Key Messages

- Reporting of polymerase chain reaction (PCR)-confirmed case counts in Ontario is an underestimate of the true epidemiology of SARS-CoV-2 infections due to changes in PCR testing eligibility and no requirement or mechanism to report positive rapid antigen test (RAT) for the general population.

- The literature suggests that three doses of a Coronavirus Disease 2019 (COVID-19) vaccine provides greater protection against severe outcomes of Omicron variant infection when compared to two doses of a COVID-19 vaccine. The duration of protection from a third dose or recent infection remains unclear.

- There is additional evidence to support previous reports that despite the numerous mutations in Omicron, T cell recognition of Omicron is largely preserved. There is additional evidence to support the benefit of a longer interval between vaccinations to improve antibody boosting, and evidence of stronger antibody responses in vaccinated, previously infected individuals compared to vaccinated individuals without previous infection, or individuals with previous infection and no vaccination.

- Early evidence suggests Omicron is more transmissible but causes less severe disease compared to Delta infections. Nonetheless, due to increased transmission of Omicron, an increase in the number of severe cases is occurring and poses a significant threat to health system capacity. There is insufficient data to comment on mortality and long-term COVID outcomes.

- The current risk of increased Omicron transmission in Ontario is high, with a low degree of uncertainty. The risk of reinfection and breakthrough infection (after two doses of Pfizer, Moderna, AstraZeneca, or a heterologous combination) in Ontario is high with a low degree of uncertainty. The risk of severe disease, particularly amongst unvaccinated individuals, is moderate with a moderate degree of uncertainty. The overall risk assessment may change as new evidence emerges.

- Based on what is known about Omicron and its rapid case growth in Ontario, increased community-based public health measures and accelerated vaccination efforts targeting those most at-risk of severe outcomes and onward transmission (e.g., those in congregate living settings and schools/daycares) can help protect Ontarians, health system capacity, and limit disruption of critical infrastructure and in-person learning.
Issue and Research Question
Since its identification on November 8, 2021 in South Africa, Omicron has become the dominant severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variant in many countries. Since the last report on January 6, 2021 more evidence has emerged of Omicron’s transmissibility, potential immune evasion, and disease severity. This brief updates the evidence since the previous Public Health Ontario (PHO) risk assessments, and summarizes available information and evidence on the Omicron variant of concern (VOC) relevant to the risk of importation and transmission in Ontario up to January 12, 2022.

Methods
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 various news feeds and custom search engines. English-language peer-reviewed and non-peer-reviewed (preprint) records that described COVID-19 variants were included.

Main Findings
Epidemiology
• As of January 7, 2022, whole genome sequencing (WGS) from surveillance testing across Canada reported that of SARS-CoV-2 samples sequenced the week of December 9, 2021, 72.1% were Omicron. On January 12, 2022, Canada reported 328,827 new cases, 114 deaths, 402,114 active cases, and the daily percent positivity (over the previous 7 days) was 27.5%.

• In Ontario, on December 28, 2021, 80.4% of samples tested at the PHO laboratory exhibited 5-Gene Target Failure (SGTF), indicating that Omicron is the dominant circulating variant. The PHO laboratory discontinued SGTF testing on December 30, 2021. Due to changes in the eligibility criteria for PCR testing in Ontario effective December 31, 2021, reported confirmed case counts are an underestimate of the true number of individuals with SARS-CoV-2 infection.

  • The Ontario 7-day confirmed case average increased from 838 on December 1, 2021 to 4,581 on December 23, 2021, and 14,669 on January 6, 2022.

  • For most of the summer and fall of 2021, the Ontario COVID-19 laboratory test positivity remained below 4%. On December 31, 2021 (i.e., the day on which changes to the eligibility criteria for PCR testing took effect), the percent positivity was 34.3%. On January 8, 2022 (i.e., just over a week since the testing eligibility update), the percent positivity was 27.7%.

