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EVIDENCE BRIEF

COVID-19 Omicron Variant Sub-lineage BA.2 and Sub-lineages of BA.2: Evidence and Risk Assessment (up to date as of May 18, 2022)

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Key Messages

- Based on representative surveillance whole genome sequencing (WGS), the most prevalent severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variant in Ontario the week of April 24 to 30, 2022 was BA.2 (67.3%), followed by BA.2.3 (11.7%), BA.2.9 (6.7%), BA.2.12 (4.9%), BA.2.12.1 (3.7%), BA.1.1 (3.5%) and BA.2.10 (0.5%).

- Although BA.2.12.1 comprises a relatively small proportion of cases by surveillance, the weekly growth rate of BA.2.12.1 has been approximately 1.7 times that of BA.2 in Ontario, and therefore could be expected to become the dominant variant. The potential impact of the currently circulating BA.2.12.1 sub-lineage in Ontario is unclear at this time.

- Evidence continues to show 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 or sub-lineages.

- Among those eligible for PCR testing in Ontario, the number of cases and percent test positivity have passed their wave six peak and are declining, with percent positivity at 11.2% on May 14, 2022. Despite a declining trend, percent positivity is higher than during most of the pandemic. Indicators of SARS-CoV-2 activity need close monitoring, particularly as we continue to learn about BA.2 sub-lineages circulating in Ontario, and measures to reduce the risk of transmission continue to be important.

- Despite decreasing epidemiological trends in Ontario, in the current context of high case rates and percent positivity (among those eligible for PCR testing), population-level measures, particularly in essential indoor public settings, can help minimize inequitable impacts on those at highest risk of severe disease (e.g., immunocompromised, older adults, racialized, and low income populations), those ineligible for vaccination (i.e., children less than 5 years) and those impacted by disruptions in educational settings (e.g., when individuals cannot attend due to being infected or symptomatic).

- A complete primary series and for those eligible, the recommended booster dose(s), provide optimal protection against severe outcomes. Additional dose(s) also reduce the risk of symptomatic infection; however, vaccine effectiveness (VE) against symptomatic infection is lower and wanes more quickly than VE against severe disease.

- Public health measures that reduce the risk of transmission can be layered onto a vaccination strategy to reduce the number of cases driven by a more transmissible dominant variant and the emergence of an even more transmissible sub-lineage (i.e., BA.2.12.1). These include ventilation, moving outdoors as the weather permits, and indoor masking in essential settings. Preventing high levels of population infection would also likely mitigate the incidence of post-acute COVID-19 syndrome (PACS, "long COVID-19") and its longer term impacts, for which evidence is still emerging.

Issue and Research Question

There are many Pango sub-lineages associated with the Omicron variant, including BA.1 and BA.2.[1,2] The BA.2 sub-lineage has led to the development of its own sub-lineages, including BA.2.12, BA.2.12.1, BA.2.3, BA.2.9 and others. Considering the increased transmissibility of BA.2 compared to previously circulating variants of concern (VOCs), and possible changes to transmissibility, severity and vaccine effectiveness of the emerging BA.2 sub-lineages, it is important to monitor the potential impact BA.2 and its sub-lineages might have in Ontario. This evidence brief updates the Public Health Ontario (PHO) report published May 20, 2022,[3] and summarizes available information and evidence on BA.2 and BA.2 sub-lineages relevant to the risk in Ontario that has emerged since the last report up to May 18, 2022. A section on animal transmission and reservoirs is included in this update and summarizes the literature on SARS-CoV-2 in animals since the March 25, 2022 PHO Risk Assessment.[4]

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 variant 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. In some of the literature, the term Omicron is used to refer to BA.1 and/or BA.1.1, which were the dominant sub-lineages in some jurisdictions. 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.2 and BA.2 sub-lineage transmissibility in Ontario is high, with a low degree of uncertainty. The risk of severe disease is low with a high degree of uncertainty. The risk of reinfection is high with a moderate degree of uncertainty. The risk of breakthrough infection is high with a high degree of uncertainty. The risk of impact on testing is moderate, with a low degree of uncertainty. The risk of impact on surveillance is moderate with a low degree of uncertainty. The overall risk assessment may change as new evidence emerges (see **Table 1**).

