Public Health Ontario | Santé publique Ontario

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 31, 2022)

Published: June 3, 2022

Key Messages

- Based on representative surveillance sequencing, the most prevalent severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variant in Ontario the week of May 8-14, 2022 was BA.2 (58.3%), followed by BA.2.12.1 (10.3%), BA.2.3 (9.0%), BA.2.12 (5.7%), BA.2.20 (4.6%), BA.2.9 (4.5%), BA.2.3.4 (1.9%), BA.1.1 (1.3%), BA.5 (0.5%) and BA.4 (0.1%).

- 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 1.73 times that of BA.2 in Ontario for several weeks 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.

- There is 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/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 8.5% on May 27, 2022. Despite a declining trend, percent positivity is higher than during most of the pandemic.

- 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 much as possible, and masking in indoor 3C settings (closed spaces, crowded places, and close contact). 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.

- 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 3C public settings, can help minimize inequitable impacts on those at highest risk of severe disease due to medical (e.g., immunocompromised, older adults) or social factors(e.g., racialized or 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 COVID-19 vaccine 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.

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 31, 2022. Evidence on other VOCs and Omicron sub-lineages may be included for context.

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 when the Omicron VOC first emerged. 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

- 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.[4-8] 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.

- The emergence of new sub-lineages of BA.2 in Ontario introduces uncertainty until more is known about their transmissibility, severity, and immune evasion.

- The evidence shows BA.2.12.1 to have a growth advantage over BA.2 (see below and Transmissibility section). 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),[9] cases of this sub-lineage may rise. The absolute number of severe cases would then be expected to rise as well. 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.

- As whole genome sequencing (WGS) and genomic surveillance 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, burnout, and surgical backlog may remain challenging during this current period of high transmission.

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);[10] 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.[11]

- The Ontario COVID-19 Genomics Network moved from sequencing 10% of eligible samples to 25% on May 12, 2022.[12]
    - The most prevalent SARS-CoV-2 VOC the week of May 8 to 14, 2022 was BA.2 (58.3%), followed by BA.2.12.1 (10.3%), BA.2.3 (9.0%), BA.2.12 (5.7%), BA.2.20 (4.6%), BA.2.9 (4.5%), BA.2.3.4 (1.9%), BA.1.1 (1.3%), BA.5 (0.5%) and BA.4 (0.1%).[12]
        - The proportion of BA.2.12.1 increased from 6.5% (May 1-7) to 10.3% (May 8-14).
        - To date, seven cases of BA.4 and eleven cases of BA.5 have been identified in Ontario. Five cases of BA.4 and ten cases of BA.5 were sequenced as part of representative surveillance, while the other cases were identified through targeted surveillance (e.g. travel related sequencing.)
    - From February 20, 2022 to May 14, 2022, the weekly growth rate relative to BA.2 was: 1.73 (95% confidence interval [CI] 1.64 - 1.82) for BA.2.12.1, 1.10 (95% CI 1.06-1.15) for BA.2.12, and 1.01 (95% CI 0.98-1.03) for BA.2.9.
- After rising for four consecutive weeks from March 20, 2022 to April 16, 2022, the weekly rate of confirmed COVID-19 cases had a decreasing trend since the week of April 17, 2022.[13] From May 15-21, 2022, 8,496 cases were reported to public health compared to 11,270 cases the previous week.[14] The number of cases should be interpreted with caution due to changes in testing eligibility. From early April, percent test positivity reported by PHO was relatively stable near 18-19%, before starting a downward trend.[15] On May 27, 2022, PHO reported 8.5% test positivity.[15] Although percent positivity is slowly declining since the end of April, it remains higher than during much of the pandemic.
- The number of outbreaks in congregate care and congregate living settings decreased to 79 cases the week of May 15-21, 2022, from 140 cases the week of May 8-14, 2022.[14] The number of outbreak-associated cases decreased across settings with the exception of correctional facilities, where cases more than doubled the week of May 15-21, 2022 compared to the previous week.

- Hospitalizations, intensive care unit (ICU) admissions and deaths are lagging indicators, often occurring days or weeks after cases are initially reported to public health, and are subject to reporting lags (i.e., reporting to public health units or entry into CCM). Therefore trends may change. Based on information included in Public Health Case and Contact Management Solution (CCM) as of May 25, 2022, from the week of April 17, 2022 to the week of May 8, 2022, weekly hospitalizations decreased from 747 to 404, weekly ICU admissions decreased from 71 to 45, and weekly deaths decreased from 97 to 83.[16]

- The Ontario Science Advisory Table has not released updated COVID-19 projections since the April 22, 2022 PHO Risk Assessment.[17] On May 31, 2022, the Ontario Dashboard indicated that COVID-19 cases, percent positivity, hospital and ICU occupancy were decreasing, and the province-wide wastewater signal is still declining, suggesting community transmission has peaked; but, uncertainty remains about whether this trend will continue.[18]

