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About the Author

Ms. Fong is a research postgraduate student at the School of Public Health, University of Hong Kong. Her research interests are the transmission and control of respiratory viruses among children, particularly in school settings.

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Address for correspondence: Benjamin J Cowling, School of Public Health, Li Ka Shing Faculty of Medicine, University of Hong Kong, 21 Sassoon Rd, Pokfulam, Hong Kong; email: bcowling@hku.hk

Risk for International Importations of Variant SARS-CoV-2 Originating in the United Kingdom

Zhanwei Du,¹ Lin Wang,¹ Bingyi Yang, Sheikh Taslim Ali, Tim K. Tsang, Songwei Shan, Peng Wu, Eric H.Y. Lau, Benjamin J. Cowling, Lauren Ancel Meyers

Author affiliations: WHO Collaborating Centre for Infectious Disease Epidemiology and Control, University of Hong Kong, Hong Kong, China (Z. Du, B. Yang, S.T. Ali, T.K. Tsang, S. Shan, P. Wu, E.H.Y. Lau, B.J. Cowling); Laboratory of Data Discovery for Health, Hong Kong (Z. Du, S.T. Ali, S. Shan, P. Wu, E.H.Y. Lau, B.J. Cowling); University of Cambridge, Cambridge, UK (L. Wang); The University of Texas at Austin, Austin, Texas, USA (L.A. Meyers); Santa Fe Institute, Santa Fe, New Mexico, USA (L.A. Meyers)

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A fast-spreading severe acute respiratory syndrome coronavirus 2 variant identified in the United Kingdom in December 2020 has raised international alarm. We analyzed data from 15 countries and estimated that the chance that this variant was imported into these countries by travelers from the United Kingdom by December 7 is >50%.

The United Kingdom has detected a variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent coronavirus disease (COVID-19), from samples initially collected in Kent on September 20 and London on September 21, 2020 (1). The variant was associated with increased transmissibility and includes deletions at amino acid sites 69 and 70 of the spike protein (2). In mid-December, the UK government tightened measures in London and southeastern England to mitigate transmission of the fast-spreading virus variant (3). On January 5, 2021, England initiated a national lockdown that included closing all schools and nonessential businesses until mid-February (4). By December 20, restrictions for travelers from the United Kingdom had been implemented by ≈40 countries (5). The new variant (501Y) has subsequently been reported worldwide, including in the United States (6), Spain, Sweden, and France, and might be spreading without detection in countries with limited virus sequencing capacity (5).

Using data from 15 countries, we estimated the probability that travelers from the United Kingdom

¹These first authors contributed equally to this article.

introduced this 501Y variant into each of the countries and estimated the extent of local transmission. Our estimations were based on the changing proportion of infections caused by the 501Y variant identified in the United Kingdom (2) and population mobility from the United Kingdom to each country, determined from Facebook Data for Good (<https://dataforgood.fb.com>). The highest risk for importation

from September 22 through December 7, 2020, was in Ireland. By October 22 (a month after the variant was first detected in the United Kingdom), the chance that 10 of the 15 countries would receive 1 imported case from the United Kingdom was at least 50% (Figure), except for Romania, Portugal, Cyprus, India, and the United States, although by November 1, this risk threshold was exceeded for all of these countries.

