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 Prystajecky, Christopher F. Lowe, Mari L. DeMarco, Daniel T. Holmes, Janet Simons, Masahiro Niikura, Marc G. Romney*, Mark A. Brockman*

***co-Principal Investigators**

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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

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

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

Francis Mwimanzi,[1] Hope R. Lapointe,[2] Peter K. Cheung,[1,2] Yurou Sang,[1] Fatima Yaseen,[1] Gisele Umviligihozo,[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 Prystajecky,[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 | IDSA Infectious Diseases Society of America | hivma hiv medicine association

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

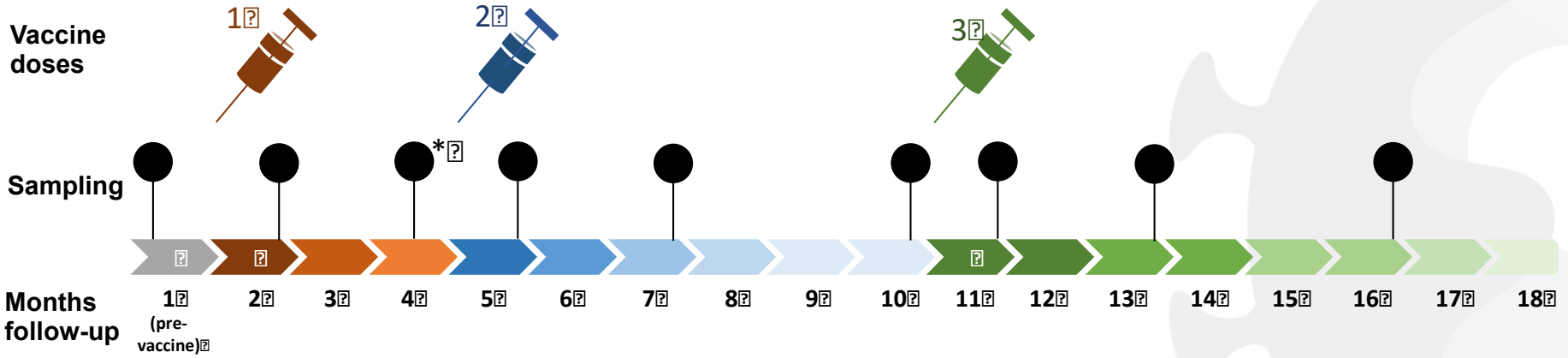
89 younger adults
(health care workers)

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

62 elder adults
(including long term care residents)

