EVIDENCE BRIEF

COVID-19 Omicron Variant Sub-lineage BA.2: Risk Assessment, February 23, 2022

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Key Messages

- The Omicron (B.1.1.529) variant of concern (VOC) consists of several sub-lineages (i.e., BA.1, BA.1.1, BA.2, and BA.3). The BA.2 sub-lineage is new and evolving with limited information available.
- As of February 23, 2022, there were 284 cases in Ontario identified as BA.2 via whole genome sequencing. The first BA.2 case was identified on November 28, 2021.
- According to data accessed on February 23, 2022, more than 96,000 BA.2 sub-lineage sequences have been reported globally from 80 countries. Denmark continues to report the majority of BA.2 cases globally, with cases increasing in several other countries, including the United Kingdom and the United States.
- While studies are ongoing to understand the apparent growth advantage BA.2 has compared to BA.1, initial data suggests that BA.2 appears more transmissible than BA.1. However, this difference in transmissibility appears to be much smaller than the difference between BA.1 and Delta.
- The impact of the BA.2 sub-lineage on testing is unknown. Variant surveillance supported by whole genome sequencing can be used to distinguish the BA.2 sub-lineage from other variants.
- The current risk of BA.2 sub-lineage transmission in Ontario is high with a moderate degree of uncertainty. The risk of severe disease in Ontario is moderate, with a moderate degree of uncertainty. The risk of reinfection and breakthrough infection in Ontario is high with a high degree of uncertainty. The risk of impact of the BA.2 sub-lineage on testing in Ontario is moderate, with a moderate degree of uncertainty. The risk of impact on surveillance in Ontario is moderate with a low degree of uncertainty.

Issue and Research Question

The Omicron variant BA.2 sub-lineage, has been identified in 80 countries with highest case counts reported in Denmark.[1] Considering evidence of increased transmissibility of the Omicron variant seen with BA.1 sub-lineage, it is important to closely monitor the potential impact that the BA.2 sub-lineage might have in Ontario. Our two main research questions were:

- What are the key characteristics of the BA.2 variant?
- What are the risks the BA.2 variant poses to Ontarians?

Methods

PHO Library Services conducted daily searches of primary and preprint literature using the MEDLINE database (search strategies available upon request). In addition, PHO performed grey literature searches daily using various news feeds and custom search engines. English-language peer-reviewed and non-peer-reviewed (preprint) records that described Coronavirus Disease 2019 (COVID-19) variants were included.

BA.2 Context in Ontario

As of February 23, 2022, there were 284 cases in Ontario identified as BA.2 via whole genome sequencing. The first BA.2 case in Ontario was identified on November 28, 2021.[2]

- The majority of BA.2 cases were among the following age groups: 20-39 (50.7%), 40-59 (21.5%) and 19 and under (19.7%).[2]
- The public health unit with the highest proportion of BA.2 cases was Peel Public Health (35.6%), followed by Toronto Public Health (22.5%).[2]
- Overall, 53.5% of BA.2 cases were identified through the border testing program led by the Public Health Agency of Canada.[2]
- Among the BA.2 cases that linked to Public Health Case and Contact Management Solution (CCM) (84.2%), the majority occurred in unvaccinated individuals (41.6%), followed by individuals who had completed their vaccination series, i.e. post-series completion (39.9%).[2]

From January 9 to February 5, 2022, there were 5,744 cases sequenced by the Ontario COVID-19 Genomics Network (OCGN) for representative surveillance.[3]

- In the most recent week for which data is available (January 30 to February 5, 2022), BA.1.1 was the most prevalent lineage (70.3%), followed by BA.1 (21.5%). The proportion of cases identified as BA.2 increased from the week of January 23 to 29 (6.4%) to the week of January 30 to February 5 (7.7%).[3]
- Over the past twelve weeks, the growth rate of BA.2 was 1.89 times that of BA.1.1.[3]

Epidemiology

- **Global:** Data accessed on February 23, 2022 reports that 80 countries have uploaded 96,479 BA.2 sub-lineage sequences to GISAID (1% sequenced samples), with the first sequences reported to GISAID on November 17, 2021.[1]
- **Canada:** According to the GISAID initiative database, as of February 6 2022, the BA.2 sub-lineage was found in 725 sequenced cases (1% of sequenced samples).[1]
- **Denmark:** According to the GISAID initiative database, as of February 12, 2022, the BA.2 sub-lineage was found in 45,309 sequenced cases (44% of sequenced samples).[1]
- **India:** According to the GISAID initiative database, the BA.2 sub-lineage was found in 8,051 sequenced cases (30% of sequenced samples).[1] Data from India up to date as of February 15, 2022.