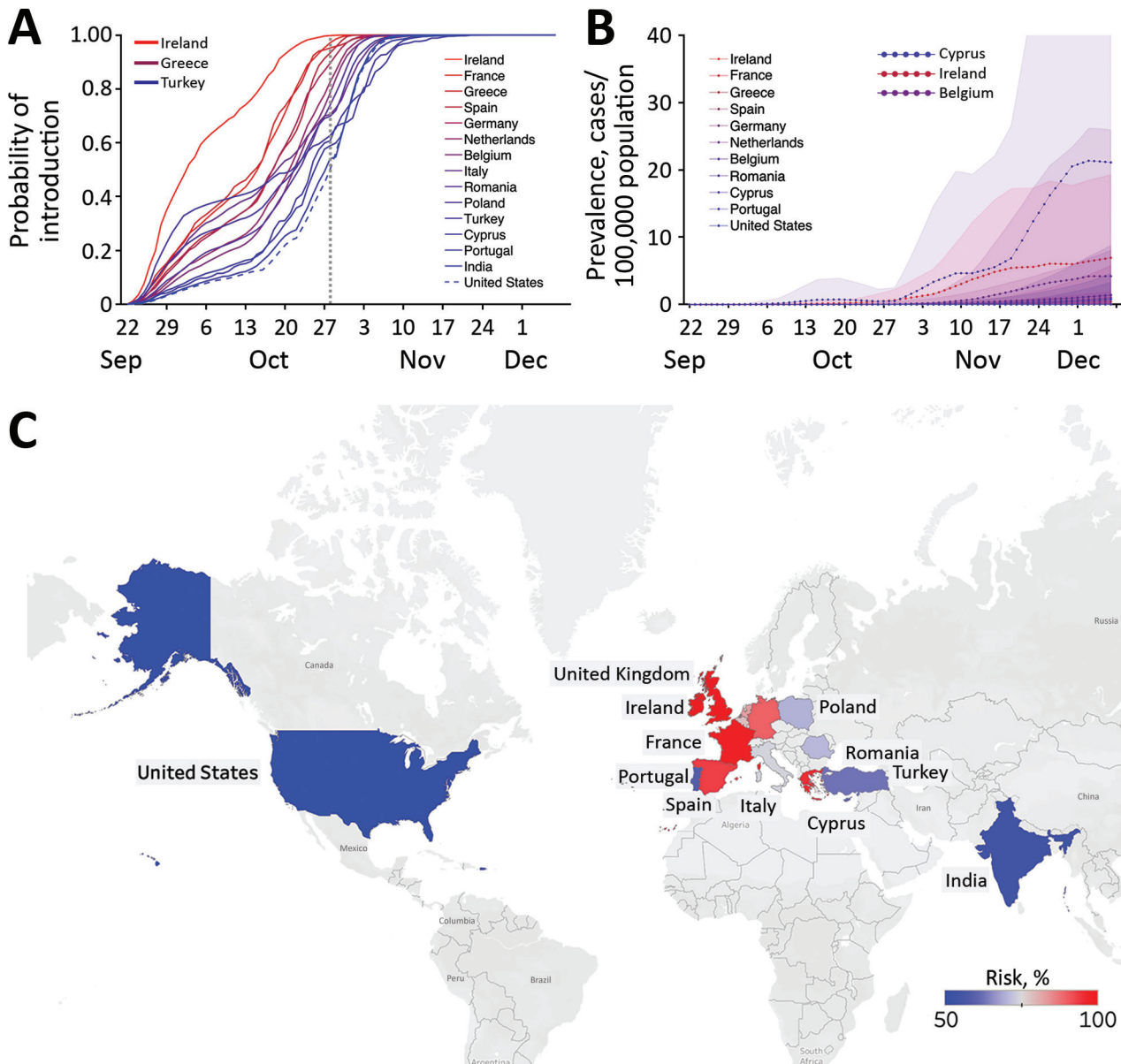


Figure. Estimated risks for introduction of the 501Y variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from the United Kingdom to 15 other countries before December 7, 2020. A) Probability that ≥ 1 person infected with this SARS-CoV-2 variant arrived at the target country from the United Kingdom by the date indicated on the x-axis, based on Facebook mobility data (<https://dataforgood.fb.com>). The dotted gray vertical line indicates October 28, 2020, the date when the introduction risk for the United States surpassed 50%; line colors correspond to the relative risk for importations as of that date. B) Estimated daily prevalence of the 501Y variant of SARS-CoV-2 in 11 countries between September 22 and December 7, 2020, assuming that the variant is σ , which means 50% more transmissible than the 501N variant (11). Points and bands indicate means and SDs based on 100 simulations. C) Probability of ≥ 1 variant importation by October 28, 2020. Grey indicates countries/regions where mobility data were not available.