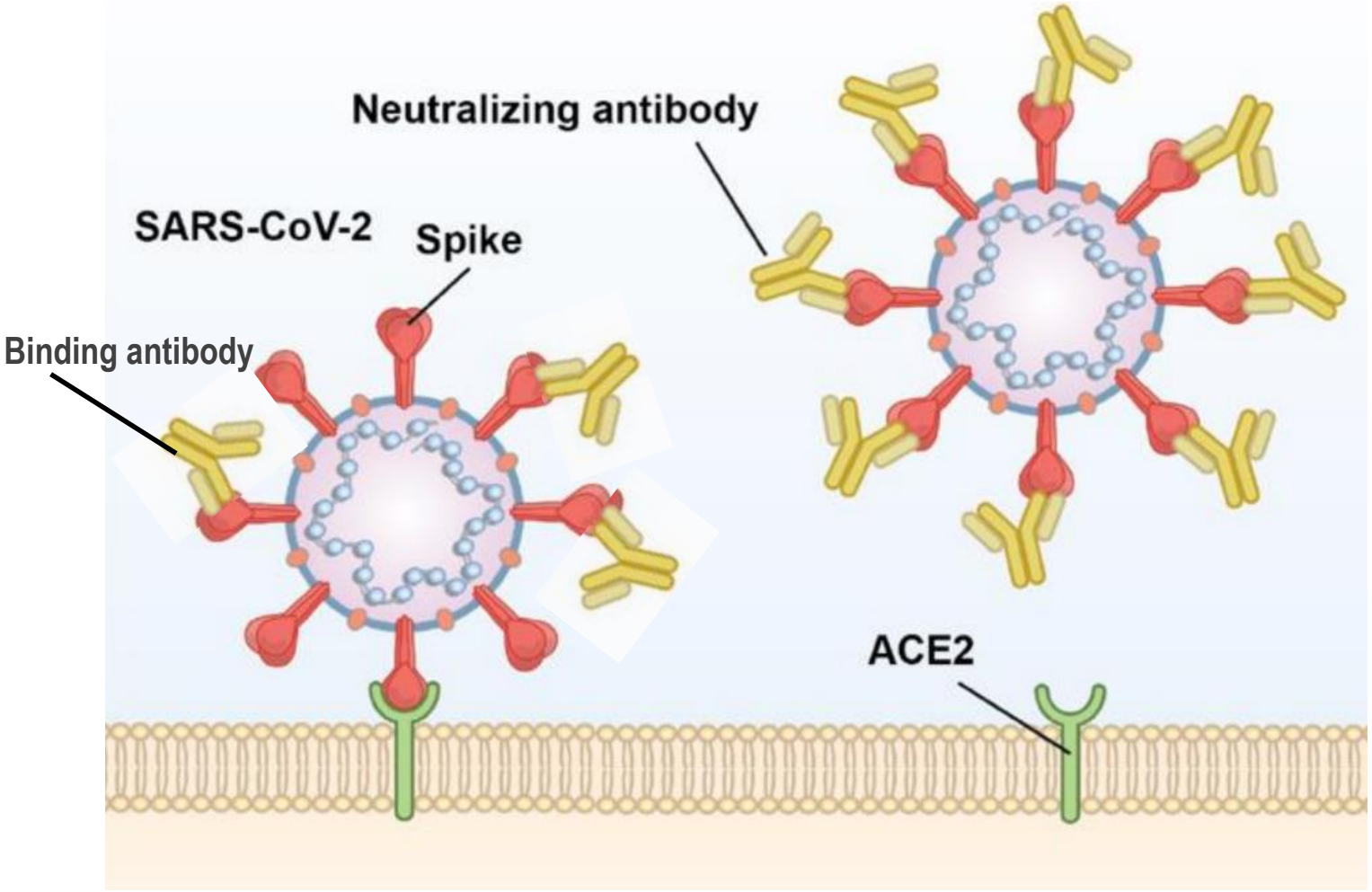
Median age 79 (IQR 73-86) years
69% female

Sampling



Plasma
Serum
PBMC

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)

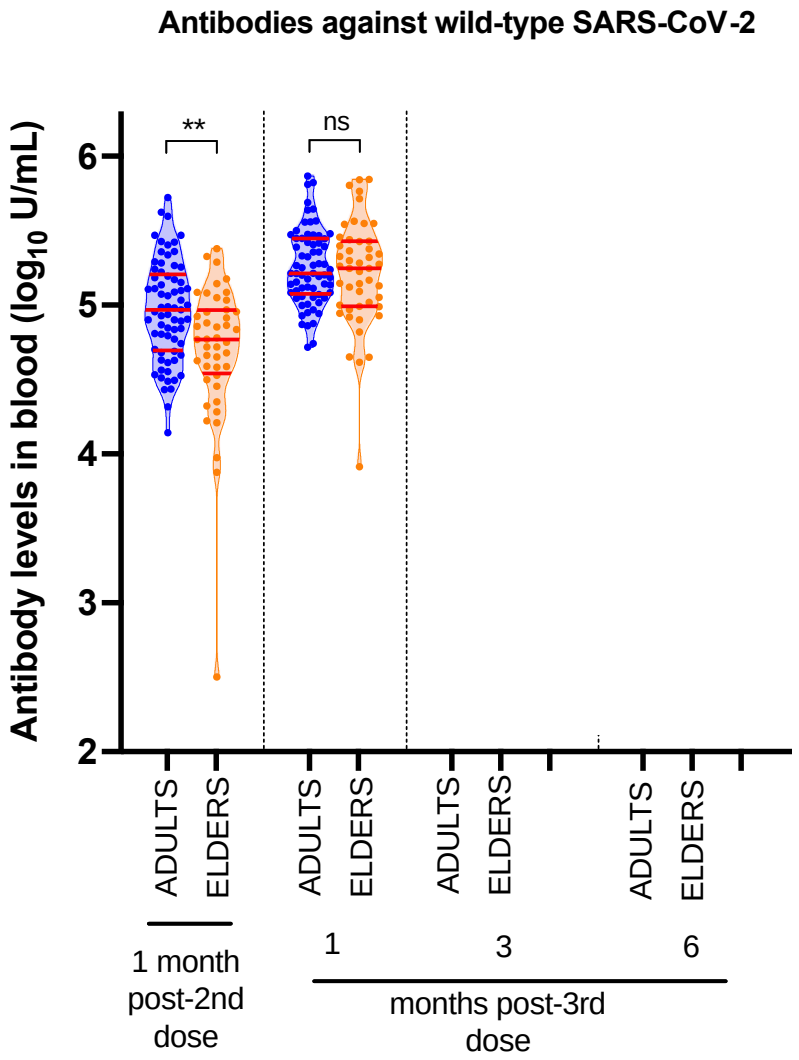
We measured both wild-type and variant -specific responses

