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

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

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Study overview

Data available online

- Preprint posted at: https://doi.org/10.1101/2021.09.06.21263149

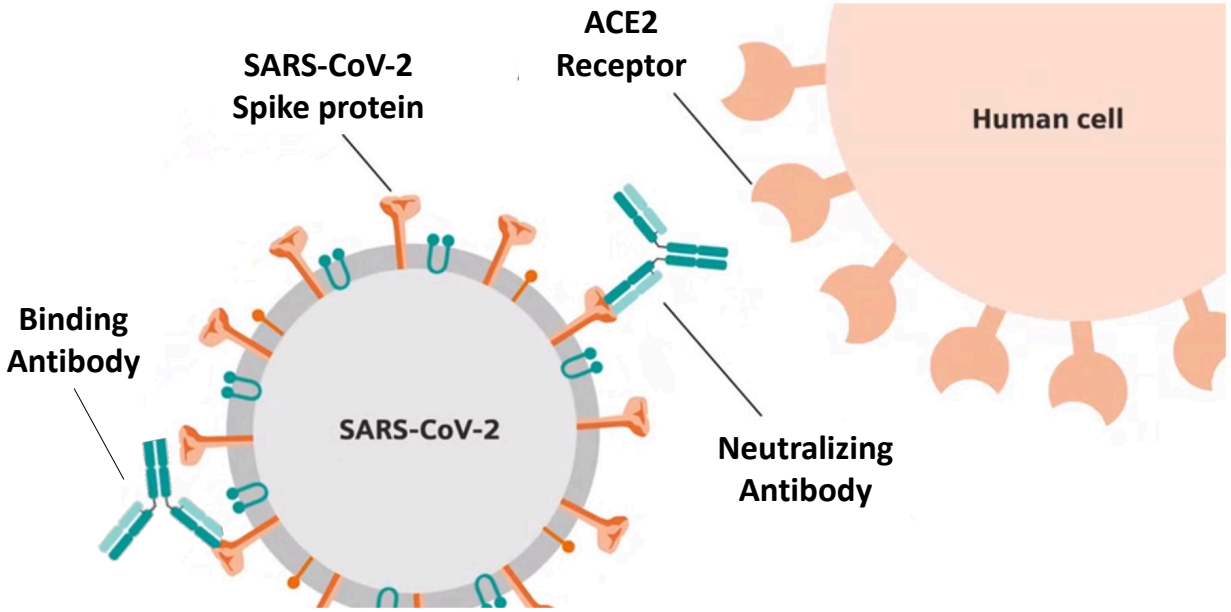
Rationale

- Third COVID-19 vaccine doses are broadly recommended.
- However, immunogenicity data remain limited, particularly in older adults and in context of the Omicron variant.

Design

- Cohort: N=151 adults aged 24-98 years (81 Health Care Workers [HCW] and 56 older adults) who received COVID-19 mRNA vaccines
- Approach: We longitudinally measured antibody concentrations and functions against ancestral and Omicron variants
- Time points: From pre-vaccine up to one month following the third dose

