Dynamics of B.1.617.2 in the UK from importations, traveller-linked and non-traveller-linked transmission

Adam Kucharski, Nicholas Davies, Rosalind Eggo, Sebastian Funk, on behalf of CMMID COVID-19 working group.

Report for SPI-M (updated), 25th May 2021

Summary

- We used a deterministic approximation of a simple continuous time branching process model to combine estimates for the number of imported B.1.617.2 cases in the UK from India with local onwards transmission, then fitted this model to reported COVID-19 cases up to 24th May 2021 and B.1.617.2 sequences in COG-UK data up to 17th May 2021 to estimate importation rate, UK-based transmission, and rate of decline of non-B.1.617.2 cases in the UK.

- We stratified transmission so that travellers to India and non-travellers could have different values of R, with $R_{traveller} \geq R_{non\text{-}traveller}$ to reflect potential for early amplification that does not persist in wider community transmission. We also allowed transmission to decline in more recent weeks (e.g. as a result of targeted local measures) to some level $R_{recent} \leq R_{non\text{-}traveller}$, where the timing and size of the decline was estimated.

- Based on importations, local sequences of B.1.617.2 and overall case patterns, we estimated that $R_{traveller}$ = 2.4 (95% CrI: 1.9-4.1), $R_{non\text{-}traveller}$ = 1.9 (95% CrI: 1.7-2) and R_{recent} = 1.2 (95% CrI: 1-1.5) in the UK assuming no change in generation interval. This corresponds to a median doubling time of 22 days for B.1.617.2 in the period since 10th May 2021.

- Our median estimate for the timing of a recent step-wise decline in transmission was 7th May 2021 (95% CrI: 2nd May to 11th May). Combined with above estimates, this suggests a decline in R of 33% (95% CrI: 21-46%) around the time B.1.617.2 was declared a variant of concern in the UK (Figure 1H–I). Consistent with our previous predictions on 12th and 18th May 2021, the majority of SARS-CoV-2 sequences in COG-UK data are now B.1.617.2.

- Note that these preliminary estimates of R for B.1.617.2 reflect the average level of transmission across the specific settings where this variant is currently circulating. The relatively large estimate of $R_{traveller}$ possibly reflects higher levels of within household transmission and lower levels of vaccine coverage in specific communities. As a result, these estimates may not generalise to other areas in the UK if there are specific risk factors for elevated transmission in areas where B.1617.2 is being reported, or additional control measures being introduced or relaxed. In particular, the effects of Step 3 of the Roadmap on 17th May will not yet be reflected fully in our estimates. Current levels of targeted measures such as testing and tracing may also become proportionally less effective as social interactions increase (Kucharski et al, Lancet ID, 2020). Analysis and model structure will continue to be refined as more data become available.

