Public Health Ontario | Santé publique Ontario

EVIDENCE BRIEF

COVID-19 Variant of Concern Omicron (B.1.1.529): Risk Assessment, January 6, 2022

01/06/2022

Key Messages

- It has become more difficult to track the epidemiology of SARS-CoV-2 due to increasing cases and limited testing capacity, which are resulting in changes to testing strategies (e.g., rapid tests as diagnostics, limited eligibility for polymerase chain reaction [PCR]), making official case counts an underestimate.

- More studies support the body of evidence that the combination of previous SARS-CoV-2 infection and vaccination provides more immune protection against Omicron than infection alone or two doses of vaccine. There are also more studies to support the body of evidence that heterologous vaccination regimens elicit a stronger immune response than homologous regimens. There is strong evidence of benefit from third doses, and preliminary evidence of third dose waning.

- While limitations remain with regards to the Omicron severity literature, the bulk of the early evidence suggests Omicron causes less severe disease than Delta; however, there is insufficient data to comment on mortality or severity of illness once in hospital.

- With epidemiological evidence indicating risks to health care system capacity (even with case counts being an underestimate), several jurisdictions are implementing more restrictive public health measures (e.g., mask mandates).

- 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 increased disease severity is moderate with a high degree of uncertainty. The overall risk assessment may change as new evidence emerges.

- Based on what is known so far about Omicron, and its rapid case growth in Ontario, increased community-based public health measures accompanied by ongoing accelerated vaccination efforts (e.g., third and fourth doses) targeting those most at-risk of severe outcomes and onward transmission (e.g., those in congregate living settings and schools/daycares) is important to protect Ontarians, health system capacity (including public health capacity), and limit the impact to key societal functions such as critical infrastructure and in-person learning.

Issue and Research Question

Since its identification on November 8, 2021 in South Africa,[1] Omicron has become the dominant severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variant in many countries. Since the last report on December 29,[2] more evidence has emerged of Omicron's transmissibility and potential immune evasion, and early evidence regarding disease severity. This brief updates the evidence since the previous Public Health Ontario (PHO) risk assessments,[2-6] 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 2, 2022. Data from Ontario was available up to January 3, 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.

Epidemiology

- The Ontario 7-day COVID-19 case average surged from 838 on December 1, 2021 to 4,581 on December 23, 2021.[7] Ontario's SARS-CoV-2 reproduction number was 1.62 (95% confidence interval [CI]: 1.61, 1.63) on December 29, 2021.[7] From October 31 to December 29, 2021, Ontario reported a total of 30,326 Omicron cases (confirmed by whole genome sequencing, WGS or based on S-Gene Target Failure [SGTF]).[8] In Ontario, from October 31, 2021 to December 29, 2021, 49.7% of Omicron/SGTF cases are females and 46.2% are between 20 and 30 years of age,[9] and there have been 166 outbreaks with Omicron or SGTF reported as the outbreak lineage or mutation.
    - SGTF is a genetic marker that can be used as a screening method for identifying the Omicron variant. On December 28, 2021, 80.4% of samples tested at the PHO laboratory exhibited SGTF, indicating that Omicron is the dominant variant circulating in Ontario. The PHO laboratory discontinued SGTF testing on December 30, 2021.[10]
- During the week December 20 to 26, 2021, the World Health Organization (WHO) global number of new COVID-19 cases increased by 11% from the previous week, and the number of new deaths remained similar to the previous week.[11] This corresponds to just under 5 million new cases and over 44,000 new deaths.

Notable epidemiological trends from select countries are:

- The US Centers for Disease Control and Prevention (CDC) had previously reported that as of December 18, 2021, 73% of new cases were linked to Omicron, but then revised the estimate for December 18, 2021 to 23% and by December 25, 2021, Omicron accounted for 58.6% of cases.[12,13]

- The UK Health Security Agency's December 29, 2021 Omicron daily overview reported 181,547 confirmed cases, 766 hospitalizations, and 53 deaths in England, which increased to 212,019 confirmed cases, 981 hospitalizations, and 75 deaths in the December 31, 2021 report.[8,14,15]

- For the week ending December 25, 2021, the number of confirmed infections in South Africa was 89,781, which was a decrease from 127,753 the previous week. South African officials have announced that cases are decreasing in all provinces,[16] suggesting the Omicron wave had peaked. The data from South Africa shows that the Omicron wave peaked around four weeks, suggesting Omicron waves may exhibit a rapid, steep peak and resolution,[17] but it remains unclear if Omicron will behave similarly in other jurisdictions.