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

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

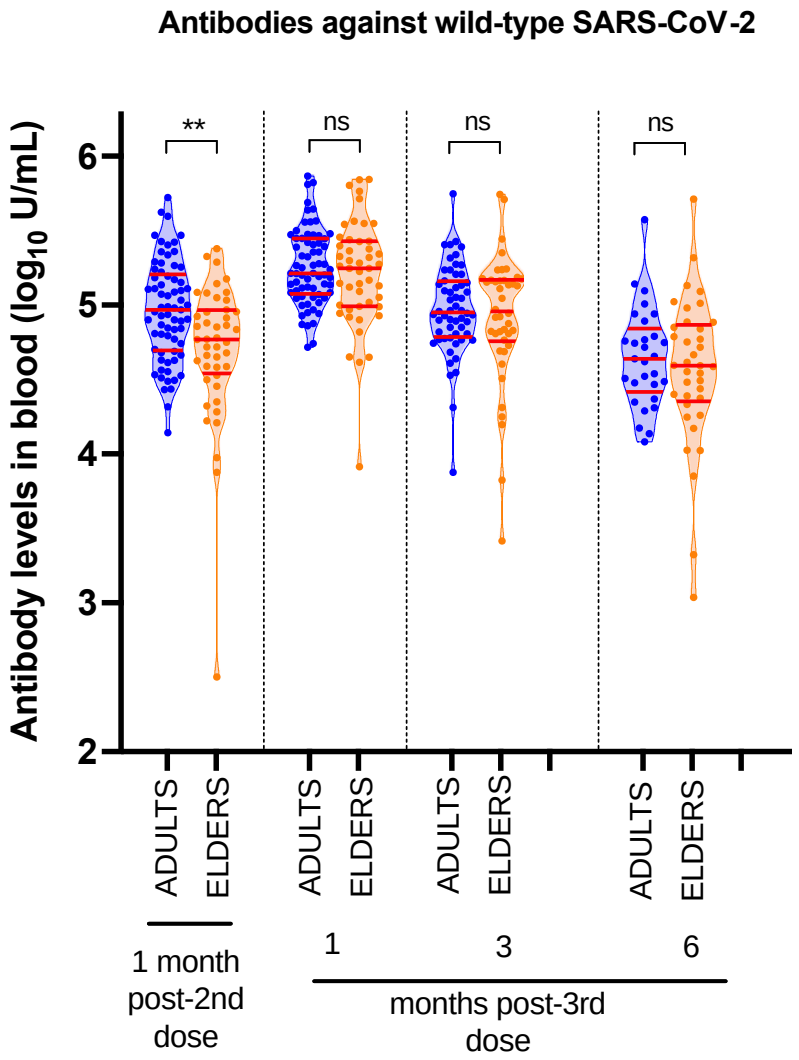
All participants displayed are COVID-19 naive



