

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

Summary report # 9

The Eighth Wave: Challenges and predictions for an uncertain future

Background

Since emerging in 2019, COVID-19 has defied prediction. Nonetheless, through the extensive and diverse resources directed against the pandemic over the course of nearly three years, we have gained tremendous insight and knowledge into the nature of SARS-CoV-2. Highly effective vaccines were created and deployed with unprecedented speed. Within the first year, <u>they were credited with preventing 20</u> million deaths worldwide, including more than 310,000 in Canada.

As Canadians emerge from this past summer's seventh wave, the CITF has assembled a panel of experts for the ninth in our *Research Results and Implications* seminar series to reflect on where we stand and what lies in wait as we continue to navigate a highly mutable situation and manage the risks presented by a virus that appears to be with us to stay.

Entitled *The eighth wave: Challenges and predictions for an uncertain future,* the panel was held on September 19, 2022.

CITF-funded researchers participating on the panel

Focus	Lead researcher(s) and affiliation	Research population	Location of study
Canada-wide seroprevalence studies	Dr. David Buckeridge Scientific Lead, Data Management and Analysis, CITF Secretariat, McGill University	General	Canada
Modelling evolution of SARS-CoV-2 variants of concern	Dr. Sarah (Sally) Otto University of British Columbia	General	Global
Variability of immunity	Dr. Charu Kausic McMaster University	General	Immune science
Future of Vaccination	Dr. Shelly Bolotin University of Toronto	General	Global
COVID-19 in context of other respiratory diseases	Dr. Mel Krajden University of British Columbia	General	Immune science

At a glance: key points from CITF-funded researchers

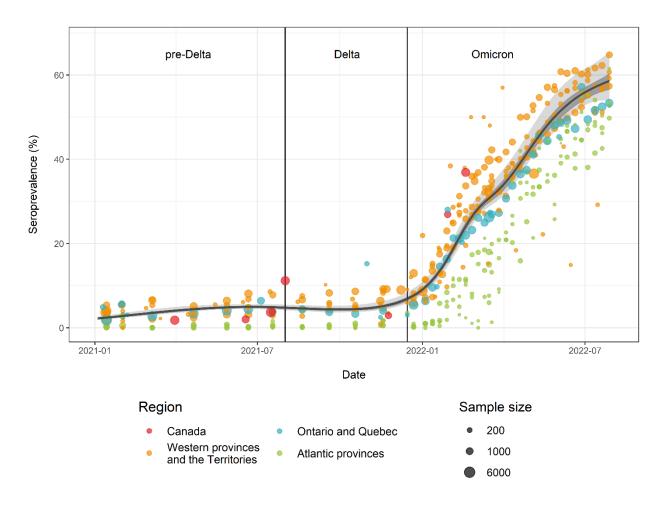
The contents of this discussion are based on forward-looking analysis and, therefore, represent the best knowledge of experts based upon existing evidence and conditions in mid-September 2022. **Most data are referenced in the** <u>panel presentation</u>.

Key Points:

- The Omicron variant of concern rapidly established its dominance across Canada. Infection-acquired antibodies were detectable in 60% of the population by the end of July 2022, as compared with 5.8% in the last week of November 2021. More than 18.2 million Canadians had been infected with SARS-CoV-2 by the end of July 2022, most during the Omicron wave. This represents an infection rate of approximately 86,000 per day over the past seven months. (Dr. Buckeridge)
- Omicron out-competed earlier versions of SARS-CoV-2 to establish dominance. Omicron is better at evading immunity, but less virulent than earlier variants of concern (VOCs). (Dr. Otto)
- BA.5 is currently the prevalent variant in circulation **there are no new VOCs on the horizon**, however, given that SARS-CoV-2 has undergone 12 million evolutionary changes since it emerged, this is not to suggest that the virus is done mutating. (Dr. Otto)
- **Immunity is not static**, but waxes and wanes over time and according to individual and communal factors. This all needs to be considered when devising strategies to contain and control the spread of infection. (Dr. Kaushic)
- It is important to keep up to date with one's vaccine status: that is, **everyone should have the recommended number of doses according to their age group, health status, and risk of exposure to infection.** (Dr. Bolotin)
- Ongoing research into **bivalent**, **intranasal**, **and pan-coronavirus vaccines hold great promise for enhancing protection** against existing and potential VOCs, as well as yet-to-emerge threats. (Dr. Bolotin)
- Going forward, it will be important to sustain a balance between normal activities of societies, on the one hand, and preventing serious illness and protecting a fragile healthcare system on the other. (Dr. Krajden)