Using COVID-19 hospital admission data, we further estimated the local prevalence of the 501Y variant in 11 of the 15 countries, assuming that the 501Y variant is 50% more transmissible than the circulating 501N strain (Figure). The variant seems to have ascended fastest in Ireland before slowing in mid-November and is expected to be spreading rapidly in many of the other countries. As of December 7, the expected prevalence of the variant and the expected proportion of coronavirus disease cases were highest in Cyprus (prevalence 13 cases, 95% CI 0–79 cases/100,000 population; proportion 6% of cases, 95% CI 0–38% of cases) (Figure; Appendix Figures 1, 2, <https://wwwnc.cdc.gov/EID/article/27/5/21-0050-App1.pdf>).

These projections suggest that countries with substantial population movement from the United Kingdom were likely to harbor cases of the 501Y variant by late October 2020. Our conclusions were based on several key assumptions. The mobility data, which include ≈ 3 million trips from the United Kingdom to the 15 countries we analyzed, might be demographically biased by the user profile of Facebook, a major social media company with ≈ 2.8 billion monthly active users in the fourth quarter of 2020 (7). We assume that all introductions during this early period occurred via asymptomatic travelers from the United Kingdom and ignore possible importations from other countries or by symptomatic case-patients traveling to seek healthcare. A sensitivity analysis suggests that these assumptions may cause a downward bias in the estimated rates of global expansion (Appendix Figure 3). Furthermore, we assume a 10-day lag between infection and hospitalization on the basis of estimates from the United States (8) and Europe (9) and estimate the daily prevalence of the 501Y variant by using the method introduced in (2), under the assumptions that the 2 variants (501Y and 501N) share the same natural history (2) and symptomatic proportion (10,11). Should future studies reveal substantial epidemiologic differences between the variant and wildtype, then these estimates can be readily updated by using the full equations provided in (2).

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About the Author

Dr. Du is a research assistant professor in the School of Public Health, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong Special Administrative Region, China. He develops mathematical models to elucidate the transmission dynamics, surveillance, and control of infectious diseases.

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Address for correspondence: Lauren Ancel Meyers, Department of Integrative Biology, The University of Texas at Austin, 2415 Speedway #C0930, Austin, TX 78712, USA; email: laurenmeyers@austin.utexas.edu

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Appendix

Data

To estimate the daily number of passengers traveling between the UK and other countries, we obtained daily mobility data from Facebook Data for Good (*I*). Based on geolocation data from Facebook mobile users that enable the ‘location history’ feature, Facebook constructed anonymized origin–destination mobility matrices between countries. However, Facebook only reports mobility flows from the UK to other countries when the daily number of recorded trips is at least 1000. We excluded countries from our analysis that had over 30% days between September 22 and October 21, 2020 falling below this threshold. For the countries we analyzed, we assumed a random number of trips (uniformly distributed between 0 and 1000) on each day of missing data. The data for those countries include ~3 million trips originating in the UK between September 22 and December 14, 2020.

Methods

Risk of COVID-19 variant introduction via infected travelers from the UK

To estimate the probability at least one case has been introduced from the UK into a given country, we first estimate the prevalence of pre-symptomatic and asymptomatic cases in the UK and then use mobility data to estimate the likelihood of introductions.

