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EVIDENCE BRIEF

(ARCHIVED) COVID-19 Delta: Risk Assessment and Implications for Public Health Measures

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Key Messages

- Since March 2021, Alpha (B.1.1.7) was the dominant circulating strain of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in Ontario. However, as of June 28, 2021, the majority (56.5%) of COVID-19 cases in Ontario are infected with a variant that test negative for both N501Y and E484K mutations, signalling that Delta (B.1.617.2) is now dominant in Ontario.
- Large-scale outbreaks with Delta have been reported especially where there was a large susceptible population (partially vaccinated or unvaccinated), and early identification and case isolation were challenging.
- Emerging data indicate that Delta has increased transmissibility and increased severity, after controlling for other variables. The case fatality rate is reported as lower than Alpha although the current estimate is subject to uncertainty.
- Vaccine effectiveness against hospitalization with Delta was similar to Alpha, but there is evidence of reduced vaccine effectiveness (VE) for symptomatic disease after one vaccine dose, meaning two-dose vaccination coverage is important in the context of Delta.
- Increased vaccination coverage of the overall population would be required to approach herd immunity given the estimated higher transmissibility and slightly lower VE of Delta compared to Alpha.
- The risk of Delta transmission in Ontario is moderate to high, and depends on the number of existing Delta cases and continued introductions into areas of the province with currently low Delta cases.

Issue and Research Question

Current evidence points to higher transmissibility and secondary attack rates (SARs), and possible higher risk of hospitalization, for the variant of concern (VOC) Delta.[1] Meanwhile, epidemiological data from Ontario indicate that Delta has replaced Alpha as the dominant strain of SARS-CoV-2 in the province.[2] Furthermore, with an effective reproduction number estimate of Delta close to 1 (threshold for exponential growth), all the gains in lowering COVID-19 case counts in the province have been from reducing Alpha transmission. With Ontario entering the Reopening Ontario roadmap on June 11, 2021 and continuing reopening as of June 30,[3] case declines will stagnate or even increase if reopening allows more Delta transmission. It is, therefore, important to consider the impact of Delta and considerations for reopening in the province.

Methods

From January 17 to June 29, 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, we 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.

For the methods in retrieving and analyzing the epidemiological data for incidence of Delta and reproduction number of the VOCs, please refer to *Estimating the Prevalence and Growth of SARS-CoV-2 Variants in Ontario using Mutation Profiles*.[4] Detailed description of the methods for estimating household SAR are presented elsewhere.[5]

As the COVID-19 outbreak continues to evolve and the scientific evidence rapidly expands, the information provided in this document is only current as of the date of respective literature searches.

Ontario Epidemiological Context

- SARS-CoV-2 cases that tested negative for the mutations N501Y and E484K (N501Y-/E484K-) include the Delta sublineage. As of June 28, 2021 PHO estimated the cases with that mutation profile represent 56.5% of all reported cases in Ontario.[4] A province-wide whole genome sequencing on 538 samples with the N501Y-/E484K- profile showed that 83% (10/12) of the samples in late May were Delta, compared to 2.2% (2/87) prior to April 4.[6] Given that there is very high concordance of N501Y-/E484K- to Delta, the dominant strain is now Delta.
- The effective reproduction number (R_e) is the average number of secondary cases of infection generated by each person infected with COVID-19 (where population includes susceptible and non-susceptible people). An $R_e > 1$ means that the overall number of new cases is growing (indication for exponential growth); an $R_e < 1$ means the overall number of new cases is decreasing and suggests that COVID-19 is coming under control. From June 22 to 28, 2021, the R_e's for the four mutation profiles are estimated as follow (note that the R_e for Delta is hovering around the threshold for exponential growth):[4]
    - N501Y+/E484K- (likely Alpha): 0.71
    - N501Y+/E484K+ (likely Beta [B.1.351, first identified in South Africa] or Gamma [P.1, first detected in Brazil]): 0.71
    - N501Y-/E484K+ (does not correspond to a VOC currently identified in Ontario): 0.93