More in depth

Over 60% of people in Canada – or roughly 18.2 million people – had infection-acquired antibodies by end of July 2022

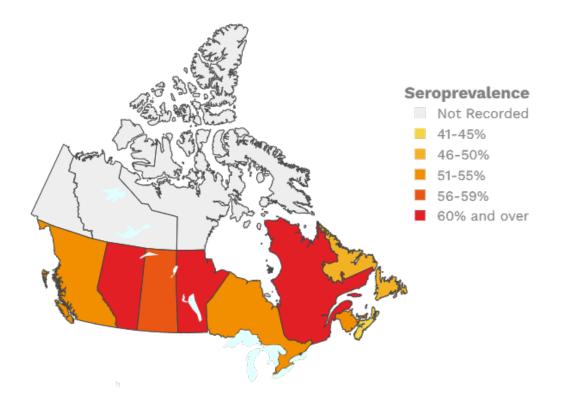


Serology (blood samples) data provides estimates on SARS-CoV-2 infections. Antibodies can distinguish between individuals vaccinated or infected by SARS-CoV-2, by SARS-CoV-2 spike antibodies or SARS-CoV-2 nucleocapsid antibodies, respectively.

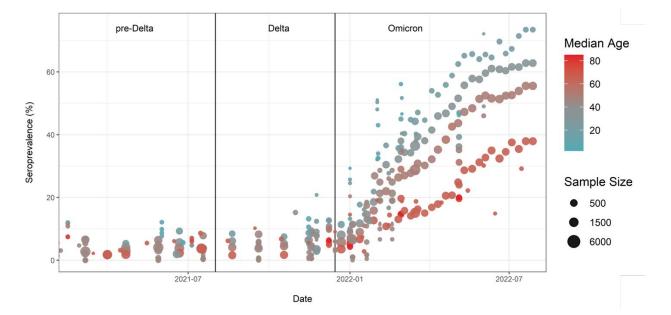
A compilation of data from blood donors, provincial and territorial surveys, and research cohorts, presented by Dr. David Buckeridge, Scientific Lead, Data Management and Analysis with the CITF Secretariat, illustrates, in the graph above, the extent of infection-acquired seroprevalence across Canada and the rapid growth of rates of infection during the Omicron era. In effect, Omicron represented a distinct phase, and not a continuation, of the pandemic from its initial outbreak in late 2019.

Dr. Buckeridge showed how **seroprevalence increased in every province and region** in the country between January 2021 and July 2022. In general, Western provinces and the Territories had the highest seroprevalence, followed by Ontario and Quebec and the Atlantic provinces had the lowest seroprevalence.

While the pandemic has not affected all of Canada equally, it has impacted and disrupted life and caused death in every part of the country.



Infections were still highest among the younger age groups (median age of 20 years old) as of July 31, 2022, while infections were low among the older age groups (median age of 60 years old of age and older).

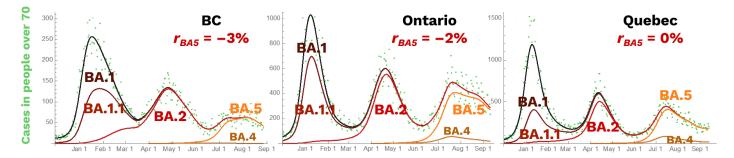


Omicron out-competed earlier versions of SARS-CoV-2 to emerge as the dominant variant of concern

Dr. Sally Otto, of the University of British Columbia and co-lead of the CoVaRR-Net's (Coronavirus Variants Rapid Response Network) Computational Biology and Modelling Pillar 6, illustrated how rapidly and extensively the SARS-CoV-2 virus has mutated from the original strain that emerged in December 2019. The virus mutated at an <u>astounding rate of once per genome every two weeks</u>. Most of the mutations were minor, she points out, but the cumulative changes eventually affected the nature of the virus.

