

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

## Summary report #2

## Protecting Canada's long-term care residents from COVID-19: The evidence behind the policies

## Key findings

- Residents of long-term care (LTC) homes experience **waning antibodies much faster** than younger, healthier adults
- Fewer LTC residents have a neutralizing antibody response compared to younger adults
- Their neutralizing antibody levels diminish 3-6 months after the second vaccine dose, suggesting **they benefit from a third dose of vaccine**
- The rate of decline in antibody levels after a first dose of vaccine suggests that 16 weeks is a reasonable upper limit of time between doses
- A two-dose series of the **Moderna vaccine seems to elicit a higher antibody response** than Pfizer in LTC residents, perhaps due to its higher mRNA concentration
- **Mixing-and-matching mRNA vaccines is equally effective** as receiving two doses of the same product
- Comorbidities are a factor in the endurance of SARS-CoV2 antibodies, indicating that **healthier people can have a longer effective antibody response against COVID-19**
- Understanding immune protection = understanding the individuals and the environments they live in

### Background

The <u>COVID-19 Immunity Task Force (CITF)</u>, through the Government of Canada, supports over 100 studies to determine the extent of SARS-CoV-2 infection in Canada. This includes the **seven studies** included in this summary that offer strong scientific evidence to aid in protecting Canada's long-term care residents, staff, and visitors. They present the evidence behind the latest policy decisions, including making this vulnerable population eligible for a third dose of a COVID-19 vaccine in many provinces and territories.

## **Research studies included**

Study	Lead researcher(s) and affiliation	Who is participating?	Where is the study taking place?
COVID-19 vaccinations & infections in long-term care	Dr. Andrew Costa, McMaster University Dr. Dawn Bowdish, McMaster University	Staff and residents of LTC homes	Hamilton, Ontario
Wellness Hub Study: Immunogenicity sub-study	Dr. Sharon Straus, University of Toronto Dr. Allison McGeer, University of Toronto Dr. Anne-Claude Gingras, University of Toronto	Staff and residents of LTC homes	Ontario
The underlying factors influencing the immune response to SARS-CoV-2 in long-term care residents, staff, and caregivers	Dr. Amy Hsu, University of Ottawa Dr. Marc-André Langlois, University of Ottawa	Residents, care-givers, and workers of LTC homes	Ontario (presented) British Columbia Quebec
UNderstanding COVID-19 Vaccination in Elderly Residents (UNCoVER)	Dr. Donald C. Vinh, McGill University Health Centre Dr. Jean-Philippe Gouin, Concordia University Dr. Diana Cruz-Santiago, Université de Montréal	Staff and residents of LTC homes	Montreal, Quebec
Study of the immune response and site-specific wastewater surveillance of SARS-CoV-2 infections in long term care homes	Dr. Xiaoli (Lilly) Pang, University of Alberta Dr. Chris Sikora, University of Alberta Dr. Bonita Lee, University of Alberta	Staff and residents of LTC homes	Edmonton, Alberta
Impact of older age on the immune response to COVID-19 mRNA vaccines	Dr. Marc Romney, University of British Columbia Dr. Zabrina Brumme, Simon Fraser University Dr. Mark Brockman, Simon Fraser University	Seniors living in LTC and in the community, as well as staff of LTC homes	Vancouver, British Columbia
Safety and Efficacy of Preventative COVID vaccines (STOP-CoV)	Dr. Sharon Walmsley, University of Toronto	Adults (aged 30 to 50) in comparison with older adults (over the age of 70) living in the community	Southern Ontario

### Latest results

# Immunity wanes more quickly than expected following a second vaccine dose

The studies consistently showed that the quantity of antibodies due to either mRNA vaccine **wane more quickly than expected** in older Canadians, especially residents of LTC homes:

- The WellnessHub study at the University of Toronto confirmed that the decline in both anti-spike and anti-RBD (the two proteins used to measure SARS-CoV-2) antibodies was quicker than expected in LTC residents. It found that the apex for seroconversion in 92% of residents was at 2 to 4 weeks post-second dose. In effect, immunity waned significantly at 4 months post-second dose (only 88% of residents had detectable antibodies; 23% had higher anti-RBD than median convalescents) and even more dramatically at 6 months postsecond dose (only 72% of residents had detectable antibodies; only 12% had higher anti-RBD than median convalescents).
- In comparing adults in the 30 to 50 and 70+ age groups, the StopCoV study discovered that the majority of adults in both groups were above the threshold for antibody detection after a second vaccine dose. The older group had exhibited weaker anti-RBD responses three weeks after the first dose, but rebounded two weeks following the second dose to where levels were similar to that of the younger cohort.

The studies found that **longer dosing intervals had a neutral or positive effect** on antibody levels following the second dose:

- The StopCoV study, studying community-living older Canadians in Ontario, suggested a longer dosing interval led to lower anti-RBD antibody levels over time. However, the longer interval did not seem to impact antibody levels two weeks following the second dose.
- The Montreal-based UNCoVER study concluded that 16 weeks between a first and second dose is likely the upper limit for the dosing interval, especially in frail LTC residents who were not previously infected, based on waning antibody levels.

#### Both mRNA vaccines induce a strong antibody response

The seven studies presented examine the prevalence and endurance of COVID-19 antibodies on residents of LTC homes, older people living in the community, and staff and caregivers at LTC homes who received mRNA vaccinations.

