Persistence of Anti-SARS-CoV-2 Antibodies in Long Term Care Residents Over Seven Months After Two COVID-19 Outbreaks

BC Centre for Disease Control
Provincial Health Services Authority

Guadalein Tanunliong[1], Aaron Liu[2], Rohit Vijh[3,4], Tamara Pidduck[5], Jesse Kustra[5], Citlali Marquez[5], Alexandra Choi[3], Meghan McLennan[5], Althea Hayden[3], Christy Kearney[6], Soren Gantt[7], Mel Krajden[1,5], Muhammad Morshed[1,5], Agatha Jassem[1,5], Inna Sekirov[1,5*]

[1]Department of Pathology and Laboratory Medicine, University of British Columbia, Vancouver, BC, Canada, [2]Department of Experimental Medicine, University of British Columbia, Vancouver, BC, Canada, [3]Office of the Chief Medical Health Officer, Vancouver Coastal Health, Vancouver, BC, Canada, [4]School of Population and Public Health, University of British Columbia, Vancouver, BC, Canada, [5]BCCDC Public Health Laboratories, British Columbia Centre for Disease Control, Vancouver, BC, Canada, [6]Haro Park Centre, Vancouver, BC, Canada, [7]Centre de Recherche de CHU Sainte-Justine, Département de microbiologie, infectiologie et immunologie, Université de Montréal, Montréal, QC, Canada

Background

Long term care facilities (LTCF) have been disproportionately affected by the coronavirus disease 2019 (COVID-19) pandemic due to [1,2]:

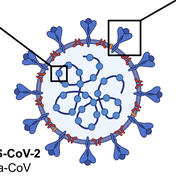
- **Increased risk of transmission** of respiratory pathogens
- Older age of residents and multiple co-morbidities lead to **increased susceptibility of severe disease**

April 2020 **Outbreak 1** — October 2020 **Outbreak 2**

SARS-CoV-2

- Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of COVID-19, emerged in December 2019 and poses an acute public health challenge worldwide

Nucleocapsid
- Viral transcription, replication, assembly

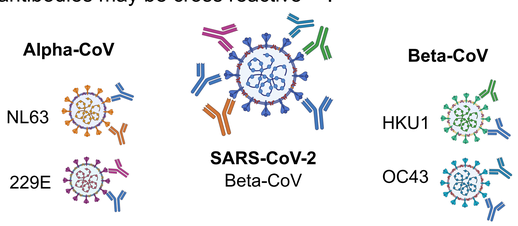


SARS-CoV-2 Beta-CoV

Spike Protein
- viral attachment, fusion, entry
- **Receptor Binding Domain (RBD)** binds to host cell receptor ACE2

Endemic Human Coronaviruses (HCoV)

- Circulating endemic human coronaviruses (HCoV) cause the common cold, and it's estimated that everyone will have acquired immune memory against them by adolescence [3].
- The endemic HCoVs OC43 and HKU1 (beta-CoV) along with NL63 and 229E (alpha-CoV) exhibit considerable sequence and structural homology to SARS-CoV-2 and antibodies may be cross reactive [4,5].



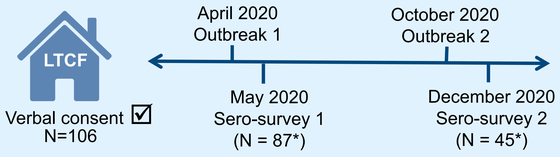
- Recent studies found a recent HCoV infection was associated with less severe disease [6], suggesting antibodies against HCoV may contribute to the immune response development during SARS-CoV-2 infection.

Objectives

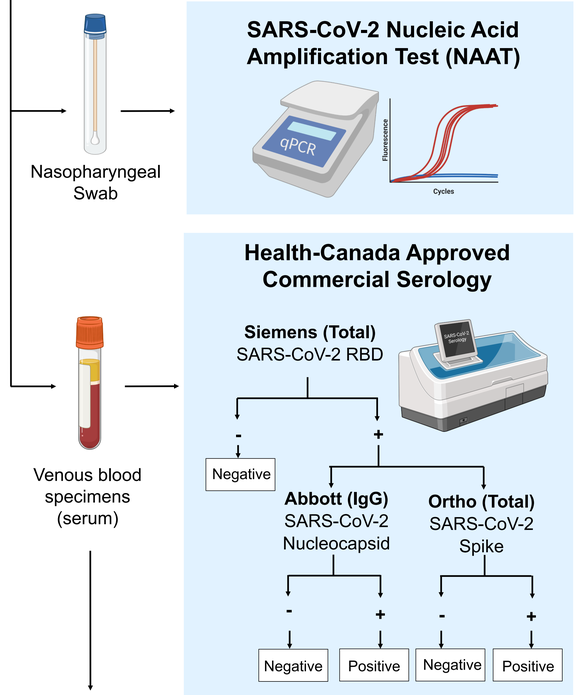
1. **To describe the serostatus of LTCF residents following the second COVID-19 outbreak**
2. **To monitor changes in their humoral immune response to SARS-CoV-2 and endemic HCoV following the second outbreak**

Methods

Outbreak investigation



*26/106 participants provided serum following both outbreaks



Meso Scale Discovery (MSD) Multiplex Immunoassay

Target (IgG)	Positivity Cut-off
1: SARS-CoV-2 Spike	**1960 AU/mL**
2: HCoV-NL63 Spike	
3: SARS-CoV-2 Nucleocapsid	**5000 AU/mL**
7: HCoV-HKU1 Spike	
8: HCoV-OC43 Spike	
9: HCoV-229E Spike	
10: SARS-CoV-2 Receptor Binding Domain (RBD)	**538 AU/mL**