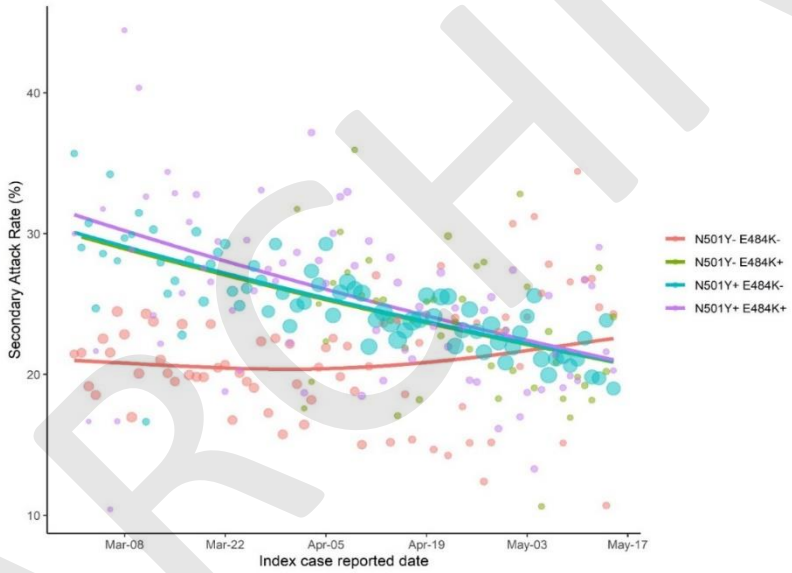
- N501Y-/E484K- (likely Delta): 0.98

- Household SAR refers to the probability that an individual with SARS-CoV-2 will transmit the disease to a household contact.[7] Starting early March 2021, SARs among household members of index cases reported between March 1 and May 15, 2021 were on the decline for mutation profiles that likely represent Alpha, Beta and Gamma, as well as those that do not correspond to a VOC currently identified in Ontario (see

- Figure 1). This decline could likely be due to increased coverage of the population by vaccination against COVID-19.

    - The red line, which represents strains of SARS-CoV-2 with neither N501Y nor E484K detected, was not in parallel with the other lines. Note that earlier in the surveillance period, this line (N501Y-/E484K-) would have represented non-VOC (i.e., pre-Alpha) specimens. Now, these profiles are a signal for Delta,[6] and since Delta is estimated to be more easily transmitted than Alpha,[8] the household secondary attack rates for that mutation profile are increasing.

Figure 1: Household Secondary Attack Rates Based on COVID-19 Mutation Profiles in Ontario, by Index Case Reported Date, March 1 to May 15, 2021



Data Source: Case and Contact Management Solution (CCM)
See also Technical Notes for data caveats and methods.

Outbreaks in Ontario

- There have been media reports of outbreaks associated with Delta in the health care[9] and residential congregate settings,[10-12] ranging in scale from under 10 cases to at least 100. Breakthrough infections that have been identified were less severe.[9] Gatherings where people were in close contact without masking and social distancing[11,12] and low vaccination rates[11,13] were deemed to be contributory factors to the scale of some of these outbreaks.

- Since its designation as a VOC, there have been 20 COVID-19 outbreaks due to Delta (including the N501Y-/E484K- mutation profile and lineage B.1.617.2 as reported by public health units).

Despite the rising incidence of Delta, a resurgence in outbreaks among long-term care homes has not been seen.[14]

Disease Severity and Implications for Health Systems

Surveillance data published from the UK provide a limited source of information as they are subject to a delay in reporting, in addition most of the cases infected with Delta, circulating more recently to Alpha, would have not completed a 28-day follow-up period which is usually used as a timeframe to report related hospitalizations and deaths.[15]

Complementary analyses undertaken in the UK and Scotland demonstrated an increased risk of hospitalisation for Delta compared to Alpha. A preprint article from Singapore suggests the potential for more severe illness with Delta compared to pre-Alpha non-VOCs.

