COVID-19 B.1.617 Variant of Concern – What We Know So Far

Introduction

Public Health Ontario (PHO) is actively monitoring, reviewing and assessing relevant information related to Coronavirus Disease 2019 (COVID-19). “What We Know So Far” documents provide a rapid review of the evidence related to a specific aspect or emerging issue related to COVID-19.

Key Findings

- Lineage B.1.617 is a new variant of concern (VOC) of Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2) and is associated with the notable mutations L452R and E484Q, which have the potential for greater transmissibility and reduced vaccine effectiveness.

- B.1.617 was first reported in India in late March 2021 and has spread to over 40 other countries around the world in less than two months’ time. However, its geographic distribution and incidence trends are not fully understood due to inconsistent testing and sequencing in different regions of the world.

- Field evidence from the United Kingdom (UK), where most B.1.617.2 sequences outside of India have been reported, suggest higher transmissibility for this lineage. Data to date are insufficient to determine if B.1.617 causes more severe disease.

- Preliminary in-vitro studies suggest that B.1.617 has reduced neutralization by vaccine-induced sera and convalescent sera, while an observational study suggests a possible small reduction in effectiveness after full vaccination.

Background

On March 24, 2021, the Ministry of Health and Family Welfare of India reported a new variant that contains two mutations in the Spike gene of SARS-CoV-2: E484Q and L452R. The discovery of this “double mutant” generated concern in India as it took place when the incidence of Coronavirus Disease 2019 (COVID-19) surged rapidly after a long decline from late September 2020 to mid-February 2021.

In less than a month’s time, this variant was detected in several other countries including the UK, Singapore, Australia and the United States (US), and was named B.1.617. Public health scientists internationally have noted that the E484Q and L452R mutations may enable B.1.617 to transmit more easily and render vaccines less effective.

In the UK, sublineage B.1.617.1 was designated as a Variant Under Investigation (VUI-21APR-01) on April 1, 2021, given its mutation profile and increasing incidence in England, while sublineages B.1.617.2 (with
a different mutation profile) and B.1.617.3 (rapid spread not apparent) were under surveillance.\textsuperscript{5} On May 6, 2021, sublineage B.1.617.2 was escalated in its designation to VOC (VOC-21APR-02) when its transmissibility was assessed to be at least equivalent to that of the VOC B.1.1.7. Meanwhile, B.1.617.3 became a VUI (VUI-21APR-03) as of April 27, 2021.\textsuperscript{6}

On May 10, 2021, the World Health Organization characterized B.1.617 as a VOC lineage which contains three sublineages: B.1.617.1, B.1.617.2 and B.1.617.3. The designation was based on early evidence of rapid increases in prevalence observed in multiple countries (for B.1.617.1 and B.1.617.2), preliminary laboratory findings of reduced effectiveness of monoclonal therapeutic antibody Bamlanivimab, and potentially slight reduction in neutralization abilities of vaccinee sera.\textsuperscript{7}

On May 14, 2021, the Canadian SARS-CoV-2 Variant Surveillance Group classified B.1.617 as a VOC, noting that the designation of the sublineages may change as evidence on their attributes is reviewed (See Appendix A for the Canadian definitions of variant of concern).\textsuperscript{8}

**Methods**

From January 17 to May 26, 2021, 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 “double mutant” or B.1.617 were included.

Prior to posting, PHO subject-matter experts reviewed the content of this document.

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.

Jurisdictional scan of involving data from England involved keyword searches conducted on May 17 and 18, 2021 in the Google search engine for literature related to COVID-19 epidemiology, vaccination programs, and public health measures in England. A formal database search was not conducted due to time constraints; thus, some relevant articles may not be included.

**Epidemiology**

- The first B.1.617 genome noted in the global database (GISAID) dates back to October 5, 2020. It was first detected in the UK on February 22, 2021 and in the US on February 23, 2021.\textsuperscript{9} As of May 17, 2021, the three sublineages of B.1.617 (B.1.617.1, B.1.617.2 and B.1.617.3) have been reported in 50 countries from Asia, Europe, North America and Australia.\textsuperscript{5,9,10} The relative frequency of B.1.617 and the sublineages in different countries is unknown due to the different sequencing capacities and strategies.

