

Impact of age and SARS-CoV-2 breakthrough infection on humoral immune responses after three doses of COVID-19 mRNA vaccine

Zabrina L. Brumme*, Francis Mwimanzi, Hope R. Lapointe, Peter K. Cheung, Yurou Sang, Fatima Yaseen, Rebecca Kalikawe, Sneha Datwani, Laura Burns, Landon Young, Victor Leung, Siobhan Ennis, Chanson J. Brumme, Julio S.G. Montaner, Winnie Dong, Natalie Prystajicky, Christopher F. Lowe, Mari L. DeMarco, Daniel T. Holmes, Janet Simons, Masahiro Niikura, Marc G. Romney*, Mark A. Brockman*
***co-Principal Investigators**



BRITISH COLUMBIA
CENTRE for EXCELLENCE
in HIV/AIDS

We established our cohort in December 2020, just as the first British Columbians were receiving their COVID-19 vaccines



The Daily Scan

HEART / LUNG KIDNEY & RENAL MENTAL HEALTH SENIORS

COVID-19 · RESEARCH · SENIORS

RESEARCHERS STUDYING IMMUNE RESPONSE TO COVID-19 VACCINE

February 10, 2021

VANCOUVER
SUN



COVID-19: As care home residents get second vaccine doses, study aims to track their antibody levels

A virologist said it may be months before restrictions for visitors are lifted, and freedoms and procedures at seniors' homes may never return to pre-COVID times.

Susan Lazaruk

Feb 18, 2021 • February 18, 2021 • 3 minute read • [Join the conversation](#)

The Journal of Infectious Diseases

MAJOR ARTICLE



Reduced Magnitude and Durability of Humoral Immune Responses to COVID-19 mRNA Vaccines Among Older Adults

Mark A. Brockman,^{1,2,3,a} Francis Mwimanzhi,¹ Hope R. Lapointe,³ Yurou Sang,¹ Olga Agafitei,¹ Peter K. Cheung,^{1,3} Siobhan Ennis,¹ Kurtis Ng,¹ Simran Basra,^{1,2,4} Li Yi Lim,^{1,2} Fatima Yaseen,² Landon Young,⁵ Gisele Umvilighozo,¹ F. Harrison Omondi,^{1,3} Rebecca Kalikawe,¹ Laura Burns,⁵ Chanson J. Brumme,^{3,6} Victor Leung,^{5,7} Julio S. G. Montaner,^{3,6} Daniel Holmes,^{7,8} Mari L. DeMarco,^{7,8} Janet Simons,^{7,8} Ralph Pantophlet,^{1,2} Masahiro Niikura,¹ Marc G. Romney,^{5,7,a} and Zabrina L. Brumme^{1,3,a}

The Journal of Infectious Diseases

MAJOR ARTICLE



Older Adults Mount Less Durable Humoral Responses to Two Doses of COVID-19 mRNA Vaccine but Strong Initial Responses to a Third Dose

Francis Mwimanzhi,¹ Hope R. Lapointe,² Peter K. Cheung,^{1,2} Yurou Sang,¹ Fatima Yaseen,¹ Gisele Umvilighozo,¹ Rebecca Kalikawe,¹ Sneha Datwani,¹ F. Harrison Omondi,^{1,2} Laura Burns,³ Landon Young,³ Victor Leung,^{4,5} Olga Agafitei,¹ Siobhan Ennis,¹ Winnie Dong,² Simran Basra,¹ Li-Yi Lim,¹ Kurtis Ng,¹ Ralph Pantophlet,¹ Chanson J. Brumme,^{2,4} Julio S. G. Montaner,^{2,4} Natalie Prystajeky,^{5,6} Christopher F. Lowe,^{3,5} Mari L. DeMarco,^{3,5} Daniel T. Holmes,^{3,5} Janet Simons,^{3,5} Masahiro Niikura,¹ Marc G. Romney,^{3,5,a} Zabrina L. Brumme,^{1,2,a} and Mark A. Brockman^{1,2,a}

Open Forum Infectious Diseases



Impact of age and SARS-CoV-2 breakthrough infection on humoral immune responses after three doses of COVID-19 mRNA vaccine

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Cohort and sampling

Cohort

89 younger adults
(health care workers)



