Key Messages

- The Omicron variant is resulting in many more SARS-CoV-2 transmissions than the Delta variant. It is estimated that each Omicron case is infecting 4.5 times more individuals than Delta in Ontario. The relative contributions of increased transmissibility inherent in the Omicron variant and immune evasion (due to Omicron mutations and waning immunity), is unclear.

- Two doses of COVID-19 vaccines are less effective at preventing Omicron breakthrough infections, compared to protection against other variants of concern (VOC) and ‘wild-type’ SARS-CoV-2. A third vaccine dose increases short-term protection against symptomatic Omicron infection. The duration of protection from a third dose is unclear.

- While limitations remain with regards to the Omicron severity literature, early data from South Africa, the United Kingdom (UK), Denmark, and Ontario, suggest a decreased odds of hospitalization for Omicron cases compared to Delta cases in the overall population. There is insufficient data to comment on mortality or severity of illness once in hospital.

- With risks to health care system capacity as a result of high community transmission levels, several jurisdictions are implementing more restrictive public health measures (e.g., closures of indoor public venues, enhanced vaccine certificates, mask mandates, and gathering limits) and changes in vaccine programs.

- 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 globally, and its rapid case growth in Ontario, increased community-based public health measures accompanied by ongoing accelerated vaccination efforts (e.g., third doses) is needed 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,⁴ Omicron has become the dominant severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variant in many countries. Since the last report on December 21,² more evidence has emerged of Omicron’s transmissibility and potential immune evasion, and early evidence regarding disease severity. This evidence brief updates the Public Health Ontario (PHO) reports from December 1, 2021, December 7, 2021, December 13, 2021, and December 21, 2021, and summarizes available information and evidence on the Omicron VOC relevant to the risk of importation and transmission in Ontario up to December 27, 2021. Data from Ontario was available up to December 30, 2021.

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

- Omicron is the dominant variant across provinces and territories in Canada, with the majority of provinces reporting record high single day case numbers on December 29, 2021.³⁴

- The Ontario 7-day COVID-19 case average surged from 838 on December 1, 2021 to 3,872 on December 22, 2021.⁵ Ontario’s SARS-CoV-2 reproduction number was below 1.1 for much of Fall 2021; however, it increased from 1.12 on December 1, 2021 to 1.62 (95%CI: 1.61, 1.63) on December 29, 2021.⁶ From October 31 to December 27, 2021, Ontario reported a total of 22,398 Omicron cases (confirmed by whole genome sequencing, WGS or based on S-Gene Target Failure [SGTF]).⁷

- SGTF is a genetic marker that can be used as a screening method for identifying the Omicron variant (99.5% sensitivity, 99.8% specificity, 99.4% positive predictive value, 99.5% negative predictive value, relative to WGS).⁸ On December 23 and December 28, 2021 the proportion of samples tested at the PHO laboratory with SGTF detected was 81.8% and 80.4% respectively, indicating that Omicron is the dominant variant circulating in Ontario.

- Of note, SARS-CoV-2 diagnostic laboratories may have discontinued submitting samples to PHO laboratory for SGTF testing as of December 25, 2021. PHO laboratory is expected to discontinue SGTF testing on December 30, 2021.⁹

- A December 23, 2021 technical brief update from the World Health Organization (WHO) Headquarters reported Omicron to be spreading significantly faster than the Delta variant in countries with documented community transmission, with a doubling time between two to three days.¹⁰ As of December 22, 2021, the Omicron variant was identified in 110 countries across all six WHO Regions. Omicron is likely present in more jurisdictions but not yet detected.
Notable epidemiological trends from several countries relevant to Ontario are:

- From November 30, 2021 to December 23, 2021, the percent of SARS-CoV-2 cases in Denmark that are Omicron increased from 0.4% to 79%.\(^{11}\)
- The UK reported a 30.3% increase in confirmed Omicron cases between December 22 to 28, 2021.\(^{12}\) Doubling times for the number of tests with SGTF in every UK region was reported to be less than 2.5 days.\(^{13}\)
- The UK Health Security Agency’s December 21, 2021 Omicron daily overview reported 56,041 confirmed cases, 129 hospitalizations, and 14 deaths in England, which increased to 181,547 confirmed cases, 766 hospitalizations, and 53 deaths in the December 29, 2021 report.\(^{14,15}\)
- In the United States (US), the first case of Omicron was identified on December 1, 2021.\(^{16}\) By December 11, 2021, Omicron accounted for 12.6% of SARS-CoV-2 infections, by December 18, 2021, 22.5% of cases, and by December 25, 2021, 58.6% of cases.\(^{17}\) A new study reported that many US cities are at risk for surges of COVID-19 during the winter and spring of 2022 that might strain hospital capacity.\(^{18}\) This finding is consistent with the Centers for Disease Control and Prevention (CDC) Center for Forecasting and Outbreak Analytics December 20, 2021 report and previous modelling from other jurisdictions, which anticipate surges of hospitalizations even if severity is reduced, because of the large number of cases in a short period of time.\(^{19-22}\)

