged ≥5 years
  - Boosters recommended for all persons aged ≥18 years
    - ≥2 months after initial Janssen vaccine, or
    - ≥6 months after completing primary series of Pfizer-BioNTech or Moderna
- Increased use of masking
- Improved ventilation
- Wider and more frequent testing, including self-testing
- Adherence to guidance on quarantine and isolation

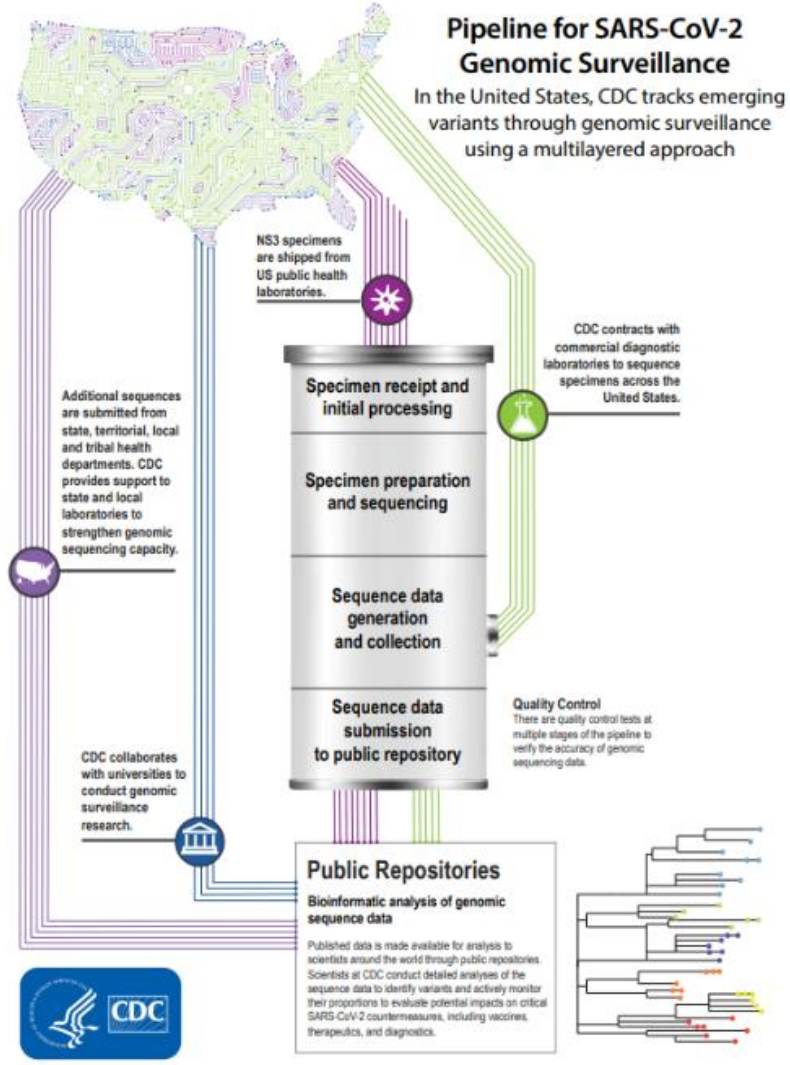
https://www.cdc.gov/mmwr/volumes/70/wr/mm7050e1.htm?s_cid=mm7050e1_w

Diagnostic Testing Updates

CDC National SARS-CoV-2 Genomic Surveillance System

CDC tracks and analyzes emerging SARS-CoV-2 variants using multiple data sources:

- The National SARS-CoV-2 Strain Surveillance (NS3) Program
- Contracts with commercial diagnostic laboratories
- Metadata tagging of sequences of randomly samples specimens



https://www.cdc.gov/coronavirus/2019-ncov/variants/cdc-role-surveillance.html

Omicron Expected to Impact Molecular Tests

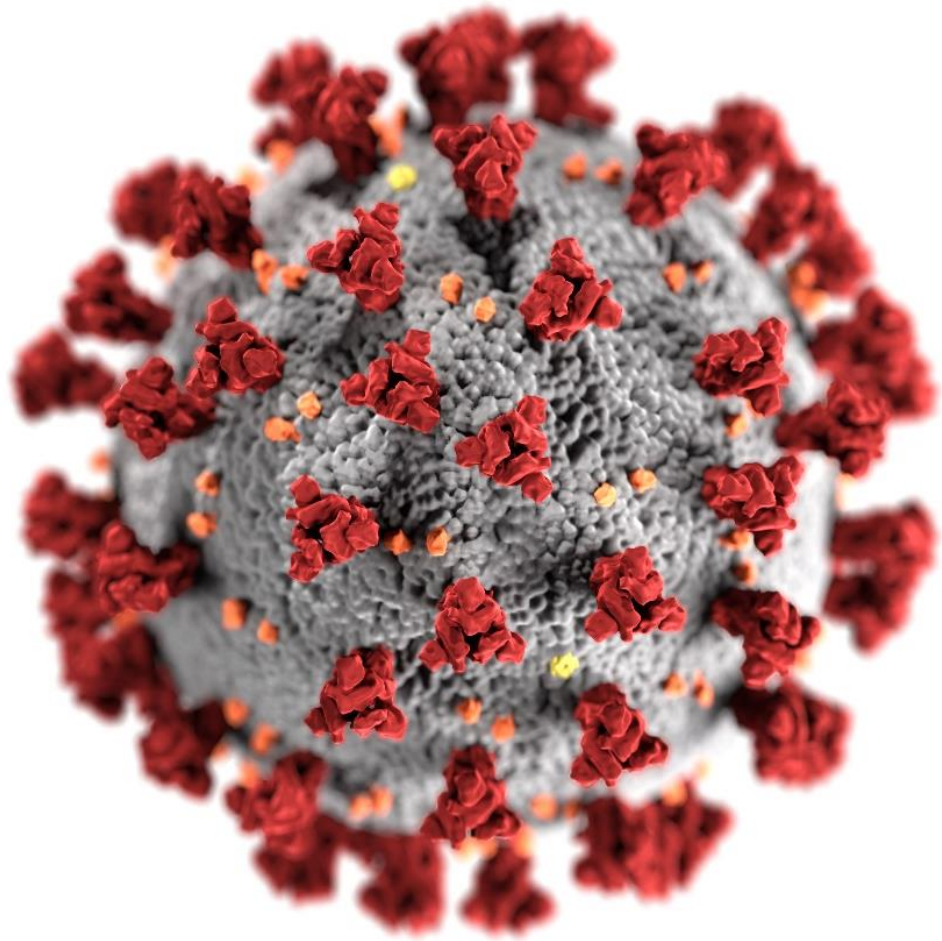
- Tests with Detection Patterns that May Be Associated with Omicron
  - To date, over FDA has identified over 25 EUA tests with a genetic target expected to have significantly reduced sensitivity due to Omicron mutations
    - **SGTF**: A specific deletion in the spike (S) gene (Δ69-70) results in an S-gene drop out, or S-gene target failure (SGTF)
    - **NGTF**: A nine-nucleotide deletion in the N-gene, spanning positions 28370-28362, results in an N-gene drop out, Since these tests are designed to detect multiple genetic targets, the overall test sensitivity should not be impacted.

https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/sars-cov-2-viral-mutations-impact-covid-19-tests#omicron

Omicron Expected to Impact Molecular Tests

- Tests Expected to Fail to Detect the SARS-CoV-2 Omicron Variant
  - Meridian Bioscience, Inc. Revogene SARS-CoV-2
  - Tide Laboratories DTPM COVID-19 RT-PCR Test
  - Applied DNA Science Linea COVID-19 Assay Kit

https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/sars-cov-2-viral-mutations-impact-covid-19-tests#omicron



For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

Re-Infection and Omicron

Juliet Pulliam, PhD

SARS-CoV-2 reinfection trends in South Africa during the emergence of Omicron

Juliet R.C. Pulliam, Cari van Schalkwyk, Nevashan Govender, Anne von Gottberg, Cheryl Cohen, Michelle J. Groome, Jonathan Dushoff, Koleka Mlisana, and Harry Moultrie

2021-12-18, CDC/IDSA COVID-19 Clinician Call

SACEMA
DSI-NRF Centre of Excellence in Epidemiological Modelling and Analysis

SOUTH AFRICAN COVID-19 MODELLING CONSORTIUM

NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES
Division of the National Health Laboratory Service

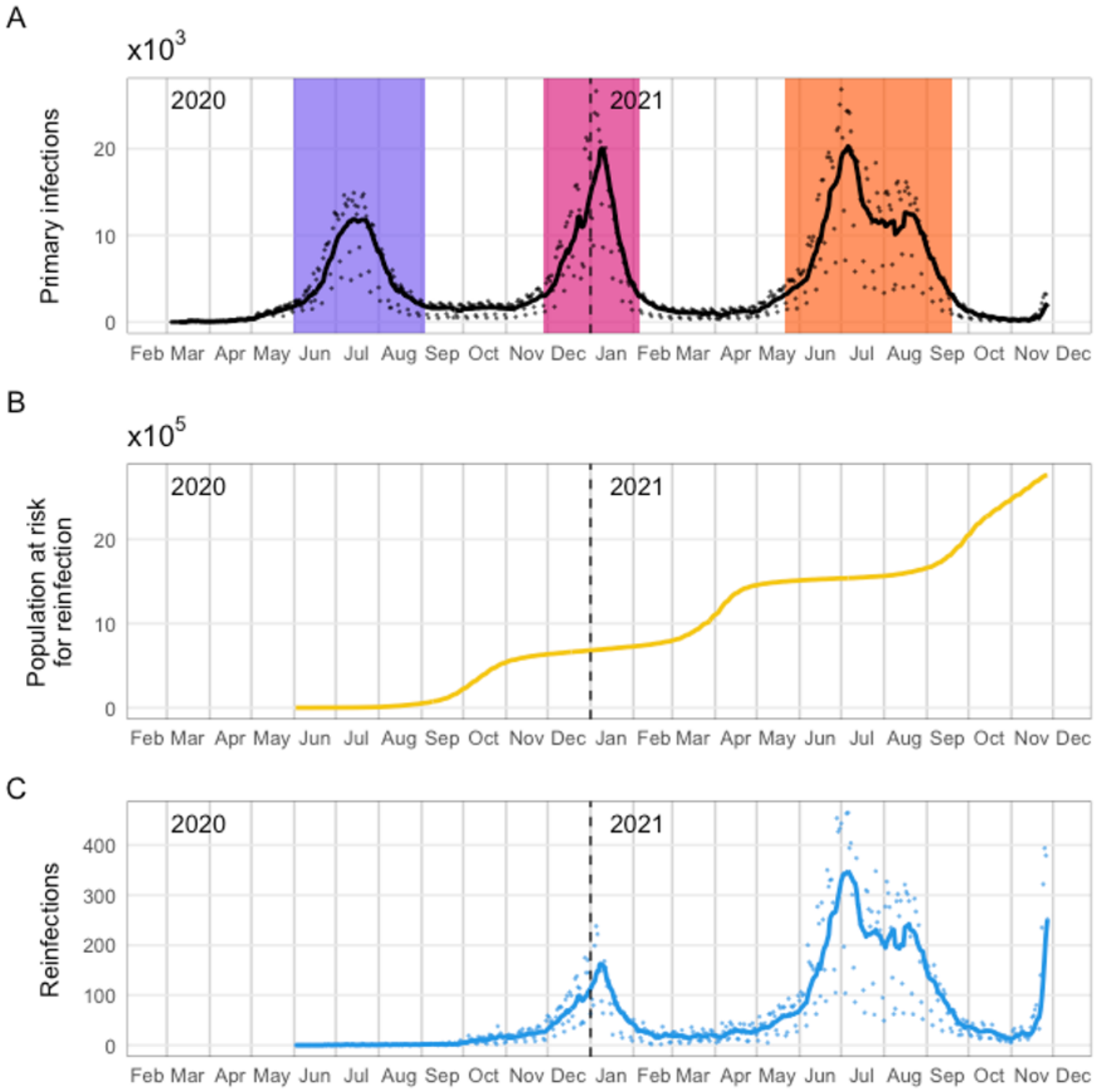
Overview

- Background:
  - Since January 2021, we have conducted regular monitoring of reinfections in routine surveillance data to detect potential changes in reinfection risk, as may occur with the emergence of new variants
- Two approaches give similar results:
  - We find no evidence that reinfection risk was higher as a result of the emergence of Beta or Delta
  - Reinfection risk has increased substantially, with timing consistent with the emergence of Omicron
- Caveats:
  - Reinfections are not confirmed by sequencing
  - Wave is used as a proxy of variant
  - Changes in testing practice and health-seeking behavior have not been accounted for
  - This analysis does not provide information on the risk of breakthrough infection in vaccinated individuals