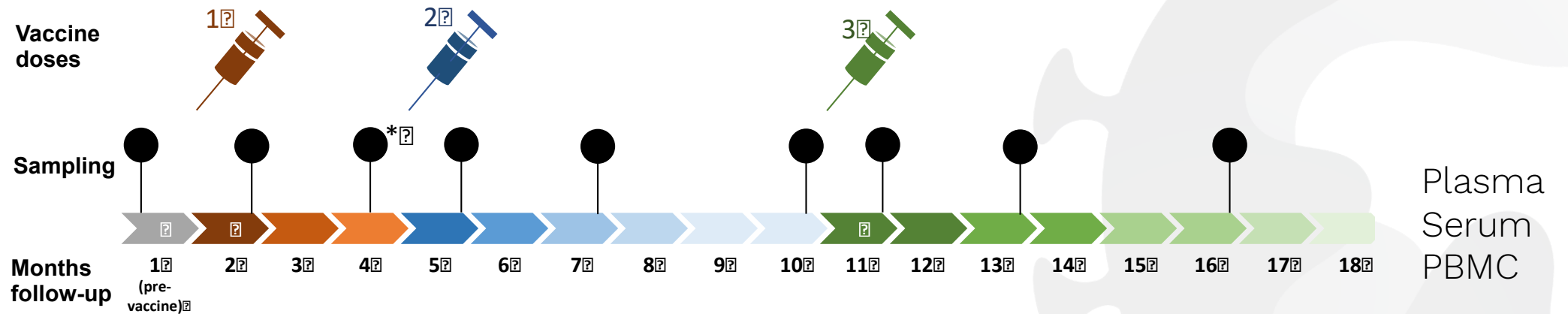
Median age 41 (IQR 35-50) years
73% female

62 elder adults
(including long term care residents)