- **Norway:** According to the GISAID initiative database, the BA.2 sub-lineage was found in 799 sequenced cases (2% of sequenced samples). Data from Norway up to date as of February 7, 2022.

- **Philippines**: The Philippines was the first country to submit BA.2 sub-lineage sequences to GISAID; however, its origin is unknown. According to the GISAID initiative database, as of February 4, 2022, the BA.2 sub-lineage was found in 948 sequenced cases (77% of sequenced samples).[1]

- **United Kingdom (UK):** According to the GISAID initiative database, as of February 12, 2022, 21,730 sequenced cases of BA.2 have been identified in the UK (4% cumulative prevalence).[1] The United Kingdom Health Security Agency's (UKHSA) most recent variant of concern and investigation report contains sequencing data complete up to January 31, 2022, at which point 95.4% of sequences were BA.1, 4.1% were BA.2 and 0.5% were other lineages.[4] The UKHSA recognizes S-gene target positive (SGTP) as a reasonable proxy for BA.2. As of February 6, 2022, the overall proportion of SGTP cases in England was 18.7% compared to 5.1% on January 24, 2022.[4]

- **United States (US):** According to sequences collected up to January 29, 2022 by the US Centers for Disease Control and Prevention (CDC), BA.2 has now been detected in more than 30 states and makes up around 3.9% of new infections.[5]

Public Health Measures

All jurisdictions included in PHO's recent public health measures reporting have implemented public health measures in response to the emergence of Omicron.[6] In January 2022, due to reported stabilizing hospitalizations, many jurisdictions eased or lifted public health measures, while at the same time, encouraged vaccination.[6] In February 2022, jurisdictions continued to lift public health measures including outdoor and/or indoor mask mandates,[7-12] capacity and/or gathering limits,[10,13-16] setting-specific closures,[14,17,18] remote work mandates,[10,19,20] and proof of vaccination.[14,15,20] Currently, there is variation in the status of implemented public health measures across jurisdictions. Largely, the remaining public health measures across the jurisdictions focus on high-risk settings rather than broad population-based measures.

Genomic Features

BA.2 differs from BA.1 in its genetic sequence, including some amino acid differences in the spike protein and other proteins.[21] BA.1 differs from BA.2 by 50 amino acids, which is approximately twice as many amino acid differences as the number of differences between four other VOC (Alpha, Beta, Gamma, Delta) and wild-type SARS-CoV-2.

The Omicron sub-variants share 39 mutations (mostly in the spike protein); however, BA.1 has an additional 20 mutations and BA.2 has 27. Further, BA.1 contains 13 unique mutations and BA.2 contains 10.[22,23]

An analysis of 13 BA.2 cases between November 28, 2021 and January 31, 2022 in south-eastern France found that viral genomes displayed a mean (± standard deviation) number of 65.9 ±2.5 (range, 61-69) nucleotide substitutions and 31.0 ±8.3 (27-50) nucleotide deletions, resulting in 49.6 ±2.2 (45-52) amino acid substitutions (including 28 in the spike protein) and 12.4 ±1.1 (12-15) amino acid deletions. Structural predictions pointed out a significant enlargement and flattening of the 21L/BA.2 N-terminal domain surface compared with that of the 21K/BA.2 Omicron variant, which may facilitate initial viral interactions with lipid rafts.[24]

Transmissibility

Studies have shown that BA.2 has a growth advantage over BA.1.[25,26] While studies are ongoing to understand the reasons for this growth advantage, the initial data suggests that BA.2 appears more transmissible than BA.1 (which remains the most common Omicron sub-lineage reported). This difference in transmissibility appears to be much smaller than, for example, the difference between BA.1 and Delta.[21]

A study of secondary attack rates in Danish households from late December 2021 to early January 2022 found an overall secondary attack rate of 39% in BA.2 infected households compared to 29% in BA.1 infected households. When comparing BA.2 relative to BA.1 infected households, there was an increased risk of infection in BA.2 infected households regardless of the vaccination status of the potential secondary case, indicating an inherent increased transmissibility of the BA.2 sub-variant.[27]

As of February 9, 2022, the transmissibility risk of BA.2 was high in the United Kingdom (UK) with a low degree of confidence due to limited available data.[28] As of February 11, 2022, BA.2 had an increased growth rate compared to BA.1 in all regions of England. While growth rates can be overestimates early in the emergence of a variant, the apparent growth advantage is currently substantial.[4]

Preliminary contact tracing analyses in the UK suggest that the average time from symptom onset of a primary case to symptom onset in their identified contacts (the mean serial interval) is approximately half a day shorter for BA.2 (3.27 days) than BA.1 (3.72 days). Both are shorter than the mean serial interval for Delta of 4.09 days. The serial interval suggests the time between primary and secondary infections is shorter, which could contribute to the increased growth rate of BA.2.[4]

Disease Severity

As of February 9, 2022, the UKHSA reported that there were no available systematic analyses comparing the disease severity of BA.1 and BA.2.[28]

An analysis of 95,470 individuals diagnosed with SARS-CoV-2 between December 1, 2021 and January 20, 2022 in South Africa concluded that the odds of severe infection (adjusted odds ratio 0.91, 95% confidence interval 0.68-1.22) and being admitted to hospital (adjusted odds ratio 0.96, 95% confidence interval 0.85-1.09) did not differ between BA.1 and BA.2 infections.[29] Limitations include restriction to samples tested with the TaqPath™ COVID-19 PCR assay which may have biased data geographically.

