Public Health Ontario | Santé publique Ontario

EVIDENCE BRIEF

Risk Assessment for Omicron BA.5 and BA.5 Sub-Lineages (as of July 26, 2022)

Introduction

This evidence brief includes evidence on SARS-CoV-2 Omicron BA.5 and BA.5 sub-lineages that has emerged since the previous Public Health Ontario (PHO) BA.4 and BA.5 Evidence and Risk Assessment,[1] relevant to the risk in Ontario. Evidence on other variants and Omicron sub-lineages may be included for context. The Key Messages, Additional Considerations, and Implications for Practice are informed by the entire Omicron Risk Assessment series; it may therefore be helpful to follow the series.

Key Messages

- The proportion of whole genome sequencing (WGS) samples identified as BA.5 (including all BA.5 sub-lineages) continues to increase in Ontario, from 60.3% (June 26-July 2, 2022) to 68.6% (July 3-9, 2022). For the week of July 3-9, 2022, two BA.5 sub-lineages were the most prevalent, BA.5.2.1 (21.9%) and BA.5.1 (17.6%), followed by BA.2.12.1 (14.6%).
    - The weekly growth of BA.5.2.1, BA.5.2, BA.5.1 and BA.5 were 3.22 (95% confidence interval [CI]: 3.08-3.37), 3.00 (2.83-3.19), 2.69 (2.59-2.80), and 2.66 (2.53-2.79) times that of BA.2 (previously the most dominant variant) over the past 12 weeks, respectively. Based on Nowcast modelling, BA.5.2.1 is projected to remain the most prevalent, reaching 37.4% (95% CI: 33.2%-41.8%) by July 27, 2022.
- Based on those eligible for molecular testing in Ontario, in the week of July 17-23, 2022, case rates in most age groups increased by less than 5% or decreased compared to the previous week. The exception is case rates increased by 23% in the 80+ years age group, compared to the previous week. The percent positivity (14.8%) and testing volumes were similar to the previous week. Hospital admissions decreased to 402, from 507 the previous week, which is the first week-over-week decrease since the beginning of wave seven. The number of deaths increased to 61, up from 46 the week before, which is the first evidence of an increasing trend in deaths since the start of wave seven.
- Evidence continues to show that BA.5 is highly transmissible, at least in part due to evasion of neutralizing antibodies. It remains unclear if BA.5 or BA.5 sub-lineages cause more severe disease than BA.1 or BA.2 due to limited and varied findings.
    - For previous sub-lineages of Omicron, a complete primary series and for those eligible, the recommended booster dose(s), provide optimal protection against severe outcomes from acute COVID-19. Public health efforts in response to the increasing SARS-CoV-2 epidemiological trends should include optimizing vaccine boosters for all eligible populations and reducing inequities in vaccine uptake.

- Based on evidence of immune evasion by BA.5 and waning immunity following vaccination, public health measures can help to reduce transmission of SARS-CoV-2, and can include: wearing a well-fitted mask when feasible in indoor spaces and close contact settings (e.g., public transit), staying home when sick or with symptoms of COVID-19, optimizing ventilation, and use of outdoor spaces.

Issue and Research Question

There are multiple PANGO sub-lineages associated with the B.1.1.529 (Omicron) variant of concern (VOC). The main BA.1, BA.2, BA.3, BA.4, and BA.5 sub-lineages also have their own sub-lineages (e.g., BA.5.1). Considering the possible changes to transmissibility, severity, and/or vaccine effectiveness (VE) of these sub-lineages compared to other VOCs, it is important to monitor the potential impact they might have in Ontario.

Methods

PHO Library Services conducted daily searches of primary and preprint literature using the MEDLINE database (search strategies available upon request). Preprints are research papers that have not undergone peer-review but are made publicly available to provide the latest data relevant to the rapidly evolving COVID-19 pandemic. Formal critical appraisal of published and preprint COVID-19 literature is out of scope for this PHO risk assessment. PHO performed grey literature searches daily using various news feeds and custom search engines. English-language peer-reviewed and preprint records that described COVID-19 variants were included. Sections from prior risk assessments for which there is no new literature of note are removed from the current update.

Risk Assessment

The current risk of BA.5 and BA.5 sub-lineage transmissibility in Ontario is high with a low degree of uncertainty. The risk of severe acute disease is low with a high degree of uncertainty. The risk of reinfection is high with a low degree of uncertainty. The risks of lowered VE and breakthrough infection are high with a moderate degree of uncertainty. The risk of impact on testing is low with a moderate degree of uncertainty. The overall risk assessment may change as new evidence emerges (see Table 1).

