

EVIDENCE BRIEF

Risk Assessment for Omicron Sub-Lineage BF.7 (as of October 11, 2022)

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Key Messages

- The variant BF.7 was first detected May 13, 2022 in Belgium.
- The convergence of spike protein mutations found in BF.7 are of concern, due to their ability to escape neutralizing antibody therapeutics.
- As of October 4, 2022, there were 385 BF.7 sequenced cases identified in Canada, with 91 from Ontario. In Ontario, the number and proportion of BF.7 cases increased from 26 (1.2%) the week of September 11, 2022, to 60 (2.7%) the week of September 18, 2022.
- In Ontario, BF.7 has a weekly growth rate that is 41% (95% CI: 33% - 51%) greater than BA.5.2.1, the current dominant lineage, and is projected to make up 5.7% (4.0% - 8.1%) of all cases by October 12, 2022.

Issue and Research Question

BF.7 (alias for BA.5.2.1.7) is a sub-lineage of Omicron BA.5.2.1. It was first reported in Belgium on May 13, 2022.¹ From mid-April to mid-July 2022, BF.7 was estimated to have a weekly growth advantage of 46% (95% confidence interval [CI]: 22%–69%) compared to BA.5.2.1 in Europe, and a weekly growth advantage of 58% (95% CI: 32%–84%) compared to BA.5.²

This evidence brief summarizes available information and evidence on the Omicron variant sub-lineage BF.7 relevant to the risk in Ontario.

Methods

Public Health Ontario (PHO) Library Services has been conducting daily searches of primary and preprint literature on Omicron variants and sub-lineages 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 risk assessment. PHO performed grey literature searches daily using various news feeds and custom search engines ending October 7, 2022. English-language peer-reviewed and preprint records that described the Omicron subvariant BF.7 were included.

Ontario Risk Assessment

There are insufficient data on the severity and immune evasion of the Omicron sub-lineage BF.7 to assess its risk to Ontario. The overall risk assessment may change as new evidence emerges (see [Table 1](#)).

Table 1. Risk Assessment for Omicron Subvariant BF.7

Issues	Risk Level	Degree of Uncertainty
Increased Transmissibility	Moderate	High
Increased Disease Severity	Unknown	High
Reduced Effectiveness of COVID-19 Therapeutics	Unknown	High
COVID-19 Reinfection	Unknown	High
Vaccine Effectiveness to Prevent Breakthrough Infection	Unknown	High
Impact on Testing and WGS* Surveillance	Low	Low

*Whole genome sequencing, WGS

Genomic Features

- BF.7 is a sub-lineage of BA.5.2.1 with a mutation at amino acid R346T on the spike protein. R346T may contribute to reduced sensitivity to monoclonal antibodies, increased binding to angiotensin converting enzyme-2 (ACE2) receptor, and increased expression of the receptor-binding domain (RBD).²⁻⁴

Epidemiology

As of October 4, 2022, 9,809 sequences of the BF.7 sub-lineage have been reported globally.⁵ Available data show that BF.7 is most prevalent in Europe.

Europe and the United Kingdom (UK)

The number of BF.7 sequences (% of all sequences sampled) are reported below for select jurisdictions.

- Belgium: From September 12, 2022 to October 5, 2022 there were 450 BF.7 sequences (23.1%). This is an increase in the proportion of BF.7 sequences from the previous month when there were 538 BF.7 sequences (14.67%).⁶
- The Netherlands: From September 12, 2022 to October 5, 2022 there were 99 BF.7 sequences (11.38%). This is an increase in the proportion of BF.7 sequences from the previous month when there were 300 BF.7 sequences (7.5%).⁷
- Germany: From September 12, 2022 to October 5, 2022, there were 501 BF.7 sequences (7.25%). This is an increase in the proportion of BF.7 sequences from the previous month, when there were 834 BF.7 sequences (3.95%).⁸

- France: From September 9, 2022 to October 5, 2022, there were 319 BF.7 sequences (10.17%). This is an increase in the proportion of BF.7 sequences from the previous month, when there were 673 BF.7 sequences (5.92%).⁹
- United Kingdom (UK): From September 9, 2022 to October 5, 2022, there were 326 BF.7 sequences (4.82%). This is an increase in the proportion of BF.7 sequences from the previous month, when there were 367 BF.7 sequences (2.47%).
- Denmark: From September 25, 2022 to October 1, 2022, there were 317 BF.7 sequences (15.83%).¹⁰ This is an increase in proportion of BF.7 sequences from three weeks earlier, when there were 208 BF.7 sequences (5.84%).