- B.1.617 was first detected in India where the majority of this lineage (412 reports as of April 22, 2021) was reported.\textsuperscript{10,11} On March 24, 2021, the Indian SARS-CoV-2 Consortium on Genomics reported that about 15%–20% of samples from Maharashtra carry the E484Q and L452R mutations, and there was an increase in the percentage of samples carrying these two mutations since December 2020. Subsequently, B.1.617 was classified as a VOC in India.\textsuperscript{1} B.1.617 was found in 61% of 361 cases sequenced between January and March, 2021 in Maharashtra, India. However, the scale of testing was too small to conclude if this lineage was driving the surge in COVID-19 cases in Maharashtra.\textsuperscript{9,12}
In the UK, B.1.617.1 was first detected in mid-February 2021. Its daily incidence rose quickly in April to peak at 15 cases in mid-April, then declined quickly in late April to <4 cases as of early May 2021. B.1.617.3 was first detected in late March 2021 and its daily incidence has remained low, peaking at 3 cases a day in mid-April and dropping to a case occasionally. On the other hand, the daily incidence of B.1.617.2 had remained low from first detection in mid-March 2021 before slowly increasing in early April, after which it rose quickly to 235 cases a day in early May 2021. The proportion of specimens belonging to the B.1.617.2 sublineage among all variants sequenced in the UK increased from 1% in the first week of April 2021, to 26% in the first week of May 2021, and reached 58% by the week of May 16, 2021. (See What’s Happening in England? for further epidemiological context and response measures).

In the US, B.1.617.1 comprised 0.2% (95% confidence interval [CI]: 0.1%–0.2%) of VOCs and variants of interest (VOIs) sequences collected through the Centers for Disease Control and Prevention’s national genomic surveillance; B.1.617.2 0.5% (95% CI: 0.3%–0.7%); and <10 observations of B.1.617.3 between April 11 and 24, 2021.

In Canada, B.1.617 and the sublineages have been reported in one territory and all provinces. The first patient identified in Quebec was reported to have been vaccinated against COVID-19 two months prior.

Genomic Features

B.1.617 contains three sublineages: B.1.617.1; B.1.617.2 and B.1.617.3 with different mutation profiles (see Appendix B). Common spike gene mutations of concern across the sublineages are L452R, P681R and D614G. In addition, B.1.617.1 and B.1.617.3 carry the amino acid mutations E484Q and G142D (the latter may also be found in some B.1.617.2 sequences).

- L452R: this amino acid mutation occurs in the receptor-binding domain and has been associated with immune escape from therapeutically relevant monoclonal antibodies and convalescent sera, and enhanced receptor binding affinity and transmissibility. A preprint by Jacobson et al. reported on the detection of L452R in breakthrough infections by SARS-CoV-2 after vaccination; however, the risk ratios were not elevated for this mutation when community prevalence was taken into consideration. It is also found in other variants including B.1.427 and B.1.429 (both first detected in California and are estimated to have increased transmissibility by up to 24%), and B.1.526.1 (first detected in New York).

- P681R: this mutation occurs near the furin cleavage site and is similar to P681H. The P681R/H mutation is also found in B.1.1.7 and has been shown to optimise spike cleavage by furin with potentially enhanced transmissibility.

- D614G: this mutation occurs in the receptor-binding domain and is linked to increased transmissibility, infectivity and viral loads.

- E484Q: this amino acid mutation has not been associated with any change in receptor-binding avidity, unlike mutation E484K which is found in VOCs B.1.351 and P.1, and which have been linked to immune escape and potentially decreased vaccine effectiveness. Findings of a preprint by Chen et al. suggest that clinical effectiveness of some monoclonal antibodies may be compromised by the E484Q mutation. Another preprint by Ranjan et al. finds lower binding energy against antibody (CR3022) and higher binding affinity for angiotensin-converting enzyme 2 (ACE2) receptor by the E484Q and L452R mutations, compared to wild-type (not defined), and suggests reduced vaccine efficacy.
• G142D: this mutation is associated with **immune escape from some monoclonal antibodies** but further studies are required to determine the impact on the effectiveness of vaccine and convalescent serum.¹⁹

**Potential Public Health Impacts**

Data on potential public health impacts are mostly for B.1.617.1 and B.1.617.2; there have been very few cases of B.1.617.3 globally.

