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EVIDENCE BRIEF

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

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Key Messages

- Ontario is experiencing a sixth severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic wave dominated by the Omicron BA.2 sub-lineage, which comprised 80.5% of whole genome sequencing (WGS) samples from March 27 to April 2, 2022.

- Epidemiological trends since the removal of public health measures, including removal of indoor masking requirements in many community settings as of March 21, 2022, suggest a corresponding temporal association with a subsequent increase in confirmed Coronavirus Disease 2019 (COVID-19) cases, testing percent positivity, and hospitalizations. In the week of April 20 to 26, the rate of confirmed cases in the eligible population increased by 1.3% from the previous week, compared to over 24.2% in the previous three weeks, which may be an early indication of a plateau.

- Evidence suggests BA.2 has similar severity compared to BA.1 in adults, but there is less evidence on severity of BA.2 in children. Due to increased transmissibility of BA.2 and removal of public health measures, the absolute number of cases and severe cases would be expected to rise. High vaccine uptake among adults and immunity from previous infections may attenuate the overall increase in severe cases. 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.

- Prevention strategies that reduce the risk of transmission can be layered onto a vaccination strategy to mitigate the current surge in cases driven by a more transmissible dominant variant with lower VE against symptomatic infection. These include ventilation, universal indoor masking in public settings, masking directives in high-risk settings, and communication on the importance of wearing masks with good fit and filtration for personal and population-level protection. Preventing high levels of population infection may mitigate the incidence of post-acute COVID-19 syndrome (PACS, “long COVID-19”) and its longer term impacts. Those at highest risk of severe disease (e.g., immunocompromised, elderly, and racialized, and low income populations), 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), can benefit from population-level interventions.

- 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. High quality surveillance, learning from prior use and removal of public health measures, and efforts to increase vaccine equity can help prepare Ontario for the next stages of the COVID-19 pandemic.

Issue and Research Question

There are currently 55 Pango sub-lineages associated with the Omicron variant, with BA.1, BA.1.1, and BA.2 as the most commonly reported.[1,2] Considering the increased transmissibility of the Omicron BA.2 sub-lineage compared to previously circulating VOCs and BA.1.1, it is important to monitor the potential impact the BA.2 sub-lineage might have in Ontario. This evidence brief updates the Public Health Ontario (PHO) report published April 5, 2022,[3] and summarizes available information and evidence on the BA.2 sub-lineage relevant to the risk in Ontario that has emerged since the last report up to April 19, 2022.

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 have been the dominant sub-lineages in most jurisdictions. Sections from prior risk assessments for which there is no new literature of note, have been removed.

Ontario Risk Assessment

The current risk of BA.2 sub-lineage transmissibility in Ontario is high, with a low degree of uncertainty. The risk of severe disease in Ontario is low, with a moderate degree of uncertainty; but, due to increased transmissibility of BA.2, the absolute number of severe cases would be expected to rise. High vaccine uptake and immunity from previous infections may attenuate the increase. 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. The risk of reinfection is high with a moderate degree of uncertainty in Ontario. The risk of breakthrough infection is high with a moderate degree of uncertainty in Ontario. The risk of impact of the BA.2 sub-lineage 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

- In the current context of a more transmissible dominant variant, and when PCR-confirmed case rates are higher than during much of the pandemic to date (despite being an underestimate) and public health measures (e.g., masking, capacity limits) have been removed, the number of infections are likely to grow to a peak, and the number of cases with severe disease are likely to increase due to the rise in cases.

- Growing evidence on the risk and prevalence of PACS shows elevated risk of several chronic, potentially disabling conditions following SARS-CoV-2 infection, even after non-severe cases.[4-15] At this time, it is not possible to know the risk of PACS from the BA.2 variant; but BA.2 infections may cause PACS in some individuals, like other SARS-CoV-2 infections.