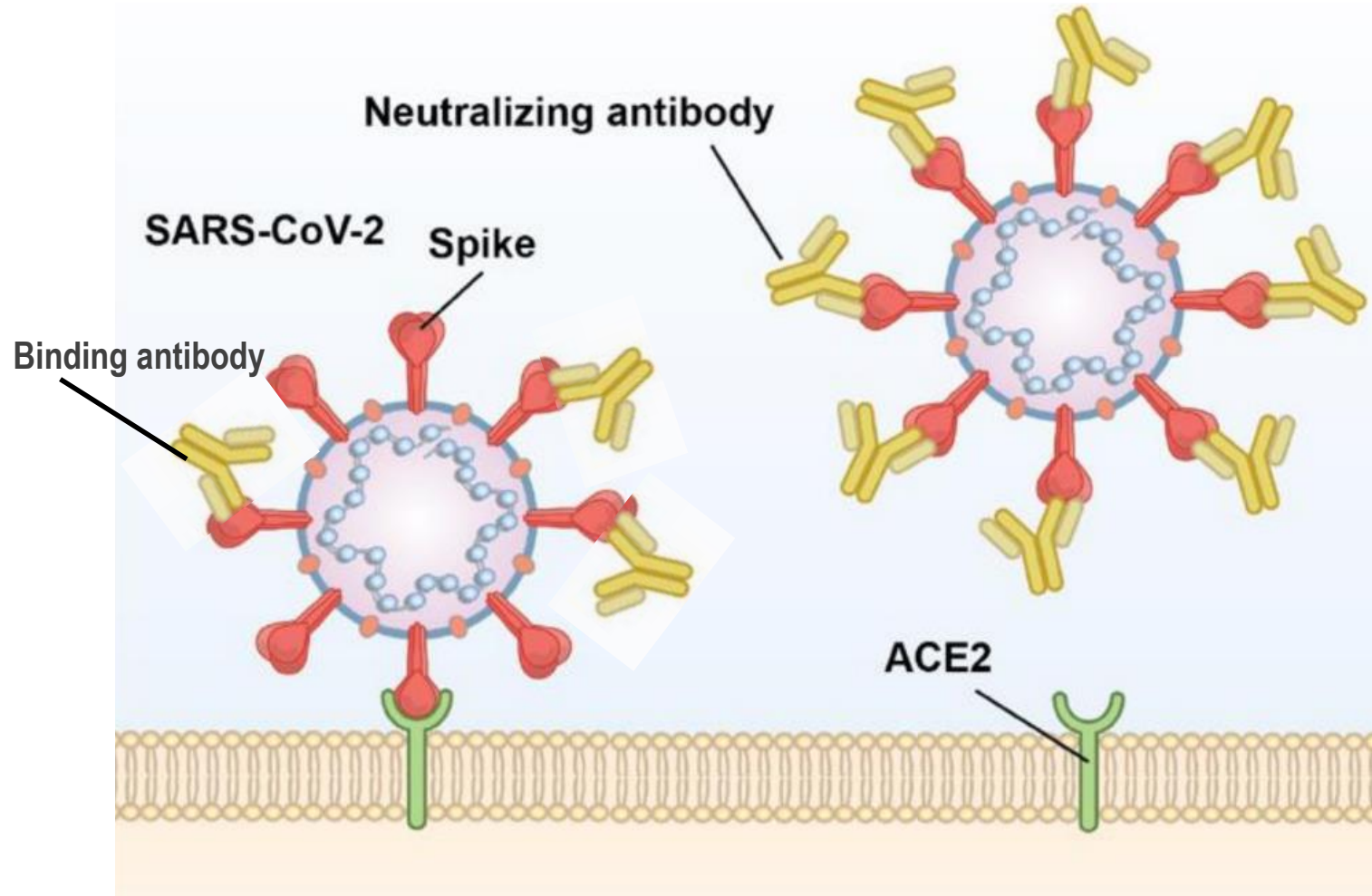


Median age 79 (IQR 73-86) years
69% female

Sampling



Assays to measure humoral immune responses



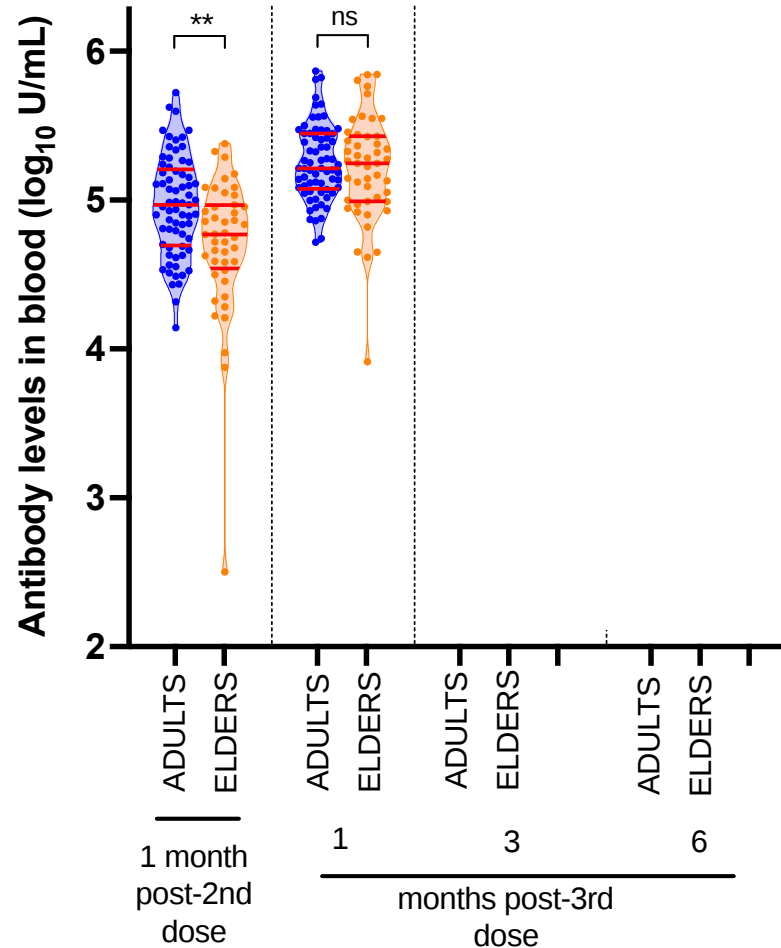
1. Total concentration of binding IgG against SARS-CoV-2 Spike-RBD (Meso Scale Diagnostics)
2. Ability of these antibodies to disrupt the Spike-RBD/ACE2 interaction (surrogate of viral neutralization – Meso Scale Diagnostics)
3. Ability of these antibodies to inhibit SARS-CoV-2 infection of target cells *in vitro* (live virus neutralization)

We measured both wild-type and variant -specific responses

SARS-CoV-2 infections identified by self-reported PCR or RAT test results and/or development of anti-N seropositivity (Roche Elecsys)

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

Antibodies against wild-type SARS-CoV-2



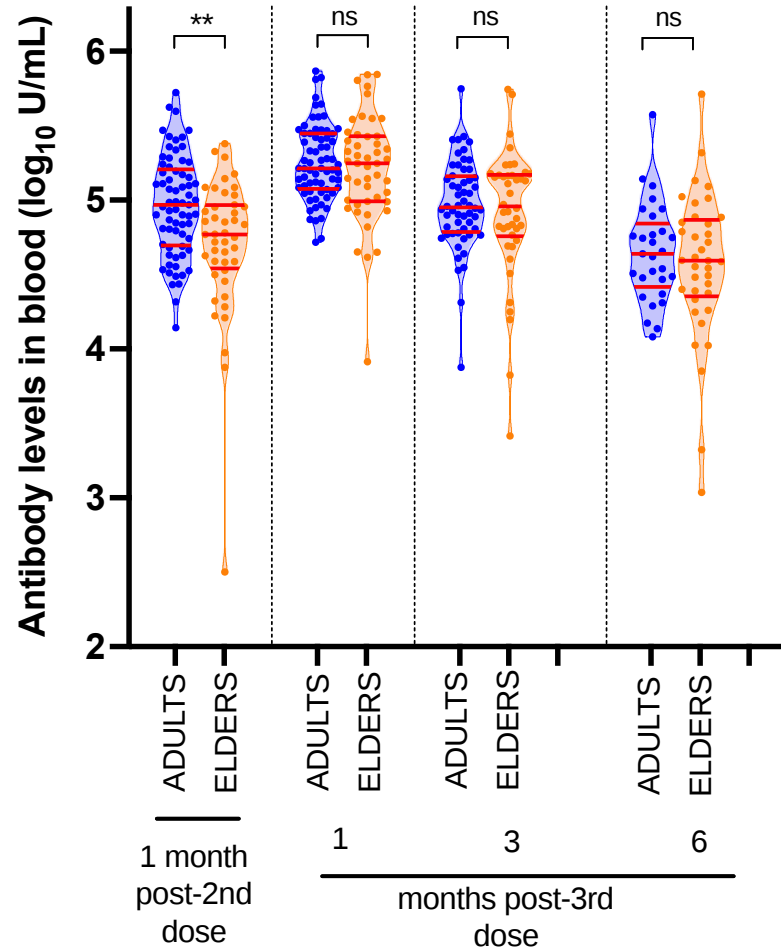
● Younger adults
(median 41 years old)