Antibody levels decline relatively quickly following vaccination

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

All participants displayed are COVID-19 naive



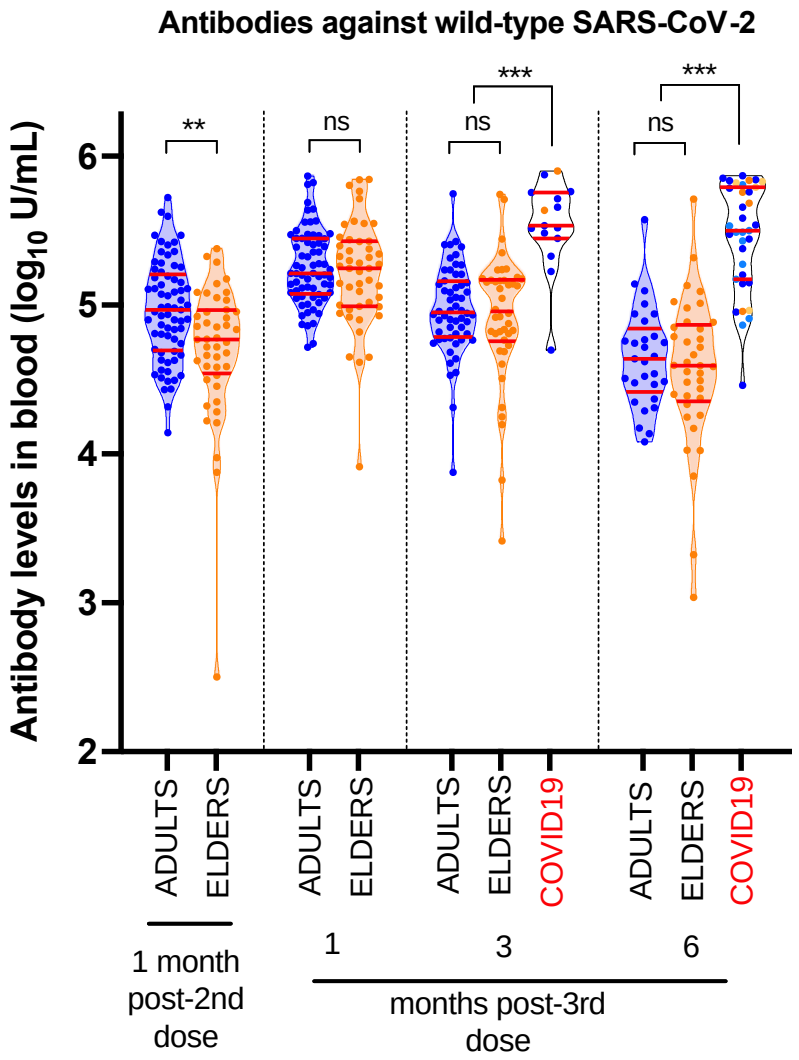
The rate of antibody decline is comparable in elder and younger adults.

