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EVIDENCE BRIEF

Risk Assessment for Omicron Sublineages BQ.1 and BQ.1.1 (as of October 20, 2022)

Published: October 2022

Key Messages

- Based on data from GISAID, in the last six months (April 20 to October 20, 2022), Canada reported 66 sequences of BQ.1 (0.08% of cases) and 82 sequences of BQ.1.1 (0.10% of cases).
- The proportion of BQ.1 cases in Ontario has grown from 1.2% (September 25 to October 1, 2022) to 2.6% (October 2 to October 8, 2022) and is projected to reach 13% (95% CI: 7.6% - 21.0%) by October 26, 2022.
- The proportion of BQ.1.1 cases in Ontario has grown from 0.6% (September 25 to October 1, 2022), to 1.0% (October 2 to October 8, 2022), and is projected to reach 7.5% (95% CI: 2.7%-17.6%) by October 26, 2022.
- While BQ.1 and BQ.1.1 currently comprise a small proportion of all COVID-19 cases globally, in some settings the proportion of cases is rapidly increasing, which suggests increased transmissibility relative to co-circulating variants. Based on the most recent analysis for Ontario, BA.2.75.2 is likely being superseded by BQ.1.1 and other variants. As such, the risk of BA.2.75.2 is lower compared to BQ.1, BQ.1.1 and other lineages at this time.
- The convergence of spike protein mutations found in BQ.1 and BQ.1.1 are concerning and merit ongoing monitoring due to their potential to cause significant immune escape.
- There is limited evidence to inform the risks of BQ.1 and BQ.1.1 with respect to transmissibility, immune evasion, and disease severity. The risk to Ontario is currently highly uncertain.
- Based on limited evidence of immune evasion by BQ.1 and BQ.1.1, and waning immunity following vaccination, public health measures can help to reduce the risk of transmission of SARS-CoV-2 in the fall. Layers of protection in addition to vaccination include: staying home when sick or with symptoms of COVID-19; wearing a well-fitted, high quality mask whenever feasible in crowded or close contact indoor settings (e.g., public transit); optimizing indoor air quality; use of outdoor spaces when weather permits; and hand hygiene.

Issue and Research Question

There are multiple PANGO sublineages associated with the B.1.1.529 (Omicron) variant of concern (VOC), and the main BA.1, BA.2, BA.3, BA.4, and BA.5 sublineages have their own sublineages (e.g., BA.1.1, BA.2.12, BA.2.12.1, BA.2.3, BA. 2.20, BA.2.9, BA.5.1, BQ.1). Considering the possible changes to transmissibility, severity, and/or vaccine efficacy (VE) of these sublineages compared to other VOCs, it is important to monitor the potential impact they might have in Ontario's context.

Based on its mutation profile, BA.5 sublineages (including BQ.1. and BQ.1.1) have been designated Omicron sublineages under monitoring by the World Health Organization (WHO).[1] This evidence brief summarizes available information and evidence on the Omicron sub-lineages BQ.1 (alias of BA.5.3.1.1.1.1.1) and BQ.1.1 (alias of BA.5.3.1.1.1.1.1.1) that emerged since the last Public Health Ontario (PHO) BQ.1 and BQ.1.1 risk assessment, relevant to Ontario.[2,3]

Methods

PHO Library Services has been conducting daily searches of primary and preprint literature on Omicron variants and sublineages 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. PHO performed grey literature searches daily using various news feeds and custom search engines beginning October 19, 2022 and concluding October 20, 2022. English-language peer-reviewed and preprint records that described the Omicron variants BQ.1 and BQ.1.1 were included if identified. Formal critical appraisal of published and preprint COVID-19 literature was out of scope for this PHO risk assessment. This is an update of the evidence brief on variant BQ.1 and BQ.1.1, which examined the literature up to October 5, 2022.[2]

Ontario Risk Assessment

The current risk of BQ.1 and BQ.1.1 with respect to transmissibility, reinfection, and breakthrough infection in Ontario is high with a high degree of uncertainty. The risk of severe disease is unknown with a high degree of uncertainty. The risk of impact on testing is unknown with a high degree of uncertainty. The overall risk assessment may change as new evidence emerges (see Table 1).

Table 1. Risk Assessment for Omicron Sublineages BQ.1 and BQ.1.1

Issues	Risk Level	Degree of Uncertainty
Increased Transmissibility	High	High
Increased Disease Severity	Unknown	High
COVID-19 Reinfection	High	High
Lowered Vaccine Effectiveness Against Infection	High	High
Impact on Testing	Unknown	High

Genomic Features

- BQ.1 is a sublineage of BA.5, and includes sublineages BQ.1.1, BQ.1.2, BQ.1.3 and BQ.1.4.[2] Within the spike (S) protein, BQ.1 and BQ.1.1 contain the mutations K444T, L452R, N460K, and F486V. BQ.1.1 additionally contains the mutation R346T.[4] It is thought that some of these S protein mutational sites are prone to antibody evasion based on previous broad mutational scanning analyses.[5]