● Elder adults
(median 78 years old)

All participants
displayed are COVID-
19 naive

Antibody levels decline relatively quickly following vaccination

Antibodies against wild-type SARS-CoV-2



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

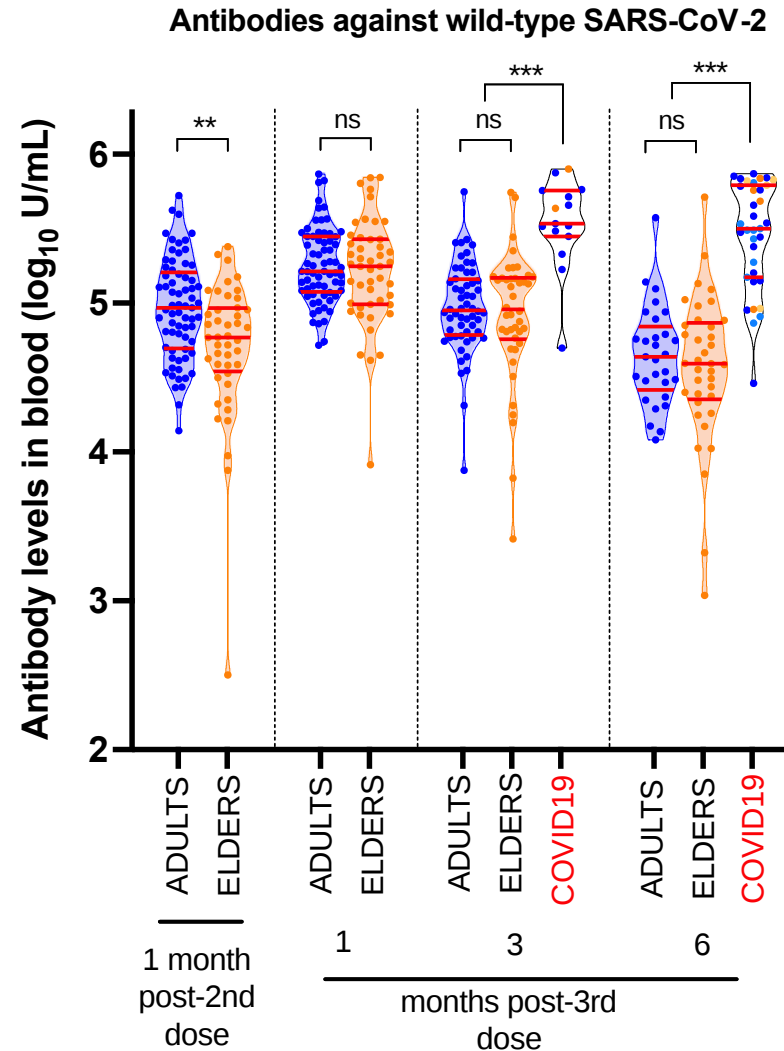
By six months after the third dose, antibody levels have generally declined to below the levels initially induced by two doses

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

● Younger adults
(median 41 years old)

● Elder adults
(median 78 years old)

COVID-19 =
participants who got
their first SARS-CoV-2
infection after three
vaccine doses