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

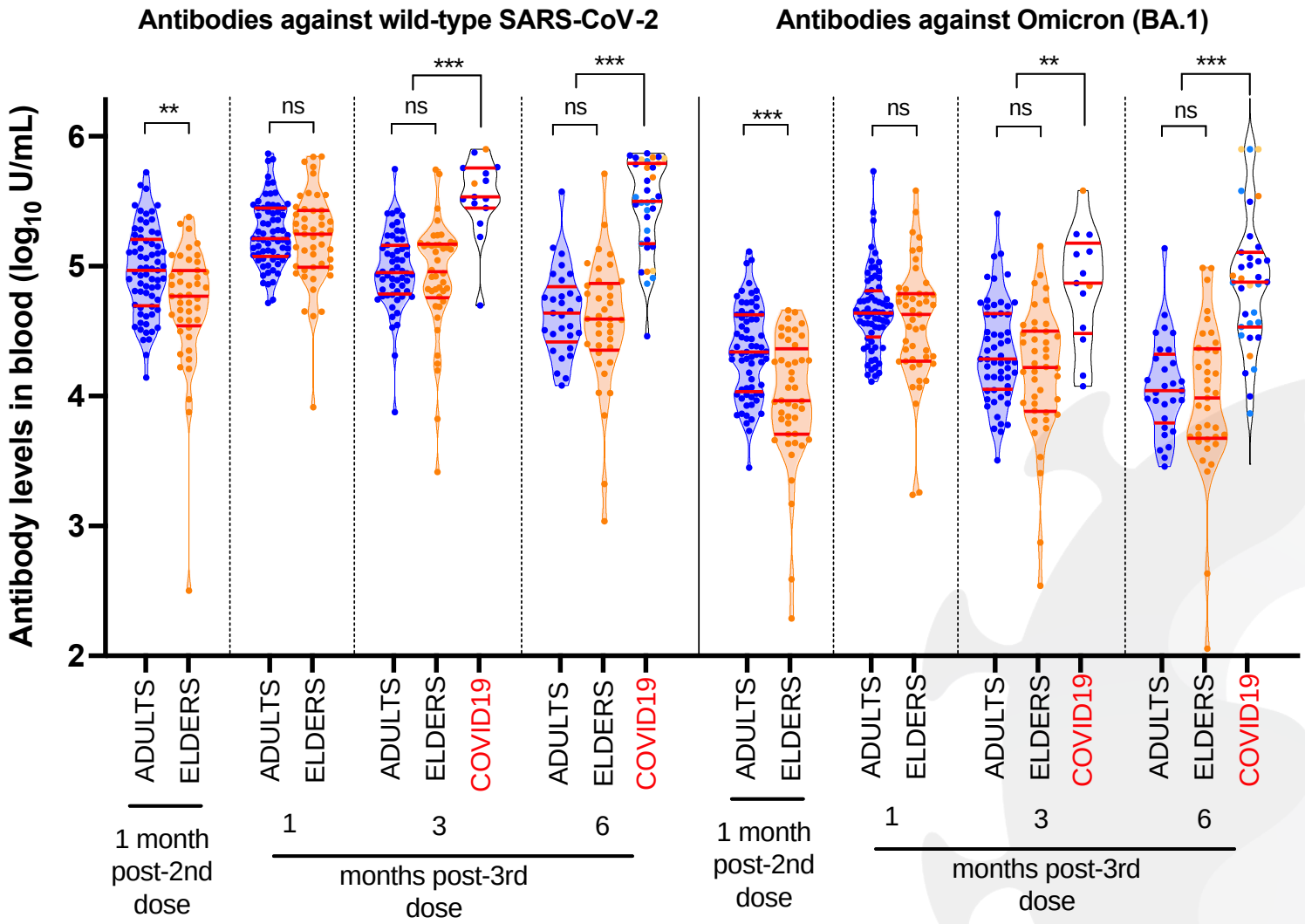


Six months after the third dose, antibody levels in this group were higher than those induced by three vaccine doses alone

