Dynamics of B.1.617.2 in England NHS regions from importations, traveller-linked and non-traveller-linked transmission

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Report for SPI-M (updated), 1st June 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 into England from India with local onwards transmission, then fitted this model to reported COVID-19 cases up to 29th May 2021 and B.1.617.2 sequences in COG-UK data up to 19th May 2021 to estimate importation rate, UK-based transmission, and rate of decline of non-B.1.617.2 cases in different NHS regions.

- 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 size of the decline was estimated, and timing was constrained to be 2 weeks either side of B.1.617.2 being declared a variant of concern on 7th May 2021.

- Based on importations, local sequences of B.1.617.2 and overall case patterns, our median estimates for $R_{non\text{-}traveller}$ ranged from 1.2–2 and R_{recent} ranged from 1.1–1.6 across the NHS regions assuming no change in generation interval (Table 1). This would imply 20–60% higher transmission for B.1.617.2 compared to non-B.1.617.2 variants circulating in the same region (Table 2). In five of the seven regions, median B.1.617.2 transmission was estimated to be at least 40% larger than non-B.1.617.2.

- Our median estimate for the timing of a recent step-wise decline in transmission ranged from 2nd to 16th May, with five out of seven regions having an estimated decline between 8th and 16th May. The largest decline was in the North West, with 26% (95% CrI: 17-33%) reduction in R around the 8th May (Figure 4).

- 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. 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.

Region	$R_{traveller}$	$R_{non\text{-}traveller}$	R_{recent}	$R_{non\text{-}617.2}$
London	1.5 (95% CrI: 1.3-2)	1.3 (95% CrI: 1.3-1.4)	1.3 (95% CrI: 1.2-1.4)	0.92 (95% CrI: 0.89-0.94)
Midlands	1.9 (95% CrI: 1.4-4.8)	1.4 (95% CrI: 1.3-1.6)	1.3 (95% CrI: 0.73-1.4)	0.97 (95% CrI: 0.96-0.97)
East of England	2.1 (95% CrI: 1.5-7.5)	1.4 (95% CrI: 1.3-1.6)	1.2 (95% CrI: 0.82-1.4)	0.95 (95% CrI: 0.94-0.97)
North West	2.3 (95% CrI: 2-3.4)	2 (95% CrI: 1.9-2.1)	1.5 (95% CrI: 1.4-1.6)	0.97 (95% CrI: 0.95-0.98)
South East	1.9 (95% CrI: 1.5-4.9)	1.5 (95% CrI: 1.4-1.7)	1.4 (95% CrI: 1.3-1.5)	0.94 (95% CrI: 0.92-0.95)
North East and Yorkshire	15 (95% CrI: 3.5-44)	1.8 (95% CrI: 1.6-2)	1.6 (95% CrI: 1.2-1.8)	0.97 (95% CrI: 0.96-0.98)
South West	4.9 (95% CrI: 1.2-35)	1.2 (95% CrI: 0.99-1.8)	1.1 (95% CrI: 0.89-1.2)	0.93 (95% CrI: 0.9-0.96)

Table 1: Posterior estimates for $R_{traveller}$, $R_{non\text{-}traveller}$ and R_{recent} in each region, with an approximation for the reproduction number of non-B.1.617.2 variants, $R_{non\text{-}617.2} \approx \exp(-a_{decline} T_g)$, where T_g is the generation time (assumed to be equal to the serial interval of 5.4 days), shown for comparison.