Transmissibility

Since the last Risk Assessment, more experiential evidence of Omicron's increased transmissibility has emerged through reports of surging cases and Omicron's rapid displacement of Delta as the dominant SARS-CoV-2 lineage in many jurisdictions.[11,18] Modelling and *in-silico* analyses support current epidemiological findings and suggest potential mechanisms behind the higher rate of transmission of Omicron. Select evidence that has emerged since the last Risk Assessment is summarized below.

Epidemiological Evidence

- Using data from Danish registers in December 2021, among 11,937 households (2,225 with Omicron), 6,397 secondary infections were identified during a one to seven day follow-up period. The secondary attack rate (SAR) was 31% and 21% in households with the Omicron and Delta VOCs, respectively.[19] Transmission was higher for unvaccinated individuals, and reduced for booster-vaccinated individuals, compared to fully vaccinated individuals. The SAR for unvaccinated individuals was 29% and 28% in Omicron and Delta households, respectively, while the SAR for fully vaccinated individuals was 32% and 19% in Omicron and Delta households, respectively. For booster-vaccinated individuals, the SAR was 25% for Omicron and 11% for Delta. Comparing Omicron households to Delta households, the authors reported a 1.17 (95% CI: 0.99-1.38) times higher SAR for unvaccinated, 2.61 times (95% CI: 2.34-2.90) higher for fully vaccinated and 3.66 (95% CI: 2.65-5.05) times higher for booster-vaccinated individuals, strongly suggesting immune evasion by Omicron. These findings ascribe the rapid spread of Omicron primarily to the immune evasion rather than an inherent increase in the basic transmissibility of the virus.

- Of 230 asymptomatic people living with HIV (PLWH) in South Africa attending routine screening as part of a vaccine trial, 71 (31%) were PCR positive for Omicron, 48% of the tested samples had cycle threshold (CT) values <25 and 18% less than 20, demonstrating high titers of asymptomatic shedding. Asymptomatic positive rates were similar in SARS-CoV-2 seropositive and seronegative persons (27% respectively).[20] Pre-Omicron, the SARS-CoV-2 PCR positivity rate at these study sites ranged from <1%-2.4%, but during the Omicron wave, asymptomatic carriage was reported to be 16% in participants. The authors therefore concluded that Omicron seems to have a much higher rate of asymptomatic cases than other VOC, which could explain its widespread, rapid dissemination, even among populations with high prior rates of SARS-COV-2 infection.

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 could impact infectivity and transmission. Since the last Risk Assessment, several *in vitro* and modelling studies have reported evidence of higher replication of Omicron early in infection (24 hours) compared to 'wildtype' and other VOCs,[21,22] and lower replication competence in lung cells compared to 'wildtype' and other VOCs.[21-25] Additional *in silico* and electron micrograph studies have analyzed Omicron Spike binding to the hACE2 receptor, with varied findings regarding binding affinity and proteolytic cleavage.[24,26-33] The mechanism of Omicron mutations enhancing transmissibility remains unclear.

Diagnostics

Current molecular and antigen tests for SARS-CoV-2 are expected to be able to detect Omicron.[9,10] Since the previous Risk Assessment, a preliminary evaluation (n=382) revealed that the Delta variant had a positive percent agreement (PPA) for saliva swabs and mid-turbinate swabs to a composite standard was 71% (95% CI: 53-84%) and 100% (95% CI: 89-100%), respectively. In contrast, the Omicron variant saliva and mid-turbinate swabs had a 100% (95% CI: 90-100%) and 86% (95% CI: 71-94%) PPA, respectively.[34] The improved sensitivity of saliva for RT-PCR detection of Omicron supports ex-vivo data of altered tissue tropism relative to other variants. Further studies are needed to evaluate saliva and throat swabs as a preferred specimen type for the Omicron variant.

Clinical Presentation

Information continues to emerge regarding the signs and symptoms of Omicron and how they differ from infection with other SARS-CoV-2 variants. In addition to the five most common symptoms for Omicron: runny nose, headache, fatigue (both mild and severe), sneezing, sore throat, and the recently reported loss of appetite and brain fog (more common in those who were fully vaccinated and boosted), there are reports of night sweats.[35] The evidence of the overall clinical presentation of Omicron remains unclear.