Both two-dose mRNA vaccine regimens (Moderna and Pfizer) were **very effective at inducing antibodies after the second dose**, though Moderna offered some advantages over Pfizer:

- The COVID in Long Term Care Study conducted at McMaster University showed that, between the two mRNA vaccines, **the quantity of antibodies is higher and lasts longer with Moderna**:
  - Among residents and staff, ~20% of Moderna recipients and ~60% of Pfizer recipients fell into the "red zone" for reduced capacity to neutralize COVID-19 within six months of full vaccination.
- Similarly, the UNCoVER study in Montreal concluded that there is a difference in the antibody responses at 16 weeks between the Moderna and Pfizer vaccines as a first dose, but this gap closes at four weeks post second dose.
  - Specifically, anti-spike and anti-RBD IgG levels decrease significantly faster in LTC residents after a first dose of Pfizer compared to Moderna, but these levels rise after the second dose of Pfizer.
- The C19 Immunity Study out of the Bruyère Institute observed a stronger immune response among older Canadians who received two doses of Moderna compared to those who received two doses of Pfizer. Anti-spike and anti-RBD immunity for both began to wane two months after the second dose.

A **mix-and-match regime** using mRNA vaccines was found to be effective:

• The UNCoVER study in Montreal compared those who received two doses of Moderna or Pfizer with people who received a Moderna-Pfizer combination, demonstrating **for the first time to our knowledge** that the serologic response at one month post-second dose was comparable for all three regimens.

#### Age and comorbidity are factors affecting vaccine effectiveness

It is also apparent that **age is a significant factor** in vaccine effectiveness, **as is the presence of comorbidities**. Among staff members who were on average several decades younger than the residents, antibodies were stronger and lasted longer, though they too diminished markedly several months after the second dose:

- The results of the antibody response study conducted in Edmonton demonstrated that age appears to be a factor in the durability of neutralizing antibodies, as staff (with a median age of 45) had a higher percentage of detectable neutralizing antibodies than residents (who had a median age of 86) both at 3 months and at 5-6 months after their second dose.
- Results were similar in the University of British Columbia/Simon Fraser study:
  - The binding antibody response after a second dose among LTC residents (median age of 86) and seniors in the community (median age of 77) was half (51%) that seen among staff (median age of 41).
  - After the second dose, neutralizing antibodies among LTC residents and seniors in the community was one-quarter (25%) that seen among staff.
  - Age, as a factor, was responsible for 20% fewer binding antibodies per decade and 15% lower neutralizing antibodies per decade.
  - $\circ$  Men exhibited 30% lower neutralizing activity than women.
  - Comorbidities were also important, and had a cumulative effect, accounting for 15% lower neutralizing activity per condition.

- The C19ImmunityStudy out of the Bruyère Institute, employing data from Ontario, discovered that residents in LTC had a lower antibody response than caregivers and staff, who are presumably younger and have fewer comorbidities.
- Further, UNCoVER study researchers found that LTC residents who were previously infected with SARS-CoV-2 before their vaccination achieved and maintained robust anti-spike and anti-RBD antibody levels, regardless of age, sex, or comorbidity.

# Wastewater analysis evaluated as early warning system for outbreaks in LTC

The Edmonton study showed the **potential of analyzing wastewater from LTC residences as an early warning system** to detect new asymptomatic and symptomatic COVID-19 cases:

- Taking wastewater samples from manholes linked to the LTC homes in question has the advantages of requiring only a single sample for an entire facility while imposing no interruption to operations and being wholly non-invasive.
- On the other hand, without daily testing, which can be costly, the system will not be comprehensive due to staff rotations, irregular visitors, and diaper use by residents.
- The team did find sewage samples positive for SARS-CoV-2, but in all cases, the LTC homes already knew an outbreak was occurring and had put testing measures into place.
- Nonetheless, the positive and suspected positive rates in LTC homes did closely correspond with overall COVID-19 cases in the community at large in Edmonton.

## Limitation to interpretation of results

There are a few notable limitations to the interpretation of these results:

- Correlation of laboratory tests with clinical outcomes is needed.
- Research into COVID-19 has not yet determined the exact "correlates of protection", meaning although it is clear antibody levels wane after a second dose of vaccine, it does not necessarily mean one is vulnerable to disease as there are other factors contributing to one's immunity.
- That said, the antibody wane in LTC residents and older Canadians living in the community is so significant compared to younger, healthier Canadians, that a third dose is certainly a safer approach to avoid more deaths and sickness.

## Implications

#### **Implications - immunity**

- LTC residents are a **vulnerable population** whose immune response to vaccination should continue to be monitored.
- The third dose may help, but some residents may **still not mount an adequate long-term antibody response** and therefore other protection measures (detailed below) in LTC homes continue to be of the utmost importance.
- In addition, as the resident population in LTC homes is so vulnerable, many older people and those with certain or numerous co-morbidities may experience **faster waning than others**, so continued close monitoring of their antibody levels is required.

#### Implications - vaccination of everyone else imperative

- It is of the utmost importance that the rest of society get vaccinated to protect this vulnerable population.
- Vaccination of all staff in LTC is of utmost importance.

#### Long-term considerations

- We need to think about the underlying structural factors that have allowed COVID-19 to be devastating in LTC homes, such as:
  - Crowding and multiple-occupancy rooms;
  - Older design standards and poor ventilation;
  - Staffing issues;
  - Poor infection prevention and control.
- The above risk factors likely contributed to past high flu mortality in LTC, so fixing these structural factors for COVID-19 would help long-term for many other conditions.

#### Focusing more research on long-term care

LTC homes were not usually included in much mainstream research. After a first wave that decimated LTC in Canada, the CITF recognized the research gap and catalyzed research into LTC in our Hot Spots funding competition.

• The results presented by this group of researchers has proven that increased research in LTC is possible and necessary and research into LTC must continue consistently post-COVID pandemic