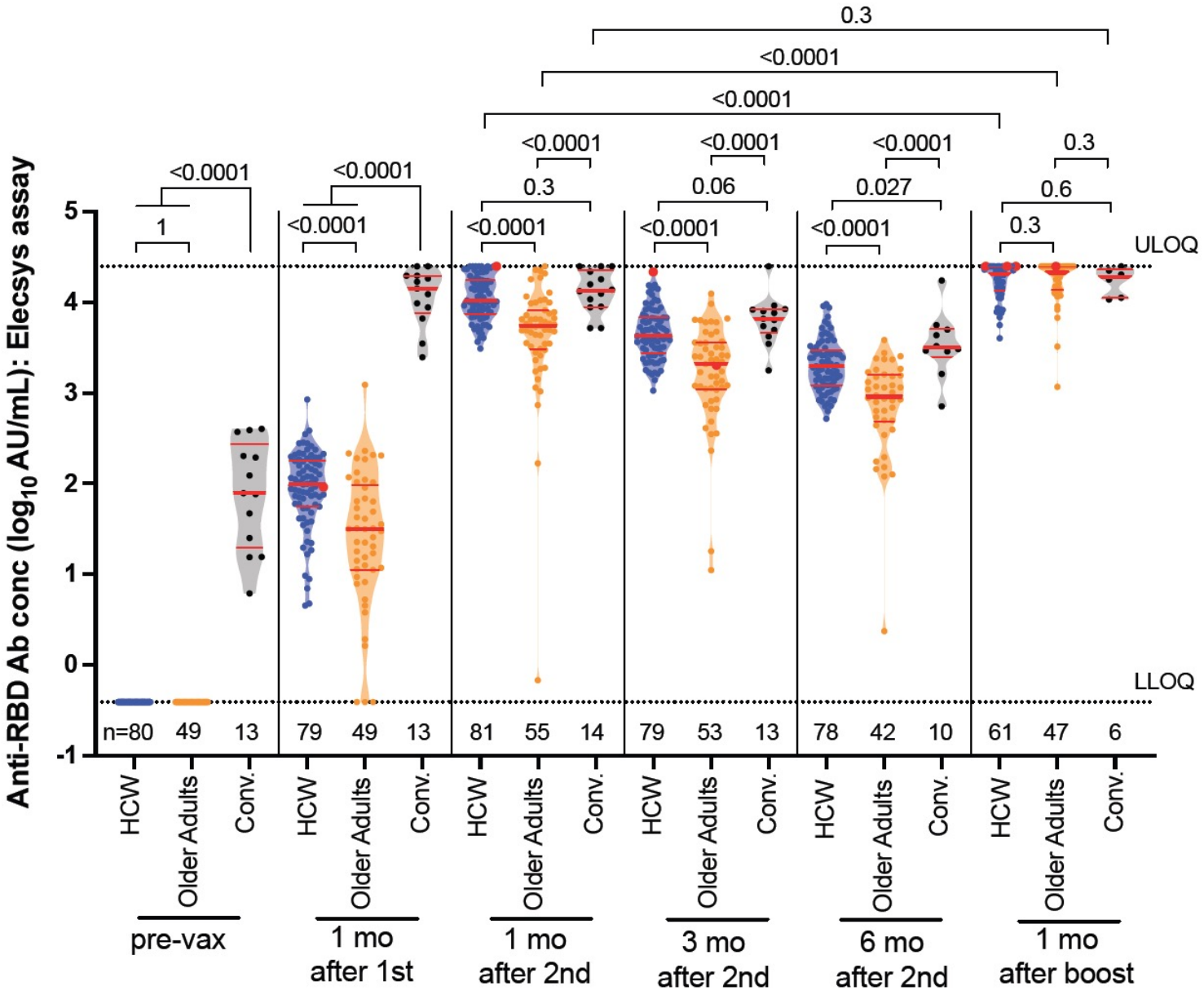
Antibody assays



1. Total binding antibodies against SARS-CoV-2 Spike-RBD (Roche Elecsys assay)
2. Ability of these antibodies to disrupt the Spike-RBD/ACE2 interaction (surrogate of viral neutralization: MesoScale Diagnostics assay)
3. Ability of these antibodies to inhibit SARS-CoV-2 infection of target cells in vitro (live virus neutralization assay)

