EVIDENCE BRIEF

Risk Assessment for Omicron BA.4 and BA.4 Variant Sub-Lineages (as of Sept 23, 2022)

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Key Messages

- The proportion of SARS-CoV-2 whole genome sequencing (WGS) samples identified as the BA.4 sub-lineage is increasing in some jurisdictions, including Ontario. It remains uncertain whether BA.4 or a BA.4 sub-lineage will become dominant in settings where they are circulating.

- BA.4 subvariant and its sub-lineages remain rarer than the variant BA.5, which represents the largest proportion of cases in Ontario (90.2% as of September 3, 2022); however, the most prominent BA.4 sub-lineage, BA.4.6, is increasing and represented 6.4% of cases the week of September 4-10, 2022, up from 5.8% the previous week. The weekly growth rate of BA.4.6 is estimated to be 1.07 (95% confidence interval [CI] 1.05 - 1.09) relative to BA.5.2.1, which is the highest relative growth rate of the most commonly circulating sub-lineages.

- As BA.4 and BA.5 have the same Spike (S) gene mutation profile and given the near simultaneous emergence of both variants of concern (VOC) in some settings, there is limited evidence specific to BA.4.
  
  - Based on what evidence exists, BA.4 is highly transmissible, largely due to evasion of neutralizing antibodies from vaccination and previous infection with other variants, with a role for declining antibody titers (the level of antibodies in a sample), and some evidence of intrinsic increased transmissibility e.g., binding rate. Evidence on severity of BA.4 is limited.

- The current risk of BA.4 and BA.4 sub-lineage transmissibility in Ontario is high with a low degree of uncertainty. The risk of severe disease is low with a moderate degree of uncertainty. The risk of reinfection is high with a low degree of uncertainty. The risk of breakthrough infection is high with a high 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 and contains a high degree of uncertainty due to the limited evidence specific to BA.4 and BA.4 sub-lineages.
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 have their own sub-lineages (e.g., BA.1.1, BA.2.12, BA.2.12.1, BA.2.3, BA.2.20, BA.2.9, BA.5.1). Considering the possible changes to transmissibility, severity, and/or VE of these sub-lineages compared to other VOCs, it is important to monitor the potential impact they might have in Ontario’s context. This report includes evidence on SARS-CoV-2 Omicron BA.4 and BA.4 sub-lineages that have emerged since the Public Health Ontario (PHO) BA.4 and BA.5 report published on April 29, 2022, and the Risk Assessment for Omicron BA.4.6 Sub-Lineage published August 11, 2022. Evidence on other variants and Omicron sub-lineages may be included for context. For example, as a result of BA.4 and BA.5 having the same S gene mutation profile, this report includes some studies that combine BA.4 and BA.5 in their analyses. The Key Messages and Implications for Practice are informed by the entire Omicron Risk Assessment series.

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.

Ontario Risk Assessment

The current risk of BA.4 and BA.4 sub-lineage transmissibility in Ontario is high with a low degree of uncertainty. The risk of severe disease is low with a moderate degree of uncertainty. The risk of reinfection is high with a low degree of uncertainty. The risk of breakthrough infection is high with a high 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 BA.4 and BA.4 Sub-Lineages

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<thead>
<tr>
<th>Issues</th>
<th>Risk Level</th>
<th>Degree of Uncertainty</th>
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<tbody>
<tr>
<td>Increased Transmissibility</td>
<td>High</td>
<td>Low</td>
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<tr>
<td>Disease Severity</td>
<td>Low</td>
<td>Moderate</td>
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<tr>
<td>COVID-19 Reinfection</td>
<td>High</td>
<td>Low</td>
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<tr>
<td>Lowered Vaccine Effectiveness or Breakthrough Infection</td>
<td>High</td>
<td>High</td>
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<tr>
<td>Impact on Testing</td>
<td>Low</td>
<td>Moderate</td>
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Genetic Features

- The genomic characteristics of BA.4 have been described previously.\(^2,3\) Of note, the BA.4 sub-lineage BA.4.6 has a mutation in a known antigenically significant site (spike protein: R346T), which could impact its immunogenicity.\(^4\)

