COVID-19 IMMUNITY TASK FORCE

GROUPE DE TRAVAIL SUR L'IMMUNITÉ FACE À LA COVID-19

Seminar Series | Research Results & Implications

The Omicron tsunami

June 23, 2022 | 11:00 a.m. to 12:30 p.m. EDT

Moderator

Catherine Hankins, MD, PhD, FRCPC, CM

Co-Chair, COVID-19 Immunity Task Force

Professor, School of Population and Global Health, Faculty of Medicine and Health Sciences, McGill University

Speakers

David Buckeridge, MD, PhD, FRCPC, Scientific Lead, Data Management & Analysis, CITF; Professor, School of Population and Global Health, McGill University.

Harriet Ware, MSc, Data Scientist, University of Toronto, on behalf of CITF-funded SeroTracker.

Ciriaco Piccirillo, PhD, Professor of Microbiology and Immunology, McGill University; CITF-funded researcher.

Michael Grant, PhD, Professor of Immunology and Associate Dean of Biomedical Sciences, Memorial University of Newfoundland; CITF-funded researcher.

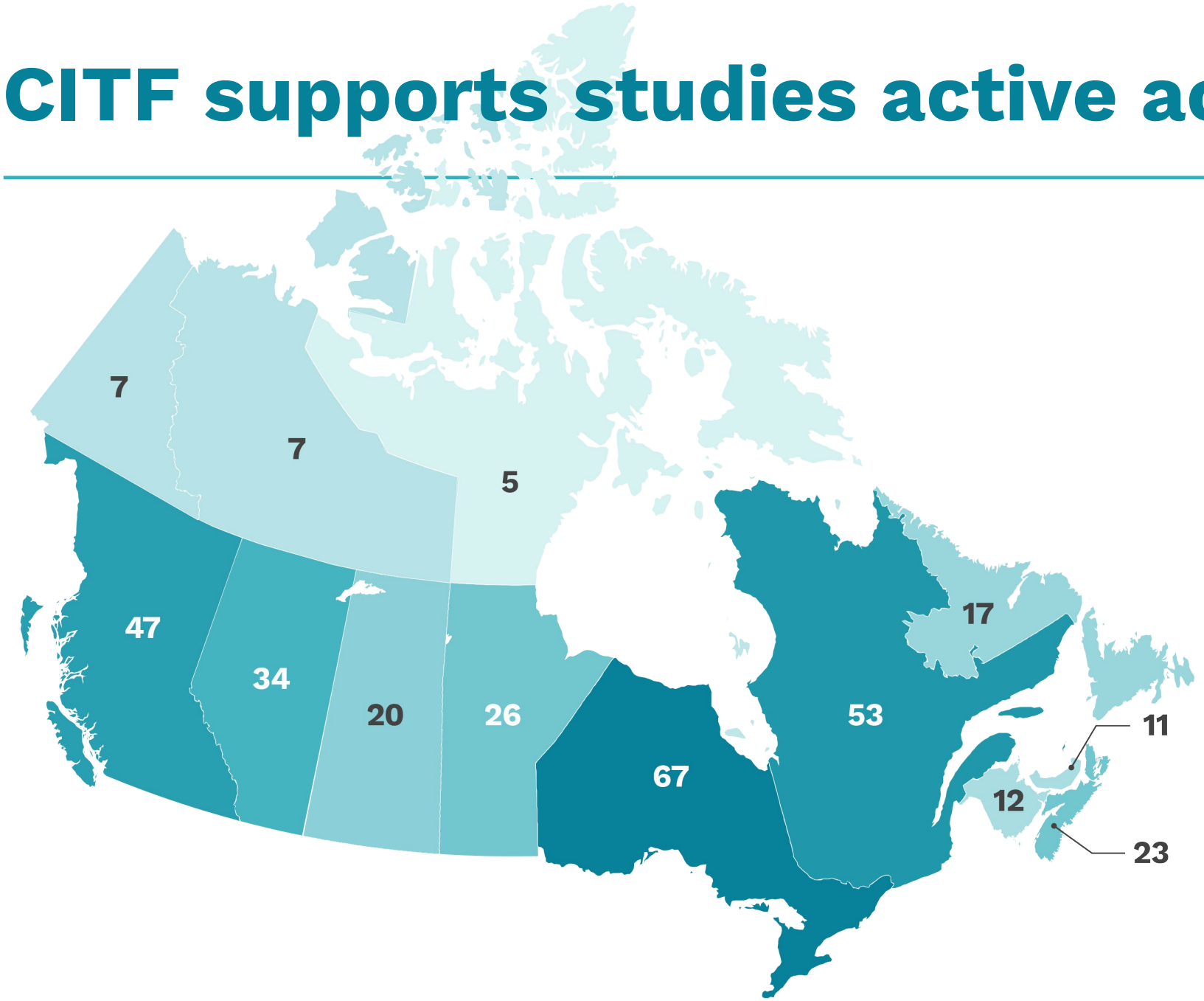
COVID-19 Immunity Task Force mandate

Established by the Government of Canada in April 2020

Mandate:

Catalyze, support, fund, and harmonize knowledge on SARS-CoV-2 immunity for federal, provincial, and territorial decision-makers to inform their efforts to protect Canadians and minimize the impact of the COVID-19 pandemic.

CITF supports studies active across Canada



113 studies

Canada-wide
seroprevalence studies

David Buckeridge, MD, PhD, FRCPC

Scientific Lead, Data Management and Analysis

CITF Secretariat

Professor, School of Population and Global Health,
McGill University

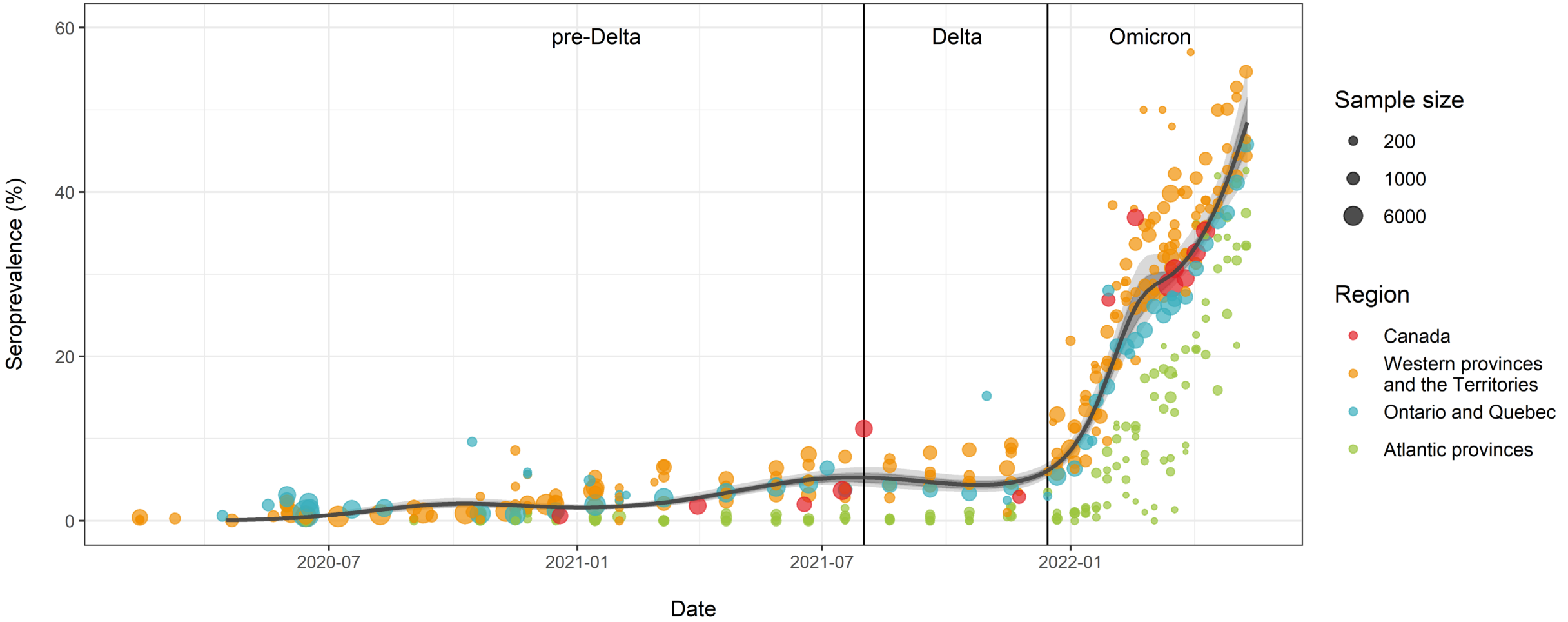
Disclaimer

I have no COIs to declare related to this study.

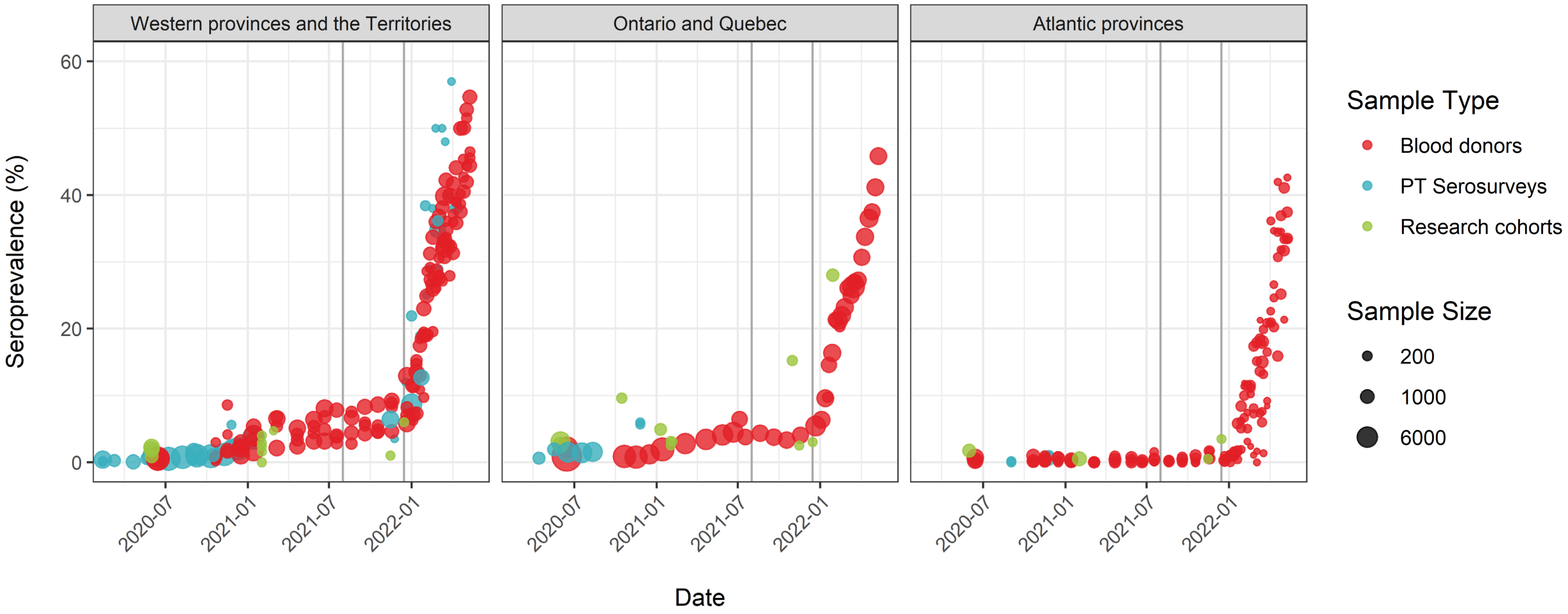
Serology provides a window on the wave

- Laboratory testing was not able to keep pace with the number of new infections, so the number of tests no longer tracked with new infections
- Other data used to track infections were affected by Omicron variant
- Serology data continue to provide a window on new infections
  - Infection (nucleocapsid) and vaccination (spike) evoke different serology
  - Change in anti-nucleocapsid serology reflects new infections over short periods
  - Estimates of serology collected from CITF partners, harmonized, and analyzed

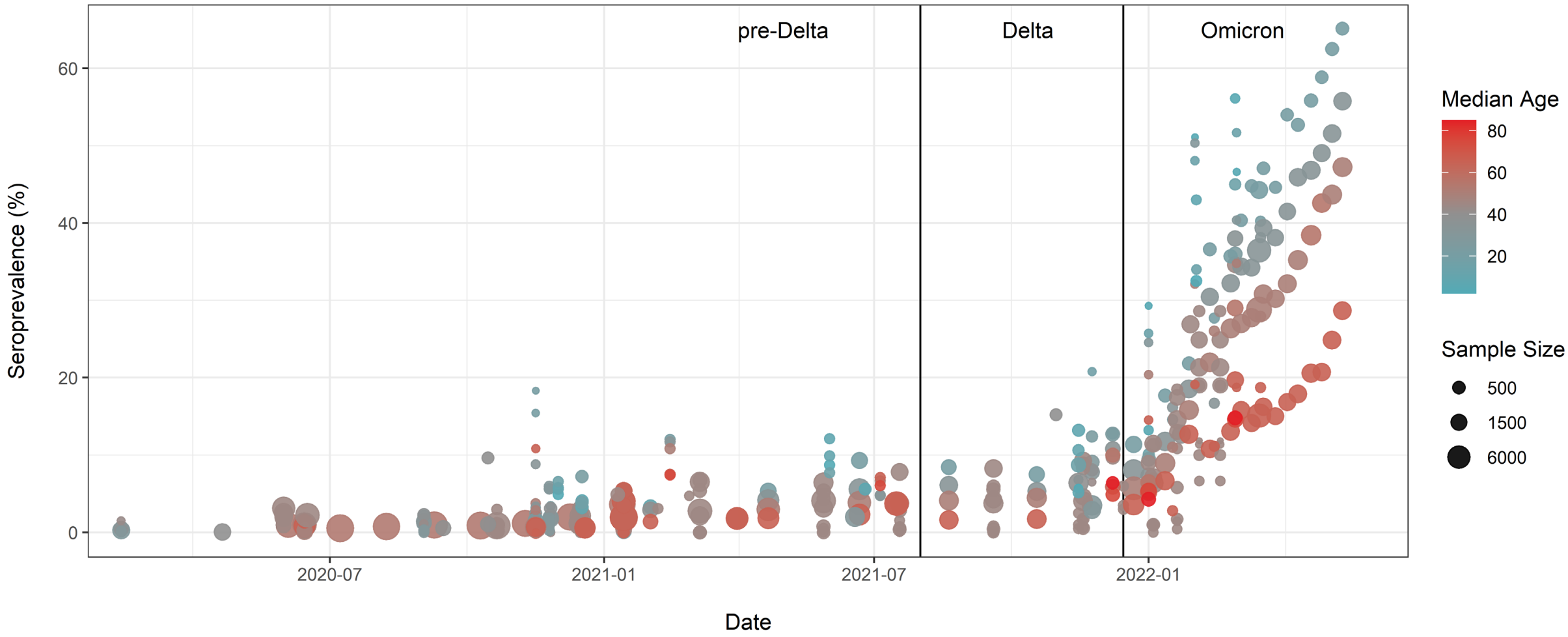
The Omicron wave caused an unprecedented rise in infection-acquired seroprevalence in Canada