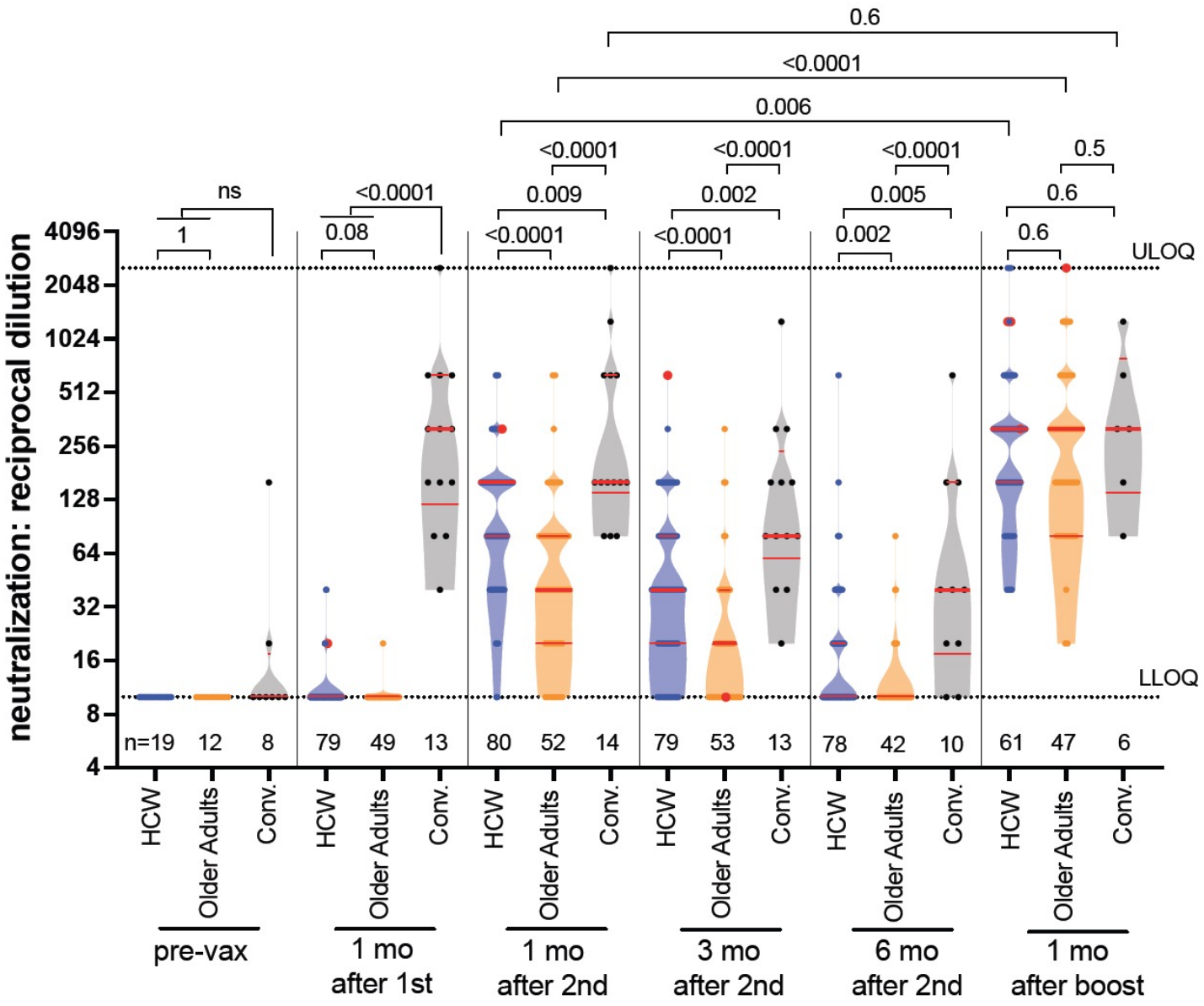
We assess responses to both wild-type SARS-CoV-2 and Omicron

Longitudinal Ab binding responses to spike RBD after COVID-19 vaccination



- All data shown are for the ancestral SARS-CoV-2 variant
- Older adults show lower binding antibody concentrations compared to younger HCW at all time points following 1 or 2 vaccine doses
- In addition, after two doses, rates of antibody decline are faster in older adults (data not shown)
- In multivariable analyses, in addition to age, a higher number of chronic conditions was also independently associated with weaker responses (data not shown)
- COVID-19 convalescent individuals ("Conv.") showed superior and more durable responses after two doses
- Third doses boost responses to higher than those seen after 2nd doses. Also, after three doses, binding antibody concentrations in older adults reached equivalence to HCW
- The data not shown are available at https://doi.org/10.1101/2021.09.06.21263149

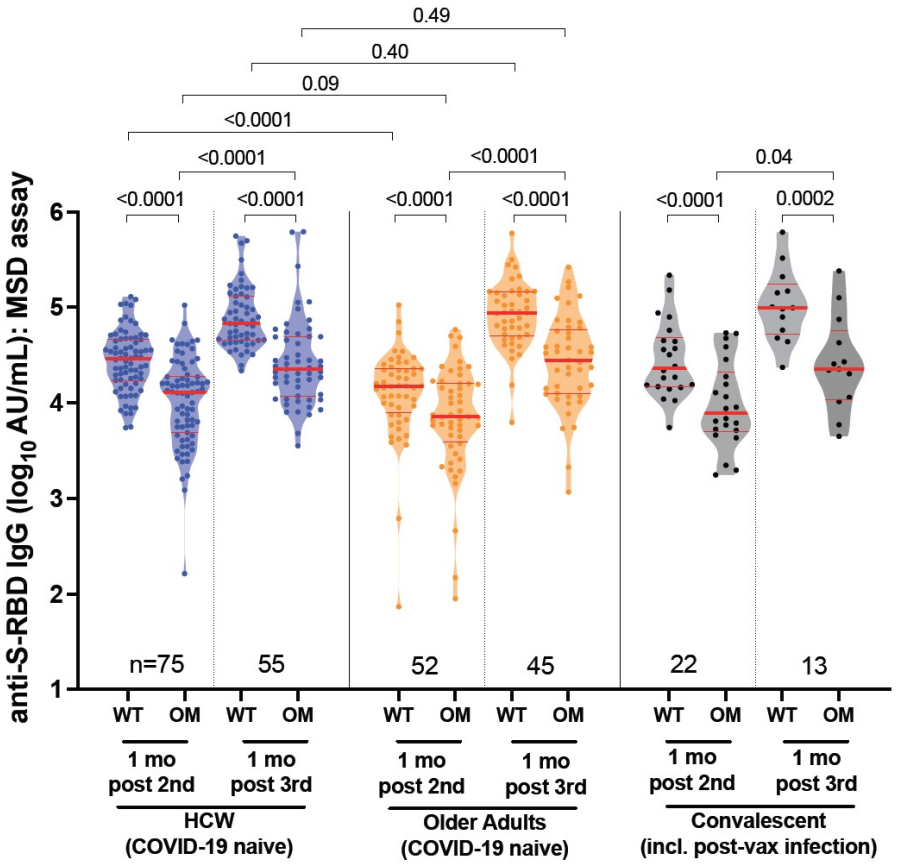
Longitudinal neutralizing antibody responses after COVID-19 vaccination