Risk of Hospitalization or Severe Outcomes

- Public Health England (PHE) reviewed a record linkage of 43,338 sequence-confirmed Delta and Alpha cases tested between March 29 and May 23, 2021 (with hospitalization data up until June 5, 2021). After adjusting for confounders (age, sex, ethnicity, area of residence, index of multiple deprivation, week of specimen date, vaccination status and international travel within 14 days prior to specimen date), COVID-19 cases with Delta, compared to Alpha, had significantly higher adjusted hazard ratios (aHR's):[15]
    - For hospitalization within 14 days of specimen date: 2.26 (95% confidence interval [CI]: 1.32–3.89, P=0.003).
    - For visiting emergency department or hospitalization within 14 days: 1.45 (95% CI: 1.08–1.95, P=0.015).
- An ongoing study by Public Health Scotland/EAVE II to estimate risk factors for the time from test to hospitalisation among individuals who tested positive for SARS-CoV-2 from April 1, 2021 (until June 21) and who were hospitalized within 14 days of a positive COVID-19 test or who had a positive COVID-19 test within 2 days of admission. The model was adjusted for age and days from 1 April 2021, number of comorbidities, gender and vaccination status.[16]
    - An increased aHR of hospitalisation (1.8, 95% CI: 1.4 to 2.4) was observed for those who were S-gene positive (proxy for Delta) compared with those with S-gene target failure (proxy for Alpha).
- A preprint examined Singapore national data of all known COVID-19 cases, and a cohort of COVID-19 patients admitted to the national outbreak clinical management centre, to assess the impact of Delta on disease severity and reported a significantly increased risk of severe outcomes.[17]
    - From the national cohort of 2,930 COVID-19 infections between January 1 and May 22, 2021, sequence data were available for 976 (33%). A significantly increased risk of severe outcome (i.e., requiring oxygen support, admission to intensive care units, or deaths) with Delta (n=464, mostly occurring in late April and May 2021) was observed compared to non-VOCs (non-Alpha, non-Beta, non-Delta) circulating in Singapore during the same period:

- Adjusted odds ratio (aOR) = 4.90 (95% CI: 1.43–30.78; P = 0.033). Adjustment for confounders include age and gender, but not time period. When compared to those < 45 years of age:
    - aOR = 2.92 (95% CI: 2.12–4.04; P < 0.0001) for those 45–64 years of age
    - aOR = 7.06 (95% CI: 3.81–13.5; P < 0.0001) for those ≥ 65 years of age

- From a cohort of COVID-19 patients at the facility, an statistically nonsignificant increase in risk of pneumonia was observed in Delta cases (n=67; admitted between December 20, 2020 and May 12, 2021) compared to wild-types (n=846; admitted from January 22 to April 15, 2021):
    - aOR = 1.88 (95% CI: 0.95–3.76; P = 0.069). Adjustment for confounders include age, gender, comorbidities and vaccination status. When compared to those < 45 years of age:
        - aOR = 2.92 (95% CI: 2.12–4.04; P < 0.0001) for 45–64 years of age
        - aOR = 7.06 (95% CI: 3.81–13.5; P < 0.0001) for ≥ 65 years of age

Vaccine Effectiveness (Delta vs Alpha)

- As of June 24, 76% of Canadians aged 12 years and older have received ≥ 1 dose of COVID-19 vaccine, and 26% were fully vaccinated. COVID-19 infection was reported in only 0.08% of fully-vaccinated people (symptom onset ≥ 7 days after the second dose) vs. 0.14% of partially vaccinated people (symptom onset ≥ 14 days after the first dose). Most of the Delta cases were identified in those who were unvaccinated or partially vaccinated,[18] suggesting that COVID-19 vaccines are highly protective, including infections caused by Delta.

- Two UK-based preprints compared VE against infection with Delta vs. Alpha: one focused on symptomatic infection,[19] the other on hospitalization, and are described in more detail below.[20]

VE against Symptomatic Infection

- Lopez Bernal et al. compared the vaccination status of sequenced COVID-19 cases in the UK between October 26, 2020 and May 16, 2021;[19] PHE updated the data to June 11 and reported absolute reductions in VE (95% CI) against symptomatic infection with Delta compared to Alpha by 14% and 10% after one and two vaccine doses, respectively:[16]
    - 35% (32%–38%) for Delta vs. 49% (46%–52%) for Alpha ≥ 21 days after the first dose up to the day before the second dose of either Pfizer-BioNTech or AstraZeneca vaccine.
    - 79% (78%–80%) for Delta vs. 89% (87%–90%) for Alpha ≥ 14 days after the second dose of either vaccine.