- The first BQ.1 and BQ.1.1 sublineage sequences reported in GISAID date from mid-July 2022 in Nigeria, and have since been reported in multiple countries including Nigeria, United Kingdom (UK), Japan, the United States (US), France, Belgium, Denmark, and Italy.[2,6]

Epidemiology

- PHO modelling of BQ.1 and BQ.1.1 growth advantages based on GISAID data from up to nine other countries showed that BQ.1 and BQ.1.1 growth rates in Canada are aligned with those seen internationally.[7]

Canada

- Based on sequences uploaded to GISAID, in Canada, between September 19 and October 19, 2022, there were 47 sequences of BQ.1 (0.65% of cases),[8] and 69 sequences of BQ.1.1 (0.96% of cases).[9] This is an increase from the previous month (August 18 to September 18, 2022) when there were 19 sequences of BQ.1 (0.14% of cases),[10] and 13 sequences of BQ.1.1. (0.09% of cases).[11] In the last six months (April 20 to October 20, 2022), Canada reported 66 sequences of BQ.1 (0.08% of cases) and 82 sequences of BQ.1.1 (0.10% of cases).

- The proportion of BQ.1 cases in Ontario has grown from 1.2% (September 25 to October 1, 2022) to 2.6% (October 2 to October 8) and is projected to reach 13% (95% CI: 7.6%–21.0%) by October 26, 2022. Based on data from July 17 to October 8, 2022, the weekly relative growth rate of BQ.1 is 2.00 (95% CI: 1.76–2.28) times that of BA.5.2.1.[12]

- The share of BQ.1.1 cases was 0.6% (September 25 to October 1, 2022), 1.0% (October 2 to October 8, 2022), and is projected to increase to 7.5% (95%CI: 2.7%-17.6%) by October 26, 2022 in Ontario. Based on data from July 17 to October 8, 2022, the weekly relative growth rate of BQ.1.1 is 2.21 (95% CI: 1.75–2.79) times that of BA.5.2.1.[12]

- Based on the most recent analysis for Ontario, BA.2.75.2 is not projected to reach 5% prevalence at any time in the most recent six week forecast window of PHO's Nowcast modelling, that variant was therefore removed from estimates of relative growth advantage.[13] Modelling estimates indicate BA.2.75.2 is likely being superseded by BQ.1.1 and other variants. As such, the risk of BA.2.75.2 is lower compared to BQ.1, BQ.1.1 and other lineages.

- In Quebec, the proportion of BQ.1 and BQ.1.1 cases based on random sequencing increased across the weeks of September 18 to 24, 2022 (0.3% and 1.0%, respectively), September 25 to October 1, 2022 (1.0% and 1.5%), and October 2 to 8, 2022 (1.8% and 4.4%).[14,15]

France

- Based on sequences uploaded to GISAID, in France, between September 19 and October 19, 2022, there were 70 sequences of BQ.1 (1.31% of cases),[16] and 505 sequences of BQ.1.1 (9.44% of cases).[17] This is an increase in proportion from the previous month (August 18 to September 18, 2022) when there were 15 sequences of BQ.1 (0.17% of cases),[18] and 55 sequences of BQ.1.1. (0.61% of cases).[19]

- PHO modelling of France's samples submitted to GISAID with a collection date since August 1, 2022 estimated BQ.1.1 prevalence to be over 50% in France.[7]

UK

- In the UK, between September 19 and October 19, 2022, there were 246 sequences of BQ.1 (1.95% of cases),[20] and 418 sequences of BQ.1.1 (3.31% of cases).[21] This is an increase in proportion from the previous month (August 18 to September 18, 2022) when there were 52 sequences of BQ.1 (0.38% of cases),[22] and 37 sequences of BQ.1.1. (0.27% of cases).[23]

US

- In the US, during the week of October 9, 2022, 5.7% of cases were BQ.1 and 5.7% of cases were BQ.1.1.[24] Between September 19 and October 19, 2022, there were 328 BQ.1 sequences (1% of cases) and 303 BQ.1.1 sequences (0.93% of cases).[25,26]

Transmissibility and Infectivity

- Studies on BQ.1 and BQ.1.1 transmissibility and infectivity are limited to one pre-print study,[4] previously described in Risk Assessment for Omicron Sublineages BQ.1 and BQ.1.1 (as of Oct 5, 2022).[2]

- Although there is limited information on BQ.1.1, informal analyses note that it appears to be highly transmissible as its relative share of COVID-19 infections has been at least doubling every week from September 4, 2022, 2022 to September 23, 2022, based on limited data from social media reports in North America and Europe, taking only 19 days to grow 8-fold from 5 sequences to 200 sequences.[27] Informal analyses posted by media and on social media estimate BQ.1 to have a growth rate advantage of almost 15% per day as compared to BA.5.2, and a 14% per day compared to BA.2.[28]

- In Canada, BQ.1 and BQ.1.1 are estimated to have daily growth rates of 0.7 (0.06–0.9) and 0.10 (0.08–0.12), respectively according to CovSpectrum.[29,30]

Disease Severity

- No reports on the severity of disease caused by BQ.1 and BQ.1.1 were identified in the evidence search.