Additional Considerations

- The emergence of new sub-lineages of BA.2 in Ontario introduces uncertainty until more is known about their transmissibility, severity, and immune evasion.
    - Evidence shows BA.2.12.1 to have a growth advantage over BA.2 (see below). If BA.2.12.1 exhibits evasion of immunity from past infections and current vaccine-acquired immunity (as New York State and other parts of the United States [US] may be experiencing),[5] and cases of this sub-lineage rise the absolute number of severe cases would be expected to rise. High vaccine uptake and immunity from previous infections may attenuate the increase. The potential impact of the currently circulating BA.2.12.1 sub-lineage in Ontario is unclear at this time.

- Planned updates to lineage assignment tools for WGS and genomic surveillance will allow for better identification of SARS-CoV-2 lineages in future Ontario VOC tracking reports. As tools improve and as new variants are assigned a PANGO lineage, additional BA.2 sub-lineage descendants and recombinants may be identified. As a result of the dynamic nature of SARS-CoV-2 variants, the process for designating a new sub-lineage, and limitations of the available tools, "BA.2" and its sub-lineages may include emerging variants that are yet to be given a PANGO designation and so are considered as "BA.2".

- Health care system capacity has improved after the decline of the BA.1 wave; however, health care worker absences and surgical backlog may remain challenging during this current period of high transmission.

- Post-COVID-19 sequelae or "long-COVID" or post-acute COVID syndrome (PACS) is not considered in the Risk Assessment table; but several reviews suggest the sequelae vary and the incidence can be relatively high.[6-10] If considering PACS in a population or individual risk assessment, the risk could be moderate to high, with a moderate to high degree of uncertainty. Preventing high levels of population infection may mitigate the incidence of PACS and its longer term impacts.

Ontario Epidemiology

On December 31, 2021, diagnostic PCR testing was restricted to high-risk populations. On April 11, 2022, provincial PCR testing guidance was updated related to eligibility for COVID-19 treatment (e.g., inclusion of all symptomatic people aged 70 and older);[11] however, Ontario case counts remain an underestimate and representative surveillance only pertains to tested populations. Although rapid antigen tests (RATs) are more available to the public, these test results are not captured in Ontario's COVID-19 surveillance, further compounding the underestimate of Ontario case counts. Changes to testing, reporting, and how epidemiological variables are defined (e.g., COVID-19 hospitalizations and deaths) have necessitated recalibration of epidemiological models and deeper understanding of new data sources (e.g., wastewater). Triangulation across indicators can provide greater confidence in trends.[12]

The Ontario COVID-19 Genomics Network (OCGN) moved from sequencing 25% of eligible samples to 10% on April 13, 2022.[13] Previously reported Ontario BA.2 WGS surveillance case counts and proportions did not distinguish between BA.2 and BA.2 sub-lineages such as BA.2.12.1, BA2.3. The OCGN data used in this report distinguishes between BA.2, BA.2.10, BA.2.12, BA.2.12.1, BA.2.3 and BA.2.9, i.e., BA.2 is mutually exclusive of BA.2.10, BA.2.12, BA.2.12.1, BA.2.3 and BA.2.9.

The most prevalent SARS-CoV-2 VOC the week of April 24 to 30, 2022 was BA.2 (67.3%), followed by BA.2.3 (11.7%), BA.2.9 (6.7%), BA.2.12 (4.9%), BA.2.12.1 (3.7%), BA.1.1 (3.5%) and BA.2.10 (0.5%).

    - One case of BA.3 was identified during the week of March 27 to April 2, 2022.
    - From February 6, 2022 to April 30, 2022, the weekly growth rate of BA.2.12.1 was 1.71 (95% confidence interval [CI] 1.55 - 1.88) times that of BA.2.

- After rising for four consecutive weeks from March 20, 2022 to April 16, 2022, the number of confirmed COVID-19 cases has been decreasing since the week of April 17, 2022.[14] From early April, percent test positivity reported by PHO was relatively stable near 18-19%, before starting a downward trend.[15] On May 14, 2022, PHO reported 11.2% test positivity.[15] On May 4, 2022, percent positivity reported by the Provincial Diagnostic Network Operations Centre was 14.3% overall, and was similar in children <13 years of age (13.5%) and 14-17 years of age (15.9%) as reported by the Ontario Laboratories Information System.[16] Although percent positivity is slowly declining since the end of April, and it remains higher than during most of the pandemic. The overall number of outbreaks is decreasing since the week of April 3, 2022.[17]