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 May 8, 2022, 100% were Omicron: 1.4% BA.1 [1.2% BA.1.1, 0.1% BA.1.17.2, 0.1% other BA.1], 97.7% BA.2 [41.5% BA.2, 4.8% BA.2.12.1, 16.5% BA.2.3, 34.9% other BA.2], and 1% other Omicron, but data were still accumulating.[19] The Public Health Agency of Canada (PHAC) reported that for the period of May 15-21, 2022: the average number of cases reported daily decreased by 22% to 1,980, the average percentage of positive tests decreased by 1.5 to 10%, and the average number of deaths reported daily decreased by 35 to 22%.[20] On May 31, 2022, Canada reported 947 new COVID-19 cases, 1 new death, and the daily percent positivity (over the previous 7 days) was 8.8%. 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: The WHO reported that Omicron is the dominant variant circulating globally, and of the Omicron lineages, BA.2 and its descendent lineages (referred to collectively as BA.2.X) are the dominant variants.[21] From May 1-7, 2022, the relative proportions of BA.2.X, BA.4, and BA.5 were 94%, 0.8%, and 1%, respectively. Among BA.2 sub-lineages, BA.2.12.1 accounted for 17%. From May 16-22, 2022, the number of cases and new weekly deaths globally decreased by 3% and 11% respectively, as compared to the previous week.[21] The WHO reports that at this time, BA.4, BA.5 and BA.2.12.1 appear to be spreading faster in countries with substantial prior waves of cases caused by BA.1, whereas countries that experienced more substantial BA.2 waves appear to have fewer cases caused by BA.4, BA.5 and BA.2.12.1; but they note that vaccination status of the country may play a role. The WHO notes that trends should be interpreted with caution because several countries have been progressively changing COVID-19 testing strategies. 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 decreased from the week of May 1-7, 2022 to the week of May 8-14, 2022.[22] Percent positivity remained stable the week of May 8-14, 2022, but continued to vary across age groups. New hospital admissions decreased by 23% the week of May 8-14, 2022, and the number of ICU admissions increased slightly. The number of COVID-19-associated deaths is decreasing. In the week of May 1-7, 2022, of 3,880 samples with WGS, the Statens Serum Institut reported that the most frequently observed variants and sub-variants were BA.2 (69.9%), BA.2.9 (21.7%), and BA.2.12.1 (1.4%), BA.2.9.1 (1.2%), BA.2.14 (1.1%), and BA.2.3 (1.1%).

England: The UK Health Security Agency's (UKHSA) most recent VOC and variants under investigation (VUI) report for England reported that of sequenced cases between April 24 to May 8, 2022, 97.0% were Omicron lineage BA.2 (VOC-22JAN-01), 0.4% were BA.1 (VOC-21NOV-01), 2.6% were comprised of BA.4 (VOC-22APR-03), Omicron lineage BA.5 (VOC-22APR-04) and Omicron recombinant XE (V-22APR-02).[23] 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.[24] COVID-19 case rates and test positivity from Pillar 1 testing (swab testing for virus in 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 16-22, 2022.[25] Around the same time, UK general practitioner sentinel swabbing schemes reported no positive tests. Between May 20-26, 2022, 36,014 people had a confirmed positive test result, which is a decrease of 18.8% compared to the previous seven days.[26] Between May 23-29, 2022, 3,114 individuals went into hospital with COVID-19, which is a decrease of 15.0% compared to the previous seven days. During May 20-26, 2022, there were 362 deaths within 28 days of a positive SARS-CoV-2 test, which is a decrease of 28.5% compared to the previous seven days.

- The final (nineteenth) round of the REal-time Assessment of Community Transmission-1 (REACT-1) study included 109,181 participants who returned a throat and nasal swab (from March 8-31, 2022).[27] The weighted prevalence of positive cases was 6.37% [95% credible interval (CrI), 6.21%, 6.53%], which was the highest weighted prevalence throughout the REACT-1 study.

US: According to NOWCAST modelling projections, the US Centers for Disease Control and Prevention (CDC) estimated that for the week ending May 28, 2022, approximately 99.9% of SARS-CoV-2 cases were Omicron (59.1% [95% PI 54.7-63.3%] BA.2.12.1, 34.7% [95% PI 30.8-38.8%] BA.2, 6.1% [95% PI 4.1-8.8%] BA.1.1.529, and 0.1% [95% PI 0.0-0.1%]) BA.1.1).[28] BA.2.12.1 has been the most rapidly growing lineage in recent weeks, and is now dominant. According to the COVID Data Tracker Weekly Review for May 20, 2022, as of May 18, 2022, the 7-day moving average of daily new SARS-CoV-2 cases (101,130) increased 18.8% compared to the previous week's 7-day moving average (85,143), and is a continuation of a rising trend in cases.[29] The 7-day average percent positivity was 10.6%. The 7-day daily average hospitalizations for May 11-17, 2022, was 3,250, which is a 24.2% increase from May 4-10, 2022 (2,617). The 7-day moving average of new deaths decreased 1.2%, from 284 down to 280 in the CDC May 20, 2022 Interpretive Summary.

Genomic Features and Evolution

The high transmissibility of the Omicron variant combined with other co-circulating VOCs, incomplete vaccination coverage and waning immunity, can result in Omicron evolution and recombination events.[30,31] A few studies are highlighted below:

- Kimura et al., reported that tracing of the emergence of BA.2 variants bearing mutations at the Spike (S) L452 residue revealed seven common ancestry groups of BA.2 variants bearing L452R, L452Q or L452M mutations in the S protein. Since BA.4 and BA.5 form a monophyletic clade with BA.2, Kimura et al.'s analyses considered BA.2, BA.4 and BA.5 as "BA.2-related Omicron variants". As of May 15, 2022, the PANGO lineage (https://cov-lineages.org) annotates four out of the seven BA.2 sub-lineages that contain mutations at the S L452 residue as BA.2.9.1 (+S:L452M) in Denmark, BA.2.11 (+S:L452R) in France, BA.2.12.1 (+S:L452Q/S704L) in the USA, and BA.2.13 in Belgium (+S:L452M).[32] The authors state that their analyses indicate that multiple BA.2-related Omicron variants containing the mutations at the S L452 residue emerged independently in several countries, and they predict that BA.4, BA.5 and BA.2.12.1, as well as others with this mutation, will spread globally and become the dominant variants in the near future.