Region	$R_{non\text{-}traveller}$ / $R_{non\text{-}617.2}$	R_{recent} / $R_{non\text{-}617.2}$
London	1.5 (95% CrI: 1.4-1.5)	1.4 (95% CrI: 1.3-1.5)
Midlands	1.5 (95% CrI: 1.3-1.7)	1.4 (95% CrI: 0.75-1.5)
East of England	1.5 (95% CrI: 1.4-1.7)	1.3 (95% CrI: 0.86-1.5)
North West	2.1 (95% CrI: 2-2.2)	1.6 (95% CrI: 1.4-1.7)
South East	1.6 (95% CrI: 1.5-1.8)	1.5 (95% CrI: 1.4-1.6)
North East and Yorkshire	1.8 (95% CrI: 1.6-2)	1.6 (95% CrI: 1.2-1.9)
South West	1.3 (95% CrI: 1-2)	1.2 (95% CrI: 0.94-1.3)

Table 2: Posterior estimates for ratio of $R_{non\text{-}traveller}$ and R_{recent} vs $R_{non\text{-}617.2}$, indicating multiplicative difference in transmission during the period analysed.

Region	Estimated decline in community R (%)	Estimated date of decline
London	2.2 (95% CrI: 0.074-12)	2021-05-09 (95% CrI:2021-04-25 - 2021-05-23)
Midlands	7.2 (95% CrI: 0.28-47)	2021-05-13 (95% CrI:2021-04-26 - 2021-05-23)
East of England	17 (95% CrI: 1.5-44)	2021-05-16 (95% CrI:2021-04-28 - 2021-05-23)
North West	26 (95% CrI: 17-33)	2021-05-08 (95% CrI:2021-05-05 - 2021-05-12)
South East	3.1 (95% CrI: 0.1-16)	2021-05-03 (95% CrI:2021-04-25 - 2021-05-23)
North East and Yorkshire	9.5 (95% CrI: 0.41-35)	2021-05-16 (95% CrI:2021-04-26 - 2021-05-23)
South West	12 (95% CrI: 0.46-42)	2021-05-02 (95% CrI:2021-04-25 - 2021-05-22)

Table 3: Posterior estimates for magnitude and timing of decline from $R_{\text{non-traveller}}$ to R_{recent} .