Asia and Australia

- Between April 11, 2022, and October 5, 2022, the BF.7 sequences and proportions were as follows:
 - Japan: From September 9, 2022 to October 5, 2022 there were 16 BF.7 sequences (0.50%). This is an increase in the proportion of BF.7 sequences from the previous month (54 sequences [0.20%]).¹¹
 - Singapore: In the past month, there were 3 BF.7 sequences (0.35%). This is an increase in the proportion of BF.7 sequences from the previous month (6 sequences [0.25%]).¹²
 - Australia: From September 9, 2022 to October 5, 2022, there were 29 BF.7 sequences (1.12%). This is an increase from the previous month (50 sequences [0.48%]).¹³

Canada

- From 150 total BF.7 sequenced cases (3.13% of overall sequenced cases) in Canada from September 12, 2022 to October 5, 2022, 54 were from Ontario (2.14%), followed by 50 from New Brunswick (8.68%) and 42 from Quebec (3.01%). This is an increase in the proportion of BF.7 cases from the previous month, August 11, 2022, to September 11, 2022, when there were 187 total sequences (1.29%), where 28 were from Ontario (0.59%), 50 were from New Brunswick (6.85%), and 53 were from Quebec (2.16%).¹⁴
- In Ontario, the number and proportion of BF.7 cases increased from 26 (1.2%) the week of September 11 to 17, 2022, to 60 (2.7%) the week of September 18 to 24, 2022.¹⁵
- From July 3 to October 15, 2022, the growth rate of BF.7 in Ontario, relative to BA.5.2.1 was 1.41 (1.33 - 1.51).¹⁵

United States (US)

- From September 12, 2022 to October 5, 2022, there were 467 BF.7 sequences (1.67%). This is an increase from the previous month of August 11, 2022 to September 11, 2022, when there were 725 sequences (0.63%)¹⁶

- Nowcast modelling projects BF.7 to account for 4.6% (95% Prediction Interval [PI] 3.9-5.4), of the circulating variants in the US for the week of October 2 to 8, 2022,¹⁷ with regional prevalence ranging from 2.6% (95% PI: 1.0%–6.0%) in Colorado, Montana, North Dakota, South Dakota, Utah and Wyoming; to 5.7% (95% PI: 4.4%–7.4%) in Alaska, Idaho, Oregon and Washington, and 5.7% (95% PI: 3.7%–8.7%) in Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island and Vermont.

Transmissibility and Infectivity

The rising prevalence and mutational profile of BF.7 are raising concern over the potential for this variant to be more transmissible and more evasive to immunity acquired from vaccination and/or prior COVID-19 infection.

- Modelling using 350 sequences of the BF.7 sub-lineage collected in England from January 1 to September 25, 2022 estimated a weekly growth advantage of 17.95% (95% CI: 16.58%–19.44%) compared to BA.5.⁵

Disease Severity

- No epidemiological reports on the severity of disease caused by BF.7 were identified for inclusion in this report.

Immunogenicity

- Jian et al., examined evasion of humoral immunity by measuring neutralizing titers against SARS-CoV-2 BA.4/BA.5 mutations, including BF.7, in China. Plasma samples from individuals who received three doses of CoronaVac (the CoronaVac vaccine is currently not used in Canada), without history of infection, showed a 1.5 to 1.7-fold decrease in 50% neutralization titers (NT50) against R346T mutation (BA.4.6 and BF.7), relative to the NT50 against BA.4/BA.5.¹⁸
- The impact of the new bivalent booster vaccines on BF.7 sub-lineages is uncertain due to a lack of data and uncertain population uptake of the new bivalent booster.
- The UK Health Security Agency’s variant of concern (VOC) technical briefing assessed BF.7 to be among the most concerning variants in terms of both growth and neutralization present based on UK data, along with BQ.X and BA.2.75.2.⁵

COVID-19 Therapeutics

- Therapeutic neutralizing antibodies (NAbs) are one tool for reducing the severity of SARS-CoV-2 infection. Preliminary data indicates reduced potency of tixagevimab and cilgavimab combined (Evusheld) against lineages with R346T substitutions such as BF.7.^{19,20} Jian et al., evaluated pseudovirus-neutralizing activities of approved neutralizing antibody drugs against the R346-mutated BA.4/BA.5 sub-lineages, including BF.7 and found that cilgavimab was completely escaped by BA.4/BA.5 with R346I/T/S, resulting in the complete loss of efficacy of Evusheld against sub-lineages with these mutations. The neutralizing activity of casirivimab-imdevimab (REGEN-COV) was also reduced due to the decreased reactivity of imdevimab against R346-mutated sub-lineages. The potency of sotrovimab was further reduced, however, bebtelovimab remained highly potent.¹⁸

