

## REPORT

# COVID-19 Variant of Concern Omicron (B.1.1.529): Risk Assessment

Published: November 29, 2021

## Key Findings

- Lineage B.1.1.529 of the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) was designated a variant of concern (VOC), Omicron, by the World Health Organization (WHO) on November 26, 2021.<sup>1</sup>
- The detection of Omicron in South Africa coincided with rapid increases in COVID-19 incidence and positivity rates there,<sup>2,3</sup> where only 24% of its eligible population is fully vaccinated.<sup>4</sup>
- Omicron carries the highest number of novel mutations compared to other VOCs.<sup>5</sup> The significance of these mutations is not yet clear,<sup>6</sup> however, some of the mutations have been associated with immune escape, transmissibility, and susceptibility to treatment.<sup>7</sup>
- As of November 28, 2021, two cases of Omicron had been detected in Ontario and no others in Canada.<sup>8</sup> At this point in time, the risk of Omicron importation in Ontario is high and the risks of further transmission, severe disease, reinfection, and breakthrough infection in Ontario is moderate with a high degree of uncertainty. The overall risk assessment may change as new evidence emerges.

## Request and Scope

- To summarize available information and evidence on the Omicron VOC relevant to the risk of importation and transmission in Ontario.

## Background

- The first known confirmed Omicron positive specimen globally was collected on November 9, 2021, although it is not yet known if the variant has been circulating before this date.<sup>1</sup>
- Prior to being designated a VOC, the B.1.1.529 lineage was designated a Variant Under Monitoring by the WHO on November 24, 2021.<sup>9</sup> In the United Kingdom (UK), it was designated as a Variant Under Investigation with Very High Priority (VUI-21-NOV-01) on November 25, 2021. That was the only variant with this designation.<sup>10</sup>
- A number of countries have or will be implementing travel-related restrictions for travellers arriving or seeking to depart from southern African countries (including at time of writing

Canada, the United Kingdom, Germany, France, Italy, the Netherlands, Austria, Belgium, Malta, the Czech Republic, Dubai),<sup>3,8,11,12</sup> a few countries have banned their citizens from travelling to southern Africa (Israel and Singapore;<sup>11</sup> Italy, the Netherlands and the Czech Republic<sup>13</sup>); and a few countries (Canada,<sup>8</sup> Germany,<sup>13</sup> the UK<sup>3</sup>) will also be quarantining and/or testing travellers returning from that area.

## Methods

From January 17 to November 26, 2021, 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.

## Genomic Features

- Omicron has over 50 mutations including 32 mutations on the spike protein.<sup>7</sup>
  - Mutations on the spike protein include: A67V,  $\Delta$ 69-70, T95I, G142D/ $\Delta$ 143-145,  $\Delta$ 211/L212I, ins214EPE, G339D, S371L, S373P, S375F, K417N, N440K, G446S, S477N, T478K, E484A, Q493K, G496S, Q498R, N501Y, Y505H, T547K, D614G, H655Y, N679K, P681H, N764K, D796Y, N856K, Q954H, N969K, L981F.
- Some of the mutations identified in Omicron are also found in other VOCs,<sup>14</sup> and may be associated in theory or through functional studies of previous variants with immune escape, enhanced transmissibility via inducing cell fusion, and susceptibility to treatment.<sup>7,15,16</sup>
  - Three mutations around the furin cleavage site may increase transmissibility and replication<sup>17</sup> as is found in Alpha (P681H) and Gamma (H655Y, N679K).
  - Six mutations in the N-terminal domain may be associated with evasion of antibody neutralization by innate, vaccine-based, or monoclonal-based antibodies. These include mutations also found in Alpha ( $\Delta$ 69-70), Delta (T95I, G142D/ $\Delta$ 143-145), as well as other mutations not yet found in VOCs (A67V,  $\Delta$ 211/L212I, ins214EPE).
  - Three mutations of the receptor binding domain, T478K (also found in Delta), N501Y (also found in Alpha, Beta and Gamma), and Q498R (not previously found in VOCs), may increase the binding affinity of the virus to the ACE2 receptors on host cells<sup>18,19</sup> and further promote immune escape mechanisms.<sup>20</sup>
  - Outside of the spike protein, the nsp6 deletion  $\Delta$ 105-107 (also found in Alpha, Beta, and Gamma VOCs) may be associated with further evasion of innate immunity and enhanced transmissibility.<sup>21</sup>
  - Two mutations of the nucleocapsid, R203K and G204R (also found in Alpha and Gamma VOCs), may be associated with increased infectivity.<sup>22</sup>

## Epidemiology

- A small but growing number of Omicron cases have been reported in South Africa (77 from samples collected between November 12-20, 2021 from Gauteng province),<sup>23</sup> Botswana (4),<sup>23</sup> and Hong Kong (1 traveller from South Africa) as of November 25;<sup>24</sup> and Israel (1 returning from Malawi),<sup>11</sup> Belgium (1 returning from Egypt)<sup>25</sup> as of November 26.
- The reported number of Omicron cases is anticipated to rise as countries begin looking for the novel variant.