- There are gaps in surveillance data to inform timely public health action related to Ontario's pediatric population, related to limited PCR testing eligibility among children,[16] as well as hospitalization lagging as an indicator and evidence of less severe disease in children than adults. Evidence from previous SARS-CoV-2 waves suggests that the majority of children are likely at low risk of complications from acute infection.[17] However, some children remain at increased risk of hospitalization and severe disease, and the numbers with severe disease may increase as the number of infections increase.

- Changes to eligibility for diagnostic PCR testing means Ontario case counts are an underestimate. Although rapid antigen testing (RAT) is more available to the public, scientific evidence on the test performance of RATs for diagnostic purposes of BA.2 is lacking. Recent evaluations performed at the National Microbiology Laboratory; however, indicate RAT sensitivity for BA.2 to be equivalent to other tested variants (report forthcoming/personal communication).

Ontario Epidemiology

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.[18]

- On December 31, 2021, diagnostic PCR testing was restricted to high-risk populations. Provincial testing guidance was updated April 11, 2022, with molecular testing eligibility updates related to eligibility for COVID-19 treatment (e.g., inclusion of all symptomatic people aged 70 and older).[19] Ontario case counts remain an underestimate and representative surveillance only pertains to tested populations.[16,20] Additionally, while RATs are more available to the public, these results are not captured in Ontario's COVID-19 surveillance, further compounding the underestimate of Ontario case counts. The Ontario COVID-19 Genomics Network (OCGN) moved from sequencing 20% of eligible samples on February 16, 2022 to 50% on March 9, 2022, and 25% on March 30, 2022.[21] Based on WGS results completed by the OCGN as of April 14, 2022:[21]

    - The proportion of cases identified as BA.2 have had an increasing trend over the past several weeks: 6.3% for week of January 23 to 29, 25.1% for February 27 to March 5, 2022, and 80.5% March 27 to April 2, 2022.

    - One case of BA.3 was identified during the week of March 27 to April 2, 2022.

    - From January 9, 2022 to April 2, 2022, the weekly growth rate of BA.2 was 1.62 (95% confidence interval [CI] 1.60 - 1.65) times that of BA.1.1.

- Despite the underestimation of cases due to testing eligibility, conclusions can be drawn from the case trends as the PCR-testing eligible population has been relatively stable since mid-January. The rate of cases increased by 1.3% in week 15 (April 10 to 16), compared to the week-over-week increases of over 24.2% in the previous three weeks. This suggests the rate of cases may be stabilizing among those eligible for testing. It is uncertain whether this trend will continue following the recent holidays and in the absence of public health measures while a highly transmissible variant is dominant.[22] The number of cases associated with outbreaks in long-term care increased by 21.2% from week 14 (April 3 to 9) to week 15 (April 10-16). The percent test positivity (among those eligible for PCR testing) began increasing at the end of February 2022. Since early April, percent positivity has been relatively stable near 18-19%, which is higher than most of the pandemic. On April 6, 2022 the percent test positivity was 18%, and was higher in children <13 years of age (22.5%), 14-17 years of age (26.94%), and 18-24 years of age (24.2%). [23]

- Hospitalizations, intensive care unit (ICU) admissions and deaths are lagging indicators, often occurring days or weeks after cases are initially reported to public health. Using data as of April 17, 2022, the Ontario Hospital Association (OHA) COVID-19 Hospital Capacity Report indicates adult critical care units with COVID-related critical illness (CRCI) patients are showing an increasing trend since the week of April 6, 2022, after a brief plateau.[24] The OHA also reports the speed signal of hospitalizations and ICU cases, which can be considered as the number of hospitalization or ICU cases per day that can be expected if the current 7-day trend continues. When the speed > 0, the trend of cases is speeding up, when < 0, the trend of cases is slowing down, and when speed=0 the cases have plateaued. Using data as of April 17, 2022, the adult hospitalization and ICU speed estimates were increasing.