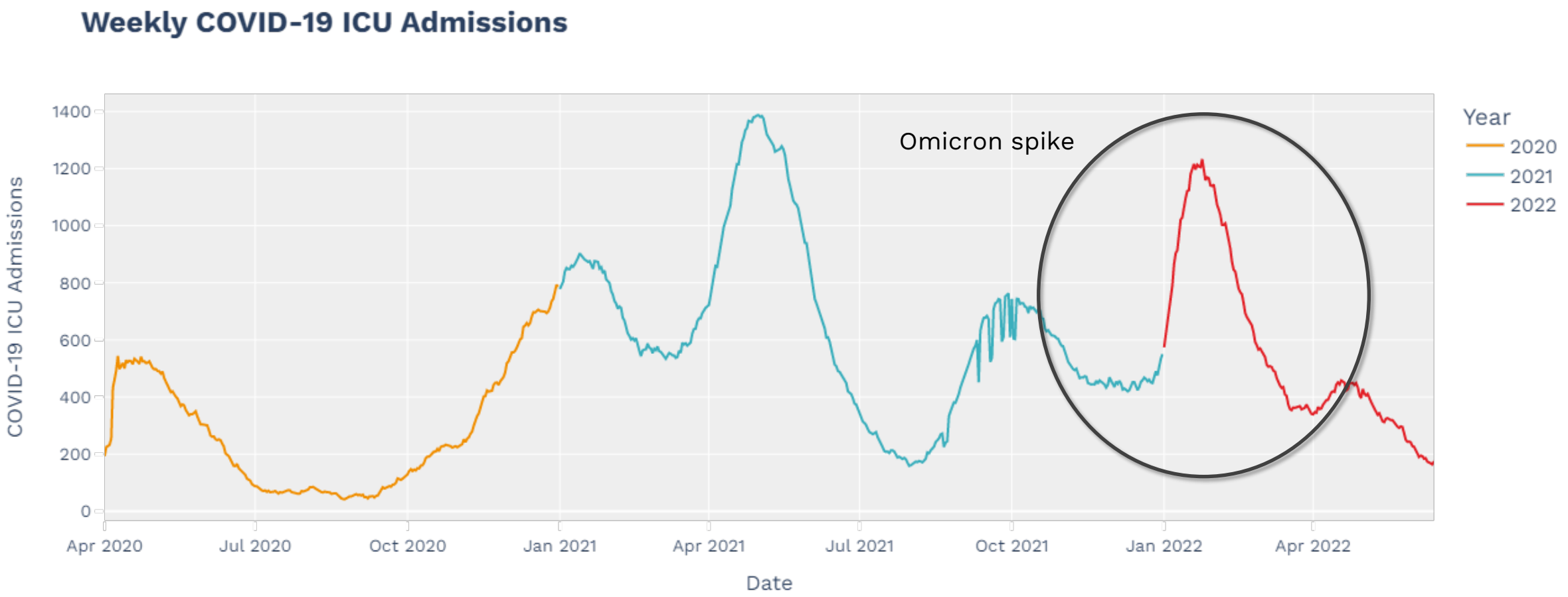
The wave affected all regions



More infections in younger age groups



Thousands sent to the intensive care unit (ICU) during Omicron

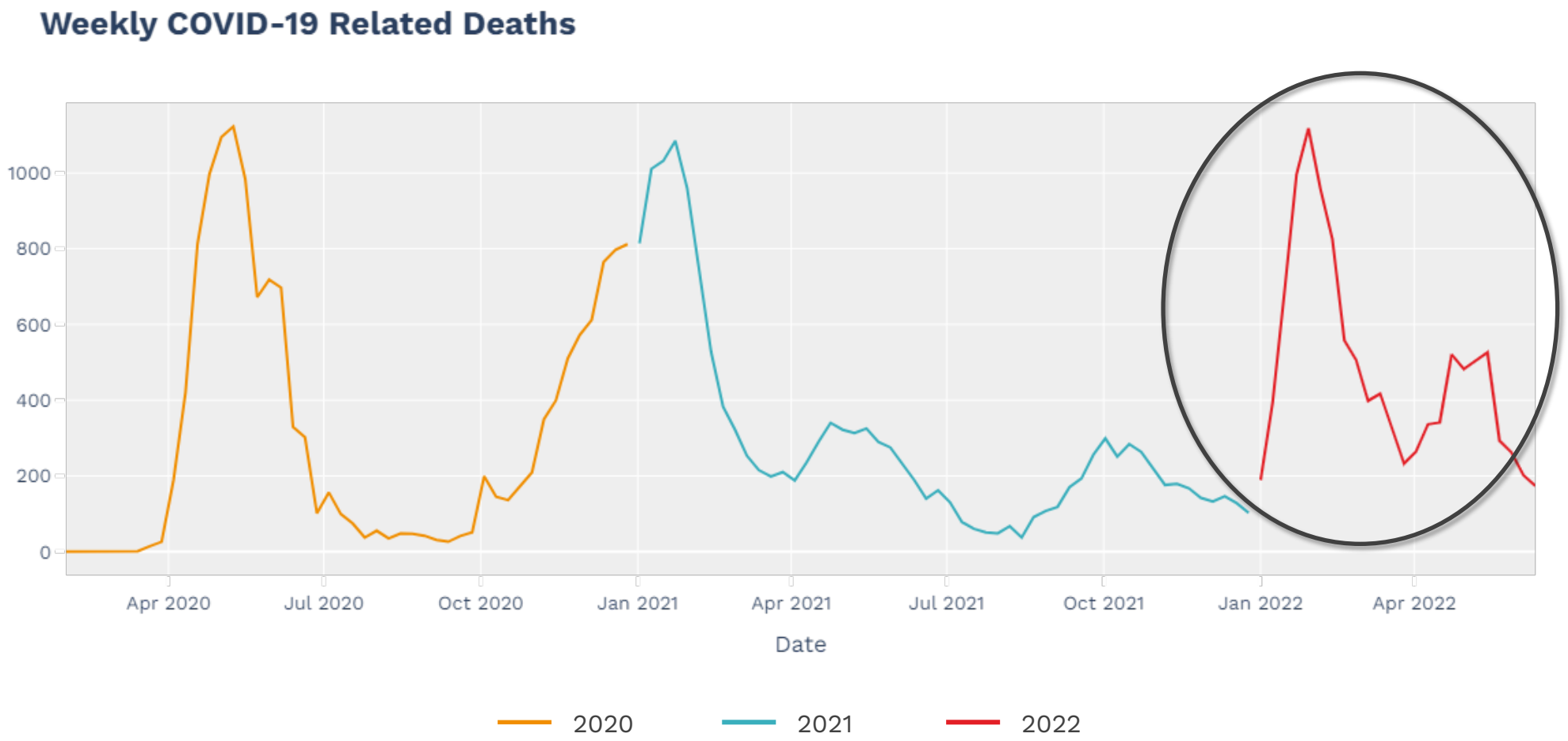


Source: https://health-infobase.canada.ca/covid-19/

Omicron caused many deaths

Younger Canadians experienced high excess mortality during Omicron

For those under 45, there were **15.6% more deaths** than expected in January 2022



Sources: https://health-infobase.canada.ca/covid-19/ and Statistics Canada

Global epidemiology of SARS-CoV-2

SeroTracker

Harriet Ware, MSc

SeroTracker, University of Calgary

World Health Organization

Disclaimer

I have no COIs to declare related to this study.

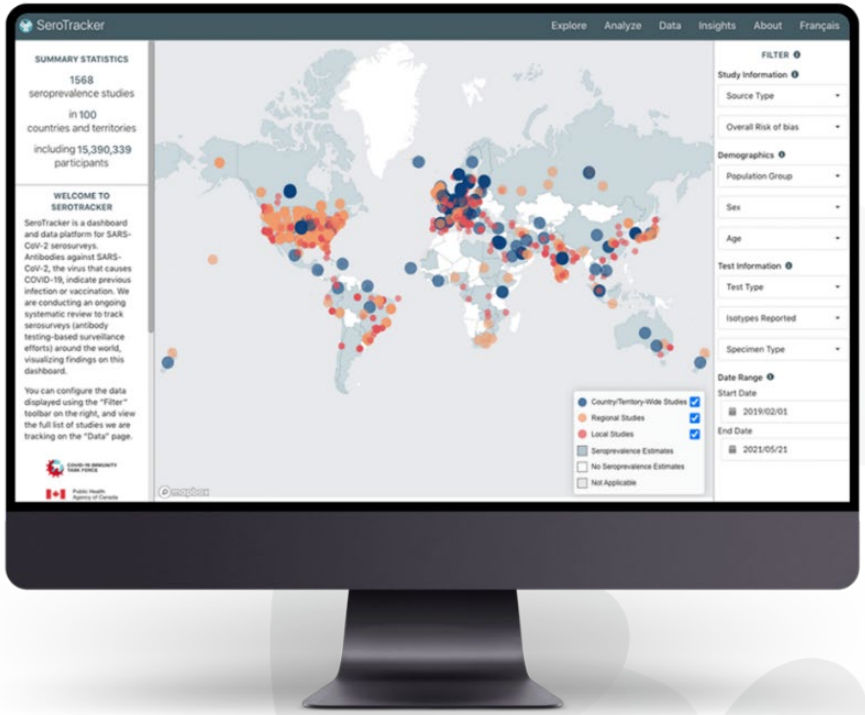
Using SeroTracker, we synthesized serosurvey data to map global and regional seroprevalence over time

SeroTracker: CITF-supported knowledge hub that tracks and synthesizes SARS-CoV-2 seroprevalence studies worldwide (living systematic review)

Data: National or subnational, gen pop serosurveys at low or moderate risk of bias, sampling between Jan 2020 and Apr 2022 (833 studies in 86 countries)

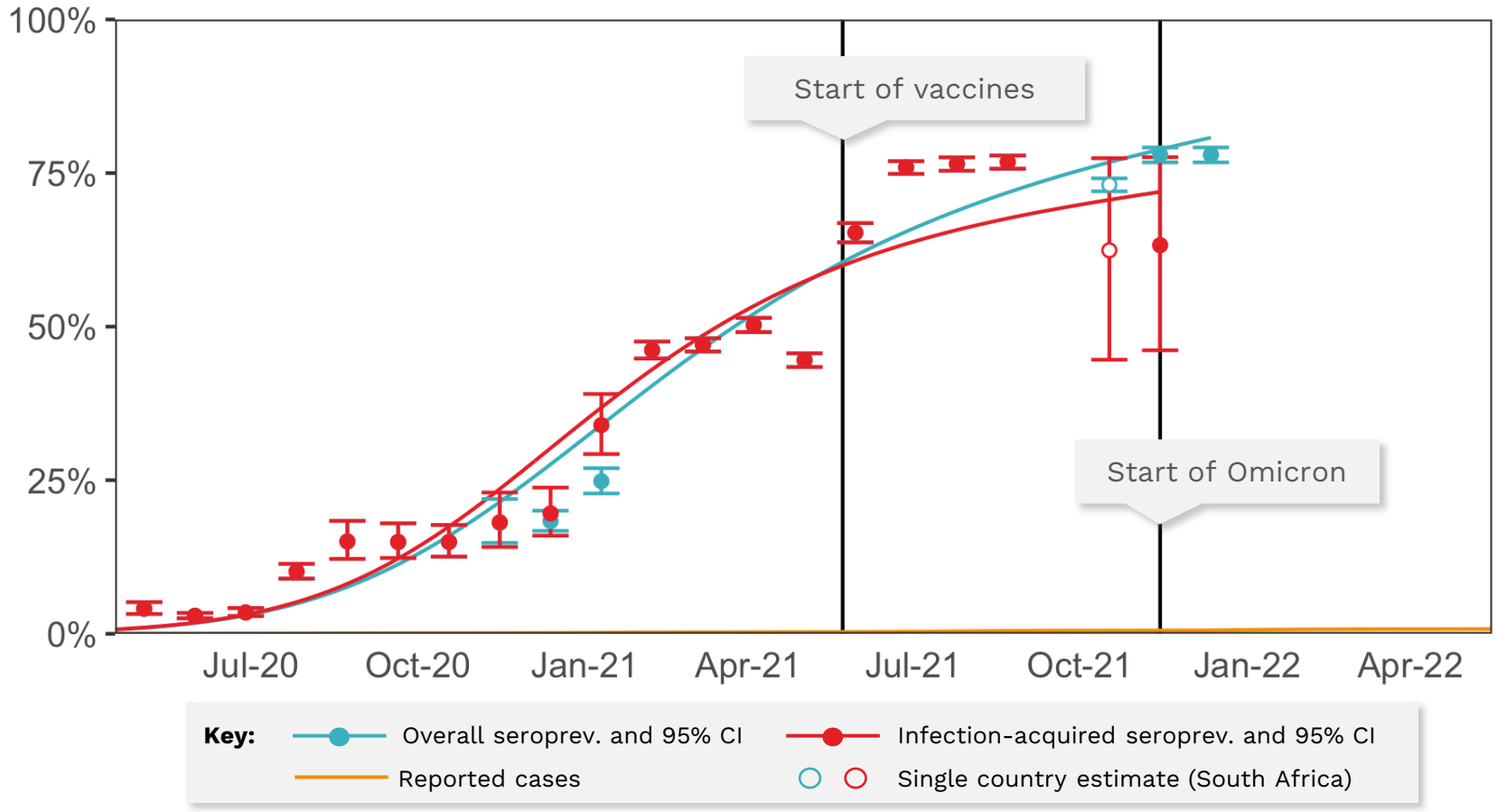
Methods:

- Calculated monthly overall and infection-acquired seroprevalence by **meta-analyzing** serosurveys by **sampling mid-point date** in each **country**
- Estimated seroprevalence for each **WHO region** as the **population-weighted average** of country estimates
- Omicron-era estimates available in **four regions**: Africa, Western Pacific, Americas (HIC), Europe (HIC)



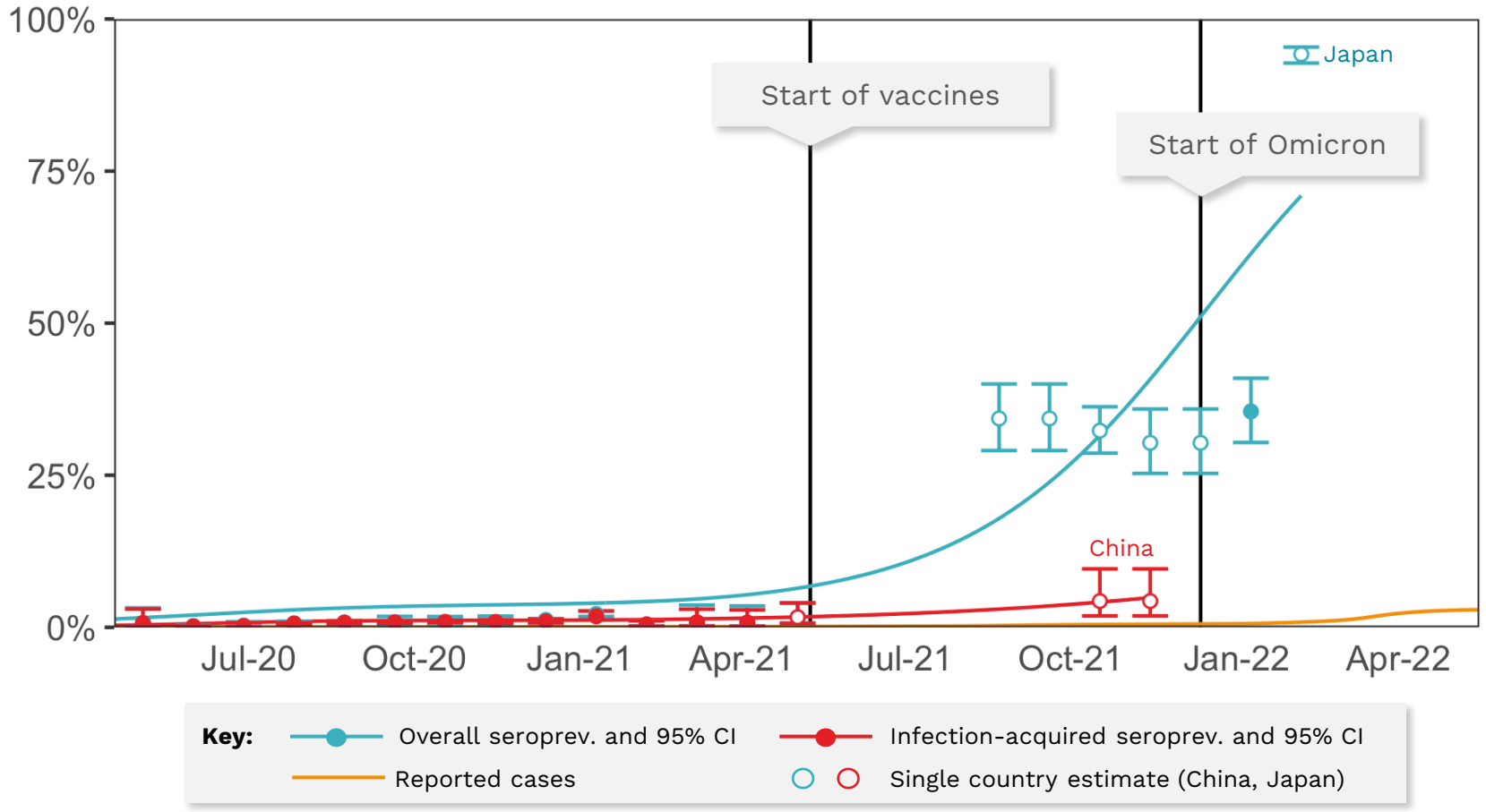
Bergeri I, Whelan M, Ware H, et al. Global epidemiology of SARS-CoV-2 infection: a systematic review and meta-analysis of standardized population-based seroprevalence studies, Jan 2020-Dec 2021. 2021. doi:10.1101/2021.12.14.21267791

In Africa, increases in seroprevalence mainly driven by infections; very high case under-ascertainment



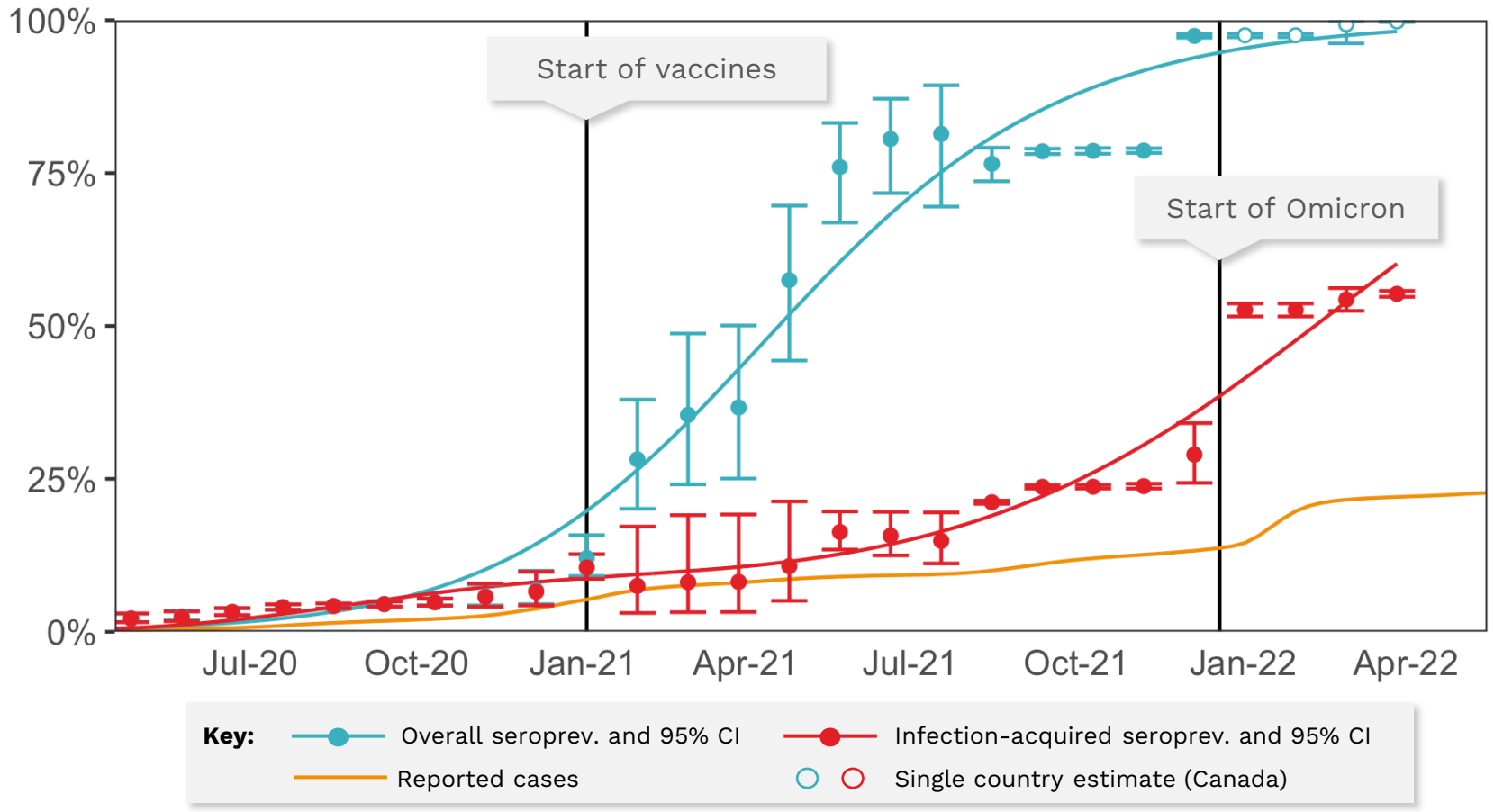
- Overall seroprevalence was 78.0% (Dec 2021) and infection-acquired seroprevalence was 63.3% (Nov 2021)
- Infection-acquired seroprevalence was **116 times higher** than reported cases

In the Western Pacific, increases in seroprevalence mainly driven by vaccination; moderate case under-ascertainment



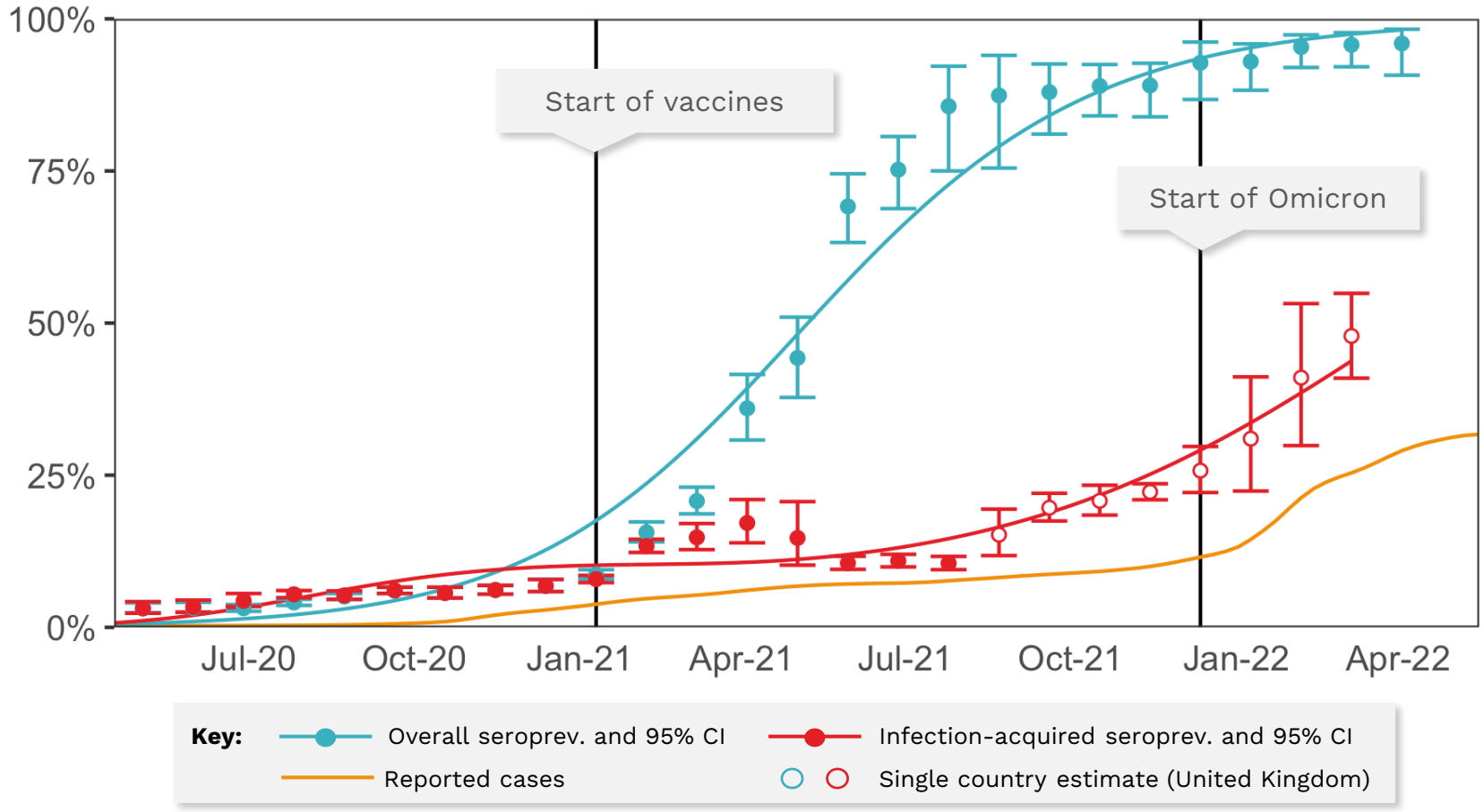
- Overall seroprevalence was 94.2% (Feb 2022) and infection-acquired seroprevalence was 4.3% (Nov 2021)
- Infection-acquired seroprevalence was **8.4 times higher** than reported cases

In the Americas (HIC), increases in seroprevalence driven by vaccination and infection; low case under-ascertainment



- Overall seroprevalence was 99.8% and infection-acquired seroprevalence was 55.2% (Mar 2022)
- Infection-acquired seroprevalence was **2.5 times higher** than reported cases

In Europe (HIC), increases in seroprevalence driven by vaccination and infection; low case under-ascertainment



- Overall seroprevalence was 95.9% (Apr 2022) and infection-acquired seroprevalence was 47.9% (Mar 2022)
- Infection-acquired seroprevalence was **1.9 times higher** than reported cases

Study Team

Informed individuals participating in investigations

Researchers and government partners conducting studies

The WHO Unity studies team, including WHO HQ, ROs, and COs

Key WHO Unity partners, including Institute Pasteur, US CDC, ECDC, BMGF, etc

The SeroTracker team

Key SeroTracker partners, including the Public Health Agency of Canada, Canada's COVID-19 Immunity Task Force, the Robert Koch Institute, and the Canadian Medical Association

Viral genetic diversity and immune escape potential

CoVaRR-Net

Dr. Ciro Piccirillo

Professor and Graduate Program Director, Department of Microbiology and Immunology, McGill University

Director, Centre of Excellence in Translational Immunology (CETI)

Research Institute of the McGill University Health Centre

CoVaRR-Net Pillar 1 Co-Lead

CITF-funded researcher

McGill | Department of Microbiology and Immunology | Département de microbiologie et d'immunologie