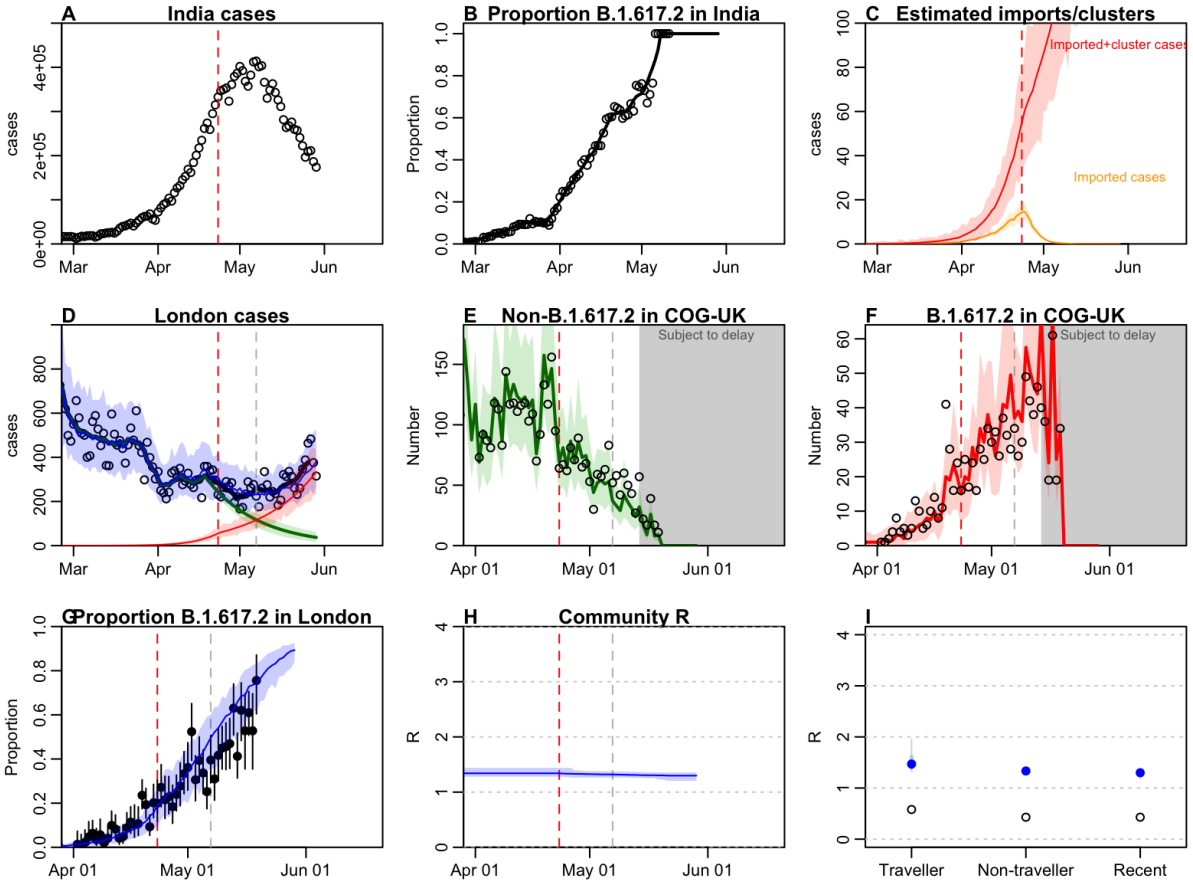


Figure 1: London analysis. A) Reported cases in India. B) Proportion of reported sequences in India that are B.1.617.2, with black line showing moving average (constrained to end at 100%). C) Estimated imported cases of B.1.617.2 into the region that contribute to onwards transmission (orange line, with 95% shaded CrI interval); 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 region. 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 region with negative binomial 95% CrI. E) Black dots show number of non-B.1.617.2 sequences in COG-UK data up to 19th 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 19th 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 19th 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.

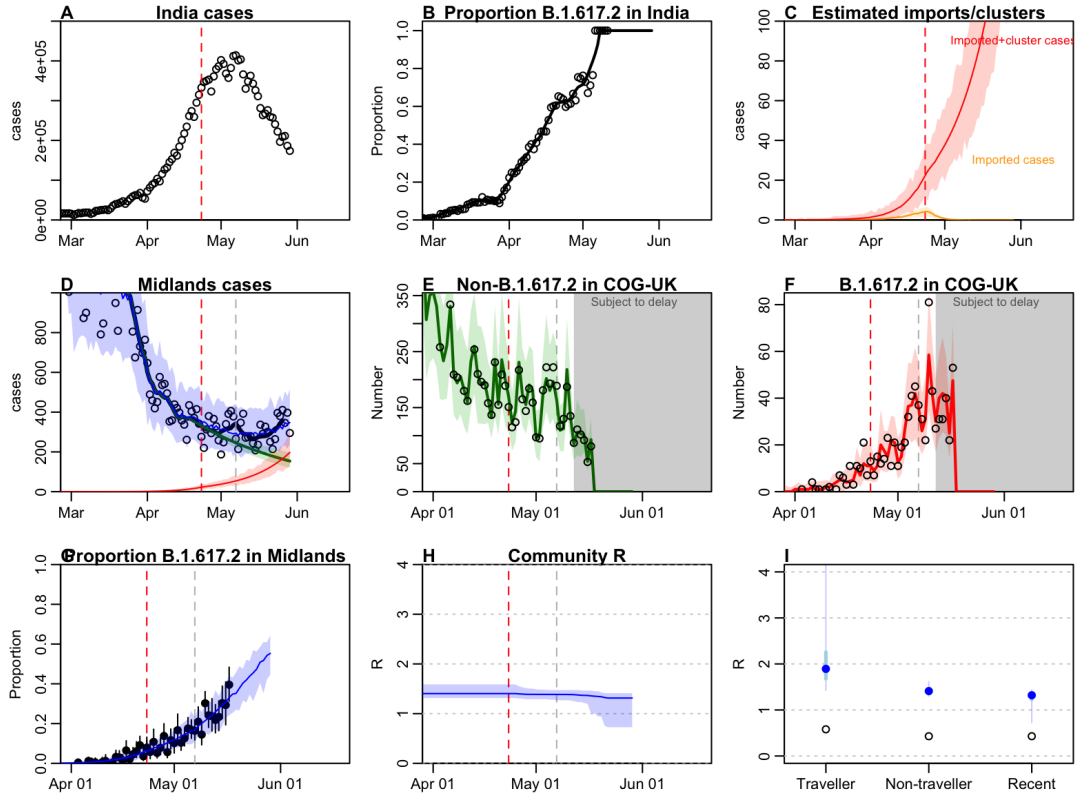


Figure 2: Midlands analysis. Panels same as Figure 1.