Data

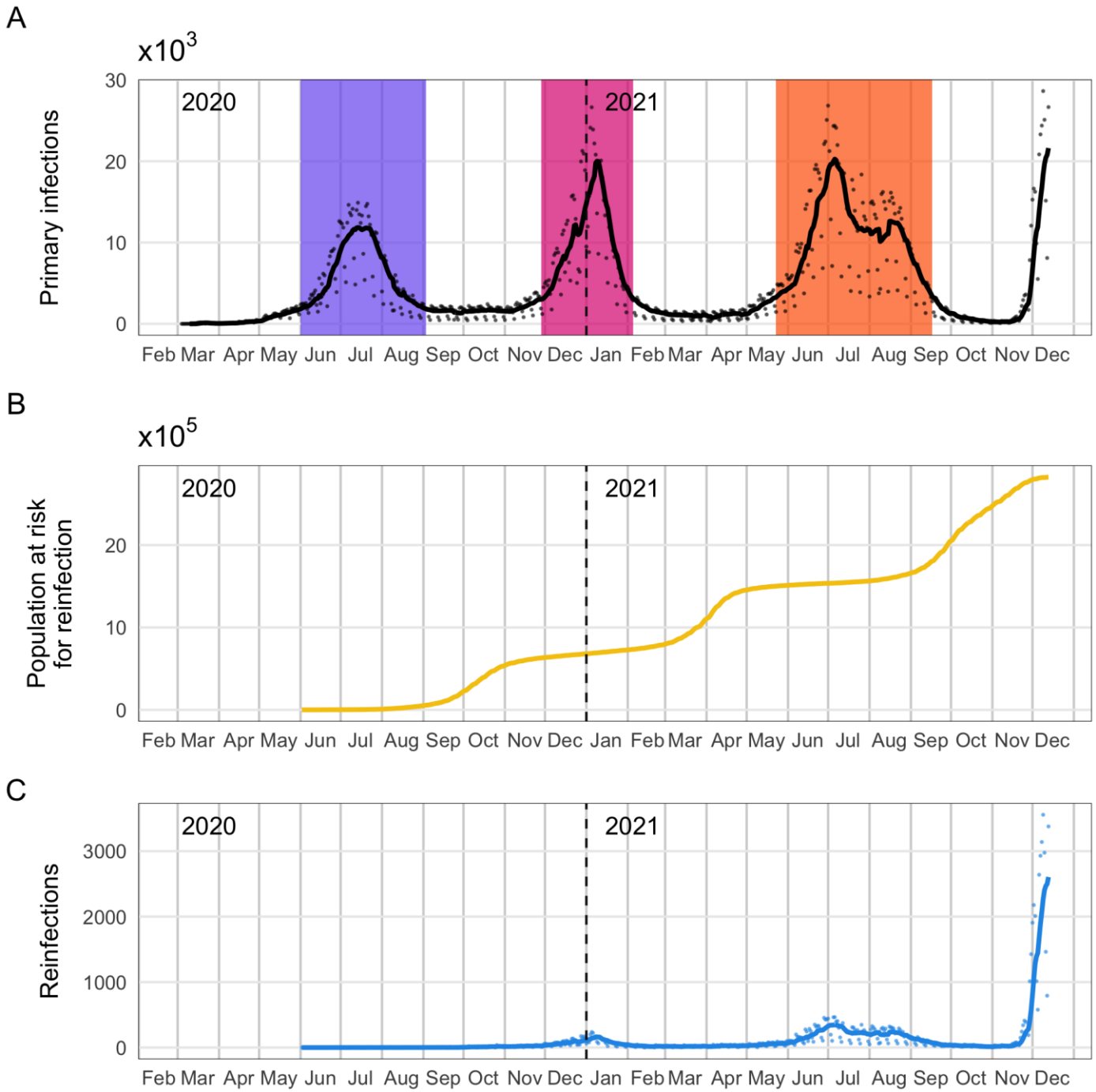
- Incidence of first infections is calculated from the NMC-SS case line list
  - Does not include incident reinfections.
- Incidence of reinfections is calculated from the line list of positive tests
  - Repeated case IDs in the line list are identified and the time between consecutive positive tests is calculated.
  - If the time between sequential positive tests is at least 90 days, the more recent positive test is considered to indicate a suspected reinfection.
- The total incidence is calculated as the sum of first infections and reinfections
- All incidence time series are calculated by specimen receipt date
  - Some dates are adjusted to account for inaccuracies in specimen receipt date for late-arriving test results (mainly associated with delayed reporting of antigen tests)

Data



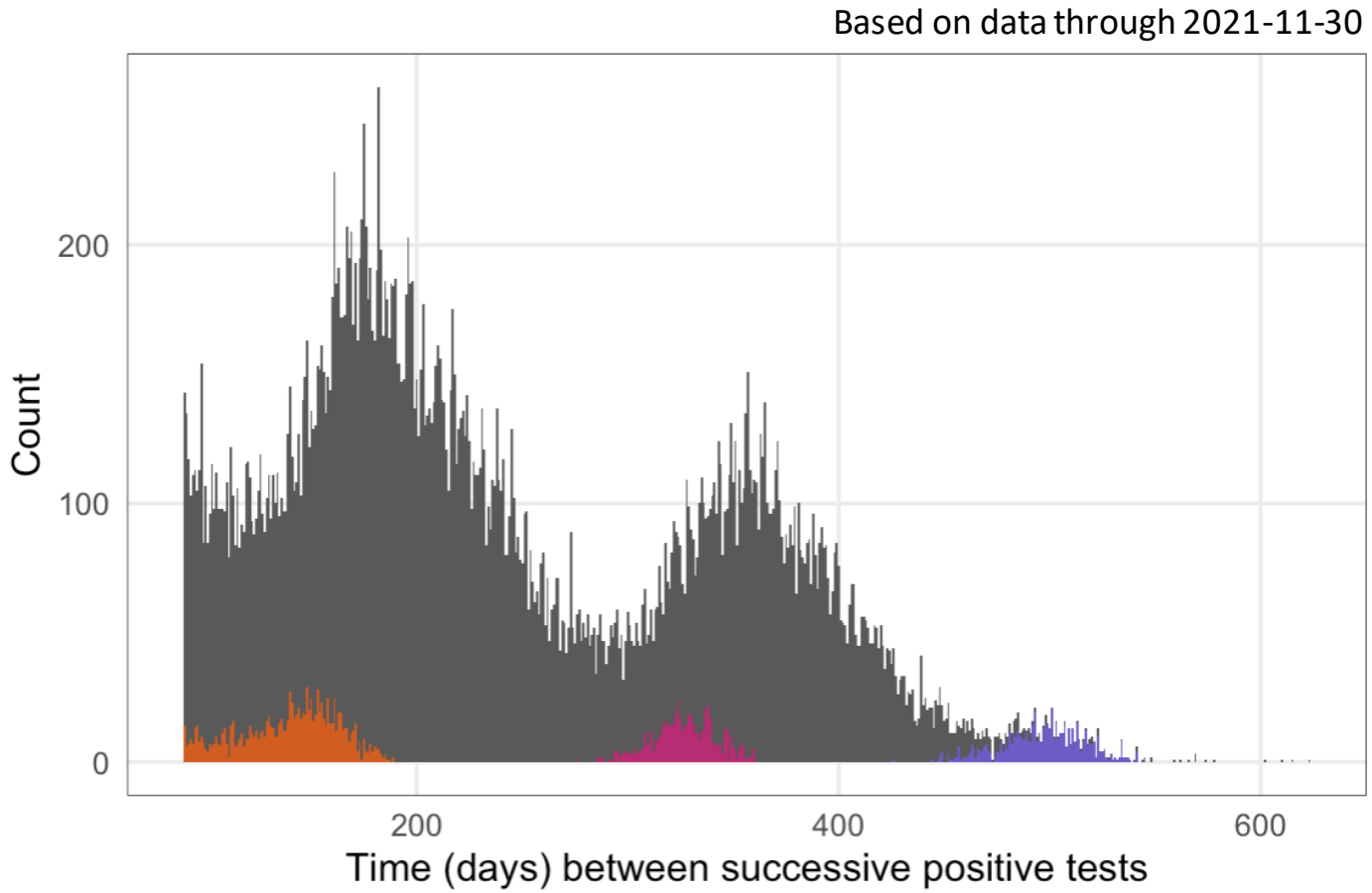
Based on data through 2021-11-27

Data



Based on data through 2021-12-13

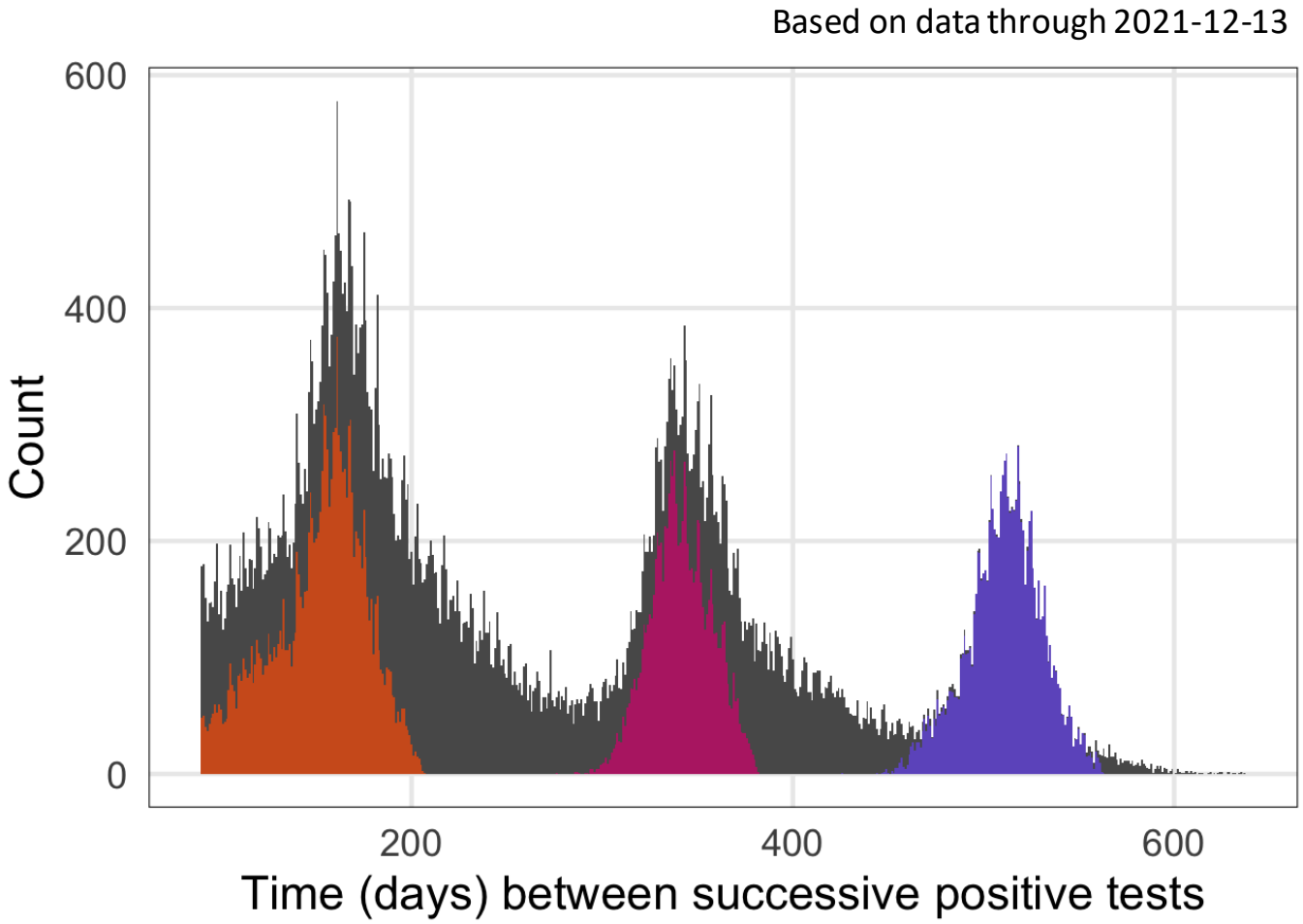
Data



- 35,670 individuals had suspected reinfections
  - 1.3% of the 2,796,982 individuals with first positive >=90 days prior to database closure on 2021-11-27
- In a 10% random sample of suspected reinfections occurring on or before 2021-01-20 (n=585):
  - Manual review of laboratory and NMC-SS records including fields not used for linkages (address, cell-phone numbers, facility and healthcare providers)
  - 562 (96%) verified as the same individual
  - 23 (4%) judged not a match or insufficient evidence

Note: Reinfections are defined as occurring at least 90 days after the previous positive test

Data



- 66,947 individuals had suspected reinfections
  - 2.3% of the 2,892,194 individuals with first positive >=90 days prior to database closure on 2021-12-13
- 33,671 individuals had suspected second infections since 2021-11-01
  - 49.7% of second infections occurred since 2021-11-01

Note: Reinfections are defined as occurring at least 90 days after the previous positive test