Table 1. Risk Assessment for Omicron Sub-Lineage BA.5 and BA.5 sub-lineages

Issues	Risk Level	Degree of Uncertainty
Increased Transmissibility	High	Low
Disease Severity	Low	High
COVID-19 Reinfection	High	Low
Lowered Vaccine Effectiveness or Breakthrough Infection	High	Moderate
Impact on Testing	Low	Moderate

Additional Considerations

As we continue to face uncertain evidence environments, the level of consideration for the following may change.

- Post-acute COVID-19 syndrome (PACS) or "long-COVID" is not included in the risk assessment table, but reviews indicate that the sequelae and their incidence vary.[2-5] Increased severity of acute SARS-CoV-2 infection has been identified as a risk factor for PACS in previous PHO work on this topic.[2] Preventing high levels of COVID-19 community transmission may mitigate the incidence of PACS or "long-COVID" and its long term impacts at the individual and population levels.

- There is increasing evidence that SARS-CoV-2 can impact the immune system, which can lead to severe acute COVID-19 or post-acute COVID-19 syndrome (PACS); however, all outcomes, risk factors and the scale of impact on the immune system remain unclear. [6-16] Evidence to date, including epidemiological indicators of severity, as well as scientific studies, suggests that most people that become infected with SARS-CoV-2 will likely have a normal immunological response.[2,3,17,18] Increased severity of acute SARS-CoV-2 infection has been identified as a risk factor for PACS in previous PHO work on this topic.[2,3]

- BA.5, and potentially BA.5 sub-lineages, evasion of neutralizing antibodies from previous infection or vaccination is likely contributing to the increasing number of SARS-CoV-2 cases in Ontario, which includes reinfections. The evidence on severity of acute and post-acute SARS-CoV-2 reinfections remains unclear.[19-22] This is due to a limited number of studies and studies with different findings, as well as differences in severity and immune evasion across variants and sub-lineages in the literature on severity of reinfections.

- The evidence on duration of shedding viable and transmissible BA.5 and BA.5 sub-lineage virus remains unclear.[23,24]

- COVID-19 hospitalizations showed the first week-over-week decline since the start of wave 7, although deaths have increased (see below). Health care worker absences, shortages, and impacts to scheduled care, could be yet more challenging in the context of BA.5 and BA.5 sub-lineages community transmission.

- Key considerations for increased risk in Ontario at this time include (in no particular order): first, evidence from variants prior to BA.5 and BA.5 sub-lineages showed that SARS-CoV-2 vaccine effectiveness against infection wanes over time; however, protection against severe infection remains against previous Omicron variants; second, BA.5 and BA.5.2.1 have significantly greater growth rates in Ontario compared to BA.2, which was a previously dominant variant and their proportional representation in Ontario is increasing according to WGS surveillance; third, although strains may share a common ancestor and sub-lineage, there can be significant point mutations and antigenic changes between evolving strains of the same sub-lineage, resulting in variable cross-protection after an infection.[25,26] As a result, reinfections and breakthrough infections can result in a resurgence of COVID-19, which is reflected in the current Ontario context.

Epidemiology

Globally

- Based on sequences submitted to GSAID from June 13 to July 13, 2022, the Omicron VOC was the dominant variant circulating globally, accounting for 95.4% of reported sequences.[27] Among Omicron sequences, from the week of June 27 to July 3, 2022, to the week of July 4-10, BA.5 increased from 51.8% to 53.6%. During the week of July 11-17, 2022, weekly new cases began to level off after having been on the rise for the five previous weeks, while the number of new weekly deaths increased by 11% compared to the previous week. The World Health Organization (WHO) advises that trends should be interpreted with caution due to limitations of surveillance systems.

Europe

- The European Centre for Disease Prevention and Control (ECDC) reported that BA.4/BA.5 are the dominant variants (90.2% of the sequenced cases, ranging from 20.7-99.9%) in the majority of countries reporting adequate surveillance coverage from June 27 to July 10, 2022.[28] While the overall number of reported COVID-19 cases fell by 7.6% in the week ending July 17, 2022 compared to the previous week, case rates among people aged 65 years and above increased by 32% in 22 out of the 24 countries reporting these data. Of 35 countries with data on hospital or intensive care unit (ICU) admissions/occupancy, 18 reported an increasing trend in at least one of these indicators in the week ending July 10, 2022, compared with the previous week.[29] The European COVID-19 Forecast Hub predicts increasing trends in cases, stable trends in hospital admissions, and increasing trends in deaths for the European Union European Economic Area overall by the end of the week ending July 31, 2022.[28] Predictions should be interpreted with caution due to changes to testing and reporting criteria.