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

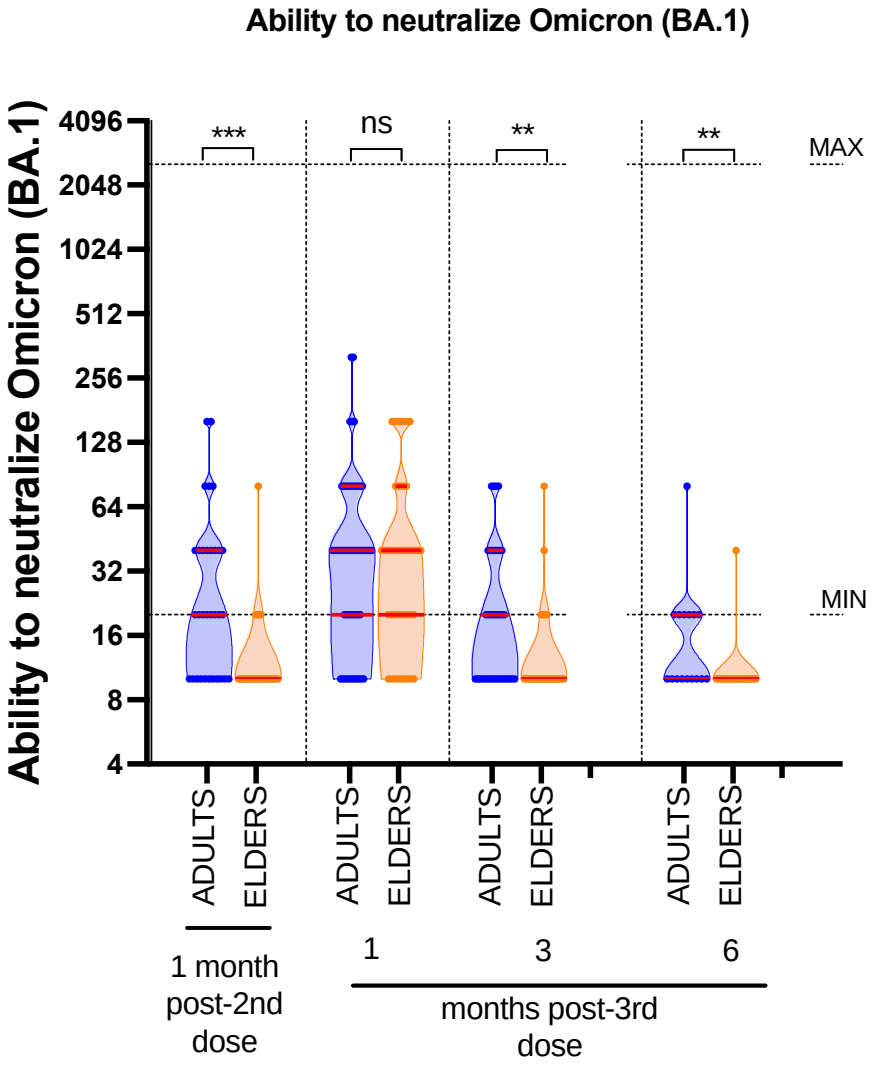
- Younger adults (median 41 years old)
- Elder adults (median 78 years old)