MSD Algorithm:
Samples above cut-off values for at least two of SARS-CoV-2 Spike, Nucleocapsid, or RBD are considered serologically reactive

Results

	Positive (N)	Negative (N)	Total (N)	Attack Rate	P-Value
Commercial					X^2, P = 0.2274
Outbreak 1	35	52	87	40.2%	Fisher, P = 0.3002
Outbreak 2	10	25	35	28.6%	
Total	45	77	122	36.8%	OR = 1.68 (0.674-4.42)
MSD					X^2, P = 0.3643
Outbreak 1	35	52	87	40.2%	Fisher, P = 0.4137
Outbreak 2	11	24	35	31.4%	
Total	46	76	122	37.7%	OR = 1.46 (0.598-3.76)

Table 1. Summary of sero-survey results. Calculations for the second outbreak do not include the individuals seropositive post-first outbreak and remained seropositive during the second outbreak.

Seroprevalence and Attack Rates of SARS-CoV-2 in LTCF

- Sero-survey results demonstrated high agreement between clinical and MSD interpretations
- Slightly greater odds of seroconversion following the first outbreak and lower attack rates following the second outbreak, although not statistically significant (Table 1)

Duration of SARS-CoV-2 IgG (Figure 1)

- Anti-SARS-CoV-2 Spike and RBD antibodies remained stable, while significant waning of anti-SARS-CoV-2 Nucleocapsid antibodies was observed over 7 months

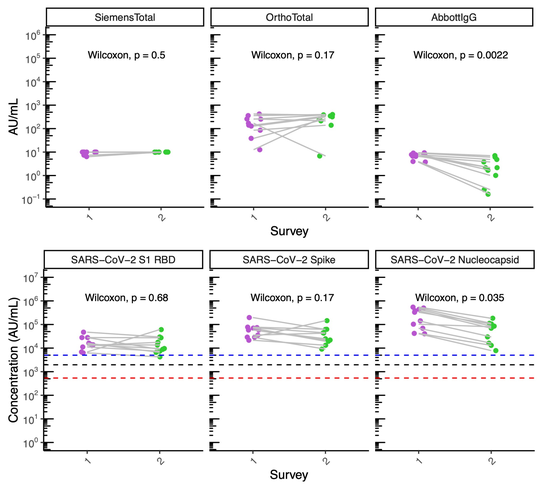


Figure 1. Sero-surveys demonstrate gradual waning of anti-nucleocapsid antibodies following the second outbreak. All participants (N=10) seropositive for SARS-CoV-2 following the first outbreak (purple) remained seropositive following the second outbreak (green) on both commercial and MSD platforms. Grey lines indicate paired samples across surveys. Dashed lines on represent positive signal cut-off for SARS-CoV-2 S1 RBD (red), spike (black), and nucleocapsid (blue). Statistical analysis was performed using Wilcoxon's Signed Rank Test.

	N (%)
Outbreak 1	87
Seropositive	35 (100%)
Negative NAAT result	0 (0%)
Positive NAAT result	30 (85.7%)
No NAAT result	5 (14.3%)
Outbreak 2	45
Seropositive	20 (100%)
Seroconverted in outbreak 1	10 (50%)
Seroconverted in outbreak 2	3 (15%)
No baseline serology results	7 (35%)
Positive NAAT result (OB1 N/A, OB2 +)	3
Positive NAAT result (OB1 +, OB2 -)	3
Positive NAAT result (OB1 -, OB2 +)	1

Table 2. Breakdown of seropositive participants based on clinical serology tests. N = Number of participants tested. OB = Outbreak. N/A = Not applicable

- 3 new seroconversions in outbreak 2, also positive by NAAT
- Among those with paired samples, all 10 individuals that were seropositive post-first-outbreak remained seropositive post-second-outbreak
- No reinfections were identified among them (Table 2)

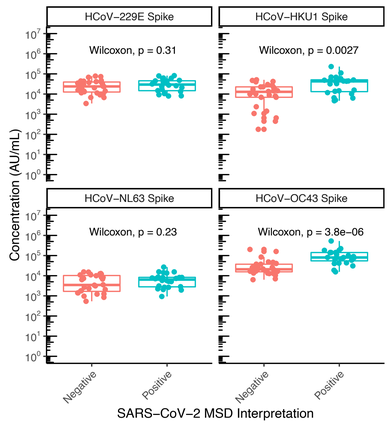


Figure 2. Significant elevation of HKU1 and OC43 antibodies in SARS-CoV-2 positive individuals. Antibody levels for all residents with paired sera collected (N=26) were plotted by SARS-CoV-2 negative (red) or positive (blue) status to assess antibody levels to endemic HCoV. Statistical analysis was performed using Wilcoxon rank-sum test.

Antibody Responses to Endemic HCoV

- Antibody levels to all 4 HCoVs remained stable in both serosurveys
- Individuals seropositive for SARS-CoV-2 were also found to have elevated antibody levels to beta-CoVs OC43 and HKU1 (Figure 2)

Limitations/Strengths

- Limitations include a small sample size from a single LTCF and may not be representative of other elderly populations
- Strength of our study includes the agreement of sero-survey results using well-validated assays

Conclusion

- SARS-CoV-2 antibodies elicited by natural infection persist over at least seven months in the elderly
- Elevated anti-beta-CoV antibodies in SARS-CoV-2 seropositive persons

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Contact:
Guadalein Tanunliong
guadalein.tanunliong@bccdc.ca
MSc Student | Pathology and Laboratory Medicine