Risk Assessment for Omicron Sub-Lineage CH.1.1 (February 1, 2023)

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Key Messages

- CH.1.1 (BA.2.75.3.4.1.1.1.1 and also given the name "Orthrus") is derived from BM.4.1.1 (and consequently BA.2.75) and is defined by the L452R mutation in the S protein.

- CH.1.1 was first detected in Southeast Asia in November 2022 and received variant status on December 19, 2022.

- The number of cases of CH.1.1 in Ontario remains low but increased from 58 cases across January 1, 2021 to December 24, 2022, to 209 cases from December 25, 2022 to January 21, 2023.

- According to one pre-print study, CH.1.1 has more immune evasion ability compared to XBB, XBB.1, and XBB.1.5.

- It is unknown whether the severity of disease caused by CH.1.1 differs from previous SARS-CoV-2 variants.

Issue and Research Question

CH.1.1 was first detected in Southeast Asia in November 2022[1] and received variant status December 19, 2022 by the United Kingdom Health Security Agency (UKHSA).[2] This evidence brief summarizes available information and evidence on the Omicron sub-lineage CH.1.1 as of February 1, 2023 that is relevant to 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 between January 23, 2023 and February 1, 2023. English-language peer-reviewed and preprint records that described the Omicron subvariant CH.1.1 were included.

Ontario Risk Assessment

The current risk of CH.1.1 with respect to transmissibility is moderate with a high degree of uncertainty. Vaccine effectiveness to prevent breakthrough infection, COVID-19 reinfection, and increased disease severity is unknown with a high degree of uncertainty. Impact on testing and Whole Genome Sequencing (WGS) surveillance is low 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 Sub-lineage CH.1.1

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

*WGS: Whole genome sequencing

Genomic Features

CH.1.1 (BA.2.75.3.4.1.1.1.1, also given the name "Orthrus")[3] is derived from BM.4.1.1 (and consequently BA.2.75) and is defined by the L452R mutation in the S protein (S:L452R).[4] The S:L452R and K444T/M mutations are potentially associated with immune evasion.[1,5] CH.1.1 contains a D1199N reversion mutation, which is associated with diminished fusogenicity.[1]

Epidemiology

The epidemiology section provides information on variant severity. 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. Therefore, trends may change and may not be fully representative of the most up-to-date situation or other local contextual factors. The severe cases i.e., hospitalizations, in the settings described below have not been attributed to CH.1.1 either due to lack of genomic information or due to CH.1.1 still comprising less than half of cases based on surveillance, but in the absence of evidence for severity of CH.1.1 settings with increasing CH.1.1 prevalence can be closely monitored for severity trends. Differences in vaccine programmes, history of infection, use of public health measures, and other contextual considerations will limit the generalizability of variant epidemiological trends to the Ontario context.

Global

For the week ending January 14, 2023, 1,672 sequences of the CH.1.1 sub-lineage have been reported globally. According to GISAID data, the countries reporting the most CH.1.1 sequences are the United Kingdom (33.0% of CH.1.1 sequences reported to CovSPECTRUM), United States (10.0%), Denmark (8.0%), New Zealand (6.0%), and Japan (6.0%).[4]

Canada

According to GISAID data, the estimated proportion of COVID-19 cases in Canada that are CH.1.1 increased from 0.52% (December 6, 2022, to January 6, 2023)[6] to 1.51% (January 6 to February 6, 2022).[7]

The number of cases of CH.1.1 in Ontario increased from 58 (January 1, 2021 to December 24, 2022) to 209 (December 25, 2022 to January 21, 2023).