  • As of January 11, 2022 there were 389 ongoing outbreaks in long-term care homes, 268 in retirement homes, and 204 in hospitals.

  • During the week of December 27, 2021 to January 2, 2022, the World Health Organization (WHO) global number of new COVID-19 cases increased by 71% (9.5 million new cases) from the previous week, and the number of new deaths decreased by 10% (41,000 new deaths).
• All WHO regions reported an increase in the incidence of weekly cases, with the highest increases in the Region of the Americas (100%), South-East Asia Region (78%), and the European Region (65%). The African Region reported a weekly increase in the number of new deaths (22%), but all other regions reported a decrease compared to the previous week.

Notable epidemiological trends from select countries are:

• According to modelling projections, the United States (US) Centers for Disease Control and Prevention (CDC) estimated that for the week ending January 1, 2022, 95.4% (90% Confidence Interval [CI]: 92.9-97.0) of SARS-CoV-2 cases were Omicron.
  • On January 10, 2022, the US reported 1.35 million new COVID-19 cases according to a Reuters tally, a global single day case count record for one country.
  • The seven-day average for new cases tripled in two weeks to over 700,000 new infections a day.
  • On January 3, 2022, the average number of daily hospitalizations in the US was 93,281, an increase of 35% in the previous two weeks. On January 10, 2022, COVID-19 hospitalizations reached a record high with 132,646 people hospitalized with COVID, surpassing the record of 132,051 set in January 2021.

• The United Kingdom (UK) Health Security Agency (UKHSA) reported >90% of a representative sample of specimens were Omicron based on SGTF in the last week of December 2021. In the UK, 129,587 new cases were reported on January 12, 2022.
  • Between January 6 to January 12, 2022, there were 1,038,500 confirmed positive tests, which is a decrease of -19.0% compared to the previous 7 days.
  • Between January 2 and January 8, 2022, there were 15,591 new COVID-19 hospitalizations, an increase of 5.2% compared to the previous 7 days.

• In Denmark, the Omicron variant represents >90% of the confirmed SARS-CoV-2 cases.
  • On January 12, 2022, Denmark reported 24,343 new COVID-19 cases in the past 24 hours.
  • The 7-day rolling average of new cases per million people increased from 740 on December 1, 2021 to 3,535 on January 10, 2022.

• Data from South Africa and other southern African countries suggests that their Omicron waves peaked rapidly, at around four weeks.
  • For the week December 27, 2021 to January 2, 2022, South Africa reported a 48% decrease in confirmed case incidence.
Transmissibility

Modelling, *in vitro* and *in-silico* analyses support current epidemiological findings and suggest potential mechanisms behind the higher rate of transmission of Omicron. It remains unclear to what extent the increased transmission of Omicron is due to inherent characteristics of the virus (i.e., enhance ability to infected cells) and/or immune evasion.

Epidemiological Evidence

Modelling of Omicron transmissibility using UK data estimated Omicron to be 5.57-fold more transmissible than Delta (95% CI: 5.26–5.90). Data from South Africa estimates Omicron to be 3.05-fold more transmissible than Delta (95% credible interval: 2.72–3.43). These estimates are in agreement with earlier statements.24

*In-vitro* and Modelling Evidence

The human ACE2 (hACE2) receptor is used by SARS-CoV-2 to enter host cells; therefore, mutations that alter binding affinity or stability or tissue tropism (e.g., faster replication in human bronchi as opposed to lungs) could impact infectivity and transmission.25,26 Since the last Risk Assessment, more *in vitro* studies have reported evidence of lower replication competence in lung cells compared to ‘wild type’ and other VOCs.23,27 Additional *in silico* and electron micrograph studies have analyzed Omicron binding to the hACE2 receptor, with varied findings regarding binding affinity and proteolytic cleavage.28–30 The mechanism of Omicron mutations enhancing transmissibility remains unclear, but there is growing evidence to support Omicron causing pandemic waves with high attack rates.31

