Quantifying the potential for dominant spread of SARS-CoV-2 variant B.1.351 in the United States

Pratha Sah1, Thomas N. Vilches1,2, Affan Shoukat1, Abhishek Pandey1, Meagan C. Fitzpatrick3, Seyed M. Moghadas2, Alison P. Galvani1*

1Center for Infectious Disease Modeling and Analysis (CIDMA), Yale School of Public Health, New Haven, Connecticut, USA
2Agent-Based Modelling Laboratory, York University, Toronto, Ontario, Canada
3Center for Vaccine Development and Global Health, University of Maryland School of Medicine, 685 W Baltimore St, Baltimore, Maryland, USA

*Corresponding author. Email: alison.galvani@yale.edu

Abstract: Recent evidence suggests that the SARS-CoV-2 variant B.1.351 exhibits partial immune evasion to antibodies generated by natural infection or vaccination. We used a dynamic transmission model to evaluate whether this variant could become dominant in the United States given mounting vaccination coverage and other circulating variants. We show that B.1.351 is unlikely to become dominant even when all fully vaccinated individuals return to their pre-pandemic behavior. However, an improved selection advantage of B.1.351 arising from a combination of increased transmission and immune escape could drive this variant to dominance as early as July 2021 and fuel a resurgence of cases and hospitalizations. Our study underscores the urgency for continued rollout of the current generation of vaccines despite the emergence of immune escape variants.

One-Sentence Summary: Within the range of early estimates for its immune evasion and transmissibility, the B.1.351 variant is unlikely to spread widely in the United States.

A key milestone in efforts towards controlling the COVID-19 pandemic has been the development and deployment of highly effective vaccines at an unprecedented rate. As of April 2021, at least seven different vaccines have been rolled out worldwide and more than 200 additional vaccine candidates are in various stages of clinical trials (1). In the United States,
more than 246 million doses of vaccines have been administered as of May 5, 2021, and 32% of the population is fully vaccinated. While the daily number of cases has declined sharply since the apex of the pandemic, new variants with a selection advantage—from increased transmissibility, immune escape or both—are increasing in prevalence. The B.1.1.7 variant, first identified in the United Kingdom, is now the predominant variant in the US and is considered 50% more contagious than the original COVID-19 strain (2) with higher mortality risk (3). Other variants, including B.1.351, P.1, and B.1427/1429 variants are also on the rise (4).

The three authorized vaccines in the US—produced by Pfizer-BioNTech, Moderna, and Johnson & Johnson—are highly effective for preventing symptomatic and severe disease caused by the originally identified Wuhan-1 strain (5–7). Since these vaccines target the spike (S) protein of the original strain (8), vaccine-mediated neutralizing antibodies may be less protective against newer variants with multiple spike mutations (9). Indeed, early laboratory data suggests significantly lower neutralizing activity for vaccine-induced antibodies against the B.1.351 variant (10, 11). Recent studies have also noted a decline in neutralizing antibody titers for B.1.351 in convalescent sera and sera from vaccinated individuals (12–14). However, the effect of reduced neutralizing activity on the protection offered by vaccines remains to be determined (15).

Although the current prevalence of the B.1.351 variant in the US is relatively low (~0.7%) (16), the growing evidence of immune evasion and vaccine escape has raised concerns about the ability of the first generation of vaccines to end the pandemic. The interim guidelines from the US Centers for Disease Control and Prevention (CDC) allow fully vaccinated individuals to resume certain pre-pandemic activities and social interactions (17). Premature relaxation of social distancing measures could enhance the selective advantage for immune escape variants, hampering the ability of vaccination to control the pandemic. Here, we examined whether vaccine and immunity-mediated selection pressures could facilitate the dominance of the B.1.351 variant in the presence of the original strain and the B.1.1.7 variant under the updated guidelines by the CDC.