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

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

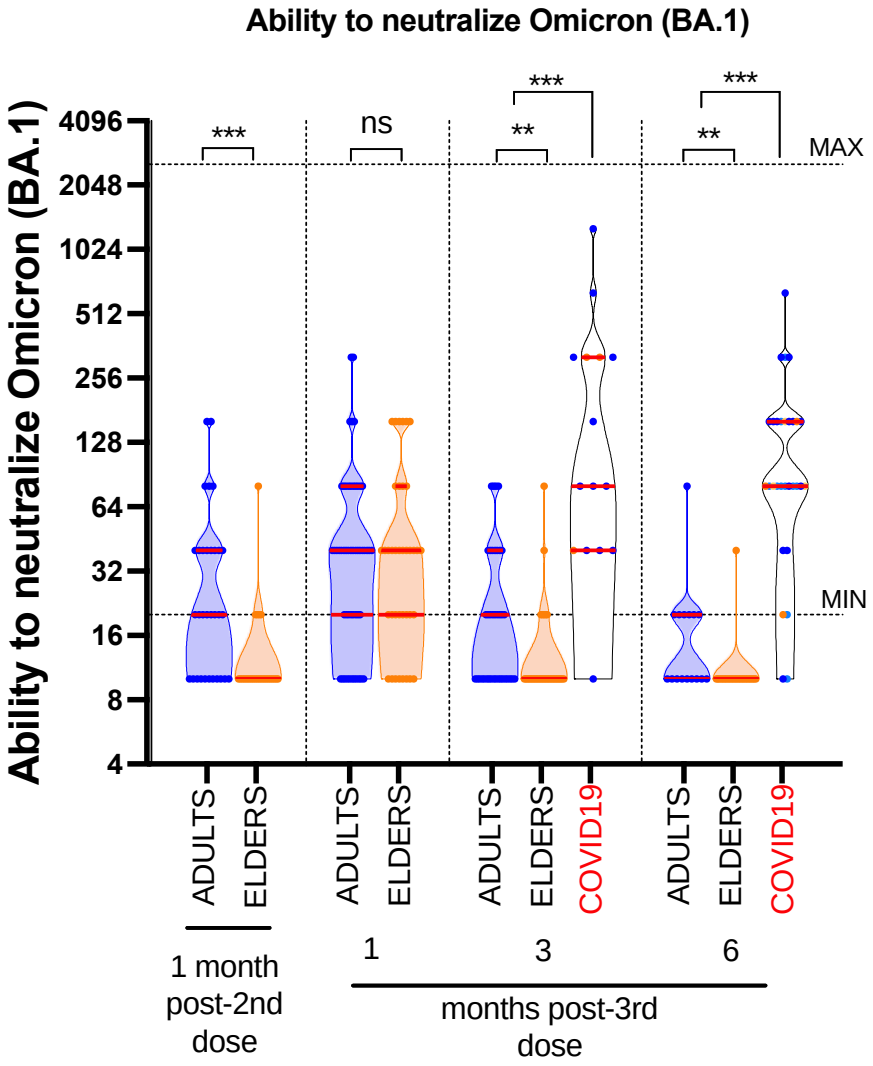


Six months after the third dose, ability to neutralize Omicron (BA.1) had declined to undetectable levels in 56% of younger adults and 96% of elder adults

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

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

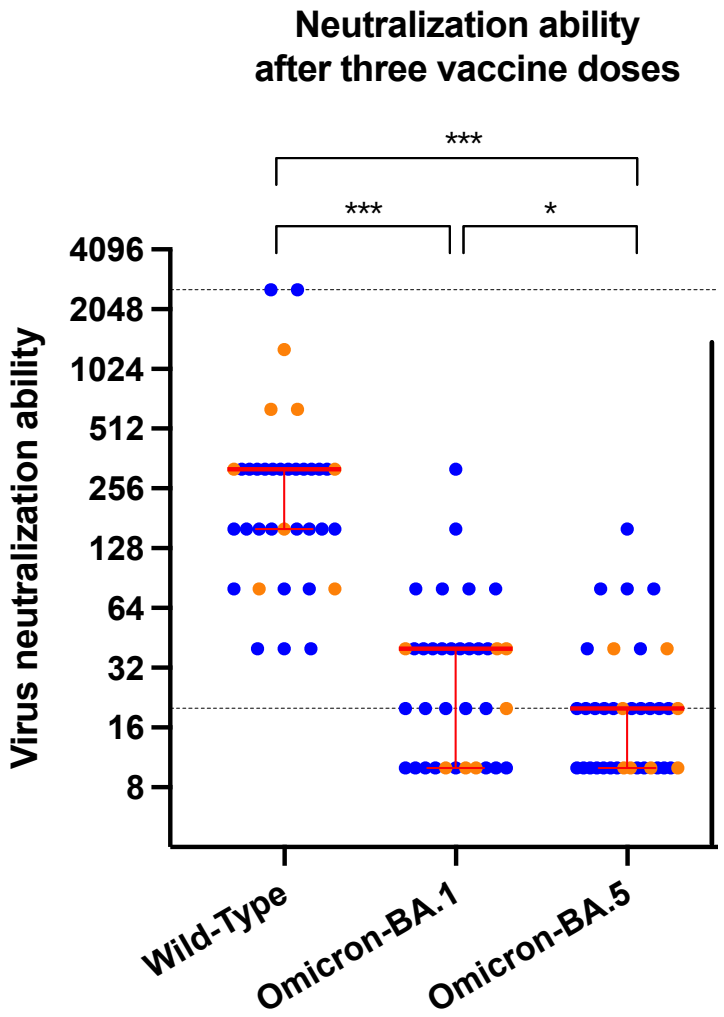
COVID-19 = participants who got COVID-19 after three vaccine doses