Transmissibility

On December 20, 2021, the CDC estimated that Omicron may have 1.6-fold increased transmissibility compared to Delta.\(^{22}\) On December 23, 2021, the WHO released their technical brief indicating that there is consistent evidence that Omicron is spreading significantly faster than Delta,\(^{10}\) which has also been suggested by other health agencies and research articles.\(^{3,23-27}\) It is also documented that there is observed community transmission, with a doubling time of two to three days.\(^{10}\) Modelling and in-silico analyses support current epidemiological findings and identify potential mechanisms behind the higher transmission of Omicron relative to previous variants and wild-type SARS-CoV-2.

Epidemiological Evidence

- Out of 33 people who attended a private gathering in early December 2021 in the Faroe Islands, 21 tested positive for SARS-CoV-2 (attack rate = 63.6%). The high attack rate triggered targeted sequencing for Omicron and found 13 samples from the gathering and 4 from infected contacts were confirmed Omicron (these being the first Omicron cases detected in the Faroe Islands). The median age was 45 years. The mean incubation period was 3.24 days (95% CI: 2.87–3.60), assuming the exposure was at the gathering.\(^{28}\)
In-Silico and Modelling Evidence

- It has been reported that the mutations on the Omicron variant may increase transmissibility by enhancing ACE2 binding, enhancing cleavage at the S1/S2 junction, and the ability to replicate faster than other variants.\(^{29-31}\)

- The human ACE2 (hACE2) receptor is used by SARS-CoV-2 to enter host cells; therefore, higher binding affinity could lead to increased infectivity and transmission. Modeling Spike protein (S-protein) mutations which may lead to potential alterations in hACE2 binding can aid in predicting the transmissibility and infectivity of Omicron. Since the last risk assessment, another in silico analysis has reported higher binding affinity between the Omicron S-protein and hACE2 (compared to other SARS-CoV-2 variants).\(^{32}\)

- Using a SARS-CoV-2 virus-like particle (SC2-VLPs) system that reflects the impact of mutations in Omicron’s four structural proteins on both infection efficiency and antibody or antisera neutralization, it was reported that Omicron showed increased infectivity compared to B.1, B.1.1 variants, attributed to S and N protein mutations.\(^{33}\)

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, but the clinical presentation remains unclear.\(^2\)

- Data from England identified that only 50% of current cases experience the classic three COVID-19 symptoms of fever, cough, and loss of taste and smell.\(^{34-36}\) Though not the most prevalent symptoms reported, new symptoms of Omicron that are being reported include loss of appetite and brain fog (e.g. memory problems, difficulty concentrating, and not being able to think clearly )\(^37\)

- In a cohort of 6,287 pediatric COVID-19 cases in Tshwane District, South Africa, 183 were hospitalized. Detailed clinical information was available for 139 (76%) of the 183 children hospitalized. Ages of those hospitalized ranged from newborn to 13 years, with most admissions in the <1 year age group (35%), and 62% of children in the 0-4 years category. Among this group symptoms included fever (47%), cough (40%), vomiting (24%), difficulty breathing (23%), diarrhoea (20%) and convulsions (20%). For those hospitalized, mean length of hospital stay was 3.2 days.\(^{38}\)

- The analysis of an Omicron outbreak at a private gathering among triple-vaccinated healthcare workers in the Faroe Islands, reported that all infected individuals (21/33 attendees) were symptomatic. The most common symptoms were muscle and joint pain, fatigue and fever.
Disease Severity

There remain limitations with the Omicron severity literature; however, more evidence of lower severity for Omicron compared to Delta cases is emerging from jurisdictions outside of South Africa, including from Ontario.\textsuperscript{39-43} There is insufficient data to comment on severity of illness once in hospital or mortality.\textsuperscript{36} Severity data have several limitations because patients with mild presentations are more likely to be admitted as a precaution, there has not been sufficient follow-up time for severe outcomes to have accumulated, and there have not been enough cases to properly represent entire populations.\textsuperscript{2} Using hospital admissions as a proxy for disease severity is also complicated by SARS-CoV-2 screening at hospitals upon admission where a patient is positive for SARS-CoV-2 but is hospitalized for an alternate reason and does not require COVID-19 related care.\textsuperscript{2}