To project the shifting dynamics of viral circulation, we extended our previous age-stratified agent-based model of COVID-19 to include the transmission dynamics of the B.1.17 and B.1.351 strains in addition to the original strain (18, 19). A two-dose vaccination campaign of Moderna vaccine was implemented based on the recommended prioritization by the US Advisory Committee on Immunization Practices (20). The model was parameterized with the population demographics of the United States, a contact network accounting for pandemic mobility patterns, and age-specific risks of severe health outcomes due to COVID-19 (Appendix). We calibrated the transmissibility of the original strain by fitting the model to
reported cases in the US per 100,000 population from October 1, 2020 to April 16, 2021. In the calibration process, we introduced the B.1.1.7 variant on December 1, 2020, with a 50% higher transmissibility compared to the original strain (2). Vaccination started on December 12, 2020 with the model recapitulating the average weekly rate of dose administration reported in the US for all authorized vaccines (21). Vaccine efficacies against infection, symptomatic and severe disease caused by the original strain were drawn from published estimates (Appendix, Table S2). We assumed that vaccines have the same efficacy against the B.1.1.7 variant. The B.1.351 variant was introduced on January 28, 2021 (22). Since the epidemiological and immunological data on the selective advantage of the B.1.135 variant are limited, we varied its transmissibility ranging from being equally transmissible as the original strain to 50% higher and reduced vaccine efficacy across the range of 20 — 80%. Following interim social distancing guidelines announced by the CDC on April 2, 2021 (17), we adjusted contact patterns in the model to allow fully vaccinated individuals to return to normal pre-pandemic behavior 14 days after the second dose of vaccine, starting from April 3, 2021.

We projected the number of cases and hospitalizations caused by the variants and the original strain between April 3 to December 31, 2021 (Fig. 1: A1, S1). We found that the B.1.1.7 variant would remain dominant in the US if the reduction in vaccine efficacy against the B.1.135 variant is less than 30% or if the relative transmissibility of B.1.135 is below 1.04 compared with the original strain (Fig. 1, A1-2, C1-6). Infections and hospitalizations caused by the B.1.135 variant would remain low unless its selection advantage determined by a combination of relative transmissibility and vaccine escape (represented by reduced efficacy) exceeds a threshold curve (Fig. 1: A2). For example, if the B.1.351 variant has a similar transmissibility to the original strain, we project that less than 28% of hospitalizations would be caused by this variant even if vaccine efficacy is reduced by as much as 80%. When the selection advantage of B.1.135 exceeds the threshold curve, the variant would become predominant as early as July 2021, fuelling a resurgence of cases and hospitalizations with magnitude dependent on the relative transmissibility and degree of vaccine escape. For example, if the B.1.135 variant is 20% more transmissible than the original strain and vaccine efficacy against this variant is reduced by 60%, we project a resurgence of 19.2 (95% CrI: 7.7 — 32.7) cases per 100,000 population at the peak (Fig. S2), causing a total of 96 (95% CrI: 68 — 126) hospitalizations per 100,000 population over the evaluation period, corresponding to 316,535 (95% CrI: 224,107 — 415,710) hospitalizations for the entire US. Incidence and hospitalizations would further be exacerbated as the selection advantage of the B.1.135 variant increases above the threshold curve. For example, the average daily cases would substantially increase to 93 (95% CrI: 58 — 131) cases per 100,000 population at the peak if the B.1.135 variant can evade 60% of vaccine-induced immunity with 50% higher relative transmissibility, causing a total of 1,228,763 (95% CrI: 1,011,794 — 1,481,841) hospitalizations in the US over the nine months. We obtained similar results substituting the base case vaccine parameters for Moderna vaccines with those for Pfizer vaccines (Fig. S3).
Our results indicate that the potential dominance of the B.1.351 variant in the US would require a relatively high selection advantage in order to evade the naturally-acquired or vaccine-induced immunity. While evidence is accumulating that convalescent and vaccine sera offer limited neutralizing antibody activities and reduced protection against the B.1.351 variant (12, 23), the selection advantage of this variant may not be sufficiently high to compete with the more transmissible B.1.1.7 variant. A recent small Phase 3 clinical study in South Africa, where the B.1.351 variant is prevalent, found Pfizer-BioNTech vaccines to remain effective against symptomatic disease (24). The high vaccine efficacy indicates that the neutralizing antibody response to the B.1.351 variant, although lower than against the original strain, is still protective (25). The selective advantage of the B.1351 variant likely lies within a range of 50% higher transmissibility and the ability to evade 21% of naturally-acquired immunity (26). While the dominance of B.1.351 variant in terms of infection and severe outcomes appears improbable at the national level in the US at these estimates, regional flare-ups or congregate outbreaks of the B.1.351 variant may still occur if the variant was introduced around the same time as the B.1.1.7 variant. Corroborating this is local dominance of other variants in California (27) and the low national prevalence but clustered outbreaks of the P.1 variant in Canada (28, 29).