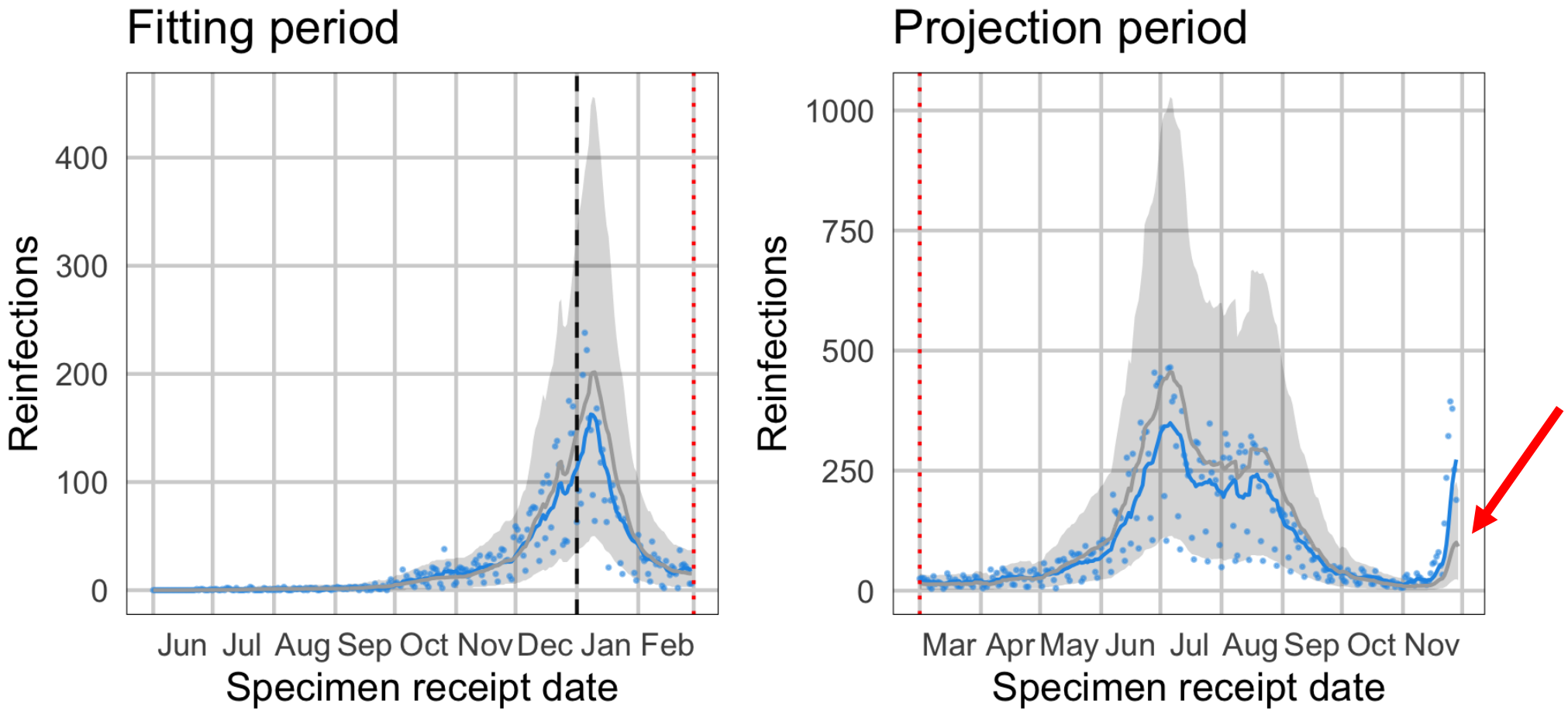
Methods: Approach 1

Catalytic model assuming a constant reinfection hazard coefficient

- Assume reinfection risk is proportional to incidence of detected cases
- Estimate a constant reinfection hazard coefficient (‘null model’)
  - Fit to data from prior to March 2021
- Project the expected number of reinfections under the null model that reinfection risk has not changed
- Compare observed reinfections to projection to assess deviation from the null hypothesis

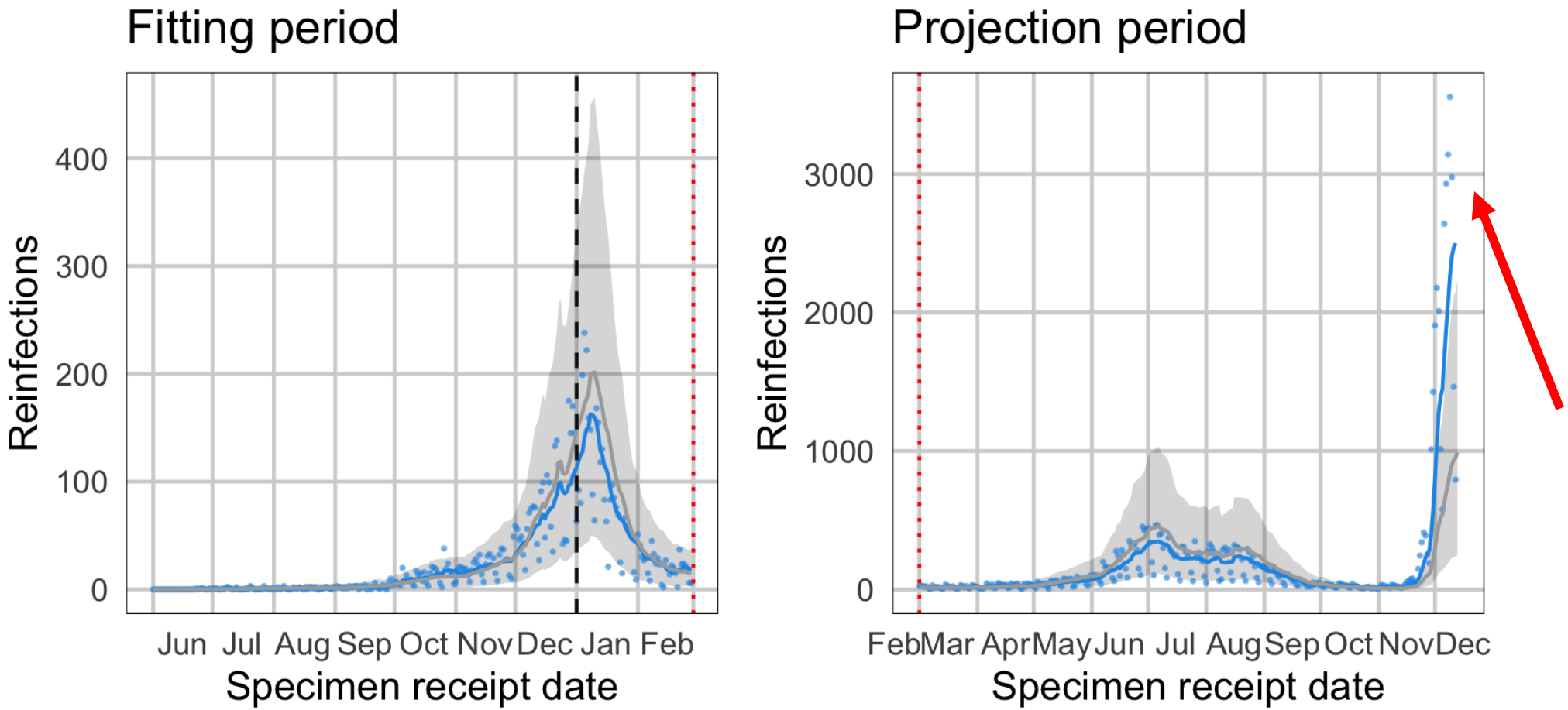
Detailed methods at:
https://www.medrxiv.org/content/10.1101/2021.11.11.21266068

Approach 1 (National)



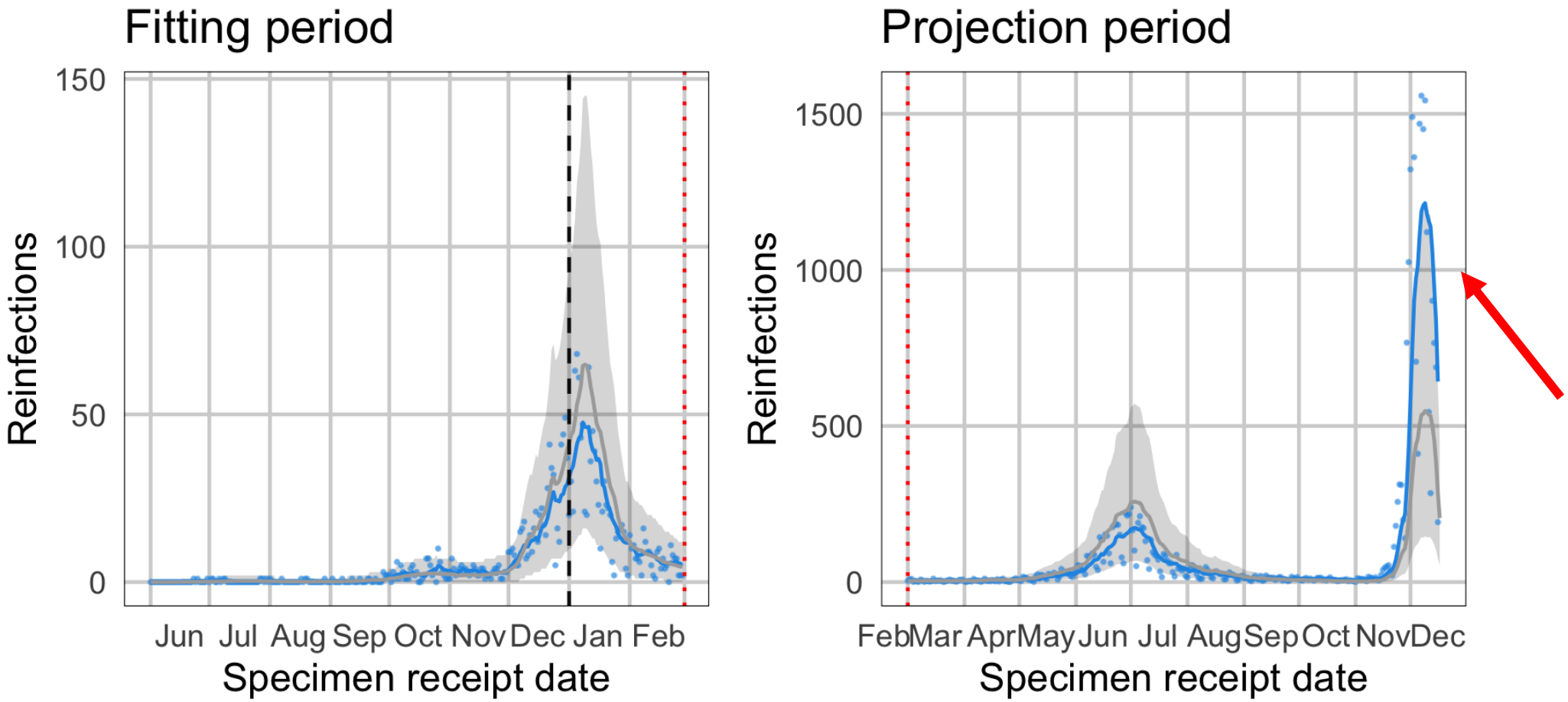
Based on data through 2021-11-27

Approach 1 (National)



Based on data through 2021-12-13

Approach 1 (Gauteng)



Based on data through 2021-12-13

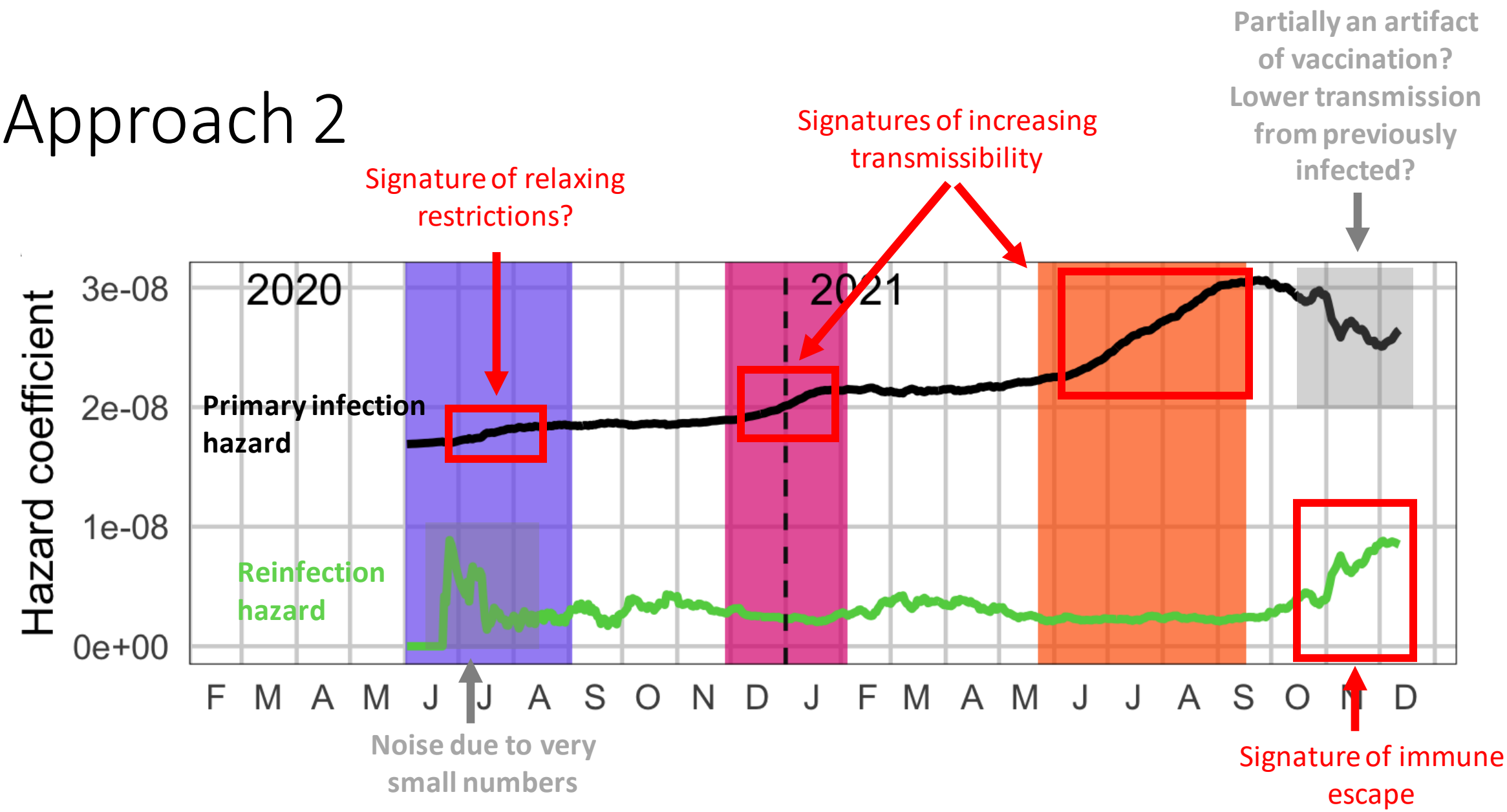
Methods: Approach 2

Empirical estimation of time-varying infection and reinfection hazards

- Estimate time-varying empirical hazards of infection and reinfection
  - Assume risk is proportional to incidence of detected cases (for both primary infections and reinfections)
  - Account for probability of detection
- Compare the temporal trend in infection and reinfection hazards