- Hospitalizations, intensive care unit (ICU) admissions and deaths are lagging indicators, often occurring days or weeks after cases are initially reported to public health. Based on information included in Public Health Case and Contact Management Solution (CCM) up to May 4, 2022, the number of confirmed COVID-19 cases hospitalized increased from the week of March 6, 2022 to the week of April 10, 2022, followed by a decrease the weeks of April 17 and 24, 2022 and May 1, 2022.[18] This trend may change, particularly for the most recent week (May 1, 2022), as a lagging indicator and because of reporting lags (i.e., reporting to public health units or entry into CCM). The number of confirmed cases admitted to ICU had an increasing trend from the week of March 20, 2022 to the week of April 10, 2022. Similar to hospitalizations, the number of ICU admissions decreased the weeks of April 17 and 24, 2022, but increased the week of May 1, 2022. From April 17 to May 7, 2022, weekly COVID-19 deaths remained between 95 and 112. The number of deaths in recent weeks may change due to being a lagging indicator and reporting lags.

- The Ontario Science Advisory Table has not released updated COVID-19 projections since the April 22, 2022 PHO Risk Assessment.[3] On May 17, 2022, the Ontario Dashboard indicated that COVID-19 cases, percent positivity, hospital and ICU occupancy were decreasing, and the province-wide wastewater signal looked to still be declining, suggesting community transmission has peaked but uncertainty remains about whether this trend will continue.[19]

Table 1. Risk Assessment for Omicron variant sub-lineage BA.2 and BA.2 sub-lineages

Issues	Risk Level	Degree of Uncertainty
Increased Transmissibility	**High**	**Low**
Disease Severity	**Low**	**High**
COVID-19 Re-infection	**High**	**Moderate**
Lowered Vaccine Effectiveness/Breakthrough Infections	**High**	**High**
Impact on Testing	**Moderate**	**Low**
Impact on Surveillance	**Moderate**	**Low**

Epidemiology in Other Jurisdictions

Canada

Surveillance WGS across Canada indicated that, of SARS-CoV-2 samples collected the week of April 24, 2022, 99.6% were Omicron: 6.1% BA.1 [0.2% BA.1, 5.3% BA.1.1, 0.6% other BA.1], 93.2% BA.2 [48.4% BA.2, 16.2% BA.2.12, 16.2% BA.2.3, 12.4% other BA.2], and 0.4% BA.4), but data were still accumulating.[20] The Public Health Agency of Canada (PHAC) reported that for the period of May 1 to 7, 2022: the average number of cases reported daily decreased by 26% to 3,429, the average percentage of positive tests decreased by 2.2% to 13.3%, and the average number of deaths reported daily increased by 8% to 39.[21] On May 17, 2022, Canada reported 1,559 new COVID-19 cases, and 7 new deaths. The daily percent positivity (over the previous 7 days) was 11.5%. PHAC notes that due to changes in COVID-19 testing policies in many jurisdictions in late December 2021, case counts will underestimate the total burden of disease.

Select Other Jurisdictions

Global: Based on sequences uploaded to GISAID (with sample collection dates from March 23 to April 21, 2022), Omicron was the dominant variant globally, at 99.7%.[22] From May 2 to 8, 2022, the number of cases and deaths globally decreased by 12% and 25% respectively, as compared to the previous week.[23] The WHO recommends maintaining strong SARS-CoV-2 surveillance through the acute phase of the pandemic.

Denmark: The Danish Health Authority changed their COVID-19 test recommendations the week of March 6, 2022 to limit testing primarily to vulnerable groups and patients admitted to hospital, which is expected to impact trends in the following weeks. COVID-19 case numbers have continued to decrease from February 10 to May 8, 2022.[24] Percent positivity stabilized the week of May 1, 2022, and continued to vary across age groups. New hospital admissions decreased by 22% the week of May 1, 2022. The number of COVID-19-associated deaths is decreasing. In the week of April 24, 2022, of 4,736 samples with WGS, the Statens Serum Institut reported that 71.4%% were BA.2, 23.3% BA.2_H78Y, 2.2% BA.2.1, 1.4% BA.2.3, 0.7% BA.2.12.1, 0.2% BA.1.1, 0.3% BA.4, and 0.0% BA.1.

