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

Seminar Series | Research Results & Implications

COVID-19 and older Canadians: Where are we now?

October 18, 2022 | 2:30-4:00 p.m. EDT

Moderator

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Provincial Lead, Ontario's Seniors Strategy

Professor of Medicine, University of Toronto

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Panelists

Timothy Evans, MD, PhD, Executive Director, COVID-19 Immunity Task Force

Manish Sadarangani, BM, BCH, DPhil, Director, Vaccine Evaluation Center, BC Children's Hospital Research Institute; Associate Professor, Division of Infectious Diseases, Department of Pediatrics, UBC; Physician Lead, Family Immunization Clinic, BC Children's Hospital; CITF-funded researcher

Sharon Walmsley, MSc, MD, FRCPC, Senior Scientist, Toronto General Hospital Research Institute; Professor, Department of Medicine, University of Toronto; CITF-funded researcher

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Land Acknowledgement

The Dish With One Spoon is a treaty between the Anishinaabe, Mississaugas and Haudenosaunee that bound them to share the territory and protect the land. Subsequent Indigenous Nations and peoples, Europeans and all newcomers have been invited into this treaty in the spirit of peace, friendship and respect.

Land Acknowledgement

I am speaking to you from my place of work at McGill University, which is on land which has long served as a site of meeting and exchange amongst Indigenous Peoples, including the Haudenosaunee and Anishinabeg nations. I'd like to acknowledge and thank the diverse Indigenous Peoples whose presence marks this territory on which peoples of the world now gather.

Land acknowledgement

BC Children's Hospital Research Institute operates on the traditional, ancestral, and unceded territory of the Coast Salish peoples — xʷməθkʷəyʼəm (Musqueam), Sḵwxw̱ú7mesh (Squamish), and Səlʼilw̓ətaʔ/Selilwitulh (Tsleil-Waututh) Nations.

Land Acknowledgement

I respectfully acknowledge that I am an uninvited settler on the unceded traditional territories of the Coast Salish peoples, the xʷməθkʷəyʼəm (Musqueam), Sḵwxw̱ú7mesh Úxwumixw (Squamish) and səlʼilwʼətaʔɬ (Tsleil-Waututh) peoples.

Land acknowledgement

McMaster University recognizes and acknowledges that it is located on the traditional territories of the Mississauga and Haudenosaunee nations, and within the lands protected by the “Dish with One Spoon” wampum agreement.

COVID-19 Immunity
Task Force

Tim Evans, MD, PhD

Executive Director, COVID-19 Immunity Task Force

Professor, Director and Associate Dean of the School of Population and Global Health, Faculty of Medicine, McGill University

Disclaimer

I have no COIs to declare related to this study.

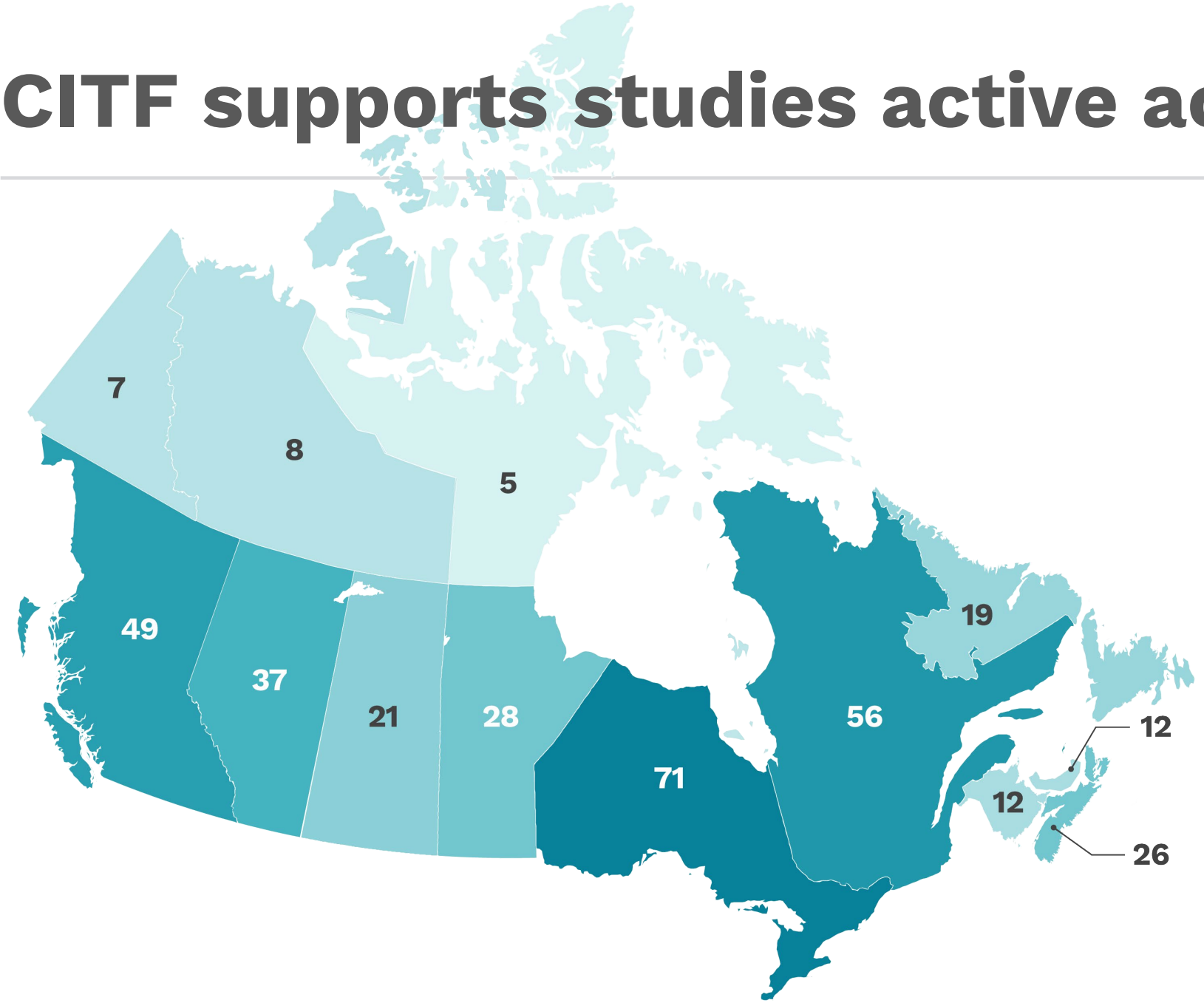
COVID-19 Immunity Task Force mandate

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



119 studies, 7 of which focus on older Canadians

Burden of the COVID-19 pandemic on older Canadians

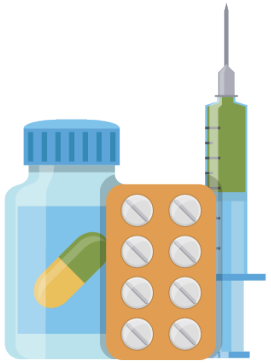
By September 16th, 2022, people aged 70+ in Canada accounted for

82%

of all COVID-19 **deaths** and **50%** of all SARS-CoV-2 related **hospitalizations**.

Why are older people more vulnerable?

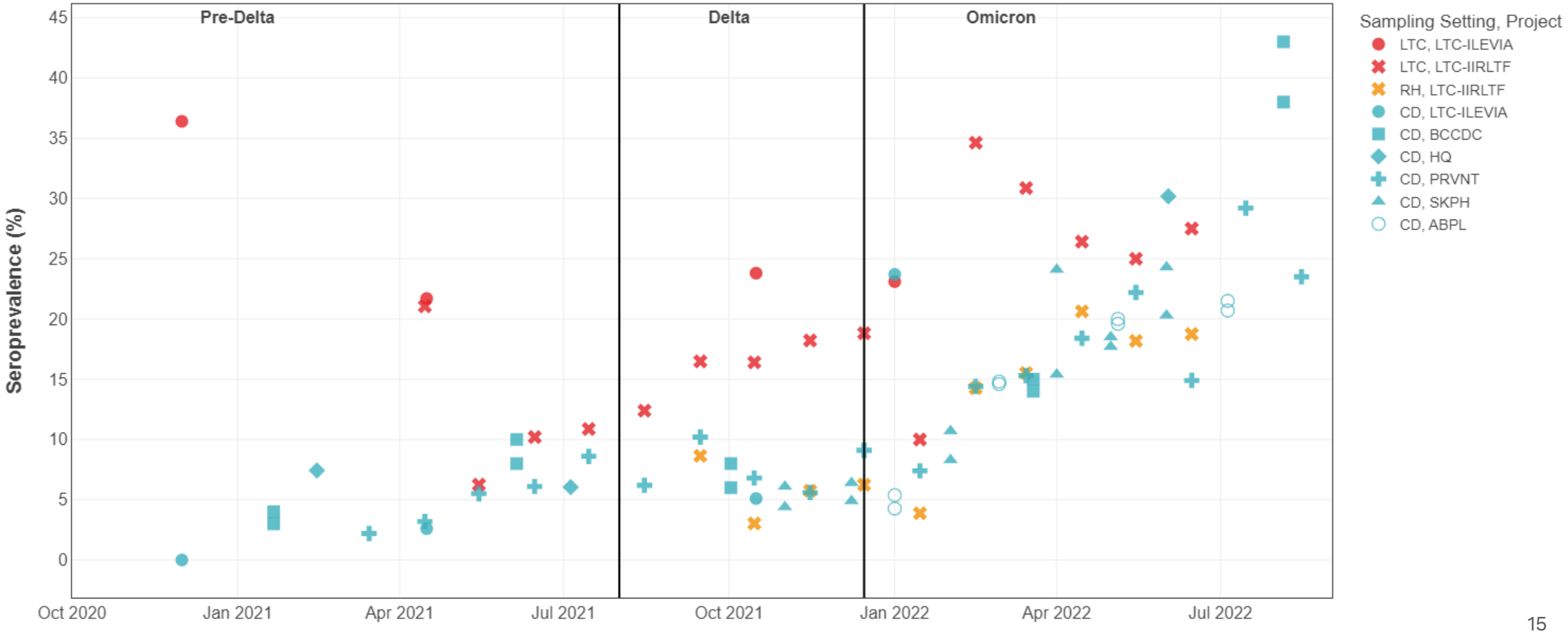
Frailty and older age
mean a weaker immune system



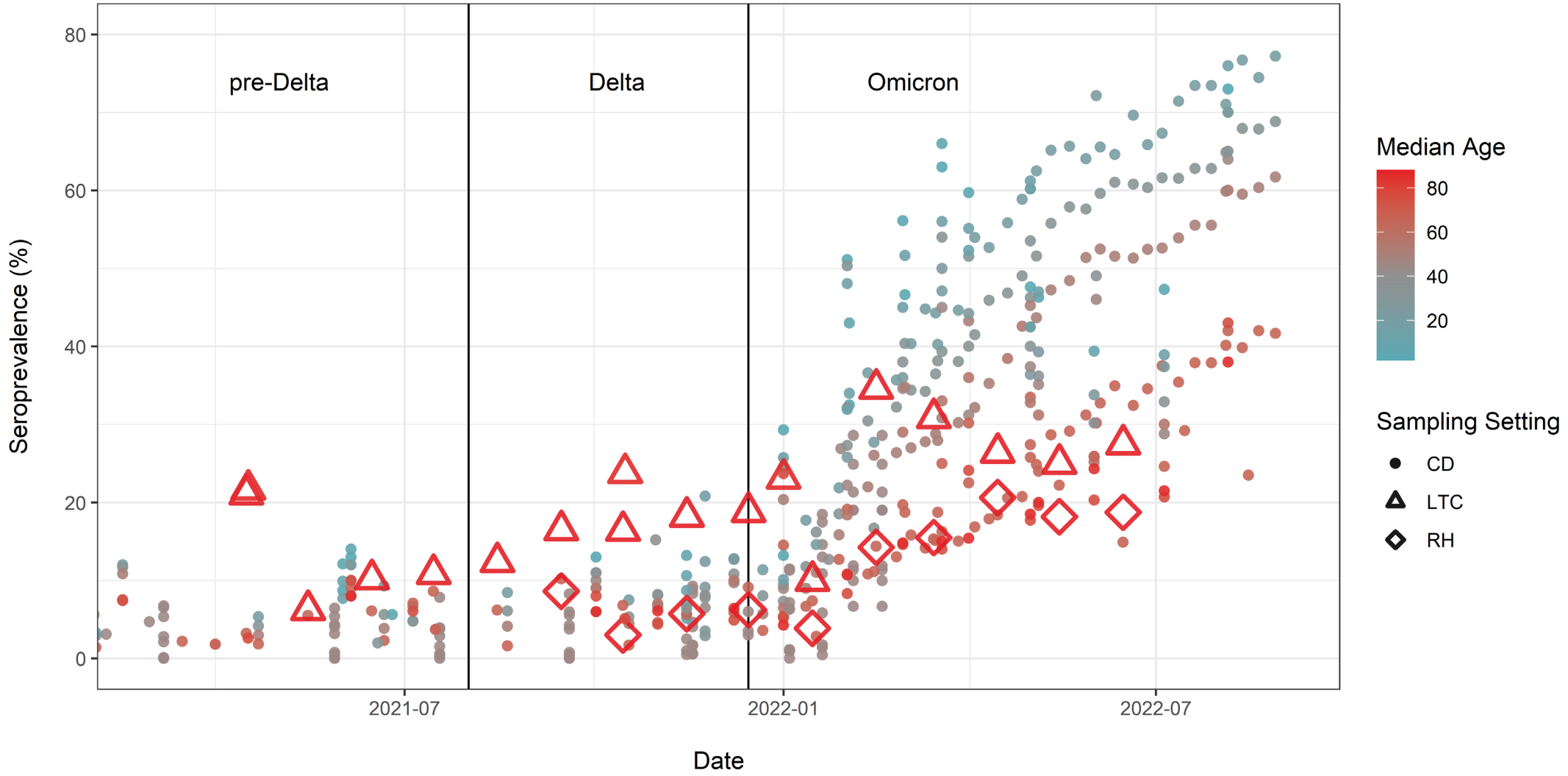
Underlying medical conditions
often accumulate with age and increase the risk

Communal living in seniors' residences
increases the risk of SARS-CoV-2 outbreaks

Rates of infection amongst seniors highest in LTC residents throughout pandemic



LTC residents had highest infection rates until Omicron wave when surpassed by younger age groups



The PREVENT-COVID Study

PRospEctiVe EvaluatioN of immuniTy after COVID-19 vaccines

British Columbia

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Disclosures

Salary awards

BC Children's Hospital Foundation
Michael Smith Foundation for Health Research

Research/Project Funding

Merck, Moderna, VBI Vaccines, GlaxoSmithKline, Pfizer, Sanofi-Pasteur, Seqirus, Symvivo

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All funds have been paid to my institute, **no personal payments** have been received.