**Transmissibility**

**Epidemiological data** from India and the UK, as well as two modelling studies from the UK, indicate that **B.1.617.1 and B.1.617.2 may be more easily transmitted** than non-variant strains of SARS-CoV-2.

**B.1.617.1**

• In India, the proportion of B.1.617.1 among the sequenced viruses uploaded to GISAID has increased to about 50% in late March 2021 before starting to decline in April 2021.³⁰

**B.1.617.2**

• In India, the proportion of B.1.617.2 among the sequenced viruses uploaded to GISAID has been increasing since early March to become the dominant variant reported in mid-April 2021.³⁰

• In the UK, the Scientific Advisory Group for Emergencies (SAGE) reported on May 13, 2021 with high confidence that **B.1.617.2 can be up to 50% more transmissible than the VOC B.1.1.7**.³¹ This is based on an observed rise in the number of sequenced cases of B.1.617.2 and of the proportion of spike-gene (S-gene)–positives being B.1.617.2 in a small number of areas.³² **S-gene–positives** are specimens with cycle threshold values ≤ 30 in all S, N and ORF1ab gene targets of a specific 3-target assay (TaqPath assay) used in some laboratories. The proportion of B.1.617.2 in S-gene–positives rose from 72.2% (570/754) in the second half of April to 93% (368/397) in early May of 2021,³² and to 97.3% in the week of May 11, 2021.³³ This happened when the proportion of B.1.1.7 among all VOCs and VOIs was declining, so local contact and behaviour patterns alone could not account for the rapid rise in B.1.617.2. However, many of these increases were detected in a small number of local regions, some of which had a higher proportion of specimens tested in laboratories using the TaqPath assay. The B.1.617.2 sublineage may also have been overrepresented as a result of targeted contact tracing in outbreak settings.³²

• A modelling study by the Centre for Mathematical Modelling of Infectious Diseases COVID-19 Working Group **estimated the reproduction number (R) of B.1.617.2 as 1.64 (95% CI: 1.61–1.67).** The working group used data on imported and local cases between February 1 and April 27, 2021 and assumed the same generation interval for B.1.617.2 and other strains. Imported cases of B.1.617.2 were estimated from three data sources: reported cases in India, proportion of sequenced cases that were B.1.617.2, and reported imported cases into the UK from India. The authors noted that the estimates may not generalize to other areas in the UK.³⁴

• Another modelling study by the Joint Universities Pandemic and Epidemiological Research Consortium using S-gene–positives as proxy of B.1.617.2 **estimated that B.1.617.2 may have a transmission advantage of >1.4 compared to S-gene negatives.** The authors used primarily community-based COVID-19 testing data and there were significant delays in sequencing results. The authors also noted that the conclusion of increased transmissibility of B.1.617.2 could not be made due to the following factors: S-gene positives may contain other VOCs, wild-type, even
some B.1.1.7; different population and behavioural patterns and superspreading events could not be ruled out; travelling status of cases were not available; uneven geographic distribution of laboratories that test for S-gene positives.\textsuperscript{35}

- A cluster analysis by Public Health England found that the size of COVID-19 \textbf{clusters initiated by travellers from India} tended to be larger if the index cases were infected with B.1.617.2 vs. B.1.1.7. However, the \textbf{difference in cluster sizes was not statistically significant} (P=0.19) after adjusting for the number of travellers at the origin of each cluster.\textsuperscript{33}

\section*{SECONDARY ATTACK RATES}

Data from the UK between March 29 and May 4, 2021 estimate \textbf{higher secondary attack rates for contacts of individuals infected with B.1.617.2 than those infected with B.1.1.7 or B.1.617.1.}\textsuperscript{33}