CETI Centre of Excellence in Translational Immunology

Centre universitaire de santé McGill Institut de recherche | McGill University Health Centre Research Institute

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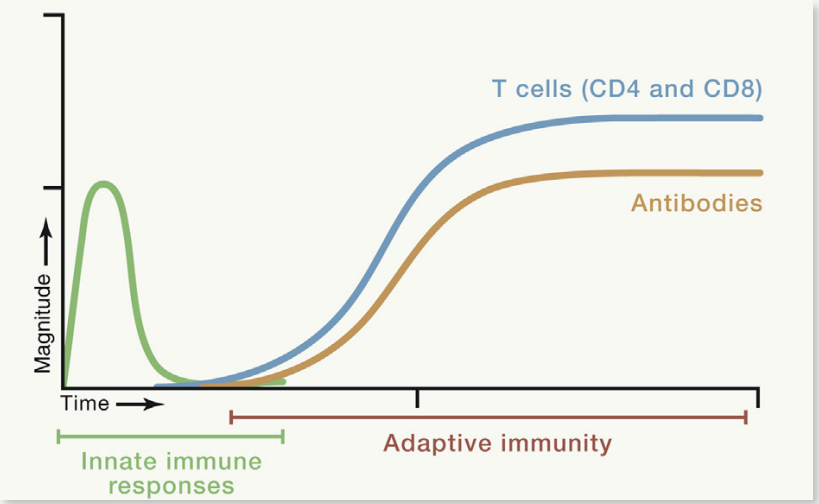
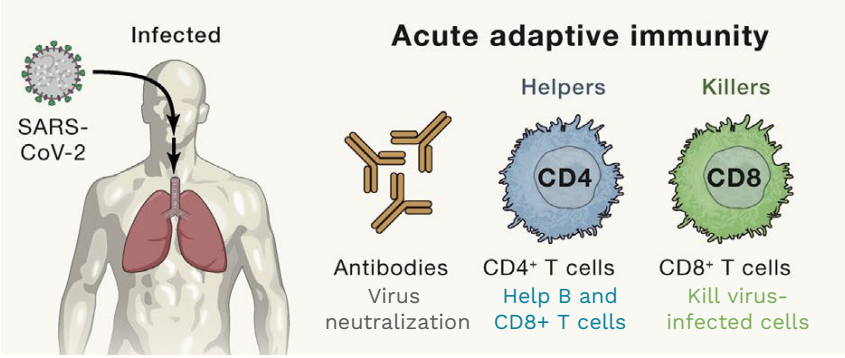
Immune teamwork in the fight against viral infections

Perfect example of generic infection:

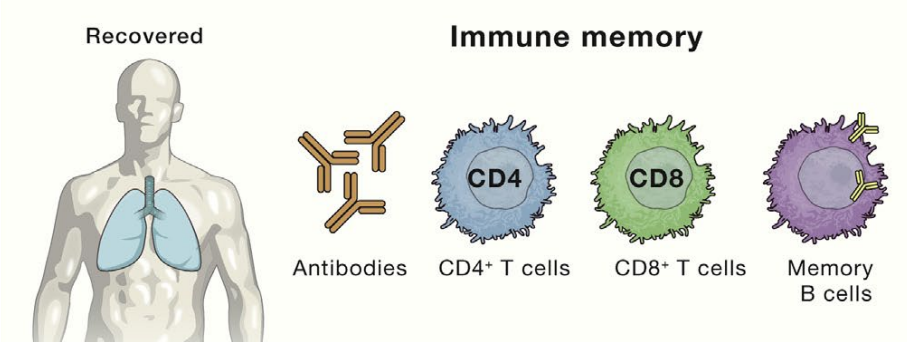


Coordinated actions of various immune players as infection develops

Primary infection



Recovery from infection or vaccine protection
(immune memory)

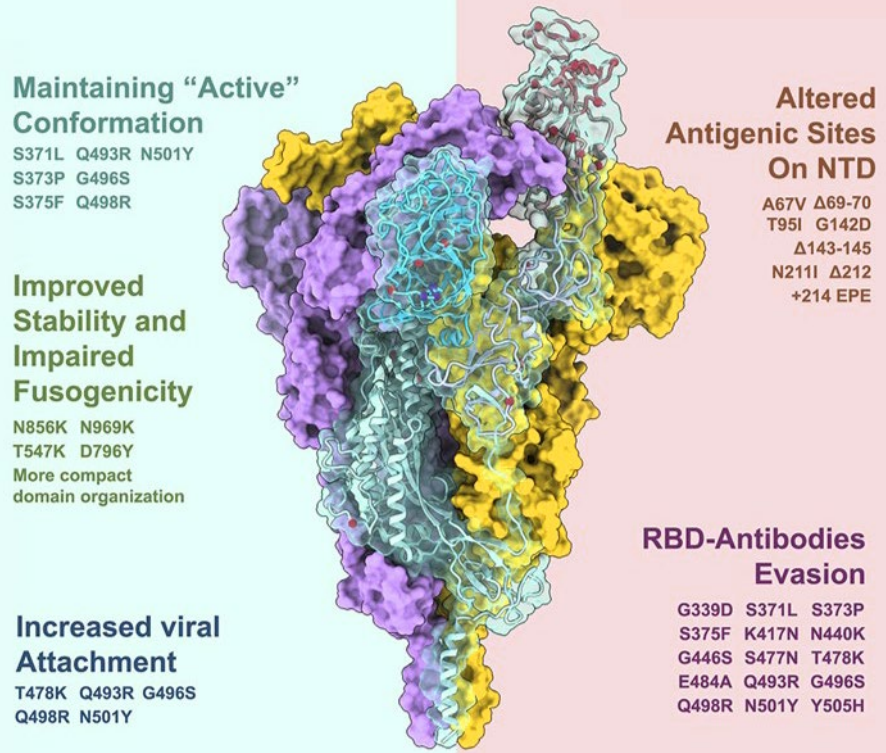


The genetic diversity of emerging viral variants (mutations) can **alter the functions** of Abs and T cells.

How does Omicron escape our immune system?

Increased infection

- Omicron's shape binds much better to the ACE2 receptor
- Because of its conformation (shape):
  - Omicron binds better to receptor (= more infectious)
  - Has weaker viral fusion (= less severe disease)

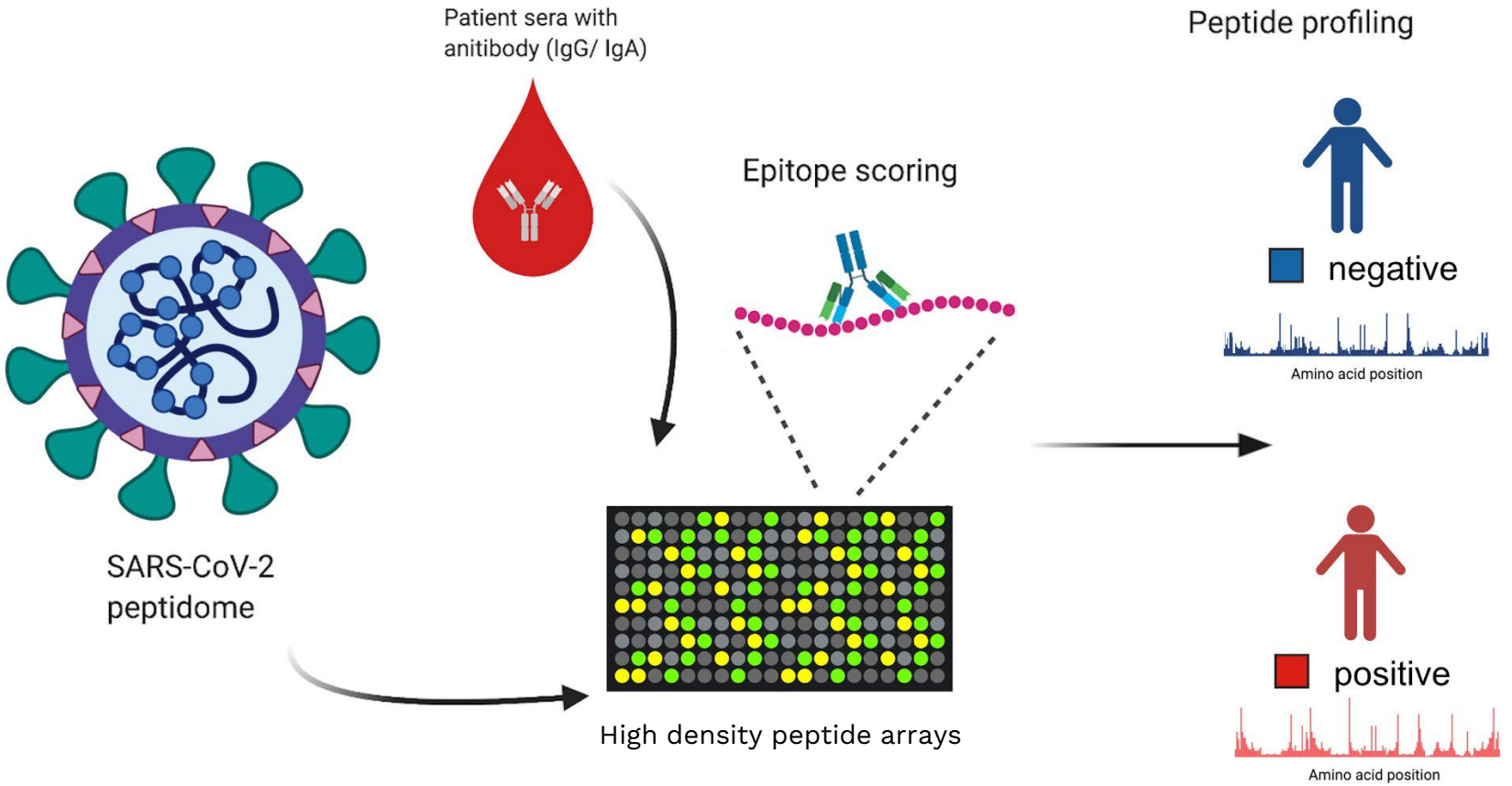


Cui et al. Cell 185, 860-871

Escape from immunity

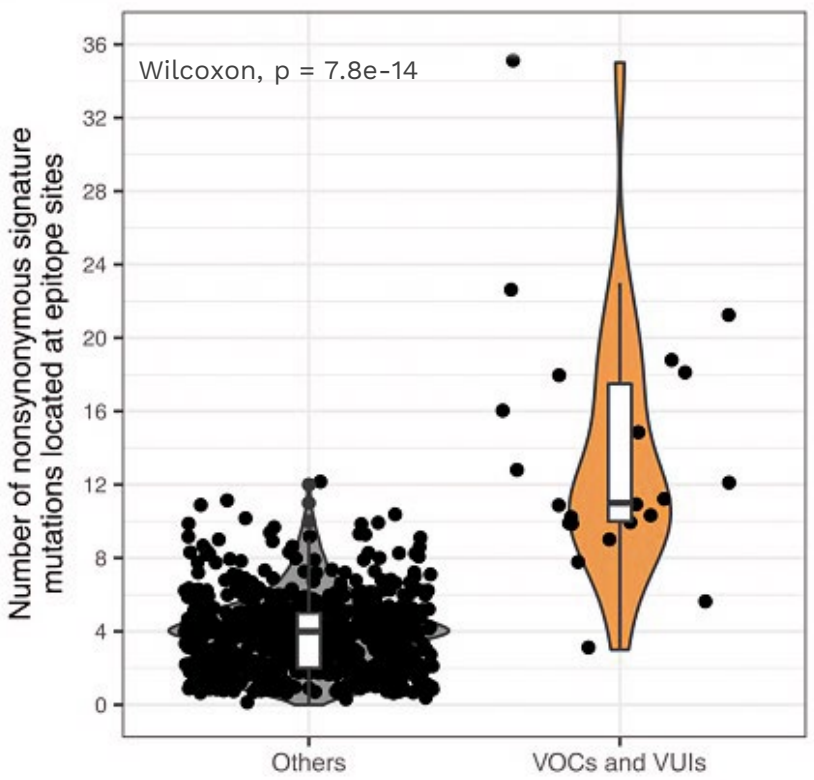
Omicron has mutations that make it look **different** from previous variants

Answering “Does Omicron evade immunity?”: Our workflow and patients



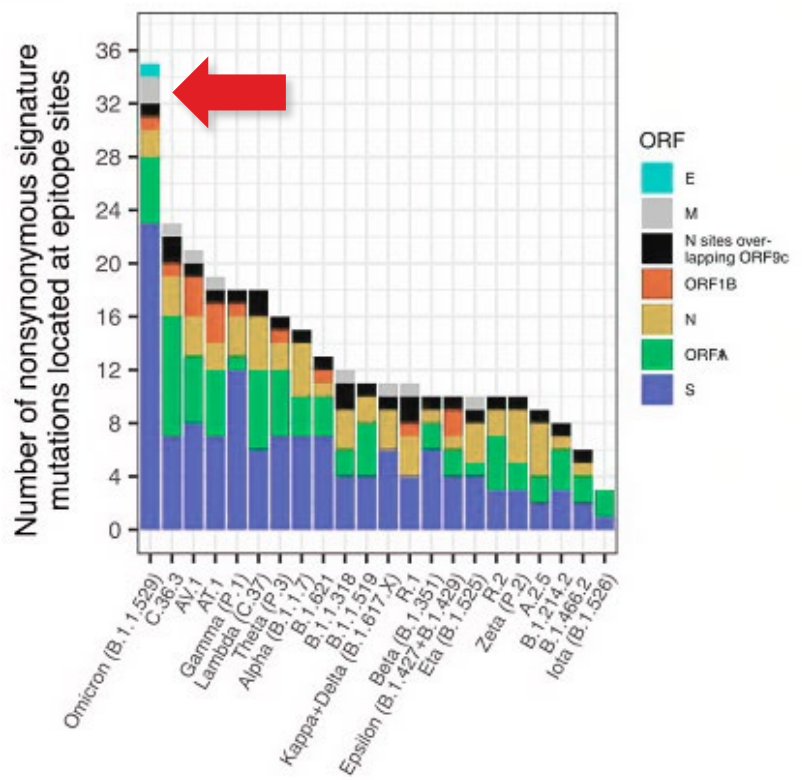
Omicron has many more mutations than other VOCs and therefore evades immune protection