PREVENT-COVID

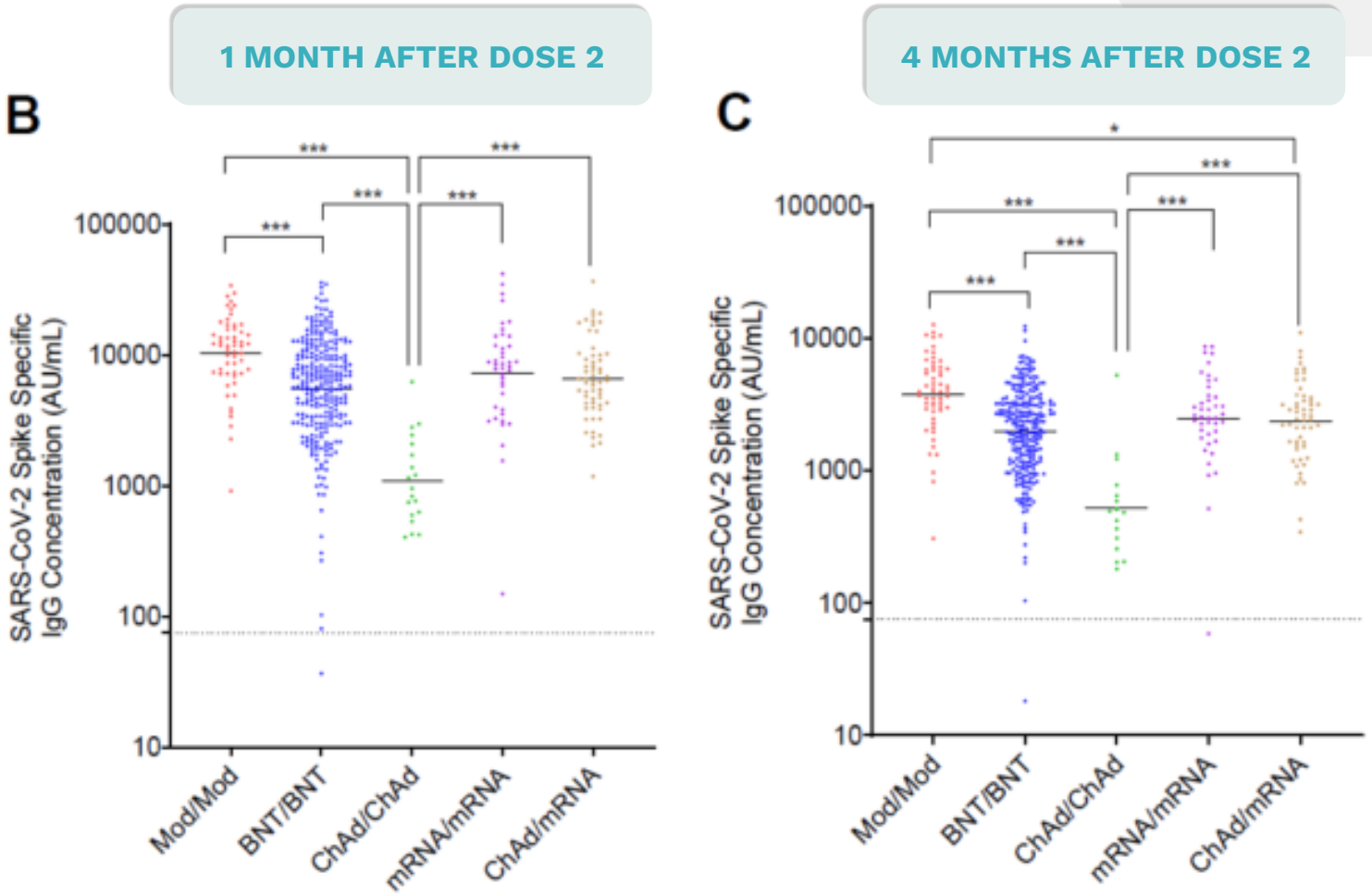
PRospEctiVe EvaluatioN of immuniTy after COVID-19 vaccines

Study Objectives

- Establish immunogenicity of COVID-19 vaccines in adults aged >50 years
  - BNT162b2 (BNT), mRNA-1273 (Mod), ChAdOx1-S (ChAd)
- Characterize the protection generated by COVID-19 vaccines
- Explore the influence of the following on the response to COVID-19 vaccines:
  - Prior hCoV infection
  - Prior SARS-CoV-2 infection
- Evaluate cell-mediated immune responses to COVID-19 vaccines

Antibody responses after 2 doses of vaccine

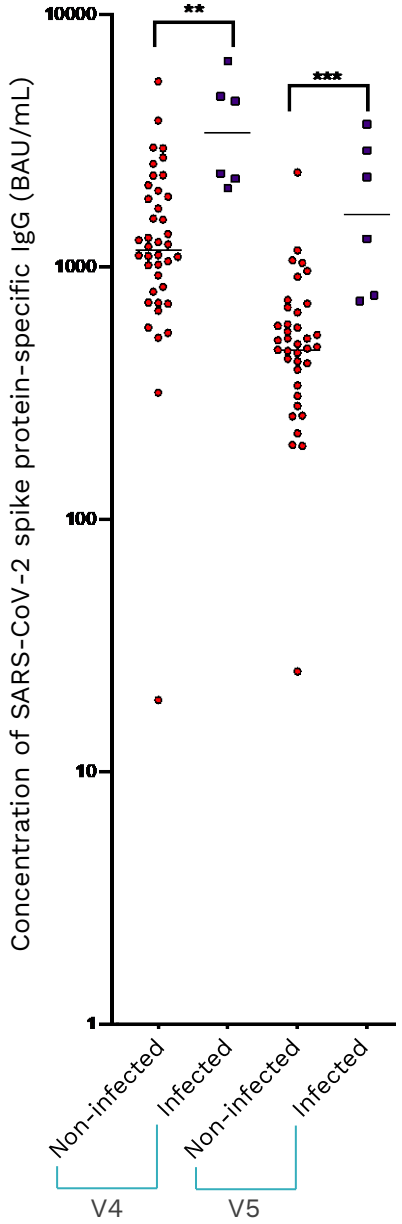
- 2 doses Moderna led to higher antibody levels than 2 doses Pfizer
- AstraZeneca followed by mRNA similar to 2 doses Pfizer
- For all regimens, antibodies were waning 1 → 4 months after dose 2



Horizontal line indicates positivity threshold.
Two-way ANOVA with Tukey-Kramer multiple comparisons tests performed on $\log_{10}$ transformed data.

* $P < .05$, ** $P < .01$, *** $P < .001$

People with prior infection had higher antibody levels after 2 doses



____ represents the geometric mean concentration

* p < 0.05
** p < 0.01
*** p < 0.001
**** p < 0.0001

V4 = visit 4, 1-month post-dose 2
V5 = visit 5, 4-months post-dose 2

Main determinants of antibody response

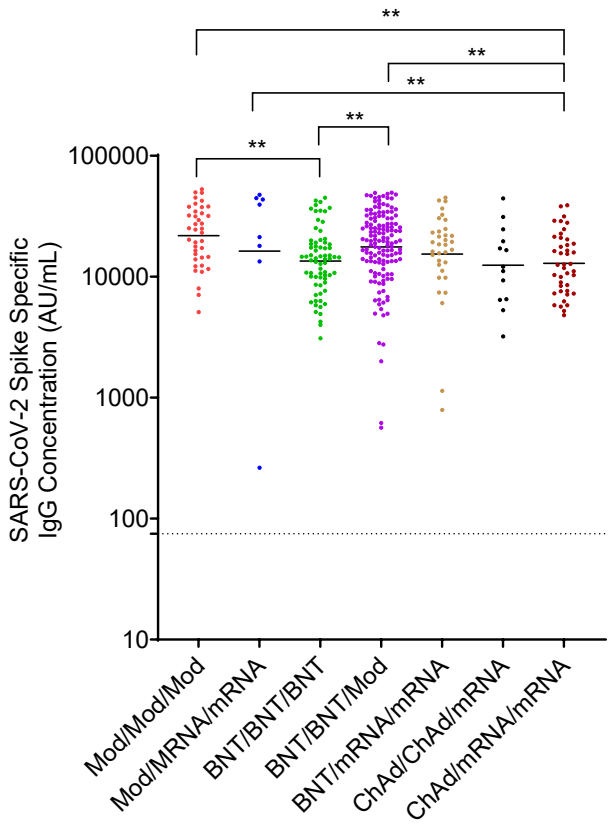
Antibody levels were higher after 2 doses in those who:

- Had a previous infection
- Received 2 doses of Moderna
- Had their 2nd dose 14 weeks or more after the 1st

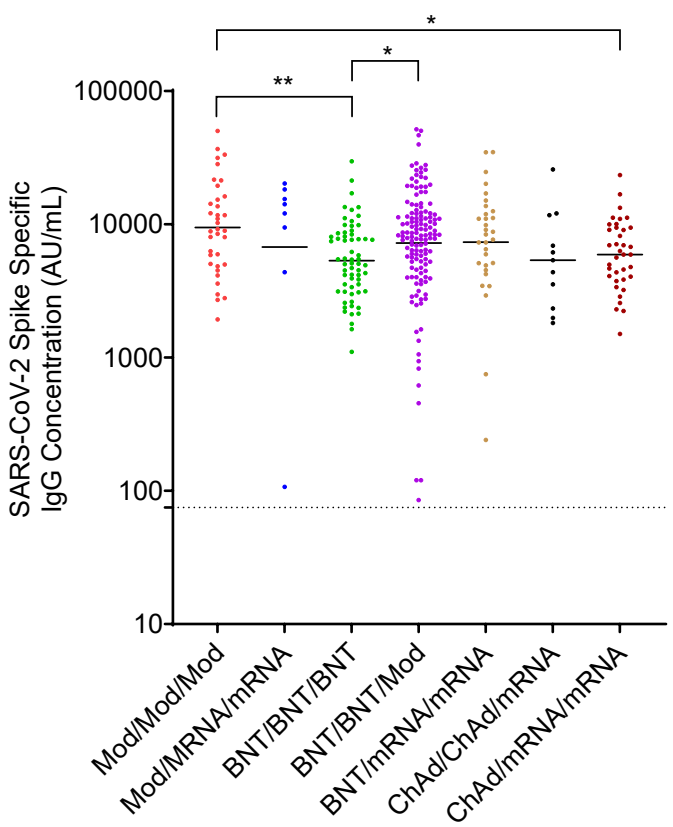
Timepoint	Variable	Regression coefficient (95% CI)	*P* value
1 month Post dose 2	Infection status		
	Uninfected	[Reference]	
	Infected	**0.68** (0.38 – 0.98)	< .001
	Vaccine type		
	BNT/BNT	[Reference]	
	Mod/Mod	**0.63** (0.38 – 0.88)	< .001
	ChAd/ChAd	**-1.56** (-1.98 – -1.15)	< .001
	mRNA/mRNA	**0.32** (0.05 – 0.60)	.02
	ChAd/mRNA	**0.23** (-0.01 – 0.48)	.063
	Vaccine interval		
	<14 weeks	[Reference]	
	≥ 14 weeks	**0.47** (0.14 – 0.80)	.005
4 months Post dose 2	Sex		
	Female	[Reference]	
	Male	**-0.27** (-0.42 – -0.12)	< .001
	Infection status		
	Uninfected	[Reference]	
	Infected	**0.91** (0.63 – 1.2)	< .001
	Vaccine type		
	BNT/BNT	[Reference]	
	Mod/Mod	**0.61** (0.39 – 0.83)	< .001
	ChAd/ChAd	**-1.35** (-1.75 – -0.95)	< .001
	mRNA/mRNA	**0.23** (-0.009 – 0.48)	.059
	ChAd/mRNA	**0.20** (-0.01 – 0.43)	.072
	Vaccine interval		
	<14 weeks	[Reference]	
	≥ 14 weeks	**0.38** (0.07 – 0.69)	.015

Booster of mRNA vaccine provides robust and durable antibody responses, irrespective of combination