- For contacts of cases with travel history:
  - B.1.617.2: 2.9% (174/5,908); 95% CI: 2.5%–3.4%
  - B.1.617.1: 2.2% (56/2,509); 95% CI: 1.7%–2.9%
  - B.1.1.7: 1.7% (452/26,934); 95% CI: 1.5%–1.8%

- For contacts of cases with no or unknown travel history:
  - B.1.617.2: 13.5% (537/3,977); 95% CI: 12.5%–14.6%
  - B.1.617.1: 11.0% (33/301); 95% CI: 7.9%–15.0%
  - B.1.1.7: 8.1% (5,587/68,713); 95% CI: 7.9%–8.3%

UK contact tracing data between March 29 and May 4, 2021 estimate \textbf{higher secondary attack rates among household and non-household contacts of the 1,446 cases with B.1.617.2 compared to those of cases with B.1.1.7 and with no or unknown travel history.}\textsuperscript{33}

- For household contacts of cases with no or unknown travel history:
  - B.1.617.2: 15.0% (490/3,274); 95% CI: 13.8%–16.2%
  - B.1.1.7: 8.9% (5,019/56,374); 95% CI: 8.7%–9.1%

- For non-household contacts of cases with no or unknown travel history:
  - B.1.617.2: 6.7% (47/703); 95% CI: 5.1%–8.8%
  - B.1.1.7: 4.6% (568/12,339); 95% CI: 4.2%–5.0%

\section*{Serial Interval and Incubation Period}

Contact tracing data from the UK between March 29 and May 5, 2021 estimate that the median serial interval (time between symptom-onset or testing date of index cases and symptom-onset household contacts) is 4 days for both B.1.617.2 (n=618; range 2–10 days) and B.1.1.7 (n=5,376; range 2–12 days). For non-household contacts, the median incubation period (time between exposure and symptom-onset) is 5 days for B.1.617.2 (n=160; range 2–7 days) and 4 days for B.1.1.7 (n=888; range 2–10 days).\textsuperscript{33}

In progress are longitudinal sampling studies to provide a clearer picture by overcoming some of the challenges in recall error.
Disease Severity

In India, anecdotal evidence from clinicians suggests that B.1.617 is less virulent (most patients do not require hospitalization). However, a sharp rise in death rates was observed at the time of increasing incidence of B.1.617, but patient-level data are not available to determine if the increase death rates was due to higher transmission and/or suboptimal access to health care services.

In the UK, there have been 12 deaths out of 5,599 cases due to B.1.617.2 as of May 25, 2021, with a case fatality rate of 0.2% (95% CI: 0.1%–0.4%), compared to 2.0% (95% CI: 1.9%–2.0%) for B.1.1.7. The actual case fatality rate may change as a high proportion of recent cases have not completed a follow up of 28 days. Meanwhile, there have been no deaths reported out of 406 cases of B.1.617.1 and 14 cases of B.1.617.3.

Impact on Testing

There is no evidence to date that indicates reduced effectiveness of molecular tests in use for diagnosing B.1.617. While the detection capability of antigen tests for B.1.617 detection has not been assessed, it is unlikely that their performance would be affected. However, it is unclear at this time if B.1.617 and the sublineages may impact on serological tests.

Immunity and Reinfection

As of May 25, 2021, 2 cases of re-infection with B.1.617.1 and 54 cases of re-infection with B.1.617.2 have been reported in the UK, as expected with any prevalent variant. Also, the SARS-CoV-2 Immunity and Reinfection Evaluation (The SIREN study), which monitors COVID-19 infections among National Health Service health care workers in the UK, reported only one reinfection (VOC status not reported) between April 22 and May 21, 2021.

On the other hand, SAGE speculates on some potential reduction in protection offered by natural infection or vaccine due to the observed antigenic distance between B.1.617.2 and wild-type virus, which is less than that for B.1.351, similar to that for B.1.617.1; greater than that for B.1.1.7. Four preprints of in vitro neutralization experiments also report on reduced neutralization of B.1.617 or the sublineages B.1.617.1 and B.1.617.2 by convalescent sera.