Diagnostics

Although current molecular tests for SARS-CoV-2 are expected to be able to detect Omicron,24 there is evidence that the large number of mutations in the S-gene may render some quantitative RT-PCR assays less sensitive to Omicron that include the S-gene target.32 Increasing use of rapid antigen tests for diagnostic purposes or to inform isolation guidance, requires a better understanding of the benefits and limitations of this testing modality.24,33,34

- An *in silico* analysis of Omicron whole genome sequencing data evaluated the potential for false negatives or test failure due to mismatches between primers/probes and Omicron mutations.32 For 5 SARS-CoV-2 BA.2 Omicron sublineage genomes, false negative results were observed for six of the assays tested.

- As observed in a previous study,35 a lag in detection of COVID-19 cases by rapid antigen tests during the early period of disease was described in a high-risk occupational case cohort of 30 individuals.36 With daily testing during an Omicron outbreak in December 2021, reported that most Omicron cases were infectious for several days before being detectable by rapid antigen tests, based on viral load and transmissions confirmed through epidemiological investigation. On Days 0 and 1, all rapid antigen tests produced false-negative results, despite 28/30 pairs having infectious viral loads within the range of confirmed Omicron transmissions in the cohort. The median time from first positive PCR to first detectable antigen positive was 3 days. After infection was detected, a subgroup (n=5) who received daily saliva PCR, nasal swab PCR, and nasal swab rapid antigen testing showed viral load peaked in saliva 1-2 days before nasal tests. All individuals in the cohort developed symptoms within two days of the first PCR positive test.
A study evaluating the performance of healthcare worker collected oral swabs compared to standard nasal swabs for detecting Omicron at a walk-up community site in California, USA, simultaneously performed rapid antigen testing (BinaxNOW) and RT-PCR testing (n=75). Among 46 nasal RT-PCR positives, 22 were positive by rapid antigen (47.8%, 22/46) that were collected using nasal swabs, while only 2 (4.3%, 2/46) were positive from oral cheek specimens. Thirteen of the 46 RT-PCR positive nasal specimens were also positive on oral cheek RT-PCR (28.3% sensitivity of oral specimens compared to nasal). Furthermore, no specimens were RT-PCR positive from the oral cheek collection and negative on the nasal RT-PCR.

Clinical Presentation

Information continues to emerge regarding the signs and symptoms of Omicron and how they may differ from infection with other SARS-CoV-2 variants.

- Reports and analysis of UK health app data suggests Omicron presents similarly to the common cold, as previously reviewed.2,5,6

- A Google Trends analysis investigating COVID-19 signs and symptoms during a period when Omicron represented >80% of cases in the UK compared to a period when the Alpha variant was dominant, found that conjunctivitis, chills, cough, aches, fever, nausea and sore throat were more searched in the Omicron period compared to the Alpha period (>15% increase). In contrast, tiredness, loss of taste or smell, sneezing and shortness of breath were less searched in during Omicron compared to Alpha periods (>15% decrease). The number of Google searches for headache, diarrhea and runny nose were nearly comparable between the two periods (i.e., <15% variation).
Disease Severity

The bulk of early evidence suggests Omicron causes less severe disease than Delta,\textsuperscript{24} and this is supported by several rodent and \textit{in vitro} studies that have emerged since the last Risk Assessment;\textsuperscript{23,27,39-41} however, there remains a moderate degree of uncertainty regarding disease severity. There is insufficient data to comment on hospitalization outcomes including progression of severity of illness, complications, and mortality.