- Nirmatrelvir/ritonavir (Paxlovid) is an oral antiviral drug used to treat mild-to-moderate COVID-19 in individuals at high risk for progression to severe disease. Nirmatrelvir is a novel protease inhibitor that binds to the main viral protease (M^{pro}) of SARS-CoV-2 to inhibit virus replication.²¹ Preliminary data indicates retained activity against BA.5 for Paxlovid.^{20,22} No literature reporting reduced activity of nirmatrelvir/ritonavir against BF.7 was identified.
- Remdesivir (Veklury) is an intravenous antiviral drug used to treat COVID-19 in hospitalized patients with moderate COVID-19 and in non-hospitalized individuals at high risk of progression to severe disease. Remdesivir is an adenosine nucleotide prodrug that inhibits viral RNA synthesis.²³ Preliminary data indicates retained activity against BA.5 for remdesivir.^{20,22} No literature reporting reduced activity of remdesivir against BF.7 was identified.

Impact on Testing and WGS Surveillance

- Antigen testing: There is limited literature on the performance of rapid antigen tests (RATs) with VOCs; however, the majority of VOC mutations occur in the spike protein and RATs used in Ontario target the nucleocapsid protein. Therefore, we expect there to be limited impact on RAT performance for BF.7 although confirmatory studies are needed.
- Molecular testing: No impact is expected on the capability of molecular tests to detect BF.7.
- WGS surveillance: No or little impact is expected on the capability of WGS to detect BF.7.

Implications for Public Health Practice

- Early and limited evidence indicates a growth advantage for BF.7 over other circulating Omicron subvariants. The emergence of BF.7 in Ontario warrants a cautious approach and ongoing monitoring of its risk in Ontario.
- Based on evidence from previous SARS-CoV-2 variants, while current COVID-19 vaccines and previous SARS-CoV-2 infection provide protection against severe disease, they do not provide 100% sterilizing immunity (i.e., full protection from infection or reinfection) or completely prevent onward transmission.²⁴ If BF.7 has increased transmissibility compared to the most frequently detected sub-lineages at present, this could lead to a risk of increased COVID-19 cases during the fall, test positivity, and province-wide wastewater signals.

References

1. SARS-CoV-2 Lineages. Lineage BF.7 [Internet]. UK: SARS-CoV-2 Lineages; 2022 [cited 2022 Oct 11]. Available from: <https://cov-lineages.org/lineage.html?lineage=BF.7>
2. Hisner R. Proposal for a sublineage of BA.5.2.1 with S:R346T and N:S33F (originally proposed by @FedeGueli) #827 [Internet]. GitHub; 2022 Jul 7 [cited 2022 Oct 6]. Available from: <https://github.com/cov-lineages/pango-designation/issues/827>
3. Cao Y, Jian F, Wang J, Yu Y, Song W, Yisimayi A, et al. Imprinted SARS-CoV-2 humoral immunity induces converging Omicron RBD evolution. bioRxiv 507787 [Preprint]. 2022 Sep 23 [cited 2022 Oct 05]. Available from: <https://doi.org/10.1101/2022.09.15.507787>
4. Liu Z, VanBlargan LA, Bloyet L-M, Rothlauf PW, Chen RE, Stumpf S, et al. Landscape analysis of escape variants identifies SARS-CoV-2 spike mutations that attenuate monoclonal and serum antibody neutralization. bioRxiv 372037 [Preprint]. 2021. Available from: <https://doi.org/10.1101/2020.11.06.372037>
5. UK Health Security Agency. SARS-CoV-2 variants of concern and variants under investigation in England: technical briefing 46 [Internet]. London: Crown Copyright; 2022 [cited 2022 Oct 7]. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1109820/Technical-Briefing-46.pdf.
6. CovSPECTRUM. BF.7 (Nextclade) Belgium [Internet]. GISAID; 2022 [cited 2022 Oct 13]. Available from: <https://cov-spectrum.org/explore/Belgium/AllSamples/from=2022-08-09&to=2022-09-09/variants?nextcladePangoLineage=bf.7&>
7. CovSPECTRUM. BF.7 (Nextclade) Netherlands [Internet]. GISAID; 2022 [cited 2022 Oct 11]. Available from: <https://cov-spectrum.org/explore/Netherlands/AllSamples/Past6M/variants?nextcladePangoLineage=bf.7&>
8. CovSPECTRUM. BF.7 (Nextclade) Germany [Internet]. GISAID; 2022 [cited 2022 Oct 11]. Available from: <https://cov-spectrum.org/explore/Germany/AllSamples/Past6M/variants?nextcladePangoLineage=bf.7&>
9. CovSPECTRUM. BF.7 (Nextclade) France [Internet]. GISAID; 2022 [cited 2022 oct 11]. Available from: <https://cov-spectrum.org/explore/France/AllSamples/Past6M/variants?nextcladePangoLineage=bf.7&>
10. Statens Serum Institut. Weekly trends: COVID-19 and others respiratory infections [Internet]. Copenhagen: Statens Serum Institut; 2022 [cited 2022 Oct 13]. Available from: <https://files.ssi.dk/covid19/tendensrapport/rapport/ugentlige-tendenser-covid19-andre-luftvejs-uge40-2022-gi85>
11. CovSPECTRUM. BF.7 (Nextclade) Japan [Internet]. GISAID; 2022 [cited 2022 Oct 13]. Available from: <https://cov-spectrum.org/explore/Japan/AllSamples/Past6M/variants?nextcladePangoLineage=bf.7&>