## Transmissibility and Disease Severity

- It is unclear if Omicron is more transmissible or causes more severe disease than other VOCs given the small number of cases detected globally so far.
- The effective reproductive number (Re) in South Africa on November 22, 2021 was estimated at 1.5 or below for all provinces, except Gauteng which had a high number of Omicron cases and an Re of 2.<sup>26</sup> As of November 26, 2021, the Re in South Africa across all provinces has been estimated to have increased to 3.<sup>27</sup>

## Vaccine Effectiveness

- It is unclear if and to what extent Omicron can evade immunity from infection and vaccination. Only 24% of the population in South Africa, one of the countries experiencing an increase in Omicron cases, have been fully vaccinated,<sup>4</sup> and it is unknown at this time how many of the infected cases have been vaccinated.
- There are media reports of breakthrough infections of B.1.1.529 in Botswana<sup>28</sup> and Israel from fully vaccinated travellers.<sup>11</sup> At time of writing, there are also reports of 61 out of 624 passengers from South Africa that tested positive for COVID-19 on arrival to Amsterdam, including infected with Omicron.<sup>29</sup> Considering that Amsterdam requires a proof of vaccination or a negative test for entry, these cases would either have been acquired very recently or despite vaccination.

## Reinfection

- WHO reported preliminary evidence of increased risk of COVID-19 reinfection with Omicron, likely based on the increasing incidence of COVID-19 in almost all provinces in South Africa.<sup>1</sup>

## Diagnostic Assays

- Current diagnostic tests are expected to be able to detect Omicron.
- Considering that the vast majority of COVID-19 cases in Canada are due to Delta (99.9% in Ontario<sup>30</sup>), markers suggestive of a non-Delta infection may be implemented to screen for the presence of Omicron. The S gene target failure (SGTF) in one widely used PCR test that can be used as a marker for Omicron while pending confirmation by sequencing.<sup>1</sup> Sequencing is required to confirm the variant as SGTF is not specific to Omicron and may be found in other

variants. Other screening methods employing PCR to target specific mutations (e.g. Δ69/70, N501Y), as implemented for other VOCs, may also be used to identify a possible Omicron infection pending further sequencing.

## Ontario Risk Assessment

- The current risk of Omicron importation in Ontario is high and the risks of further transmission, reinfection, or breakthrough infection in Ontario is moderate with a high degree of uncertainty. As of November 28, 2021, two cases of confirmed Omicron have been detected in Ontario. Ontario’s proportionate WGS surveillance is expected to detect a variant at a prevalence of 1% for samples with a Ct ≤30 and sufficient volume remaining. Of note, the Ontario COVID-19 Genomics Network moved from sequencing 25% of eligible samples on October 8 to 100% on November 5, 2021. However, Ontario’s Re is above 1 (i.e., epidemic growth is occurring), with multiple local surges.<sup>31,32</sup> In terms of the risk of importation, travel-related restrictions were implemented after Omicron was known to have been circulating in southern Africa, and the list of affected countries has expanded quickly. The overall risk assessment may change as new evidence emerges (see [Table 1](#)).
- Further epidemiological and laboratory studies are in progress to assess if Omicron confers any additional phenotypic impacts based on its extent of novel mutations (e.g., change in transmissibility, disease severity, or antibody evasion from innate immunity, vaccines, and/or therapeutics).

**Table 1. Risk Assessment for Omicron B.1.1.529**

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

## Implications for Public Health Practice

- Emerging evidence and information on Omicron is expected to evolve rapidly, and close monitoring to inform the public health response in Ontario is needed. Of note, this summary mostly reflects publicly available information current to November 26, 2021.
- VOC PCR testing in Ontario, previously implemented but discontinued as of November 12, 2021, has been rapidly leveraged to enhance the ability to identify suspected Omicron cases from travellers to affected countries through the detection of the N501Y mutation found in Omicron.

The N501Y mutation may also be found in Alpha, Beta, or Gamma, which are currently accounting for < 0.1% of cases in the province, but not Delta, which is currently accounting for up to 99.9% of cases in the province.

- Noting concerns about Omicron's potential increased transmissibility and mutations that may have implications for vaccine/immune escape, as well as uncertainty about its virulence (i.e., clinical severity among those with disease), as a precautionary approach a temporary containment strategy could help delay importation and spread of this VOC in Ontario.
- In addition to federal travel-related restrictions and requirements for returning travellers, a containment strategy in Ontario requires rapid consideration and implementation of enhanced public health measures, including case and contact management approaches. Given the rapid and ongoing expansion of countries where Omicron has been detected to date, including jurisdictions outside of southern Africa, a cautious approach to enhanced measures in Ontario could consider any recent travel outside Canada (including but not limited to countries/regions with confirmed Omicron cases) as a potential increased risk for Omicron acquisition.
- Population-level and individual-level public health measures should continue to be implemented to help limit the spread of COVID-19 in Ontario using a multi-layered approach, including vaccination, masking, physical distancing, ventilation, handwashing, and staying home when sick or with any symptoms of COVID-19.
- Vaccination remains one of the most effective layers of protection against SARS-CoV-2, including for the 99.9% of Delta strains currently representing the COVID-19 disease burden in Ontario. Global efforts to optimize vaccination coverage, especially in low and middle income nations that have limited resources to prevent and control COVID-19 transmission, is also a key measure to combat VOC spread as each transmission event plays a role in fostering mutations of the virus that risk the development of further variants.<sup>33</sup>

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## Citation

Ontario Agency for Health Protection and Promotion (Public Health Ontario). COVID-19 Variant of Concern Omicron (B.1.1.529): Risk Assessment. Toronto, ON: Queen's Printer for Ontario; 2021.

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