Transmissibility

The BA.2 variant is highly transmissible, even overcoming China's "dynamic zero-COVID policy".[33] 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.[34-36] 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, which is supported by evidence that it is more transmissible than BA.2.[9]

- The aforementioned study by Kimura et al., provided insights into infectivity and transmissibility of BA.2 and its sub-lineages.[32] Infectivity assays in cell lines, using BA.2-related pseudoviruses showed significantly higher infectivity by BA.2.9, BA.2.11 and BA.2.12.1 compared to BA.2, and comparable infectivity to ancestral D614G-bearing B.1.1. For additional context, BA.4/5 pseudovirus infectivity was 18.3-fold higher than that of BA.2 pseudovirus. Cell-based fusion assays showed that the L452R mutation (in BA.2.11) significantly increased S expression on the cell surface, but the L452Q and L452M mutations (in BA.2.9.1) did not. Surface expression of S proteins from BA.2.12.1 (S704L) and BA.4/5 (HV69-70del; F486V; R493Q) was significantly lower than that of original BA.2. The results of the cell-based fusion assays and co-culture assays led the authors to suggest that the L452R-bearing S proteins (i.e., BA.2.11 and BA.4/5) exhibited higher fusogenicity than BA.2 S in three independent experimental setups. Additional *in vitro* assays showed that the replication kinetics of L452R/M/Q-bearing BA.2-related Omicron variants were similar to that of BA.2 in human airway epithelial cells; but rBA.2.12.1 and rBA.4/5 more efficiently replicated in human alveolar epithelial cells compared to BA.2, with 61-fold and 34-fold higher levels of viral RNA in the supernatant at 24 hours post-infection compared to rBA.2-infected culture, providing additional evidence that viral load may play a role in increased transmissibility of BA.2 and its sub-lineages.[34-36]

- The most recent round of the REACT-1 study (N=109,181) in England, from March 8-31, 2022,[27] reported that the weighted prevalence of positive cases was 6.37% [95% credible interval (CrI), 6.21%, 6.53%], which was the highest weighted prevalence throughout the REACT-1 study. The authors estimated the March 18-31, 2022 doubling time in weighted prevalence to be 30.5 days (95% CrI 25.8, 37.0), which corresponds to an R of 1.07 (95% CrI 1.06, 1.09) with >0.99 posterior probability that R>1. The authors note that March 2022 corresponded to a period of high and increasing mobility, with indices for driving, walking and transit by March 31 reaching, respectively, 92.9%, 85.0%, and 84.2% of the maximum observed throughout the study period. The estimated 56.4 days (95% CrI 54.2, 58.7) for the proportion of BA.2 to grow from 5% to 95%, which is approximately two-fold lower than the estimated rate for the Delta-to-Omicron transition (28.5, 95% CI 26.3, 30.7 days), is over 20% higher than the Alpha-to-Delta transition, and almost four-fold higher than the wild-type-to-Alpha transition.

- In Ontario, from February 20 to May 14, 2022, the weekly growth rate of BA.2.12.1 was 1.73 (95% CI 1.64-1.82) times that of BA.2,[37] which is the highest relative growth rate of the BA.2 sub-lineages circulating in Ontario (i.e., BA.2.12.1, BA.2.3, BA.2.12, BA.2.20, BA.2.9, BA.2.3.4).[12] The only other BA.2 sub-lineages to have a relative growth rate >1.0 during the same time period were BA.2.12 at 1.10 (95% CI 1.06-1.1) and BA.2.9 at 1.01 (95% CI 0.98-1.03).

Disease Severity

- Gautret et al., described the first 207 BA.2 cases diagnosed at a hospital in Marseille, France, in order to compare the severity of disease to that of 2,793 BA.1 variant (B.1.1.529.1) cases diagnosed at the same timeframe.[38] The hospitalization rate for BA.1 cases was 1.4%, only three patients (0.1%) were transferred to ICU, and 10 (0.4%) died (eight were >65 years old with comorbidities including cancer, chronic respiratory diseases, and diabetes; two had leukemia and asthma; five were unvaccinated, one had received one dose of vaccine, one received two doses, and three received three doses). In contrast, the hospitalization rate for BA.2 cases was 6.3% ($p < 10-2$), none were transferred to ICU, and three (1.5%) died (aged 80, 97, and 99 years, two had diabetes; two had received three doses of COVID-19 vaccine). They observed that the median age of patients who died with BA.2 infection (97 years old, 100% ≥80 years old) was significantly higher than that of those who died with Omicron BA.1 infection (72.5 years, 30% ≥80 years old). In multivariate analysis, independent risk factors for hospitalization were older age and infection with the BA.2 variant but only older age (>80 years) was associated with risk of death.

- The aforementioned study by Kimura et al also provided insights into BA.2 and BA.2 sub-lineage pathogenicity.[32] Infection in hamsters using recombinant viruses suggested that rBA.2.12.1 and rBA.4/5 more efficiently spread in the lung tissues compared to rBA.2. Lung pathology at various time points post-infection showed that bronchitis/bronchiolitis, hemorrhage/congestion and alveolar damage, as well as the total score of histology of rBA.2.12-infected hamsters were significantly higher than those of rBA.2-infected hamsters, but there was no statistically significant difference between rBA.2.12.1 and rBA.2 infections for inflammation with type II alveolar pneumocyte hyperplasia. For additional context, all histopathological parameters were highest in rBA.4/5-infected hamsters. Based on these and additional analyses across variants and sub-lineages, the authors state that their observations strongly suggest that SARS-CoV-2 does not necessarily evolve to attenuate its pathogenicity.