Variants of Concern: Enriched in epitope mutations



SARS-CoV-2 lineage type

Omicron has lots of escape mutations, especially in spike

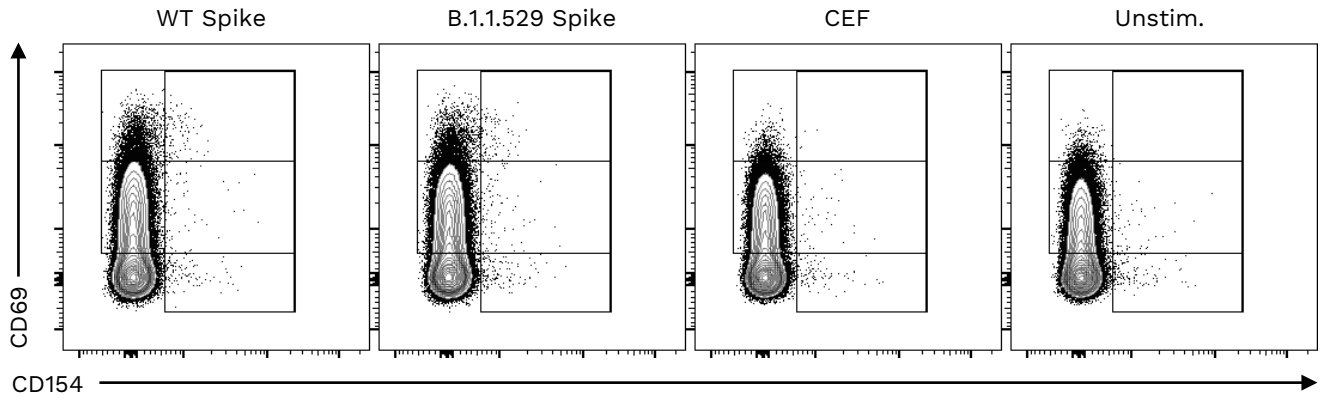


SARS-CoV-2 VOCs and VUIs

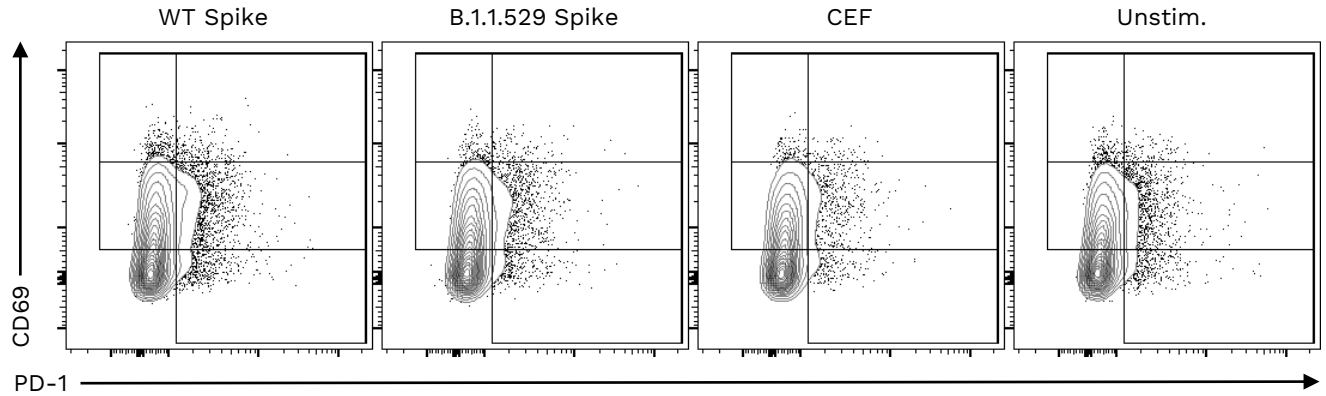
McGill | Department of Microbiology and Immunology | Département de microbiologie et d'immunologie
CETI Centre of Excellence in Translational Immunology
Centre universitaire de santé McGill Institut de recherche | McGill University Health Centre Research Institute

People with Omicron have good T cell response

CD4+ ”Helper” T cells



CD8+ “Killer” T cells

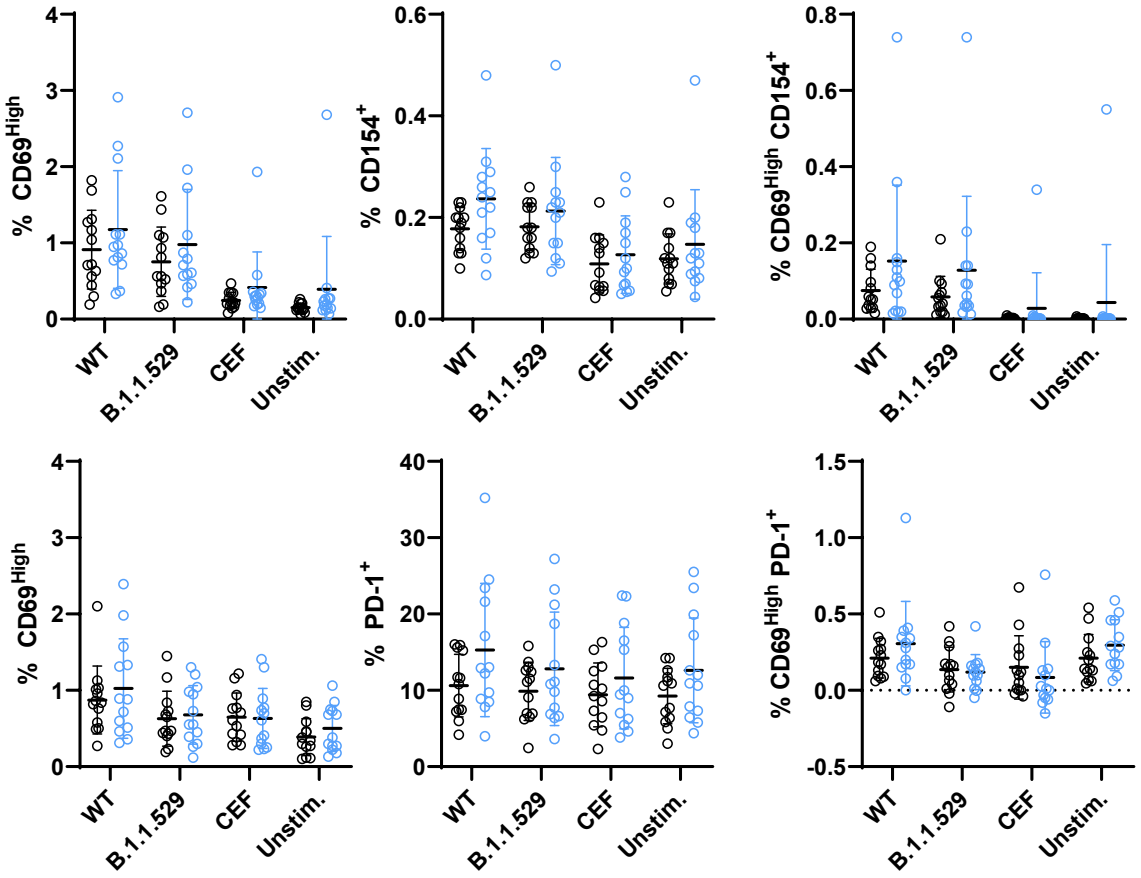


- People with Omicron generally respond very well in terms of T cell responses (both Helpers and Killers)
- Omicron elicits an immune response equivalent to a 3rd dose
- Omicron induces weaker antibodies than other variants, but it induces good T cell responses
- More long-term investigation is needed

People with Omicron have good T cell response

CD4+ "Helper" T cells

CD8+ "Killer" T cells



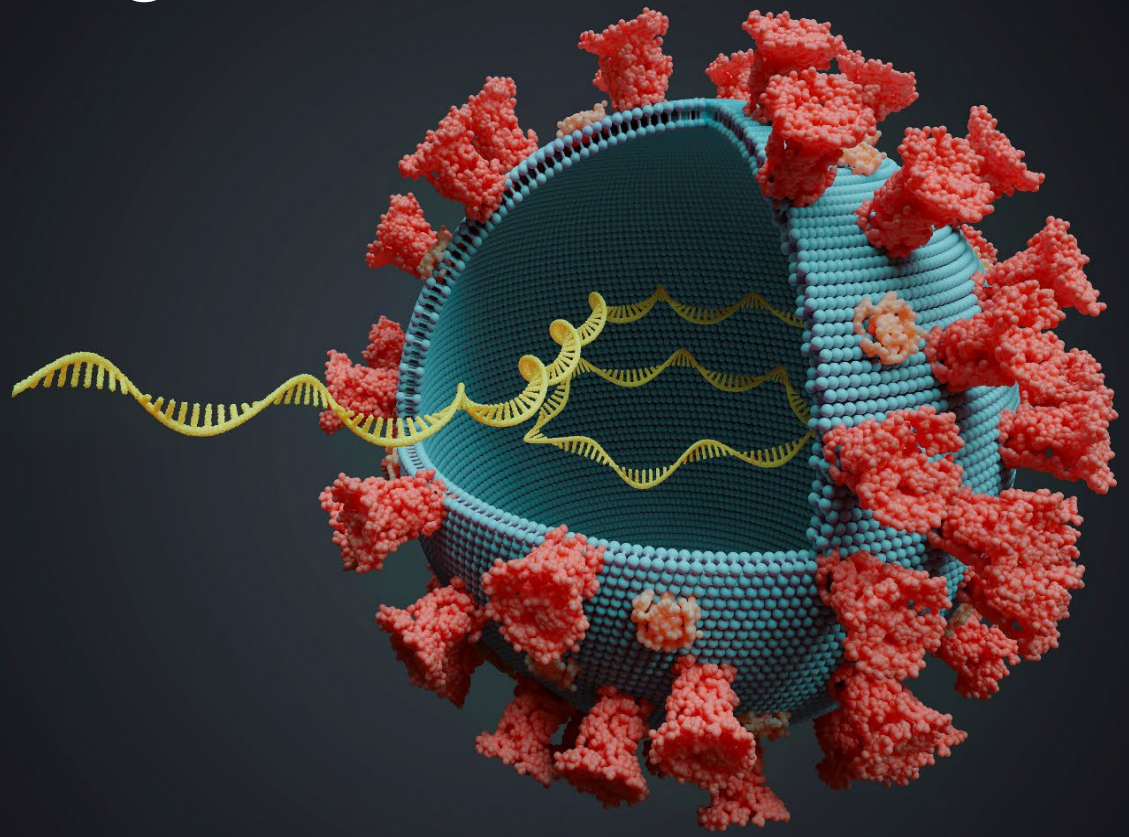
Legend:

- 3rd booster
- 2nd booster + Omicron infection

- People with Omicron generally respond very well in terms of T cell responses (both Helpers and Killers)
- Omicron elicits an immune response equivalent to a 3rd dose
- Omicron induces weaker antibodies than other variants, but it induces good T cell responses
- More long-term investigation is needed

Coming up in our study…

- Does an individual’s age or immune status favor emergence of variants with immune escape potential?
- Viral genome sequencing
- * Epitope mapping



Study Team

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McGill Interdisciplinary Initiative in Infection and Immunity (MI4)

Funded by

CoVaRR-Net

COVID-19 IMMUNITY TASK FORCE
GROUPE DE TRAVAIL SUR L'IMMUNITÉ FACE À LA COVID-19

Hybrid immunity

St. John’s,
Newfoundland
and Labrador

Dr. Michael Grant

Professor of Immunology and
Associate Dean of BioMedical Sciences,
Memorial University of Newfoundland,