- The Ontario Science Table's April 14, 2022 Update on COVID-19 Projections reported that there is significant uncertainty around the impact of case growth on the Ontario health system and deaths. They reported that wastewater surveillance suggests that community transmission may have peaked but uncertainty remains about whether this trend will continue following the holidays. Their modelling indicates hospital occupancy is likely to continue increasing for some time, and the timing and height of the peak remain uncertain. They also reported that COVID-19 infections in healthcare workers were as high as in the last Omicron wave, with the table suggesting the high infection rates among healthcare workers combined with potentially high hospitalization rates, will reduce Ontario's ability to provide care for non-COVID-19 patients.[25]

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

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

Epidemiology in Other Jurisdictions

Canada

In an April 12, 2022 statement, the Chief Public Health Officer of Canada reported that the recent 7-day averages across the provinces and territories showed a continued marked increase in average daily case counts, and rising trends in severe illness in most jurisdictions.[26] Laboratory test positivity from April 4-10, 2022 increased to 19% nationally, and community wastewater data continue to indicate sharply rising trends in several jurisdictions.

- Surveillance WGS across Canada indicated that of SARS-CoV-2 samples collected the week of March 27, 2022, 99.9% were Omicron (1.1% BA.1, 19.2% BA.1.1, 53.0% BA.2, 26.6% other Omicron), but data were still accumulating.[27] This is an increase in the proportion of BA.2 samples compared to the week of March 13, 2022 (100% Omicron: 4.1% BA.1, 38.4% BA.1.1, 34.1% BA.2, 23.4% other Omicron). On April 19, 2022, Canada reported 2,295 new COVID-19 cases, 7 new deaths and 220,306 active cases. The daily percent positivity (over the previous 7 days) was 19.9%, and is a continuation of the increasing trend in test positivity observed since late February/early March. The Public Health Agency of Canada (PHAC) notes that due to changes in COVID-19 testing policies in many jurisdictions starting in late December 2021, case counts will underestimate the total burden of disease.

Select Other Jurisdictions

- Denmark: The Danish Health Authority changed their COVID-19 test recommendations the week of March 6, 2022to 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 27 to April 2, 2022.[28] In the week March 27 to April 2, 2022, of 6,011 samples with WGS, the Statens Serum Institut reported that 71.5% were BA.2, 23.8% BA.2_H78Y, 2.8% BA.2.1, 0.3% BA.1.1, 0.1% BA.1, and 0.0% BA.3. The Danish COVID-19 Genome Consortium reported 99.4% of sequenced samples were BA.2 in the week of April 3 to 9, 2022 .[29]

- United Kingdom (UK): Effective April 1, 2022, the UK Health Security Agency (UKHSA) is using a revised variant classification system to better indicate which variants have significant changes in biological properties, and BA.2 is now designated as a variant of concern (VOC).[30] The Office of National Statistics reported that in the week ending April 9, 2022, the percentage of infections compatible with the Omicron BA.2 variant decreased in England, Northern Ireland and Scotland, and remained high in Wales. In parallel, the percentage of infections compatible with BA.1 decreased in England and Scotland, but the trend was less certain in Wales and Northern Ireland.[31]

    - England: The UKHSA most recent VOC and variants under investigation (VUI) report for England reported that of all WGS cases between March 27 to April 3, 2022, 11.0% were BA.1 (VOC-21NOV-01), 88.5% were BA.2 (VUI-22JAN-01), and 0.5% were other variants.[30] The UKHSA, like other jurisdictions, has used S-gene target failure (SGTF) as a proxy for the Omicron BA.1 and BA.1.1 variants due to the amino acid deletion at position 69 and 70 of the S protein, and S-gene target positivity (SGTP) as a proxy for BA.2 because it is usually missing this deletion. The proportion of SGTP cases increased from 93.7% on March 20, 2022, to 97.6% on April 3, 2022.[30] There is, however, a growing proportion of BA.2 sequences in the UK containing the deletion at 69 and 70. As of March 2, 2022, 123/93,937 BA.2 sequences in the UK genomic database had a deletion at 69 and 70 (0.13% of BA.2

cases), and as of March 30, 2022 this increased slightly to 516/320,144 (0.16% of BA.2 cases).