United States (US)

In the US, the estimated proportion of CH.1.1 among circulating variants the week of January 29 to February 4, 2023 was 1.6% (95% Prediction Interval [PI]: 1.2–2.0%).[8] This remains unchanged from four weeks prior (January 8 to 14, 2022), when it was 1.6% (95% PI: 1.3–2.1%).[9] During the week of January 29 to February 4, 2023, across the US Health and Human Services (HHS) Regions, Region 5 (Illinois, Indiana, Michigan, Minnesota, Ohio, and Wisconsin) had the highest proportion of CH.1.1 with an estimated proportion of 3.1% (95% PI: 2.1–4.4%),[10] an increase from four weeks prior (January 8 to 14, 2023) when it was 1.9% (95% PI: 0.8–3.7%).[11]

United Kingdom (UK)

According to GISAID data, the estimated proportion of COVID-19 cases in the UK that are CH.1.1 increased from 9.37% (December 6, 2022, to January 6, 2023)[12] to 14.72% (January 6 to February 6, 2022).[13] CH.1.1 has demonstrated a 21.56% (95% credible interval (CrI): 19.25 to 23.97) relative growth rate advantage over BQ.1.1.[2]

Despite an increasing proportion of cases attributable to CH1.1, overall hospital admission rates for COVID-19 have been decreasing in the UK. Between January 16 to 22, 2023, COVID-19 hospital admission rates were 5.97 per 100,000 people a decrease from 6.59 per 100,000 people for January 9 to 15, 2023.[14]

Asia

In Hong Kong, GISAID data shows that the estimated proportion of COVID-19 cases that are CH.1.1 has increased from 24.23% overall proportion (63 sequences) from December 6, 2022 to January 6, 2023,[15] to 34.09% overall proportion (15 sequences) from January 6 to February 6, 2023.[16]

Transmissibility and Infectivity

CH.1.1 has been noted to bind well to angiotensin-converting enzyme 2 (ACE2) receptors.[1] Qu et al. (2023), used lentiviruses pseudotyped with different subvariant S proteins and reported that similar to most other Omicron subvariants, CH.1.1 exhibited reduced infectivity in CaLu-3 cells (lung epithelial cell line), with a titer 2.5 times ($p < 0.05$) that of ancestral D614G.[1] Analysis of S protein biological function revealed that similar to BQ.1.1 and BA.2.75.2, the subvariant CH.1.1 exhibited enhanced fusogenicity (fusing with the surface of the host cell) compared to BA.4/5. The authors reported no obvious differences in S processing for CH.1.1 as compared to their parental BA.2.75.2 subvariant.

Disease Severity

There was no specific data for CH.1.1 on disease severity at the time of the literature search.

Immunogenicity

According to one pre-print, CH.1.1 is more immune-evasive compared to XBB, XBB.1, and XBB.1.5.[1] Qu et al. (2023), investigated the sensitivity of CH.1.1 to neutralizing antibodies from bivalent and monovalent mRNA COVID-19 vaccine recipients in the US, as well as from individuals with a previous infection with BA.4/5.[1] In the bivalent vaccinated cohort (n=14), the nAb titers against CH.1.1 were 16.7-fold lower than titers against BA.4/5. In the three-dose monovalent cohort (n=15), the nAb titers against CH.1.1 were 24.6-fold lower than titers against BA.4/5. Neutralizing antibody titers against CH.1.1 were 3.0-fold lower in the cohort with previous BA.4/5 infections (n=20), compared to BA.4/5 titers. The authors conclude that escape by subvariant CH.1.1 is still prominent after administration of a bivalent booster. Qu et al. state that CH.1.1 has a stronger neutralization resistance than XBB, XBB.1 and XBB.1.5, which warrants continued monitoring.

Impact on Testing and Whole Genome Sequencing

- 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 CH.1.1 although confirmatory studies are needed.

- Molecular testing: Little to no impact is expected on the capability of molecular tests to detect CH.1.1.

- WGS surveillance: Little to no impact is expected on the capability of WGS to detect CH.1.1 as several instances have already been detected in Ontario.

Implications for Practice

- It remains unclear how increased CH.1.1 prevalence might impact overall COVID-19 epidemiological trends.[17]

- COVID-19 severity trends in jurisdictions with a high prevalence of CH.1.1 should be monitored closely to help assess risk of severe cases associated with CH.1.1 variants in Ontario.

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