Disease Severity

There are limitations with the Omicron severity literature (see previous Risk Assessments), which may be exacerbated by degrading data quality due to changes in testing strategies. The bulk of the early evidence suggests Omicron causes less severe disease than Delta, but new evidence is still emerging. There is insufficient data to comment on severity of illness once in hospital, or mortality.[36] Select evidence that has emerged since the last Risk Assessment is summarized below.

- An update of the UK Health Security Agency's last report found that the risk of presentation to emergency care or hospital admission with Omicron was roughly half of that for Delta (Hazard Ratio 0.53, 95% CI: 0.50 to 0.57).[37] The risk of hospital admission from emergency departments with Omicron was approximately one-third of that for Delta (Hazard Ratio 0.33, 95% CI: 0.30 to 0.37). The analyses were adjusted for age, sex, ethnicity, local area deprivation, international travel, vaccination status, and whether the current infection was a known reinfection. The authors report that the risk of hospitalization is lower for Omicron cases after two and three doses of vaccine, with an 81% (77 to 85%) reduction in the risk of hospitalization after three doses as compared to unvaccinated Omicron cases.

- In Denmark, from November 21 to December 28, 2021, 0.9% of Omicron cases were hospitalized, whereas 1.2% of other VOC cases were hospitalized.[18]

- A study of sentinel hospitals in the Greater Manchester area found that the proportion of Omicron in hospital samples follows a similar trajectory to the SGTF proportion in cases, but with a two-day offset, which is consistent with the lag between testing positive to hospital admission, suggesting a similar proportion of Omicron cases are becoming hospital admissions as was the case for Delta.[38] Similar trends are observed in national hospitalization data, suggesting no signal of a substantial reduction in hospital admission risk with Omicron.

- A White House briefing on December 29, 2021 announced that the 7-day daily average of COVID-19 infections was 240,400, which was an increase of 60% since the previous week; however, hospital admissions only increased by 14%, at 9,000 per day.[39] Deaths were averaging 1,100 per day, a decrease of about 7%. It remains unclear whether the difference in hospitalization and cases is due to the hospitalization trend lagging behind cases by about two weeks, or if it is an indication of less severe disease from Omicron.

- An analysis of first-time COVID-19 infections in the US compared 14,054 infections in the last two weeks of December, when Omicron was emerging, and 563,884 infections from September 1 to December 15, 2021, when Delta was predominant. Outcomes were measured from the time of positive test to three days after infection. The overall risk among the Omicron cohort was 4.55% for emergency department visit, 1.75% for hospitalization, 0.26% for intensive care unit (ICU) admission, and 0.07% for mechanical ventilation. The authors used propensity-score matching to adjust for demographics, socio-economic determinants of health, comorbidities, medications, and vaccination status. The adjusted risk ratio for the Omicron cohort as compared to the Delta cohort was 0.30 for an emergency department visit, 0.44 for hospitalization, 0.33 for ICU admission, and 0.16 for mechanical ventilation.[40]

- In a cohort of COVID-19 infections identified by a hospital system in Houston, Texas (accounting for approximately 5% of cases in Houston), individuals with the Omicron variant were much younger, much more likely to have received at least two vaccinations, and were less likely to be hospitalized or die from their infection. Of 862 Omicron infections, 15% of cases were admitted and 0.9% of cases died. Of 15,639 Delta infections, 43% were admitted, and 5.3% died.[41]

- Individuals admitted to a hospital in Tshwane District, South Africa during the Omicron wave (n = 466) were compared to individuals admitted during previous waves (n = 3976). Risk of in-hospital death was lower during the Omicron wave than during previous waves (4.5% vs. 21.3%).[42]

- Researchers compared health outcomes during four waves of COVID-19 cases at a hospital system in South Africa. They defined each wave as the period of time when positivity rates exceeded 26%. Cases during the Omicron wave tended to be younger, were less likely to have comorbidities, were less likely to present to hospital in an acute respiratory condition, and were more likely to be vaccinated. They reported decreased risk of requiring oxygen therapy (17.6% in wave 4 vs 74% in the Delta wave), decreased risk of admission to intensive care (18.5% in wave 4 vs 29.9% in the Delta wave), and decreased risk of death (19.7% in wave 1, 29.1% in the Delta wave, 2.7% in Omicron wave).[43]

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 protection against other VOCs and 'wild-type' SARS-CoV-2, and a third vaccine dose increases short-term protection against symptomatic Omicron infection. Select evidence is summarized below.