Detailed methods at:
https://www.medrxiv.org/content/10.1101/2021.11.11.21266068

Approach 2

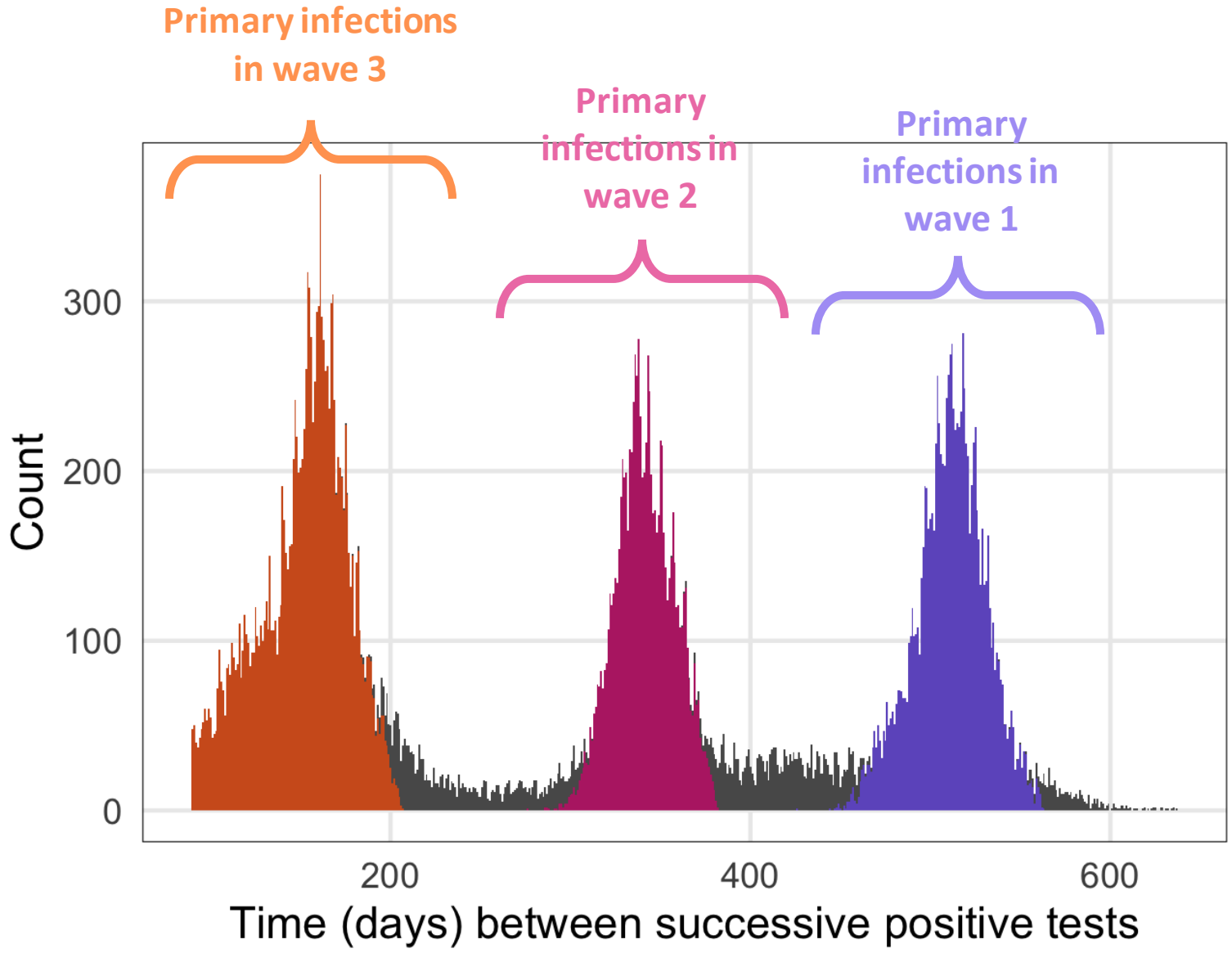


Note: Exact estimates are sensitive to assumptions regarding the detection probabilities, but conclusions are robust.

Based on data through 2021-12-13

Recent reinfections (detected since 1 Nov. 2021)

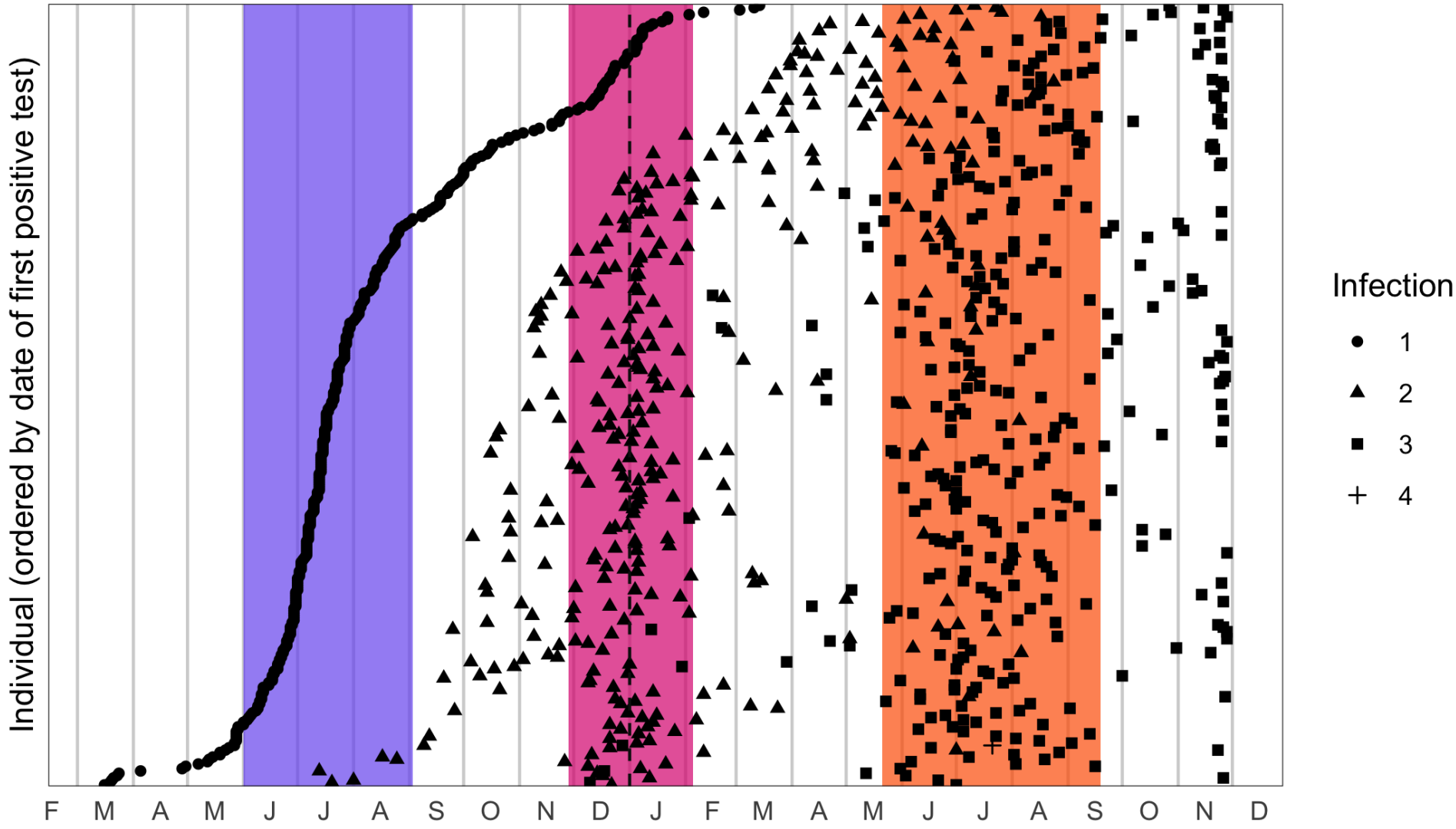
- Recent reinfections appear concentrated in individuals whose primary infection was during wave 3
- Increase in reinfections among individuals infected during waves 1 and 2 since early-to-mid November



Based on data through 2021-12-13

Individuals with multiple reinfections

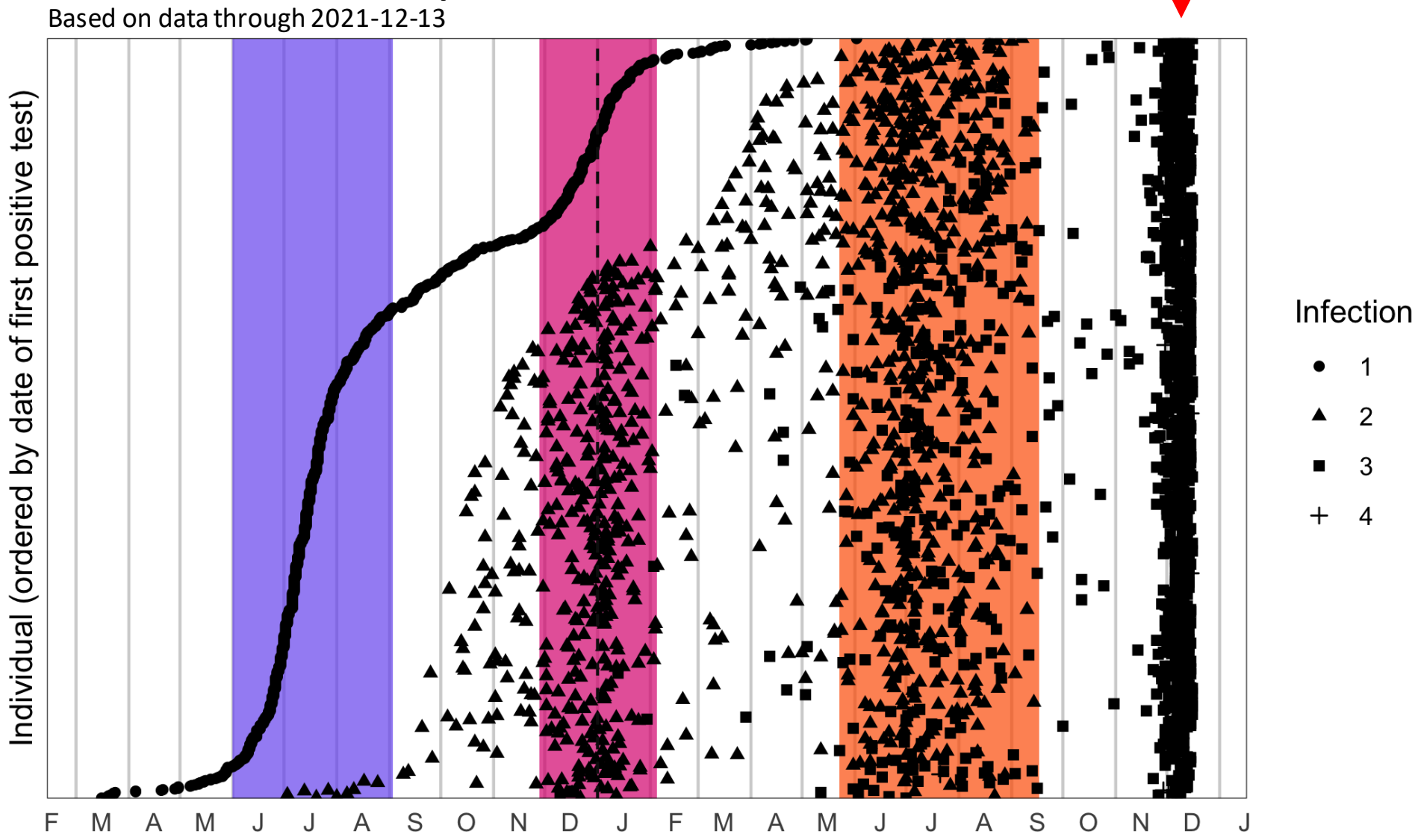
- Emerging signal of increase in individuals who have already had 2 or more infections



Based on data through 2021-11-27

Individuals with multiple reinfections

- Strong signal of increase in individuals who have already had 2 or more infections
- 659 of 945 (69.7%) of suspected 3rd infections since 1 Nov