VE against Hospitalization

- Stowe et al. compared the vaccination status of individuals in England hospitalized within 14 days of a positive COVID-19 test between April 12 and June 4, 2021;[20] PHE updated the data to June 11 and reported similar VE (95% CI) against hospitalization with Delta compared to Alpha:[16]

- 80% (69%–88%) for Delta vs. 78% (64%–87%) for Alpha ≥ 21 days after the first dose up to 13 days after the second dose of either Pfizer-BioNTech or AstraZeneca vaccine.
- 96% (91%–98%) for Delta vs. 93% (80%–97%) for Alpha ≥ 14 days after the second dose of either vaccine.

Impact on Herd Immunity

- The herd immunity threshold is the estimated immunity level required to keep a virus from circulating in a population without physical distancing or public health measures. The threshold applies to whole populations, but also includes contact networks like neighbourhoods, schools, etc.
- Immunity can be acquired naturally (by infection) or by vaccination, and is never complete, meaning that there remains a probability of being infected after vaccination or having a prior infection. Vaccine effectiveness quantifies this probability of infection outcome after vaccination.
- Herd immunity calculations include estimates of reproduction number and vaccine effectiveness. The herd immunity threshold may change as more information on these estimates becomes available.
- In Canada, vaccine coverage targets (fully vaccinated) were set at 75% of the population ≥ 12 years of age,[21] or 67% of the overall population. On the assumption that Delta is 1.5 times more transmissible than and twice as virulent as Alpha, and that two doses of vaccine offer 80% protection against infection with Delta, a modelling study by Public Health Agency of Canada estimates a greater than expected resurgence of COVID-19 cases this Fall/Winter as Delta becomes dominant; restrictive measures are lifted when ≥ 20% of Canadians aged 12 years and older are fully vaccinated; and personal protective measures are lifted when ≥ 75% of Canadians aged 12 years and older are fully vaccinated. However, such potential resurgence of Delta cases could be reduced if restrictive measures are lifted when ≥ 40% of Canadians aged 12 years and older are fully vaccinated, and personal protective measures are lifted when ≥ 83% of Canadians aged 12 years and older are fully vaccinated.[18]
- This means the equivalent of 67% vaccine coverage for Alpha is 90% for Delta. Because 11% of the Ontario population is <12 years old and currently ineligible for the vaccine, coverage of 90% would require complete two-dose coverage of the population 12 years and older. This indicates that some public health measures to prevent the circulation of SARS-CoV-2 will likely remain necessary societally to reduce introductions and spread among unvaccinated/partially vaccinated individuals.

Relevant Jurisdictions Experiencing Delta Surge: England

Epidemiology

- As of June 24, 2021:
  - Rate of cases in a 7-day period per 100,000 people was 145.4 (up from 134.3 on June 23, 2021).[22]

    - There were 116 weekly deaths in the week ending June 18, 2021 (up from 93 the week ending June 11, 2021).[22]

- As of June 23, 2021, there were 111,157 sequenced and genotyped cases of the B.1.617.2 (Delta) in England (up from 75,953 cases on June 16, 2021)[23]

    - Delta comprises 95% of sequenced cases in England.[16]

Public Health Measures

- To respond to the spread of the Delta:

    - Their "stage 4" re-opening was paused until July 19, 2021 to accelerate vaccinations.[24]

        - Second vaccine dose was brought forward to 8 weeks for individuals ≥ 40 years of age to provide strongest protection against Delta sooner.

    - Additional support (June 11 to 19, 2021) including surge testing, tracing, isolation support and maximising vaccine uptake, was rapidly deployed in:

        - Birmingham, Blackpool, Cheshire East, Cheshire West and Chester, Liverpool City Region and Warrington, Reigate and Banstead, Lambeth and Cumbria.[25-28]

    - Re-opening can be moved earlier if:[24]

        - Vaccine deployment continues to be successful.

        - Vaccines are sufficiently effective in reducing hospitalisations or deaths.

        - Infection rates do not risk a surge in hospitalisations.

        - Risk assessment is not changed by new VOCs.

Vaccination

- All individuals ≥ 18 years of age are now eligible for vaccination.[29] As of June 28, 2021:[22]

    - 77.3 million doses administered

    - 84.6% of the population had received at least one dose

    - 62.1% of the population were fully vaccinated

- Starting October, 2021 anyone working in a registered care home must be fully vaccinated[30]

Ontario Risk Assessment

- **Overall, the risk of B.1.617.2 or Delta transmission in Ontario is moderate to high. It is the predominant variant and transmission will depend on the number and spread of existing cases and continued introductions into areas of the province.**

    - While mutation profiles estimated that 61.7% of all reported cases in Ontario could include cases due to Delta, the prevalence can rise sharply with outbreaks of high case

numbers,[31,32] driven by close contact[10,33] due to Delta's higher transmissibility, pockets of population with suboptimal vaccine coverage and slightly reduced vaccine effectiveness.