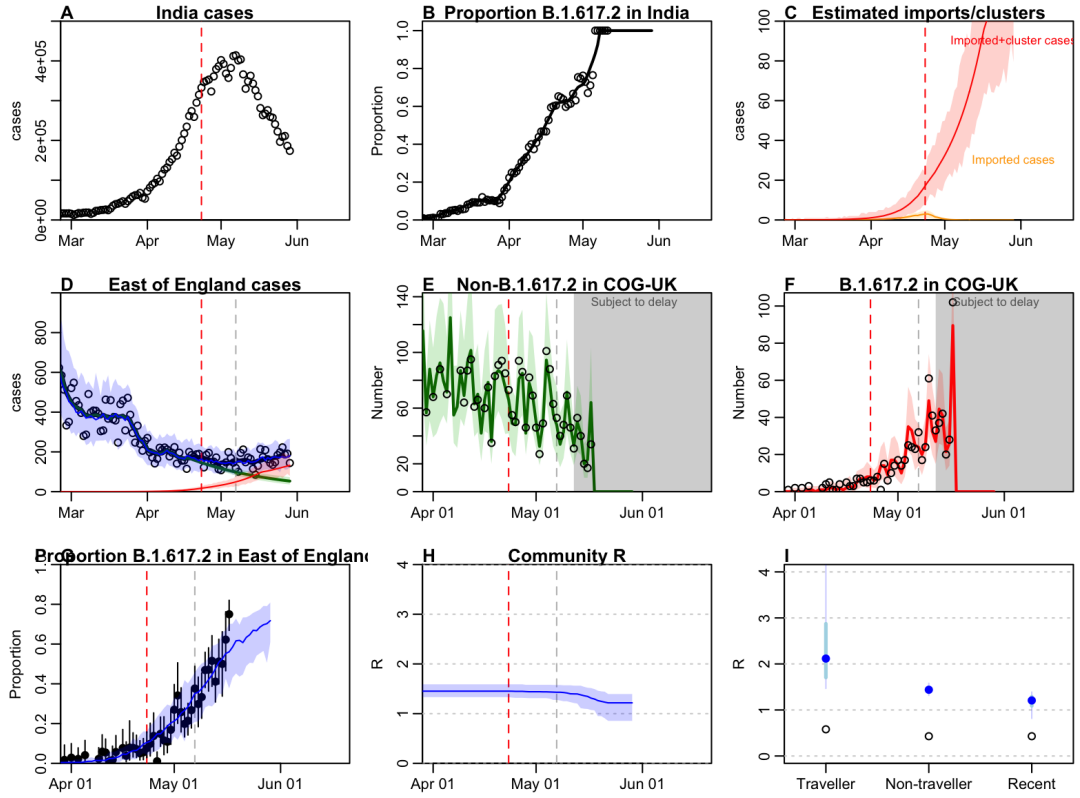


Figure 3: East of England analysis. Panels same as Figure 1.

