Modelling importations and local transmission of B.1.617.2 in the UK

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Summary

- We used 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 B.1.617.2 sequences in COG-UK data (Figure 1).
- Based on importations and local cases of B.1.617.2, we estimated that the R of B.1.617.2 was 1.64 (95% CI: 1.61–1.67) in the UK assuming no change in generation interval. This would suggest that the majority of sequenced cases in the UK would consist of this variant by mid-May 2021, under the assumption that non-B.1.617.2 variants continue to decline at 3% per day as they did in late April 2021.
- We obtained similar conclusions but poorer fits to the data if we assumed 50% of imported B.1.617.2 cases were reported (R≈1.2–1.3), there was less potential for superspreading (R≈1.6) or a daily decline of only 1% for non-B.1.617.2 variants (R≈1.7) (Appendix Figures 1–4).
- 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. 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. 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 (black line), reported traveller cases of B.1.617.2 in PHE Technical Report 10 (black dots); simulated imported cases and onwards transmission in branching model (red line shows median, shaded region shows 95% PI). D) Reported cases in the UK. Black dots show data, black line shows 7 day moving average, dashed black line shows extrapolation assuming non-B.1.617.2 declines at 3% per day from 23rd April onwards. Red line as in (C); orange line and shaded region shows predicted total cases in UK. E) Black lines show proportion of B.1.617.2 sequences in COG-UK data up to 3rd May 2021, with 95% CI; blue line shows fitted model with 95% PI. F) Profile log likelihood for R.

Methods

- We estimated imported cases of B.1.617.2 into the UK by combining three data sources: reported cases in India, proportion of sequenced cases that were B.1.617.2 and reported imported cases into the UK from India. Details of these three data sources:
 - Reported cases in India from 1st February 2021 onwards were extracted from the covidregionaldata R package (Figure 1A).
 - Proportion of sequences in India were based on sequences reported in GISAID, aggregated by <u>outbreak.info</u> (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 there were 1079 imported cases from India between 1st February 2021 and 27th April 2021 (based on: Shingleton, SPI-M report, 27/4/21)
- We assumed that all imported infections from India ceased after the red listing on 23rd April 2021 (i.e. no leaks from hotel quarantine), and assumed a lognormal incubation period with mean 5.1 days and s.d. log(1.65) (McAloon al, BMJ Open, 2020) to estimate onsets occuring after the red list date among travellers (Figure 1C). Given the possibility of incomplete traveller information, sensitivity analysis assuming only 50% of imported cases are reported are shown in Appendix Figures 1–2.
- As a validation, we compared estimated imported to traveller cases reported during the same period (<u>PHE Technical Report 10</u>), omitting the most recent 5 days to reflect possibly incomplete data. These corresponded closely to our estimates (Figure 1C). If we instead use the full raw sequence data for imported cases (which are likely to be censored as a result of reporting delays), we obtain a higher estimate for R (because there are fewer imported cases to initial local clusters).
- To estimate overall B.1.617.2 cases resulting from initial imports, we used a continuous time branching process model (<u>Kucharski et al, EID, 2016</u>), with the serial interval assumed to be lognormal with mean = 5.4 days and s.d. log(1.5) (<u>Rai et al, Clin Epi Glob Health, 2021</u>). We assumed secondary transmission followed a negative binomially distributed offspring distribution with reproduction number R and k=0.2. Sensitivity analysis assuming k=0.8 shown in Appendix Figure 3.
- To estimate non-B.1.617.2 cases in the UK, we calculated the 7 day moving average of cases overall in the UK up to 23rd April 2021, then extrapolated forward assuming a 3% daily decline, based on the SPI-M consensus estimate (-5% to -1% per day). A sensitivity analysis assuming a daily decline of 1% is shown in Appendix Figure 4.
- We estimated R by simulating 100 stochastic outbreaks for each value of R, then calculating the binomially distributed likelihood of sequencing the number of B.1.617.2 cases observed in reality in COG-UK data on a given day (y_{ib}), given the mean number of B.1.617.2 cases on each day in the simulated outbreaks (E(x_{ib})) and non-B.1.617.2 cases in the UK (y_{ic}) and the number of cases sequenced (y_{in}). Specifically:

 $L(R \mid y) = \sum_{i} \log B(x = y_{ib} \mid n = y_{in}, p = E(x_{ib})/(E(x_{ib}) + y_{ic}))$

• The model trajectory using the MLE is shown in Figure 1C–D, with comparison to COG-UK data shown in Figure 1E and profile likelihood (with GAM fitted to raw estimates to calculate MLE and 95% CI) shown in Figure 1F.



Appendix Figure 1: Same as Figure 1, but assuming only 50% of imported B.1.617.2 cases are reported.



Appendix Figure 2: Same as Figure 1, but assuming only 50% of imported B.1.617.2 cases are reported, and assuming non-B.1.617.2 cases decline at 1% per day from 23rd April onwards.



Appendix Figure 3: Same as Figure 1, but assuming k=0.8.



Appendix Figure 4: Same as Figure 1, but assuming non-B.1.617.2 cases decline at 1% per day from 23rd April onwards.