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

Table 1. Risk Assessment for Delta

Issue	Risk level	Degree of Uncertainty
Increased Transmissibility	**High** Data from India, the UK and Ontario suggest Delta can be up to 64% more transmissible than Alpha. SARs of Delta are higher than Alpha.	**Low**
Disease Severity	**Moderate** Increased risk of hospitalization based on sequenced cases in UK and from comparison of S-gene–positive (proxy for Delta) with S-gene–negative (proxy for Alpha). A greater proportion of cases admitted to hospital were unvaccinated compared to fully-vaccinated with two doses of COVID-19 vaccine.	**Low**
Re-infection	**Low**	**High**
Lowered Vaccine Effectiveness	**Moderate** There is ~14% lower VE against symptomatic infection after first dose, and ~10% lower after two doses compared to Alpha. VE against hospitalization for Delta is high and similar compared to Alpha.	**Moderate**
Impacts on Testing/ Surveillance	**Low** The risk of Delta cases not being detected in Ontario's surveillance program is low.	**Low**

Practice Implications

- The Delta variant is a recently emerged global VOC which has replaced Alpha as the dominant SARS-CoV-2 strain in Ontario, and has impacted multiple jurisdictions worldwide. It is a more transmissible strain with evidence of increased severity. England is an example of a jurisdiction which modified some public health measures in response to Delta surge.

- Completion of the two-dose vaccination series will be important to protect Ontarians from the more severe and transmissible Delta variant. Vaccination should target those who have not had a first dose, and continue with second doses promptly particularly in areas and settings that have seen high incidence of SARS-CoV-2 overall and Delta specifically. Timely administration of second doses may represent a balance between increased vaccine effectiveness afforded by a two-dose vaccine schedule and the possibility of a longer duration of protection afforded by longer intervals between doses. What interval between doses in a COVID-19 vaccine series provides the most optimal duration of protection is currently unknown, but an area of emerging evidence.

- The herd immunity threshold for Delta is higher than for Alpha. Essentially, everyone who is eligible for COVID-19 vaccination and can be vaccinated should receive 2 doses. This has important implications for vaccination program targets in Ontario. Public Health Agency of Canada modelling recommends very high two-dose coverage for full reopening, such as increasing vaccination coverage target to at least 83% of the population that is ≥ 12 years of age;[18] thus, a high (90%) vaccination coverage target is recommended. Based on projected approvals for vaccines for those < 12 years old by approximately September 2021,[34] planning should start for rapid roll-out of vaccine in younger age groups in the fall to increase overall coverage in the population before winter.

- Sufficient time for assessment of sustained response to reopening stages by appropriate epidemiologic, vaccination and health system indicators will be important to understand how Delta is spreading in Ontario, to ensure that gains achieved in spring 2021 are maintained through summer and in preparing for fall and winter.

Technical Notes

Below is the data caveats and methods for Figure 1.

- Index cases included case reported dates from March 1 to May 15, 2021; congregate settings are excluded.
- Index cases are the first case in the household based on symptom onset date (or specimen collection date, if symptom onset date was not available); secondary cases were those with a symptom onset 1 to 14 days after the index case.
- Household sizes are reported in Case and Contact Management solution and was used to calculate SARs by dividing the number of secondary cases by the total number of household secondary contacts (i.e., household size minus one).
- The points are the mean household SAR for a given day, per mutation profile; the size of the points represent the number of households used to calculate the mean. The lines are the predictive values generated by a general additive model, with mutation profile and index case reported date as predictors of SAR.
    - N501Y+ and E484K- (blue) mutation detected are likely to be lineage Alpha.
    - N501Y+ and E484K+ (purple) mutation detected are likely to be lineage Gamma or Beta.
    - N501Y- and E484K+ (green) does not correspond to a variant of concern currently identified in Ontario.
    - N501Y- and E484K- (red) are cases with neither mutation detected and includes Delta.

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