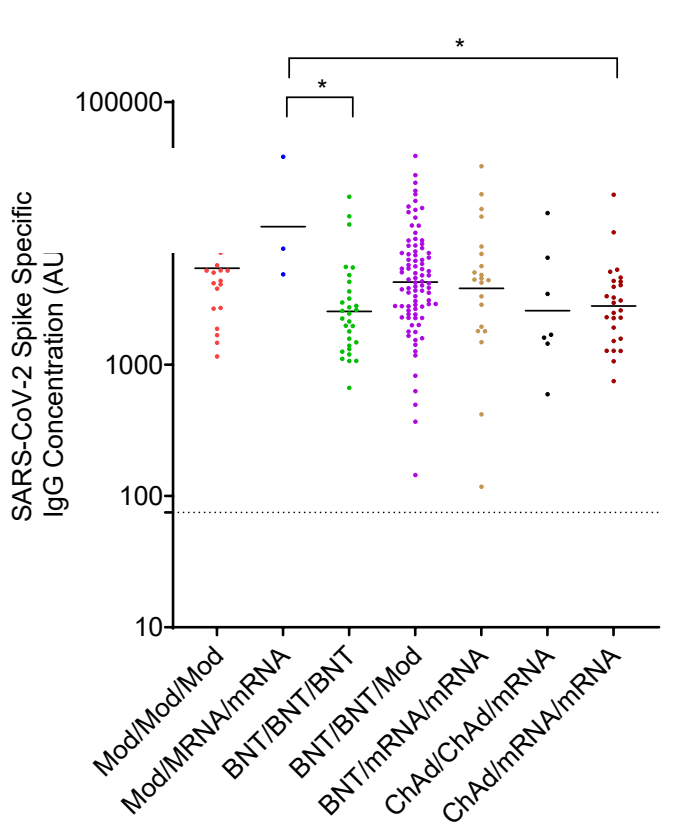
1 MONTH AFTER DOSE 3



4 MONTHS AFTER DOSE 3



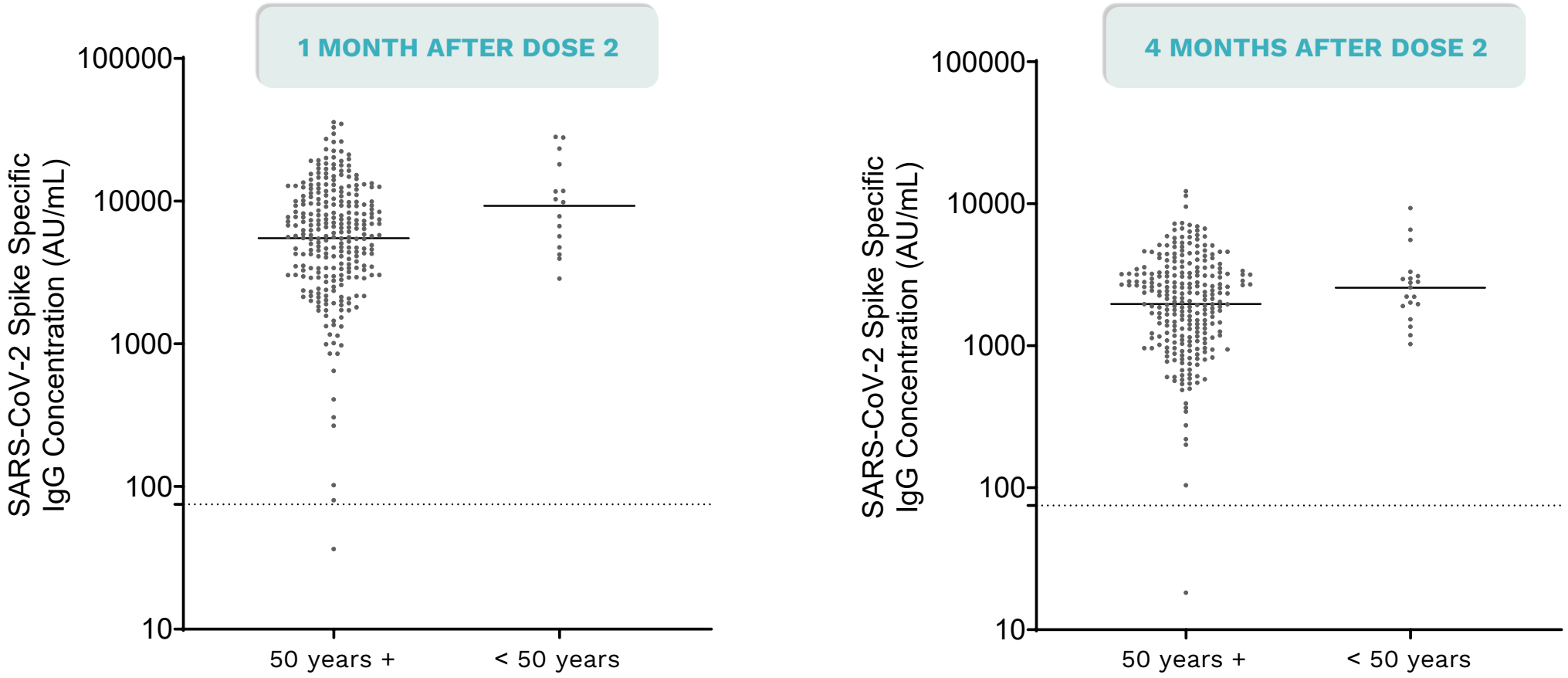
7 MONTHS AFTER DOSE 3



One way ANOVA with Kruskal Wallis multiple comparisons test

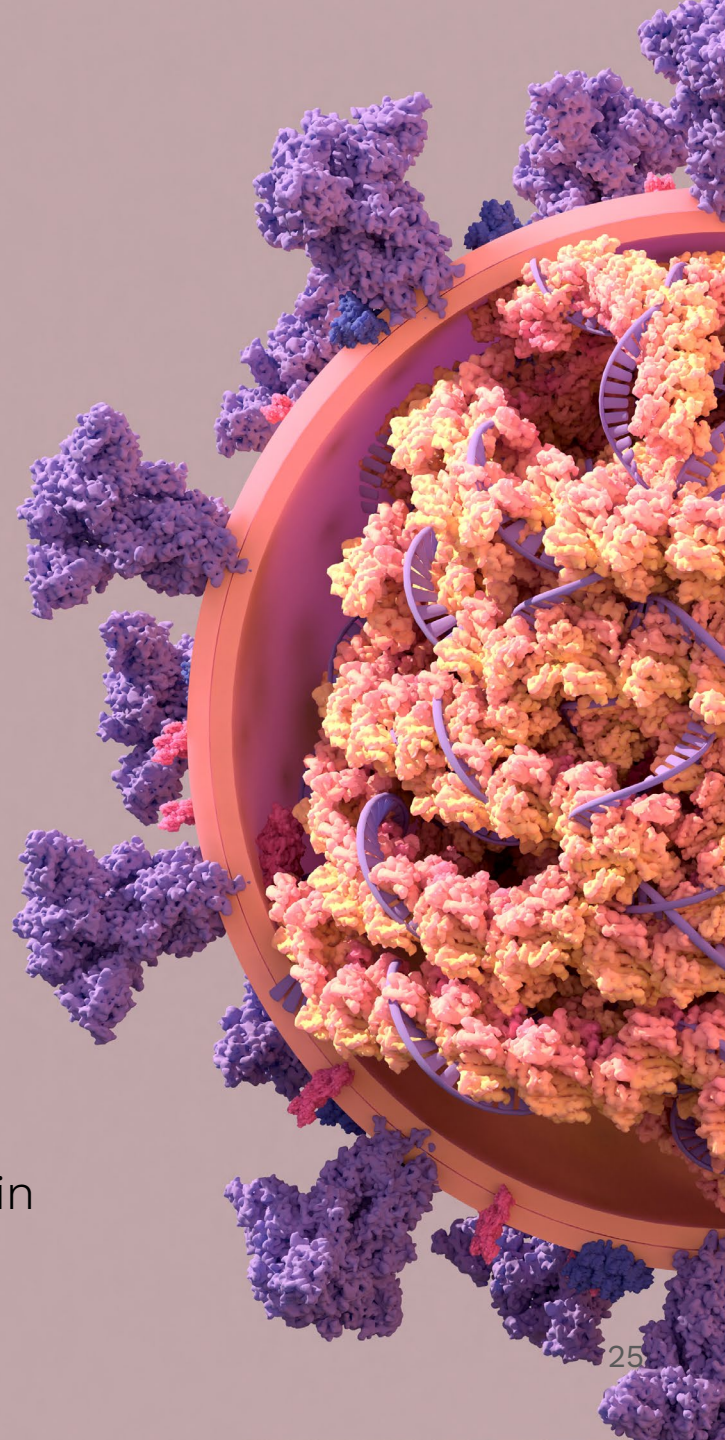
** P < 0.01,
* P < 0.05

Similar antibody response in individuals >50 yrs *vs.* younger adults



Conclusions

- mRNA vaccines elicit higher antibody responses than AstraZeneca after 2 doses, particularly Moderna; smaller differences after booster
  - Note there is no correlate of protection, so this does not indicate clinical significance
  - mRNA vaccines give higher effectiveness against any symptomatic COVID-19
  - All 3 vaccines similarly effective against severe disease endpoints
- Antibody amount correlates with some functions, but not all
  - Functional activity is likely important in protection and may explain incomplete correlation between antibody level and clinical outcomes
- Prior infection and longer interval → higher antibody responses
  - Sex may also be an important determinant and should be considered in all vaccine/immunity studies
- Highlights utility of DBS, which may be valuable in future studies



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BC's health research funding agency

Public Health Agency of Canada
Agence de la santé publique du Canada

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

CIRN
CANADIAN IMMUNIZATION RESEARCH NETWORK

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

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Thank you

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STOP-CoV

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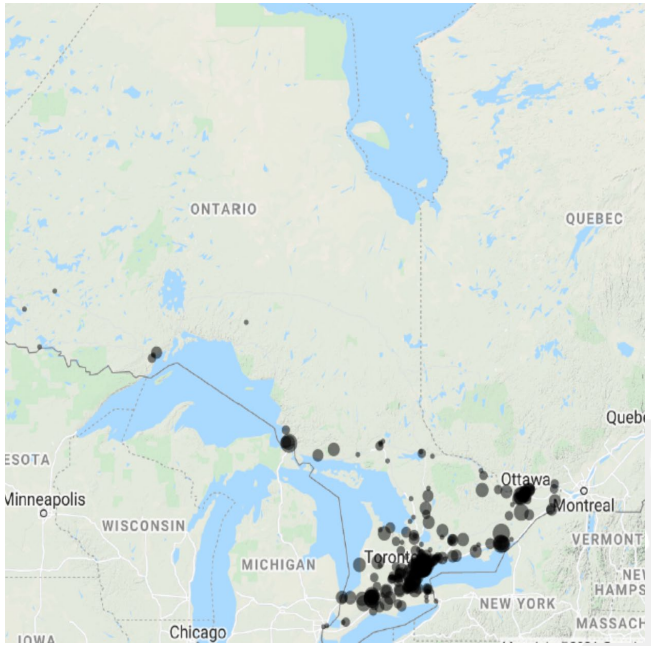
Disclaimer

I have no COIs to declare related to this study.

Our decentralized study follows people aged 70+ in Ontario and compares them to those 30-50 years

www.stopcov.ca



Study population

70+ years (n= 853)
30-50 years (n= 341)

Procedures online

- Consent
- Questionnaires
- Monthly check-in
- Schedule of activities
- Email reminders
- Results

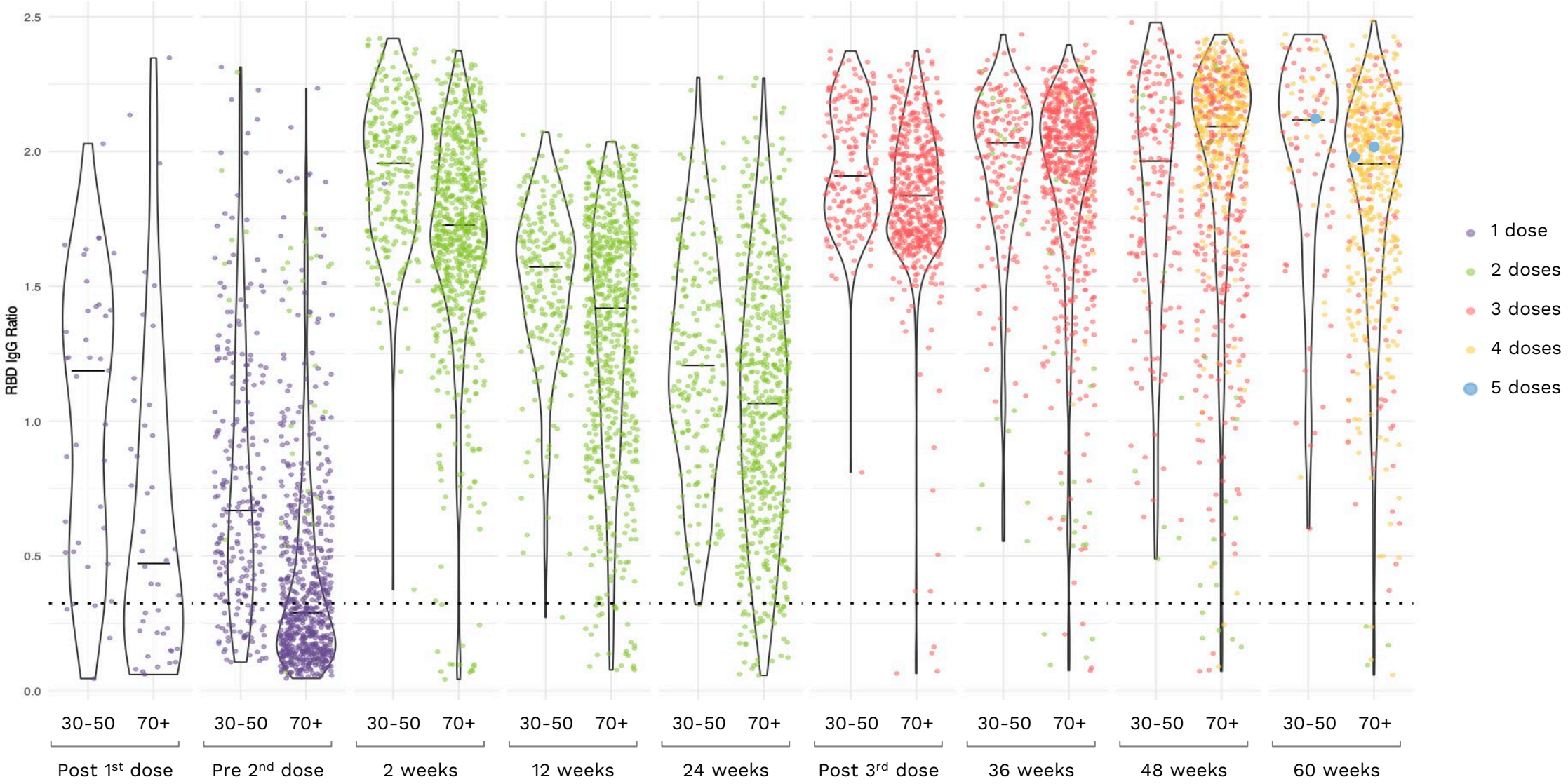
Self-collected

- Dried blood spots

Differences in baseline characteristics of cohorts & vaccines received

	30-50	70+	p
N	340	852	
Age	41 (36, 45)	73 (71, 76)	<0.0001
Female or Non-Binary	254 (75.6)	505 (59.5)	<0.0001
Racial background			0.0005
Arab / West Indian	3 (0.9)	7 (0.8)	
Black	11 (3.3)	9 (1.1)	
Southeast Asian	20 (6.0)	12 (1.4)	
White	253 (75.3)	791 (93.2)	
Smoking status			<0.0001
Never	237 (70.5)	431 (50.8)	
Previous	68 (20.2)	384 (45.2)	
Current	31 (9.2)	34 (4.0)	
Comorbidities			
Diabetes	5 (1.5)	121 (14.3)	<0.0001
Cardiovascular disease	16 (4.8)	409(48.2)	<0.0001
Cancer	9 (2.7)	171 (20.1)	<0.0001
Asthma	48 (14.3)	76 (9.0)	0.0094
Vaccine Types			<0.0001
Two doses of BNT162b2	161 (48.6)	572 (68.2)	
Two doses of mRNA-1273	61 (18.4)	70 (8.3)	
One dose of BNT162b2, one dose of mRNA-1273	57 (17.2)	145 (17.3)	
One dose of AstraZeneca Vaxzevria, one dose of BNT162b2 or mRNA-1273	38 (11.5)	30 (3.6)	
Other combinations or unknown	14 (4.2)	22 (2.6)	
Weeks between vaccine doses	8 (6.3, 9.4)	11 (9.6, 12)	<0.0001

Anti-RBD antibody ratios increase with each dose but decline faster in the older cohort