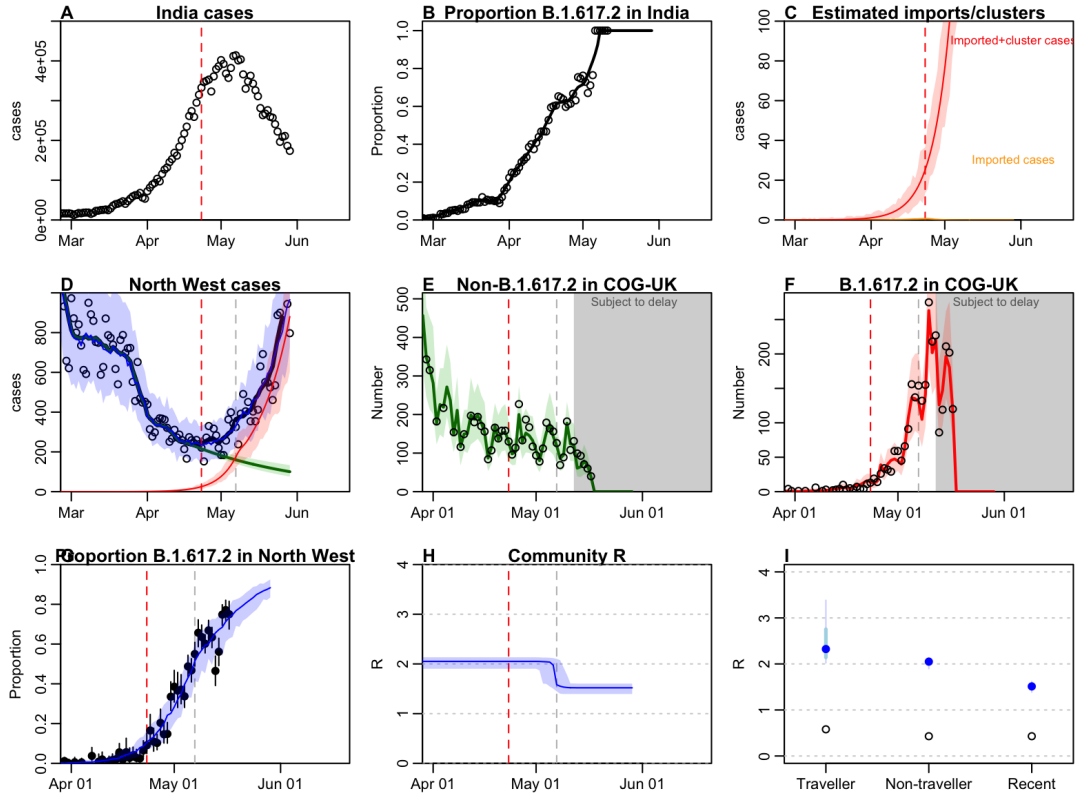


Figure 4: North West analysis. Panels same as Figure 1.