CITF-funded researcher

MEMORIAL UNIVERSITY

Disclaimer

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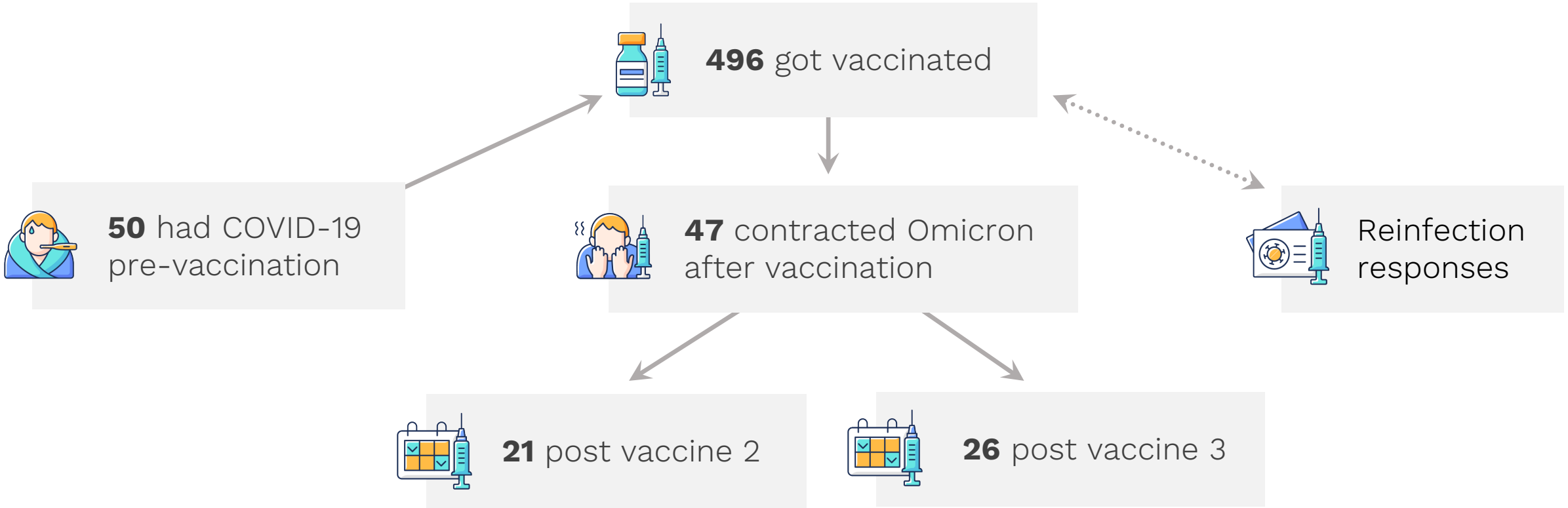
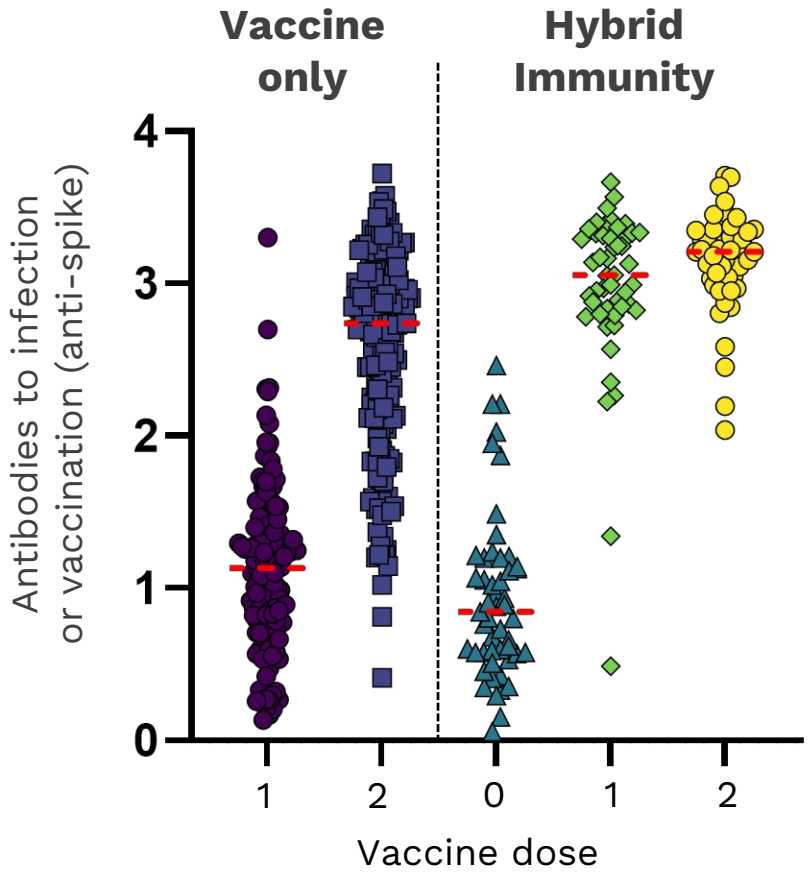
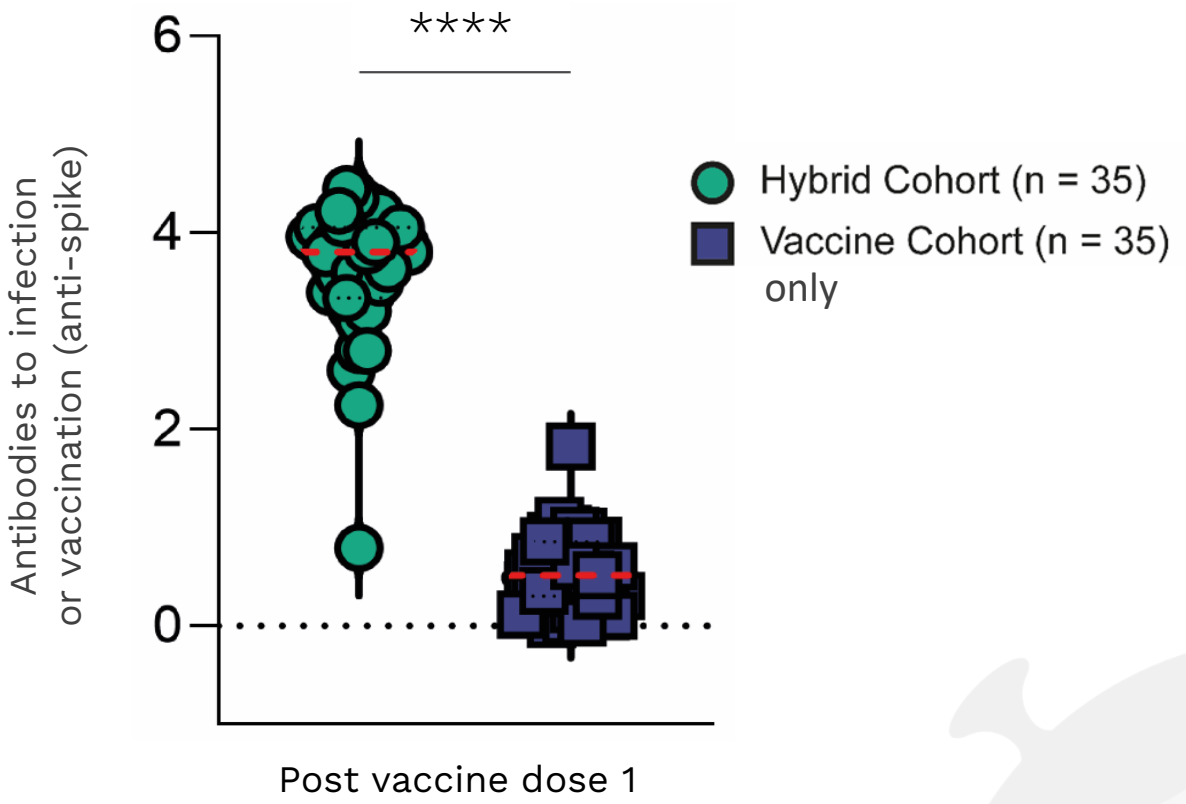
Study cohort (n=517)



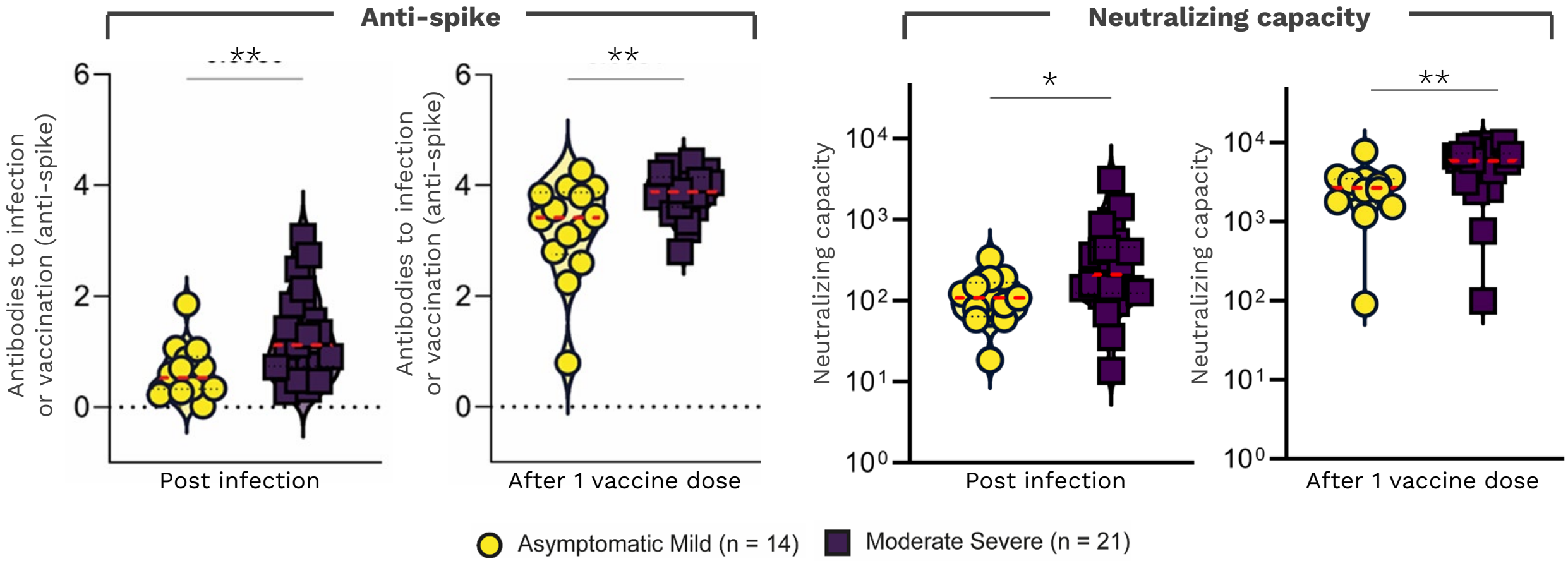
Quarterly blood draws monitor anti-spike and anti-nucleoprotein

Hybrid immunity boosts antibody responses

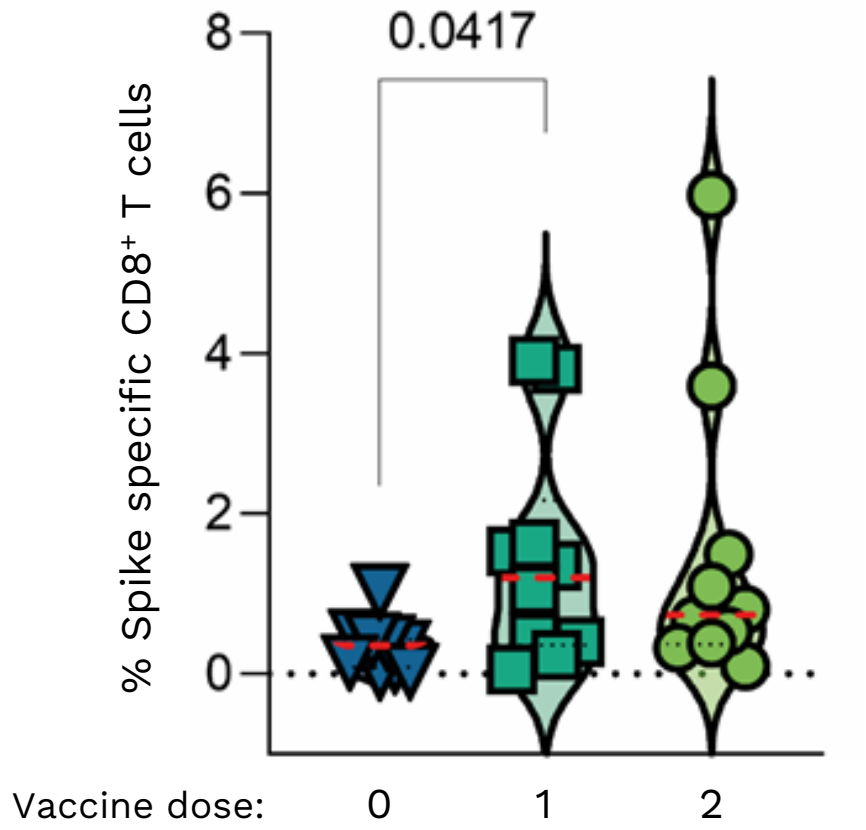


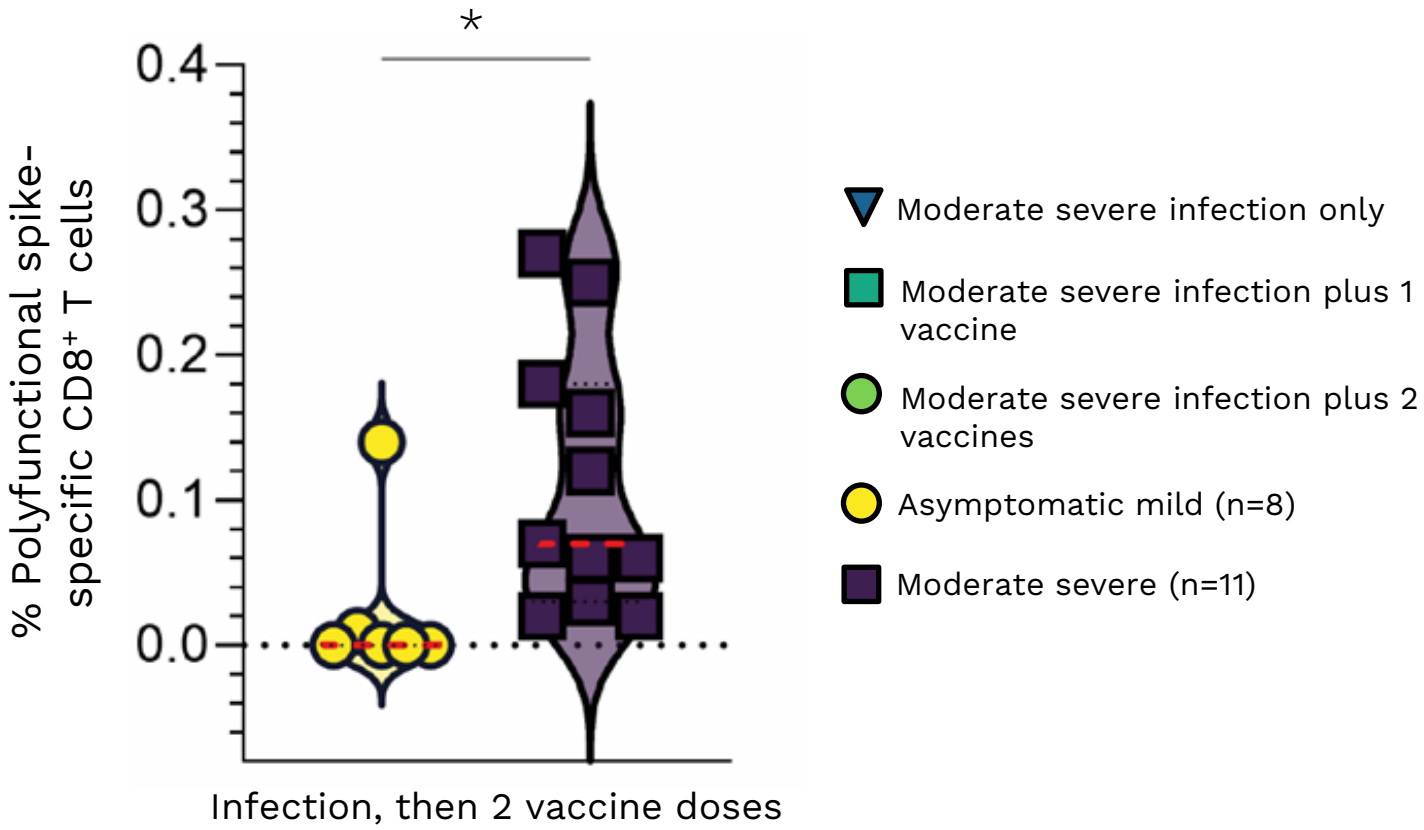


Mild infections do not induce as strong an immune response as severe infections



Severe COVID-19 + vaccination boosts long lasting memory T cells





Hybrid immunity: Infection *before* vaccination

Infection, then vaccination = higher levels of:

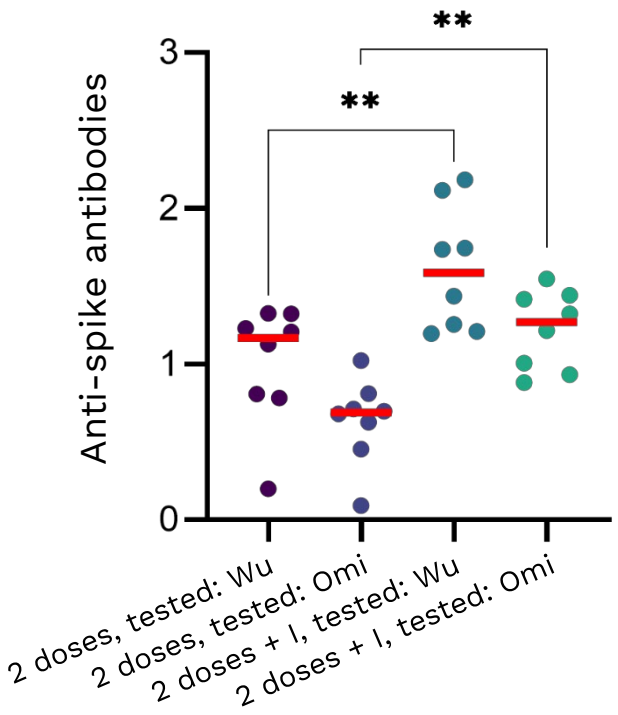
- Anti-spike antibodies
- Neutralization capacity
- Spike-directed antibody-dependent cell-mediated cytotoxicity
- Spike-specific T cells

vs. vaccination alone

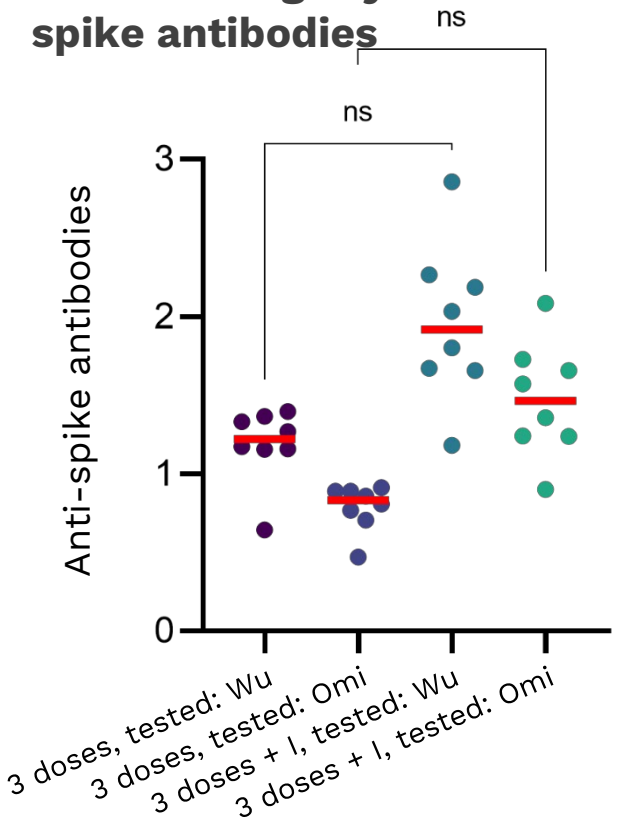
- Severe infection + vaccination = **stable memory** and **greater function**

Hybrid immunity: Infection *after* vaccination boosts anti-spike antibodies

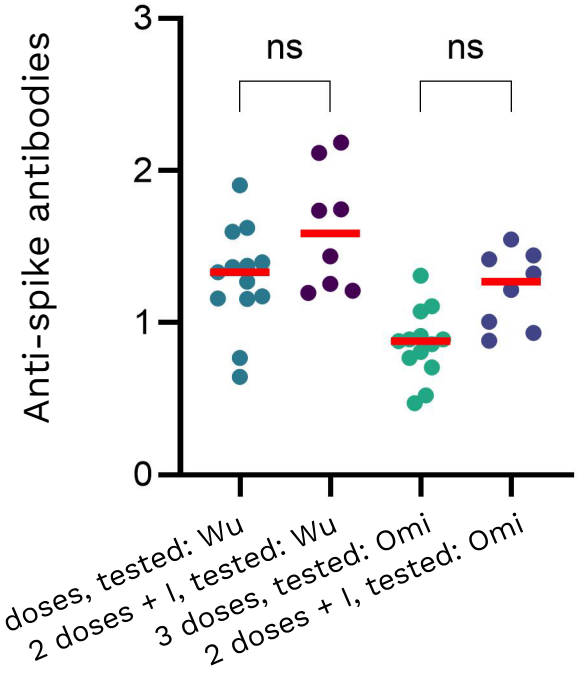
2 doses + Omicron infection boost spike antibodies



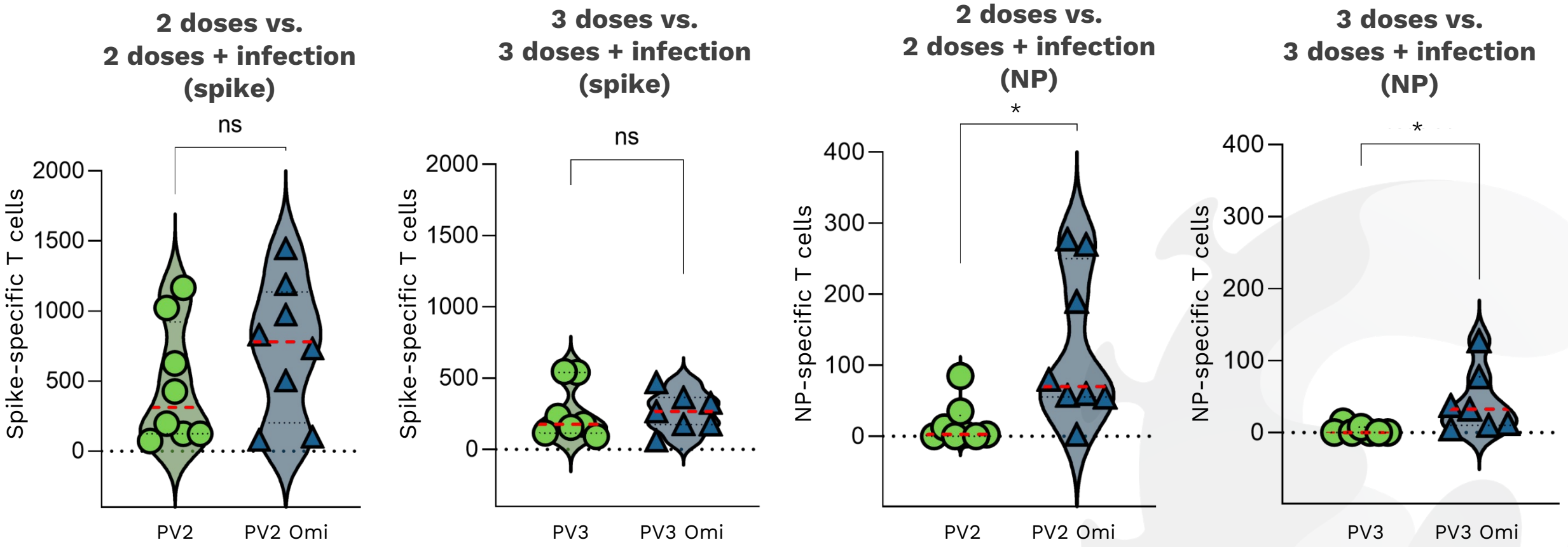
3 doses + Omicron infection slightly boost spike antibodies



3rd dose or breakthrough infection doesn't always induce stronger antibody response

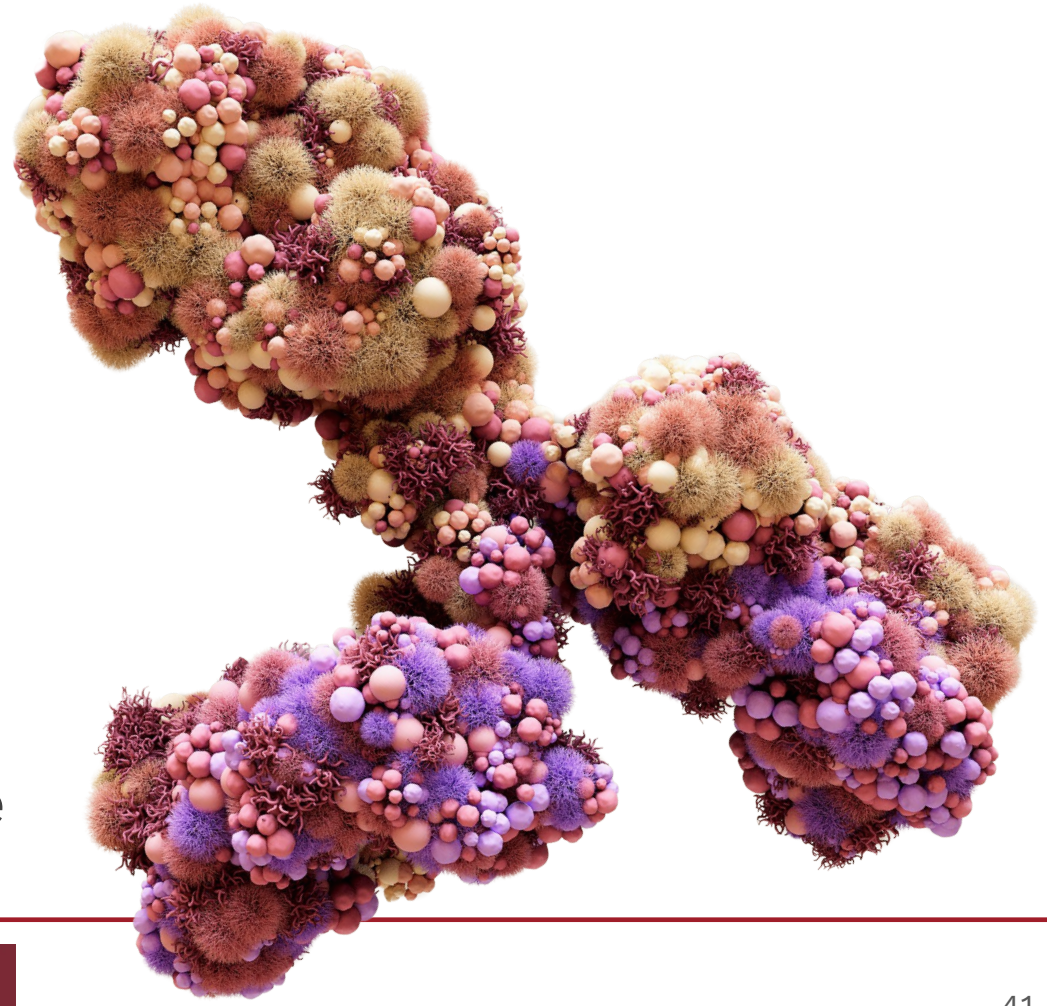


Hybrid immunity: Infection *after* vaccination boosts T cell response against nucleoprotein (NP)



Hybrid immunity: Infection *after* vaccination

- Anti-spike antibody levels boosted by infection after 2 vaccine doses – similar to 3rd vaccine dose
- Omicron infection after 2 or 3 vaccine doses induces *de novo* nucleoprotein-specific T cells
- A vaccinated person infected with Omicron makes more antibodies against Wuhan spike than against Omicron spike



Conclusions - hybrid immunity

- Antibody and T cell immunity against SARS-CoV-2 greater than seen with vaccination or infection alone
- Immunity is functionally enhanced when hybrid
- More is not necessarily better:
  - A 3rd dose or a breakthrough infection doesn't always have a major effect on Ab levels
- Incomplete immune response from Omicron infection
  - Omicron infection does not significantly boost vaccine-induced T cell immunity against spike

Study Team

Principal Investigators

Michael Grant, PhD
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Kayla Holder, PhD

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Danielle Ings, MSc
Kathleen Fifield, PhD
Debbie Harnum, RN
Donette O'Brien, RN

Funding:

COVID-19 IMMUNITY TASK FORCE
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b|e|i RESOURCES
SUPPORTING INFECTIOUS DISEASE RESEARCH

CIHR IRSC
Canadian Institutes of Health Research
Instituts de recherche en santé du Canada

National Research Council
NRC·CNRC Canada

Who has been most at risk?