- An Ontario matched cohort study of hospitalization and death associated with Omicron (6,314 cases) compared to Delta (8,875 cases)(with adjustment for vaccine doses and time since vaccination) reported a 54% lower (hazard ratio=0.46, 95%CI: 0.27, 0.77) adjusted risk of hospitalization or death among Omicron cases compared to Delta cases. Omicron cases had 21 (0.3%) hospitalizations and 0 (0%) deaths, compared to 116 (2.2%) hospitalizations and 7 (0.3%) deaths among matched Delta cases.

- In Scotland, the observed hospitalizations among SGTF cases was 0.32 times the expected hospitalizations compared to non-SGTF cases.\textsuperscript{41} This analysis included patients who tested positive for COVID-19 between November 1 and December 19, 2021, including 119,100 non-SGTF cases and 22,205 SGTF cases.\textsuperscript{41}

- In a technical briefing by the UK Health Security Agency,\textsuperscript{42} it was reported:
  - As of December 20, 2021, a total of 14 people have died within 28 days of an Omicron COVID-19 diagnosis in England. The median time from Omicron specimen date to death was four days (range 1 to 10). The age of those dying ranged from 52 to 96 years.
  - A preliminary analysis of 114,144 Omicron cases and 461,772 Delta cases occurring between November 22 and December 19, 2021 was undertaken to assess the risk of hospital admission and emergency care attendance among cases. Stratified Cox proportional hazard regression assessed that the risk of presentation to emergency care or hospital admission with Omicron was approximately three-fifths of that for Delta (hazard ratio 0.62, 95% CI: 0.55 to 0.69). The risk of hospital admission alone with Omicron was approximately two-fifths of that for Delta (hazard ratio 0.38, 95% CI: 0.30 to 0.50).

- Imperial College examined hospitalization data in England for cases with specimen collection dates between December 1 – 14, 2021 and indicated a reduction in the risk of hospitalization for infection with Omicron relative to the Delta variant.\textsuperscript{43} Omicron cases were estimated to have a 20-25% reduced risk of any hospitalization (including Accident and Emergency departments) and a 41% (95% CI: 37%-45%) reduced risk of a hospitalization resulting in a stay of one or more nights.\textsuperscript{43}

- Data from Denmark published on December 21, 2021 show that 0.6% of cases of Omicron have been hospitalized, compared with 1.6% of those infected with other SARS-CoV-2 variants.\textsuperscript{10}
Using samples collected from the lower respiratory tract, researchers at Hong Kong University found that the Omicron variant replicates faster (up to 70 times faster) in the human bronchi compared to the Delta variant and wild-type SARS-CoV-2 virus. In contrast, the Omicron variant demonstrated slower replication in the lung relative to the other strains. This replication pattern is thought to explain the less severe clinical presentation of patients infected with the Omicron variant.

In a media report, the chief medical officer and vice president at Texas Children's Pediatrics & Urgent Care stated that an increase in the number of children hospitalized in the United States is to be expected in January 2022. However, at other hospital sites, although the number of COVID-positive children is increasing in the hospital setting, many are presenting to hospital for other treatments, screening positive and not necessarily coming in with COVID symptoms. While there is little evidence the Omicron variant is causing more severe disease in children than previous variants did, there is also no evidence it is milder.

An analysis of 11,495 COVID-19 infections in South Africa compared risk of hospitalization between SGTF infections (presumed Omicron) and non-SGTF infections. The study included those diagnosed with TaqPath PCR between October 1 and November 30, 2021 (about 7% of COVID-19 cases reported nationally during that time). The crude hospitalization rates were 2.5% of SGTF infections and 12.8% of non-SGTF infections. After adjusting for age, sex, and co-morbidities, the odds of hospitalization for individuals with SGTF infections was 0.2 the odds of hospitalization for those with non-SGTF infections. Among those hospitalized, SGTF infections had equal odds of severe disease compared to non-SGTF infections (adjusted odds ratio 0.7, 95% CI 0.3-1.4).

During a six-week period (October 31, 2021 to December 11, 2021), 6,287 pediatric (≤ 19 years) COVID-19 cases were recorded in Tshwane District, South Africa. Of these, 462 (7.2%) were hospitalized which was an unexpected rise from the first three waves.