Epidemiology

Globally

- As of September 4, 2022, descendent lineages of BA.5 (BA.5X) are most prevalent globally (76.6%), followed by BA.4X with a 7.5% prevalence,\(^5\) which has been declining.\(^6\) BA.4X comprised 8% of prevalent cases August 22-28, 2022, and dropped to 6.1% the week of August 29 to September 4, 2022.\(^7\)

- The earliest sample of BA.4.6 in GISAID was a genome from Spain, with a collection date April 25, 2022.\(^4\) According to the September 9, 2022 United Kingdom Health Security Agency (UKHSA) SARS-CoV-2 technical briefing, a total of 14,181 genomes have been identified from outside the UK, which are assigned to BA.4.6 by Pangolin lineage designation.\(^4\) Countries with BA.4.6 sequences in GISAID according to the UKHSA September 9, 2022 briefing include: the United States of America (USA) (9,526), Canada (1,007), Denmark (500), France (400), Australia (288), Germany (248), Chile (242), Dominican Republic (173), Peru (149), Luxembourg (123), Belgium (102), Israel (101), Italy (94), Ireland (93), Sweden (92), Spain (85), Netherlands (84), Brazil (76), Argentina (68), Japan (67), New Zealand (60), Switzerland (54), Puerto Rico (53), South Africa (53), Ecuador (49), Mexico (39), Colombia (34), Trinidad and Tobago (30), Czech Republic (27), Costa Rica (23), Jamaica (21), Portugal (20), South Korea (19), Austria (17), Botswana (17), Indonesia (13), Saint Maarten (12), Senegal (11), and other countries (less than 10 samples) (115), and 31 countries had less than 10 BA.4.6 samples.

- Denmark’s Statens Serum Institut reported the estimated proportion of BA.4.6 in weeks August 28–September 3, 2022, September 4 –10, 2022, and September 11–17, 2022 as 3.17%, 3.68%, and 3.6%, respectively.\(^8\)
  - BA.4 continued to decrease over three weeks, starting at 0.80% August 28-September 3, 2022, decreasing to 0.27% the following week, and 0.19% the week after. Variant BA.4.1 fluctuated, at 0.31%, then 1.51%, and 0.76%.
  - BA.5 showed little change over three weeks at 4.24% August 28-September 3, 2022, to 3.74%, and 3.6% in the following weeks.

- In the United States of America (USA), weekly proportions of BA.4.6 have increased from 9.9% to 11.9% from September 10, 2022 to September 24, 2022.\(^9\) In the same period, the estimated proportion of BA.4 has fallen from 2.3% to 1.4%.\(^9\) BA.5 has decreased slightly week over week from 85% to 83.1% from September 10, 2022 to September 24, 2022.\(^9\)
The UKHSA’s June 22, 2022 Risk Assessment categorized the overall growth advantage of BA.4 and BA.5 as the highest level (red) with high confidence. The Omicron sub-lineage BA.4.6 was identified as part of horizon scanning on August 15, 2022 and was designated as variant V-22SEP-01 on September 1, 2022. BA.4.6 represented 3.31% of UK samples for the week beginning August 14, 2022. Of sequenced episodes from August 21 to 28, 2022, 0.5% were BA.2 (VOC-22JAN-01), 1.6% BA.2.75 (V-22JUL-01), 8.3% BA.4 (including BA.4.6), 87.2% BA.5 (VOC-22APR-04), and 2.4% were classified as other. Preliminary estimates of the relative fitness advantage of BA.4.6 suggest a 6.55% (95% credible interval (CrI) 5.53 to 7.57) advantage over BA.5, which is considerably smaller than the advantage of BA.5 over BA.2 (45 to 55%). Variant modelling suggests that the relative growth rate of BA.4 lineages (other than BA.4.6) is negative, meaning it is slowly declining as a share of sequenced cases, with a relative daily halving time of 20.5 days (CI: 10.36 to 960.76). By contrast, the modelling showed BA.4.6 was slowly increasing as a share of sequenced cases, and comprised 8.94% (CI: 7.46 to 10.71) of cases, with a relative daily doubling time of 25.35 days (CI: 29.56 to 22.19). The relative growth rate of BA.5 was stable, with both a slow increase and slow decline in its representation.