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 and BA.2 sub-lineage VE and reinfections important for assessing the risks associated with a BA.2 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.[39] A recent study in mice reported that a fourth vaccination with the Omicron BA.1 receptor binding domain (RBD) elicited a broadly neutralizing antibody response that included neutralization of BA.2.[40] 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:

- Kirsebom et al.'s pre-print study that was previously reviewed,[41] was updated and published in a peer-reviewed journal.[42] They used a test-negative case-control study design, with cases from January 17 to March 31, 2022 in the UK. The study included 265,820 individuals positive for BA.1, 246,069 positive for BA.2, and 615,628 negative controls, and hospitalization included 1,662 positive for BA.1, 623 positive for BA.2, and 12,758 controls. After 25 or more weeks post-second dose, VE was 14.8% (95% CI 12.9-16.7) against BA.1 and 27.8% (25.9-29.7) against BA.2. A week after a third dose, protection increased to 70.6% (68.9-72.2) against BA.1 and 74.0% (70.8-76.9) against BA.2, and waned to 37.4% (35.8-39.0) against BA.1 and 43.7% (42.3-45.1) against BA.2 at 15 or more weeks after receiving the booster dose. For individuals with a booster/third dose, VE against hospitalization peaked at 90.8% (85.1-94.3) against BA.1 and 89.1% (80.5-94.0) against BA.2, then decreased to 80.4% (75.6-84.3) and 56.5% (38.4-69.3), respectively, after 15 or more weeks. The authors note that the sample sizes were smaller for the hospitalization VE compared to VE for symptomatic diseases, and the confidence intervals overlapped. Overall, the authors reported no reduction in VE against symptomatic disease with BA.2 compared with BA.1, and no difference in the rate of VE decline between the two sub-lineages.

- The aforementioned study by Kimura et al., also provided insights into immune evasion of BA.2 and its sub-lineages.[32] Since BA.4 and BA.5 form a monophyletic clade with BA.2, Kimura et al.'s analyses considered BA.2, BA.4 and BA.5 as "BA.2-related Omicron variants". Using pseudoviruses bearing the S proteins of BA.2.9.1, BA.2.11, BA.2.12.1 and BA.4/5, as well as their derivatives and original BA.2, the authors found BA.2 was highly resistant to convalescent sera from 14 individuals previously infected with BA.1, and all BA.2-related Omicron variants tested were also resistant. Using the sera from 16 individuals who were 2- or 3-dose vaccinated and had a BA.1 breakthrough infection, the sensitivity of BA.2.9.1 and BA.2.11 to these sera was comparable to that of BA.2, but BA.2.12.1 was 1.3-fold more sensitive than BA.2 ($P = 0.021$ by the Wilcoxon signed-rank test). In comparison, BA.4/5 was 2.3-fold more resistant to the BA.1 breakthrough sera than BA.2 ($P < 0.0001$ by the Wilcoxon signed-rank test). Assays using S derivatives with single mutations showed that the F486V mutation confers resistance, whereas HV69-70del and R493Q mutations confer sensitivity. Based on these and additional analyses, the authors state that the data suggests the sensitivity of BA.2 HV69-70del mutant is due to BA.1 infection, whilst sensitivity of BA.2 R493Q is due to vaccination, and BA.2 is less resistant to BA.1 breakthrough-induced immunity than BA.4/5. Analyses of human and mouse convalescent and breakthrough sera showed that BA.2 infection does not induce efficient antiviral immunity and BA.4/5 is resistant to the immunity induced by BA.1 and BA.2 infection.

- Cheng et al., investigated the neutralizing antibody response from vaccination or prior SARS-CoV-2 infection against symptomatic infection by BA.2 or other variants.[43] They reported that sera from individuals who were previously vaccinated or previously wild-type-SARS-CoV-2-infected, had similar BA.2 and BA.1 plaque reduction neutralization test (PRNT50) titers but they were significantly ($p < 10\text{-}5$) lower than against wildtype. Comirnaty (Pfizer-BioNTech) vaccination elicited higher titres to BA.2 than CoronaVac (Sinovac). In individuals with a wild-type-SARS-CoV-2 infection, a single vaccine dose induced higher BA.2 titers than three Pfizer-BioNTech doses ($p = 0.02$) or Sinovac ($p = 0.00001$) doses in infection-naïve individuals. Uninfected and unvaccinated individuals who had a BA.2 infection had low (PRNT50 titer ≤ 80) responses and little cross-neutralization of other variants. In contrast, vaccinees with BA.1 or BA.2 breakthrough infections had broad cross-neutralising antibodies to wild-type viruses, and BA.1, BA.2, Beta and Delta variants. They report that overall, for vaccinated individuals and those who had a previous wild-type-SARS-CoV-2 infection with or without vaccination, the PRNT50 titers to BA.2 were significantly lower than those for wild-type virus, but PRNT50 titers to BA.1 and BA.2 were comparable to each other.

