

Letters

RESEARCH LETTER

S-Gene Target Failure as a Marker of Variant B.1.1.7 Among SARS-CoV-2 Isolates in the Greater Toronto Area, December 2020 to March 2021

A novel variant of SARS-CoV-2, B.1.1.7, originally discovered in the UK, is rapidly overtaking wild-type SARS-CoV-2 globally,¹ due to a substantial transmission advantage. This variant is estimated to be 40% to 80% more transmissible² and 35% more lethal³ than the wild-type virus.

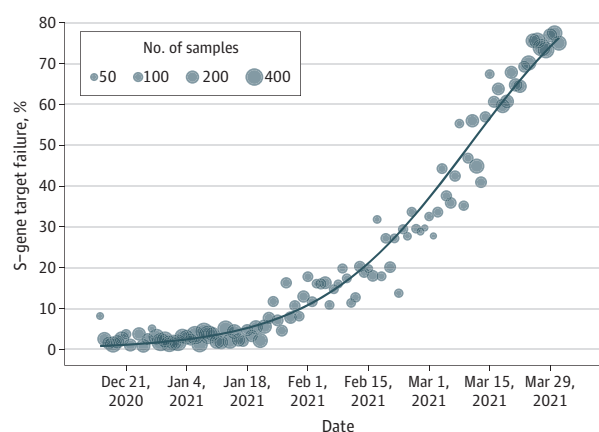
Deletion of amino acids 69 and 70 within the spike (S) gene of SARS-CoV-2 B.1.1.7, sometimes attributable to the N501Y mutation, can result in an undetectable S-gene target (S-gene target failure, SGTF) for some real-time reverse transcriptase polymerase chain reaction (RT-PCR) testing methods. A rapid increase in the proportion of SARS-CoV-2 samples with SGTF was identified in regions of England affected by B.1.1.7, and, after validation with whole genome sequencing, SGTF was determined to be a reliable marker of B.1.1.7 across the country.²

To quantify the spread of B.1.1.7 in the Greater Toronto Area, we tracked SGTF prevalence between December 2020 and March 2021.

Methods | All SARS-CoV-2 clinical samples received by Dynacare Laboratory Ontario, which draws from the Greater Toronto Area including Markham, Brampton, Maple, and Etobicoke, and with results available between December 15, 2020, and March 31, 2021, were included. Samples were primarily collected with nasopharyngeal swabs. All samples were tested using RT-PCR (TaqPath COVID-19 PCR, Thermo Fisher Scientific). SGTF was defined as nondetection of the S-gene target among samples that tested positive (cycle threshold <37) for both the N-gene and *ORF1ab* gene targets. We modeled the daily count of samples that tested positive for SGTF and non-SGTF samples using a count quasi-Poisson regression with the date modeled as a flexible spline and a linear interaction capturing the relative growth rate for SGTF vs non-SGTF samples. The estimated daily SGTF proportion was calculated from the modeled counts. The relative reproduction number was estimated assuming a generation interval of 5.2 days.⁴ Statistical analyses used the mgcv package within R (version 4.0.2). In the period up to January 27, SGTF samples with an N-gene or *ORF1ab*-gene target cycle threshold of 30 or less were forwarded to Public Health Ontario for confirmatory testing. The Public Health Ontario Ethics Review Board determined that this project did not require research ethics committee approval or informed consent because it involved deidentified population data and was considered to be public health practice.

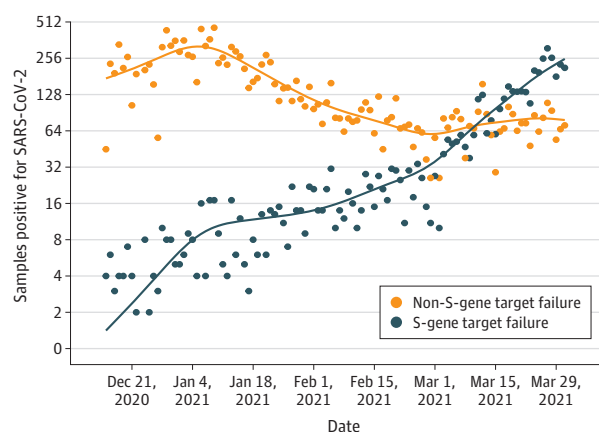
Results | We identified 20 051 samples that tested positive for COVID-19, of which 4692 had SGTF (23.4%). Baseline SGTF prevalence was 2% in mid-December 2020 and reached 75%

Figure 1. Percentage of Samples Positive for SARS-CoV-2 With S-Gene Target Failure



In the most recent week, March 25 to March 31, 2021, model-based estimates of S-gene target failure prevalence increased from 68.4% to 76.2% (7.8%; 95% CI, 7.3%-8.4%).

Figure 2. Daily Counts of SGTF (n = 4692) vs Non-SGTF Samples (n = 15 359)



In the most recent week, March 25 to March 31, 2021, model-based estimates of daily samples that tested of positive for S-gene target failure (SGTF) increased from 176 per day to 254 per day (weekly growth rate, 1.45; 95% CI, 1.18-1.75), whereas daily samples that tested positive for non-SGTF decreased from 81 per day to 79 per day (weekly growth rate, 0.97; 95% CI, 0.80-1.18). SGTF case counts increased in spite of a 6-week province-wide lockdown from December 26, 2020, to February 9, 2021.

(213 of 284) on March 31 (Figure 1). In the most recent week (March 25 to March 31), model-based estimates of daily samples positive for SGTF increased from 176 per day to 254 per day (Figure 2, weekly growth rate, 1.45; 95% CI, 1.18-1.75), while daily non-SGTF samples decreased from 81 per day to 79 per day (weekly growth rate, 0.97; 95% CI, 0.80-1.18). The weekly growth rate of SGTF samples was 1.49 times greater (95% CI, 1.43-1.54) than it was for non-SGTF samples; this suggests that

the mean number of secondary transmissions per SGTF case was 1.34 times greater (95% CI, 1.31-1.38).

Fifty-nine of 69 samples meeting confirmatory testing criteria had valid results. B.1.1.7 was identified in 33% (2 of 6) of samples by whole-genome sequencing in late December 2020 and probable B.1.1.7 was confirmed in 96% in January 2021 (51 of 53 screened positive by a laboratory-developed N501Y RT-PCR test,⁵ of which the 25 subjected to whole-genome sequencing were confirmed as B.1.1.7).

Discussion | This study found that SGTF was a reliable marker of B.1.1.7, and that prevalence of B.1.1.7 has consistently grown more rapidly than preexisting variants, suggesting increased transmissibility.² As in the UK,³ the prevalence of B.1.1.7 increased during a province-wide lockdown period (December 26, 2020, to February 9, 2021) when non-B.1.1.7 variants were effectively brought under control.

This study has limitations. Prevalence trends may have been affected by unperceived changes in testing patterns. Furthermore, the SGTF approach has imperfect specificity (approximately 98% in this study), because non-B.1.1.7 variants with low viral burden or possessing the 69-70 deletion can trigger SGTF.⁶ Despite this, SGTF prevalence was concordant with B.1.1.7 prevalence from an independent point prevalence survey.⁵

B.1.1.7 became the dominant lineage in the Greater Toronto Area in March 2021. To plan public health measures to control COVID-19, timely early warning systems for new variants are essential.

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