As of September 5, 2022, BA.4.6 in England had a logistic growth rate of 36%, relative to the dominant lineage in England, BA.5. As of September 6, 2022, there were 1,697 cases with BA.4.6 in England.

Canada and Ontario

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 performed on a proportion of cases with positive molecular tests. Thus, triangulation across indicators can provide greater confidence in trends. Uncertainty remains about whether this trend will continue.

WGS surveillance across Canada indicated that BA.4X (BA.4 and all sub-lineages) represented 12.8% of cases for the week of August 28-September 4, 2022, an increase from 10.1% for the week Aug 21-28, 2022.

Although the proportion of sequenced cases that are BA.4X remains low in Ontario, the lineage with the most cases among the BA.4X strains, BA.4.6, is increasing. BA.4.6 represented 6.4% of cases the week of September 4-10, 2022, a slight increase from the week prior at 5.8%. The weekly growth rate of BA.4.6 is estimated to be 1.07 (95% CI 1.05 - 1.09) relative to BA.5.2.1 (prevalence of 31% [September 4-10]), and is the highest relative growth rate among the most common circulating lineages. For context, the proportion of BA.5 (and all sub-lineages) represents the most cases in Ontario at 89.8% the week of September 4-10.

Transmissibility

Since the previous reports describing evidence of increased transmissibility of BA.4, an additional study further supports these findings. The study, a preprint, analyzed Gibbs energies of binding comparing Omicron variants BA.1 through BA.4, and examined infectivity and the incubation period. The author suggests that the BA.4 has increased infectivity and a decreased incubation period compared to the other variants.
Disease Severity

Given its emergence during a time period with a more prevalent BA.5 subvariant, it is unclear if BA.4 specifically can be attributed to no difference or less severe disease than other SARS-CoV-2 variants, including BA.5. Recent evidence in two pre-print studies suggests that mortality risk was lower during BA.4/BA.5 (in those who were vaccinated or had prior natural infection). A UKHSA report noted that BA.4/BA.5 disease severity seems similar to BA.2.

- Jassat et al. reported that unlike during the D614G (ancestral SARS-CoV-2), Beta and Delta waves, the rise in cases during the BA.1/BA.2 and BA.4/BA.5 waves were not accompanied by a concomitant rise in hospital admissions and in-hospital deaths. In BA.1/BA.2 and BA.4/BA.5 waves, hospital admission incidence was highest in individuals ≥60 years followed by those <1 year old. In adults and in children aged 5-18 years, admission incidence risk was lower in the BA.1/BA.2 and BA.4/BA.5 waves than in any other previous wave. The in-hospital case fatality ratio (CFR) was 25.9% (37,537/144,798), 10.9% (6,074/55,966) and 7.1% (837/11,860) in the Delta, BA.1/BA.2, and BA.4/BA.5 periods, respectively. After adjusting for age, sex, race, comorbidity, health sector, and province, compared to the BA.4/BA.5 wave, patients had a higher risk of mortality in the BA.1/BA.2 (adjusted odds ratio [aOR] 1.43; 95% CI 1.32-1.56) and Delta (aOR 3.22; 95% CI 2.98-3.49) waves. Being partially vaccinated (received one dose of BNT162b)(aOR 0.89, CI 0.86-0.93), fully vaccinated (received two doses of BNT162b or one dose of Ad26.COV2.S with the most recent dose at least 14 days earlier)(aOR 0.63, CI 0.60-0.66), boosted (aOR 0.31, CI 0.24-0.41), or having a prior laboratory-confirmed infection (aOR 0.38, CI 0.35-0.42) were associated with reduced mortality.

- Lewnard et al., compared clinical outcomes and characteristics of BA.2 (n = 48,941) and BA.4/BA.5 (n = 16,753) cases during a period of mixed co-circulation, and did not identify evidence of differential severity of infections. Adjusted hazard ratios comparing BA.4/BA.5 cases to BA.2 cases for out-patient diagnosed follow-up events were 1.07 (adjusted hazard ratio (aHR): 0.92-1.25) for any emergency department (ED) presentation, 1.07 (aHR: 0.92-1.26) for symptomatic ED presentation, 1.06 (aHR: 0.66-1.70) for any inpatient admission, 1.04 (aHR: 0.62-1.72) for symptomatic hospital admission, and 0.93 (aHR: 0.17-5.28) for ICU admission. No BA.4/BA.5 cases died or received mechanical ventilation.