- A retrospective cohort study examined electronic health record data of 577,938 first-time SARS-CoV-2 infected patients from a multicenter, nationwide database in the US between September 1, 2021 to December 24, 2021 including 14,054 infected between December 15 to 24, 2021 (Omicron cohort) and 563,884 infected September 1 to December 15, 2021 (Delta cohort).\textsuperscript{42}

- After propensity-score matching for demographics, socio-economic determinants of health, comorbidities, medications and vaccination status, the risk of severe outcomes in the three days following infection in the Omicron cohort were less than half those in the Delta cohort: ED visit: 4.55\% vs. 15.22\% (risk ratio [RR]: 0.30, 95\%CI: 0.28-0.33); hospitalization: 1.75\% vs. 3.95\% (RR: 0.44, 95\% CI: 0.38-0.52); intensive care unit (ICU) admission: 0.26\% vs. 0.78\% (RR: 0.33, 95\% CI:0.23-0.48); mechanical ventilation: 0.07\% vs. 0.43\% (RR: 0.16, 95\% CI: 0.08-0.32).

- In children <5 years old, the overall risks of ED visits and hospitalization in the Omicron cohort were 3.89\% and 0.96\% respectively, significantly lower than 21.01\% and 2.65\% in the matched Delta cohort (RR for ED visit: 0.19, 95\% CI:0.14-0.25; RR for hospitalization: 0.36, 95\% CI: 0.19-0.68). Similar trends were observed for other pediatric age groups, adults (18-64 years) and older adults.

- First time SARS-CoV-2 infections that occurred during the Omicron period were associated with significantly less severe outcomes than first-time infections during the Delta period.

Vaccine Effectiveness (VE)

Since the last Risk Assessment, more evidence has emerged demonstrating that two doses of COVID-19 vaccines are less effective at preventing Omicron breakthrough infections compared to other VOCs and ‘wild-type’ SARS-CoV-2.\textsuperscript{43} A third COVID-19 vaccine dose increases short-term protection against symptomatic Omicron infection.

- A test negative study of individuals aged ≥18 years testing positive by RT-PCR (n=6657) with specimens collected between December 6, 2021 and December 23, 2021 with 44\% Delta and 56\% Omicron estimated the two dose VE against Omicron infection to be 30.4\% (95\% CI, 5.0\%-49.0\%) at 14-90 days after vaccination, 15.2\% (0.0\%-30.7\%) at 91-180 days and 0.0\% after 180 days.\textsuperscript{44} Three dose VE was 95.2\% (93.4\%-96.4\%) against Delta infection and 62.5\% (56.2\%-67.9\%) against Omicron infection, but the time since third dose vaccination was not clear in the report. Three dose VE against Omicron infection was lower among immunocompromised individuals (11.5\%; 0.0\%-66.5\%). None of the Delta or Omicron cases vaccinated with three doses were hospitalized compared to 53 Delta and two Omicron unvaccinated cases.
In-Vitro and Modelling Evidence of Vaccine Efficacy

Since the previous risk assessment, additional studies have reported reduced antibody levels and function against Omicron compared to ‘wildtype’ and other VOCs in two-dose vaccinated and/or previously infected individuals, with some evidence of relatively well-preserved Fc effector function and neutralization against Omicron. There is additional evidence to support previous reports that despite the numerous mutations in Omicron, T cell recognition of Omicron is largely preserved. There is additional evidence to support the benefit of a longer interval between vaccinations to improve antibody boosting, and evidence of stronger antibody responses in vaccinated, previously infected individuals compared to vaccinated individuals without previous infection, or individuals with previous infection and no vaccination. Select reports are highlighted below.

- In health care workers (n=328) two doses of Pfizer, Moderna, or AstraZeneca, or heterologous vaccinations induces equally high levels of anti-SARS-CoV-2 spike antibodies and neutralizing antibodies against Omicron when administrated with a 12-week dose interval. Geometric mean titres at three weeks after the second dose were 127 for 2x Pfizer, 158 for 2x Moderna, 142 for 2x AstraZeneca, 87 for AstraZeneca + Pfizer, and 158 for AstraZeneca + Moderna, suggesting a high induction of antibody levels by the second immunization with all five vaccine combinations. Two doses of Pfizer with a short, three week interval resulted in 2-3-fold lower titers of neutralizing antibodies compared to the long interval. And at the time of the third dose (7-9 months after the second dose), only 5% (3/59) of health care workers had neutralizing antibodies against Omicron. A third mRNA dose for the short dose interval group increased the antibody levels 4-fold compared to the levels after the second dose.