Substudy: Breakthrough infections and the performance of Rapid Antigen Tests

n=806

588 in older cohort,
218 in younger cohort

90%

completed at least one
Rapid Antigen Test (RAT)

7116 tests

January 28 - March 29, 2022

n=25

tested positive (3.4%), all
mild, 20/25 had booster prior

64%

had positive anti-NP
mean of 60 days later

36%

had negative NP mean
40 days later

No difference

in anti-RBD levels in those
with or without positive RAT

For those without a positive RAT:

105

reported at least
one symptom

96

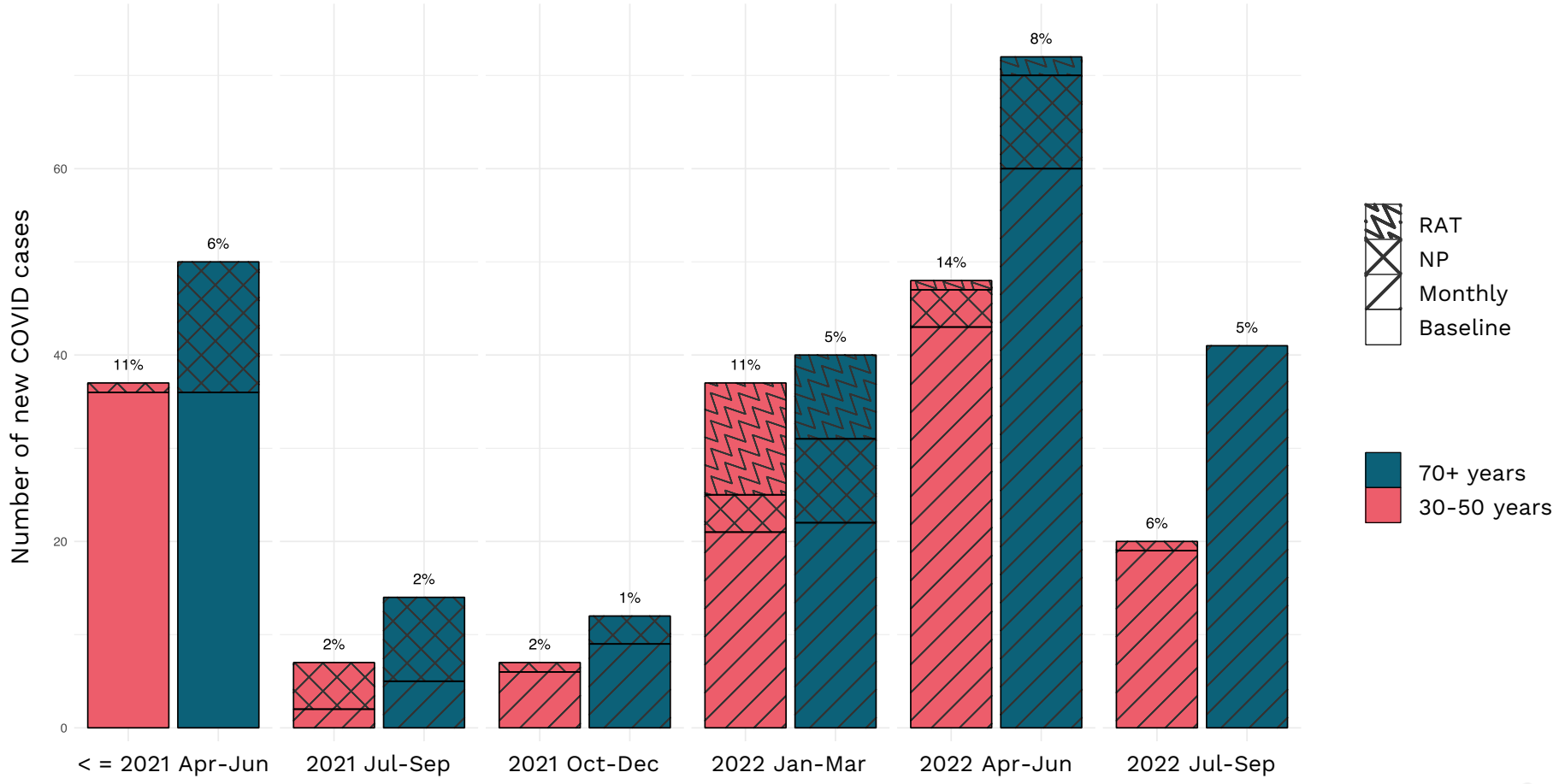
reported two or
more symptoms

4-6.6%

False negative RAT rate
compared to subsequent NP

JAMMI, in press, 2022

Older cohort had fewer infections than younger



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Antibody responses to COVID-19 vaccination in elder adults

Results from Vancouver, BC

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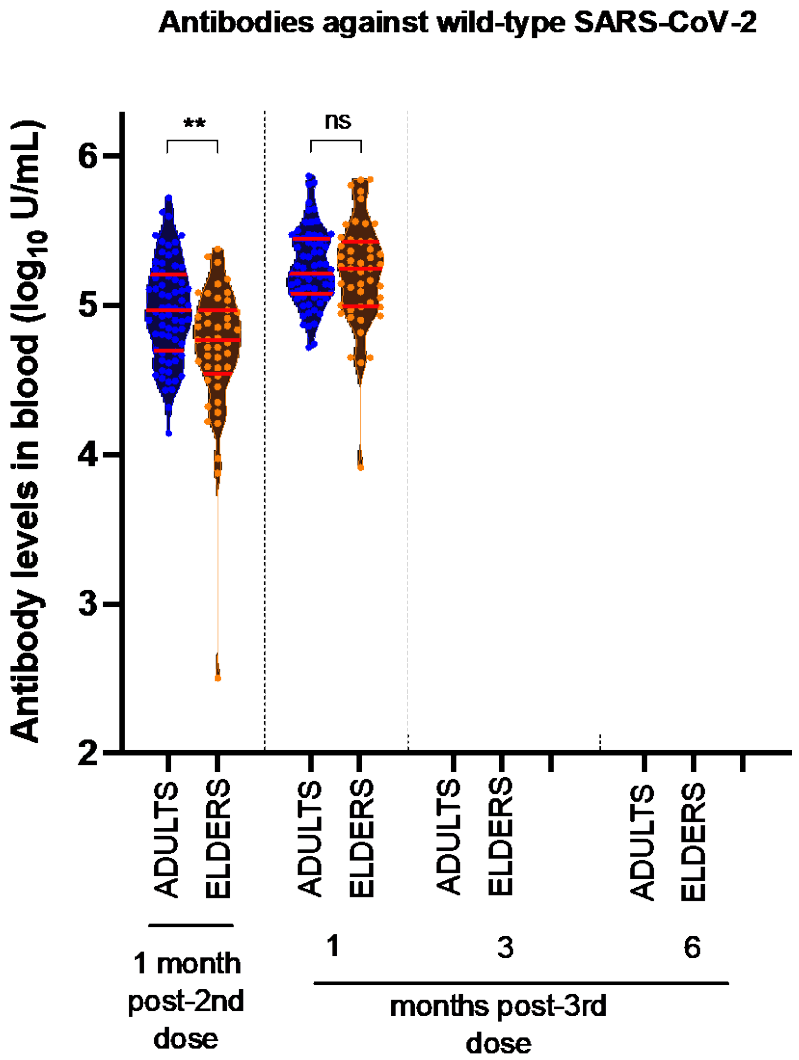
BRITISH COLUMBIA CENTRE *for* EXCELLENCE *in* HIV/AIDS

Disclaimer

I have no COIs to declare related to this study.

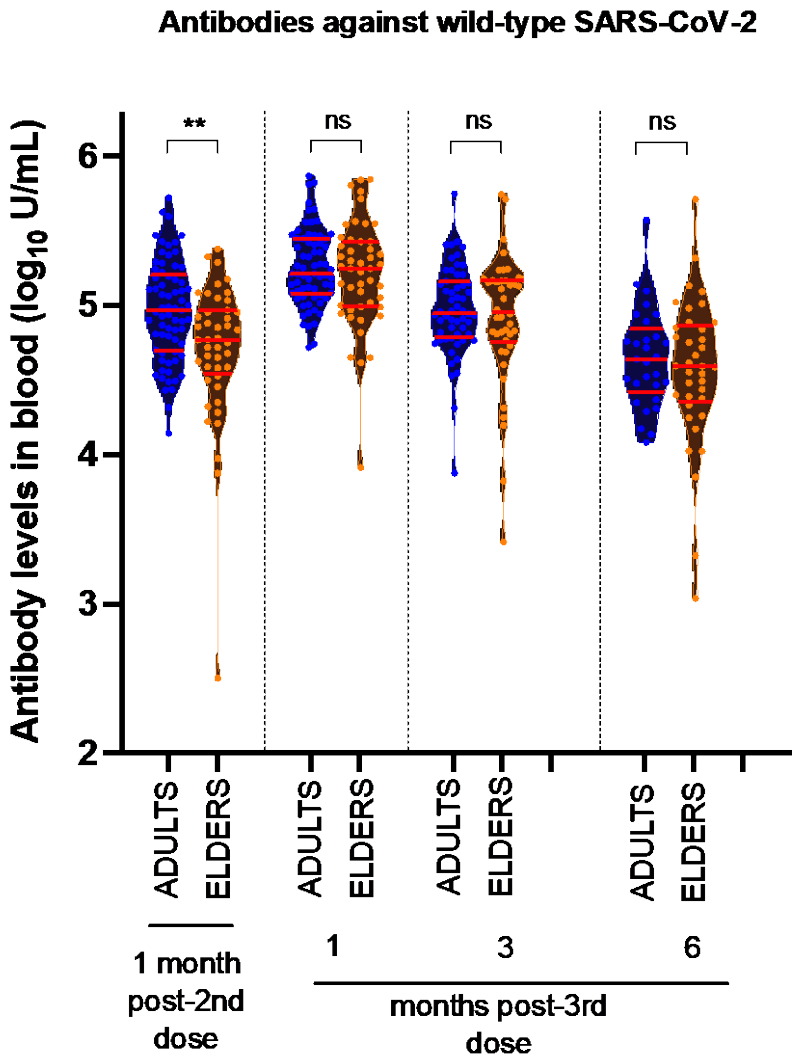
It takes three COVID-19 mRNA vaccine doses for antibody levels in elder adults to reach equivalence to younger adults

- Younger adults (median 41 years old)
- Elder adults (median 78 years old)



Antibody levels decline relatively quickly following vaccination

- Younger adults (median 41 years old)
- Elder adults (median 78 years old)



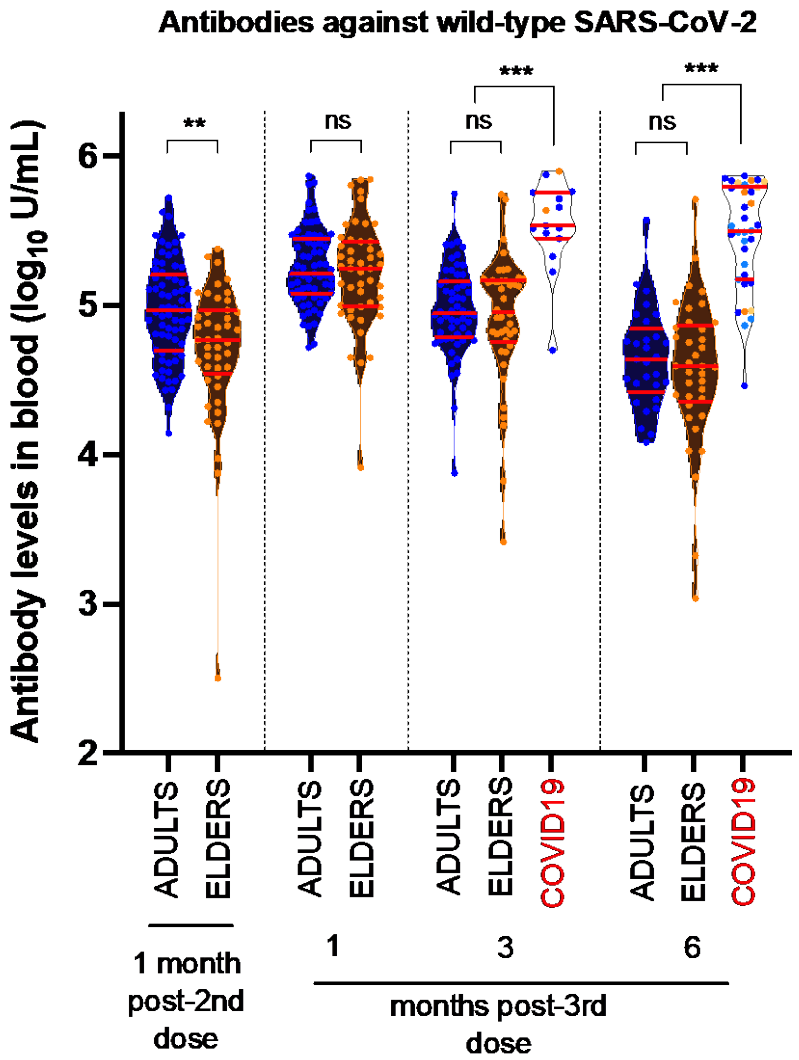
The rate of antibody decline is **comparable** in elder and younger adults.

By 6 months after the 3rd dose, antibody levels have generally **declined** to below the levels initially induced by 2 doses.