- The UKHSA reported a case-control study that examined the risk of being admitted to hospital as an inpatient, among people presenting to emergency care within 14 days of a positive SARS-CoV-2 test, for BA.4 (n = 2,530), BA.5 (n = 12, 026), and BA.2 (n = 17, 022). After adjustment (age, sex, vaccination status, week of test, and for admissions occurring over the two days of extreme heat), there was no statistically significant difference in the risk of admission between people infected with BA.4 compared to BA.2 (odds ratio (OR): 0.96, 95% CI: 0.86 to 1.08). There was no statistically significant difference in the risk of admission between people infected with BA.5 compared to BA.2 (OR: 0.97, 95% CI: 0.89 to 1.07).
Immunogenicity

Evidence continues to show that BA.4 is more immune evasive than previous SARS-CoV-2 variants.\textsuperscript{2,13,16}\textsuperscript{19} Evidence from recent pre-prints and peer-reviewed publications report individuals as having lower antibody levels against BA.4 compared to other Omicron variants,\textsuperscript{20-22} including lower levels of neutralizing antibodies,\textsuperscript{4,20-26} evidence of waning SARS-CoV-2 immunity,\textsuperscript{20,27} as well as further evidence of differing cross-neutralization of BA.4 after a SARS-CoV-2 infection depending on the variant that caused the infection.\textsuperscript{19,28-30} Similar to earlier Omicron variants, evidence shows that a vaccine booster dose can provide similar, or somewhat similar, VE against hospitalization for BA.4 as other VOCs.\textsuperscript{18} A sample of studies are reported below.

- Studies illustrate that BA.4/BA.5 may spread more easily and have a shorter immunity time period, supporting the need for a bivalent vaccine. Burkholz et al, found that those who initially were infected with ancestral SARS-CoV-2 (Alpha) may show increasingly higher reinfection frequencies with subsequent variants.\textsuperscript{27} In addition, authors found that Omicron-to-Omicron reinfections could appear in as little as three weeks after initial infection. Bhiman et al.,\textsuperscript{24} reported that 14 days after two doses of Novavax, Omicron sub-lineages BA.1 and BA.4 were resistant to neutralization in 72.0% (n=21/29) and 59.0% (n=17/29) of samples. However, 35 days after a third dose of Novavax, high titers against Omicron BA.1 and BA.4 were observed with responses similar in magnitude to those triggered by three doses of Ad26.COV2.S or BNT162b22. Tauzin et al., support the need for a bivalent vaccine as they state the BA.4/5 Spike is markedly less recognized and neutralized compared to the D614G and Omicron BA.2 in those who received three doses of the mRNA vaccine.\textsuperscript{26} Newer COVID-19 Vaccines (e.g. bivalent vaccines) that target recent variants have the potential to generate a stronger immune response against current variants, generate broader cross-neutralization against future variants, and extend durability of current SARS-CoV-2 protection. It has been reported that a fourth COVID-19 mRNA vaccine dose (second booster) using Moderna’s BA.1 Omicron bivalent booster (mRNA1273.214) yielded higher neutralizing antibody titers (level of antibodies in a sample) against Omicron BA.4 and BA.5 than the original mRNA-1273 vaccine used as the fourth dose (second booster).\textsuperscript{31,32} Data currently available on Moderna’s BA.4/BA.5 bivalent booster are from rodent studies.

- The September 9, 2022 UKHSA technical briefing reported that preliminary pseudoviral neutralization assays performed on BA.4.6 showed that titers are reduced 2-fold, compared to neutralisation of BA.4 or BA.5 using sera from triple dosed recipients of the BNT162b2 vaccine.\textsuperscript{4}