A hamster trial performed by Yamasomaba et al. demonstrated that BA.2 was more pathogenic than BA.1.[30]

Vaccine Effectiveness

The UKHSA has reported that there is no evidence of difference in vaccine effectiveness between BA.1 and BA.2.[28]

In the UK, vaccine effectiveness of BA.2 was compared against the BA.1, with all vaccine brands combined, by conducting a test-negative case control design.[31] It was noted that the vaccine effectiveness for symptomatic disease was similar for both BA.1 and BA.2. The vaccine effectiveness of two doses at 25+ weeks was 10% and 18% for BA.1 and BA.2, respectively. At two to four weeks following a booster vaccine, the vaccine effectiveness increased to 69% (BA.1) and 74% (BA.2), but decreased to 49% (BA.1) and 46% (BA.2) after 10+ weeks following a booster dose.

In a separate study, neutralizing antibody titres for BA.2 were overall similar to BA.1, however, the BA.2 titres trended to be 1.3-1.4 fold lower. The authors suggested that the BA.2 frequency is more likely due to increased transmissibility than enhance immunologic escape.[25] Yamasomba noted that BA.2 had a reproductive number that was 1.4 fold higher than BA.1.[30]

Re-infection

As of February 11, 2022, there is no detected sequence-confirmed BA.2 reinfection following a BA.1 infection at any interval in England.[4] Denmark conducted a study of more than 1.8 million infections between November 22, 2021 and February 11, 2022 and found that although rare, BA.2 re-infection can occur within 20 to 60 days after a BA.1 infection. Out of 187 re-infections, 47 were BA.2 reinfections that occurred after a BA.1 infection and these affected mainly young unvaccinated people with mild disease who did not require hospitalization.[32]

Diagnostics

Currently only sequencing technology can confirm a BA.2 infection.[22] Variant surveillance supported by whole genome sequencing can be used to distinguish the BA.2 sub-lineage from other variants.

Given the BA.2 sub-lineage does not contain the deletion at S:69-70 it is S-gene target positive (or SGTP) on PCR diagnostic tests. Given that it is SGTP, the SGTF screening method previously used to differentiate the Omicron BA.1 sub-lineage from other SARS-CoV-2 strains (i.e., Delta) cannot be used to rapidly identify the Omicron BA.2 sub-lineage.[4]

The use of rapid antigen tests for BA.2 sub-lineage diagnostic purposes requires a better understanding of the test characteristics when used for BA.2.[33]

Ontario Risk Assessment

The current risk of BA.2 sub-lineage transmissibility in Ontario is high, with a moderate degree of uncertainty. The risk of severe disease in Ontario is moderate, with a moderate degree of uncertainty and at this time is assumed to be the same as the BA.1 sub-lineage. The risk of reinfection and breakthrough infection is high with a high degree of uncertainty in Ontario. Early evidence suggests the risk of reinfection and degree of vaccine effectiveness is similar for BA.1 and BA.2. The risk of impact of the BA.2 sub-lineage on testing is moderate, with a moderate 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).

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

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

Implications for Practice

- Given the recent emergence of BA.2 globally, a cautious approach in assessing its risk in Ontario is warranted.

- Initial data suggests that BA.2 is more transmissible than BA.1, however, current evidence does not suggest a significant difference in disease severity or vaccine effectiveness.

- Although current epidemiological trends[34] for SARS-CoV-2 are favourable (e.g. decreasing test-confirmed case counts, decreasing test-positivity, decreasing COVID-19 related hospitalizations and intensive case unit admissions), current plans in Ontario to lift many existing public health measures in March 2022[35] (e.g., increasing gathering limits, removing proof of vaccination) will require close surveillance and monitoring of BA.2. Close monitoring of epidemiological trends in jurisdictions with BA.2 pre-dominance that have already removed public health measures (e.g. Denmark) will be useful.

- Continued measures such as promoting and offering booster COVID-19 vaccinations and encouraging masking, especially in high-risk settings, are likely to remain important measures to mitigate impacts of this more transmissible Omicron sub-lineage in Ontario.

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