As vaccine rollout proceeds slowly in many countries, emergence and circulation of new variants will continue to pose challenges to global pandemic control. Selection pressure from naturally-acquired or vaccine-mediated immune responses will inevitably foster resistant mutations to arise if community transmission remains high. Although emergence of novel variants cannot be completely averted, steps can be taken to mitigate the risks. Reducing community transmission also lowers the probability of more transmissible variants emerging. While increasing vaccine uptake, continued adherence to non-pharmaceutical mitigation measures should be followed until viral circulation is driven low. Our results further show that despite the evidence of immune escape, rollout of the current generation of vaccines remains an effective strategy to combat the pandemic. In the longer term, development of multivalent or universal vaccines targeting more conserved regions of the virus can improve our ability to prevent resurgence of emerging SARS-CoV-2 variants.
Fig. 1. Projected hospitalizations and infections caused by the variants and the original strain between April 3 to December 31, 2021 (A1) Percentage of hospitalizations due to infections by different variants, with varying transmissibility of B.1.351 relative to the original strain, and reduced efficacy of Moderna vaccines against B.1.351. (A2) Dominance regions in percentage of hospitalizations caused by B1.1.7 and B.1.351 separated by the threshold curve.

(B1-B6) Total hospitalizations per 100,000 population for B.1.351 transmissibility increased by a factor of: 1 (B1), 1.1 (B2), 1.2 (B3), 1.3 (B4), 1.4 (B5), 1.5 (B6) relative to the original strain.

(C1-C6) Percentage of total infections caused by different variants corresponding to the relative transmissibility of B.1.351 in B1-B6.
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**Funding:**

National Science Foundation Expeditions grant 1918784 (APG)
National Science Foundation grant RAPID-2027755 (APG)
National Institutes of Health grant 1R01AI151176-01 (APG)
Centers for Disease Control and Prevention grant U01IP001136 (APG)
Notsew Orm Sands Foundation (APG). SMM acknowledges support from the Canadian Institutes of Health Research grant OV4 – 170643, COVID-19 Rapid Research (SMM) Natural Sciences and Engineering Research Council of Canada, NSERC EIDM grant (SMM)

**Author contributions:**
Conceptualization: PS, TNV, AS, AP, MCF, SMM, APG
Methodology: TNV, SMM
Investigation: PS, TNV, AS, AP, MCF, SMM, APG
Visualization: TNV, SMM
Funding acquisition: SMM, APG
Writing – original draft: PS, SMM
Writing – review & editing: PS, TNV, AS, MCF, SMM, APG

Competing interests: Authors declare that they have no competing interests.

Data and materials availability: All data are available in the main text or the supplementary materials. The simulation codes are available at: https://github.com/thomasvilches/Third_strain

Supplementary Materials:
Materials and Methods
Tables S1 to S2
Figs. S1 to S3
References (1–43)
Reduced efficacy of vaccine (%) against B.1.351 variant

Relative transmissibility of B.1.351 variant

% of hospitalizations caused by different variants