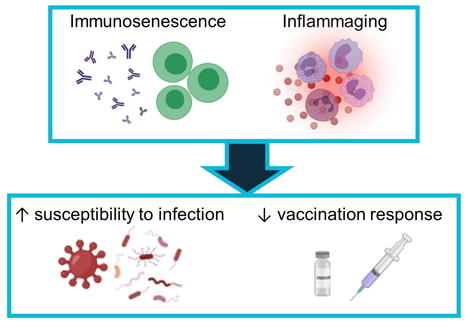
The COVID in Long-Term Care Study: assessing SARS-CoV-2 vaccination and infection in older adults

Jessica A. Breznik, Ali Zhang, Angela Huynh, Ahmad Rahim, Tara Kajaks, Lucas Bilaver, Hina Bhakta,
Jonathan L. Bramson, Ishac Nazy, Dawn M. E. Bowdish, Andrew P. Costa, and the COVID-in-LTC Study Group

BACKGROUND

- Older adults in have experienced the highest rates of infections and deaths throughout the COVID-19 pandemic.
- Age-associated ***immunosenescence*** (deterioration of cellular and antibody-mediated immunity) and ***inflammaging*** (increased systemic inflammation) may contribute to increased SARS-CoV-2 infection risk and decreased protective immunity after vaccination.



Key Questions

- How does immunological aging impact immune responses after vaccination with novel SARS-CoV-2 mRNA vaccines?
- What factors predict individual infection risk and vaccine efficacy?

STUDY OVERVIEW

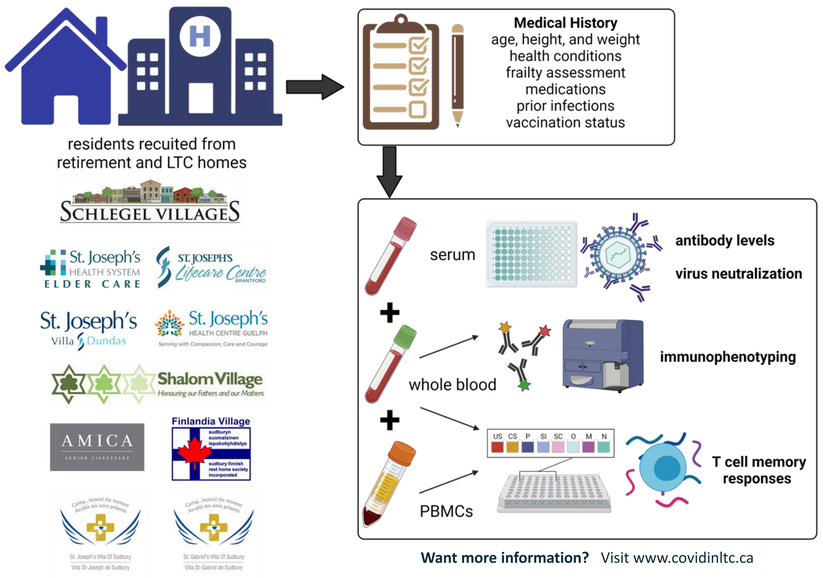
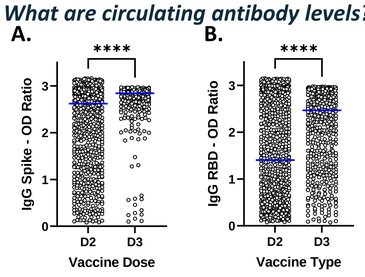


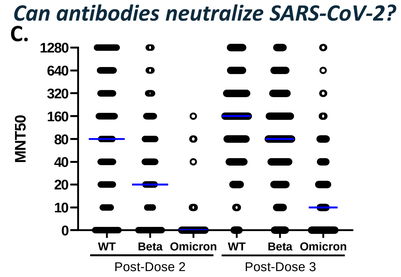
Figure 1. Study design and methodology.
Long-term care and retirement residents from partner homes in Ontario are eligible for the study. For all study participants, in addition to obtaining data on medical history, approximately every 3 months after each vaccine dose assays are performed on serum, whole blood, and PBMCs. These assays include ELISAs to measure the levels of antibodies in circulation, microneutralization assays to assess the ability of those antibodies to bind the live SARS-CoV-2 virus and prevent it from infecting cells, as well as flow cytometry and activation-induced marker assays to measure numbers of T cells and memory T cell responses.

Vaccinated older adults produce antibodies, including neutralizing antibodies, as well as memory T cells

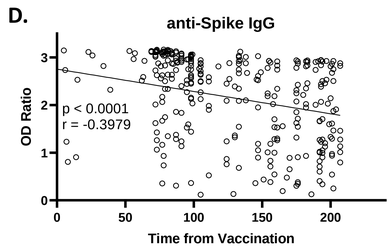
What are circulating antibody levels?



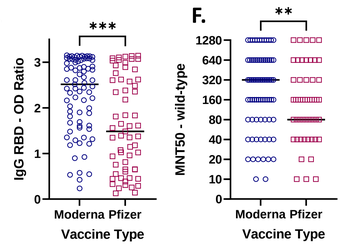
Can antibodies neutralize SARS-CoV-2?



How do antibody levels change over time?



Does vaccine type matter?



Are there T cell memory responses?

