# Comparison of SARS-CoV-2 antibody response by demographic and clinical characteristics following natural infection and vaccination: the CANCOV study

**Victoria Russell**[1], Jennifer Taher[2,3], Anne-Claude Gingra[3,4], Karen Colwill[4], Ian Fraser[5], Kendiss Olafson[6], Gloria Vazquez-Grande[6], Anita Palepu[7], Michelle Kho[8], Sarah Manske[9], Juthaporn Cowan[10], Hilary Meggison[10], Jennifer Tsang[11], Alexandra Binnie[12], Karen Britto[12], Neill Adhikari[3,13], Margaret S. Herridge[1,3], Angela M. Cheung[1,3]

1. University Health Network 2. Sinai Health 3. University of Toronto 4. Lunenfeld-Tanenbaum Research Institute 5. Michael Garron Hospital 6. University of Manitoba 7. University of British Columbia 8. St. Josephs Healthcare Hamilton 9. University of Calgary 10. The Ottawa Hospital Research Institute 11. Niagara Health 12. William Osler Health System. 13. Sunnybrook Research Institute

## Introduction

**CANCOV** is an ongoing ambi-directional cohort study of patients with SARS-COV-2 infection. Serology samples from Ontario, British Columbia, Alberta and Manitoba are included.

## Objectives

**Primary:** To compare the long-term trajectory of SARS-CoV-2 antibody response following natural infection with and without vaccination.

**Secondary:**

- To describe the differences between antibody response by sociodemographic factors.
- To examine the characteristics of those who do not produce an antibody response following COVID-19 vaccination.
- To examine the characteristics of those who have a long-term sustained antibody response following SARS-CoV-2 infection without vaccination.

## Methods

Participants include non-hospitalized patients, hospitalized non-ICU patients and hospitalized ICU patients following confirmed SARS-CoV-2 infection (PCR or RAT).

Two Health Canada approved Roche antibody tests using the Cobas platform, targeting total antibodies (IgG, IgM, IgA) to the nucleocapsid antigen (qualitative test) and the spike antigen (quantitative test) were used.

Sociodemographic variables include age, sex, ethnicity, alcohol consumption and smoking behavior. Clinical factors include acute illness hospitalization, number of initial symptoms and pre-existing comorbidities.

## Results

**Figure 1.** Natural & vaccine induced anti-spike antibody levels over time.

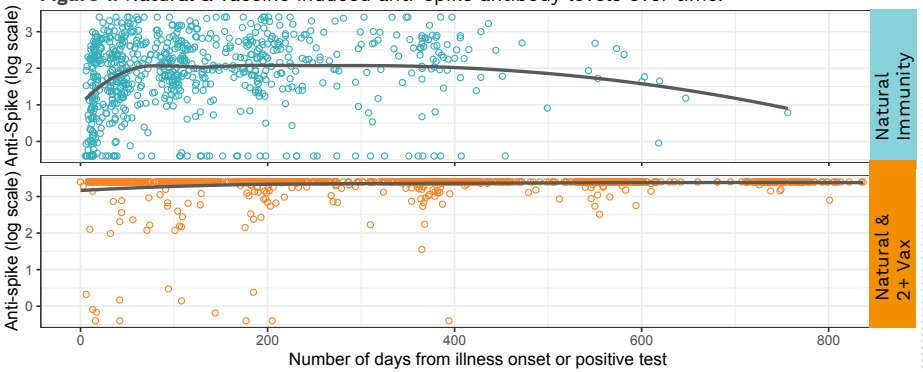
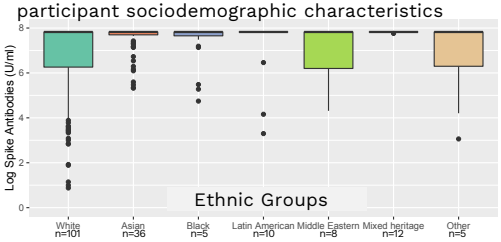



**Figure 2.** Anti-spike antibodies from natural immunity 6-months after illness onset and participant sociodemographic characteristics




After adjusting for sociodemographic & clinical variables, **female** is associated with **lower Spike Ab levels** compared to male (p=0.03) (not shown)

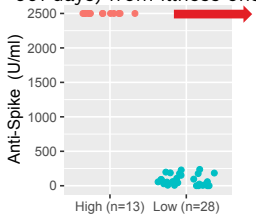
Asian (p=0.04), Latin American (p=0.02) and Mixed heritage (p=0.04) ethnic groups are all associated with **higher Spike Ab levels** compared to White.

**Table 1.** Characteristics of participants that do not generate a substantial spike Ab response to vaccination (< 50 U/ml 30-90 days from last dose)

| | <50 U/ml Spike n=7 | Remaining participants n= 412 | Total & p-value n= 419 |
|---|---|---|---|
| **Nucleocapsid Ab** | | | **< 0.001** |
| Negative | 6 (85.7%) | 53 (13.0%) | 59 (14.2%) |
| Positive | 1 (14.3%) | 355 (87.0%) | 356 (85.8%) |
| Missing | 0 | 4 | 4 |
| **Pre-existing Comorbidities** | | | **0.090** |
| No | 0 (0.0%) | 114 (29.2%) | 114 (28.7%) |
| Yes | 7 (100.0%) | 276 (70.8%) | 283 (71.3%) |
| Missing | 0 | 22 | 22 |

**71%** (5/7) of those **without substantial response** are immunocompromised (ex. organ transplant, CF)

**Figure 3.** Unvaccinated Participants with "high" (2,500 U/ml) Spike Ab vs "low" (<=250 U/ml) levels in unvaccinated participants more than 1 year (366-561 days) from illness onset.




Univariate analysis showed "high" responders more likely to be **hospitalized** during acute illness (p=0.01) and **male** (p=0.03). No other significant differences.

## Conclusions

- Participants' spike Ab responses have **high variability.** 3 months from symptom onset, 6% of unvaccinated participants are negative for nucleocapsid antibodies and 2% are negative for spike Ab. **Hybrid immunity** (vaccination and infection) greatly reduces the variability of antibody response and most participants approach the maximum reported threshold.
- Participants that are **vaccine "non-responders"** are associated with more negative nucleocapsid Ab levels suggesting a depressed immune response to initial infection. There is also a potential association with pre-existing comorbidities.
- **Sex, ethnic group and initial illness severity** account for some of the variability of antibody response, but there are likely other factors.

**Acknowledgements:**
We thank the participants of the CANCOV study for providing blood samples for this study. Funding was provided by Canadian Institutes Of Health Research and Covid-19 Immunity Task Force. Roche Canada provided reagents. AM Cheung is supported by a Tier 1 Canadian Research Chair.