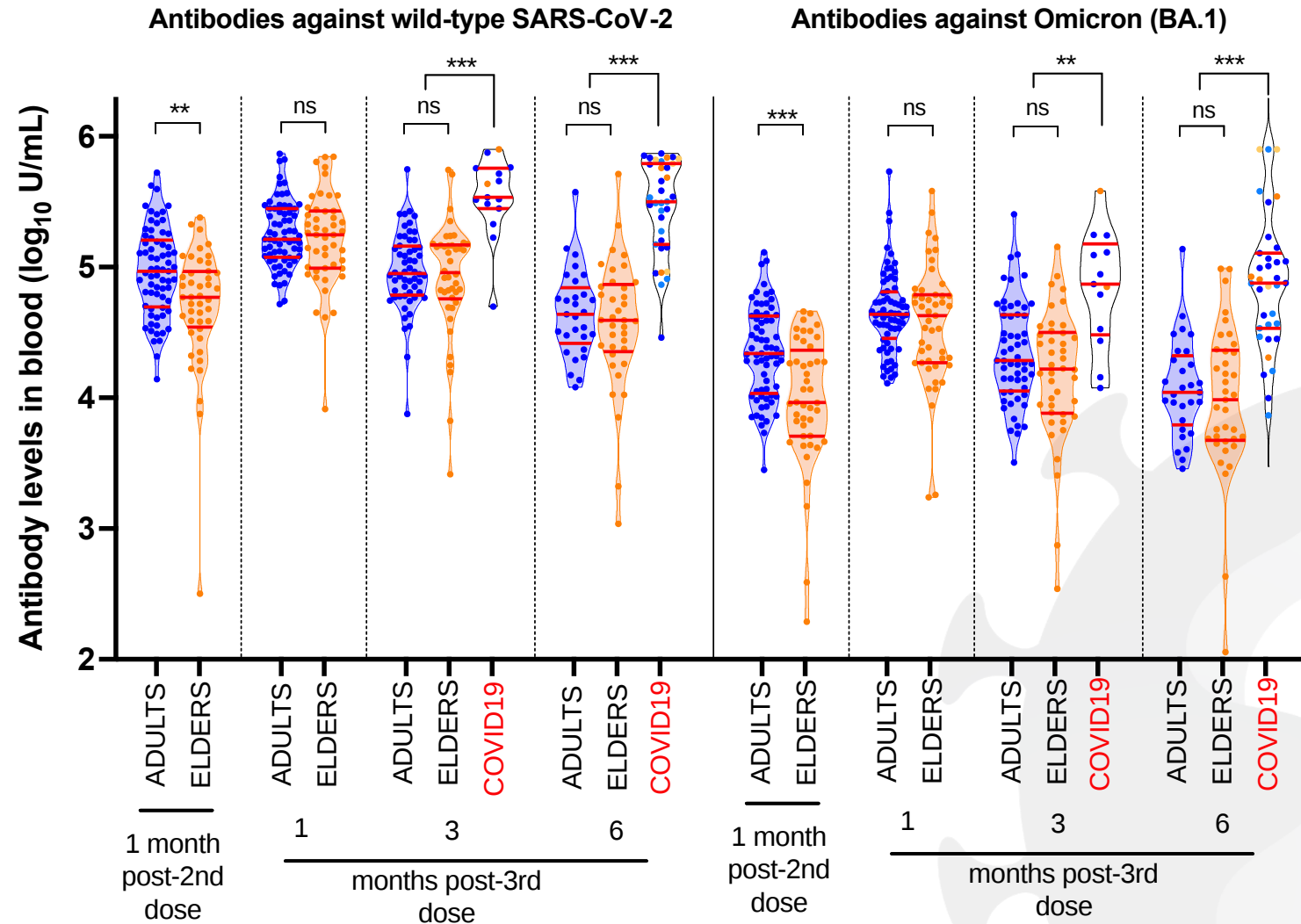


Six months after the third dose, antibody levels in this group were higher than those induced by three vaccine doses alone

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

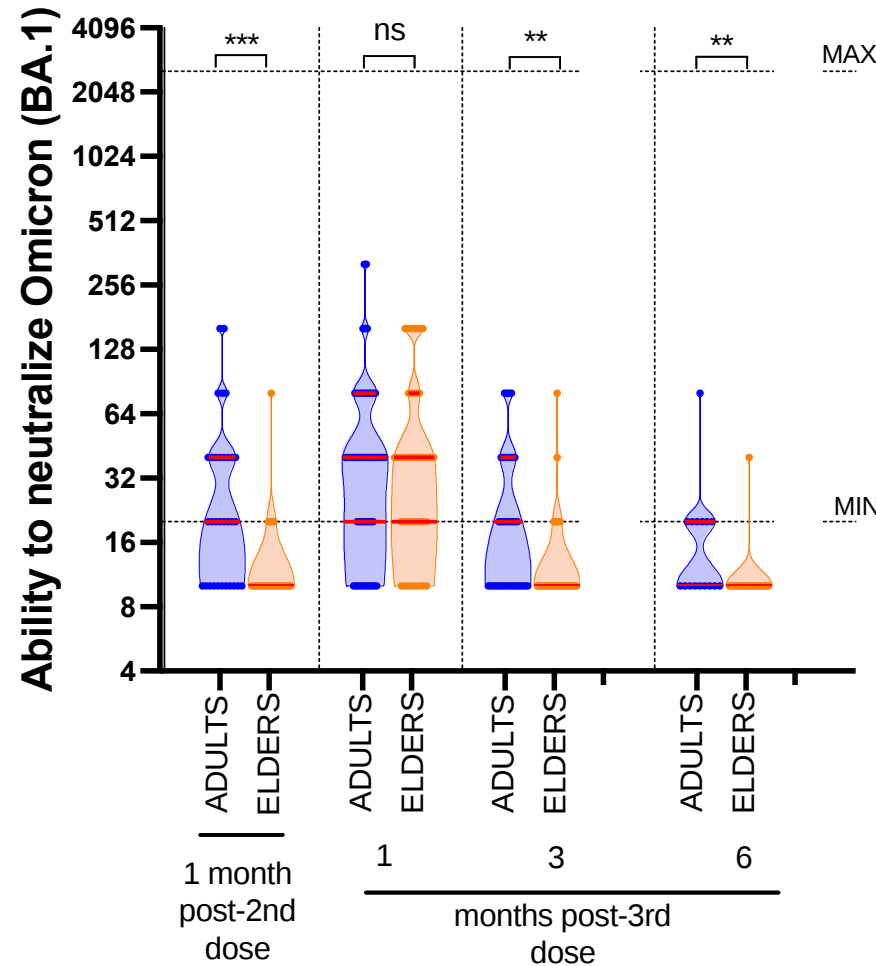
- Younger adults (median 41 years old)
- Elder adults (median 78 years old)