Individuals who got COVID-19 after 3 vaccine doses got a big antibody boost

- Younger adults (median 41 years old)
- Elder adults (median 78 years old)

COVID19 Participants who got COVID-19 after 3 vaccine doses

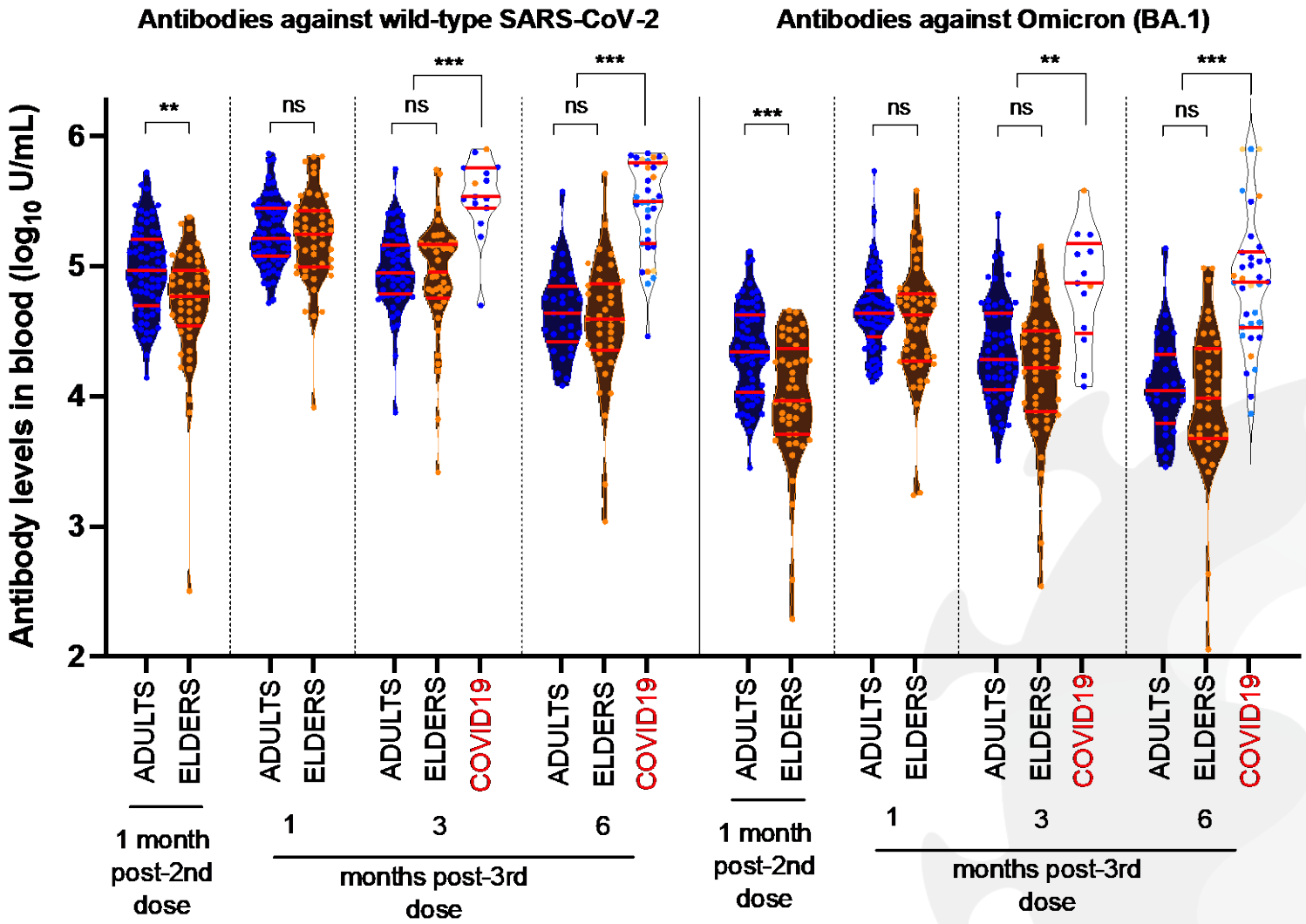


Six months after the 3rd dose, antibody levels in this group were **higher** than those induced by 3 vaccine doses alone.

Identical trends are seen for Omicron BA.1-specific antibodies, though these levels are far lower than to the wild-type strain

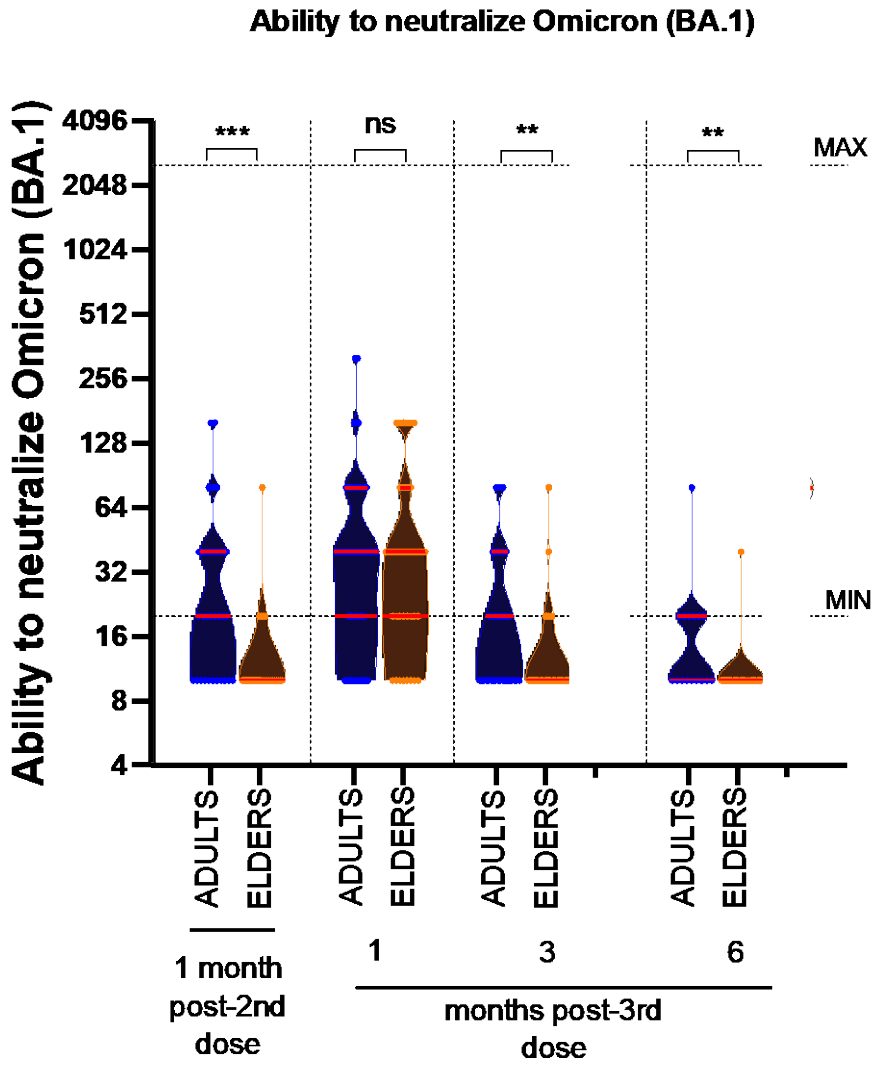
- Younger adults (median 41 years old)
- Elder adults (median 78 years old)

COVID19 Participants who got COVID-19 after 3 vaccine doses



Antibody *function* against the Omicron (BA.1) strain declines more quickly in elder adults

- Younger adults (median 41 years old)
- Elder adults (median 78 years old)



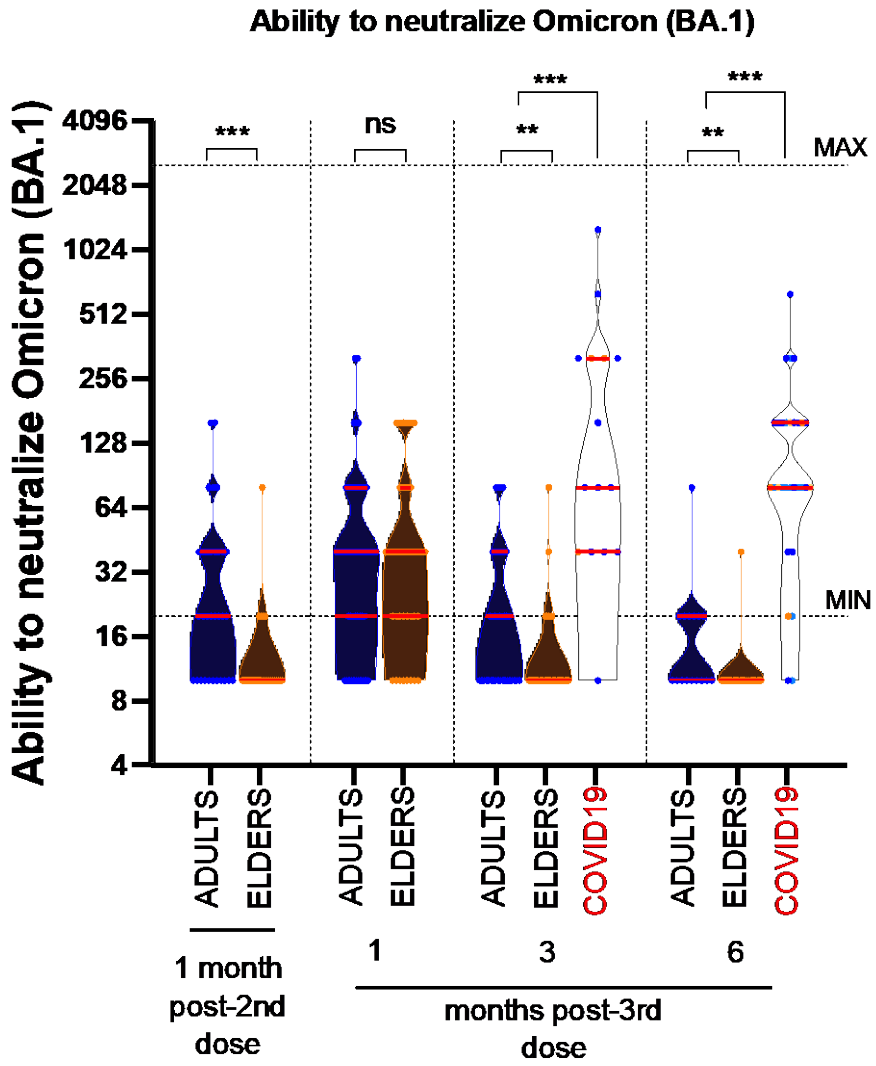
Six months after the 3rd dose, ability to neutralize Omicron (BA.1) had declined to undetectable levels in **56% of younger adults** and **96% of elder adults**.

This demonstrates the need for 4th doses within 3-6 months in elder adults to maintain antibody levels.

Individuals who got COVID-19 after 3 vaccine doses got a boost to their ability to neutralize Omicron (BA.1)

- Younger adults (median 41 years old)
- Elder adults (median 78 years old)

COVID19 Participants who got COVID-19 after 3 vaccine doses

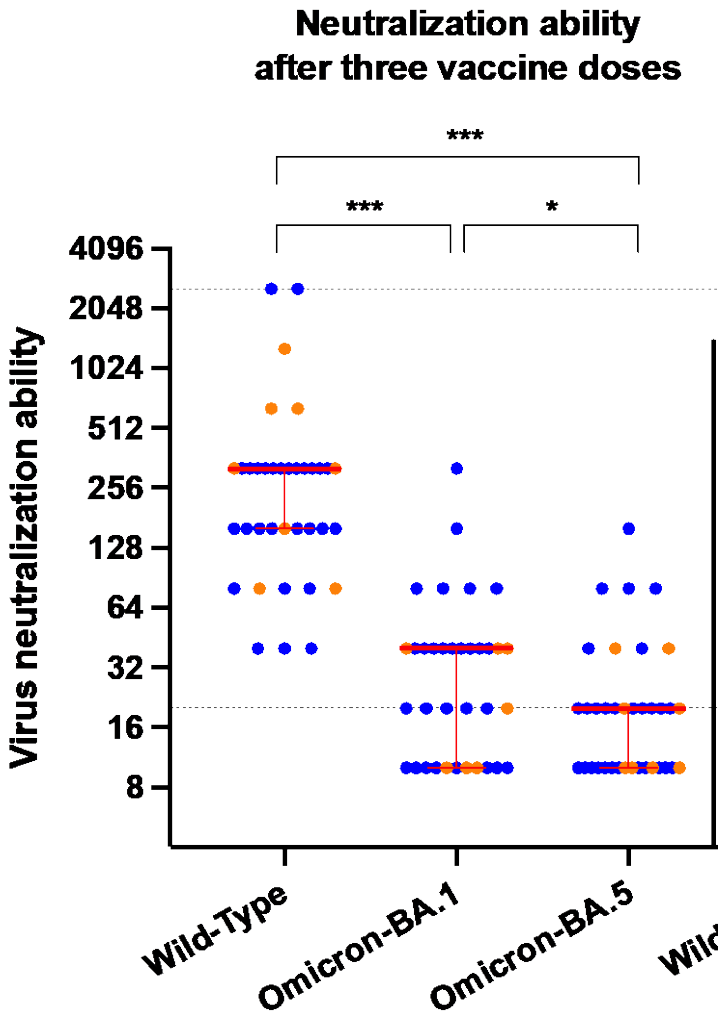


Six months after the 3rd dose, **ability to neutralize Omicron** in this group was **higher** than after 3 vaccine doses alone.

People who experienced COVID-19 after 3 vaccine doses can likely delay their 4th dose (to recommended maximum of 6 months following infection).

Ability to neutralize Omicron BA.5 after 3 vaccine doses is even poorer than BA.1

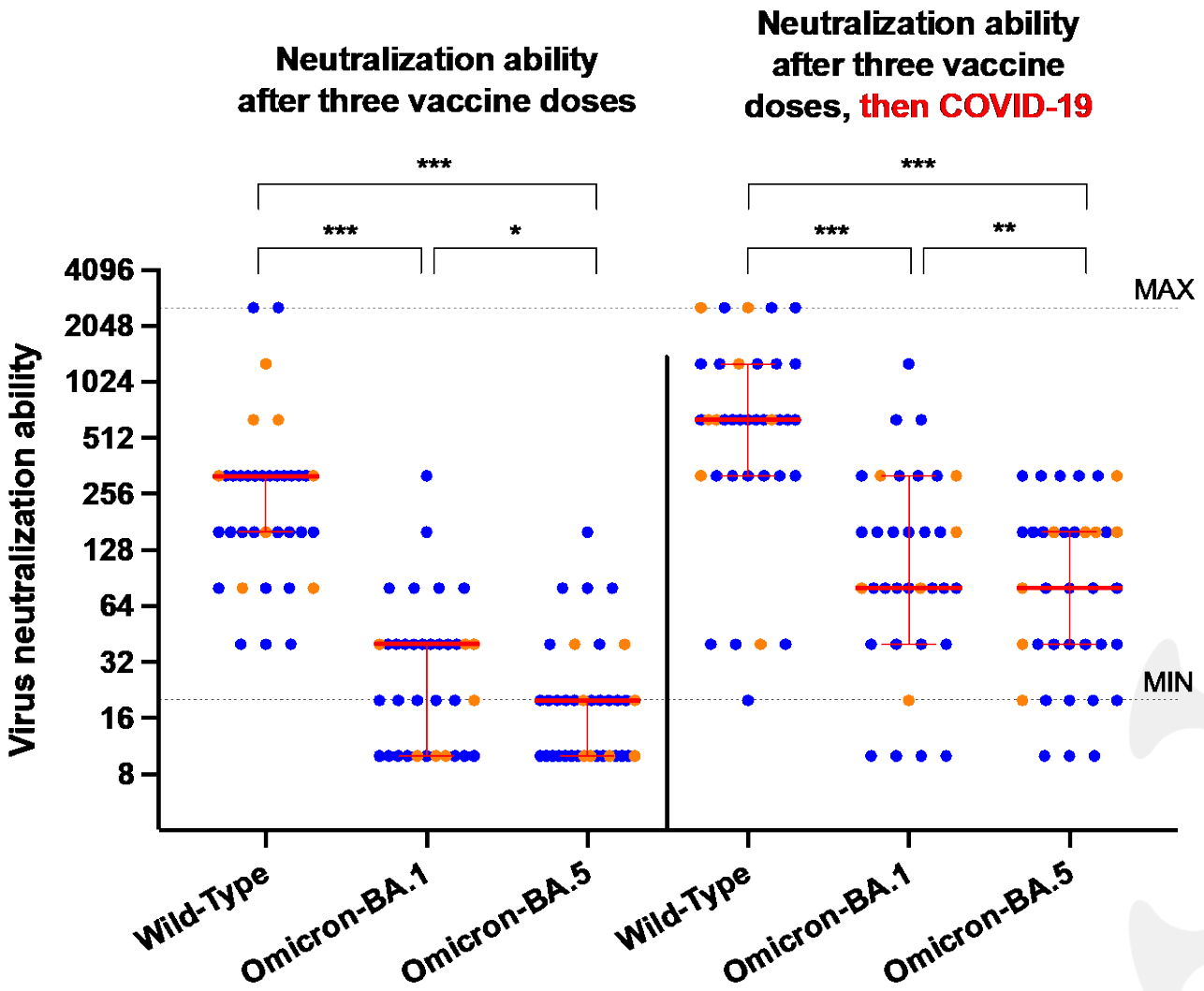
- Younger adults (median 41 years old)
- Elder adults (median 78 years old)



This is true for everyone, regardless of age.