- Edara et al. reported that 19/24 (79%) of convalescent sera were able to neutralize live virus of B.1.617.1 despite a significant 6.8-fold reduction in neutralization titre, compared to that against the WA1/2020 wild-type.
- Planas et al. reported 6-fold reduction in neutralization titres against live virus of B.1.617.2 compared to B.1.1.7 by convalescent sera of a cohort of unvaccinated individuals (n=56) at 6 months post-infection.
- Hoffmann et al. reported an approximately 2-fold reduction in neutralization titre against pseudovirus bearing B.1.617 S protein by convalescent sera (n=15), compared to the Wuhan-1 wild-type. The authors suggest that B.1.617 might evade with moderate efficiency humoral immunity in convalescent patients.
• Tada et al. reported approximately 2-fold reduction in neutralization titre against pseudovirus bearing L452R/E4384Q/P681R S protein by convalescent sera (n=8), compared to the wild-type with D614G mutation.41

Vaccine Effectiveness

REAL-WORLD EXPERIENCE FROM THE UK: B.1.617.2

Lopez Bernal et al. compared the vaccine effectiveness against symptomatic COVID-19 in individuals tested for COVID-19 in the UK up to May 16, 2021. The authors reported that after only one dose, vaccine effectiveness against symptomatic COVID-19 with B.1.617.2 was reduced by approximately 20% compared to that for B.1.1.7: 33.2% (95% CI: 8.3%–51.4%) vs. 49.2% (95% CI: 42.6%–55.0%) for the Pfizer vaccine, 32.9% (95% CI: 19.3%–44.3%) vs. 51.4% (95% CI: 47.3%–55.2%) for the ChAdOx1 (i.e., AstraZeneca) vaccine. However, the reduction in vaccine effectiveness after two doses of vaccine was very small: 87.9% (78.2%–93.2%) vs. 93.4% (95% CI: 90.4%–95.5%) for the Pfizer vaccine; 59.8% (95% CI: 28.9%–77.3%) vs. 66.1% (95% CI: 54.0%–75.0%) for the ChAdOx1 vaccine. The study included 12,675 sequenced COVID-19 variant cases (11,621 cases with B.1.1.7 and 1,054 cases with B.1.617.2). The authors noted that shorter follow-up time after two doses of ChAdOx1 (i.e., AstraZeneca) vaccine may explain the lower vaccine effectiveness.42

Experience from Bolton, UK (where clusters of B.1.617.2 are have been detected) suggests that COVID-19 vaccines are effective against B.1.617.2, as nearly 90% of the 25 people hospitalized with COVID-19 as of May 19, 2021 were not fully vaccinated.43 (COVID-19 vaccines used in the UK include Pfizer BNT162b2 mRNA, Moderna mRNA-1273, and Oxford/AstraZeneca.)44

IN VITRO NEUTRALIZATION ASSAYS

Findings from seven preprints and one peer-reviewed study, however, suggest potential slight to moderate reduction in effectiveness of four COVID-19 vaccines (Pfizer-BioNTech BNT162b2 mRNA, Moderna mRNA-1273, AstraZeneca, and Covaxin) compared to the wild-type or the B.1.1.7 strains. Three of the studies looked at B.1.617 while the other four focused on sublineage B.1.617.1.

B.1.617

• Hoffmann et al. reported approximately 3-fold reduction in neutralization ability by sera from fully-vaccinated Pfizer vaccinees (n=15) against pseudovirus with B.1.617 S protein, compared to the Wuhan-1 wild-type.40

• Yadav et al. reported a 2-fold reduction in neutralization ability by sera from Covaxin vaccinees (n=28; vaccination status not reported) against live virus of B.1.617, compared to the B.1 (D614G) prototype and VOC B.1.1.7.45

• Tada et al. reported approximately 4-fold reduction in neutralization ability by sera from Pfizer vaccinees (n=6; vaccination status not reported) and Moderna vaccinees (n=3; vaccination status not reported) against pseudovirus with L452R, E484Q and P681R spike mutations, compared to the wild-type with D614G mutation.41