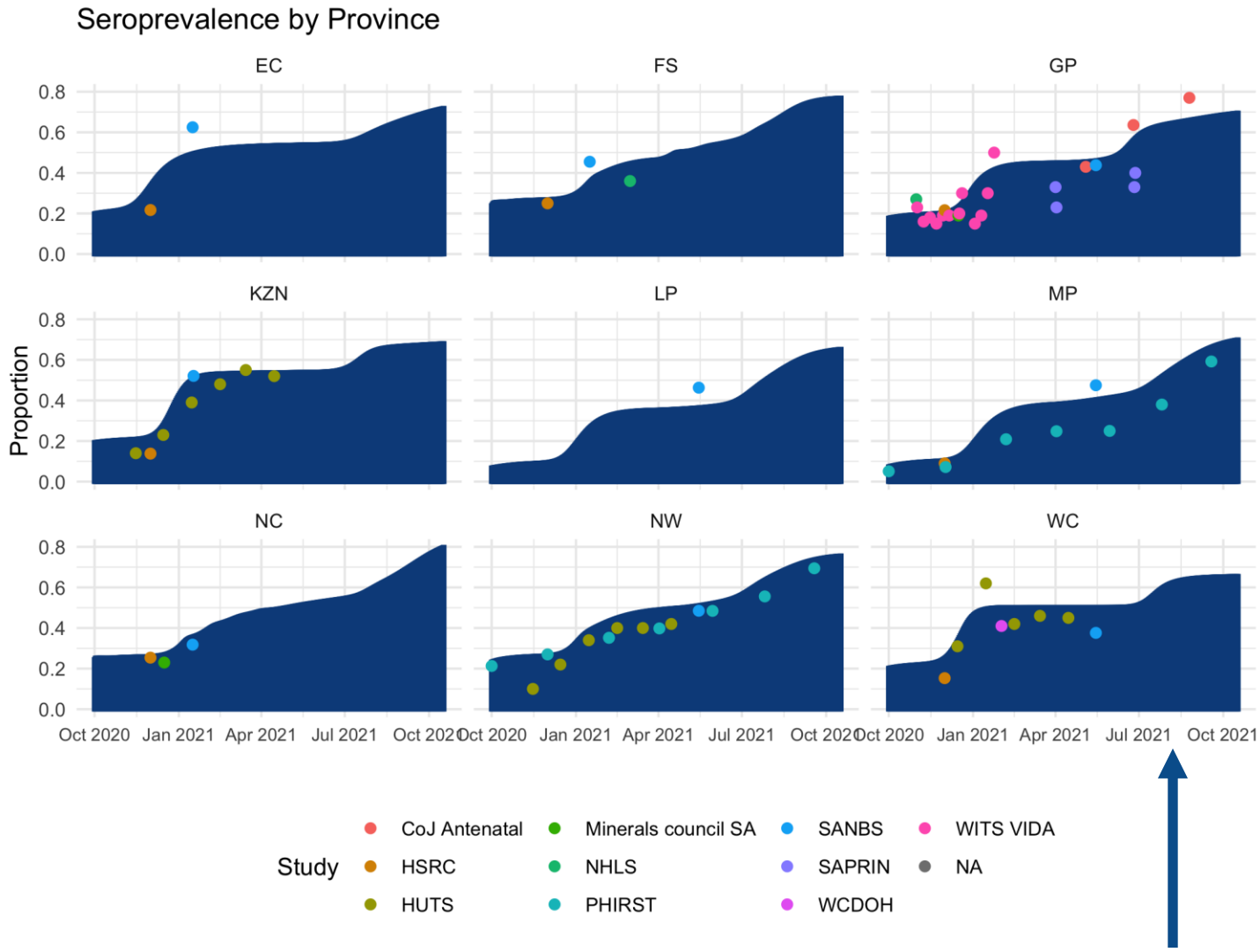


Key messages

- Reinfection risk has increased markedly, with timing consistent with the emergence of the Omicron variant
- Reinfections are occurring in:
  - people whose primary infection occurred in all 3 prior waves
  - people who had already experienced 2 infections prior to the emergence of Omicron
- Preliminary data suggest prior infection and vaccination may reduce severity of a second infection
  - No robust data yet on severity of Omicron in unvaccinated people without a prior infection
  - Given low detection rates in South Africa, best data likely to come from elsewhere

Thinking about context

- South Africa likely has high seroprevalence compared to much of the world
  - Higher selective pressure for immune escape
  - Stronger signal of increased reinfection risk?
- This also means that early findings re: severity from SA may not be applicable elsewhere



Calibrated seroprevalence based on National COVID Epi Model v6.0

Acknowledgements

2021 MMED Reinfections Project Group

Network for Genomic Surveillance - South Africa (NGS-SA) led by Prof Tulio de Oliveira for its role in the discovery of the Omicron variant

Carl A.B. Pearson and colleagues in the **SARS-CoV-2 Variants Research Consortium in South Africa** for useful discussions

NICD Epidemiology team: Andronica Moipone Shonhiwa, Genevie Ntshoe, Joy Ebonwu, Lactatia Motsuku, Liliwe Shuping, Mazvita Muchengeti, Jackie Kleynhans, Gillian Hunt, Victor Odhiambo Olago, Husna Ismail, Nevashan Govender, Ann Mathews, Vivien Essel, Veerle Msimang, Tendesayi Kufa-Chakezha, Nkengafac Villyen Motaze, Natalie Mayet, Tebogo Mmaborwa Matjokotja, Mzimasi Neti, Tracy Arendse, Teresa Lamola, Itumeleng Matiea, Darren Muganhiri, Babongile Ndlovu, Khuliso Ravhuhali, Emelda Ramutshila, Salaminah Mhlanga, Akhona Mzoneli, Nimesh Naran, Trisha Whitbread, Mpho Moeti, Chidozie Iwu, Eva Mathatha, Fhatuwani Gavhi, Masingita Makamu, Matimba Makhubele, Simbulele Mdleleni, Bracha Chiger, Jackie Kleynhans

NICD Information Technology team: Tsumbedzo Mukange, Trevor Bell, Lincoln Darwin, Fazil McKenna, Ndivhuwo Munava, Muzammil Raza Bano, Themba Ngobeni

Funders:

221003/Z/20/Z

Evusheld for Pre-Exposure Prophylaxis in Adults & Children: Update and Clinical Considerations for Use

Cameron R. Wolfe, MBBS (Hons), MPH, FIDSA

Monoclonal Antibody Therapy Updates

‘Evusheld’ for *Pre*-Exposure Prophylaxis in Adults /Children
Update and Clinical Considerations for Use

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MBBS(Hons), MPH, FIDSA
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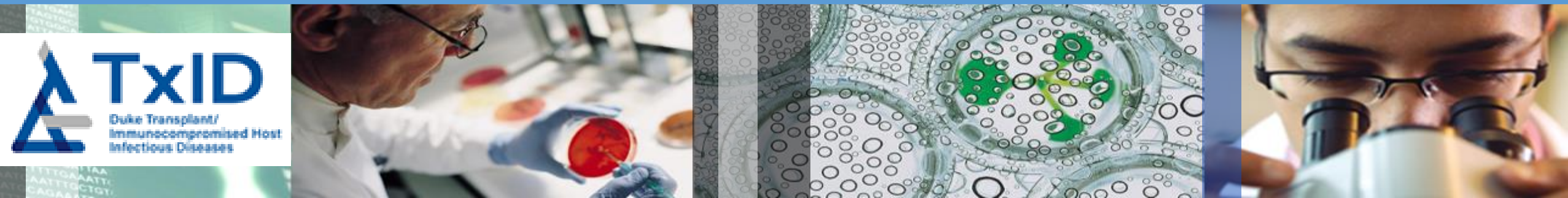
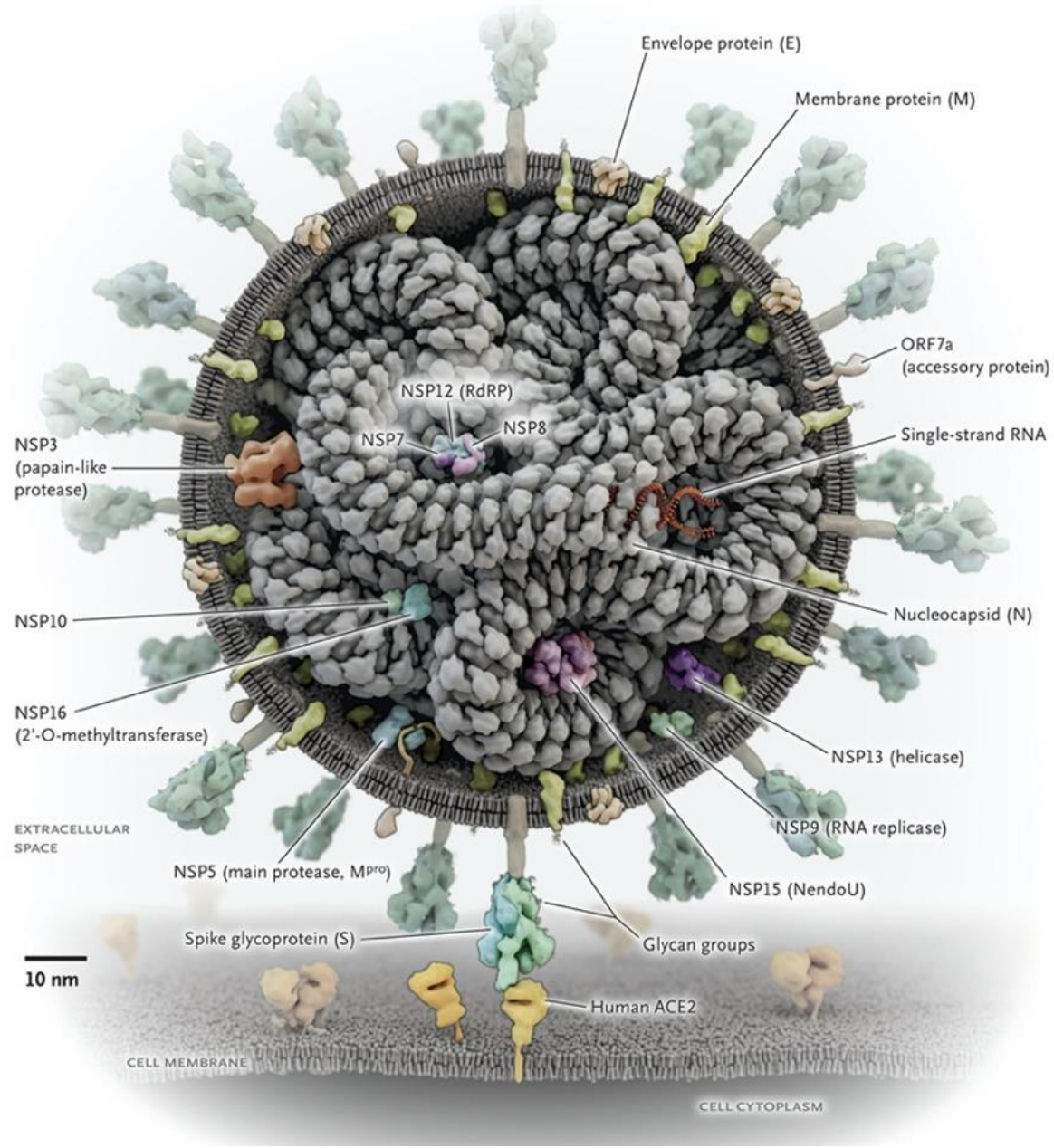


DISCLOSURES:

- DSMB:
  - Janssen – RSV Vaccines
  - Biogen – Covid, SLE therapeutics
  - Atea – Covid therapeutics
- Advisory Boards:
  - MedinCell – Antibiotics
  - Enzychem – Covid therapeutics
  - Adagio – Covid therapeutics
  - Regeneron – Covid therapeutics



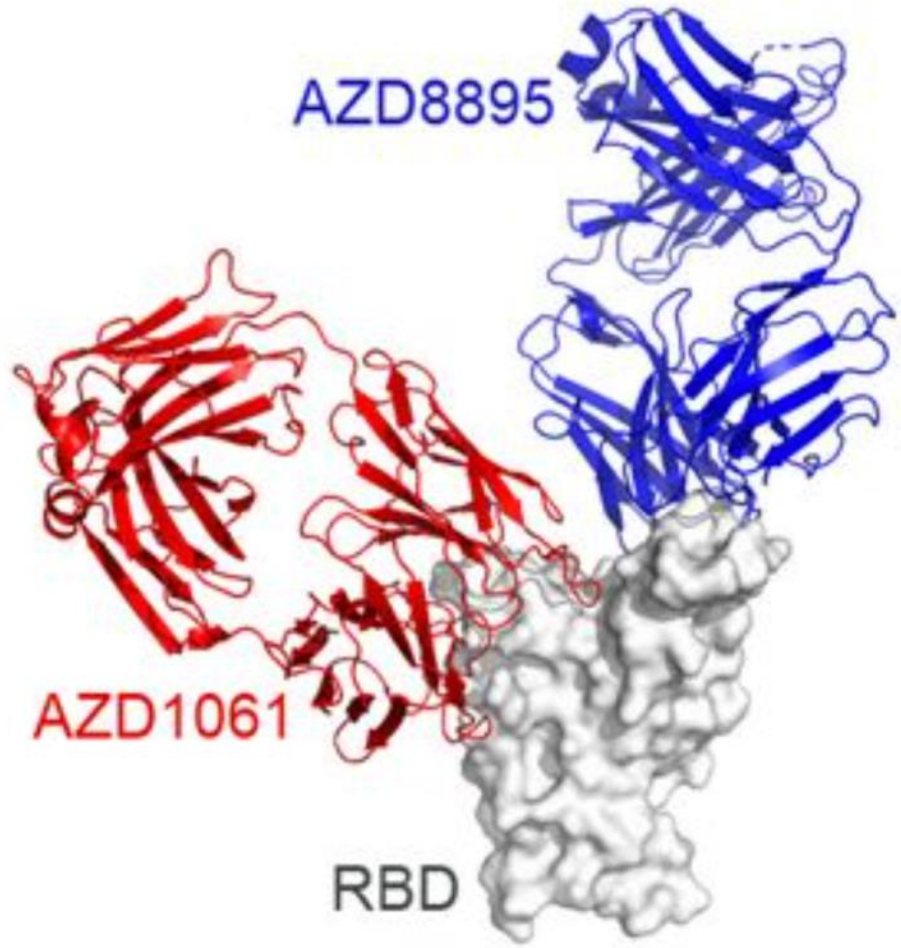
Tixagevimab / Cilgavimab:

- AstraZeneca – “Evusheld”

- AZD8895 and AZD1061 simultaneously bind to distinct, non-overlapping epitopes on the spike protein receptor binding domain (RBD) and sterically block RBD binding to ACE2.