United Kingdom (UK): In the four weeks leading up to May 7, 2022, 96.5% of cases in UK countries were BA.2.[25] From April 4 to May 1, 2022, 96.8% of COVID-19 cases were BA.2.[26] The week of May 10, 2022, the number of positive SARS-CoV-2 decreased 38.0% compared to the previous week, and is a continuation of decreasing cases (e.g., confirmed cases decreased 43.3% the week of April 27, 2022).[27,28] Between May 4 to 10, 2022, the number of people admitted to hospital with COVID-19 decreased by 17.0% compared to the previous 7 days, which is a continuation of a decreasing trend (e.g., decreased 23.6% from April 19 to 25). From May 10 to 16, 2022, the number of deaths within 28 days of a positive coronavirus test decreased 34.8% compared to the previous seven days. The UK includes BA.1/BA.2 recombinant (with unique mutation C3583T) and BA.2.12.1 as signals currently under monitoring and investigation, along with BA.3, Delta and Omicron recombinant lineages (UK), and XF recombinant.[29]
England: As of April 1, 2022, free universal symptomatic and asymptomatic testing is no longer available to the general public in England, which will impact epidemiological trends from Pillar 2 testing (swab testing for virus in the wider population, through commercial partnerships, either processed in a lab or more rapidly via RATs).[30] COVID-19 case rates and test positivity from Pillar 1 testing (swab testing for virus in UK Health Security Agency [UKHSA] labs and National Health Service [NHS] hospitals for those with a clinical need, and health and care workers) decreased in the week of May 1, 2022. According to the UK general practitioner sentinel swabbing schemes, the overall positivity around the same time was 0.0% (0 out of 29). Overall COVID-19 hospitalizations decreased the week of May 1, 2022. From March 27 to April 2, 2022, 11.6% of all first or reinfection episodes were reinfections. There was no updated UKHSA VOC and variants under investigation (VUI) report for England since the last PHO Risk Assessment update.

US: According to NOWCAST modelling projections, the US Centers for Disease Control and Prevention (CDC) estimated that for the week ending May 14, 2022, 99.9% of SARS-CoV-2 cases were Omicron (50.2% [95% PI 44.9-56.9%] BA.2, 47.5% [95% PI 41.5-53.5%] BA.2.12.1, 1.2% [95% PI 0.6-2.2%] BA.1.1.529, and 0.3% [95% PI 0.2-0.4%])BA.1.1).[31] BA.2.12.1 has been the most rapidly growing lineage in recent weeks, comprising a growing proportion of cases since its emergence. As of May 11, 2022, the 7-day moving average of daily new SARS-CoV-2 cases (84,778) increased 30.7% compared to the previous week's 7-day moving average (64,863), and is a continuation of a rising trend in cases.[32] The 7-day daily average hospitalizations for May 4 to 10, 2022, was 2,629, which is a 17.5% increase from April 27 to May 3, 2022 (2,238).

SARS-CoV-2 Animal Reservoirs and Zoonotic Transmission

SARS-CoV-2 is known to infect non-human animal species.[33,34] Although animals do not have a documented considerable role in spread to humans, SARS-CoV-2 transmission in animal species can impact the health of animals and can result in the emergence of new variants. The latter is of particular concern when considering future scenarios and the potential risk of 'spillover' of animal-adapted SARS-CoV-2 lineages back into humans. New evidence on animal reservoirs and zoonotic transmission that emerged since the last PHO Risk Assessment that addressed this,[4] are described below. This evidence is not specific to BA.2 and BA.2 sub-lineages. A summary of animals and COVID-19 can be found on the PHAC website.[35]

- Evidence of SARS-CoV-2 spillover infection into wild mustelids was reported in Eurasian river otter found near a water reservoir in the Valencian Community (Spain).[36]
- The risk of zoonotic spillover or spillback infections could be higher for domestic pets than wild animals due to shared living space. Additional evidence of SARS-CoV-2 in cats and dogs was reported,[37-42] suggesting a risk of SARS-CoV-2 zoonotic transmission in common pets such as cats and dogs, but the findings overall are varied.[43-48] There are; however, also reports of possible false-positive results for SARS antibodies in felines based on pre-pandemic samples.[49,50]
- There is evidence that Golden Syrian hamsters are very susceptible to SARS-CoV-2 infection,[51] which builds on earlier evidence of hamster-to human transmission,[52-54] and concern about human-hamster-human infections.
- Efforts are underway to understand the risk of zoonotic transmission,[55,56] and monitor reports of SARS-CoV-2 in animals globally.[57]