COVID-19 Therapeutics

- Information on activity of therapeutic neutralizing antibodies (NAbs) and nirmatrelvir/ritonavir (Paxlovid) against BQ.1 and BQ.1.1 is currently limited. Please refer to Risk Assessment for Omicron Sublineages BQ.1 and BQ.1.1 (as of Oct 5, 2022) for a summary of the available data as no new literature was identified.[2]

Immune Evasion

- Studies on BQ.1 and BQ.1.1 immune evasion are limited to one pre-print study, which was previously described in Risk Assessment for Omicron Sublineages BQ.1 and BQ.1.1 (as of Oct 5, 2022).[2] In summary, Cao et al., reported higher likelihood of BQ.1.1 evading neutralizing antibodies from vaccination (with CoronaVac) and breakthrough Omicron infections, when compared to BA.5.[4]

Testing and Whole Genome Sequencing (WGS) Surveillance

- The impact of BQ.1 and BQ.1.1 on the performance of current antigen and molecular testing methods is currently unknown, but testing has not been known to be significantly impacted by other Omicron sublineages with diverse mutation profiles. No impact is expected on the capability of WGS to detect BQ.1 or BQ.1.1 in the provincial lineage surveillance program as numerous cases have already been identified to date through current testing algorithms.

Implications for Public Health Practice

- The emergence of BQ.1 and BQ.1.1 in Canada and other parts of the world, alongside rapid increases in the proportion of cases attributable to BQ.1 and BQ.1.1, compared to co-circulating variants in some settings, warrant a cautious approach and ongoing monitoring of the risk of these sublineages in Ontario.

- In Ontario, a gradual increase in COVID-19 case numbers and percent positivity has been observed over approximately the past four weeks, with projections made the week of October 2, 2022 suggesting weekly case numbers may continue to gradually rise over the following two weeks.[31] Recent changes in epidemiology may be further impacted by BQ.1 and BQ.1.1 emergence.

- Limited pre-print evidence indicates that BQ.1 and BQ.1.1 may be more immune evasive than earlier variants. Despite an absence of data on BQ.1 and BQ.1.1 disease severity, even if these sublineages are no more severe than BA.5, the increased immune evasiveness and transmissibility potential of BQ.1 and BQ.1.1 may result in a rise in the number of cases, including a potential increase in the absolute number of severe cases if BQ.1 and/or BQ.1.1 were to increase in prevalence in Ontario.

    - Of note, hospitalizations in Quebec show an increasing trend since the end of September 2022,[14,15] and Our World in Data for France depicts low prevalence (but an increasing trend) in COVID-19 mortality, hospitalizations, and ICU admissions over the last several weeks.[32-34] Both of these settings are reported to have among the higher BQ.1 and BQ.1.1 prevalence and growth in their larger jurisdictions i.e., Canada and the EU. The severe cases in these settings have not been attributed to BQ.1 and BQ.1.1, but in the absence of evidence for severity of these variants, settings with increasing BQ.1 and BQ.1.1 prevalence should be closely monitored for severity trends.

- COVID-19 vaccination remains an essential component of the public health response in the current context, with an emphasis on initiation and completion of a primary series in all (especially under-vaccinated) communities, as well as boosters for eligible individuals.[35] Groups at higher risk for severe outcomes should be prioritized.

    - While vaccination is a key public health tool for the pandemic, current COVID-19 vaccines authorized for use in Canada and previous SARS-CoV-2 infection do not provide sterilizing immunity. In addition, vaccine protection against infection is time-limited. Though integral to the COVID-19 response, the limitations of vaccines are more evident in the context of variants that evade vaccine and infection-acquired immunity (e.g., BA.4, BA.5, limited evidence for BQ.1 and BQ.1.1). Related, growing evidence shows variable antibody cross neutralization across SARS-CoV-2 variants after an infection, making it difficult to gauge the level of immunity against reinfection by future variants. The new BA.1 and BA.4/5 bivalent vaccines were only recently implemented in vaccination programs, and their effectiveness against BQ.1 and BQ.1.1 (a sublineage of BA.5) is still unknown. Therefore, a COVID-19 pandemic strategy that relies entirely on immunity from current vaccines and past infection will be limited in its ability to affect transmission. Continuous WGS surveillance, monitoring of the impacts of implementation/removal of public health measures, and efforts to increase vaccine equity can all help prepare Ontario for the next stages of the COVID-19 pandemic.

- With the transition to colder weather, return to more indoor settings including offices and schools, public health measures can be effective to reduce the risk of SARS-CoV-2 transmission and consideration should be given to the least restrictive and most equitable measures. Layers of protections in addition to vaccination include: staying home when sick or with symptoms of COVID-19; wearing a well-fitted, high quality mask whenever feasible in crowded or close contact indoor settings (e.g., public transit); optimizing indoor air quality; use of outdoor spaces when weather permits; and hand hygiene.

- Clear risk communication to Ontarians regarding current levels of SARS-CoV-2 transmission and COVID-19 disease risk, risk factors for severe disease, protective effects of infection-acquired and vaccine-acquired immunity, and the risks associated with post-acute COVID-19 syndrome,[36-39] will be important, especially in the context of third-dose COVID-19 vaccine uptake.

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Citation

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