- A test negative study of VE against infection (regardless of symptoms) from Delta (9,201) or Omicron (3,442) with 471,545 test-negative controls between November 22 and December 19, 2021 in Ontario, Canada reported that after two doses of COVID-19 vaccine, VE against Delta infection decreased steadily over time but recovered to 93% (95% CI, 92-94%) ≥7 days after a third dose of an mRNA vaccine.[44] In contrast, two dose VE against Omicron was 37% (95% CI, 19-50%) ≥7 days after receiving an mRNA vaccine for the third dose.

- The UK Health Security Agency reported that VE against symptomatic disease is lower for Omicron than for Delta, with waning by 10 weeks after the third dose.[37] After three doses of vaccine, the risk of hospitalization for a symptomatic Omicron case was estimated to be reduced by 68% (42 to 82%) when compared to similar individuals with Omicron who were not vaccinated (after adjusting for age, gender, previous positive test, region, ethnicity, clinically extreme vulnerable status, risk group status and period). Combined with protection against being a symptomatic case, this results in a VE against hospitalization of 88% (78 to 93%) against Omicron after three doses of vaccine. The duration of protection against hospitalization is unclear, but is expected to last longer than protection from symptomatic disease.

- Using Danish nationwide databases, a time-to-event analysis of VE against Omicron was conducted up to five months after a primary vaccination series with the Pfizer or Moderna vaccines.[45] Among those who had recently completed primary vaccination, VE against Omicron was 55.2% (95% confidence interval: 23.5 to 73.7%) and 36.7% (-69.9 to76.4%) for recipients of the Pfizer vaccine and Moderna vaccine, respectively, but both waned rapidly within five months. VE for individuals who had received a booster dose 14 to 44 days earlier was 54.6% (30.4 to 70.4%)

- The Sisonke 2 trial enrolled healthcare workers just before the onset of the Omicron wave in South Africa, permitting an evaluation of a homologous boost of the Johnson & Johnson vaccine in preventing hospital admissions.[46] The authors estimated the VE of the Johnson & Johnson vaccine booster (given six to nine months after initial dose) in 69,092 healthcare workers as compared to unvaccinated individuals enrolled in the same managed care organization. Using a test negative design and adjusting for confounders, the authors reported that VE for hospitalization increased over time since booster dose, from 63% (95%CI 31-81%) to 84% (95% CI 67-92%) and then 85% (95% CI: 54-95%), 0-13 days, 14-27 days, and 1-2 months post-boost.

- A study by Beth Israel Deaconess Medical Center comparing different vaccine regimens, demonstrated that a heterologous Johnson & Johnson booster in individuals who initially received the Pfizer vaccine generated a 41-fold increase in neutralizing antibody responses by four weeks, and a 5-fold increase in CD8+ T-cells to Omicron by two weeks.[47] In contrast, a homologous boost with Pfizer generated a 17-fold increase in neutralizing antibodies by four weeks following the boost and a 1.4-fold increase in CD8+ T-cells by two weeks.

- Using a logistic additive model with a test negative case control design to estimate relative VE against becoming a confirmed case with Delta (2,553 cases) and/or Omicron (1,001 cases) in a population of 1.2 million people in Scotland, it was reported that protection from vaccine-acquired and infection-acquired immunity was greatly reduced against Omicron compared to Delta. VE in individuals 14 days post full primary course of AstraZeneca vaccine were negative against Omicron and only 16% against Delta. VE in individuals with two doses of Pfizer or Moderna was significantly lower for Omicron than Delta (6.84% versus 56.53%) and (8.83% versus 60.07%), respectively.[24] VE increased significantly following a third booster dose of Pfizer or Moderna to 91.87% and 89.28% against Delta and 67.57% and 71.15% against Omicron. Waning of protection lead to very low levels of protection against Omicron in double vaccine recipients of AstraZeneca, Pfizer or Moderna (5.19%, 24.39% and 24.86% respectively). The authors estimated current protection against Omicron in recipients of a third booster dose of Pfizer or Moderna to be approximately 59.21% and 64.9%, respectively. The level of protection from previous infection was 53.2% for Omicron, and 88.7% for Delta. This was greater than two doses of vaccine but not as high as three doses in those without previous infection.