COVID-19 = participants who got their first SARS-CoV-2 infection after three vaccine doses



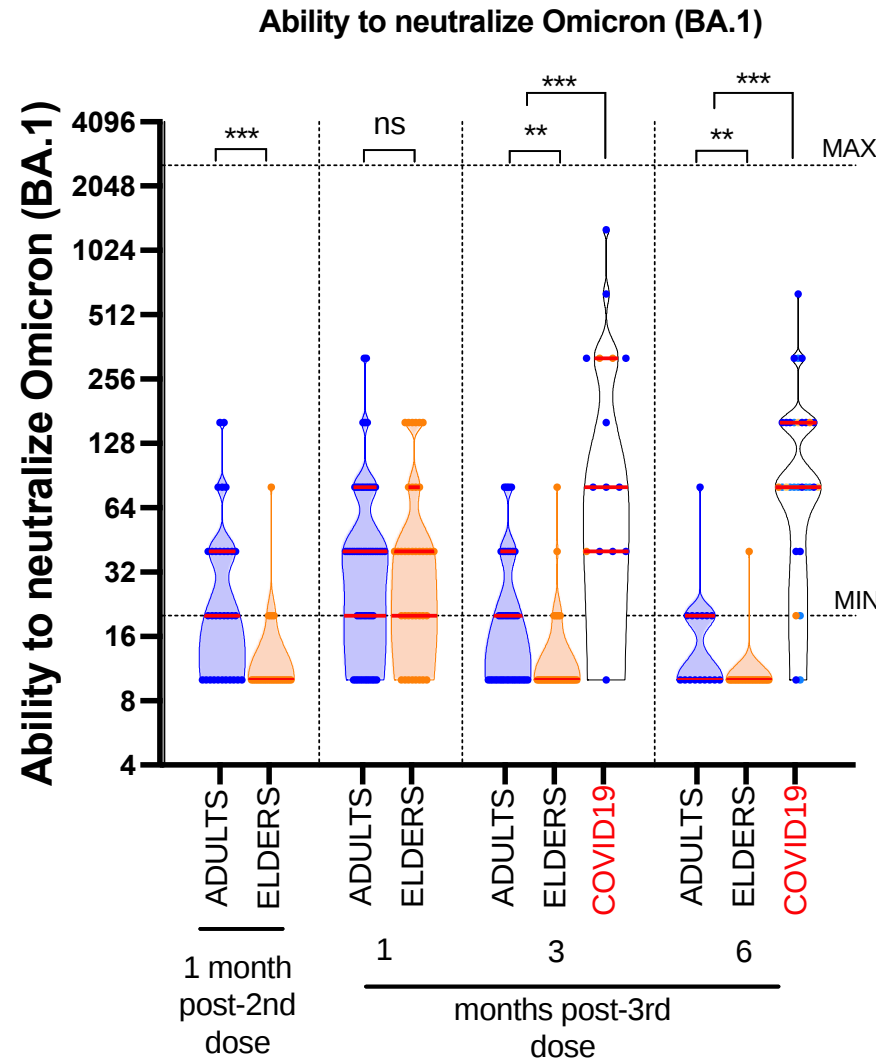
Antibody function against the Omicron (BA.1) strain declines more quickly in elder adults

Ability to neutralize Omicron (BA.1)