United Kingdom

- Based on data from July 10-17, 2022, the United Kingdom (UK) Health Security Agency (UKHSA) estimated that 78.7% of the sequenced episodes in England were BA.5. Modelling of sequenced cases from mid-April to mid-July of 2022 in England suggests that the relative growth rates for BA.5, BA.4 and BA.2.12.1 are declining although BA.5 still has a higher relative growth rate (relative double time = 45 days) compared to BA.4 (relative doubling time = -25.8 days) and BA.2.12.1 (relative doubling time = -8.87 days).[30] In England, from July 9-15, 150,591 people had a confirmed positive SARS-CoV-2 test result, which is a decrease of 14.4% compared to the previous 7 days.[31] As of July 22, 2022, the R range for England was 0.9 to 1.2 and the growth rate range was -1% to +3% per day.[32] Between July 12-18, 2022, 12,038 individuals tested positive for SARS-CoV-2 upon admission to hospital, which is a decrease of 7.6% compared to the previous 7 days.[31] Between July 9-15, 2022, there were 908 deaths within 28 days of a positive coronavirus test, which is an increase of 15.2% compared to the previous 7 days.

South Africa

- BA.4 and BA.5 together became dominant (73%) in April, and comprised 93%, 91%, and 91% of all sequenced samples in May, June, and July, respectively.[33] Epidemiological data showed that the BA.4 and BA.5 wave in South Africa has passed its peak.[34] The BA.4 and BA.5 epidemic curve experienced in South Africa may not be generalizable to the Ontario context due to differences in history of previous SARS-CoV-2 infection, COVID-19 vaccination coverage and schedules, public health measures, as well as age distribution of the population.[35]

    - Weekly test positivity rates for COVID-19 had been declining from 28.2% for the week starting May 1, 2022 to 4.5% for the week starting June 26, 2022. Weekly test positivity rates rose slightly to 4.9% for the week starting July 10, 2022, with the highest rate of 9.1% in individuals 80 years of age or older.[36] The number of new cases decreased by 12.8% from 2,289 (week ending July 9, 2022) to 1,997 (week ending July 16, 2022).[34]

    - There was a 31% decrease in the number of new hospital admissions in the week ending July 9, 2022 compared to the number of admissions the previous week.[37] Delays in reporting of hospital admissions may affect the numbers reported in the most recent week.

United States

- The estimated proportion of BA.5 among circulating variants has been increasing, from 55.0% (95% CI: 53.3%-56.8%) the week ending July 2, 2022, to 77.9% (95% PI: 75.8%-79.9%) the week ending July 16, 2022.[38] During the same period, the estimated proportion of BA.2 dropped from 4.8% (95% CI: 4.3%-5.4%) to 0.6% (95% PI: 0.6%-0.7%), while that for BA.2.12.1 dropped from 25.7% (95% CI: 24.3%-27.1%) to 8.6% (95% PI: 7.8%–9.5%). As of July 20, 2022, the 7-day moving average of daily new cases (125,827) increased 0.5% compared with the previous 7-day moving average (125,185).[39] The 7-day daily average for new hospital admissions for July 13-19, 2022 was 6,180, which is a 4.7% increase from the prior 7-day average (5,902) from July 6-12, 2022.

Canada and Ontario

- WGS surveillance across Canada indicated that BA.5 represented 60.5% of the samples sequenced for the week ending July 3, 2022, up from 52.6% the week before (data still accumulating).[40] On July 19, 2022, the reported 7-day average percent positivity was 16.1%, which is an increase compared to 15.0% reported on July 12, 2022.[40]

- Testing and case, contact, and outbreak management in Ontario was restricted to high-risk populations and settings in January 2022.[41] Ontario case counts are based on positive molecular tests from populations eligible for molecular testing and therefore remain an underestimate of total COVID-19 cases in the province. Representative WGS surveillance is also only performed on cases with positive molecular tests. Thus, triangulation across indicators can provide greater confidence in trends.