- Modified Fc Ig tail, so half life extended to beyond 6m

- Reduced Fc receptor and complement C1q binding, to minimize risk of antibody mediated disease enhancement.



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Duke Transplant/
Immunocompromised Host
Infectious Diseases

Trials for EUA:

- PROVENT Trial:
  - >18yrs, 2:1 randomization, 5197 patients (3460 active arm)
  - 87 sites, US, UK, Europe
  - At 'high-risk' for COVID19
  - Endpoints: Symptomatic COVID+ Infection ; Hospitalizations / Mortality
  - Demographics:
    - Mean age 57yrs, 36% HTn, 14% DM, 8% CVD

Incidence of Symptomatic COVID-19 in Adults (PROVENT)

	N*	Number of events, n (%)	Relative Risk Reduction, % (95% CI)
EVUSHELD†	3,441	8 (0.2%)	77% (46, 90)
Placebo	1,731	17 (1.0%)	

N = number of subjects in analysis; CI = Confidence Interval
* subjects were censored after receiving the vaccine or being unblinded to consider the vaccine, whichever occurred earlier
† EVUSHELD dose (150 mg tixagevimab and 150 mg cilgavimab)

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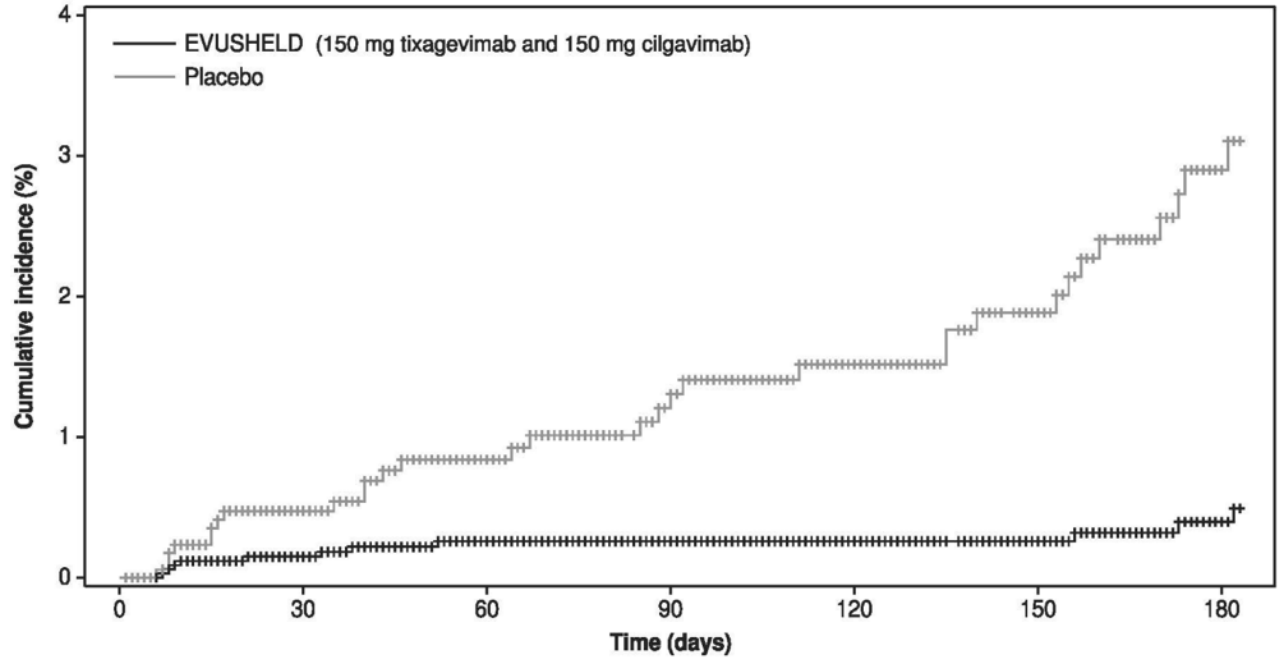
Trials for EUA:

Figure 1 Kaplan Meier: Cumulative Incidence of Symptomatic COVID-19* (PROVENT)



Number of participants at risk

EVUSHELD	3441	2957	2393	2054	1815	1667	1044
Placebo	1731	1483	1177	991	856	774	472

* Subjects who do not experience a primary endpoint event (and had not discontinued) are censored at Day 183. Subjects who were unblinded/vaccinated prior to an event are also censored at the earlier time of unblinding/vaccination.

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Trials for EUA:

Adverse Events (All Grades) Regardless of Causality Occurring in at Least 3% of Subjects Receiving EVUSHELD or Placebo in Primary Safety Analysis

	EVUSHELD N= 3,461	Placebo N= 1,736
Headache	6%	5%
Fatigue	4%	3%
Cough	3%	3%

Cardiac SAEs Regardless of Causality in PROVENT with Onset Prior to Day 183 Using the Median 6-Month Data Cut-off Date

	EVUSHELD N= 3,461	Placebo N= 1,736
Subjects with any cardiac SAE*	22 (0.6%)	3 (0.2%)
SAEs related to coronary artery disease or myocardial ischemia†	10 (0.3%)	2 (0.1%)
Myocardial infarctions‡	8 (0.2%)	1 (0.1%)
SAEs related to cardiac failure§α	6 (0.2%)	1 (0.1%)
SAEs related to an arrhythmia¶	4 (0.1%)	1 (0.1%)
Other (cardiomegaly, cardiomyopathy, and cardio-respiratory arrest)	3 (0.1%)	0

- Likely no issue in renal failure, cirrhosis, older adults
- No data for pregnancy / lactation
- For 12-18yrs: “comparable serum exposures of tixagevimab/ cilgavimab expected, if > 40kg”

Available at: www.fda.gov/media/154701/download

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Trials for EUA:

Storm Chaser

- 1121 exposed adults, 2:1 randomized vs placebo
- 33% (95%CI -26, 65) reduction in symptomatic covid
- No cardiac signal seen in this cohort

Table 1: STORM CHASER analyses

Baseline subgroup	Onset of case post dose	Number of cases / number of participants		Relative risk reduction (95% confidence interval)
		AZD7442 (300mg IM)	Placebo	
All participants (Primary analysis)	All cases	23 / 749	17 / 372	33% reduction[a] (-26 to 65)
PCR-negative[b] (Pre-planned subgroup analysis)	All cases	6 / 715	11 / 358	73% reduction (27 to 90)
PCR-negative[b] (Post hoc subgroup analysis)	≤7 days	5 / 715	5 / 358	51% reduction (-71 to 86)
	>7 days	1 / 710	6 / 353	92% reduction (32 to 99)

a: Not statistically significant.
b: Includes 974 participants (15 cases) confirmed PCR negative at baseline and 99 participants (2 cases) with PCR status missing at baseline.
48 participants were confirmed PCR positive at baseline with 23 cases (AZD7442: 17/34; placebo: 6/14).

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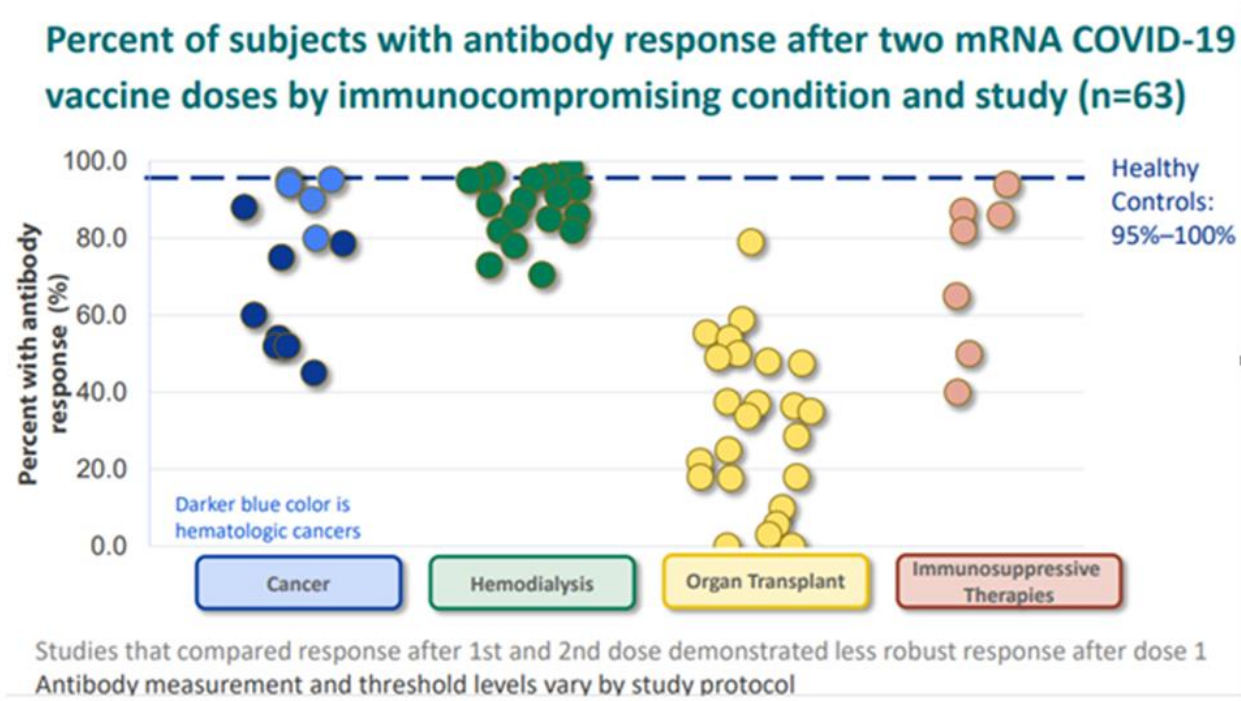
So who is *really* “high risk”?

High-risk for severe disease:

- Elderly
- Obese
- Diabetic
- Immunosuppressed
- Cardio-respiratory illness

High-risk for vaccine failure:



(https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-08-13/02-COVID-Dooling-508.pdf

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Tixagevimab / Cilgavimab:

EVUSHELD* (tixagevimab co-packaged with cilgavimab)	Antibody dose	Number of vials needed	Volume to withdraw from vial(s)
	tixagevimab 150 mg	1 vial (dark grey vial cap)	1.5 mL
	cilgavimab 150 mg	1 vial (white vial cap)	1.5 mL

* 150 mg of tixagevimab and 150 mg of cilgavimab are to be administered as separate, consecutive intramuscular injections

The product is only authorized for those individuals who are not currently infected with the SARS-CoV-2 virus and who have not recently been exposed to an individual infected with SARS-CoV-2. The authorization also requires that individuals either have:

- moderate to severely compromised immune systems due to a medical condition or due to taking immunosuppressive medications or treatments and may not mount an adequate immune response to COVID-19 vaccination (examples of such medical conditions or treatments can be found in the fact sheet for health care providers) or;
- a history of severe adverse reactions to a COVID-19 vaccine and/or component(s) of those vaccines, therefore vaccination with an available COVID-19 vaccine, according to the approved or authorized schedule, is not recommended.

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Dispensing:

Proposed Prioritization Tiers:

1) Received B-cell depleting therapies (e.g. rituximab, obinutuzumab, ocrelizumab, alemtuzumab) within last 6 months & age > 65

2) Received B-cell depleting therapies , within the last 6 months, and age < 65yrs. Any ongoing use of BTK inhibitors (ibrutinib, acalabrutinib)

3) Received allogeneic HCT or CAR-T therapy within the past 6-12 months

4) Lung transplants, other SOT recipients on continual belatacept therapy, or multiple myeloma (actively receiving treatment);

5) Autologous HCT, or other solid organ transplants age > 65 yrs and within 6 months of transplant

6) Other actively treated hematologic malignancies or severe congenital immunodeficiency syndromes; patients receiving high-dose cyclophosphamide or similarly immunosuppressive regimens

7) Solid tumor malignancies or inflammatory syndromes on immunomodulatory chemotherapy (eg: high-dose cyclophosphamide); advanced AIDS

8) Other groups not previously mentioned.

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Dispensing:

Other Considerations:

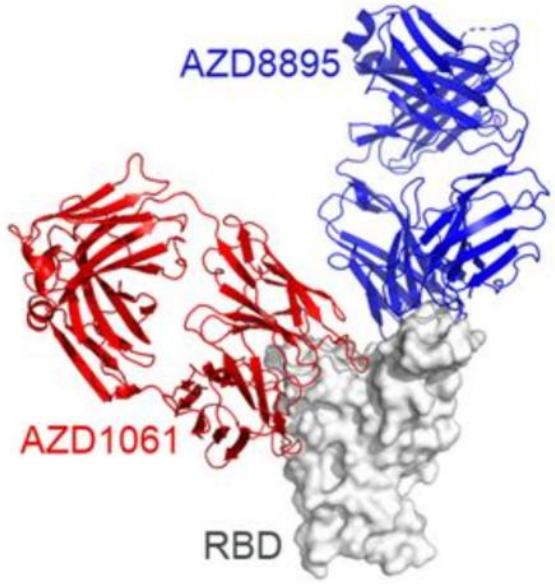
- Aligning with hospital “Scarce Resource Policy”

- Balancing rapid dissemination (and resupply) Vs Precise medical hierarchical ”need"
- Balancing risk of vaccine non-responsiveness Vs Risk of severe disease
  - Stratifying by predicted severity of illness,
  - Stratifying by risk of being exposed (eg: HCWs)

- Administration in different location than usual mAbs
  - Currently no infection at play, so don’t want cross contamination

- Plan for nursing to allow monitoring for 1hr after dose.