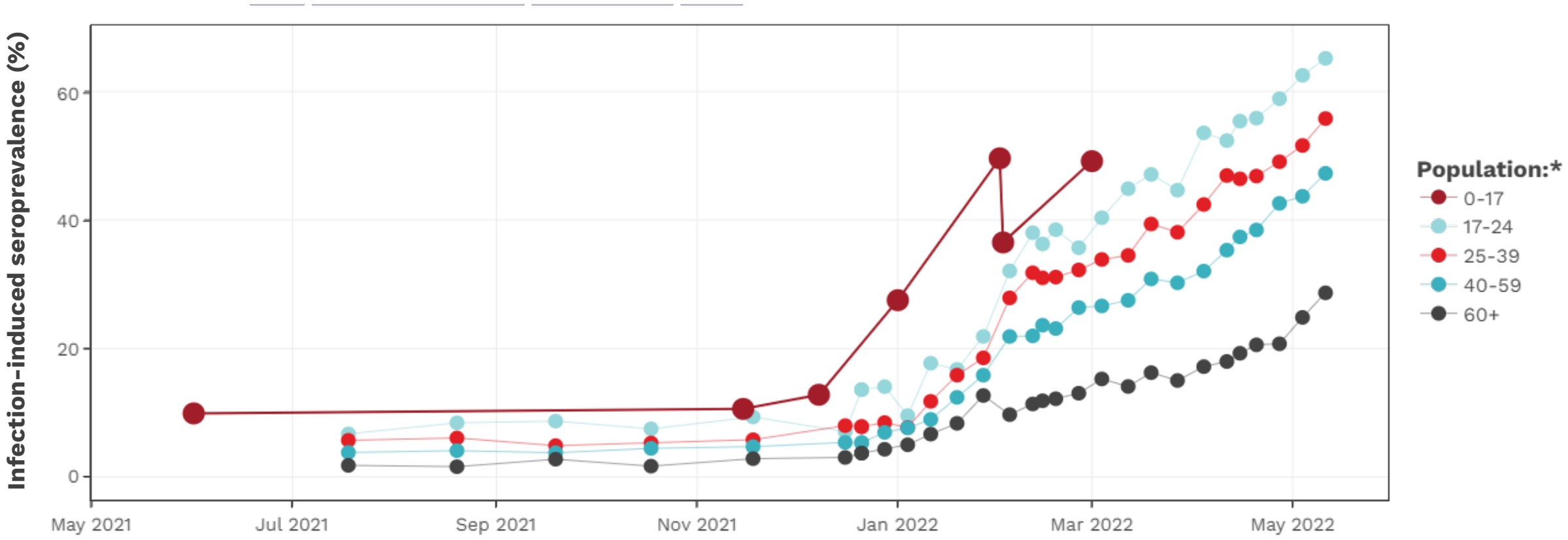
Conclusion & Implications

Dr. Catherine Hankins

Co-Chair, COVID-19 Immunity Task Force

Professor, School of Population and Global Health, Faculty of Medicine and Health Sciences, McGill University

Now, over 50% of young adults have infection-acquired antibodies



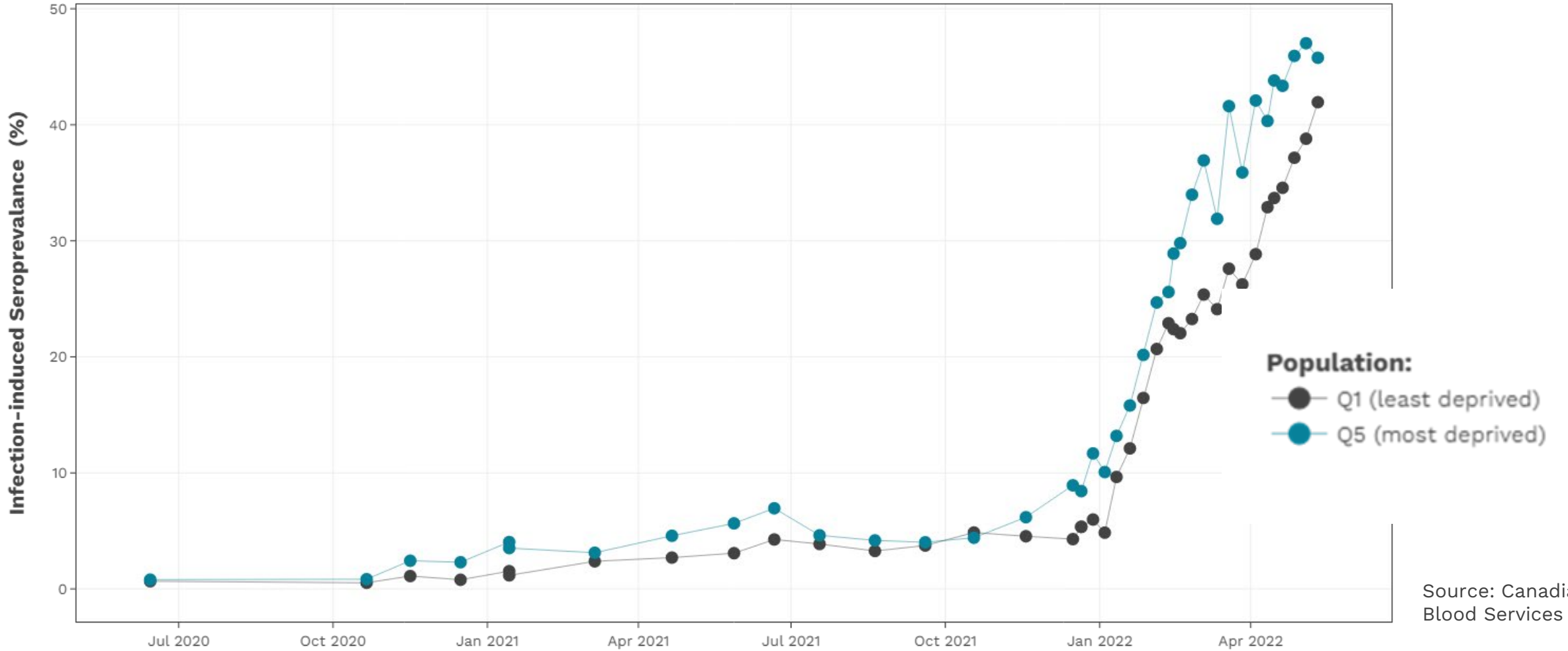
*Estimates for age groups 17-24, 25-39, 40-59 and 60+ were provided from Canadian Blood Services.

*Estimates from the 0-17 category were provided from EnCORE, Manitoba Seroprevalence, Saskatchewan Seroprevalence and Ste. Justine Hospital

Why are children and young adults so at risk of infection?

- Group settings such as school/university
- Greater social networks
- Front-line service jobs: coffee shops, restaurants
- Living situations: group settings, dormitories
- Lower perceived risk of COVID-19 (role of social media)
- More likely to have asymptomatic or mild disease, therefore
  - Less likely to get tested
  - May not test positive with rapid tests

Higher incidence of COVID-19 among lower-income Canadians



Source: Canadian Blood Services

Seroprevalence from infection higher among lower socioeconomic communities throughout pandemic

Population	Study	Infection-acquired seroprevalence	Comparator
Montreal-North (community with lower SES)	Jack Jedwab	12%, Aug.-Dec. 2021	5% in rest of Montreal, same period
Montreal-North children (community with lower SES)	EnCORE, Kate Zinszer	16.7% Nov- Dec 2021 *Most samples before Omicron	3.2% in children from West Island (high SES), same period
Multicultural dense urban neighbourhoods (tends to be lower SES)	Canada-wide household antibody study (StatCAN)	** Age-standardized mortality rate per 100,000 population **66.7**/100,000 in May 2021	**33.9**/100,000 in high SES urban neighbourhoods in May 2021

Why are those in lower income neighbourhoods more at risk?

> The pandemic has exposed **fault lines** in many aspects of society

Housing

- Multigenerational housing
- High population density

Reduced ability to self-isolate outside of work

- Essential workers
  - Children in daycare
- Reliance on public transit

Working conditions

- Many work in health care
- Inadequate PPE
- Public-facing roles
- Lack of sick days and health benefits
- Insecure employment

Why are those in lower income neighbourhoods more at risk?

> The pandemic has exposed **fault lines** in many aspects of society

Access to healthcare

- Reduced access to COVID testing
- Minority groups disproportionately affected by chronic medical conditions e.g., hypertension, diabetes, asthma, etc.
- Racial bias
- Lack of primary health provider
- Reticence to seek care
- Language barriers

Increased vaccine hesitancy in lower SES neighbourhoods

- 11% of Montreal-North residents likely to not vaccinate vs. 4% in rest of Montreal

Preparing for the next wave – likely in the fall

Everybody needs to keep up-to-date on vaccines… even post-infection

- The Omicron wave affected millions
- Breakthrough infections in vaccinated individuals have generated hybrid immunity
- Hybrid immunity helps protect against severe outcomes, but infection is not one size fits all
  - Variants offer different immune protection and duration
  - Severity of disease impacts your immune response

Infection is not a viable strategy to achieve or maintain immunity

- Risk of severe disease and death
- Threat of long COVID
- Spread of infection to others
- Unlike vaccination, infection is not guaranteed to induce immunity
  - 1 in 8 infected individuals do not seroconvert following an infection

Infection from one Omicron variant does not promise immunity against the next

Preparing for the next wave – likely in the fall

Continue to engage the public on the dangers of COVID-19

- The pandemic is **not over**
- The Omicron tsunami underscores the need to **resist pandemic fatigue**, get all recommended vaccines and respect public health efforts
- COVID presents **real risks**
- After effects of COVID (ex: **long COVID**) are still undetermined
- SARS-CoV-2 **can be transmitted** to people who can get very sick and die

Encourage Canadians to continue public health measures

- Despite public health measures no longer being mandated by provinces and territories, Canadians should use their common sense to protect themselves and their loved ones from COVID-19

Preparing for the next wave – likely in the fall

Increase vaccine confidence

- Vaccines have proven effective against severe disease and death from all variants of concern
- Highlight that vaccines do work: we must evaluate immune protection in terms of severe disease and death, not just the number of people infected
- Implement campaigns tailored to parents, young adults, those in lower-income areas, racialized communities… and everyone!

Discussion

What **strategy should people use** to decide when and whether to vaccinate?

- Another dose now? Wait until the fall?
- How long should one wait after infection to get another dose?
- Does everyone need a booster?

What vaccine strategy should **public health** adopt for the fall?

- Tailored for priority populations?
- Strategies by age grouping 5-17 years, 18-69 years, 70+ years?

What should **public messaging** include in preparation?

- Getting and staying up-to-date on vaccine protection?
- Importance of smart, common sense, assessments of risk (crowded, poorly ventilated settings)?
- Respect for those who wear and do not wear masks?
- Other?

Questions?

You'll find our summary of this seminar at

covid19immunitytaskforce.ca

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Annex | SeroTracker

We meta-analyzed serosurvey data in rolling windows to map changing seroprevalence over time and provide snapshot through Omicron

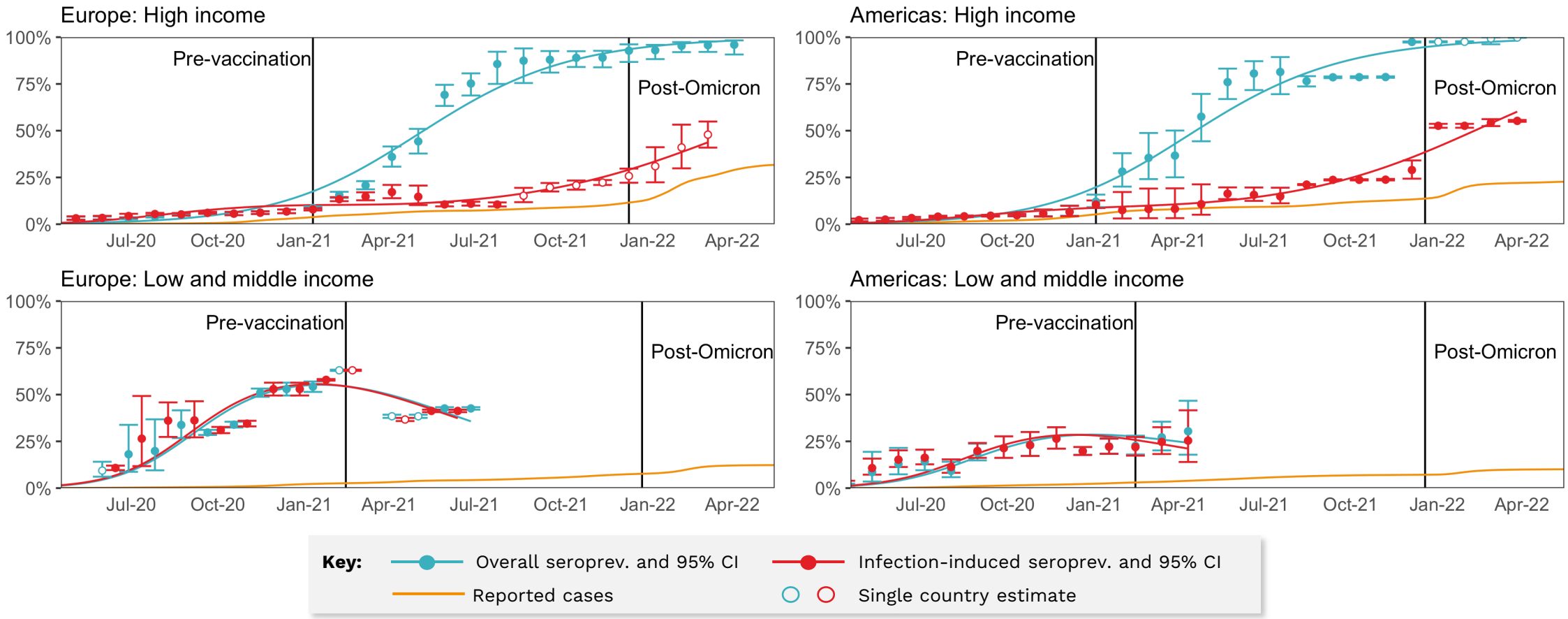
Identify eligible serosurvey data	Identify seroprevalence from infection	Pool by country, time	Aggregate by WHO region and globally	Smooth estimates
Identify national or subnational serosurveys at low or moderate risk of bias published through **May 27 2022** that estimate seroprev in the gen pop **(n = 733 in 84 countries)**[1]	**Where only S protein vaccines were used,** select only studies that detected anti-N seroprevalence. **Where inactivated vaccines were used,** adjust the observed seroprev using a standard formula[2]	Calculate **monthly overall and infection-induced seroprevalence** by pooling serosurveys by **sampling mid-point date** in each country in 12-week rolling windows with **random-effects meta-analysis**[3]	Estimate seroprevalence for each WHO region (and globally) as the **weighted average** of country (and WHO region) meta-analysis estimates	Fit a **generalized additive model** (GAM) to produce smooth model estimates of seroprev. over time. Estimate frequency varies by region due to publication delay. **Results are updated regularly**

Notes:

1. Includes household and community samples, residual sera, blood donors, pregnant or parturient women, and multiple general population sampling frames.
2. Institute for Health metrics and Evaluation (IHME) (2021) COVID-19: Estimating the historical time series of infections. IHME, University of Washington, Seattle, Washington, USA
3. This step is repeated twice: using all serosurveys and using only serosurveys detecting seroprevalence from infection.

'Sampling midpoint' date of the study - the date halfway between seroprevalence study sample collection start and end.
Refer to pre-print for additional methods: https://www.medrxiv.org/content/10.1101/2021.12.14.21267791v2.full-text

Seroprevalence over time in all regions



Seroprevalence over time in all regions (continued)