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

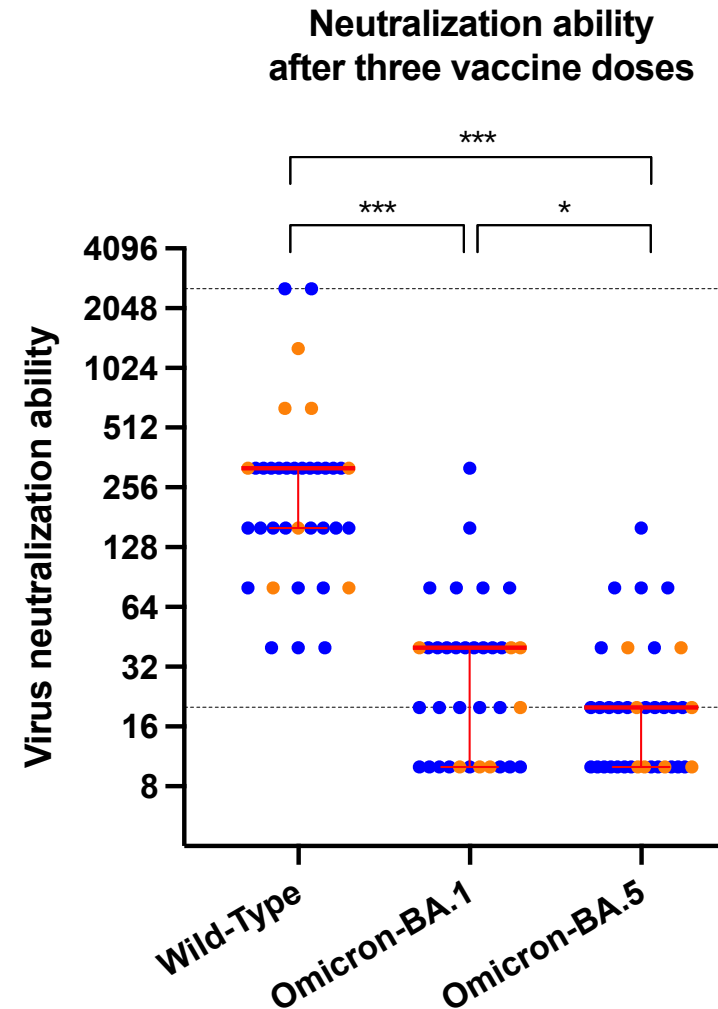
Individuals who got COVID-19 after three vaccine doses got a boost to their ability to neutralize Omicron (BA.1)



Six months after the third dose, ability to neutralize Omicron in this group was higher than after three vaccine doses alone

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

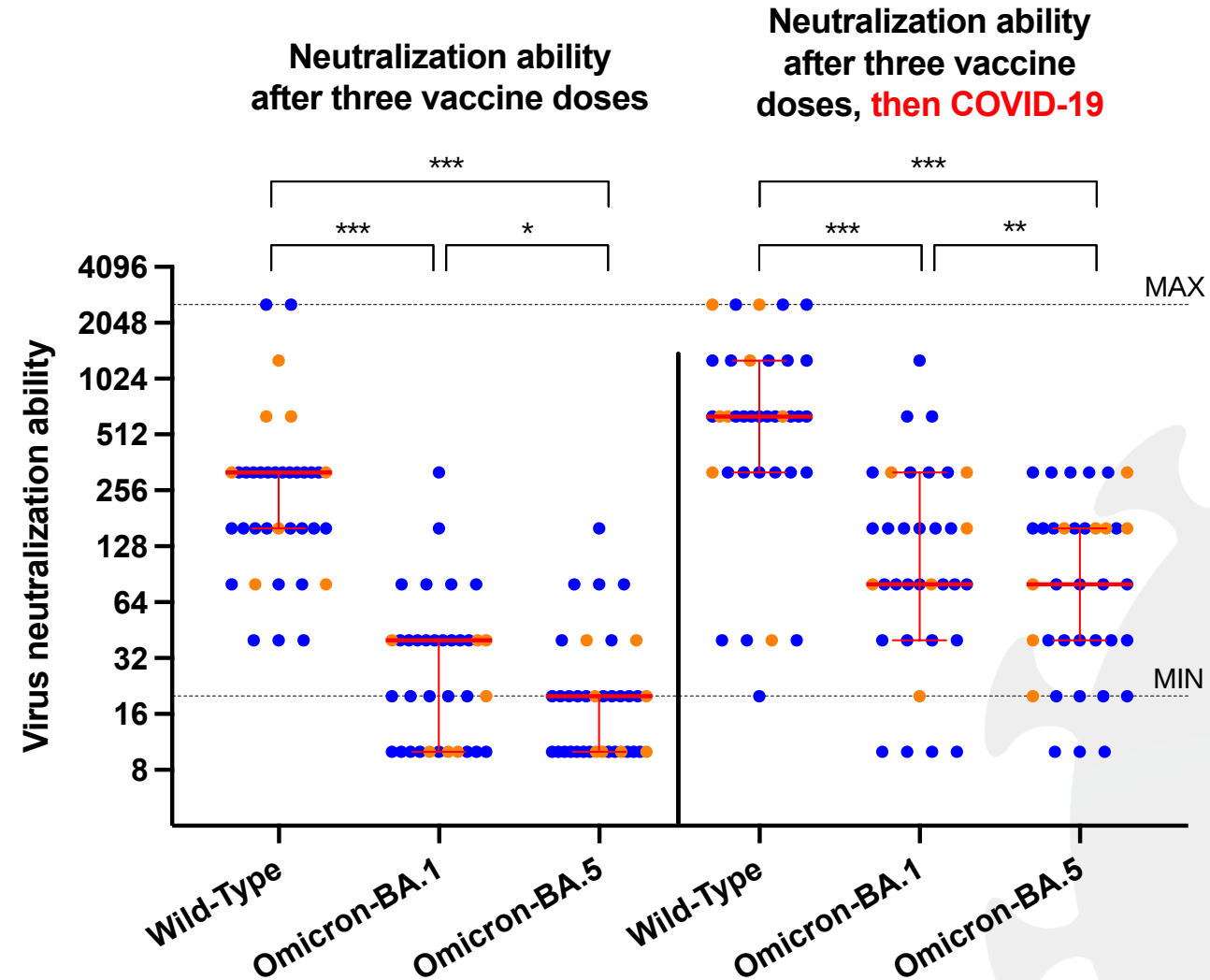
- Younger adults (median 41 years old)
- Elder adults (median 78 years old)