In-Vitro and Modelling Evidence of Vaccine Efficacy

Since the previous risk assessment,[2] more *in vitro* and *in silico* evidence has emerged demonstrating reduced ability of convalescent sera or vaccine-induced antibodies to neutralize Omicron compared to 'wildtype' or other SARS-CoV-2 VOCs.[24,29,48-57] Additional studies have reported evidence that heterologous vaccination regimens (adenoviral and mRNA platforms) elicit a stronger antibody immune response than homologous regimens, though the relative benefit to CD4+ and CD8+ T cell immunity remains unclear.[27,55,56,58] Several studies have reported that despite the numerous mutations in Omicron, CD4+ and CD8+ T cell recognition of Omicron is largely preserved.[50,56,58-61] There is also 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.[57,62,63] Lastly, there are more *in silico* and electron micrograph studies reporting evidence of immune evasion resulting from Omicron mutations.[31,32,64,65] A few reports are highlighted below.

- A study of the neutralizing antibodies and T-cell responses to wildtype, Beta, Delta, and Omicron in a cohort of 60 health care workers after immunization with Johnson & Johnson, AstraZeneca, Moderna and Pfizer showed high binding antibody levels against 'wildtype' spike (S) 28 days after vaccination with both mRNA vaccines, but it significantly decreased after 6 months.[50] In contrast, antibody levels were lower after Johnson & Johnson vaccination but did not wane. Neutralization assays with authentic virus showed Omicron-specific responses were significantly lower or absent (up to a 34-fold decrease compared to 'wildtype'). Pfizer booster vaccination after either two Moderna or AstraZeneca priming partially restored neutralization of the Omicron variant, but responses were still as high as 17-fold decreased compared to 'wildtype'. CD4+ T-cell responses were detected up to 6 months after all vaccination regimens; S-specific T-cell responses were highest after Moderna vaccination. No significant differences were detected between 'wildtype'- and variant-specific T-cell responses, including Omicron, suggesting minimal escape of T-cell immunity.

- A longitudinal study of AstraZeneca/AstraZeneca (n=41) and AstraZeneca/Pfizer (n=88) vaccinated individuals showed that a third dose greatly augmented anti-spike (S) IgG but only moderately increased spike-specific CD4+ and CD8+ T cells in both groups.[56] The third dose restored neutralizing antibody responses against Alpha, Beta, Gamma, and Delta, but neutralizing activity against Omicron remained severely impaired. Boosting of the heterologous AstraZeneca/Pfizer immunized group led to a significant 47.9-fold increase for anti-S IgG ($p<0.0001$) and 8.0-fold increase in individuals after homologous AstraZeneca vaccination ($p<0.0001$). 9/29 (31%) and 27/58 (47%) of vaccinees in the AstraZeneca/AstraZeneca and AstraZeneca/Pfizer group, respectively, had no detectable neutralization activity after boost. Therefore, homologous AstraZeneca/AstraZeneca vaccination can be well boosted by a heterologous Pfizer vaccination. However, prior heterologous AstraZeneca/Pfizer vaccination provides no additional benefit for spike-specific T cell immunity or neutralizing Omicron after the third dose.

- An assessment of Omicron-specific humoral and cellular immune responses in 65 individuals who were vaccinated with two doses of Pfizer and were then boosted after at least 6 months with either Johnson & Johnson (n=41) or Pfizer (n=24) showed detectable but low pseudovirus neutralizing antibody responses to the 'wildtype', Delta, and Beta variants and largely undetectable to the Omicron variant.[58] Johnson & Johnson-boosted median Omicron-specific neutralizing antibody titers 41-fold. Pfizer-boosted median Omicron-specific neutralizing antibody titers 17-fold increase. Johnson & Johnson boosting led to peak antibody titers at week four or later, whereas Pfizer boosting led to peak antibody titers at week two that declined by week four. Antibody responses were substantially reduced to Omicron compared with 'wildtype', but CD8+ and CD4+ T cell responses were similar for Omicron and 'wildtype', suggesting substantial cellular immune cross-reactivity. Johnson & Johnson boosted median Omicron-specific CD8+ T cells by 5.5-fold from 0.017% to 0.093% and Omicron-specific CD4+ T cells by 3.1-fold from 0.030% to 0.092%. Pfizer increased Omicron-specific CD8+ and CD4+ T cells by 1.4-fold.