In the first year of the pandemic, there was no competition among lineages. By the second year of the pandemic, **VOCs had emerged from earlier lineages, not currently common strains. VOCs started to "leap-frog" past one another** in a "survival of the fittest" competition for superiority, Dr. Otto explained. Though Omicron is proving less virulent than earlier VOCs, it is better able to evade the immune responses induced by existing vaccines or acquired through previous infections – including previous Omicron infection.

Since the seventh wave struck, **researchers who are tracking the virus' genome have observed no new major VOC on the horizon beyond the current BA.5 strain**, despite the fact that sub-variants BA.5.2 and BF.5 show a minor growth advantage over BA.5.1. While the vaccines developed to combat the first wave of SARS-CoV-2 are less effective against BA.5 infection, they continue to afford strong protection against severe COVID-19 disease and death.



We can combine evolutionary changes with case data (here **cases among those over 70, a more reliably tested age group**) to understand how new variants drive waves.

Estimates of growth rate, r, for BA.5 are estimated on the last day and change with changing immunity and with protective health measures, both mandated and voluntary (e.g., wearing effective masks, increasing ventilation, and avoiding crowded indoor spaces)

As seen in the graph above, the last three Omicron waves were observed to be declining over time in each of the provinces. However, with each decline of one Omicron subvariant, there is a rise of another variant. The BA.5 wave is extending longer than predicted for an epidemic model, reflecting waning of immunity in those individuals infected with BA.1.1 and vaccination early in January 2022. In the future, says Dr. Otto, **COVID-19 cases will be driven by the drop in immune protection over time**, thus necessitating regular vaccine boosts.

Immunity is variable

There is no single, static definition of immunity. Some infections and vaccines generate longer lasting immunity than others. For example, a measles vaccine lasts a lifetime while we need a fresh influenza vaccination annually.

At the moment, multiple studies have shown that **immunity to COVID-19 - from vaccination, previous infection, or a hybrid of the two – wanes within approximately six months**. But even this is variable, according to a variety of personal and communal circumstances: i.e. whether one is over the age of 60 or immunocompromised and the extent of ongoing transmission within a particular geographic location. This is why all all panellists insisted **it is essential for people to keep up-to-date with their vaccines and take the recommended doses appropriate to their circumstances**, as per their local health authorities and personal healthcare provider:

- This could mean a different number of doses, depending on the individual.
- This definition will be modified over time, as new doses or vaccine types become available.

Vaccine timing, previous infections, variants and individual factors contribute to a complex immunity landscape, said Dr. Charu Kaushic (McMaster University and Member of the CITF Leadership Group). She presented the following chart by way of illustration:

	Lev	Level of immune protection against variants					
	Non-Om	Non-Omicron		Omicron			
	Ancestral	Delta	BA.1	BA2.12.1	BA.4, BA.5		
· · · · · · · · · · · · · · · · · · ·	High	High	Low	Low	Low		
	Medium	Medium	Low	Low	Low		
	High	High	High	Low	Low		
	High	High	High	Not known	Not known		
	High	High	Many reinfections	Many reinfections	Low		
Ancestral or Alpha infection	Adapted from: Omicron infection SARS-CoV-2 hybrid immunity: silver bullet or silver lining? Nature Reviews Immunology (2022)						

BA.2.12.1, BA.4 and BA.5 escape antibodies elicited by Omicron infection, *Nature* (2022)

Periodic boosting of immunity is necessary to sustain a high level of protection against severe disease and death because Omicron is so effective at evading our immune defenses. Even those who are up to date with their vaccines may still be susceptible to infection, but vaccination is still highly protective against severe illness.

Delta

infection

Vaccination

Hybrid immunity offers the strongest protection, but with an important caveat

Dr. Kaushic showed that hybrid immunity offers effective, longer lasting protection against Omicron than either vaccination or infection alone. However, she emphasizes that this is not an argument in favour of becoming infected. **SARS-CoV-2 remains a dangerous disease with unpredictable effects**, including exacerbated inflammatory responses and long COVID. For this reason, continued use of masks, proper hand hygiene and physical distancing is still important even if one has been vaccinated. Moreover, **broad vaccine uptake will determine the impact of future COVID-19 waves**. Left to spread unchecked, the virus will continue to mutate and spawn new VOCs.