Even after 3 vaccine doses and COVID-19, ability to neutralize Omicron BA.5 is still poorer than BA.1

- Younger adults (median 41 years old)
- Elder adults (median 78 years old)



This is true for everyone, regardless of age.

This supports the current roll-out of bivalent (combined wild-type and Omicron) vaccines, but indicates that **maintaining additional precautions is still important**.

Study Team

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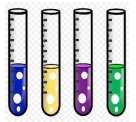

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Thank you to the clinics **and above all to the participants**. Without you, research would not be possible.

Don’t Count Doses, Think about **“Packages of Protection”**

COVID-19 vaccinations & infections in long-term care

Ontario

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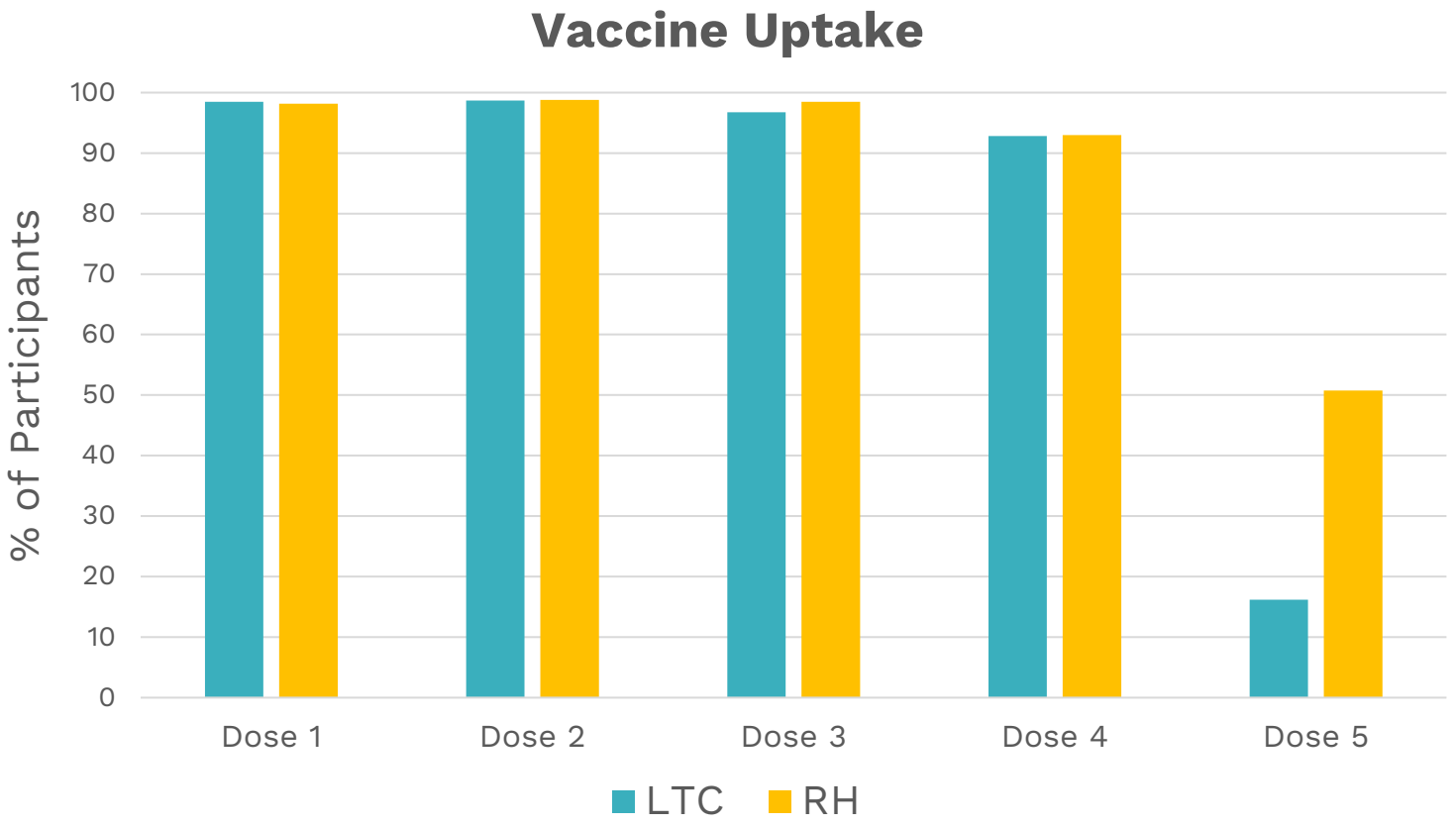
RIA Research Institute for Aging
Schlegel • UWaterloo • Conestoga

Health Sciences North Research Institute
Institut de recherches d’Horizon Santé-Nord

Disclaimer

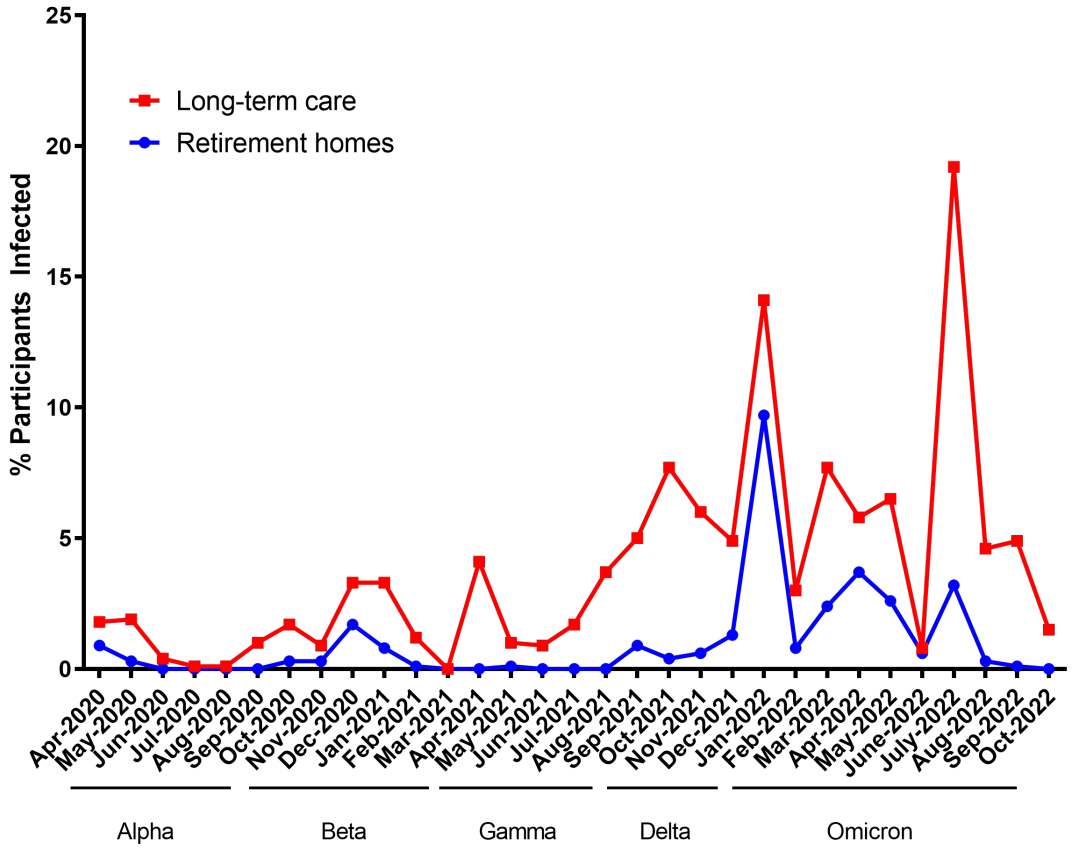
I have no COIs to declare related to this study.

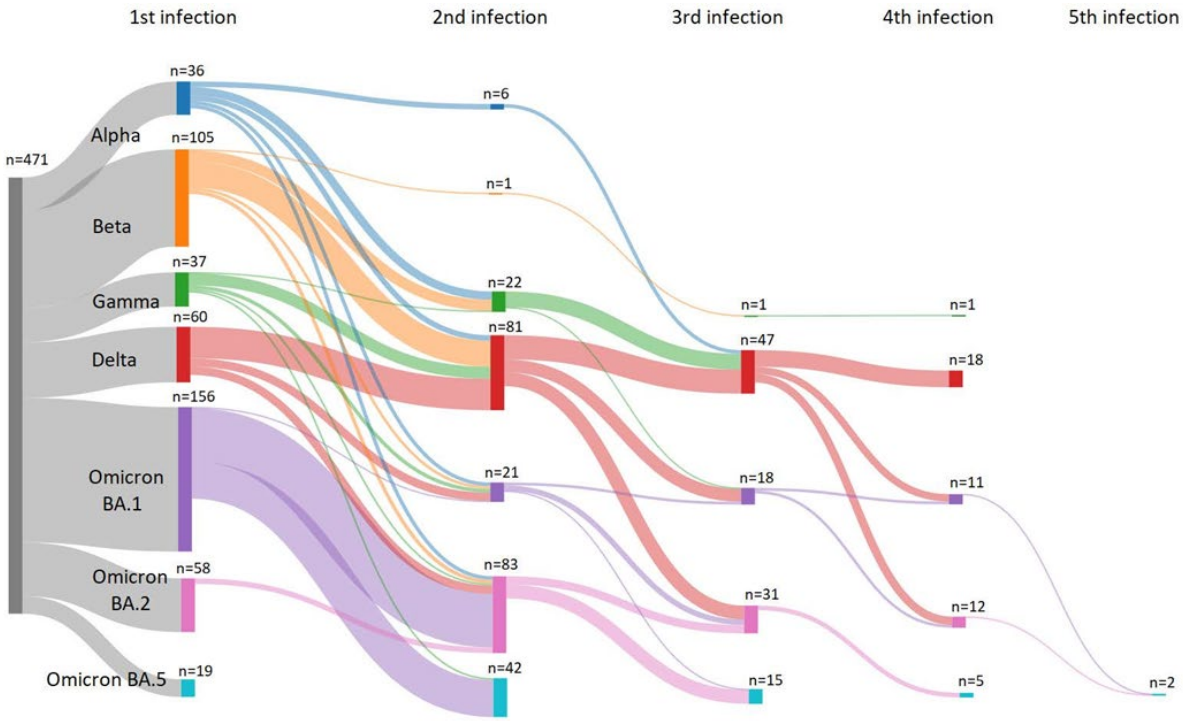
High vaccine uptake



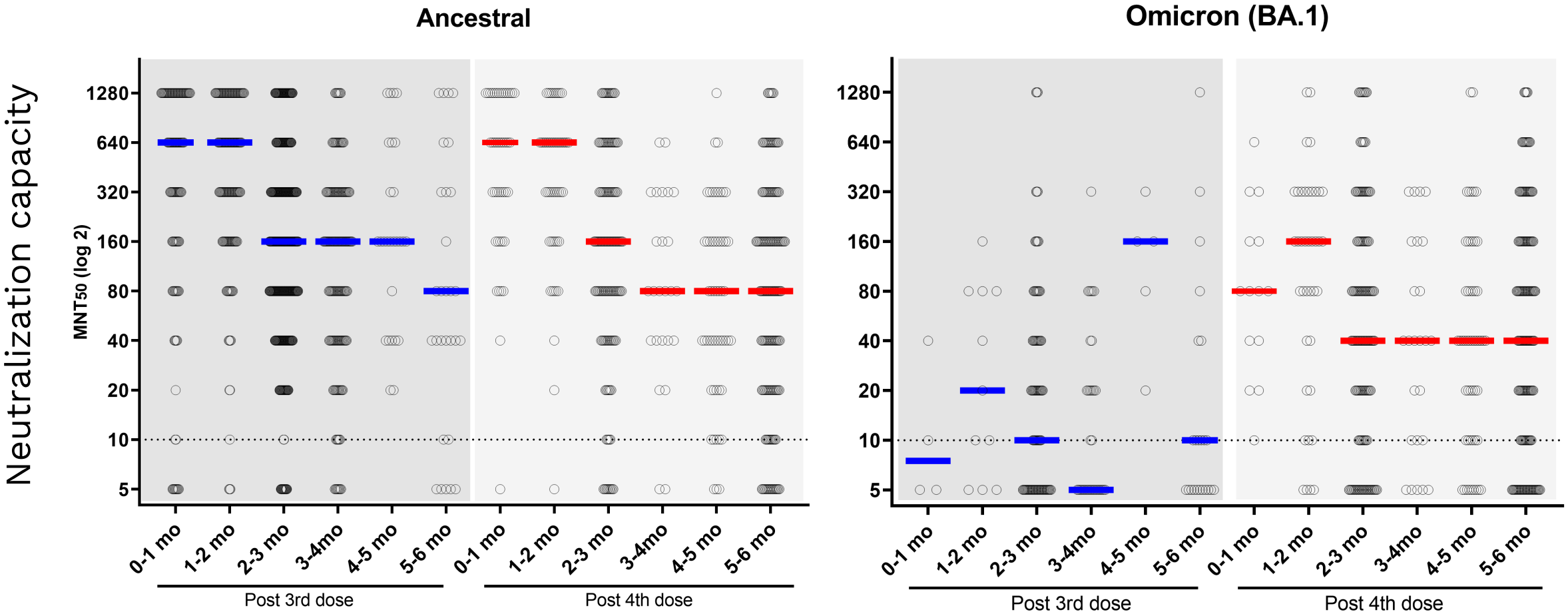
- Vaccine uptake is over 96.7% for doses 1-3
- Vaccine update is over 92.8% for dose 4
- Most eligible participants are currently getting their 5th dose

Residents are getting infected, sometimes multiple times ….but why?