    - The proportion of BA.5 (including all BA.5 sub-lineages) increased from 60.3% (June 26-July 2, 2022) to 68.6% (July 3-9, 2022).[42]

    - For the week of July 3-9, 2022, BA.5.2.1 was the most prevalent lineage (21.9%), followed by BA.5.1 (17.6%), and BA.2.12.1 (14.6%). Based on Nowcast modelling, the proportion of BA.5.2.1 is projected to reach 37.4% (95% CI: 33.2%-41.8%) by July 27, 2022.

- The weekly growth of BA.5.2.1, BA.5.2, BA.5.1 and BA.5 were 3.22 (95% CI: 3.08-3.37), 3.00 (2.83-3.19), 2.69 (2.59-2.80), and 2.66 (2.53-2.79) times that of BA.2 over the past 12 weeks, respectively.

- In the week of July 17-23, 2022,[43]

    - Based on those eligible for molecular testing in Ontario, case rates in most age groups increased by less than 5% or decreased compared to the previous week. The exception is case rates increased by 23% in the 80+ years age group, compared to the previous week. The percent positivity (14.8%) and testing volumes were similar to the previous week.

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    - The number of outbreaks in high-risk settings decreased 16%, to 203.

- Hospitalizations, ICU admissions and deaths are lagging indicators, often occurring days or weeks after cases are initially reported to public health units, and are subject to reporting lags (i.e., reporting to public health units or entry into the Public Health Case and Contact Management Solution [CCM]). Therefore, trends may change and may not be fully representative of the most up-to-date situation.

    - Hospital admissions decreased to 402, from 507 the previous week, which is the first week-over-week decrease in hospital admissions since the beginning of wave seven.[43] The number of deaths increased to 61, up from 46 the week before, which is the first evidence of an increasing trend in deaths since the start of wave seven. Hospitalizations and deaths are lagging indicators.

- Outbreaks in high-risk settings decreased 16%, from 241 to 203 the week of July 17-23, 2022.[43]

- On July 26, 2022, the Ontario Dashboard indicated that COVID-19 cases, percent positivity, hospital occupancy, and the province-wide wastewater signal were increasing, indicating increasing community transmission.[44]

Transmissibility

- Reuschl et al., reported that Omicron lineages of BA.1, BA.2 and BA.5 replicated similarly in human airway epithelial cells but replicated faster than Delta by 24 hours post-infection.[45] The authors also report that the evaluated Omicron lineages have lower tolerance to changes in temperature compared to Delta, as Omicron replication was reduced at 32°C versus 37°C. Lower temperature also reduced the innate immune response to infection by BA.5.

Symptoms and Severity

There is no clear evidence to date that BA.5 or BA.5 sub-lineages cause more severe disease than BA.1 or BA.2. The lack of clarity stems from limited and varied findings in the scientific literature. This is complicated by variation in severity of Omicron waves across different jurisdictions (likely impacted by differences in history of infection, vaccination rates, vaccine programs, reporting, etc.). Hospitalizations are increasing in several jurisdictions experiencing BA.5 waves (see Epidemiology), but it remains unclear if the increase in hospitalizations is due to intrinsic severity of BA.5 and BA.5 sub-lineages, or the overall increase in case number.[48] Limited data exists on acute and post-acute SARS-CoV-2 reinfections in the context of BA.5.

- Hansen et al., compared the severity of BA.5 infections relative to BA.2 in Denmark.[49] In contrast to evidence from South Africa and Portugal,[50-52] Hansen et al., report that BA.5 may be more severe than BA.2. Among individuals infected with BA.5, 1.4% (87/6,154) were admitted to hospital for COVID-19, and similarly, 1.4% (487/35,830) of those infected with BA.2 during the same period were admitted to hospital. After adjusting for several confounders, the odds ratio (OR) for hospitalization was 1.65 (1.16 to 0.34) among those infected with BA.5 relative to BA.2. Of the potential confounding factors, only time and age had a strong effect on the estimate. Restricting the analysis to include only 3-dose-vaccinated individuals (OR: 1.78; 95% CI: 1.21 to 2.63) did not have a substantial impact on the estimate. The authors conclude that the increased risk of hospitalization after BA.5 infection found in their study merits further investigation.