Breakthrough Infections

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

- In Ontario, from October 31, 2021 to December 29, 2021, 14.4% of Omicron/SGTF cases were reported as unvaccinated and 77.3% were reported as breakthrough cases[9] (breakthrough cases include those with a symptom onset date that was 14 days following completion of a vaccine series or 0 to <14 days after a booster dose).A high proportion of the cases being breakthrough cases is because the majority of people in Ontario are vaccinated. Individuals with at least two doses of vaccine are significantly less likely to contract COVID-19, be hospitalized for COVID-19, or admitted to the ICU, compared to those who are unvaccinated.[66]

- A study of 1,313 symptomatic Omicron patients in Texas from late November 2021 through December 20, 2021 reported that 675/1313 (51.4%) Omicron patients met the CDC definition of vaccine breakthrough cases.[41] There was no clear relationship between time since vaccination and the breakthrough infection. The patients had either received two doses of Pfizer (n=485, 72%) or Moderna (n=157, 23%), or one dose of Johnson & Johnson (n =33, 5%) vaccine. Compared to either Alpha or Delta patients, a significantly greater percentage of breakthrough cases were caused by Omicron (51.4% compared to 3.2% and 24.3% for Alpha and Delta VOCs, respectively). The authors reported that 140 (10.7%) of the 1,313 Omicron patients had a breakthrough infection after having a booster vaccine.

- In Denmark, from November 21 to December 28, 2021, 82.7% of Omicron cases were in individuals 12 years and older who had completed a primary vaccination schedule.[18]

- Between November 22 and December 19, 2021, 70,983 PCR positive SARS-CoV-2 samples in the Netherlands were analyzed to compare the risk of Omicron (based on SGTF) compared to Delta in vaccinated and previously infected individuals.[67] Of the Omicron cases, 789 (85%) were fully vaccinated compared to 62% of non-SGTF (other VOC) cases, and 2.8% had a previous infection compared to 1.3% of the non-SGTF cases. The authors reported an adjusted odds ratio of 5.0 (95% CI: 4.0-6.1) for the association between full vaccination and an Omicron infection. Similarly, an adjusted odds ratio of 4.9 (95% CI: 3.1-7.7) was reported for previous infection and Omicron infection.

- A study describing the genomic profile and early transmission dynamics of Omicron in South Africa reported that the proportion of the population with immunity against Delta and earlier VOCs was likely above 60%.[68] Therefore, the authors suggest that partial immune evasion was a major driver for the observed dynamics of Omicron in South Africa, but an increase, or decrease in transmissibility of Omicron compared to Delta cannot be ruled out.

Reinfection

The following new findings since are consistent with previous reports that Omicron can evade immunity after natural infection.[2,4,5]

- An analysis of UK data revealed that SARS-CoV-2 reinfections were occurring at 1-3% across all age groups throughout September to November 2021 (likely Delta), but in early December 2021, there was a significant increase in the reinfection rate in nearly all age groups, but in particular the young.[69]

- A high-throughput neutralization assay reported that from one and six months post- non-Omicron SARS-CoV-2 infection, the neutralization titers against Omicron were 15.8- and 4.4-fold lower than those against 'wildtype'.[70]

- A study evaluating whether neutralizing immunity elicited by Omicron also enhances neutralizing immunity of the Delta variant investigated samples from previously vaccinated (n=3 with two doses of Pfizer, n=4 with Johnson & Johnson) and unvaccinated (n=4) individuals who were infected during the Omicron wave in South Africa. The authors reported that neutralization of Omicron (live virus) increased 14-fold from enrollment to a median of 14 days, as well as enhanced Delta virus neutralization, which increased 4.4-fold.[71] The increase in Delta variant neutralization in individuals infected with Omicron may result in decreased ability of Delta to re-infect those individuals.

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 4, 2022: Denmark, England, Finland, France, Germany, Ireland, Israel, Italy, Netherlands, Norway, and Portugal.