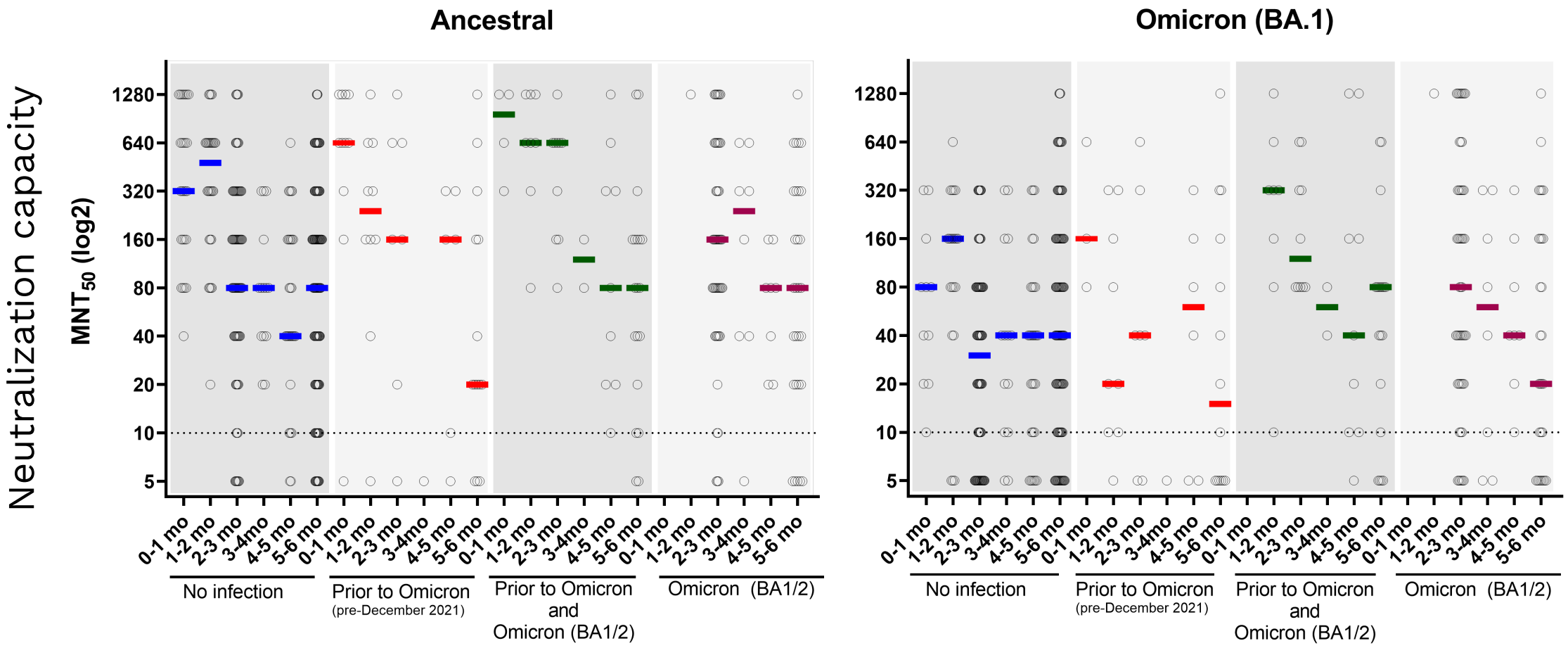




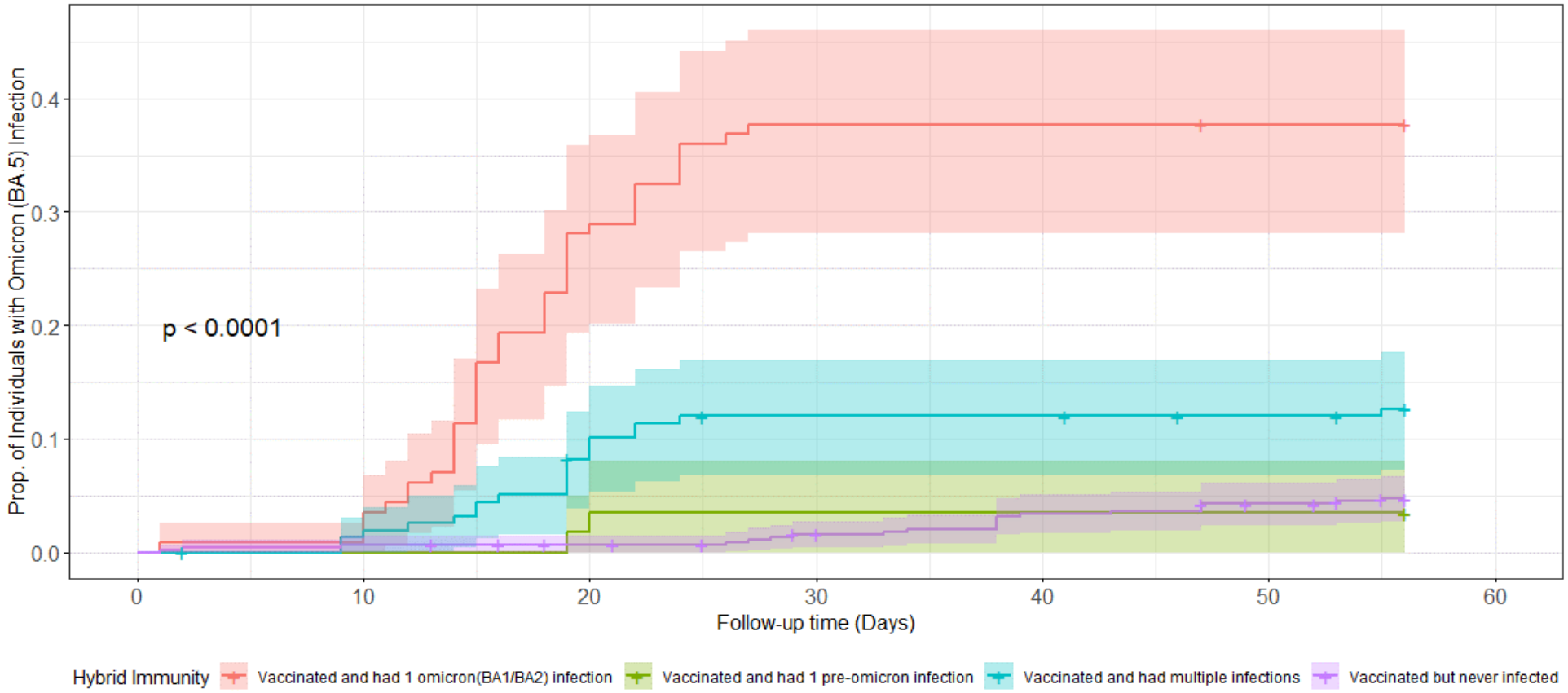
4 doses are better than 3, especially against Omicron



Role of previous infections is mixed, and hybrid immunity is short lived



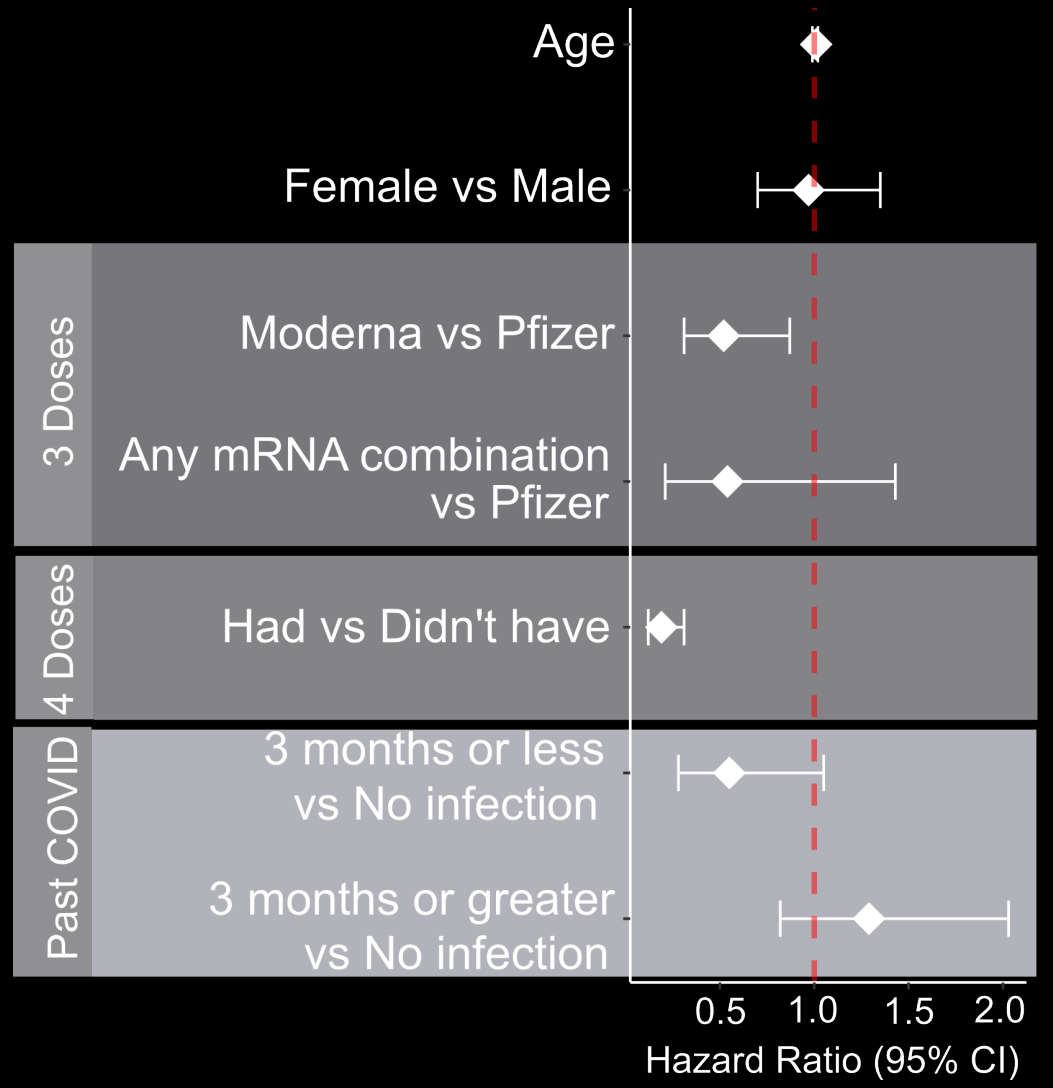
How likely are people to get a BA.5 infection? Recent past infections predict new infections



- Hybrid immunity with an Omicron BA.1/BA.2 infection is not protective against Omicron BA.5

Omicron BA.1/BA.2 Infection Risk

- Age and sex do not influence Omicron BA.1/BA.2 infection risk
- Receiving 3 doses of Moderna was more protective than 3 doses of Pfizer against Omicron BA.1/BA.2
- Any 4th dose helped reduce risk of Omicron BA.1/BA.2 infection



Breznik, J. et al., *medRxiv* 2022.06.28.22277016;

Recommendations

- Don’t count doses, think about **“packages of protection”**
  - Vaccine = 3-6 months of protection
  - Infection = 3 months or less of protection
- Vaccinate at the start of a wave
- Get infected as few times as possible
- Vaccine-induced immunity, protecting against infection, is strongest soon after vaccination

Study Team

Co-Leads


Project Management


Analytics



Data Facility





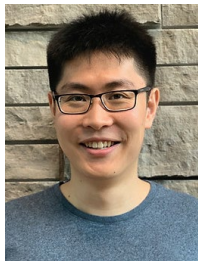

Immunology












Saliva Testing

Logistics & Comms

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Research Coordination

Over 20 admin and healthcare workers

...and many more...