- Andreano et al., tested the neutralizing activity against BA.4 and BA.5 of a panel of 482 human monoclonal antibodies isolated from people who received two or three doses of a COVID-19 mRNA vaccine or from individuals who were vaccinated after infection.\textsuperscript{30} Overall, less than 15% of the antibodies retained neutralizing activity against BA.4 and BA.5 variants. None of the 52 antibodies from the seronegative-two-dose vaccinated cohort were able to neutralize BA.4. Of the 206 neutralizing antibodies (nAbs) from the seronegative-three-dose vaccinated cohort, 14.6% (n = 30) cross-neutralized BA.4. Of the 224 nAbs from the cohort that was infected and then two-dose vaccinated, 15.5% (n = 32) cross-neutralized BA.4. The overall nAbs neutralization potency against Omicron BA.4 in the triple vaccinated, seronegative and in the infected, two-dose vaccinated groups, reported as geometric mean 100% inhibitory concentration (GM-IC100), was 2.62- and 5.34-fold decreased compared to the ancestral SARS-CoV-2.
• Yang et al., examined 215 participants for naïve or breakthrough infections with Delta (N=46), Omicron BA.1 (N = 47), and BA.2 variants (N = 122), comparing the neutralizing profiles against Delta, BA.1, BA.2 and BA.4/BA.5 variants based on the SARS-CoV-2 viral infection rate. Both naïve and breakthrough infections with BA.2 maintained comparable neutralizing activities against other variants, including BA.4/BA.5 variant. Authors state that this indicates a possibly broader cross-immunity induced by BA.2 variant. Authors note that for broad spectrum protection, Omicron BA.2-based vaccine might be a better candidate than BA.1.

• Jian et al., examined BA.4/BA.5 sub-lineages with R346 mutations (a mutation of concern for evading neutralizing antibodies) to examine the efficacy of vaccines against the BA.4/BA.5 sub-lineages. Plasma samples from individuals with three doses of CoronaVac without infection, showed 1.5 to 1.7 fold decrease in 50% neutralization titers against BA.5/5 with R346 (BA.5.9) and R346T (BA.4.6 and BF.7) and R346S (BA.4.7), in comparison to the neutralization titers against BA.4/BA.5. Authors state that these findings suggest that R346-mutated sub-lineages contribute to immune evasion against BA.4/BA.5 breakthrough infection.

• Hachmann et al., examined neutralizing antibody titers against the reference WA1/2020 isolate of SARS-CoV-2 along with Omicron subvariants BA.1, BA.2, BA.2.12.1, and BA.4 or BA.5, using specimens from n=27 individuals who had been vaccinated and boosted with BNT162b2 and in n=27 individuals who had been infected with the BA.1 or BA.2 subvariant a median of 29 days earlier. Among individuals with a previous SARS-CoV-2 infection, the median neutralizing antibody titre was 11,050 against the WA1/2020 isolate, 1740 against the BA.1 subvariant, 1910 against the BA.2 subvariant, 1150 against the BA.2.12.1 subvariant, and 590 against the BA.4 or BA.5 subvariant. In individuals with just two vaccine doses, the median neutralizing antibody pseudovirus titre was less than 20 against all tested Omicron subvariants.

• Kiresbom et al., reported that there was no evidence of reduced VE against hospitalization for BA.4 or BA.5 as compared to BA.2, based on the mRNA-1273 and BNT162b2 vaccines used in the UK. The incremental VE was 56.8% (95% C.I. 24.0-75.4%), 59.9% (95% C.I. 45.6-70.5%) and 52.4% (95% C.I. 43.2-60.1%) for BA.4, BA.5 and BA.2, respectively, at 2 to 14 weeks after a third or fourth dose. The authors state that their data provide evidence of the protection conferred by the current vaccines against severe disease with BA.4 and BA.5. Shirley et al., examined the effectiveness and durability of the BNT162b2 vaccine against the BA.4/BA.5 variants. The authors examined VE against hospitalization with two doses of vaccine. The VE was 56.3% (95% CI, 51.6 to 60.5) during the BA.1–BA.2 wave and 47.4% (95% CI, 19.9 to 65.5) during the BA.4–BA.5 wave. Boosting with a third dose of vaccine increased VE against severe disease for BA.1, BA.2, BA.4 and BA.5 in the first 1-2 months, but decreased in 3-4 months with an effectiveness of 50% (95% CI, 4.4 to 73.9) during the BA.1–BA.2 wave and 46.8% (95% CI, 35.3 to 56.2) during the BA.4–BA.5 wave. The authors state that these findings indicate that boosting increases VE against hospitalizations caused by BA.4/BA.5 but there is a need for regular boosting as early as four months after the last dose.
Impact on Testing and WGS Surveillance

- Antigen testing: The performance of rapid antigen tests for BA.4 is currently unknown, but has been maintained to be slightly reduced (depending on the study, specimen source, and assay) for Omicron in general compared to other variants. Furthermore, the BA.4 sub-lineage contains an additional mutation on the nucleocapsid (N) protein, P151S, and its impact on antigen tests detecting the N protein is not yet established.