12. CovSPECTRUM. BF.7 (Nextclade) Singapore [Internet]. GISAID; 2022 [cited 2022 Oct 11]. Available from: <https://cov-spectrum.org/explore/Singapore/AllSamples/Past6M/variants?nextcladePangoLineage=bf.7&>
13. CovSPECTRUM. BF.7 (Nextclade) Australia [Internet]. GISAID; 2022 [cited 2022 Oct 11]. Available from: <https://cov-spectrum.org/explore/Australia/AllSamples/Past6M/variants?nextcladePangoLineage=bf.7&>
14. CovSPECTRUM. BF.7 (Nextclade) Canada [Internet]. GISAID; 2022 [cited 2022 Oct 06]. Available from: <https://cov-spectrum.org/explore/Canada/AllSamples/Past6M/variants?nextcladePangoLineage=bf.7&>
15. Ontario Agency for Health Protection and Promotion (Public Health Ontario). Epidemiologic summary: SARS-CoV-2 whole genome sequencing in Ontario, October 7, 2022 [Internet]. Toronto, ON: King's Printer for Ontario; 2022 [cited 2022 Oct 13]. Available from: https://www.publichealthontario.ca/-/media/Documents/nCoV/epi/covid-19-sars-cov2-whole-genome-sequencing-epi-summary.pdf?sc_lang=en
16. CovSPECTRUM. BF.7 (Nextclade) United States [Internet]. GISAID; 2022 [cited 2022 Oct 11]. Available from: <https://cov-spectrum.org/explore/United%20States/AllSamples/Past6M/variants?nextcladePangoLineage=bf.7&>
17. Centers for Disease Control and Prevention. Variant proportions [Internet]. Atlanta, GA: Centers for Disease Control and Prevention; 2022 [cited 2022 Oct 11]. Available from: <https://covid.cdc.gov/covid-data-tracker/#variant-proportions>
18. Jian F, Yu Y, Song W, Yisimayi A, Yu L, Gao Y, et al. Further humoral immunity evasion of emerging SARS-CoV-2 BA.4 and BA.5 subvariants. bioRxiv 503384 [Preprint]. 2022 Aug 10 [cited 2022 Oct 11]. Available from: <https://doi.org/10.1101/2022.08.09.503384>
19. Wang Q, Li Z, Ho J, Guo Y, Yeh AY, Liu M, et al. Resistance of SARS-CoV-2 Omicron subvariant BA.4.6 to antibody neutralization. bioRxiv 506628 [Preprint]. 2022 Sep 06 [cited 2022 Oct 13]. Available from: <https://doi.org/10.1101/2022.09.05.506628>
20. Wollins D. CDC/IDSA clinician call [Internet]. Infectious Diseases Society of America; 2022 [cited 2022 Oct 13]. Available from: <https://www.idsociety.org/globalassets/idsa/multimedia/clinician-call-slides--qa/9-24-22-clinician-call.pdf>
21. Pfizer Canada ULC; Health Canada. Product monograph including patient medication information: PAXLOVID (Submission Control Number: 261884) [Internet]. Ottawa, ON: Government of Canada; 2022 [cited 2022 Oct 7]. Available from: <https://covid-vaccine.canada.ca/info/pdf/paxlovid-pm-en.pdf>.
22. Takashita E, Yamayoshi S, Simon V, van Bakel H, Sordillo EM, Pekosz A, et al. Efficacy of antibodies and antiviral drugs against Omicron BA.2.12.1, BA.4, and BA.5 subvariants. N Eng J Med. 2022;387(5):468-70. Available from: <https://doi.org/10.1056/NEJMc2207519>
23. Gilead Sciences Canada. Product monograph including patient medication information [Internet]. Mississauga, ON: Gilead Sciences Canada; 2020 [revised 2022 Apr 22; cited 2022 Oct 13]. Available from: <https://covid-vaccine.canada.ca/info/pdf/veklury-pm1-en.pdf>

24. Centers for Disease Control and Prevention. Science brief: SARS-CoV-2 infection-induced and vaccine-induced immunity [Internet]. Atlanta, GA: Centers for Disease Control and Prevention; 2022 [cited 2022 Oct 07]. Available from: <https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/vaccine-induced-immunity.html>

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