This is true for everyone, regardless of age

Even after three 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

Does the magnitude of vaccine-induced humoral responses predict SARS-CoV-2 breakthrough infection risk?



Does the magnitude of vaccine-induced humoral responses predict SARS-CoV-2 breakthrough infection risk?

We used univariable and multivariable logistic regression to investigate whether humoral responses one month post-3rd dose could predict breakthrough infection in COVID-19-naïve participants.

We investigated the following 3 antibody functions:

- Anti-RBD IgG concentration (both WT and Omicron-BA.1-specific)
- ACE2% displacement (both WT and Omicron-BA.1-specific)
- Live virus neutralization (both WT and Omicron-BA.1-specific)



Does the magnitude of vaccine-induced humoral responses predict SARS-CoV-2 breakthrough infection risk?

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The sole measure associated with protection against breakthrough infection was the magnitude of Omicron-BA.1-specific live virus neutralization one month post-3rd dose

This remained significant after controlling for sociodemographic, health and vaccine-related variables.

Summary

Third COVID-19 vaccine doses provide immune benefits to individuals of all ages, and particularly to older adults.

Antibody levels decline over time - and the ability of antibodies to neutralize Omicron decline particularly quickly in older adults – supporting the need for fourth doses within 3-6 months in older adults to maintain antibody levels.

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

Antibody responses against the first-generation COVID-19 mRNA vaccines – and even generated by COVID-19 itself – do not neutralize Omicron BA.5 as well as previous variants, supporting the roll-out of bivalent vaccines

antibody levels and function are just one aspect of the immune response (albeit an important one!). Analysis of cellular immune responses are ongoing

Study Team

Nominated Principal Investigator



PHC

Marc Romney, MD
Division Head,
Medical Microbiology & Virology,
Providence Health Care

Co-Principal Investigators



CfE

Zabrina Brumme, PhD
Professor, SFU
Laboratory Director, BC Centre
for Excellence in HIV/AIDS



SFU

Mark Brockman, PhD
Associate Professor, SFU
Canada Research Chair in
Viral Immunopathogenesis

Partners and Knowledge Users

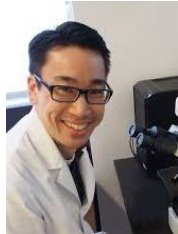


Dr. Patricia Daly, Chief Medical Health Officer, Vancouver Coastal Health
Fiona Dalton, President and Chief Executive Officer, PHC
Deborah Mitchell, former Vice President, Seniors Care, PHC
Sutinder Kaba, Director of Resident Experience, Seniors Care, PHC
Dr. John Harding, Medical Health Officer, Vancouver Coastal Health
Isobel Mackenzie, BC Senior's Advocate

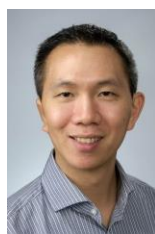
Project team members



C. Brumme, PhD
Asst Lab
Director, BC-CfE



J. Choy, PhD
Associate Prof,
SFU



C. Lowe, MD
Head,
SPH Virology Lab



V. Leung, MD
Medical Director,
Infection Prevention
and Control, PHC



M. DeMarco, PhD
Clinical Chemist,
SPH



N. Matic, MD
SPH Virology Lab



J. Montaner, MD
Executive Director and
Physician-in-Chief,
BC-CfE



M. Niikura, DVM
Associate Prof, SFU



G. Ritchie, PhD
SPH Virology Lab



R. Pantophlet, PhD
Assoc. Prof, SFU



H. Lapointe, PharmD
BC-CfE



Y. Sang, PhD
Scientist, SFU



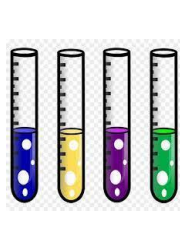
F. Mwimanzi, PhD
Scientist, SFU



F. Yaseen
Scientist, SFU



P. Cheung
BC-CfE



Laura Burns
PHC



N. Prystajek
Program Head, Environ.
Microbiol., BCCDC/PHSA



D. Holmes
Division Head,
Clinical Chem., PHC



J. Simons
Medical Biochemist,
PHC



W. Dong
BC-CfE



S. Datwani, MD
Scientist, SFU



R. Kalikawe
MD/PhD
Scientist, SFU

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above all to the participants.
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be possible.**