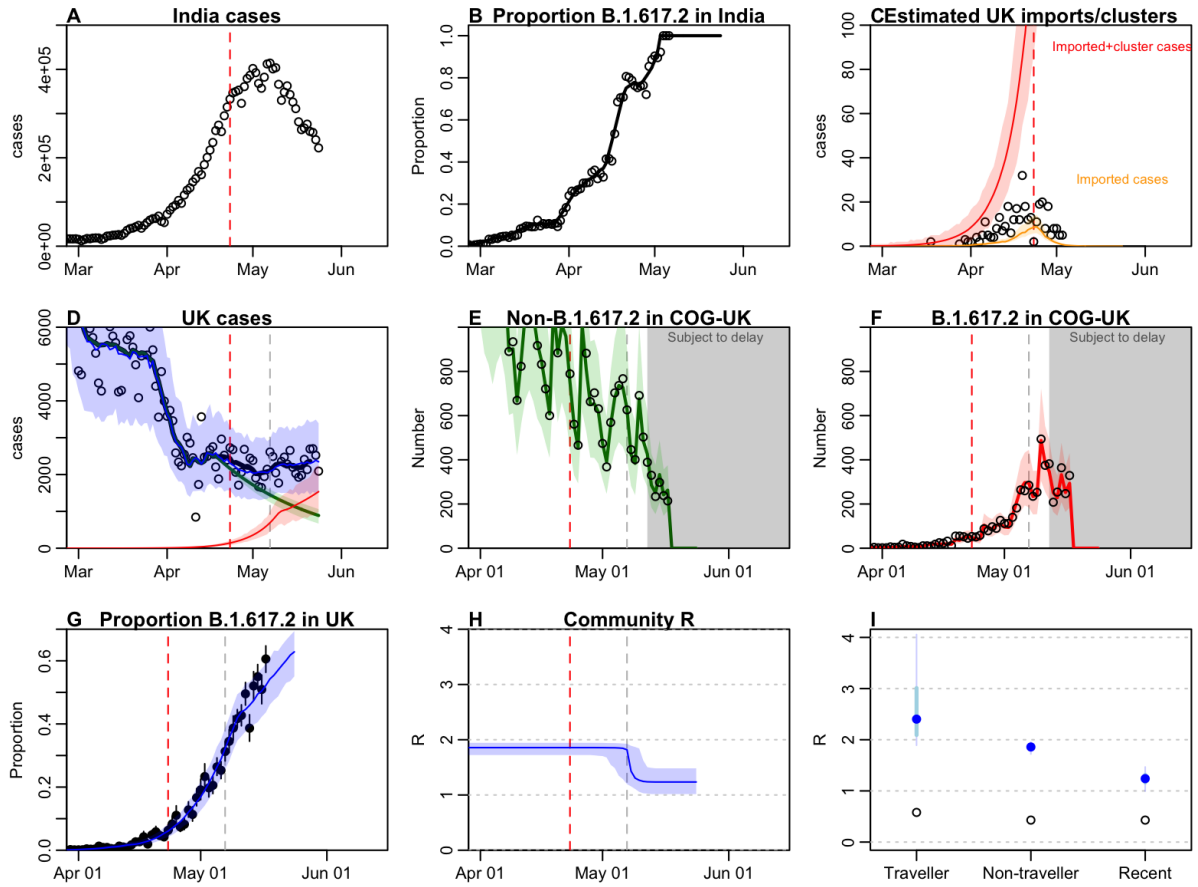
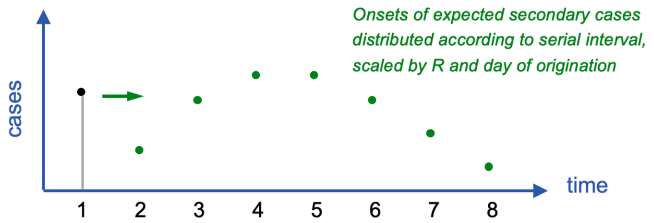


Figure 1: A) Reported cases in India. B) Proportion of reported sequences in India that are B.1.617.2, with black line showing moving average (constrained to end at 100%). C) Estimated imported cases of B.1.617.2 into the UK that contribute to onwards transmission (orange line, with 95% shaded CrI interval), reported traveller cases of B.1.617.2 as described in PHE Technical Report 12 (black dots); simulated imported cases and onwards transmission using maximum a posteriori (MAP) model estimate (red line with 95% negative binomial CrI). D) Reported cases in the UK. Black dots show data, black line shows 7 day centred moving average; green line shows estimated non-B.1.617.2 cases with 95% CrI; red line as in (C); blue line and shaded region shows predicted total cases in UK with negative binomial 95% CrI. E) Black dots show number of non-B.1.617.2 sequences in COG-UK data up to 17th May 2021; green line shows fitted model with 95% negative binomial CrI. Grey region shows data in the past week, which is likely subject to reporting delays. F) Black dots show number of B.1.617.2 sequences in COG-UK data up to 17th May 2021; red line shows fitted model with 95% negative binomial CrI. G) Black dots show proportion of B.1.617.2 sequences in COG-UK data up to 17th May 2021; blue line shows MAP model estimate. H) Estimated change in R among non-travellers over time, assuming a step-change at some point during the observed period. Line shows median and shaded region 95% CrI; as in other panels, dashed grey line shows date B.1.617.2 was declared VOC in UK. I) Estimate of $R_{traveller}$, $R_{non\text{-}traveller}$ and R_{recent} in model, with thick line showing 50% CrI and thin line showing 95% CrI. Dots show implied R based on contact tracing data in PHE Technical Report 12.