Our notation and parameter values are provided in Appendix Table. Briefly, we assume that a fraction p_{sym} of cases eventually develop symptoms and the remaining $1 - p_{\text{sym}}$ remain asymptomatic throughout the course of their infection. The total periods of infection for asymptomatic and symptomatic cases are $D_{\text{inf,a}}$ and $D_{\text{inf,s}}$ days, respectively, with symptomatic cases developing symptoms following a D_{presym} day incubation period. A proportion is denoted r

of symptomatic cases require hospitalization and enter the hospital D_h days following infection. We use dH_t^{UK} and ω_t to denote the number of new COVID-19 hospital admissions and the proportion of the new variant among all sequenced SARS-CoV-2 samples in the UK on day t , respectively. We assume that the numbers of new pre-symptomatic and asymptomatic variant-caused infections in the UK at time t are given by

$$dI_{\text{presym},t}^{\text{UK}} = \frac{dH_{t+D_h}^{\text{UK}} \omega_t}{r}$$

$$dI_{\text{asym},t}^{\text{UK}} = dI_{\text{presym},t}^{\text{UK}} \left(\frac{1 - p_{\text{sym}}}{p_{\text{sym}}} \right).$$

Then, the numbers of pre-symptomatic and asymptomatic cases in the UK at time t are given by

$$I_{\text{presym},t}^{\text{UK}} = \sum_{i=t-D_{\text{presym}}}^{t-1} dI_{\text{presym},i}^{\text{UK}}$$

$$I_{\text{asym},t}^{\text{UK}} = \sum_{i=t-D_{\text{inf,a}}}^{t-1} dI_{\text{asym},i}^{\text{UK}}$$

The prevalence of asymptomatic cases infected by the variant as a proportion of the UK population is given by

$$\xi_t^{\text{UK}} = \frac{I_{\text{presym},t}^{\text{UK}} + I_{\text{asym},t}^{\text{UK}}}{N_{\text{UK}}}$$

where N_{UK} is the population size of the UK.

Assuming that travelers from the UK to other countries are infected with the variant according to the overall prevalence of pre-symptomatic and asymptomatic cases (assuming symptomatic cases will not travel), the rate of introductions from the UK to country c on day t is approximated by

$$\gamma_t^c = \xi_t^{\text{UK}} \cdot \Omega_t^c,$$

where Ω_t^c is the daily number of travelers from the UK to country c .

Assuming that the introduction of variant cases from the UK to each country c is essentially a non-homogeneous Poisson process (2–4), we estimate the probability of at least one introduction by time t (starting at time t_0) using

$$1 - \exp\left(-\sum_{i=t_0}^t \gamma_i^c\right)$$

Estimating the prevalence of the variant in each country

We assume the variant and wildtype share the same generation time (5). Let dH_t^c denote the number of new COVID-19 hospitalizations in country c on day t . We assume that the number of new symptomatic and asymptomatic COVID-19 cases in country c on day t are given by

$$dI_{\text{presym},t}^c = \frac{dH_{t+D_h}^c}{r}$$

$$dI_{\text{asym},t}^c = dI_{\text{presym},t}^c \left(\frac{1 - p_{\text{sym}}}{p_{\text{sym}}} \right)$$

Let σ denote the ratio between the reproduction number of the 501Y variant and the reproduction number of the 501N variant. Then, the incidence of the 501Y and 501N variants are given by

$$dI_{Y,t}^c = (dI_{\text{presym},t}^c + dI_{\text{asym},t}^c) \frac{\sigma I_{Y,t-1}^c}{\sigma I_{Y,t-1}^c + I_{N,t-1}^c}$$

$$dI_{N,t}^c = (dI_{\text{presym},t}^c + dI_{\text{asym},t}^c) \frac{I_{N,t-1}^c}{\sigma I_{Y,t-1}^c + I_{N,t-1}^c}$$

We estimate the prevalence of the 501Y and 501N variants as a proportion of the population, as given by

$$I_{Y,t}^c = \frac{1}{N_c} \left(\sum_{i=t-D_{\text{inf},s}}^{t-1} dI_{Y,i}^c p_{\text{sym}} + \sum_{i=t-D_{\text{inf},a}}^{t-1} dI_{Y,i}^c (1 - p_{\text{sym}}) \right)$$

$$I_{N,t}^c = \frac{1}{N_c} \left(\sum_{i=t-D_{\text{inf},s}}^{t-1} dI_{N,i}^c p_{\text{sym}} + \sum_{i=t-D_{\text{inf},a}}^{t-1} dI_{N,i}^c (1 - p_{\text{sym}}) \right)$$