Transmissibility

It remains unclear to what extent the increased transmission of BA.2 compared to BA.1 or BA1.1, and BA.2.12.1 compared to BA.2 is due to inherent characteristics of this sub-lineage (i.e., viral load, enhanced ability to infect cells, tissue tropism) or due to immune evasion or antibody waning; but, evidence suggests higher viral load plays a role in the BA.2 advantage over BA.1 and BA.1.1.[58-60] For context, when BA.1/BA.1.1 emerged, they were the most transmissible variants up until that time. Then BA.2 emerged, and it was more transmissible than BA.1/BA.1.1. At the moment, BA.2.12.1 has emerged in Ontario and is comprising a growing proportion of cases since its emergence in the US, and it is more transmissible than BA.2.[5]

- Gjorgievska et al., reported two cases of BA.1 and BA.2 co-infection in co-exposed, cohabitating individuals.[61] In both individuals, BA.1 was identified at early time points (using genome sequencing and/or S-gene specific PCR), and was then replaced by BA.2 at later time-points of the infection. The authors suggest that their observations support other evidence that BA.2 outcompetes BA.1 in a real-life scenario and BA.2 has biological properties allowing it to outcompete BA.1 in the host, at least in the immunological and genetic context of these two individuals and in time becomes the dominant variant in the upper respiratory tract of the host.

- In Ontario, from February 6 to April 30, 2022, the weekly growth rate of BA.2.12.1 was 1.71 (95% CI 1.55-1.88) times that of BA.2,[13] which is the highest relative growth rate of the BA.2 sub-lineages circulating in Ontario (i.e., BA.2.10, BA.2.12, BA.2.12.1, BA.2.3 and BA.2.9). The only other BA.2 sub-lineage to have a relative growth rate >1.0 during the same time period was BA.2.9 at 1.01 (95% CI 0.98-1.04).

Immunogenicity and Reinfections

Genomic evidence indicates that BA.2 is as genetically different from BA.1 as Alpha, Beta and Delta VOCs were from each other, which makes monitoring of BA.2 VE and reinfections important for assessing the risks associated with a BA.2 or BA.2 sub-lineage wave in Ontario. A review of VE evidence before the BA.2 wave shows that a primary series and one booster dose of COVID-19 vaccine exhibits less waning against severe outcomes, including hospitalization and death, than for symptomatic infection.[62] Evidence on VE and reinfections will continue to be confounded by differences in public health measures and vaccination programs, history of infections, and recentness of booster programs across jurisdictions. New studies that emerged since the last PHO Risk Assessment are described below:

- Bjork et al., attempted to estimate VE against severe COVID-19 using all individuals residing in Scania county in southern Sweden.[63] Most vaccinated individuals were vaccinated with the Pfizer-BioNTech COVID-19 vaccine (77%), with some vaccinated with Moderna or Oxford-AstraZeneca's COVID-19 vaccines. The authors created three calendar periods: (i) BA.1 dominant (respective proportions of VOCs – BA.1: 60%, Delta: 25%, BA.2: 15%), (ii) transition period (BA.1: 47%, Delta: 4.5%, BA.2: 49%), and (iii) BA.2 dominant (until date of data extraction on March 15, 2022 – BA.1: 17%, Delta: 0.5%, BA.2: 82%). Previous SARS-CoV-2 infection (with zero or one dose) offered similar protection against new onset severe COVID-19 as compared to two or three vaccine doses during either the BA.1 dominant or the transition period. In the BA.2 dominant period, protection against severe outcomes among those with prior infection (with zero or one dose) and two doses (with or without prior infection) markedly decreased. Protection following a third dose declined in the BA.2 period but to a much lesser degree and remained above 80% across the three calendar period. In an analysis that adjusted for comorbidities and infection at least 90 days before the case date, while the VE after at least three doses remained above 80% over the study periods, the VE from two doses declined markedly from 90% (95% CI: 78–95) during BA.1 dominance to 54% (95% CI: 13–75) during BA.2 dominance. The authors suggest that the relatively stable protection among individuals with at least three doses during follow-up suggests that a robust immune response is needed to confer protection against BA.2.