- Recognizing your variant mix in your region, and discussing limitations



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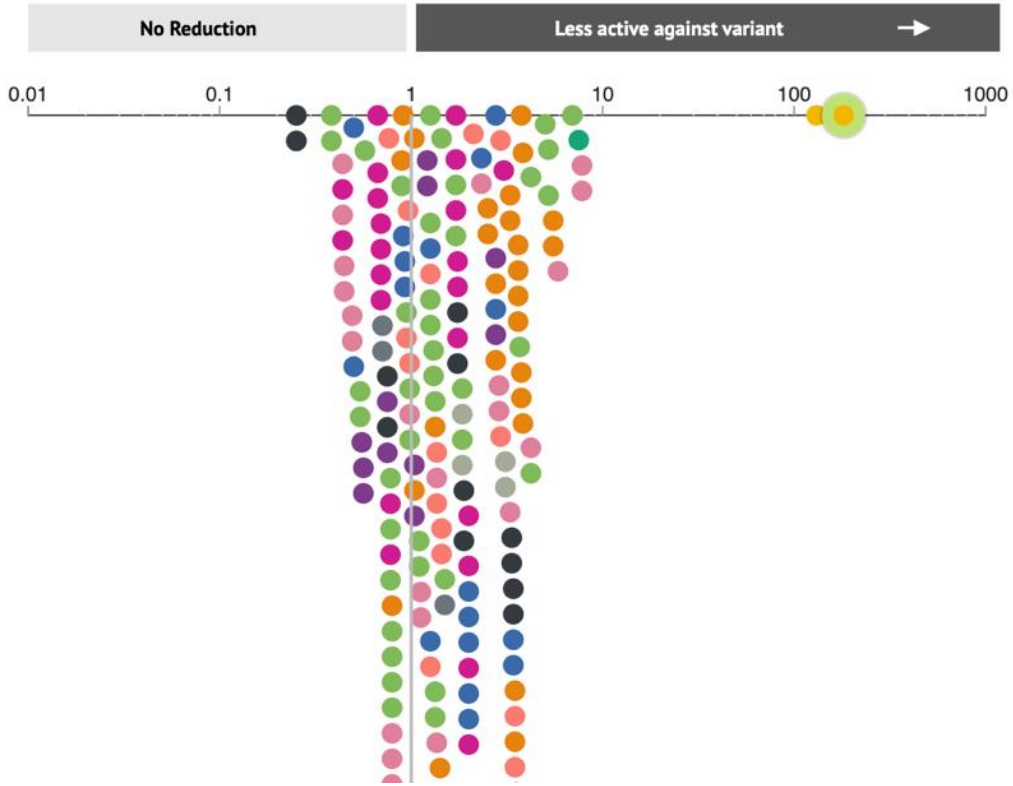
Activity against Omicron:

EXPANDED THERAPEUTIC VIEW

AZD7442



SELECTED POINT DETAIL

Viral Lineage: B.1.1.529

Viral Type: Pseudovirus

Full / Partial Variant: Full variant

Fold Change: 183

Therapeutic Name: AZD7442

Therapeutic Class: Neutralizing antibody

Data Source: AZD7442 (AZD8895 and AZD1061; mAbs for SARS-CoV-2) Omicron Antiviral Resistance Information

Data Source Type: Directly submitted data

Data Uploaded: 12/15/2021

Assay: Pseudotyped virus assay

Spike Mutations: A67V, H69del, V70del, T95I, G142D, V143del, Y144del, Y145del, N211del, L212I, ins214EPE, G339D, S371L, S373P, S375F, K417N, N440K, G446S, S477N, T478K, E484A, Q493R, G496S, Q498R, N501Y, Y505H, T547K, D614G, H655Y, N679K, P681H, N764K, D796Y, N856K, Q954H, N969K, L981F

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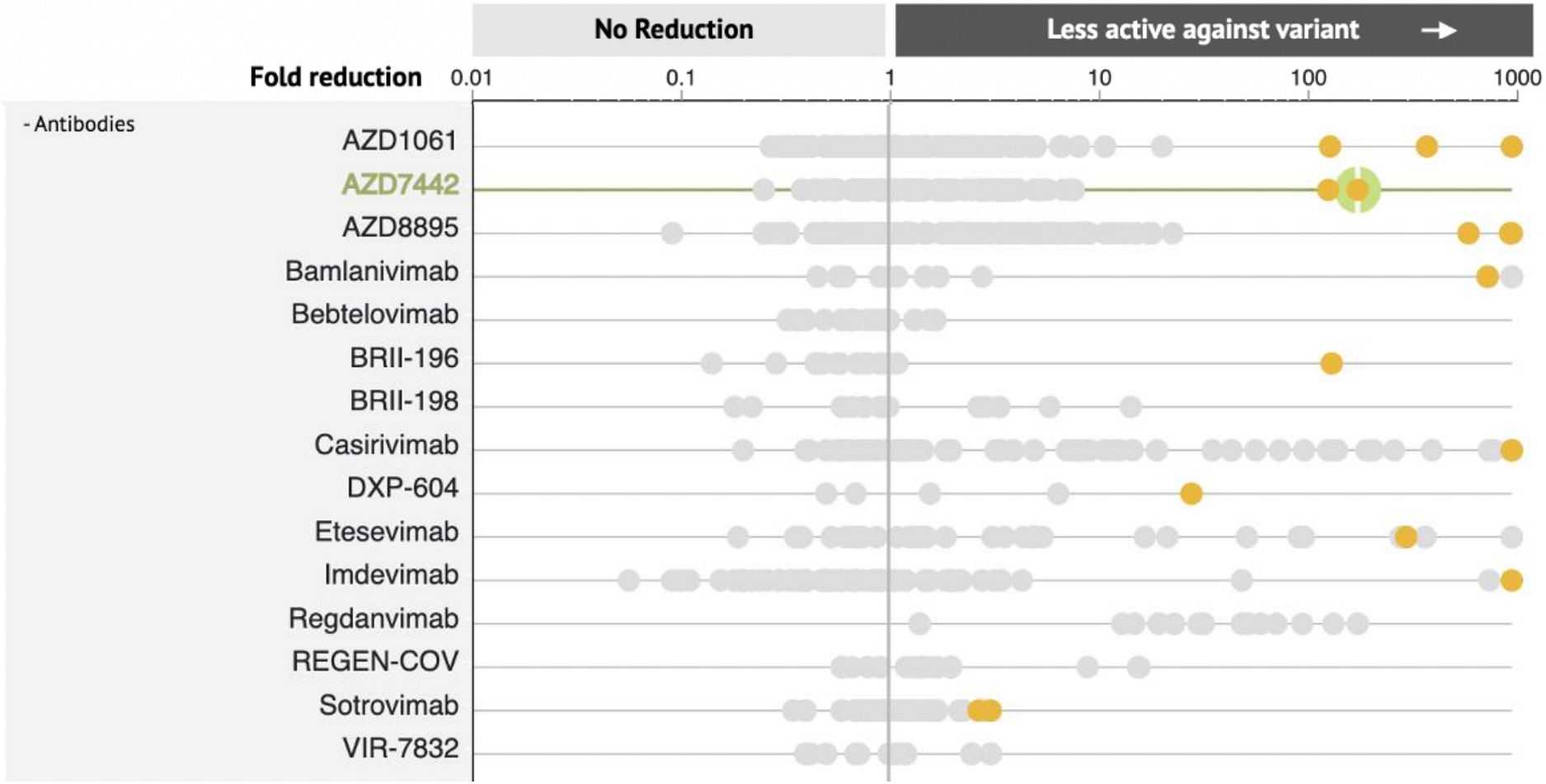
Available at: https://opendata.ncats.nih.gov/

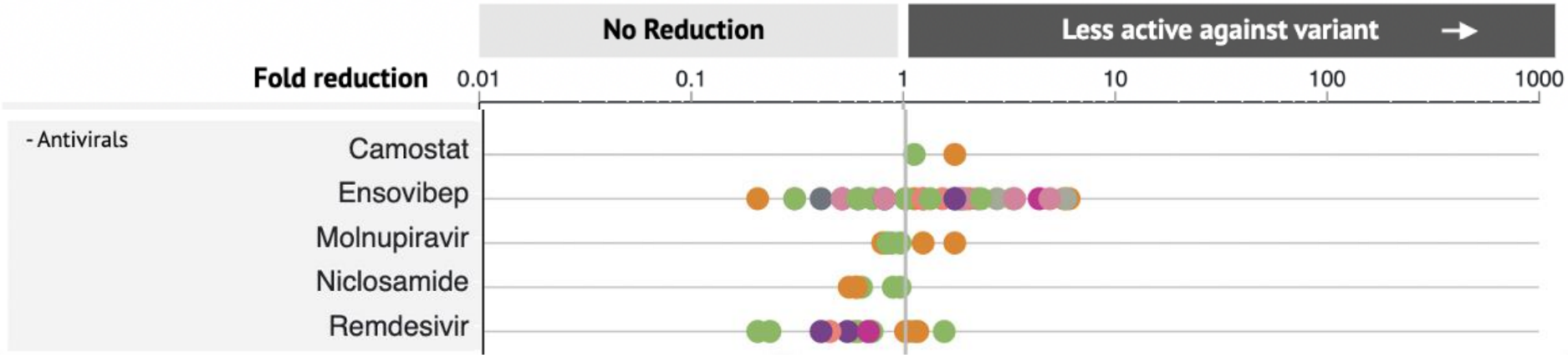
Activity against Omicron:



TxID
Duke Transplant/ Immunocompromised Host Infectious Diseases

Available at: https://opendata.ncats.nih.gov/

Activity against Omicron:



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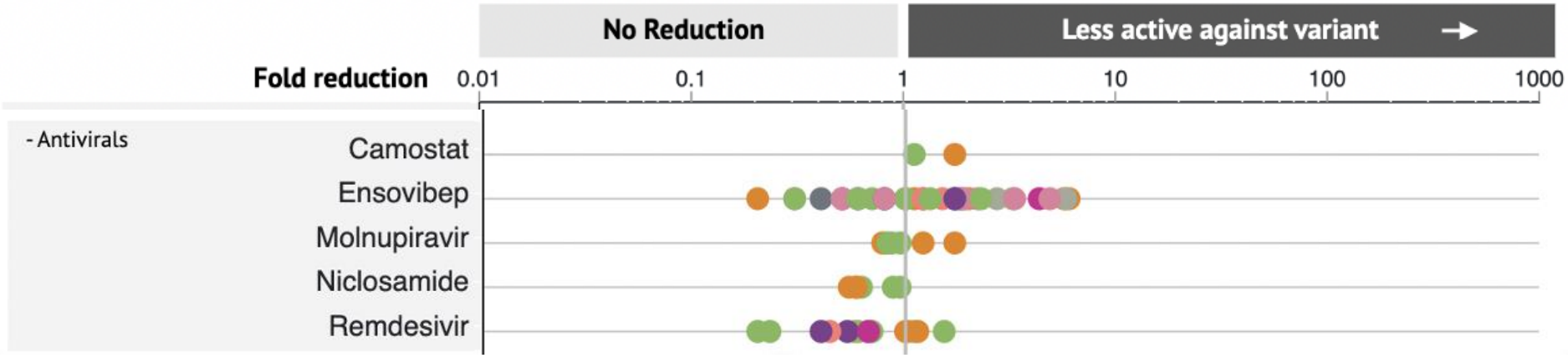
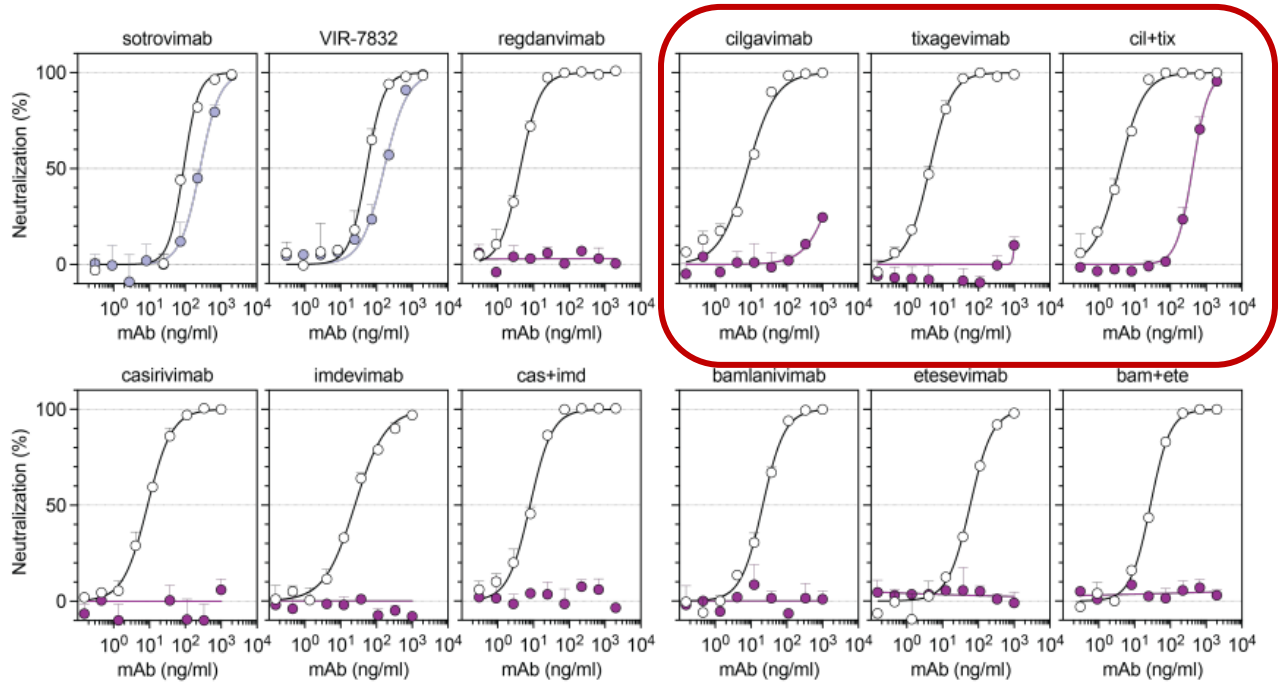




TxID
Duke Transplant/ Immunocompromised Host Infectious Diseases

Available at: www.biorxiv.org/content/10.1101/2021.12.12.472269v1.full.pdf

Bamlanivimab and Etesivimab for Treatment & Post-Exposure Prophylaxis in Pediatric Patients

Sameer J. Patel, MD

U.S. FOOD & DRUG ADMINISTRATION

Subject: FDA Expands Authorization of Bamlanivimab and Etesevimab to Allow Use in Certain High-Risk Pediatric Patients from Birth to Less Than 12 Years of Age

- Bamlanivimab and etesevimab are authorized to be administered together in adults and pediatric patients, including neonates, who are at high risk for progression to severe coronavirus disease 2019 (COVID-19), including hospitalization or death for the **treatment of mild to moderate** COVID-19, or **post-exposure prophylaxis** of COVID-19.
- Given the similar course of COVID-19, the authorization of bamlanivimab and etesevimab for treatment and post-exposure prophylaxis in younger pediatric patients, including neonates, is supported by safety and efficacy data in adolescents and adults, together with additional pharmacokinetic and safety data from the clinical trial in pediatric patients studying bamlanivimab and etesevimab for the treatment of mild to moderate COVID-19.