- Ho et al., conducted a systematic antigenic analysis of the Omicron subvariants to investigate their potential immune evasion. To understand antigenic differences between BA.2.12.1 and BA.4/5 from BA.1, BA.1.1, BA.2, and the wild-type SARS-CoV-2 (D614G), they made each pseudovirus and assessed its sensitivity to neutralization by a panel of 21 monoclonal antibodies (mAbs) directed to known neutralizing epitopes on the viral S protein. 18 mAbs lost neutralizing activity completely or partially against BA.2.12.1. BA.2 and BA.2.12.1 had similar neutralization profiles, with the exception of Class 3 RBD antibodies which were either inactive or further impaired against BA.2.12.1. Using surface plasmon resonance (SPR) to measure the binding affinity of variant S proteins to hACE2 showed that S proteins of the Omicron subvariants had similar affinities to hACE2. Dimeric hACE2 neutralization assays confirmed that BA.2.12.1 has not lost hACE2 affinity. Sera from individuals who had three doses of mRNA vaccines had titers for BA.2.12.1 lower by 8.1-fold relative to D614G, and by 1.8-fold relative to BA.2. Relative to BA.2, BA.2.12.1 showed 1.2-fold to 1.4-fold greater resistance to neutralization by sera from individuals who had both mRNA vaccination and SARS-CoV-2 infection. Using the results from the three mRNA dose samples, they mapped the antigenic distances among D614G, various Omicron subvariants, and individual point mutants. Their antigenic cartography showed that BA.1, BA.1.1, and BA.2 are approximately equidistant from D614G, with each about 3-4 antigenic units away. BA.2.12.1 is further away from BA.2 by 1 antigenic unit. And BA.4/5 is 4 antigenic units from BA.2.

Public Health Measures in Other Jurisdictions

Since the last risk assessment, the US CDC recommended a booster for children aged 5 to 11 at least five months after their primary series.[44] Although travel is out of scope for the jurisdictional scan, it should be noted that international jurisdictions are starting to lift mask mandates on planes[45,46] and restrictions for travellers (e.g., proof of vaccination, testing).[47,48]

Implications for Practice

The implications for practice remain largely unchanged from the previous PHO BA.2 and sub-lineages of BA.2 Risk Assessment.[3]

- 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) and BA.4/5 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 3C 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).

- 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. Consideration should be given to the least restrictive and most equitable measures to achieve pandemic response goals based on epidemiological trends 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 3C public settings (e.g., public transit), and practicing respiratory etiquette and washing hands should continue to be promoted for all.[49]

- 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.

- The evidence that a new SARS-CoV-2 VOC could emerge and alter the course of the pandemic again, continues to grow.[50-52] 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."[53] 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,[54] and BA.4 and BA. 5 in South Africa,[55] 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.

References

1. World Health Organization. Weekly epidemiological update on COVID-19 - 22 March 2022 edition 84 [Internet]. Geneva: World Health Organization; 2022 [cited 2022 May 03]. Available from: https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19---22-march-2022

2. Outbreak.info. BA.2 lineage report [Internet]. Munich: GISAID; 2022 [cited 2022 May 03]. Available from: https://outbreak.info/situation-reports?pango=BA.2&selected=DNK&loc=USA&loc=USA_US-CA&loc=DNK&loc=NOR&loc=CAN&overlay=false

3. Ontario Agency for Health Protection and Promotion (Public Health Ontario). 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) [Internet]. Toronto, ON: Queen's Printer for Ontario; 2022 [cited 2022 May 31]. Available from: https://www.publichealthontario.ca/-/media/Documents/nCoV/voc/covid-19-omicron-risk-assessment.pdf?sc_lang=en

4. Nguyen NN, Hoang VT, Dao TL, Dudouet P, Eldin C, Gautret P. Clinical patterns of somatic symptoms in patients suffering from post-acute long COVID: a systematic review. Eur J Clin Microbiol Infect Dis. 2022;41(4):515-45. Available from: https://doi.org/10.1007/s10096-022-04417-4

5. Raman B, Bluemke DA, Lüscher TF, Neubauer S. Long COVID: post-acute sequelae of COVID-19 with a cardiovascular focus. Eur Heart J. 2022;43(11):1157-72. Available from: https://doi.org/10.1093/eurheartj/ehac031

6. Stefanou M-I, Palaiodimou L, Bakola E, Smyrnis N, Papadopoulou M, Paraskevas GP, et al. Neurological manifestations of long-COVID syndrome: a narrative review. Ther Adv Chronic Dis. 2022;13:20406223221076890. Available from: https://doi.org/10.1177/20406223221076890

7. Ontario Agency for Health Protection and Promotion (Public Health Ontario). Impact of vaccination on post-acute COVID-19 syndrome (PACS) – what we know so far [Internet]. Toronto, ON: Queen's Printer for Ontario; 2022 [cited 2022 May 17]. Available from: https://www.publichealthontario.ca/-/media/Documents/nCoV/COVID-WWKSF/2022/04/impact-vaccination-post-acute-covid-19-syndrome.pdf?sc_lang=en

8. Ontario Agency for Health Protection and Promotion (Public Health Ontario). Post-acute COVID-19 syndrome (PACS) in adults [Internet]. Toronto, ON: Queen's Printer for Ontario; 2022 [cited 2022 May 17]. Available from: https://www.publichealthontario.ca/-/media/Documents/nCoV/ipac/2022/04/post-acute-covid-syndrome-pacs.pdf?sc_lang=en

9. Centers for Disease Control and and Prevention. Transcript for CDC media telebriefing: update on COVID-19 [Internet]. Atlanta, GA: Centers for Disease Control and and Prevention; 2022 [cited 2022 May 18]. Available from: https://www.cdc.gov/media/releases/2022/t0426-covid-19-update.html

10. Government of Ontario. COVID-19 clinical assessments and testing [Internet]. Toronto, ON: Queen's Printer for Ontario; 2022 [modified 2022 Apr 11; cited 2022 May 03]. Available from: https://covid-19.ontario.ca/covid-19-clinical-assessments-and-testing

11. Ontario Agency for Health Protection and Promotion (Public Health Ontario). Omicron in Ontario: risk analysis for approaching public health measures in Winter 2022 [Internet]. Toronto, ON: Queen's Printer for Ontario; 2022 [cited 2022 May 17]. Available from: https://www.publichealthontario.ca/-/media/Documents/nCoV/phm/2022/01/covid-19-omicron-ontario-risk-analysis.pdf?sc_lang=en

12. Ontario Agency for Health Protection and Promotion (Public Health Ontario). Epidemiologic summary: SARS-CoV-2 whole genome sequencing in Ontario, May 31, 2022. Toronto, ON: Queen's Printer for Ontario; 2022. Forthcoming.

