

EVIDENCE BRIEF

COVID-19 Omicron Variant Recombinant
Lineage: XE

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Key Messages

- The XE lineage is one of eight recombinant lineages of the BA.1 and BA.2 Omicron variant of concern sub-lineages.
- First detected in the United Kingdom (UK) on January 19, 2022, 1,365 XE sequences have been reported in the UK as of April 18, 2022 (<1% of all sequenced COVID-19 cases).
- Media report 6 XE cases in Canada as of April 20, 2022. No XE cases have been identified in Ontario based on preliminary analysis of recent COVID-19 cases.
- Preliminary data from community testing in the UK suggest that XE had a higher growth rate by 12.6% compared to BA.2.
- The risk of XE transmission in Ontario is moderate. The overall risk assessment may change as new evidence emerges.

Issue and Research Question

- Recombination of viral genetic material can occur when different viral strains infect the same host and large sections of the genome in one strain recombine with that of the other strain(s), yielding a new strain.¹ While recombination is common and expected among coronaviruses,² the high rates of ongoing global transmission of the Omicron variant of concern have raised potential for emerging variants (including recombinants) that can impact vaccine effectiveness and further alter SARS-CoV-2 transmissibility and severity.¹
 - Eight recombinants of BA.1 and BA.2 have been reported as of April 18, 2022:³
 - XE, XL, XN (UK lineages). XE is the most frequently reported recombinant lineage of BA.1/BA.2 with evidence of transmission in the community.⁴
 - XG, XH (Denmark lineages)
 - XJ (Finland lineage)
 - XK (Belgium lineage)
 - XT (South Africa lineage)

- This evidence brief summarizes available information and evidence on the Omicron recombinant lineage XE relevant to the risk of transmission in Ontario.

Methods

From January 17, 2021 to April 20, 2022, Public Health Ontario (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 news feeds in the Shared Library Services Partnership. English-language peer-reviewed and non-peer-reviewed (preprint) records that described COVID-19 variants were included.

Main Findings

Genomic Features

- The XE recombinant lineage is mostly BA.2 mutations with mutations from BA.1 for nonstructural proteins 1-6, as well as three mutations that are not seen in all BA.1 or BA.2.⁴ It includes 62 nucleotide substitutions and 48 amino acid substitutions (28 of which are in the S protein).⁵

Epidemiology

- As of April 18, 2022, 1,365 XE sequences have been reported to GISAID from at least 13 countries, including the United Kingdom (1,322 sequences); the United States (15 sequences); Israel (7 sequences); Germany (5 sequences); Denmark (4 sequences); Ireland and Switzerland (3 sequences each); Australia, Belgium, Brazil, France, India and Sweden (1 sequence each).⁶
- In addition, media have reported 6 cases in Canada;⁷ <5 cases in Northern Ireland;⁸ 2 cases in South Korea;⁹ and 1 case in Thailand,¹⁰ Japan¹¹ and New South Wales¹² each as of April 20, 2022.
- The actual prevalence of the XE recombinant lineage is unknown, as COVID-19 testing strategies and capacities vary across jurisdictions, with some countries progressively reducing the overall number of tests performed.²
- XE was classified on April 6, 2022 as a variant in the UK based on evidence of community transmission and possible higher growth rate compared to BA.2 sub-lineage.¹³

Transmissibility

- Using COVID-19 community testing in the UK and adjusted for geographic and temporal variations, the median growth rates of XE compared to that of the BA.2 sub-lineage were estimated by logistic regression as:¹³
 - 12.6% higher (between January 15 and March 30, 2022).
 - 20.9% higher (limiting the data to the three weeks prior to March 30, 2022).
- Variable growth rates have been seen across regions in the UK, and epidemiological confounders (e.g., founder effects, sampling strategies) could not be ruled out.¹³ Further data are needed to determine the transmissibility of XE compared to BA.2.

Severity, Immune Evasion

- There is insufficient evidence to inform how infections by the XE recombinant lineage may differ from those by the BA.2 sub-lineage in clinical severity and ability to evade immunity from natural infection and/or vaccination.

Ontario Risk Assessment

- PHO is in the process of evaluating changes to the program used to identify variants that has recently been updated to include the "X" recombinants. During the course of this evaluation, PHO Laboratory have run all of PHO's recent sequences and none have been identified as XE to date. There is still considerable uncertainty around the tool's ability to identify these "X" recombinants, and PHO Laboratory have not yet moved to implement the new version for the entire Ontario COVID-19 Genomics Network. Once implemented, all previously identified sequences will be run on this new version and an update on any XE variant will be provided.
- The current risk of the XE recombinant lineage transmission in Ontario is moderate with a high degree of uncertainty. The prevalence of XE can rise with outbreaks of high case numbers due to pockets of the population with suboptimal vaccine (and booster) coverage, waning immunity, and the ability of the Omicron variant of concern to escape immunity from natural infection and/or vaccination. The overall risk assessment may change as evidence emerges (see [Table 1](#)).

Table 1. Risk Assessment for Omicron Recombinant Lineage XE

Issue	Risk Level	Degree of Uncertainty
Importation in Ontario	High	High
Increased Transmissibility	Insufficient information	High
Disease Severity	No information	High
COVID-19 Re-infection	No information	High
Lowered Vaccine Effectiveness/Breakthrough Infections	No information	High
Impacts on Testing/Surveillance	Insufficient information	High

Implications for Public Health Practice

- The risk of mutation occurrence increases with ongoing transmission, and the risk of new recombinants emerging is very high given the high transmissibility and immune evasion of the currently dominant Omicron variant, the current high levels of Omicron transmission in the province, and the lifting of public health restrictions across Canada (and globally).
- To mitigate the emergence and spread of new variants (including recombinants), a combination of public health and personal efforts are important to reduce the ongoing transmission of SARS-CoV-2 and to identify new variants when they arise, including:
 - Implementation of proactive screening and genomic sequencing for prompt identification of new variants that facilitates timely public health interventions to reduce their local introduction and spread.
 - Achieving high, equitable vaccination coverage globally as quickly as possible.
 - Staying home when sick.
 - Wearing a well-fitting mask in indoor public settings.
 - Maintaining good ventilation in indoor spaces.

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