- A longitudinal cohort of 98 convalescent individuals infected in spring 2020, and 73 naïve individuals matched for sex, age, working conditions and risk factors were monitored after the first, second and third Pfizer COVID-19 vaccination. Sera were characterized for anti-spike IgG titers, IgG antibody avidity and neutralizing capacity.

  - COVID-19 convalescents showed a more sustained neutralization capacity after one Pfizer vaccination approximately 9 months after infection (63-fold increase) than naïve individuals vaccinated twice. A third vaccination was needed in naïve individuals to develop the high antibody avidity needed for protection against VOCs with humoral immune escape.

  - 40.6% (95% CI: 29.4 – 52.9 %) of naïve, vaccinated individuals, but only 4.0% (95% CI: 1.1 – 13.5 %) of vaccinated convalescents showed no neutralization activity against Omicron seven months after the initial vaccinations.

  - In convalescents, the ratio between the IC50 neutralization and anti-spike IgG titers (i.e., efficacy of antibodies for virus neutralization) slightly increased after the second vaccine and was more pronounced after a third dose, but for naïve individuals, the ratio was low after first and second doses of vaccine, then increased over four and seven months, and after a third vaccination reached levels comparable those in convalescents.
• Using a cohort of 29 vaccinated individuals (28 had a two dose schedule, one had a single dose of Johnson & Johnson) with 16 Delta and 13 Omicron breakthrough infections, the authors reported an average of five months to breakthrough infection. Neutralization titers were significantly higher among the 29 individuals with Delta or Omicron breakthrough infections compared to the twice vaccinated naïve study participants of the first cohort and comparable titers two weeks after third vaccination in convalescent and naive individuals of the first cohort.

**Breakthrough Infections**

As more of a population are vaccinated, a greater proportion of SARS-CoV-2 infections will be in vaccinated individuals. This does not mean that vaccinated individuals are more likely to get infected.

• Using longitudinal samples from individuals who experienced clinically mild breakthrough infections four to five months after vaccination with Johnson & Johnson vaccine, a study showed dramatically boosted binding antibodies, Fc effector function and neutralization.\(^\text{48}\) The high titer responses were of similar magnitude to humoral immune responses measured in severely ill, hospitalized donors, and were cross-reactive against diverse SARS-CoV-2 variants, including against Omicron.

**Reinfection**

The following new findings since are consistent with previous reports that Omicron can evade immunity after natural infection.

• Using a test-negative, case-control study design, cases (PCR-positive persons with a variant infection) and controls (PCR-negative persons) were exact-matched by sex, 10-year age group, nationality, and calendar time of PCR test, to control for known differences in the risk of exposure to SARS-CoV-2 infection.\(^\text{55}\) The study found that the protection against symptomatic reinfection was 90.2% (95% CI: 60.2-97.6) for Alpha, 84.8% (95% CI: 74.5-91.0) for Beta, 92.0% (95% CI: 87.9-94.7) for Delta, and 56.0% (95% CI: 50.6-60.9) for Omicron. Protection against hospitalization or death due to reinfection was estimated at 69.4% (95% CI: -143.6-96.2) for Alpha, 88.0% (95% CI: 50.7-97.1) for Beta, 100% (95% CI: 43.3-99.8) for Delta, and 87.8% (95% CI: 47.5-97.1) for Omicron. Protection against reinfection with Omicron at 60% was lower than for other VOCs. Protection from previous SARS-CoV-2 infection appears to protect against severe disease leading to hospitalization or death for those re-infected, regardless of variant.