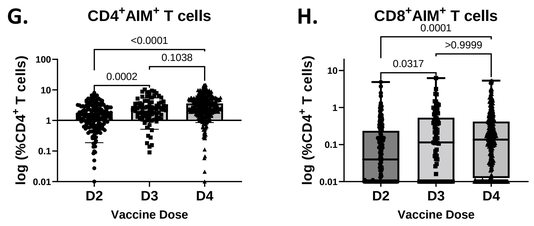
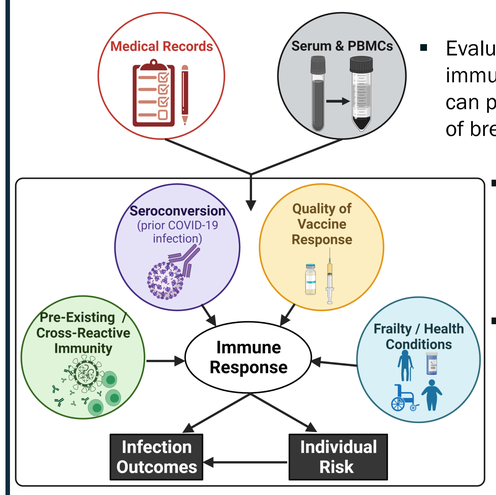


Figure 2. Serum antibody levels, neutralization, and whole blood T cell memory responses after SARS-CoV-2 vaccination.
Antibodies were measured by ELISA (A-B; D-E) and neutralization by MNT50 assay (B; F). T cell memory responses were assessed by flow cytometry in an activation-induced marker (AIM) assay.

What factors explain heterogeneity of immune responses?



- Evaluation of combined measures of immunity with health history to assess if we can predict vaccination responses and risk of breakthrough infections in older adults.
- **Chronological age** and **biological sex** alone do not explain variability in antibody and cellular responses after vaccination.
- High antibody levels / neutralization and T cell responses alone do not always positively correlate.

Chronic CMV infection does not prevent antibody or cellular vaccine responses in older adults

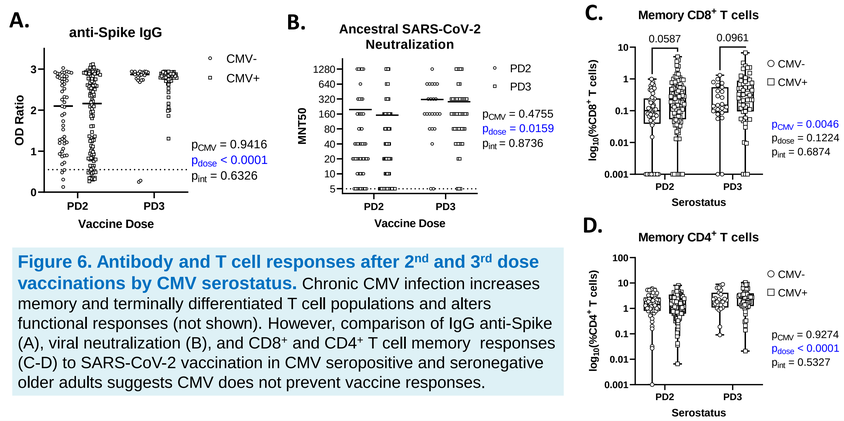


Figure 6. Antibody and T cell responses after 2nd and 3rd dose vaccinations by CMV serostatus. Chronic CMV infection increases memory and terminally differentiated T cell populations and alters functional responses (not shown). However, comparison of IgG anti-Spike (A), viral neutralization (B), and $CD8^+$ and $CD4^+$ T cell memory responses (C-D) to SARS-CoV-2 vaccination in CMV seropositive and seronegative older adults suggests CMV does not prevent vaccine responses.

What factors provide protection against Omicron infection?

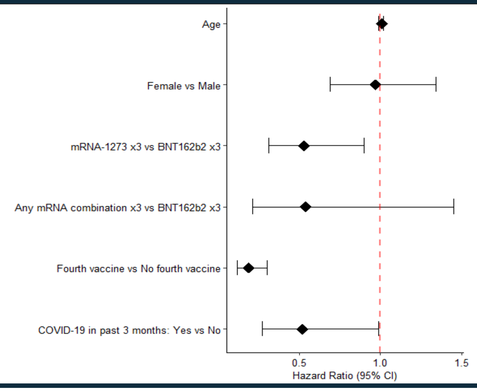
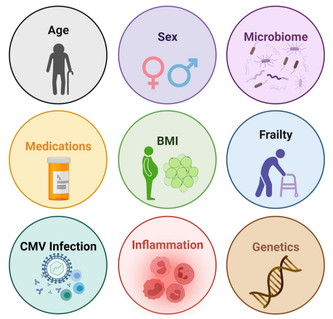


Figure 5. Cox regression analysis.
Variables (age, sex, mRNA vaccine combination received, and previous infection status) reflect time to baseline hazard on December 15, 2021 (beginning of Omicron wave in Ontario). To estimate the change in risk of Omicron infection due to receiving a fourth mRNA vaccine during the follow-up period, we included a binary time-dependent covariate (i.e., received a fourth vaccine or did not receive a fourth vaccine) in the regression analysis. Regression results are presented as hazard ratios with 95% confidence intervals based on robust standard errors, accounting for the clustering of participants by facility.

CONCLUSIONS & ONGOING RESEARCH

- Older adults, despite immunosenesce and inflammaging, produce heterogeneous antibody and cellular responses to SARS-CoV-2 mRNA vaccination; vaccination has been successful in reducing incidence of and morbidity and mortality from COVID-19.
- Heterogeneity in immune responses to vaccination is influenced by vaccine type and number of vaccine doses, as well as prior COVID-19 and chronic CMV infection.
- Vaccine dose, recent vaccination, and hybrid immunity influence risk of Omicron variant infection.

Continue post-4th dose collections and assessments



Continue evaluation of additional predictors / correlates of immunity and individual infection risk

Figures were created with BioRender.com