Vaccine Effectiveness (VE)

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. There is increasing evidence that a third vaccine dose increases short-term protection against symptomatic Omicron infection, and early evidence of reduced vaccine effectiveness around nine to ten weeks after a third dose.

In a test-negative study, researchers in Scotland reported a third vaccine dose was associated with a 57% reduction in the odds of developing symptomatic disease from SGTF COVID-19, relative to ≥25 weeks post second vaccine dose. In a test-negative case study, it was found that among individuals who received an AstraZeneca primary course, VE was around 60% two to four weeks after either a Pfizer or Moderna booster, then by 10 weeks dropped to 35% and 45%, for Pfizer and Moderna, respectively. Among those who received a Pfizer primary course, vaccine effectiveness was around 70% after a Pfizer booster, dropping to 45% after 10-plus weeks and stayed around 70 to 75% after a Moderna booster up to nine weeks after booster.
Breakthrough Infections

- In Denmark, of individuals ≥12 years infected with Omicron from November 22 to December 18, 2021, 76.5% had completed a two-dose vaccine series, compared to 64.6% of other VOC cases. This suggests that breakthrough Delta cases due to waning immunity can also contribute to cases in settings where Delta is still circulating and immunity is waning from the primary vaccination series. It is worth noting that 13.5% (3,650/27,132) of Omicron cases were boosted, and 8.5% (7,276/85,967) of other VOC cases were boosted.

- The analysis of an Omicron outbreak at a private gathering in the Faroe Islands, reported that all infected participants had received a third dose of BNT162b2 vaccine within the last two and a half months.

Reinfection

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

- A study found that the risk of re-infection for SGTF COVID-19 was 10 times higher than for non-SGTF. This analysis included patients who tested positive for COVID-19 in Scotland between November 1, 2021 and December 19, 2021, including 119,100 non-SGTF cases and 22,205 SGTF cases. 7.6% of SGTF cases had been previously infected, while only 0.7% of non-SGTF cases had previously been infected.

- Of 116,683 individuals identified with an Omicron infection between November 1 and December 18, 2021, 11,103 individuals (9.5%) were linked to previous confirmed infection (by PCR or rapid antigen testing). The interval to reinfection from previous SARS-CoV-2 infection ranged from 90 to 650 days, with a median of 343 days. This was the third episode of infection for 69 individuals (>=90 days between each episode).

In-Vitro and Modelling Evidence of Vaccine Efficacy

Since the previous risk assessment, more in vitro and in silico evidence has emerged demonstrating reduced ability of existing convalescent or vaccine-induced (largely Pfizer, Moderna, AstraZeneca) antibodies to neutralize Omicron, compared to other VOCs. Although sample sizes continue to be small, and studies are largely not peer-reviewed, the trends are consistent across studies. Since the last risk assessment, there are more studies reporting that a third dose significantly boosts the neutralization of Omicron compared to two doses of Pfizer, Moderna, AstraZeneca or heterologous vaccine combinations (based on in vitro neutralization using sera from vaccine recipients); however, neutralization ability is still reduced compared to wild-type and other VOCs. A few reports are highlighted below.

- Four weeks after two standard Moderna vaccines, it was found that Omicron was 41 to 84-fold less sensitive to neutralization than the D614G variant and 5.3 to 7.4-fold less sensitive than the Beta variant. Seven participants received 50 ug booster doses at least four months from their second dose and neutralization titers post-boost were more modestly reduced than after second doses.
• Using a SARS-CoV-2 virus-like particle (SC2-VLPs) system that reflects the impact of mutations in Omicron’s four structural proteins on antibody neutralization, a study (n = 38) reported the sera from individuals four to six weeks post-vaccination with Pfizer or Moderna showed strong neutralizing activity of the ‘wildtype’ spike protein (B.1, B.1.1), but a 3-fold reduced efficacy against Delta and 15-reduced neutralization against Omicron VLPs. The sera from individuals vaccinated with Johnson & Johnson showed minimal neutralization.33

• One study reported that plasma from recipients of two mRNA vaccine doses were 30- to 180-fold less potent against Omicron than Wuhan-hu-1. Individuals who were previously infected or had two doses of an mRNA vaccine who received additional mRNA vaccine dose(s) had 38 to 154-fold increases in neutralizing activity against Omicron.53

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 December 27, 2021: 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) (e.g., Denmark, England, Finland, France, Ireland, Italy, Norway, Portugal, Israel).