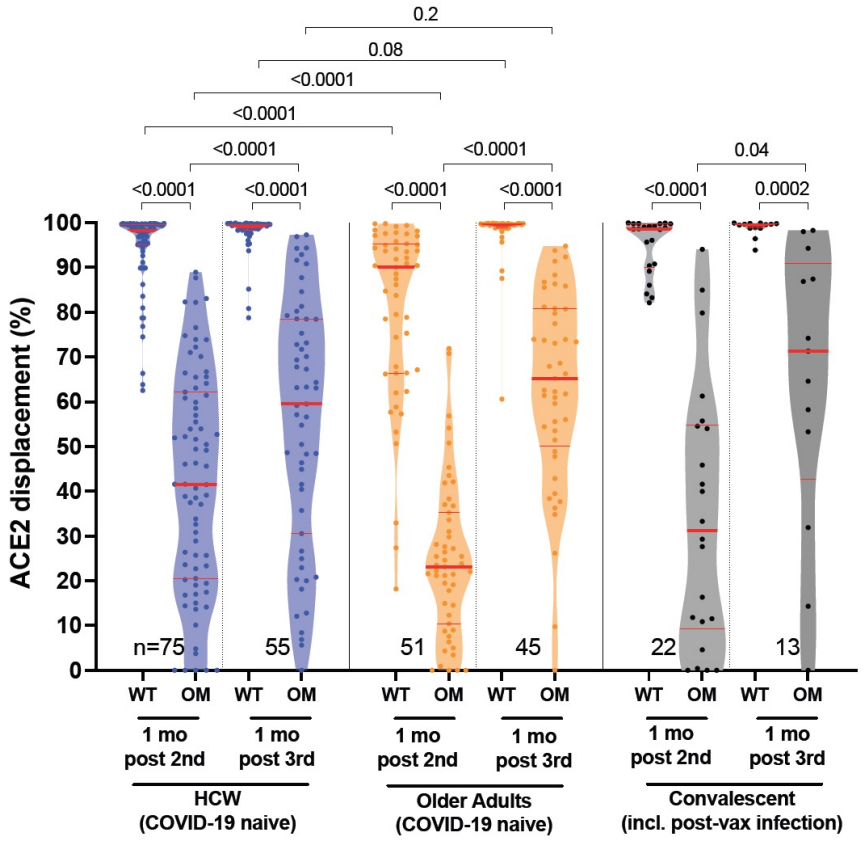
- All data are for the ancestral SARS-CoV-2 variant, from live virus neutralization assays
- Older adults show poorer neutralization compared to younger HCW at all time points following 1 or 2 vaccine doses
- 6 months after the second dose, neutralization activity had declined to below the limit of detection in all COVID-19 naïve individuals, regardless of age
- Multivariable analyses confirmed older age as the strongest significant correlate of poorer neutralization after 2 doses (data not shown)
- COVID-19 convalescent individuals ("Conv.") showed superior neutralization responses at all time points after two doses
- Third doses boost neutralization to higher than that seen after 2nd doses. Also, after three doses, neutralization function in older adults reached equivalence to HCW
- The data not shown are available at https://doi.org/10.1101/2021.09.06.21263149

Comparing “peak” Ab responses against WT and Omicron after 2 and 3 vaccine doses

Binding antibodies



ACE2 competition (surrogate viral neut)



- Humoral responses against Omicron were universally weaker than against the ancestral strain after both second and third doses
- Nevertheless, after three doses, anti-Omicron responses in older adults reached equivalence to those in younger adults
- Consistent results obtained in live virus neutralization assays; data available at https://doi.org/10.1101/2021.09.06.21263149

Conclusion: Results underscore the immune benefits of third COVID-19 vaccine doses, particularly in older adults. It will be important however to monitor the decline in these responses over time in this population.