B.1.617.1

• Ferreira et al. reported significant reduction in neutralization ability (actual titre not reported) compared to the Wuhan-1 D614G wild-type, when pseudovirus bearing spike mutations in L452R and E484Q (proxy of B.1.617.1) were tested with sera from Pfizer vaccinees (n=9; vaccination status not reported).46
Edara et al. reported that all sera from Moderna fully-vaccinated vaccinees (n=15) and Pfizer fully-vaccinated vaccinees (n=10) were able to neutralize live virus of B.1.617.1 despite a significant 6.8-fold reduction in neutralization ability compared to that against the WA1/2020 wild-type.\(^{38}\)

Yadav et al. reported that 22/43 (51%) of sera from fully-vaccinated Covishield vaccinees without prior COVID-19 infection did not show any neutralizing antibodies against B.1.617.1. A significant 2-fold reduction in neutralization ability against B.1.617.1 was observed compared to the B.1 (D614G) prototype. With a geometric mean titre of 21.92 ± 4.42 (95% CI: 24.4–62.64) against B.1.617.1, the authors speculate that the vaccine are likely to protect against severe infection and death from that sublineage.\(^{47}\)

Shi et al. reported that all sera from Pfizer fully-vaccinated vaccinees (n=20) were able to neutralize pseudovirus bearing mutations in G142D, E154K, L452R, E484Q, D614G, P618R, Q1071H, H1101D and D111 as proxy of B.1.617.1, despite a 0.26 times reduction in plaque reduction neutralization testing (PRNT\(_{50}\)) compared to that of the wild-type WA1/2020.\(^{48}\)

**B.1.617.2**

Planas et al. reported that 94% of sera (n=16) at 8 weeks after two doses of Pfizer vaccine were able to neutralize live virus of B.1.617.2, despite a 3-fold reduction in neutralization titres compared to that for B.1.1.7. Even at 16 weeks after vaccination, neutralization ability was retained by 85% of the sera. On the other hand, only 8% of sera (n=12) from vaccinees with one dose of AstraZeneca vaccine were able to neutralize the virus. However, even one dose of vaccine (9 with Pfizer, 9 with AstraZeneca, 3 with Moderna) was observed to increase the median neutralizing titres in convalescent sera (n=23) by 130-fold against both B.1.1.7 and B.1.617.2 even at 12 months after infection, suggesting a single dose of vaccine could boost cross-neutralizing antibody responses.\(^{39}\)

What’s Happening in England?

**Epidemiological Context**

- The 7-day rolling average daily cases of COVID-19 rose slowly from late February 2020 to plateau around 4,500 to 4,800 in April 2020, then declined to stay below 700 during late-June to late-July 2020. Daily cases started to climb in September 2020 and plateaued around 21,000 and 24,600 from mid-October to mid-November 2020, dipped quickly to around 14,500 in late November before shooting to the peak of 61,239 in early January 2021. Since then, daily cases have been declining rapidly to around 12,000 in mid-February, then slowly to a low of 1,847 at the end of April 2021, and hovering around 1,900 to 2,100 for the first week of May. As of May 15, 2021, the 7-day rolling average number of daily new COVID-19 cases in England was 1,563 (22 cases per 100,000). As of May 14, 2021, the cumulative number of cases in England was 4.4 million.\(^{49}\)

- The 7-day average daily admission to hospitals due to COVID-19 rose sharply from late March 2020 to a peak at 3,116 in early April 2020, then dropped slowly to a low of 97 in late August 2020. Daily admission then rose to a high of 1,777 in mid-November 2020 and peaked at 4,232 in mid-January 2021. Daily admission was at 234 at the start of April and hovered around 100 and 120 for the first week of May in 2021.\(^{50}\)
• In the past 7 days (as of May 17, 2021) the areas with the greatest rates of cases per 100,000 were the Yorkshire and The Humber regions (2151 cases or 39.1 per 100,000) and the North West region (2764 cases or 37.7 per 100,000).\(^{51}\)