13. Ontario Agency for Health Protection and Promotion (Public Health Ontario). Ontario COVID-19 data tool: case trends [Internet]. Toronto, ON: Queen's Printer for Ontario; 2022 [cited 2022 May 31]. Available from: https://www.publichealthontario.ca/en/Data-and-Analysis/Infectious-Disease/COVID-19-Data-Surveillance/COVID-19-Data-Tool?tab=trends

14. Ontario Agency for Health Protection and Promotion (Public Health Ontario). Weekly epidemiologic summary: COVID-19 in Ontario – focus on May 15, 2022 to May 21, 2022 [Internet]. Toronto, ON: Queen's Printer for Ontario; 2022 [cited 2022 May 31]. Available from: https://www.publichealthontario.ca/-/media/Documents/nCoV/epi/covid-19-weekly-epi-summary-report.pdf?sc_lang=en

15. Ontario Agency for Health Protection and Promotion (Public Health Ontario). Ontario COVID-19 data tool: lab tests [Internet]. Toronto, ON: Queen's Printer for Ontario; 2022 [cited 2022 May 31]. Available from: https://www.publichealthontario.ca/en/data-and-analysis/infectious-disease/covid-19-data-surveillance/covid-19-data-tool?tab=labTests

16. Ontario Agency for Health Protection and Promotion (Public Health Ontario). COVID-19 cases with severe outcomes: December 12, 2021 to May 21, 2022 [Internet]. Toronto, ON: Queen's Printer for Ontario; 2022 [cited 2022 May 31]. Available from: https://www.publichealthontario.ca/-/media/Documents/nCoV/epi/covid-19-cases-severe-outcomes-epi-summary.pdf?sc_lang=en

17. Ontario Agency for Health Protection and Promotion (Public Health Ontario). COVID-19 Omicron variant sub-lineage BA.2: evidence and risk assessment (up to date as of April 19, 2022) [Internet]. Toronto, ON: Queen's Printer for Ontario; 2022 [cited 2022 May 31]. Available from: https://www.publichealthontario.ca/-/media/Documents/nCoV/voc/2022/04/omicron-variant-ba2-risk-assessment-apr-19.pdf?sc_lang=en

18. Jüni P, Maltsev A, Katz GM, Perkhun A, Yan S, Bodmer NS; Ontario COVID-19 Science Advisory Table. Ontario dashboard: tracking Omicron [Internet]. Toronto, ON: Queen's Printer for Ontario; 2022 [cited 2022 May 31]. Available from: https://covid19-sciencetable.ca/ontario-dashboard/

19. Government of Canada. COVID-19 daily epidemiology update: current situation [Internet]. Ottawa, ON: Government of Canada; 2022 [cited 2022 May 31]. Available from: https://health-infobase.canada.ca/covid-19/epidemiological-summary-covid-19-cases.html?stat=rate&measure=total_last7&map=pt#a2

20. Government of Canada. Canada COVID-19 weekly epidemiology report: 15 May to 21 May 2022 (week 20) [Internet]. Ottawa, ON: Government of Canada; 2022 [cited 2022 May 31]. Available from: https://www.canada.ca/content/dam/phac-aspc/documents/services/diseases/2019-novel-coronavirus-infection/surv-covid19-weekly-epi-update-20220527-en.pdf

21. World Health Organization. Weekly epidemiological update on COVID-19 – 25 May 2022: edition 93 [Internet]. Geneva: World Health Organization; 2022 [cited 2022 May 31]. Available from: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20220525_weekly_epi_update_93.pdf?sfvrsn=e8162ad9_5&download=true

22. Statens Serum Institut. Ugentlige tendenser: covid-19 og andre luftvejsinfektioner [Internet] Copenhagen: Statens Serum Institut; 2022 [cited 2022 May 31]. Danish. Available from: https://filesssidk/covid19/tendensrapport/rapport/ugentlige-tendenser-covid19-andre-luftvejs-uge20-2022-id74

23. UK Health Security Agency. SARS-CoV-2 variants of concern and variants under investigation in England: technical briefing 42 [Internet]. London: Crown Copyright; 2022 [cited 2022 Jun 3]. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1077180/Technical-Briefing-42-20May2022.pdf

24. UK Health Security Agency. Weekly national influenza and COVID-19 surveillance report: week 19 report (up to week 18 data) 12 May 2022 [Internet]. London: Crown Copyright; 2022 [cited 2022 May 17]. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1075079/National_flu_and_COVID-19_surveillance_report_12_May_2022_week_19.pdf

25. UK Health Security Agency. Weekly national influenza and COVID-19 surveillance report: week 21 report (up to week 20 data) 26 May 2022 [Internet]. London: Crown Copyright; 2022 [cited 2022 May 31]. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1078858/Weekly_Flu_and_COVID-19_report_w21.pdf

26. UK Health Security Agency. Coronavirus (COVID-19) in the UK: simple summary for United Kingdom [Internet]. London: Crown Copyright; 2022 [cited 2022 May 31]. Available from: https://coronavirus.data.gov.uk/easy_read