• In some jurisdictions, immunity certificates are now required in more settings than previously (e.g., Denmark, England, Finland, France, Germany, Ireland, Italy, Portugal, California, Israel),70 and eligibility for immunity certificates is more restrictive (e.g., how long a negative test result is valid or the duration of validity of the most recent vaccine dose) in some jurisdictions (e.g., Denmark, France, Italy).71-83

• Some jurisdictions implemented mask mandates in indoor settings (e.g., Denmark, England, France, Ireland, Netherlands, Norway, Portugal, California, New York State), on public transport (e.g., Denmark, England, Ireland, Norway), or at outdoor events (e.g., Germany, Italy).71-73,75,77-79,84-92

• Capacity limits were introduced at hospitality and cultural venues and/or places of worship (e.g., Denmark, Germany, Ireland, Netherlands), business hours were reduced at non-essential businesses (e.g., Denmark, Ireland, Netherlands), venues and schools temporarily closed (e.g., Denmark, France, Ireland, Italy, Norway, Portugal, the Netherlands), and large events were cancelled (e.g., Denmark, Germany, Netherlands). In some jurisdictions, there is national guidance limiting private gatherings as well (e.g., France, Germany, Ireland, Norway, Netherlands).73-76,79,88,91-102 Remote work was recently recommended in some jurisdictions (e.g., Denmark, France), while other jurisdictions mandated it (e.g., England, Finland, Ireland, Norway, Portugal, the Netherlands).80,88,93,103-105 Additional vaccine mandates were announced and/or implemented for some workforces (e.g., healthcare workers, police force, military) (e.g., Finland, Italy).106,107

• There is increasing discussion of calling for a state of emergency or ‘lockdown’ (e.g., England), with some jurisdictions implementing “a partial lockdown” (e.g., Norway) or a ‘lockdown’ (e.g., Netherlands).91,108,109
Changes to Vaccination Programming

- Since the identification of Omicron, some of the jurisdictions reviewed here have updated their COVID-19 vaccination programs.  

- On December 13, 2021, the UK announced more than 750 Armed Forces personnel would be administering COVID-19 vaccines and helping to plan a large-scale booster rollout to maximize effectiveness. The armed forces and pharmacies in Norway have also been called upon to speed up delivery of vaccinations.

- Several jurisdictions have expanded eligibility for booster doses (e.g., Denmark, England, Finland, France, Germany, Ireland, Norway, Portugal, the Netherlands) and/or shortened the minimum interval between completion of a vaccination series and a booster dose (e.g., three months in England, Ireland, Israel, five to six months in Finland, five months in France, Italy and Portugal, 4.5 months in Denmark). Israel will offer a fourth dose to residents who got their third dose at least four months ago.

- Some jurisdictions have started vaccinating vulnerable children and children residing with vulnerable individuals (e.g., Germany) or children 5 to 11 years old in general (e.g., Denmark, England, Finland, France, Ireland, Italy, Portugal).

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.

- Using projections that account for time lags in the incubation period (five days) and case presentation (two days), most cases infected on December 20, 2021 (>90%) are likely to be of the Omicron variant.

- 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.

- The overall risk assessment may change as new evidence emerges (see Table 1).
Table 1. Risk Assessment for Omicron B.1.1.529

<table>
<thead>
<tr>
<th>Issue</th>
<th>Risk Level</th>
<th>Degree of Uncertainty</th>
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<tbody>
<tr>
<td>Increased Transmissibility</td>
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<td>Low</td>
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<tr>
<td>Disease Severity</td>
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<td>High</td>
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<tr>
<td>COVID-19 Re-infection</td>
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<td>Low</td>
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<td>Lowered Vaccine Effectiveness/Breakthrough Infections</td>
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<td>Low</td>
</tr>
<tr>
<td>Impacts on Testing/Surveillance</td>
<td>Moderate</td>
<td>Low</td>
</tr>
</tbody>
</table>

Implications for Practice

The epidemiology of Omicron will become more challenging to interpret, and changes in reproduction number will need to consider additional variables. For example, the exponential increase in Omicron cases has resulted in a rapid increase in testing demand, which is increasing the lag time for results and causing underestimates in metrics such as effective reproduction number and case rate. Increased capacity of rapid antigen testing in the community is also likely contributing to an underestimation in case rate as these results are not reported to local public health units.

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.

Although the current challenges require increased efforts on public health measures and vaccination, the unknown duration of third dose protection from Omicron needs consideration in future planning and response.
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Citation


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