• On April 9, 2021, B.1.617.2 made up 0.1% of COVID-19 cases in England, and by May 7, 2021, the lineage made up 19.6% of cases.\(^{52}\) UK experts expect B.1.617.2 to become the dominant lineage by the end of the week of May 18, 2021, if not already.\(^{53}\) As of May 17, 2021, there were 2,323 confirmed cases of B.1.617 in the UK, which represents a 77% increase from just five days earlier.\(^{54}\)

• North West and South Central England have the highest proportions of B.1.617.2 cases, but cases are being reported across the country.\(^{54}\)

• In Blackburn and Bolton (North West England) where the B.1.617 variant are spreading the fastest,\(^{55}\) the number of cases among those under 60 years of age has increased significantly more than among those over 60 (who are more likely to be vaccinated) suggesting the effectiveness of vaccines.\(^{56}\) The majority of the cases in Bolton were individuals in their teens, 20s and 30s, most of whom had not been vaccinated against Covid-19.\(^{57}\)

**Vaccine Context**

• As of May 18, 2021, 57.9 million doses of the COVID-19 vaccine had been administered; 70.2% of the population had received at least one dose of the COVID-19 vaccine and 39.6% were fully vaccinated.\(^{58}\)

• As of May 13, 2021, the vaccine is currently being offered to: individuals aged 36 and over and individuals who will turn 36 before July 1, 2021, individuals at high risk from COVID-19 (clinically extremely vulnerable), individuals who live or work in care homes, health and social care workers, individuals with a condition that puts them at higher risk (clinically vulnerable), individuals with a learning disability, and individuals who are a main carer for someone at high risk from COVID-19.\(^{44}\)

• To address the rising cases of B.1.617.2, the government announced on May 14, 2021 that it would shorten the interval for second doses from 12 weeks to 8 weeks for the country’s top 9 priority groups.\(^{59}\) England is also accelerating COVID-19 vaccinations in regions with a high proportion of B.1.617.2 cases.

**Public Health Measures**

• As of May 17, 2021, the English government started loosening restrictions for a variety of public health measures, including indoor settings such as hospitality and organized sports.\(^{55}\)

• The government recommends that particular caution be used in certain areas of England (i.e., Bolton Metropolitan Borough and Blackburn with Darwen Borough) where variants are spreading the fastest.\(^{55}\)

• In a press conference on May 14, 2021, the prime minister stated that if the B.1.617 variant turns out to be only marginally more transmissible, the country can continue to move forwards with their re-opening plan; however, if it is significantly more transmissible the roadmap to re-opening may have to be delayed or adapted (particular Step 4 in June\(^{60}\) which involves removing all legal limits on social contact\(^{61}\)).
Actions Taken to Control the Spread of Variants

- A press release from May 13, 2021 stated that due to the recent surge in B.1.617.2 cases in select regions, “a new Surge Rapid Response Team is being deployed in Bolton, additional surge testing will shortly launch in areas such as Formby, and enhanced contact tracing is in place across England”. Additionally, in areas where clusters of cases have been identified additional contact tracing, increased genomic sequencing of positive cases, increased community engagement and support for individual to get tested and self-isolate, and ensure access to vaccination and encourage uptake.

- England has also accelerated genomic sequencing, enhanced contact tracing and implemented surge testing in the North West in efforts to rapidly break chains of B.1.617.2 transmission.

Ontario Context

- Currently, all positive SARS-CoV-2 specimens in Ontario with a cycle threshold (Ct) value ≤35 are tested for presence of the N501Y and E484K mutations, and only specimens positive for E484K mutation with Ct value ≤30 will be sequenced. It is unclear at this time whether the current E484K assay will detect the E484Q mutation associated with B.1.617.

- Approximately 90%–95% of positive specimens that undergo VOC testing in Ontario have either N501Y and/or E484K mutations. As these mutations are not associated with the B.1.617 lineage, the vast majority of specimens in Ontario are highly unlikely to be B.1.617. A proportion of non-VOC specimens are routinely sent for sequencing, in addition to all travel-related positive specimens, as part of Ontario’s ongoing surveillance for emerging variants.