At the start of each simulation, we assume that all cases on September 22, 2020 are the wildtype (501N). That is, $I_{Y,0}^c = 0$ and $I_{N,0}^c = dI_{\text{presym},0}^c + dI_{\text{asym},0}^c$. Variant (501Y) cases are then introduced according to our travel model. Prior to the first introduction of the variant into country c , we draw a poisson random variable with a mean of γ_t^c each day t (representing the number of asymptomatic and presymptomatic cases of 501Y traveling from the UK to c). At the first instance of a nonzero number of importations into country c , we set $dI_{Y,t}^c = \gamma_t^c$ and do not consider subsequent importations into c .

Sensitivity Analyses

Appendix Figures 1 and 2 provide a sensitivity analysis with respect to the relative transmission rate of the variant, with σ ranging from 25% to 75% more transmissible than the wildtype (Appendix Figures 1 and 2). Appendix Figure 3 provides a sensitivity analysis in which we simultaneously change the following two assumptions, both of which accelerate our estimates for importation times: (i) non-hospitalized symptomatic cases are allowed to travel and (ii) the mobility values are roughly doubled (scaled by 741/419) to account for the FaceBook data sample size (419 million regular users (6) out of a Europe population of 741 million (7) in 2020).

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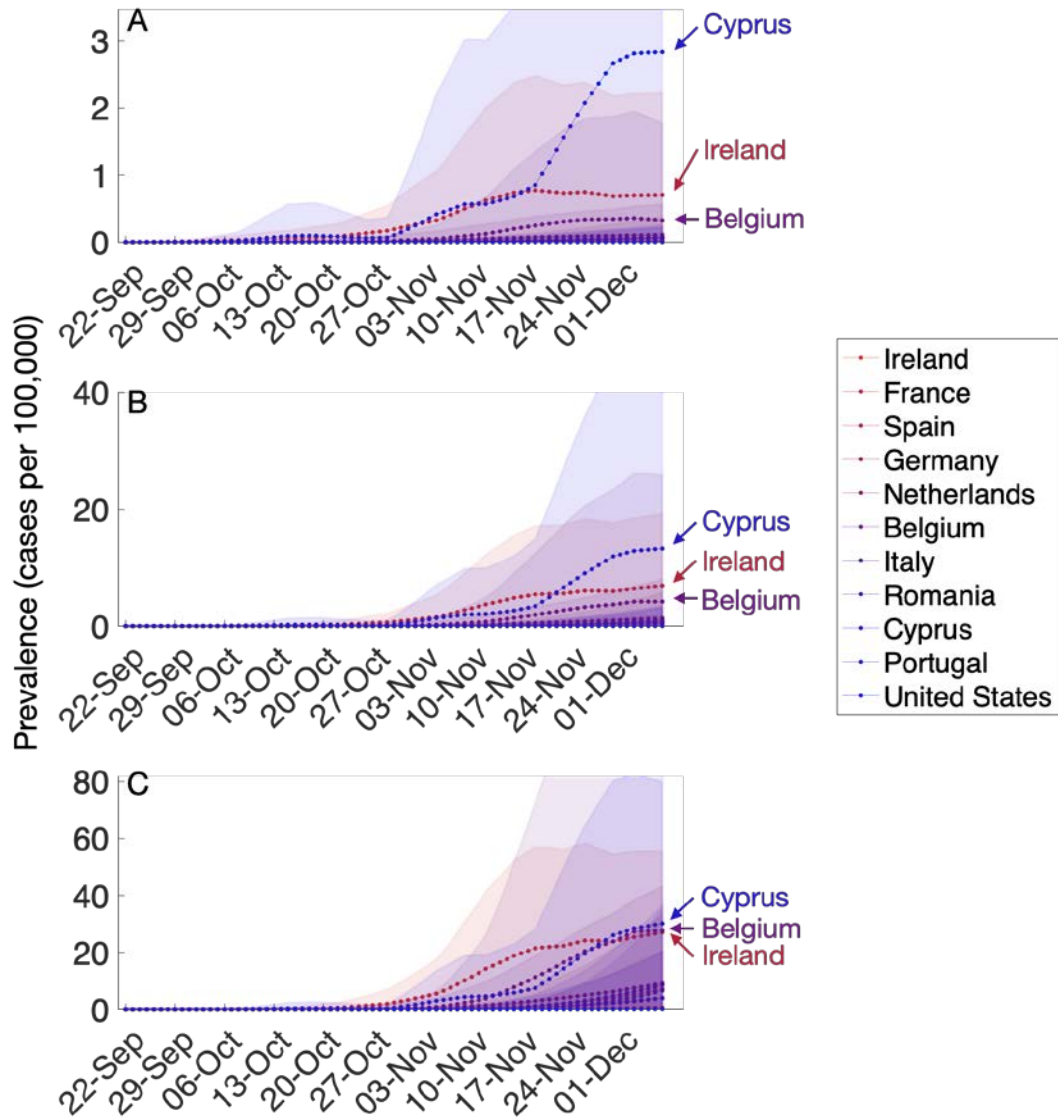
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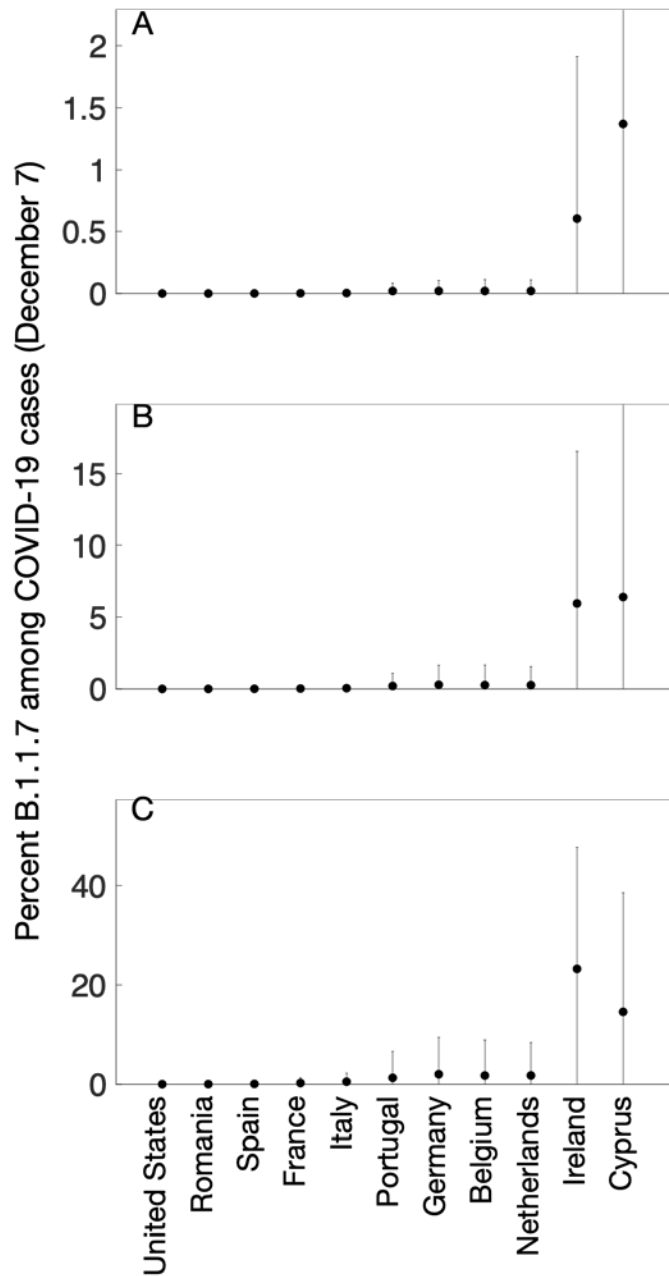
Appendix Table. Model Parameters and Data Sources