Methods

- We estimated imported cases of B.1.617.2 into the UK by combining two data sources: reported cases in India, proportion of sequenced cases that were B.1.617.2 in India. We then scaled these estimates by a parameter a_{import} to produce an expected number of importations over time. Details of the two data sources:
    - Reported cases in India from 1st February 2021 onwards were downloaded using from the covidregionaldata R package (Figure 1A).
    - Proportion of sequences in India were based on sequences reported in GISAID, aggregated by outbreak.info (Figure 1B). Note that these are based on relatively low numbers of sequences collected, which may not be representative, and assumed to converge to 100% eventually.
- We assumed that all imported cases from India ceased after the red listing on 23rd April 2021 (i.e. no leaks from hotel quarantine), and assumed a lognormal incubation period using dlnorm() with mean = 5.1 days and s.d. log = 0.5 (McAloon al, BMJ Open, 2020) to estimate onsets occuring after the red list date among travellers (Figure 1). We assumed that reported onsets in India reflect onset timings in UK, but in practice any timing difference would have little impact on results given the exponential shape of the Indian epidemic pre-red listing date.
- As a validation, we compared estimated imported to traveller cases reported during the same period (PHE Technical Report 12). These corresponded reasonably closely to our estimates (Figure 1C), although it is worth noting that the model estimates the number of imports that contribute to onward transmission; if reported imported cases do not transmit (e.g. because of strict quarantine) then these would not be reflected in model estimates.
- To estimate overall B.1.617.2 cases resulting from initial imports, we used a deterministic approximation of a continuous time branching process model (Kucharski et al, EID, 2016), with the serial interval (here defined as time from test-to-test if cases were to be reported) assumed to be positive, distributed according to a lognormal with mean = 5.4 days and s.d. log 0.4 (Rai et al, Clin Epi Glob Health, 2021). The expected secondary number of cases from onsets on each day is iteratively propagated forward, with transmission depending on R and temporal pattern based on the serial interval. An illustrative schematic of this process is illustrated below:



- To estimate non-B.1.617.2 cases in the UK, we calculated the 7 day centred moving average of cases overall in the UK up to 23rd April 2021 given fluctuations in day-to-day reporting, then extrapolated forward based on the value of an exponential daily decline, $a_{decline}$, which was fitted.
- We assumed that imported cases transmit with reproduction number $R_{traveller}$, non-travellers initially transmit with $R_{non\text{-}traveller}$, then there is a step-wise change in transmission at some point in time d_{time} , after which all individuals with onset on or

after this point have reproduction number R_{recent}, similar to the piecewise parameterisation approach of Auranen et al, JASA, 2000.

- We estimated the vector θ of eight parameters ($a_{decline}$, a_{import} , $R_{traveller}$, $R_{non\text{-}traveller}$, R_{recent} , σ_1 ,σ_1 , d_{time}) by simulating case trajectories from the model, then calculating two likelihoods:
    - the negative binomially distributed log likelihood of sequencing the number of B.1.617.2 cases reported in reality in COG-UK data on a given day *i* (y_{ib}), given the mean number of B.1.617.2 onsets on each day in the simulated outbreak ($E(x_{ib})$ and overall number of cases by date of specimen collection in the UK (y_{io}) and the number of cases sequenced (y_{in}). The negative binomial distribution had dispersion parameter σ_1. Specifically:

      $L_1(\theta) = \sum_i \log NB(x = y_{ib} \mid mu = E(x_{ib})\, y_{in} / y_{io} , size = 1/\sigma_1))$

    - the negative binomially distributed log likelihood of the number of overall cases reported in reality on a given day (y_{io}), given the mean number of B.1.617.2 onsets on each day in the simulated outbreak ($E(x_{ib})$ and estimated non-B.1.617.2 cases in the UK (y_{ic}) from 1st April 2021 onwards, which are assumed to declined exponentially from mid-April onwards as described above. We assumed the negative binomial distribution also had dispersion parameter σ_2. Specifically:

      $L_2(\theta) = \sum_i \log NB(x = y_{io} \mid mu = E(x_{ib}) + y_{ic} , size = 1/\sigma_2))$

- We then calculated the overall log likelihood as $L(\theta) = L_1(\theta) + L_2(\theta)$, and estimated the parameters using MCMC (adaptive Metropolis-Hastings, implemented with the doMC R package). We estimated a daily decline of 2.8% (95% CrI: 2.3-3.6%) for non-B.1.617.2 cases (Figure 1D). This is consistent with mid point of the SPI-M consensus estimate for England on 23rd April (i.e. –5 to –1%).
- The posterior model estimates are shown in Figure 1C–I, with comparison to COG-UK data and overall cases.