Changes to Public Health Measures

All included jurisdictions have implemented public health measures in response to the emergence of Omicron, and some jurisdictions are continuing to tighten public health measures and increase vaccination programs as Omicron continues to surge (i.e., since the last Omicron risk assessment). Since the last Risk Assessment, the following changes to public health measures were identified in select jurisdictions:

- In Israel, effective December 30, 2021, masks are required for outdoor gatherings over 50 people.[72]
- In France, effective January 3, 2021 (for three weeks), all public gatherings will be limited to 2,000 people for indoor events and to 5,000 people for outdoor events. Spectators at concerts will all have to be seated. Consumption of drinks and food will be banned in long-distance transport and cinemas, and work from home will become mandatory for at least three days per week where possible. Mask-wearing will be mandatory in town centres, with local authorities in charge of enforcing the measure, and in bars and restaurants only seated customers will be able to consume food and drinks.[73]
- In Italy, effective December 30, 2021 to March 31, 2022, visits to residential, social-welfare, social-health and hospice facilities are permitted only to those with a super Green Pass (i.e., vaccine certificate showing proof of vaccination or recovered from COVID-19) and negative swab or vaccination with a third dose.[74]

Changes to Vaccination Programming

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

- On January 3, 2022, the US Food and Drug Administration (FDA) authorized the use of a third dose of the Pfizer COVID-19 vaccine for children ages 12 to 15, and narrowed the interval for booster shot eligibility to five months from six.[75] The CDC's immunization advisory panel will meet January 5, 2022 to discuss recommendations.
- As of January 3, 2021, children ages 5 – 11 in Ireland are eligible for the COVID-19 vaccine.[76]
- On January 2, 2022, Israel's Prime Minister announced approval of a fourth COVID-19 vaccine dose for people over 60 and medical staff.[77] Previously, fourth doses were approved for high-risk populations.[78]

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 increased disease severity is moderate with a high 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 sheer volume of severe cases due to increased transmission also presents risks to health system capacity.
- It is estimated that each Omicron case is infecting 4.5 times more individuals than Delta (95% CI: 4.0 to 5.1) in Ontario during the November 28 to December 16, 2021 period.[79]
- The overall risk assessment may change as new evidence emerges (see Table 1).

Table 1. Risk Assessment for Omicron B.1.1.529

Issue	Risk Level	Degree of Uncertainty
Increased Transmissibility	**High**	**Low**
Disease Severity	**Moderate**	**High**
COVID-19 Re-infection	**High**	**Low**
Lowered Vaccine Effectiveness/Breakthrough Infections	**High**	**Low**
Impacts on Testing/Surveillance	**Moderate**	**Low**

Implications for Practice

The epidemiology of Omicron has become more challenging to interpret due to the exponential increase in Omicron cases and rapid increase in testing demand. Consequently, some jurisdictions have changed their testing policies, thereby making metrics such as the reproduction number and case rate less accurate.

While limitations remain with regards to the Omicron severity literature, the bulk of the evidence suggests Omicron causes less severe disease than Delta, with some reports suggesting Omicron causes similar disease severity as Delta. In either case, the sheer number of cases is predicted to overwhelm many health systems. The increasing community prevalence of Omicron will likely result in many individuals presenting at hospitals for non-COVID-19 reasons but with a SARS-CoV-2 infection. The potential impact of SARS-CoV-2 infection on chronic and underlying medical conditions — that have been unmonitored due to the pandemic – remains unclear, but an anecdotal report early in the hospitalization surge in the US suggests those being admitted for chronic conditions are also testing positive for SARS-CoV-2 and we do not know the nature of the correlation at this time.[80]

Many studies have emerged reporting measures of vaccine effectiveness and many more studies of measures related to vaccine effectiveness (e.g., antibody neutralization assays). Nevertheless, generalizability of these studies is made challenging by differences in the history of infection in the study participants, vaccination programming (i.e., homologous vs. heterologous vaccine schedules, interval between doses, third dose eligibility criteria), population age distribution, and whether public health measures were in place during the study period (e.g., vaccine certificates, mask mandates, 'lockdowns'). Increased transmissibility of the Omicron variant leading to exponential growth, coupled with immune evasion (due to Omicron mutations and waning immunity), remains highly concerning for health system capacity. 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.[81,82]

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