Symbol	Description	Values	Source (Reference)
Ω_t^c	Number of travelers from the UK to country c at time t	Daily mobility	Facebook Data for Good (1)
p_{sym}	Proportion of infections that are symptomatic	57%	(8), assuming 501Y and 501N have the same symptomatic proportion (9,10)
dH_t^{UK}	Number of COVID-19 hospital admissions in the UK at time t	Daily admissions	(11,12)
$dI_{\text{presym},t}^{\text{UK}}$	Number of new pre-symptomatic variant infections in the UK at time t	Daily cases	Estimated
$dI_{\text{asym},t}^{\text{UK}}$	Number of new asymptomatic variant infections in the UK at time t	Daily cases	Estimated
ξ_t^{UK}	Prevalence of asymptomatic variant cases as a percentage of the UK population at time t	Daily prevalence	Estimated
γ_t^c	Rate of variant introductions from the UK to country c on day t	Daily rate	Estimated
dH_t^c	Number of COVID-19 hospital admissions in country c at time t	Daily admissions	(11,12)
$dI_{\text{presym},t}^c$	Number of new pre-symptomatic variant infections in country c at time t	Daily cases	Estimated
$dI_{\text{asym},t}^c$	Number of new asymptomatic variant infections in country c at time t	Daily cases	Estimated
r	Proportion of symptomatic cases that are hospitalized	3.4/77	(13)
ω_t	Proportion of the 501Y variant (with deletions at amino acid sites 69/70 of the S protein) among new SARS-CoV-2 cases at time t	Proportion of sequenced SARS-CoV-2 specimens in UK (weekly data)	(5)
D_h	Expected delay from infection to hospital admission	10 d	5 d from infection to symptom onset (14); 5 d from symptom onset to hospital admission (15,16)
D_{presym}	Expected incubation period between infection and symptom onset for symptomatic cases	5 d	(14)
$D_{\text{inf},s}$	Expected time from infection to recovery, for symptomatic cases	11 d	Sum of expected 5-d incubation (14) and expected 6-d symptomatic (15) period
$D_{\text{inf},a}$	Expected time from infection to recovery, for asymptomatic cases	11 d	(15)
N_{UK}	Population of United Kingdom	66,796,807 (2019)	(17)