- Evans et al., reported neutralizing antibody responses in mRNA-vaccinated health care workers, as well as hospitalized and ICU COVID-19 patients, against viruses harbouring the Spike protein of the SARS-CoV-2 variants.[64] Similar to BA.1 and BA.1.1-ΔEPE, BA.2 exhibited reduced neutralization by two-dose mRNA vaccination sera (n=10) compared to D614G (an early mutant of SARS-CoV-2) but showed increased sensitivity to neutralization by the booster dose sera (n=10)($p < 0.05$). A sample of four representative hospitalized, unvaccinated patients exhibited neutralizing antibody repertoires that were most potent against BA.1- and BA.1.1-derived sub-lineages but only weakly effective against D614G and BA.2.

- Zhou et al., reported the VE of two or three doses of Pfizer-BioNTech COVID-19 vaccine during a BA.2 outbreak in Hong Kong.[65] The COVID-19 incidence was significantly lower in recipients of three doses Pfizer-BioNTech (16.6%) compared to two doses (49.2%)($p < 0.0001$). The frequency of asymptomatic infections was low at 3.8% and 3.4% in two and three dose recipients, respectively. The hospitalization rate was 3.4% in the three dose group and 19.2% in the two dose group). Using a pseudovirus assay, the authors reported that BA.2 was the most resistant to neutralization (out of Alpha, Beta, Delta, and BA.1) with a 4.67-fold reduction in three dose Pfizer-BioNTech, compared to D614G.

- Cao et al., investigated the ability of BA.2.12.1, BA.4 and BA.5 to escape neutralization by antibodies elicited by an Omicron infection.[66] Using sera and pseudoviruses, they found three dose-vaccinated individuals exhibited no significant difference in neutralization of BA.1, BA.1.1 and BA.2; but, BA.2.13 and BA.2.12.1 showed increased immune evasion compared to BA.2, with BA.2.12.1 having stronger evasion than BA.2.13, and BA.4/BA.5 having even stronger antibody evasion. The plasma neutralizing titers of individuals previously infected with BA.1 was reduced against BA.2.13, BA.2.12.1 and BA.4/BA.5 (compared to against BA.1), with reductions of 2.0-, 3.7- and 8.0- fold, respectively. Plasma from vaccinated convalescents showed a different phenotype than normal vaccine recipients, such that BA.2.12.1, BA.2.13 and BA.3/BA.4/BA.5 could cause a neutralization loss. Based on these and other observations, the authors suggest that BA.2.13, BA.2.12.1 and BA.4/BA.5 display stronger and distinct humoral immune evasion than BA.1 and BA.2. The authors also report evidence that they believe shows that post-vaccination infection with BA.1 primarily recalls ancestral SARS-CoV-2-induced memory B cells, supporting the "original antigenic sin" theory.

- Rossler et al., reported that previously naïve individuals infected with BA.2 had detectable neutralizing antibodies against BA.2, but neutralizing antibodies against pre-Omicron and BA.1 were only occasionally above the limit of detection.[67] Individuals with hybrid immunity (infections after two doses of Pfizer-BioNTech or two doses AstraZeneca) exhibited broad neutralizing antibody response against all variants analyzed. They also observed that multiple exposures improved neutralizing antibody titers against BA.2, including in individuals that had no contact with BA.2 itself. Compared to D614G and Delta, neutralizing antibody titers against BA.2 were higher in unvaccinated BA.1- or BA.2-convalescent persons but lower in most individuals after a pre-Omicron variant infection or multiple exposures; but, the reduction in neutralizing titers against BA.2 was not as pronounced as has been observed against BA.1.[68,69] Applying antigenic cartography to the titer data from convalescent and double vaccinated serum groups showed BA.2 to be located between the pre-Omicron variants and BA.1, approximately equidistant to Delta and BA.1. By constructing antibody landscapes, the authors observed that BA.1 and BA.2 convalescent landscapes showed unique antibody profiles focused on the area of their root variant, in agreement with the neutralizing antibody titer data.