VE and Immunogenicity

Scientific studies and WGS surveillance continue to show that BA.5 has a marked ability to evade neutralizing antibodies from SARS-CoV-2 vaccination and previous infections.[1,25,46]

- Reuschl et al., reported that induction of interferon β (IFNB) and other interferon-stimulated genes was reduced in BA.4 and BA.5 infected cells, as compared to cells infected with BA.1/BA.2, and secretion of IFNβ and CXCL10 were reduced.[45] They also reported enhanced expression of the innate immune antagonist proteins Orf6 and N, similar to the Alpha variant, which the authors suggest could indicate BA.5 has combined evolution of antibody escape with enhanced antagonism of human innate immunity to improve transmission and possibly reduce immune protection from severe disease.

- Altarawneh et al., conducted a test-negative case-control study to evaluate protection of pre-Omicron SARS-CoV-2 infection against reinfection with Omicron BA.4 or BA.5 in Qatar.[53] Effectiveness of a pre-Omicron infection against symptomatic BA.4/BA.5 reinfection was 15.1% (95% CI: -47.1-50.9%), and against any BA.4/BA.5 reinfection, irrespective of symptoms was 28.3% (95% CI: 11.4-41.9%). Effectiveness of an Omicron infection against symptomatic BA.4/BA.5 reinfection was 76.1% (95% CI: 54.9-87.3%), and against any BA.4/BA.5 reinfection was 79.7% (95% CI: 74.3-83.9%). Qatar's unique population demographics (e.g., young population, large proportion expatriates) may impact the generalizability of some of the study's results.

- Lyke et al., investigated the magnitude and short-term durability of neutralizing antibodies against Omicron after homologous and heterologous boosting with mRNA and Johnson & Johnson Ad26.COV2.S vaccines.[54] An analysis of a subset (n = 16) showed that in day 29 post-homologous COVID-19 mRNA vaccine boosted individuals, the Pseudovirus neutralization antibody (PsVNA) titers to BA.2 and BA.3 were similar to BA.1, whereas BA.4/BA.5 were 2.5 times less susceptible than BA.1.

- Arora et al., compared the neutralization of BA.2.12.1 and BA.4/BA.5 using plasma from ten unvaccinated individuals in Germany who had mild infections when BA.1 and BA.2 were circulating.[55] Neutralization of BA.2.12.1 was similar to that of BA.2, whereas BA.4/BA.5 neutralization was markedly reduced compared with BA.2 and BA.2.12.1. Analysis of neutralization by antibodies induced by Pfizer-BioNTech vaccination revealed that neutralization of BA.4/BA.5 was 8.1-times reduced compared with B.1.

- Hansen et al., also estimated infection and vaccine immunity of BA.5 relative to BA.2 in Denmark.[49] Of the 4,809 triple-vaccinated cases who had a BA.5 infection during a particular outcome period, only 98 (2.0%) also tested positive when BA.1 and BA.2 were dominant. In contrast, among 164,369 triple-vaccinated controls who tested negative during the outcome period, 29,832 (18.1%) had tested positive when BA.1 and BA.2 were dominant. The authors estimate protection of an Omicron infection in a triple-vaccinated population to be 93.6% (95% CI: 92.1 to 94.8%), suggesting that a previous Omicron infection is highly protective against a new infection with BA.5. In contrast, a previous delta or alpha infection provided much weaker protection of 46.9% (27.0 to 61.3%) and 65.4% (49.8 to 76.2%), respectively, against a new BA.5 infection. Triple-vaccinated individuals compared to individuals who had two doses over 4.5 months earlier, the adjusted OR for an infection being due to BA.5 rather than BA.2 was 1.203 (0.964 to 1.503). For triple-vaccinated individuals compared to unvaccinated individuals, the adjusted OR for the effect of the vaccine on the likelihood of an infection being due to BA.5 rather than BA.2, was 1.021 (0.827 to 1.261). The authors conclude that there is little evidence that current mRNA vaccines protect less well against BA.5 than BA.2, and suggest that the impact of the current BA.5 wave will be limited in populations with a high degree of hybrid immunity.

- Studies performed by Bowen et al. aimed to assess the plasma neutralizing activity and immune evasion associated with the spike protein (S) mutations.[56] The authors measured entry of vesicular stomatitis virus (VSV) pseudotyped with the SARS-CoV-2 Wuhan-Hu-1 S harboring the D614G, BA.1, BA.2, BA.2.12.1, or BA.4 and BA.5 mutations into VeroE6 cells in the presence of vaccine or convalescent plasma.

    - Combining data for Moderna (mRNA-1273) and Pfizer-BioNTech (BNT162b2) COVID-19 vaccine cohorts revealed an ≥23-fold geometric mean titer (GMT) reductions against BA.4/5 S VSV compared to ancestral Wuhan-Hu-1/G614.