- Molecular testing: No impact is expected on the capability of molecular tests to detect BA.4. Of note, BA.4 and BA.5 have the del69-70 mutation leading to the S gene target failure (SGTF) pattern which could help distinguish it from BA.2 sub-lineages (which do not have the SGTF pattern).

- WGS surveillance: No impact is expected on the capability of WGS to detect BA.4.

Implications for Public Health Practice

- BA.4.6 is more transmissible than earlier sub-lineages and its proportional representation in Ontario is increasing. Despite an absence of data on BA.4.6 sub-lineage disease severity, and limitations of evidence on BA.4 subvariant disease severity, and even if BA.4.6 is no more severe than BA.1 and BA.2, the increased transmissibility potential of BA.4.6 would be expected to result in a rise in the number of cases and potentially the total number of severe cases if BA.4.6 were to increase in prevalence. Similar to the BA.2 wave that emerged in the midst of Ontario’s BA.1 and BA.1.1 wave, BA.4.6 could emerge after the BA.4/BA.5 wave leading to an increase in COVID-19 cases during the fall of 2022.

- 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 (e.g., BA.4 versus BA.4.6), resulting in variable antibody cross-neutralization after an infection. Evidence since the start of the pandemic shows that ancestral mRNA and adenoviral vector intramuscular COVID-19 vaccines and previous SARS-CoV-2 infection do not provide sterilizing immunity (i.e., full protection from infection or reinfection) nor prevent onward transmission.

- 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.

- While vaccination is a key public health tool for the pandemic, current COVID-19 vaccines authorized for use in Canada and previous SARS-CoV-2 infection do not provide sterilizing immunity. A COVID-19 pandemic strategy that relies entirely on immunity from current vaccines and past infection will be limited in its ability to affect transmission. In addition, vaccine protection against infection is time-limited. Though integral to the COVID-19 response, the limitations of vaccines are more evident in the context of variants that evade vaccine and infection-acquired immunity (e.g., BA.4, BA.5). Related, growing evidence shows variable antibody cross neutralization across SARS-CoV-2 variants after an infection, making it difficult to gauge the level of immunity against reinfection by future variants. The BA.1 bivalent vaccine was only recently implemented in vaccination programs, and therefore, its effectiveness against BA.4/5 in the Ontario population is still unknown. Continuous WGS surveillance, monitoring of the impacts of implementation/removal of
public health measures, and efforts to increase vaccine equity can all help prepare Ontario for the next stages of the COVID-19 pandemic.

- Based on evidence of significant immune evasion by BA.4, waning immunity following vaccination and infection, incomplete vaccination coverage in Ontario and uncertain future uptake of COVID-19 bivalent booster vaccines and their effectiveness in the Ontario population, as well as the transition to colder weather, return to more indoor settings including offices and schools, basic principles of public health indicate that use of public health measures can be the most effective way to reduce the risk of SARS-CoV-2 transmission and consideration should be given to the least restrictive and most equitable measures. Layers of protections in addition to vaccination include: Staying home when sick or with symptoms of COVID-19, wearing a well-fitted high quality mask whenever feasible in indoor spaces, crowded places, and close contact settings (e.g., public transit), hand hygiene, optimizing indoor air quality, and use of outdoor spaces when weather permits.

- Clear risk communication to Ontarians regarding current levels of SARS-CoV-2 transmission and COVID-19 disease risk, including acute disease, risk factors for severe disease, protective effects of natural and vaccine-acquired immunity and post-COVID-19 sequelae, will support informed assessments of risk, especially in the context of approximately 50% third dose COVID-19 vaccine uptake, low uptake of primary COVID-19 vaccine series among children >12 years of age, and the emergence of more transmissible sub-lineages, including BA.4.6, in Ontario.36
References