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COVID IN LONG-TERM CARE STUDY

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Partners

McMaster University

Schlegel Villages

St. Joseph's Health System Elder Care

AMICA Senior Lifestyles

Shalom Village — Honouring our Fathers and our Mothers

Health Sciences North Research Institute

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WELLNESS HUB

COVID-19 Long Term Care Immunogenicity Sub-Study

Ontario
(Toronto and
Simcoe Region)

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Sinai Health

UNIVERSITY OF TORONTO

Disclaimer

Honoraria / consulting / advisory boards / DSMB:

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Other:

I am an external expert member of the NACI influenza and pneumococcal working groups, and a member of the Ontario Immunization Advisory Committee

Study cohort – enrolled Dec 2020/Jan 2021

4 LTC homes, 203 residents enrolled

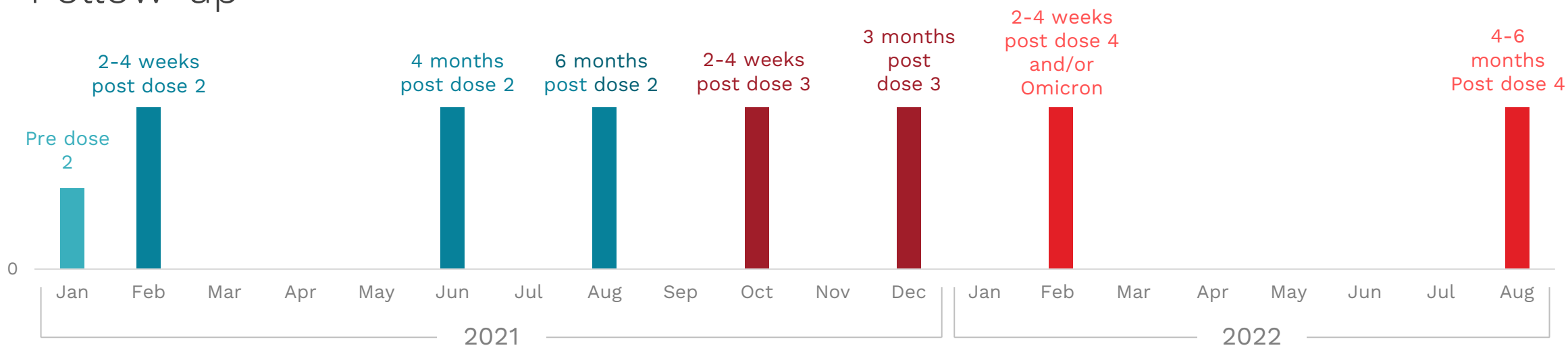
- 3 homes (115 residents) primary vaccination with Moderna (manufacturer schedule)
- 1 home (88 residents) primary vaccination with Pfizer (manufacturer schedule)
- 3rd dose same manufacturer as first
- 4th dose all Moderna (as per Ontario policy)

Resident characteristics:

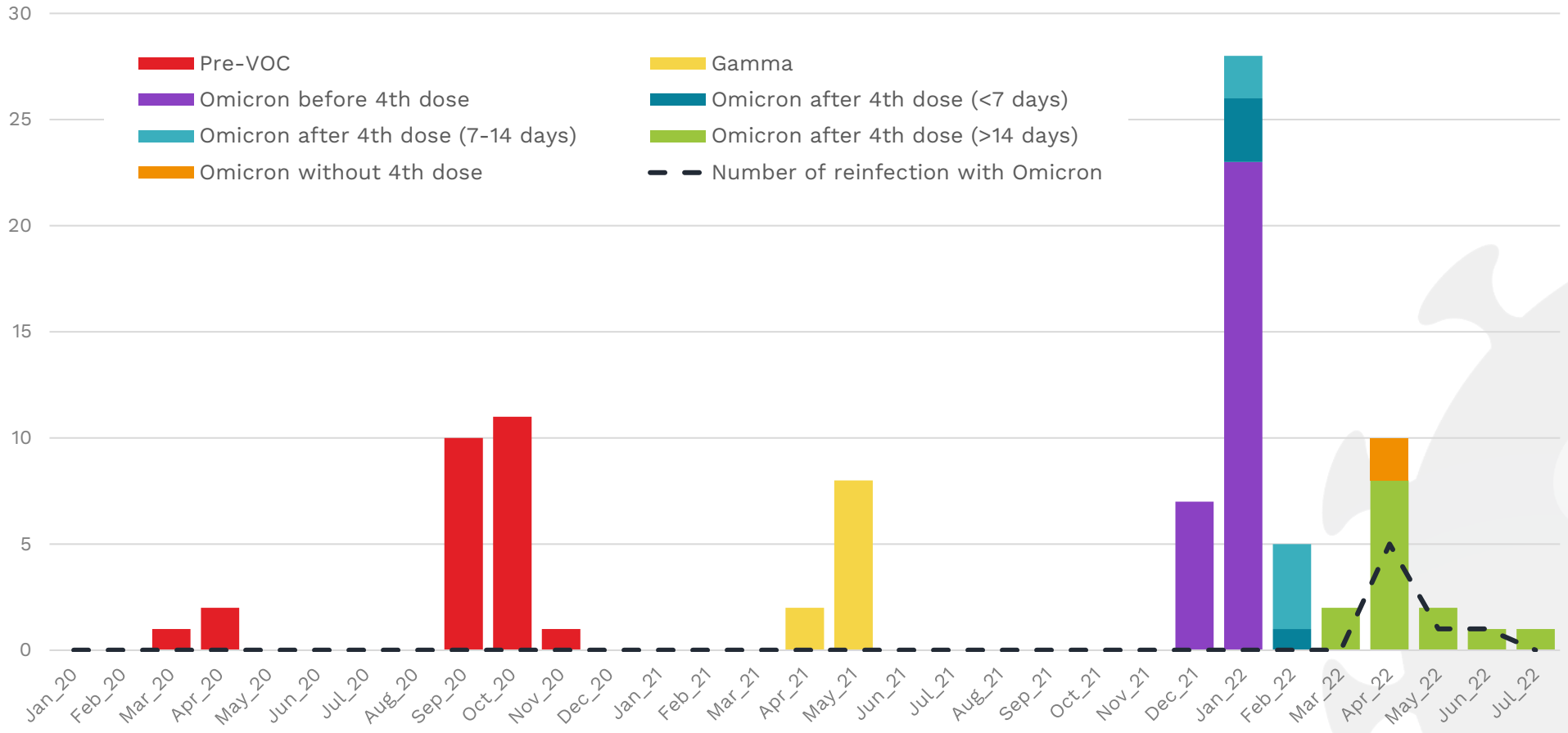
- Median age 88 years (range 53-105)
- 137 (69%) female
- Median Charlson index 2 (range 0-8)
- Median BMI 26 (range 15-45)
- 8 residents (4%) immunosuppressed
- 25 residents (13%) with prior laboratory-confirmed COVID-19

Methods

- Antibody concentrations
  - Spike trimer, receptor binding domain, nucleocapsid by enzyme immunoassays (EIA)
  - Pseudo-neutralization, and PRNT neutralization
- Follow-up



COVID infections



50% of LTCF residents have NOT (yet) been infected with COVID-19

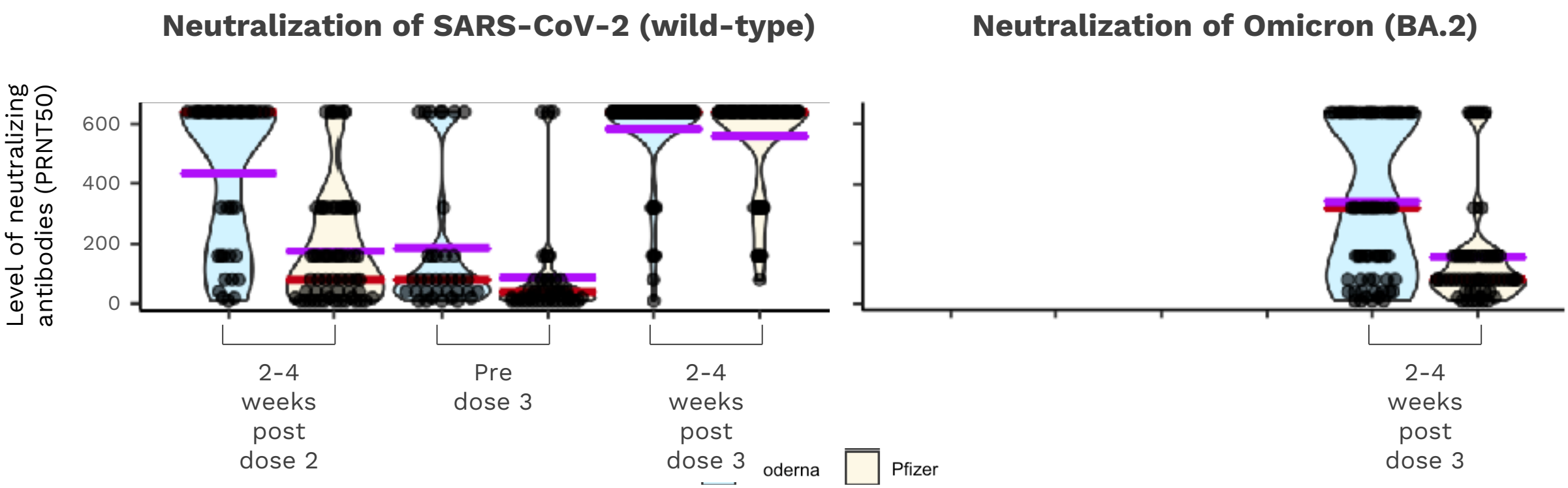
WELLNESS HUB

ST. MICHAEL'S UNITY HEALTH TORONTO

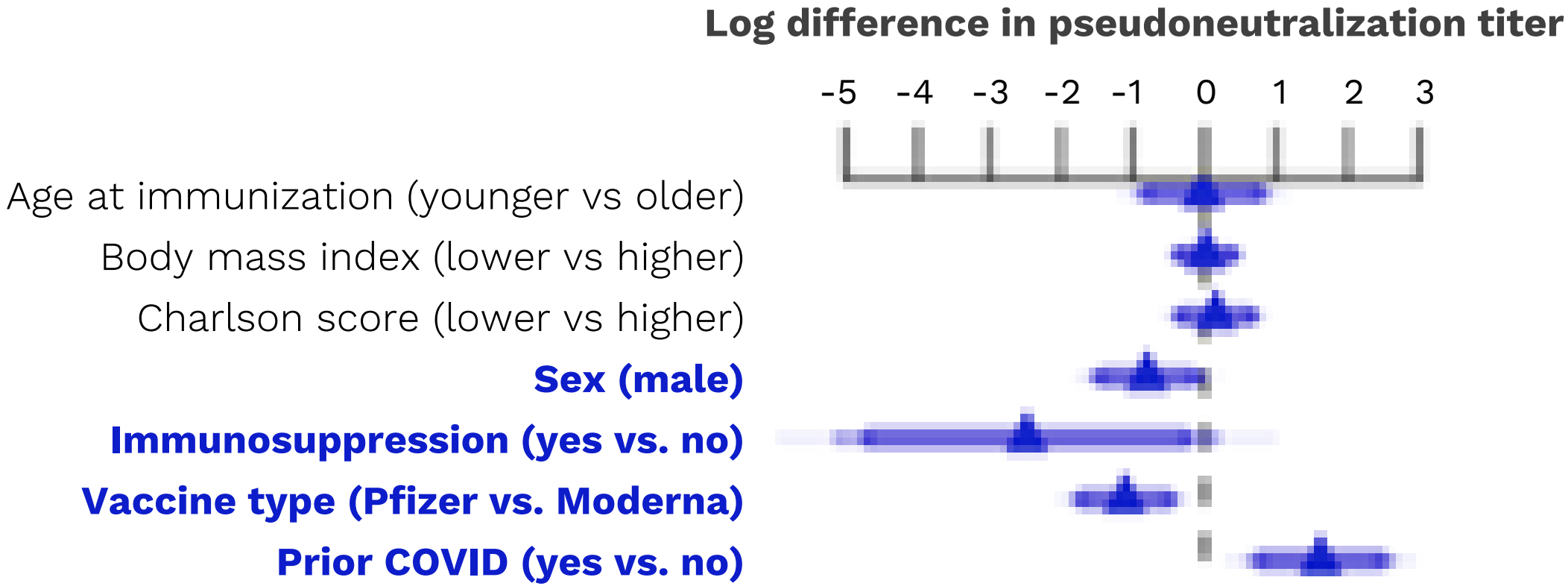
Sinai Health

UNIVERSITY OF TORONTO

Omicron immune escape: post dose 3 antibody levels



Factors associated with pseudo-neutralization titers against Omicron post-dose 3



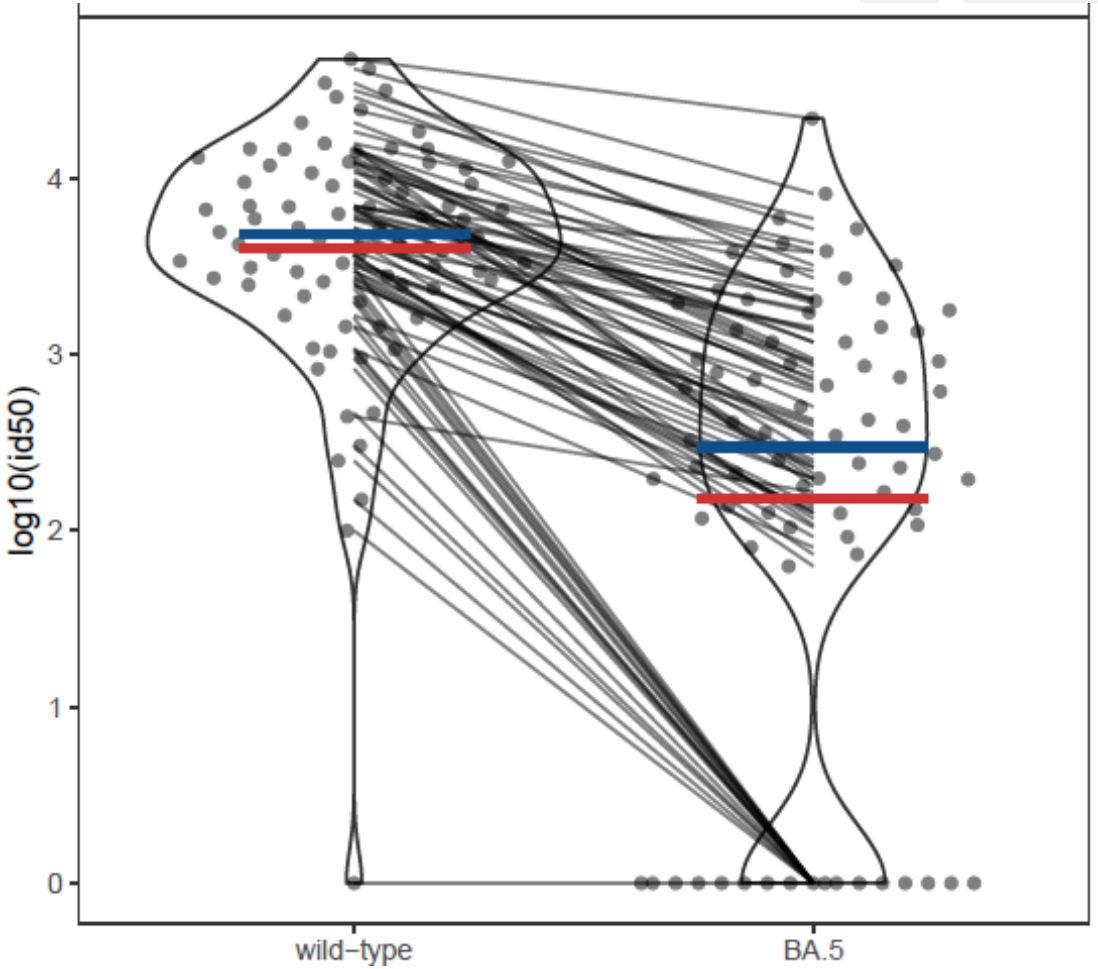
Pseudo-neutralization titres August 2022

In this very highly vaccinated cohort:

- Almost all residents have maintained neutralizing antibodies against the original virus
- But 22% of residents have no neutralizing antibodies, and another 15% have borderline levels against BA.5
- Prior COVID-19 infection is best predictor of neutralizing antibodies:

93% of previously infected and **60%** of not previously infected

have neutralizing antibodies against BA.5



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TIBDN Toronto Invasive Bacterial Diseases Network

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

You'll find our summary of this seminar at

covid19immunitytaskforce.ca

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