- United States (US): According to NOWCAST modelling projections, the US Centers for Disease Control and Prevention (CDC) estimated that for the week ending April 9, 2022, 100% of SARS-CoV-2 cases were Omicron (13.1% [95% PI 11.3-15.2%] BA.1.1, 1.0% [95% PI 0.8-1.3%] B.1.1.529 [BA.1 and BA.3] 85.9% [95% PI 83.6-87.8%] BA.2).[32] As of April 13, 2022, the 7-day moving average of daily new SARS-CoV-2 cases (31,391) increased 19% compared to the previous week's 7-day moving average (26,357).[33]

Genomic Features and Evolution

Comparison of BA.1 and BA.2 shows that BA.2 has 10 unique mutations and BA.1 has 18 unique mutations.[34] Unlike BA.1, which shares nine spike mutations with most VOCs, BA.2 shares only six mutations in its spike protein with most VOCs.[35] 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.[36,37] A few studies are highlighted below:

- Suradana et al., conducted a whole genome comparison of several SARS-CoV-2 variants and the BA.2 sub-variant to describe insertion/deletion and amino acid substitution patterns.[38] The authors used GISAID to obtain 10 to 20 randomly selected complete sequences for each definitive variant. One observation was that three deletions in the nucleocapsid protein are unique to Omicron and BA.2. Evolutionary analysis using the maximum likelihood method revealed that Omicron, BA.2, and GKA clade ("Deltacron") share a common cluster emerging from the Delta variant sequence with bootstrap support of 98%.

- Leuking et al., describe two cases of Delta/Omicron and two cases of Omicron sub-lineage BA.1/ BA.2 co-infection.[39] The authors predict SARS-CoV-2 co-infections will continue to occur when one variant takes over another, and are likely to occur in immunocompromised hosts due to trouble clearing the virus.

- Xu et al., investigated cross-species angiotensin converting enzyme-2 (ACE2) binding to the spike trimer from an ancestral, BA.1 and BA.2 strains to gain insight into a possible evolutionary map of Omicron.[40] The authors reported that ACE2 from horse, pig, and sheep had decreased BA.1 and BA.2 spike binding compared to the ancestral strain, whereas cat ACE2 had similar binding between ancestral and Omicron variants. Rat and dog ACE2 exhibited no binding with ancestral, BA.1 or BA.2 trimers. Mouse ACE2 bound to both BA.1 and BA.2 spike trimer with high affinity but did not bind the ancestral spike trimer. The mouse ACE2 bound the BA.2 spike trimer with approximately 3-fold higher affinity than the BA.1 spike trimer. The authors propose mouse is likely a host for evolution of Omicron variants.

Diagnostics

Previous PHO BA.2 Risk Assessment reports have not identified any published literature on the test performance characteristics of RATs for BA.2.[41,42] However, based on the antigen target (nucleocapsid protein) of RATs used in Ontario, the differences in observed amino acid substitutions between BA.1, BA.1.1 and BA.2,[43] *in theory*, RAT performance for BA.2 is expected to be similar to that of BA.1 and BA.1.1.2.[34] This notion is further supported by a recent internal evaluation performed by the National Microbiology Laboratory (personal communication/report forthcoming), where no difference in RAT performance was found for BA.2 compared to other SARS-CoV-2 variants (Alpha, Delta, Omicron_B.1.1.529 and Wuhan) tested. Differences between Omicron sub-lineages in terms of other variables, such as viral load dynamics and tissue tropism, can impact when and which specimen collection sites are best for detection of BA.2 when using a RAT. Use of RATs for BA.2 sub-lineage diagnostic purposes requires a better understanding of the test characteristics of this modality.