27. Elliott P, Eales O, Steyn N, Tang D, Bodinier B, Wang H, et al. Twin peaks: the Omicron SARS-CoV-2 BA.1 and BA.2 epidemics in England. Science. 2022 May 24 [Epub ahead of print]. Available from: https://doi.org/10.1126/science.abq4411

28. Centers for Disease Control and Prevention. COVID data tracker [Internet]. Atlanta, GA: Centers for Disease Control and Prevention; 2021 [cited 2022 May 31]. Available from: https://covid.cdc.gov/covid-data-tracker/#variant-proportions

29. Centers for Disease Control and and Prevention. COVID data tracker weekly review [Internet]. Atlanta, GA: Centers for Disease Control and and Prevention; 2022 [cited 2022 May 31]. Available from: https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covidview/index.html

30. Bolze A, Basler T, White S, Rossi AD, Wyman D, Roychoudhury P, et al. Evidence for SARS-CoV-2 Delta and Omicron co-infections and recombination. medRxiv 22272113 [Preprint]. 2022 Mar 28 [cited 2022 Apr 4]. Available from: https://doi.org/10.1101/2022.03.09.22272113

31. Gu H, Ng DY, Liu GY, Cheng SS, Krishnan P, Chang LD, et al. Detection of a BA.1/BA.2 recombinant in travelers arriving in Hong Kong, February 2022. medRxiv 22273020 [Preprint]. 2022 Apr 2 [cited 2022 Apr 5]. Available from: https://doi.org/10.1101/2022.03.28.22273020

32. Kimura I, Yamasoba D, Tamura T, Nao N, Oda Y, Mitoma S, et al. Virological characteristics of the novel SARS-CoV-2 Omicron variants including BA.2.12.1, BA.4 and BA.5. bioRxiv 493539 [Preprint]. 2022 May 26 [cited 2022 May 31]. Available from: https://doi.org/10.1101/2022.05.26.493539

33. Dai Y. Rapid epidemic expansion of the SARS-CoV-2 Omicron BA.2 subvariant during China's largest outbreaks. Res Sq 1516063 [Preprint]. 2022 May 31 [cited 2022 Jun 1]. Available from: https://doi.org/10.21203/rs.3.rs-1516063/v8

34. Lentini A, Pereira A, Winqvist O, Reinius B. Monitoring of the SARS-CoV-2 Omicron BA.1/BA.2 variant transition in the Swedish population reveals higher viral quantity in BA.2 cases. medRxiv 22272984 [Preprint]. 2022 Mar 27 [cited 2022 May 3]. Available from: https://doi.org/10.1101/2022.03.26.22272984

35. Qassim SH, Chemaitelly H, Ayoub HH, AlMukdad S, Tang P, Hasan MR, et al. Effects of BA.1/BA.2 subvariant, vaccination, and prior infection on infectiousness of SARS-CoV-2 Omicron infections. medRxiv 22271771 [Preprint]. 2022 Mar 4 [cited 2022 May 3]. Available from: https://doi.org/10.1101/2022.03.02.22271771

36. UK Health Security Agency. SARS-CoV-2 variants of concern and variants under investigation in England: technical briefing 38 [Internet]. London: Crown Copyright; 2022 [cited 2022 May 3]. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1060337/Technical-Briefing-38-11March2022.pdf

37. Ontario Agency for Health Protection and Promotion (Public Health Ontario). Epidemiologic summary: SARS-CoV-2 whole genome sequencing in Ontario, May 17, 2022. Toronto, ON: Queen's Printer for Ontario; 2022. Forthcoming.

38. Gautret P, Hoang VT, Jimeno MT, Lagier J-C, Rossi P, Fournier PE, et al. The severity of the first 207 infections with the SARS-CoV-2 Omicron BA.2 variant, in Marseille, France, December 2021–February 2022. J Med Virol. 2022 Apr 1 [Epub ahead of print]. Available from: https://doi.org/10.1002/jmv.27760

39. Ontario Agency for Health Protection and Promotion (Public Health Ontario). Confirmed cases of COVID-19 following vaccination in Ontario: December 14, 2020 to March 27, 2022 [Internet]. Toronto, ON: Queen's Printer for Ontario; 2022 [cited 2022 May 3]. Available from: https://www.publichealthontario.ca/-/media/Documents/nCoV/epi/covid-19-epi-confirmedcases-post-vaccination.pdf?sc_lang=en

40. Rodino KG, Peaper DR, Kelly BJ, Bushman F, Marques A, Adhikari H, et al. Partial ORF1ab gene target failure with Omicron BA.2.12.1. medRxiv 22274187 [Preprint]. 2022 Apr 28 [cited 2022 May 31]. Available from: https://doi.org/10.1101/2022.04.25.22274187

41. Ontario Agency for Health Protection and Promotion (Public Health Ontario). COVID-19 Omicron variant sub-lineage BA.2: evidence and risk assessment (up to date as of April 5, 2022) [Internet]. Toronto, ON: Queen's Printer for Ontario; 2022 [cited 2022 May 31]. Available from: https://www.publichealthontario.ca/-/media/Documents/nCoV/voc/2022/04/omicron-variant-ba2-risk-assessment-apr-5.pdf?sc_lang=en

42. Kirsebom FCM, Andrews N, Stowe J, Toffa S, Sachdeva R, Gallagher E, et al. COVID-19 vaccine effectiveness against the omicron (BA.2) variant in England. Lancet Infect Dis. 2022 May 24 [Epub ahead of print]. Available from: https://doi.org/10.1016/S1473-3099(22)00309-7