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

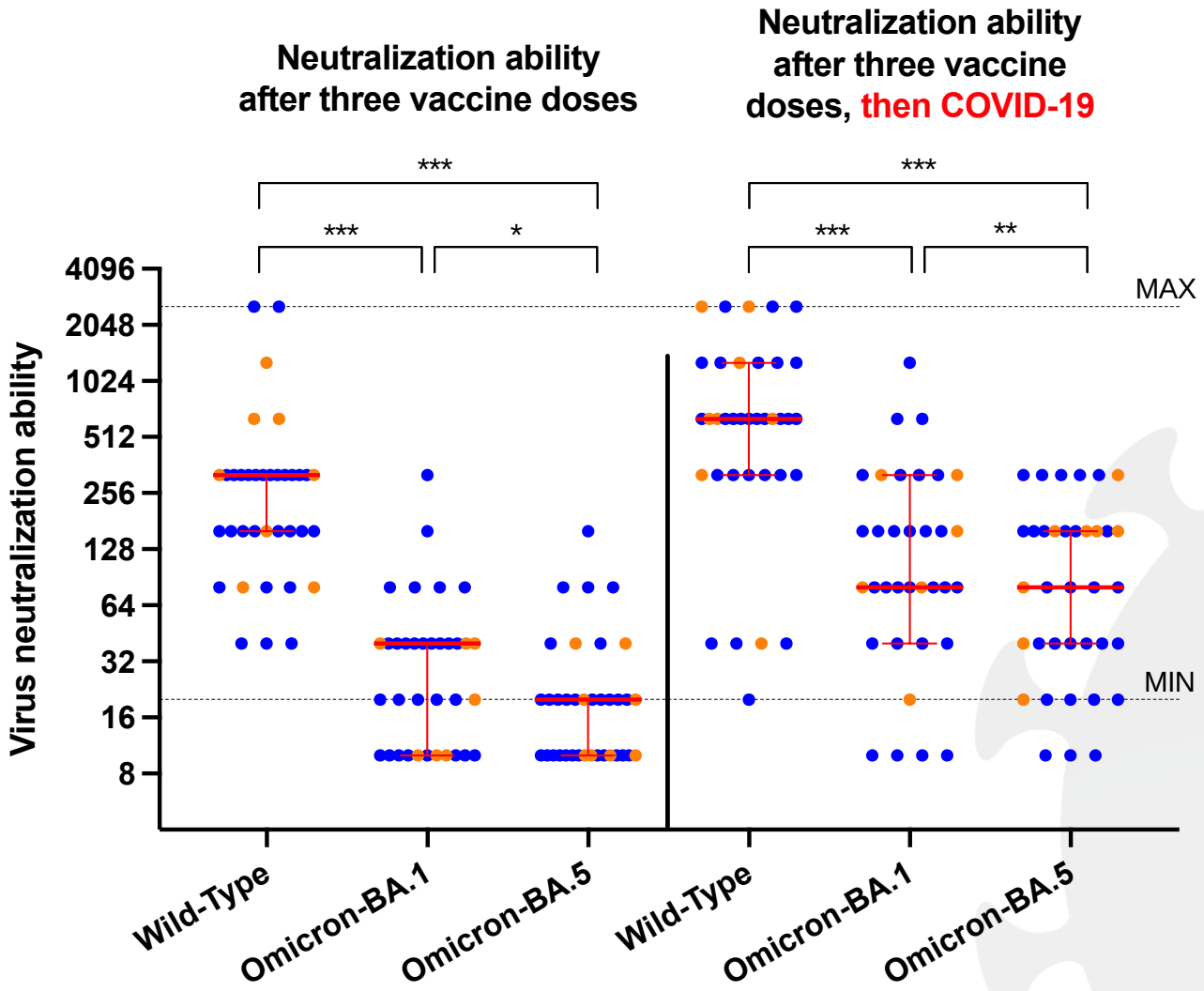
- Younger adults (median 41 years old)
- Elder adults (median 78 years old)



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?

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

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- Live virus neutralization (both WT and Omicron-BA.1-specific)

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

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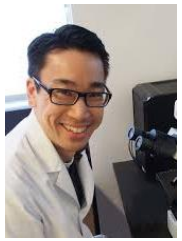

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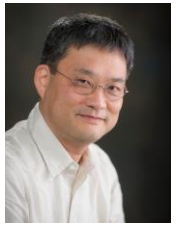

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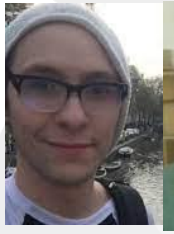

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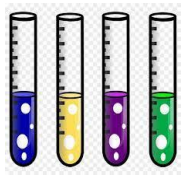

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Thank you to the clinics and above all to the participants. Without you, research would not be possible.