Transmissibility

Since the last PHO BA.2 Risk Assessment,[44] additional studies have described BA.2 growth advantage over BA.1 and other SARS-CoV-2 variants. It remains unclear to what extent the increased transmission of BA.2 compared to BA.1 or BA1.1 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 growing evidence suggests higher viral load plays a role.[45-47]

- Eales et al., used data from the REal-time Assessment of Community Transmission-1 (REACT-1) study, which has tested randomly selected cross-sections of England from September 9, 2021 to March 1, 2022, to describe the dynamics of the Omicron wave in England as it replaced the previously dominant Delta wave.[48] On December 30, 2021, at peak Omicron prevalence, BA.1 represented 84.6% (82.9%, 86.2%), BA.1.1 represented 15.2% (13.6%, 16.9%) and BA.2 represented only 0.2% (0.1%, 0.3%) of cases; however, by March 1, 2022, the proportion of BA.1 was 9.6% (8.1%, 11.3%), BA.1.1 was 21.6% (18.7%, 24.9%) and BA.2 was 68.7% (64.6%, 72.7%). The daily log-odds of BA.2 infection increased with a daily growth rate of 0.133 (0.122, 0.144) relative to BA.1, and 0.091 (0.081, 0.102) relative to BA.1.1. On March 1, 2022, the estimated time-varying reproduction number (Rt) for BA.2 was 1.17 (1.08, 1.28) and for non-BA.2 Omicron it was 0.77 (0.69, 0.87). The difference in Rt over time resulted in an estimated multiplicative advantage of 1.5 for BA.2 over non-BA.2 Omicron (daily estimates range 1.46 [1.40, 1.52] on January 31, 2022 and 1.54 [1.46, 1.60] on February 18, 2022).

- Xu et al., also reported potential structural and biochemical mechanisms for the increased infectivity of BA.1 and BA.2 variants using biochemical analyses and cryogenic electron microscopy (cryo-EM).[40] The authors report that dimeric human ACE2 (hACE2) bound to the BA.2 spike trimer with a dissociation constant (KD) value that was approximately 11-fold higher than that with an ancestral SARS-CoV-2 spike trimer and almost 2-fold higher than with BA.1 spike trimer. Analysis of the Omicron BA.2 spike trimer-hACE2 complex revealed that the spike trimer bound to at least two or three hACE2, suggesting a stronger hACE2 binding tendency of the BA.2 spike trimer compared to what the same authors observed for BA.1.[49] The cryo-EM revealed BA.1 and BA.2 to have a similar RBD-ACE2 but some BA.2 mutations resulted in enhanced ACE2 binding. The authors conclude that increased hACE2 binding is a key factor in increased BA.2 infectivity.

Disease Severity and Symptoms

Early evidence suggests BA.2 has similar severity compared to BA.1 in adults, but there is less evidence on severity of BA.2 in children.[3] Since the last PHO BA.2 Risk Assessment, a report by Eales et al., used data from the REACT-1 study in England (September 9, 2021 to March 1, 2022) to describe the dynamics of the Omicron wave in England as it replaced the previously dominant Delta wave.[48] The authors reported that a greater proportion of BA.2 cases exhibited the most predictive COVID-19 symptoms (loss or change of sense of smell or taste, fever, new persistent cough) compared to BA.1 cases. A comparison of BA.2 and Delta cases was not performed.

Although it is too early to assess the risk of PACS from BA.2 infections, there is growing evidence of significant sequelae after SARS-CoV-2 infection.[4]

Vaccine Effectiveness (VE) 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 wave in Ontario. A review of VE evidence before the BA.2 wave shows that a primary series and a booster dose of COVID-19 vaccine exhibits less waning against severe outcomes, including hospitalization and death, than for symptomatic infection.[50] 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:

- Gruell et al., compared polyclonal serum activity against BA.1, BA.1.1, and BA.2 from convalescent (n=20) or vaccinated (n=30 healthcare workers) individuals, and characterized monoclonal antibody sensitivities using 163 antibodies.[51] Both study groups received a Pfizer-BioNTech booster after a median of 14 and 9 days post-infection or two doses of Pfizer-BioNTech, respectively. Convalescent, boosted individuals had neutralizing titers of 1,688, 1,578, and 2,388 against BA.1, BA.1.1, and BA.2, respectively. Individuals who had three doses of Pfizer-BioNTech had neutralizing titers of 648, 557, and 592 against BA.1, BA1.1, and BA.2, respectively. For both convalescent and two-dose vaccine recipients, the booster dose significantly increased the neutralizing antibody response against Omicron sub-lineages investigated. The authors also tested 158 Omicron-specific monoclonal antibodies isolated from convalescent individuals in order to compare neutralization across Omicron sub-lineages. All antibodies neutralized the ancestral SARS-CoV-2 strain, but only 18%, 17% and 22% were active against BA.1, BA.1.1, and BA.2, respectively. Although the geometric mean IC50s were lower for BA.1, BA.1.1, and BA.2 than for the ancestral strain, the study identified a small number of monoclonal antibodies that retained high potency against BA.1, BA.1.1, and BA.2. The authors reported a strong correlation between the antibodies that neutralized BA.1 and BA.1.1, whereas BA.1 and BA.2 exhibited more divergent antibody profiles. Based on the observation that 72.5% of antibodies had comparable activity against BA.1 and BA.2, 25% had higher potency against BA.2, and 10/40 monoclonal antibodies had a 1.1 to 3.9 log10 fold higher potency against BA.2, the authors conclude that there is less immune escape by BA.2 compared to BA.1 and BA.1.1.

- Parn et al., characterized CD4+ and CD8+ T cell epitopes that target the spike protein of BA.1 and BA.2 in a first step towards identifying epitope-based peptide vaccine candidates that could elicit a strong and long-lived immune response against the Omicron variant.[52] The authors used Immune Epitope Database to predict CD8+ and CD4+ T cell epitopes with high binding affinity to MHC class I and II alleles. Immunogenicity, population coverage, antigenicity, allergenicity, toxicity, IFNγ secretion, half-life, GRAVY (grand average of hydropathicity), and other amino acid physiochemical properties were also predicted. After identifying potential epitopes, the authors attempted to identify the most immunogenic CD8+ peptides within IFNγ-inducing CD4+ epitopes. The authors also predicted the structure of the peptide-MHC and TCR-MHC. The authors suggest their study could provide Omicron peptides for future pre-clinical trials.

- Knabl et al., reported the immune response to BA.1 and BA.2 in naïve and previously infected individuals.[53] Naïve and unvaccinated individuals anti-Omicron and ancestral spike IgG titers were 4- to 5-fold lower after BA.2 infection compared to BA.1 infection. The data showed that in individuals who had never been previously infected or vaccinated, the immunologic response after an Omicron BA.2 infection was lower than after a BA.1 infection. In individuals previously infected with an earlier SARS-COV-2 variant, titers were 11- to 86-fold higher, with no difference in titers from those infected with BA.1 or BA.2 variants. The differential antibody response following BA.1 or BA.2 infection was consistent across all SARS-COV-2 variants tested. Neutralizing activities (based on ACE2 neutralization) against ancestral and Omicron were similarly low in antigen naïve individuals infected with either BA.1 or BA.2, and was higher in previously infected individuals. The authors suggest that the lower neutralization response after a BA.2 infection could contribute to prolonged SARS-CoV-2 circulation in the population due to attenuated protection from re-infection.