New vaccines hold the hope of greater protection

Vaccines have had a significant impact during the COVID-19 pandemic by preventing millions of deaths globally since its first introduction in December 19, 2020. Most current vaccines were formulated to induce immunity against the original strain (wild-type) of SARS-CoV-2. The BA.5 VOC, which is now dominant around the world, is significantly different from that virus. Three novel approaches to vaccination are currently being developed:

- A bivalent formulation was approved for use in Canada in September 2022 and is now available. This particular mRNA vaccine has proven effective in clinical trials against the BA.1 version of Omicron. While more data is needed to evaluate its efficacy against BA.5, Dr. Shelly Bolotin (University of Toronto, Public Health Ontario and Co-lead of the CITF's Vaccine Surveillance Working Party) reports, this vaccine seems to provide good protection against all Omicron variants.
- Several intranasal vaccines are under development. The advantage promised by intranasal vaccines is their capacity to induce an immune response in the mucosal tissue of the upper respiratory tract (nose and throat) where the virus enters the body. The hope is to stave off infection altogether and attenuate transmission. Intranasal vaccines have a proven track record against influenza.
- **Pan-coronavirus vaccines are the "holy grail" of immunology**, said Dr. Bolotin. However, she notes that these vaccines are very difficult to develop. Many teams, including here in Canada, are doing significant research to bring them to fruition.

SARS-CoV-2 is here to stay

COVID-19 has established itself in the human population and is, thus, here to stay for the foreseeable future, Dr. Kaushic stated.

We must mitigate against the impact of COVID-19 and other respiratory infections without unduly disrupting our normal lives, said Dr. Mel Krajden (University of British Columbia and Member of the CITF Leadership Group).

Dr. Krajden offered guidance on how we should think about COVID-19 at this stage of the pandemic:

- Vaccine-induced and infection-acquired immunity are transforming SARS-CoV-2 into a manageable endemic respiratory virus.
- It is time to return to normalcy for our COVID-19 traumatized population and health system, but normalcy is not zero risk! Humans cannot live in a microbe-free bubble, nor is the immune system designed to function in such an environment.
- Focusing only on COVID-19 morbidity and mortality is bad because our response to protect more vulnerable older and immunocompromised Canadians has come at a very high cost to our youth.
- It is not about preventing every infection; it is about preventing severe disease and protecting our health system one that was already fragile pre-COVID-19.

He predicts that the unexpectedly severe seventh wave of the pandemic has generated enough hybrid immunity that **the Canadian fall will likely be quiet from a COVID-19 perspective, but that early winter may bring a different story**. He raised concern about a potentially serious influenza season this year because our immune response may have been lessened by a lack of exposure to flu during the previous seasons' lockdowns. In essence, he says, we skipped over an entire cycle of flu and must beware of the potential for the 2022-23 season ahead.

Dr. Krajden warns that:

- We should continue to exercise caution (i.e. distancing, masking, avoiding confined spaces).
- **More severe measures come at a price** and should be avoided so long as severe disease is controlled and the healthcare system continues to function. We should take a strategic approach to addressing endemic respiratory disease.
- We need contextualized public health surveillance and planning beyond COVID-19 to identify sensible interventions to protect the various at-risk populations.
- Rational plans are needed for the co-existence of SARS-CoV-2 variants with other respiratory agents, including ongoing surveillance and other preventative measures.

Policy implications

The eighth wave and beyond

- **COVID-19 is now well-established in populations around the world**. It is now endemic at a very high rate of infection.
- Extreme measures, such as lockdowns and curfews, are unsustainable over the long run.
- We need widespread acceptance of mitigation measures such as vaccination and reasonable public health precautions, such as masking and testing where infection rates are high and/or where there are people more likely to get severely sick.
- Everybody needs to be encouraged to keep up to date on vaccines, however what this means is defined by individual circumstances. People need to be prepared to adopt regular updating of their vaccine status for the foreseeable future.
- COVID-19 remains a dangerous infection and the public must not become complacent. The protection afforded by hybrid immunity does not mitigate against the dangers of complications from the virus.
- **Preventing severe illness and safeguarding our healthcare system are attainable goals**, but only so long as vaccine uptake remains high, and people take precautions against becoming infected and transmitting the disease.
- New vaccine research is critical for arresting the spread and continued mutation of SARS-CoV-2. So long as the virus circulates, it has the potential to evolve into new VOCs that threaten new dangers.

The views expressed herein do not necessarily represent the views of the Public Health Agency of Canada.