- As of May 19, 2021, there have been 260 cases with B.1.617 detected in Ontario (an increase from 45 as of May 12). Of the 260 cases, 203 were tested by the National Microbiology Laboratory as part of international travel arrival quarantine procedures, while 57 were detected by PHO, most of whom were associated with out-of-country travel.

Risk Assessment and Practice Implications

**Overall risk assessment:** The risk of B.1.617 transmission in Ontario is moderate to high and depends on the number of existing B.1.617 cases and continued introductions into the province. Given the rapid emergence of B.1.617, PHO’s level of confidence in the existing primary literature, preprint literature and grey literature is low but building up quickly with emergence of new evidence. This overall risk assessment may change as new evidence emerges.

- **Transmissibility:** The risk of increased transmissibility by B.1.617 is high, with a relatively low degree of uncertainty.

- **Disease severity:** The risk of B.1.617 causing severe disease is unknown.

- **Immunity and re-infection:** The risk of re-infection with B.1.617 in convalescent patients is low, with a high degree of uncertainty.

- **Vaccine effectiveness:** The risk of B.1.617 causing lowered vaccine effectiveness is moderate, with a moderate degree of uncertainty.

- **Surveillance:** The risk of B.1.617 cases not being detected in Ontario’s surveillance program is moderate, with a moderate degree of uncertainty.
Surveillance testing (including genomic sequencing of a sufficient sample of positive cases) will help us better understand the epidemiology of B.1.617. Currently, there is no indication that individual or societal public health measures such as case and contact management, vaccination rollout and non-pharmaceutical interventions such as physical distancing in Ontario need to be changed. However, ongoing monitoring of single-dose vaccine effectiveness and the impact of England’s shortened second-dose schedule will help to inform Ontario’s second-dose roll-out. Heightened surveillance, close monitoring of case rate indicators, and local assessment of transmissibility are also needed to inform public health measures and Ontario’s new recovery plan.⁶⁷
References


3. Davis N. COVID variant first detected in India is found in the UK. The Guardian [Internet], 2021 Apr 15 [cited 2021 Apr 23]; Coronavirus. Available from: https://www.theguardian.com/world/2021/apr/15/covid-variant-first-detected-india-found-uk


Appendix A

For the purposes of this document, the definition of variants of interest (VOI) and variants of concern (VOC) as proposed by the Canadian SARS-CoV-2 Variants Expert Working Group (CSVEWG) are used.8

Variant of Interest (VOI)

A SARS-CoV-2 variant is a variant of interest (VOI) if it:

- has a genome with mutations associated with changes in epidemiology, antigenicity, or virulence, or changes that potentially have a negative impact on available diagnostics, vaccines, therapeutics or public health measures; AND is known to cause community transmission/multiple COVID-19 cases/clusters in Canada or has been detected in multiple countries; OR
- is otherwise assessed to be a VOI by WHO; OR
- is otherwise assessed to be a VOI by the CSVEWG.

Variant of Concern (VOC)

A variant is a VOC if, through a comparative assessment, it:

- has been demonstrated to be associated with one or more of the following:
  - increased transmissibility or detrimental change in COVID-19 epidemiology;
  - increased virulence or change in clinical disease presentation;
  - decreased effectiveness of available diagnostics, vaccines, therapeutics or public health measures; OR
- is otherwise assessed to be a VOC by WHO; OR
- is otherwise assessed to be a VOC by the CSVEWG.
### Appendix B

**Notable mutations in the spike protein (non-synonymous) found in the B.1.617 sublineages**

<table>
<thead>
<tr>
<th>Amino acid substitution or deletion</th>
<th>B.1.617.1</th>
<th>B.1.617.2</th>
<th>B.1.617.3</th>
</tr>
</thead>
<tbody>
<tr>
<td>D614G</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>D950N</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>E484Q</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>G142D</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>E154K</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>L452R</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>P681R</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Q1071H</td>
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<td>No</td>
<td>No</td>
</tr>
<tr>
<td>T19R</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>T478K</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Δ157/158</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

§ Characteristic spike mutations detected in more than 60% of sequences.
Citation

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