Public Health Measures in Other Jurisdictions

Since the last risk assessment, France eased their mask mandate so that masks are no longer required on public transportation.[70] Finland expanded eligibility for a second booster dose.[71] Although airports and planes are out of scope for the jurisdictional scan, it should be noted that effective May 16, 2022, Europe's Aviation Safety Authority and the European Centre for Disease Prevention and Control no longer recommend that masks be required on planes nor in airports.[72] It was stated that this change was made to align with the lifting of mask mandates on public transportation across European countries.

Implications for Practice

- Although epidemiological indicators show that the BA.2 wave has peaked and is declining in Ontario, the emergence of sub-lineages of BA.2 (e.g., BA.2.3, BA.2.12.1) requires close monitoring of the potential impact and characteristics of these sub-lineages. Similar to the BA.2 wave that emerged in the midst of Ontario's BA.1.1 wave, a BA.2 sub-lineage or recombinant could emerge and reverse these current trends.

- 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.

- Despite decreasing epidemiological trends in Ontario, in the current context of high case rates and percent positivity, population-level measures, particularly in essential indoor public settings, can minimize inequitable impacts on those at highest risk of severe disease (e.g., immunocompromised, older adults, racialized, and low income populations), those ineligible for vaccination (i.e., children less than 5 years) and those impacted by disruptions in educational settings (e.g., when individuals cannot attend due to being infected or symptomatic).

- Public health measures can mitigate COVID-19 transmission at a time when early epidemiological indicators have started to decrease, late indicators show signs of plateau or decrease, and yet percent positivity remains high among those eligible for PCR testing. Consideration should be given to the least restrictive and most equitable measures to achieve pandemic response goals based on epidemiological trends. Due to limitations of individual public health efforts (i.e., vaccination, masking, measures to reduce contacts), an approach that layers various measures can be used to mitigate community spread.

    - COVID-19 vaccination remains an essential component of public health response in the current context, with an emphasis on initiation and completion of a primary series in relevant, under-vaccinated populations, as well as first and second boosters for the eligible populations.

    - As we continue to learn about the BA.2 sub-lineages circulating in Ontario, to achieve the overarching pandemic response goals of minimizing morbidity and mortality (including PACS/long-COVID), as well as minimizing societal disruption, current public health responses could be augmented with interventions aimed at reducing SARS-CoV-2 transmission, and current public health measures could remain in place. Layers of protection, including getting vaccinated, staying home when sick or with symptoms of COVID-19, practicing physical distancing and avoiding crowded spaces, spending time outdoors or in well-ventilated indoor spaces, wearing a well-fitted mask in indoor or enclosed public settings (e.g., public transit), and practicing respiratory etiquette and washing hands should continue to be promoted for all.[73]

    - Ongoing risk communication to the population regarding high levels of SARS-CoV-2 transmission and COVID-19 disease risk may be helpful, especially in the context of decreasing case counts but high test positivity(among those eligible for testing), and the emergence of new BA.2 sub-lineages in Ontario.

- There are gaps in surveillance data to inform timely public health action related to Ontario's pediatric population. These relate to limited PCR testing eligibility among children,[74] hospitalization as a lagging indicator and evidence from previous waves that the majority of children are at low risk of complications from acute infection. In the context of a highly transmissible BA.2-dominant wave in Ontario and emerging BA.2 sub-lineages, and given the educational, social and health impacts of cumulative educational disruption for children and families,[75,76] a cautious approach to less restrictive community-based public health measures can minimize disruption to in-person learning (e.g., due to staying home when infected or symptomatic). Optimizing layers of prevention in K-12 schools, including improved ventilation/air quality, avoiding congregation of large unmasked groups, and access to well-fitted, high quality masks when indoors can reduce the risk of in-school transmission and disruptions due to staying home when infected or symptomatic.[76,77]

- The evidence that a new SARS-CoV-2 VOC could emerge and alter the course of the pandemic again, continues to grow.[78-80] At a May 11, 2022 press conference, the WHO's technical lead for the COVID-19 response said, "The virus continues to evolve. The more the virus circulates, the more opportunities it has to change."[81] The emergence of the BA.2 sub-lineage when jurisdictions were experiencing the decline of the BA.1 and BA.1.1 waves, and the identification of BA.2 sub-lineages in Ontario,[82] and BA.4 and BA. 5 in South Africa,[83] underscore the need for high quality surveillance. It is essential we learn from prior use and removal of public health measures, increase efforts toward vaccine equity, and continue to prepare for the next stages of the COVID-19 pandemic.

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