43. Cheng SM, Mok CKP, Chan KC, Ng SS, Lam BH, Luk LL, et al. SARS-CoV-2 Omicron variant BA.2 neutralisation in sera of people with Comirnaty or CoronaVac vaccination, infection or breakthrough infection, Hong Kong, 2020 to 2022. Eurosurveillance. 2022;27(18):2200178. Available from: https://doi.org/10.2807/1560-7917.ES.2022.27.18.2200178

44. Mishra M, Erman M. U.S. CDC backs COVID boosters for children 5 to 11. Reuters [Internet], 2022 May 19 [cited 2022 May 31]. Available from: https://www.reuters.com/world/us/us-advisory-panel-weigh-covid-boosters-children-2022-05-19/?utm_source=Sailthru&utm_medium=newsletter&utm_campaign=daily-briefing

45. RFI. France lifts Covid restrictions, no longer requiring masks on planes, trains as of Monday. Yahoo! News [Internet], 2022 May 12 [cited 2022 May 31]. Available from: https://ca.news.yahoo.com/france-lifts-covid-restrictions-no-054300731.html

46. Israel. Ministry of Health. Mask mandate on board international flights to be lifted on 23.5.22 [Internet]. Jerusalem: State of Israel; 2022 [cited 2022 May 31]. Available from: https://www.gov.il/en/departments/news/17052022-02

47. Euronews. Italy drops last COVID entry rules, ditches testing and vaccination restrictions. Yahoo! News [Internet], 2022 May 31 [cited 2022 May 31]. Available from: https://uk.news.yahoo.com/italy-drops-last-covid-entry-103011518.html?guccounter=1&guce_referrer=aHR0cHM6Ly93d3cuYmluZy5jb20v&guce_referrer_sig=AQAAAHaom5khDQ9GBgrStZA7YcYErpq761fV_oEEdR_03x5Vx5vYyTgXe3eQ0ycoK__mtVCrM_RGl87XZwHskHdiVecV79729NQkQACYP8f_UxkqEnNf9goBkgL1etlZFw_3Za_OteuhO1OaIbRS2PCIutX4VDtIF-UCfyPl0eYoslj4

48. DW Staff. COVID: Germany to relax entry restrictions for summer. Guardian TV [Internet], 2022 May 29 [cited 2022 May 31]; World. Available from: https://tv.guardian.ng/news/world-news/covid-germany-to-relax-entry-restrictions-for-summer/

49. Ontario. Ministry of Health. Management of cases and contacts of COVID-19 in Ontario [Internet]. Version 14.1. Toronto, ON: Queen's Printer for Ontario; 2022 [modified 2022 Apr 19; cited 2022 Apr 20]. Available from: https://www.health.gov.on.ca/en/pro/programs/publichealth/coronavirus/docs/contact_mngmt/management_cases_contacts.pdf

50. Bedford T. Continuing SARS-CoV-2 evolution under population immune pressure 6 Apr 2022 [Internet]. Presented at: FDA. Vaccines and Related Biological Products Advisory Committee Meeting. 2022 Apr 6 [cited 2022 Apr 19]; Washington, DC. Available from: https://bedford.io/talks/sars-cov-2-continuing-evolution-vrbpac/#/15. Available from:

51. Colson P, Delerce J, Marion-Paris E, Lagier J-C, Levasseur A, Fournier P-E, et al. A 21L/BA.2-21K/BA.1 "MixOmicron" SARS-CoV-2 hybrid undetected by qPCR that screen for variant in routine diagnosis. medRxiv 22273010 [Preprint]. 2022 Mar 31 [cited 2022 Apr 4]. Available from: https://doi.org/10.1101/2022.03.28.22273010

52. Ou J, Lan W, Wu X, Zhao T, Duan B, Yang P, et al. Tracking SARS-CoV-2 Omicron diverse spike gene mutations identifies multiple inter-variant recombination events. bioRxiv 484129 [Preprint]. 2022 Mar 14 [cited 2022 Apr 4]. Available from: https://doi.org/10.1101/2022.03.13.484129

53. World Health Organization. Live Q&A on COVID-19 virtual press conference transcript - 11 May 2022 [Internet]. Geneva: World Health Organization; 2022 [cited 2022 May 17]. Available from: https://www.who.int/publications/m/item/live-q-a-on-covid-19-virtual-press-conference-transcript---11-may-2022

54. Doucleff M. 2 new omicron variants are spreading in N.Y. and elsewhere. Here's what we know. NPR News [Internet], 2022 Apr 14 [cited 2022 May 3]. Available from: https://www.npr.org/sections/goatsandsoda/2022/04/14/1092812456/two-new-omicron-variants-are-spreading-in-n-y-and-elsewhere-heres-what-we-know

55. Prater E. BA.4 and BA.5, two new Omicron variants sweeping South Africa, detected in U.S. Fortune [Internet], 2022 Apr 30 [cited 2022 May 3]; Health. Available from: https://fortune.com/2022/04/30/are-ba4-ba5-in-united-states-detected-omicron-covid-stealth-omicron-more-transmissible/

Citation

Ontario Agency for Health Protection and Promotion (Public Health Ontario). COVID-19 Omicron variant sub-lineage BA.2 and sub-lineages of BA.2: evidence and risk assessment (up to date as of May 31, 2022). Toronto, ON: Queen's Printer for Ontario; 2022.

Disclaimer

Public Health Ontario

Public Health Ontario is an agency of the Government of Ontario dedicated to protecting and promoting the health of all Ontarians and reducing inequities in health. Public Health Ontario links public health practitioners, front-line health workers and researchers to the best scientific intelligence and knowledge from around the world.

For more information about PHO, visit publichealthontario.ca.

Ontario