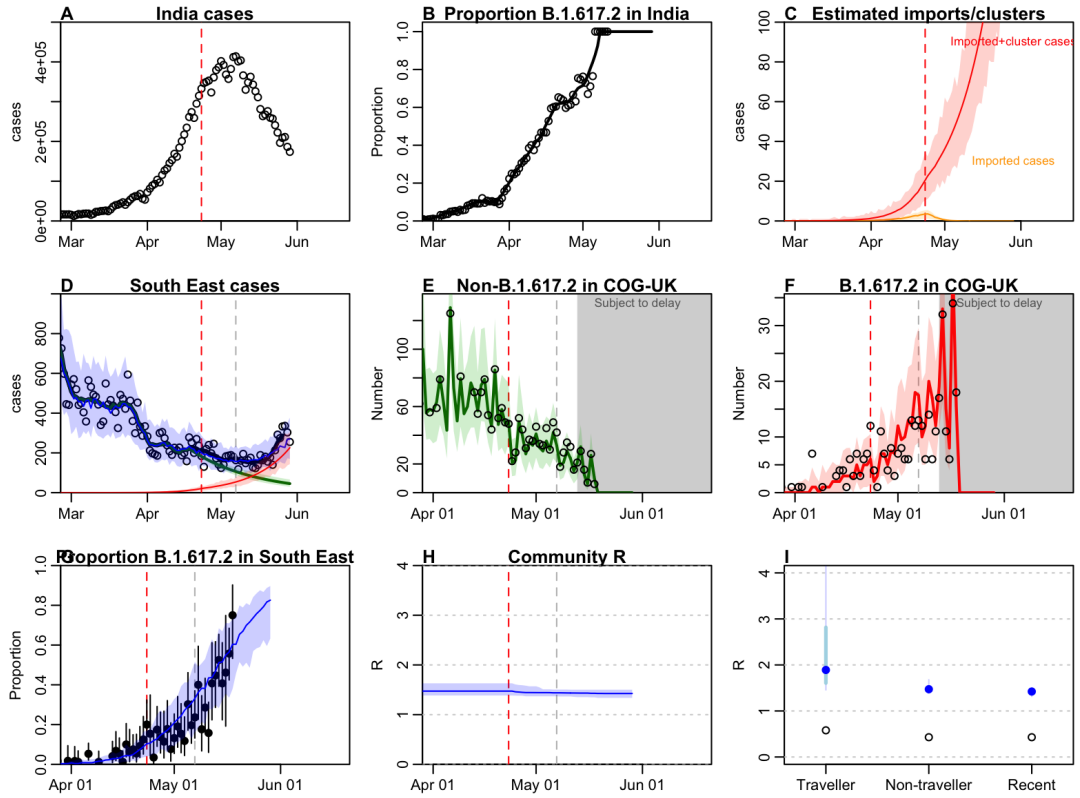


Figure 5: South East analysis. Panels same as Figure 1.

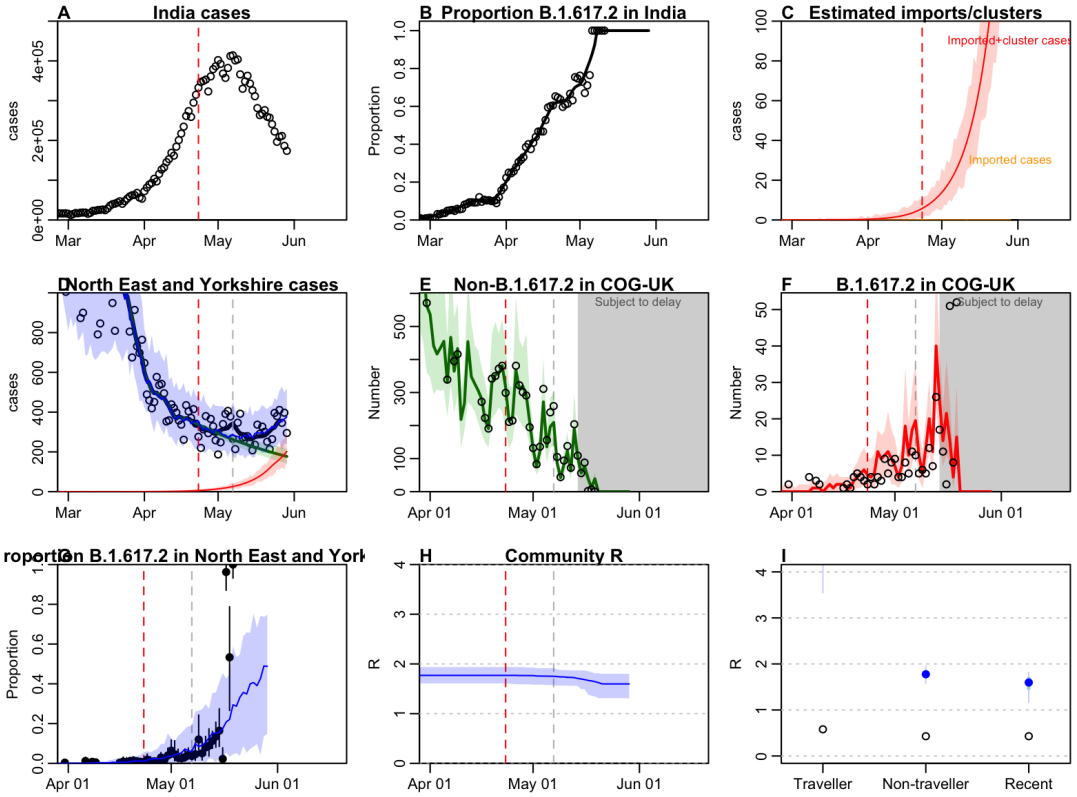


Figure 6: North East & Yorkshire analysis. Panels same as Figure 1.