Pediatric EUA Criteria

- <1 year old
- obesity or being overweight
- pregnancy
- chronic kidney disease
- diabetes
- immunosuppressive disease or immunosuppressive treatment
- cardiovascular disease (including congenital heart disease) or hypertension
- chronic lung diseases (for example, chronic obstructive pulmonary disease, asthma [moderate-to-severe], interstitial lung disease, cystic fibrosis and pulmonary hypertension)
- sickle cell disease
- neurodevelopmental disorders (for example, cerebral palsy) or other conditions that confer medical complexity (for example, genetic or metabolic syndromes and severe congenital anomalies)
- having a medical-related technological dependence (for example, tracheostomy, gastrostomy, or positive pressure ventilation (not related to COVID-19)

Limitations of Benefit and Potential for Risk in Patients with Severe COVID-19

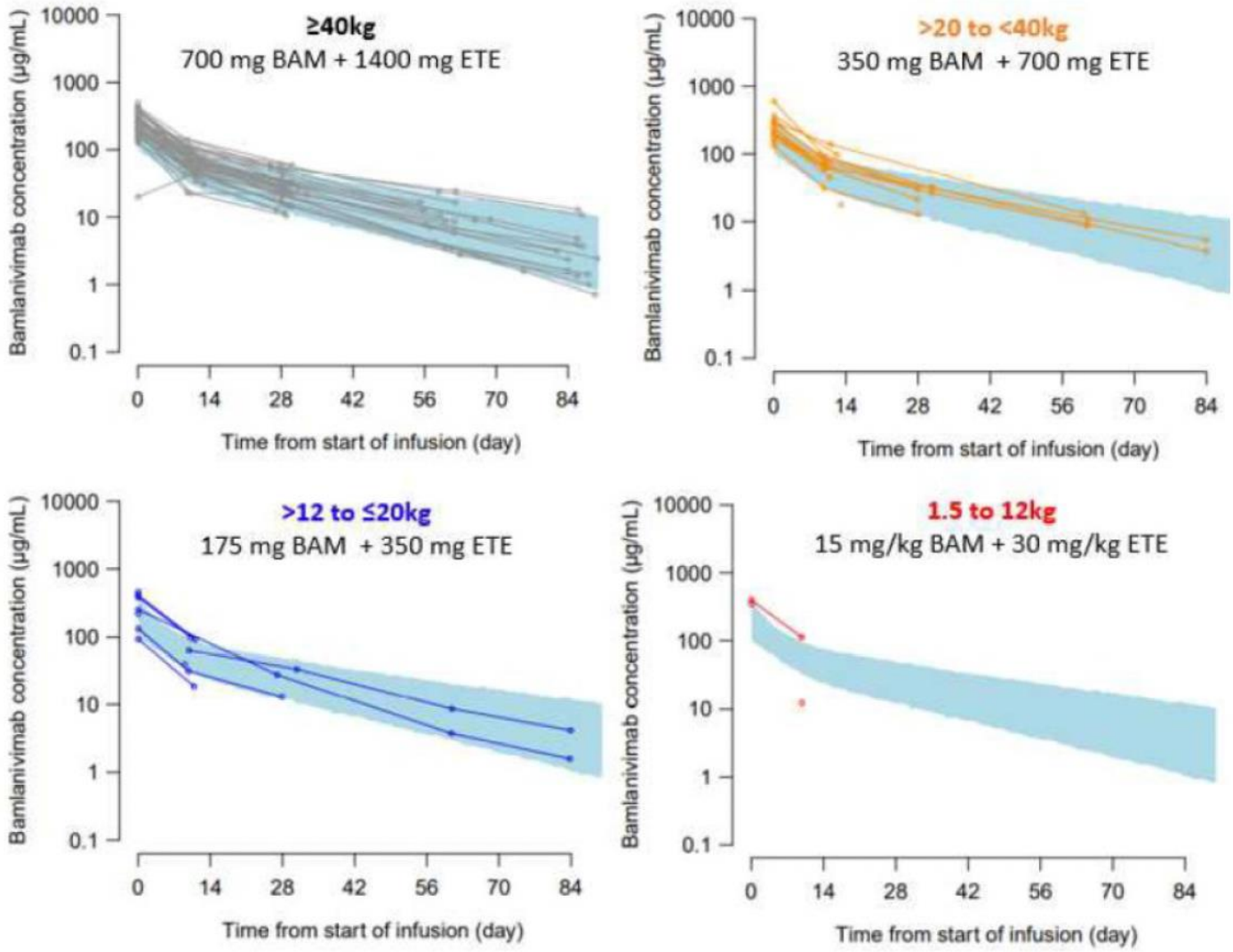
- Bamlanivimab and etesevimab are not authorized for use in patients **2 years and older** who are hospitalized due to COVID-19
- Bamlanivimab and etesevimab are not authorized for use in patients, regardless of age, who:
  - require oxygen therapy and/or respiratory support due to COVID-19, OR
  - require an increase in baseline oxygen flow rate and/or respiratory support due to COVID-19 and are on chronic oxygen therapy and/or respiratory support due to underlying non-COVID-19 related comorbidity

Dosing

- >20 kg to <40 kg: 350 mg bamlanivimab and 700 mg etesevimab
- >12 kg to 20 kg: 175 mg bamlanivimab and 350 mg etesevimab
- 1 kg to 12 kg: 12 mg/kg bamlanivimab and 24 mg/kg etesevimab

Body Weight	Bamlanivimab/Etesevimab Dose
>20 kg to < 40 kg	350 mg / 700 mg
>12 kg to < 20 kg	175 mg / 350 mg
>11 kg to 12 kg	138 mg / 276 mg
>10 kg to 11 kg	126 mg / 252 mg
>9 kg to 10 kg	114 mg / 228 mg
>8 kg to 9 kg	102 mg / 204 mg
>7 kg to 8 kg	90 mg / 180 mg
>6 kg to 7 kg	78 mg / 156 mg
>5 kg to 6 kg	66 mg / 132 mg
>4 kg to 5 kg	54 mg / 108 mg
>3 kg to 4 kg	42 mg / 84 mg
>2 kg to 3 kg	30 mg / 60 mg
>1.5 kg to 2 kg	21 mg / 42 mg
1 kg to 1.5 kg	15 mg / 30 mg

Pediatric Serum Concentration Profiles by Weight Category Matched Adult Concentration Profiles Administered Bamlanivimab 700 mg[3]



- Pediatric weight-based dosing resulted in comparable concentration-time profiles as has been observed in adults who received bamlanivimab 700 mg and etesevimab 1400 mg together
- Blue shading represents 90% prediction interval of modeling of bamlanivimab 700 mg in adults.
- Circles represent individual pediatric data.

Clinical Trial Information

- The safety and efficacy of bamlanivimab and etesevimab together was evaluated in a total of 125 pediatric patients enrolled in the phase 2/3 BLAZE-1 trial (NCT04427501), in which patients were treated for mild to moderate COVID-19.
- Pediatric patients were not hospitalized, and treatment was initiated within 3 days of obtaining the clinical sample for the first positive SARS-CoV-2 viral infection determination.
- All pediatric patients met the criteria for high-risk.
- Pediatric patients weighing 40 kg or more received the same dose as adults (700 mg bamlanivimab and 1400 mg etesevimab).
- Pediatric patients weighing less than 40 kg received weight-based dosing

Clinical Trial Information

- Of the 125 pediatric subjects, 33 subjects ages 12 to <18 were evaluated in double-blind, placebo-controlled Phase 3 cohorts of BLAZE-1, and 1 subject age 12 to <18 was evaluated in a controlled addendum to BLAZE-1.
- Of the 33 pediatric subjects
  - 14 received placebo,
  - 14 received the authorized dose or a higher dose for their age, and
  - 5 received a lower dose than authorized for their age.
- A total of 91 pediatric subjects were evaluated in an open-label addendum to BLAZE-1, with
  - 40 subjects ages 12 to <18,
  - 36 ages 6 to <12,
  - 10 ages 2 to <6, and
  - 5 ages 0 to <2.1
- The youngest participant in the trial was 10 months of age and weighed 8.6 kg.

Baseline Characteristics of Pediatric Patients Who Received Bamlanivimab and Etesevimab Together for the Treatment of COVID-19[1]

	BLAZE-1 Trial (N=125)
Median age, years	12
Female, %	46
Race/ethnicity, %	
White	38
Hispanic or Latino	20
Black or African-American	57
COVID-19 severity, %	
Mild	88
Moderate	12
Mean duration of symptoms, days	4
Mean baseline viral load by cycle threshold	5.92

Results

- No pediatric patients died or required hospitalization due to COVID-19.
- Change in viral load to day 7 by dose was -4.23 for patients treated with 700 mg bamlanivimab and 1400 mg etesevimab (n=9), and -4.23 for patients who received weight-based dosing with bamlanivimab and etesevimab (n=75).
- The median time to complete symptom resolution as recorded in a trial-specific daily symptom diary was 7 days for patients treated with bamlanivimab 700 mg and etesevimab 1400 mg together (n=10), and 5 days for patients treated with weight-based dosing of bamlanivimab and etesevimab together (n=91).

Safety

- The adverse drug reaction profile in pediatric patients is consistent with the established profile.
- A total of 16 (12.8%) patients had a treatment-emergent adverse event (TEAE) in BLAZE-1 clinical trial data
  - 14 patients who received weight-based dosing of bamlanivimab and etesevimab
  - 1 patient who received bamlanivimab 700 mg plus etesevimab 1400 mg, and
  - 1 patient who received bamlanivimab 350 mg plus etesevimab 700 mg via rapid intravenous (IV) infusion over 3 minutes.
- No TEAEs occurred in ≥5% of the total study participants.

Post-exposure Prophylaxis of COVID-19 (BLAZE-2)

- In BLAZE-2, all patients were ≥18 years of age
- Therefore, there are no data regarding the use of bamlanivimab and etesevimab for post-exposure prophylaxis of COVID-19 in patients <18 years of age.

Challenges With COVID Risk Stratification In Children

- All Infants < 12 months vs. high-risk infants
  - Prematurity (29 weeks)
  - Chronic lung disease of prematurity
- Effect modification of age on obesity risk
- Determination of respiratory impact of medical-related technological dependence
- Impact global developmental delay and failure to thrive in patients with neurodevelopmental disorders and other conditions that confer medical complexity

Additional Challenges

- Communication of risk and benefit when very limited pediatric data
- Active screening to limit referral bias for chronically ill children
- Allocation of limited supply of monoclonal Ab between adult and pediatric patients
- Impact of Omicron VOC

Q&A/Discussion

Today's Links

Program Links:

- This webinar is being recorded and can be found with the slides online at https://www.idsociety.org/cliniciancalls
- RTLN Survey - https://www.surveymonkey.com/r/BFBJ5CK
- COVID-19 Real-Time Learning Network: https://www.idsociety.org/covid-19-real-time-learning-network/
- Vaccine FAQ: https://www.idsociety.org/covid-19-real-time-learning-network/vaccines/vaccines-information--faq/

Dr. Pulliam's Link:

- https://www.medrxiv.org/content/10.1101/2021.11.11.21266068

Dr. Wolf's Links:

- www.fda.gov/media/154701/download
- https://opendata.ncats.nih.gov/
- www.biorxiv.org/content/10.1101/2021.12.12.472269v1.full.pdf

COVID-19 Real-Time Learning Network

Brought to you by CDC and IDSA

Real-Time Learning Network Needs your Feedback

Help shape future plans for the COVID-19 Real-Time Learning Network (RTLN).

Your responses to this short survey will ensure that the RTLN is useful for front-line clinicians.

https://www.surveymonkey.com/r/BFBJ5CK

Continue the conversation on Twitter

@RealTimeCOVID19
#RealTimeCOVID19

We want to hear from you!

Please complete the post-call survey.

Next Call

Saturday, Jan. 8th

A recording of this call will be posted at
www.idsociety.org/cliniciancalls
-- library of all past calls now available --

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