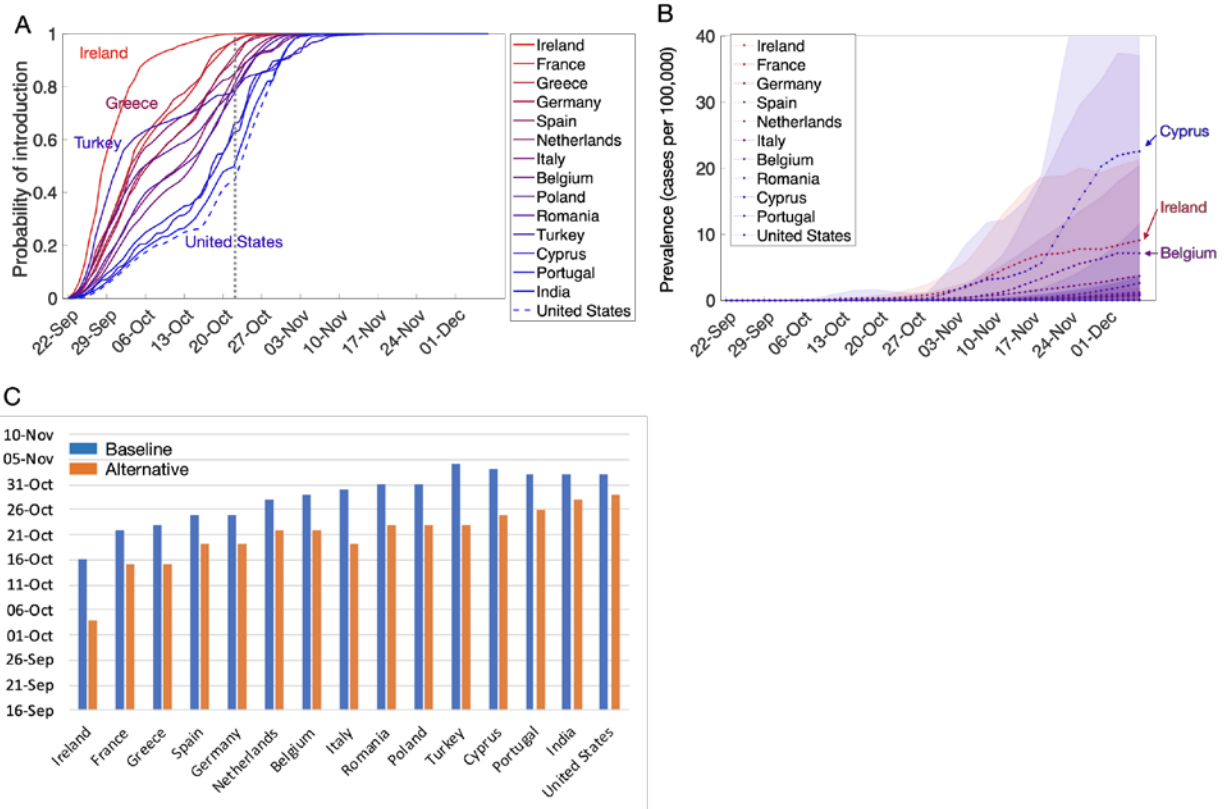
Symbol	Description	Values	Source (Reference)
N_c	Population of country c	2019 populations	(18)
σ	Ratio of the reproduction numbers for the 501Y versus 501N variant	1.25, 1.5, and 1.75	Assumed based on (5, 10, 19)



Appendix Figure 1. Estimated daily prevalence of the 501Y variant of SARS-CoV-2 in 15 countries between September 22 and December 7, 2020, assuming the variant is $\sigma =$ (A) 25%, (B) 50%, and (C) 75% more transmissible than 501N. Points and bars indicate means and standard deviations based on 100 simulations. Countries with highest estimated prevalence on December 7th are labeled.



Appendix Figure 2. Estimated proportion of the 501Y variant among all SARS-CoV-2 cases in 11 countries on December 7, 2020, assuming the variant is $\sigma =$ (A) 25%, (B) 50%, and (C) 75% more transmissible than 501N. Points and bars indicate means and standard deviations across 100 simulations.



Appendix Figure 3. Sensitivity analysis assuming that symptomatic cases can travel and increasing the mobility flows by a factor of 1.8. (A) The probability that at least one person infected with the 501Y SARS-CoV-2 variant has arrived at the target country from the UK by the date indicated on the x-axis, based on Facebook mobility data. The dotted gray vertical line indicates October 23; line colors correspond to the relative risk of importations as of that date. (B) Estimated daily prevalence of the 501Y variant of SARS-CoV-2 in 11 countries between September 22 and December 7, 2020, assuming that the variant is $\sigma = 50\%$ more transmissible than the 501N variant (Davies NG, unpub. data, <https://www.medrxiv.org/content/10.1101/2020.12.24.20248822v1.full-text>). Points and shaded bands indicate means and standard deviations based on 100 simulations. (C) The calendar day that the probability of a 501Y variant introduction first exceeds 0.8, for the baseline (blue) versus alternative (red) assumptions of elevated mobility and symptomatic travel.