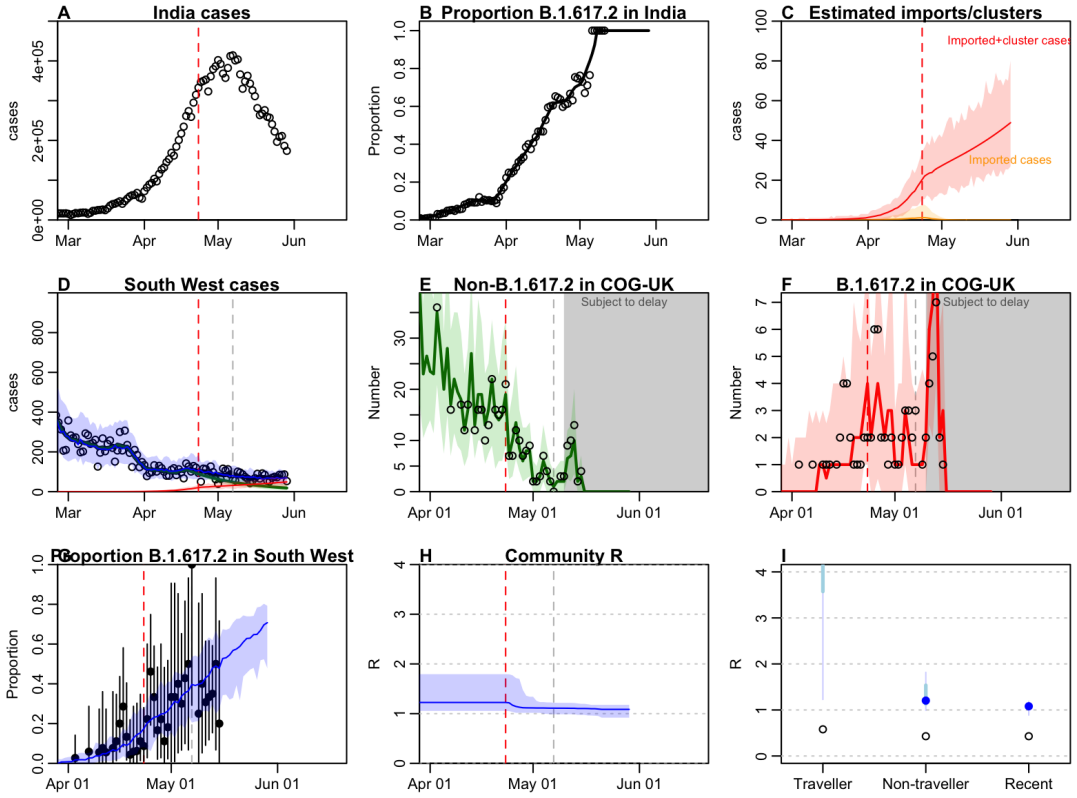
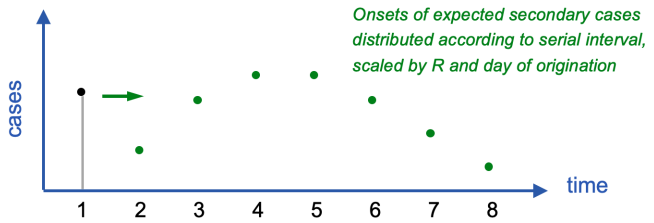


Figure 7: South West analysis. Panels same as Figure 1.

Methods

- We estimated imported cases of B.1.617.2 into each region 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.
- 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 each region, we calculated the 7 day centred moving average of cases overall in each region 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.

- For each region, 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 region (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 region (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). The posterior model estimates are shown in Figures C–I, with comparison to COG-UK data and overall cases.