    - Individuals that received two doses of Oxford-AstraZeneca (AZD1222) followed by an mRNA booster had neutralizing GMTs of 2167 and 135 against Wuhan-Hu-1/G614, and BA.4/5 S VSV, respectively, corresponding to a 16-fold potency reduction.

    - Individuals vaccinated with two doses of Novavax (NVX-CoV2373) followed by a booster of BNT162b2, mRNA-1273 or Ad26.COV2.S had neutralizing GMTs of 9298 for Wuhan-Hu-1/G614, and 575 for BA.4/5, corresponding to a 16-fold reduction.

- The authors conclude that the improved plasma neutralizing activity in boosted individuals highlights the importance of vaccine boosters for eliciting potent neutralizing antibody responses against Omicron sub-lineages. Of note, most participants had approximately four week intervals between first and second doses, except for Ad26.COV2.S doses, which may not be generalizable to other settings with longer dose intervals that are recommended in Ontario.

Impact on Testing and WGS Surveillance

- Rapid antigen testing: The performance of rapid antigen tests (RATs) for BA.5 and BA.5 sub-lineages is currently unknown. However, no difference in RAT analytical sensitivity has been described for BA.1 and BA.2 and its sub-lineages compared to other VOCs.[57,58] As the majority of VOC mutations occur in the S protein and the rapid antigen tests currently deployed in Ontario target the nucleocapsid protein, RAT performance is not expected to be impacted. Despite no reported difference in analytical sensitivity, it has been shown that Omicron detection by RATs can differ from Delta depending on specimen type (e.g. nasal vs oral-nasal) and stage of illness.[59]

- Molecular testing: No impact is expected on the capability of molecular tests to detect BA.5. Of note, BA.5 has the del69-70 mutation leading to the S gene target failure (SGTF) pattern which could help distinguish it from BA.2 sub-lineages (these don't have the SGTF pattern).

- WGS surveillance: No impact is expected on the capability of WGS to detect and differentiate BA.5 and its sub-lineages.

Implications for Practice

- Although Ontario summers have been lower transmission periods for COVID-19 during the past two years, COVID-19 cases, percent positivity, hospital occupancy, and the province-wide wastewater signal were increasing in Ontario in recent weeks, causing a seventh wave in summer. There are early signs of stabilizing case rates, percent positivity and hospitalizations. Nevertheless, waning VE against infection, variable antibody cross-neutralization across SARS-CoV-2 sub-lineages after an infection, and the reduction in public health measures, require that Ontario COVID-19 epidemiology be closely monitored.

- COVID-19 vaccination remains an essential component of the public health response in the current context, with an emphasis on initiation and completion of a primary series in all (including under-vaccinated) communities, as well as boosters for eligible individuals. Groups at higher risk for severe outcomes should be prioritized.

- As we continue to learn about BA.5 and BA.5 sub-lineage severity, to minimize risk of morbidity and mortality (including PACS or "long COVID") as well as societal disruption (e.g., due to individuals being infected or symptomatic), current public health responses could be augmented with interventions that reduce SARS-CoV-2 transmission. Consideration should be given to the least restrictive and most equitable measures to achieve pandemic response goals based on epidemiological trends. Layers of protection can include improving equitable access to vaccines, staying home when sick or with symptoms of COVID-19, spending time outdoors, improving ventilation and air quality in indoor spaces,[60-64] wearing a well-fitted high quality mask in indoors or enclosed public settings (e.g., public transit).[65] Clear risk communication to the population regarding current levels of SARS-CoV-2 transmission and COVID-19 disease risk can be helpful.

- Population-level measures, particularly in essential indoor public settings (e.g., grocery stores, pharmacies) and those where highest risk populations are served (e.g., health care facilities, long-term care homes), can minimize inequitable impacts on those at highest risk of severe disease (e.g., immunocompromised, older adults, racialized, and low income populations), and those only recently eligible for COVID-19 vaccination (i.e., infants and children six months to five years).

- Evidence that a new SARS-CoV-2 VOC could emerge and alter the course of the pandemic remains a concern.[66-68] The emergence of sub-lineages such as BA.2.12.1, BA.4, BA.5, BA.5.2.1 in Ontario, South Africa, and Portugal soon after they experienced the decline of their BA.1 or BA.2 waves, underscores the need for sustained WGS surveillance.

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