- Stiasny et al., investigated antibody neutralization against Omicron BA.1, BA.2, and Delta variants by sera from individuals who had recovered from primary Omicron BA.1 or BA.2 infection or who had been vaccinated with or without previous infection.[54] Cases with primary BA.1 infections exhibited a strongly reduced neutralizing antibody response to SARS-CoV-2 strains circulating before Omicron, but vaccine-boosting led to efficient cross-neutralization that may protect from disease. Serum from vaccinees three weeks or three months after the third dose of an mRNA vaccine efficiently and similarly cross-neutralized BA.1 and BA.2 variants (Mann-Whitney test, $p > 0.05$), although neutralization titers were significantly lower than for ancestral SARS-CoV-2. Individuals who had a previous ancestral strain infection before receiving 3-doses of vaccination exhibited Omicron cross neutralization activity. Not unexpectedly, serum from primary infections with ancestral, BA.1, and BA.2 neutralized the heterologous strain to a much lesser extent than the homologous virus. Sera from BA.1 convalescents neutralized ancestral and Delta to a lesser extent than homologous BA.1, and neutralized BA.2 significantly less. Sera from individuals previously infected with BA.2 did not cross-neutralize any other virus strain tested. Sera from individuals who were vaccinated and then infected by Omicron neutralized BA.1 and BA.2 as efficiently as the ancestral and Delta viruses. The authors conclude that primary infections with BA.1 and BA.2 result in sub-lineage-specific neutralization.

Public Health Measures in Canada

Public Health Measures and Epidemiology in Select Canadian Provinces

A jurisdictional scan of public health measures and epidemiology in other Canadian provinces (i.e., British Columbia (BC), Alberta, Saskatchewan, Manitoba and Quebec) was conducted up to April 14, with these provinces starting to lift public health measures in February 2022.[55-59] Currently, all included provinces have removed capacity limits and proof of vaccination. BC, Manitoba, and Saskatchewan have all lifted their mask mandate. Alberta still requires masks on public transportation and Quebec requires masks in most indoor settings, with some exceptions. On April 21, 2022, Quebec announced that their mask mandate for indoor public settings is extended to mid-May.[60]

Despite case counts being an underestimate due to changes to testing strategies, case rates in all included provinces are higher than at most other points since the pandemic began.[27] Since the beginning of March, COVID-19 hospitalizations have steadily increased in Saskatchewan and Quebec.[61,62] The most recently available data on wastewater surveillance in the examined provinces indicates that wastewater surveillance indicators are increasing in Alberta, BC and Saskatchewan.[63-65]

Implications for Practice

The implications for practice remain largely unchanged from the previous PHO BA.2 Risk Assessment.[3]

- Timely, temporary use of public health measures can be expected to help mitigate COVID-19 transmission at a time when early epidemiological indicators may have plateaued, late indicators continue to rise, and percent positivity remains high. Consideration should be given to the least restrictive 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 population. Groups at higher risk for severe outcomes should be prioritized.[66] While vaccination is a key public health tool, because COVID-19 vaccination and previous SARS-CoV-2 infection do not provide sterilizing immunity, and because VE against infection wanes over time, a COVID-19 strategy that relies entirely on vaccination and previous infection will not contain transmissions in the context of variants that lower vaccine effectiveness (i.e., Omicron sub-lineage BA.2).

    - 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. Options include re-implementing universal indoor masking in public settings, and extending masking directives in high-risk settings (e.g., long-term care).[67,68] During the current BA.2-driven surge, maintaining a cautious approach to isolation and quarantine requirements is another component of a layered approach, which, together with other measures, can help break chains of SARS-CoV-2 transmission.

- Ongoing risk communication to the population regarding high levels of SARS-CoV-2 transmission and COVID-19 disease risk may be helpful, including in the context of collective actions such as community masking.[69,70] 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, and practicing respiratory etiquette and washing hands should continue to be promoted for all.[71] Enhanced and timely access to oral outpatient treatment may mitigate the impact of severe illness on the health care system and the individual.

- 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,[72] 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 given the educational, social and health impacts of cumulative educational disruption for children and families,[73,74] a cautious, temporary approach to re-implementing some 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, masking indoors, avoiding congregation of large unmasked groups, and access to well-fitted, high quality masks can reduce the risk of in-school transmission and disruptions due to staying home when infected or symptomatic.[67,74]

- The evidence that a new SARS-CoV-2 VOC could emerge and alter the course of the pandemic again, continues to grow.[35,75,76] 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 recent identification of BA.3 in Ontario, 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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