**Measures in Response to Omicron**

This section was informed by scanning government websites and searches in the Google search engine for literature related to Omicron, public health measures, and vaccination programming; thus, some relevant articles may not be included. The following jurisdictions were searched on January 11, 2022: Denmark, England, Finland, France, Germany, Ireland, Israel, Italy, Netherlands, Norway, Portugal, New York State, and California.
Changes to Public Health Measures
All included jurisdictions have implemented public health measures in response to the emergence of Omicron. This continues to be the trend across most jurisdictions; however, some jurisdictions are relaxing temporary measures that were previously brought in for the holidays. Since the last Risk Assessment, the following changes to public health measures were identified in select jurisdictions:

- Some jurisdictions are introducing general vaccine mandates (e.g., Italy made vaccines mandatory for individuals 50 years and older) or workplace-specific mandates (e.g., New York State made a booster dose a requirement for healthcare workers). Ireland is considering general vaccine mandates, although no official announcement has been made.

- Some jurisdictions require proof of negative test result to enter some settings in addition to proof of vaccination or recovery (e.g., Germany, California).

- Italy expanded the use of the COVID-19 health pass to additional settings (e.g., swimming pools, gyms and team sports, spas, casinos).

- Some jurisdictions are reopening settings that were temporarily closed (e.g., Portugal is reopening bars and nightclubs or extending the open hours of some activities (e.g., Netherlands is extending children’s outdoor sports from 5 PM to 8 PM).

Changes to Vaccination Programming
Since the last Risk Assessment, the following changes to vaccination programming were identified in select jurisdictions:

- On January 7, 2022, the UKHSA released a statement saying that the Joint Committee on Vaccination and Immunisation advises the following based on recent UKHSA data showing that three months after the third dose, protection against hospitalization among those aged 65 and over remains at about 90%:
  - There is no immediate need to administer second booster doses (fourth doses), to the most vulnerable (care home residents and those aged over 80).
  - Priority should continue to be given to rolling out first booster doses to all age groups.

- As of January 7, 2022, everyone over the age of 18 in Netherlands is able to book a booster dose.

- On January 4, 2022, the CDC changed the interval between second and booster doses from six to five months. It also recommended immunocompromised children ages 5-11 years receive an additional primary dose 28 days after their second dose.

- On January 5, 2022, the CDC recommended expanded booster dose eligibility for individuals ages 12-15 years to five months after their second dose.
Ontario Risk Assessment

- The current risk of increased Omicron transmission in Ontario is high, with a low degree of uncertainty. The risk of reinfection and breakthrough infection in Ontario is high with a low degree of uncertainty, while the risk of severe disease, particularly amongst unvaccinated individuals, is moderate, with a moderate degree of uncertainty. The volume of cases due to the increased transmission of Omicron presents risks to testing capacity and as a result, risks to surveillance quality. The incidence of severe cases due to increased transmission is a threat to health system capacity.

- The overall risk assessment may change as new evidence emerges (see Table 1).

Table 1. Risk Assessment for Omicron B.1.1.529

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<th>Issues</th>
<th>Risk Level</th>
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<td>Impacts on Testing/Surveillance</td>
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Implications for Practice

The epidemiology of Omicron in Ontario has become more challenging to interpret due to the rapid increase in Omicron cases and changes in eligibility for PCR testing, which makes metrics such as the reproduction number and confirmed case rate an underestimate. The evidence for three vaccine doses providing good protection from hospitalization is strong, making three dose vaccinations a key public health tool in the current Omicron context. Public health measures and accelerated booster vaccinations are important to mitigate the surge in Omicron cases, reduce population morbidity and mortality, and address impacts to the health system.
References


46. Peiris M, Cheng S, Mok CKP, Leung Y, Ng S, Chan K, et al. Neutralizing antibody titres to SARS-CoV-2 Omicron variant and wild-type virus in those with past infection or vaccinated or boosted with mRNA BNT162b2 or inactivated CoronaVac vaccines. Res Sq 1207071 [Preprint]. 2022 Jan 05 [cited 2022 Jan 11]. Available from: https://doi.org/10.21203/rs.3.rs-1207071/v1


