Methods

**Epidemiological data**

Serial interval: mean of 5.4 and standard deviation of 1.5 days (Rai et al. 2021, and Neil’s spi-M report)

***Data from France***

<https://www.data.gouv.fr/fr/datasets/donnees-de-laboratoires-pour-le-depistage-indicateurs-sur-les-variants/> last accessed in early June

Use all age-class combined, include metropolitan France and oversee regions and departments, available at regional level(Admin2, 18 units). Data available from 28th of febrary2021 to 30th of may 2021.

Strain tested by Nextstrain code: 20I/501Y.V1 (alpha), 20H/501Y.V2 (beta) and 20J/501Y.V3 (gamma). The available data aggregated count of beta and gamma variant. Absence of strain detection was interpreted as wild type infection.

***Data from England***

[[Reference]] last accessed in ??

Use all age-class combined, include all England, data available for each NHS region (7 geographical units). Data available from 1st of September 2020 until 20th of June 2021.

Tested presence of S-protein marker?? [Need the specific info]. Throughout the available data, the presence of the mutation is interpreted as an alpha strain infection. Prior to the 15th of March 2021, the absence of S-protein was interpreted as an infection by the wild type virus. After the 15th of March 2021, the absence of S-protein was interpreted as an infection by the delta variant.

We therefore obtain 3 datasets:

* French dataset: include incidence of 3 strains. i.e. wild, alpha and combined beta-gamma
* England early dataset: include incidence of 2 strains, i.e. wild and alpha
* England late dataset: include incidence of 2 strains, i.e. alpha and delta

**Estimation of the time varying instantaneous reproduction number**

We use the package EpiEstim [REF] to estimate the instantaneous reproduction number. We obtained daily estimate for each region independently (i.e. 18 Admin 2 units in France, and 7 NHS region in England) using a weekly sliding window, and setting the prior Rt with a mean and standard deviation of unity.

To obain ‘indirect’ estimates of a variant’s transmission advantage over a reference variant, we divided both Rt estimates. We discarded Rt’s estimates as too uncertain when the width of 95%CrI exceeded 0.5. We also discarded all Rt’s estimates prior to the 11days of the data. The threshold was chosen so that as on day 11, over 99% of cases having been infected by a case on day 1 would be observed (i.e. 99th percentile of the serial interval distribution).

Posterior samples of this indirectly estimated transmission advantage were obtain for each region and each day where the conditions above were met using 100 Rt’s posterior samples per day and per variant. National aggregate of this indirectly estimated transmission advantage were obtained by simply pooling all regional estimates.

To gain insight into the potential temporal heterogeneity, we also estimated the transmission advantage during each of four non-overlapping quarters. Each quarter corresponded to 23, 46 and 22 days for the French, early England and late England datasets respectively.

**Joint estimate of the transmission advantage and transmissibility**

Using the new framework outlined above allow us to extract more information about the transmission advantage by relying on common information across region and time and assuming similar temporal trend affect all variant circulating.

For the joint estimation, serial interval distribution and Rt prior were set as described above. We set the transmission advantage prior with mean and standard deviation of unity. From the gibbs sampling procedure, we extracted a 1,000 posterior samples after a 100 sample burin period, and thinning by one in 10 sample.

Posterior samples of the transmission advantage were obtained for (i) each region independently and (ii) nationally by assuming a single underlying transmission advantage and region-specific Rt temporal trends. As this analysis focuses on estimating the transmission advantage, the instantaneous reproduction number was estimated daily.

Again independent estimates were obtained for each non-overlapping quarter.

Results

**Transmission advantage of alpha variant**

Estimating the daily reproduction numbers of both the alpha and wild type independently (i.e. using EpiEstim independently on each time series), we found some evidence for higher transmission of the alpha variant compared to the wild virus (Fig. heatmap 1). This was observed in both England and France. Combining all periods and regions where the reproduction number estimates were deemed accurate (see methods), we estimate a transmission advantage of the alpha variant over the wild type of 1.41 (95%CrI 0.86 ; 2.01) in England and of 1.21 (95%CrI 0.75 ; 1.65) in France.

The trends were consistent across regions (Figure errobar), with IQR of medians estimates of transmission advantages in England: [1.39 ; 1.42], and in Fance:[1.18 ; 1.25]. The trends across quarters were more variables (Fig. errbar), reflecting the level of incidence and therefore statistical power to estimate transmission advantage, range of median transmission advantage in England:0.89 ; 1.45, and in France: 1.00 ; 1.45

Using our novel framework, we were able to jointly infer a single transmissibility profile over time for each region assuming a single transmission advantage across region and time. As expected the novel framework gave estimates of the transmission advantage that were consistent with the ‘naïve’ approach above, but with greater accuracy. Combining all periods and regions, we estimate a transmission advantage of 1.45 (95%CrI 1.44 ; 1.46) in England and 1.29 (95%CrI 1.28 ; 1.30) in France.

Again, with our joint method, the trends were consistent across regions (Figure errobar), with IQR of medians estimates of transmission advantages in England: [1.40 ; 1.48], and in Fance:[1.28 ; 1.39]. The trends across quarters were still more variables (Fig. errbar), again reflecting variation in statistical power linked to incidence level, range of median transmission advantage in england:0.98 ; 1.50, and in France: 0.97 ; 1.43.

**Transmission advantage of delta and beta/gamma variants**

In England, we were also able to estimate the transmission advantage for the delta variant compared to the alpha variant (figure Heatmap and errorbar from SI). Using our joint estimation, we estimate the transmission advantage of the delta over alpha variant at 1.68 (95%CrI 1.61 ; 1.75). Again relying solely on independent daily estimates of the reproduction number, the estimate of transmission advantage were comparable but with much wider confidence intervals (median 2.10 ; 95%CrI 1.11 ; 6.09). As previously, the pattern were very consistent across regions, but less so across quarters, reflecting period of low incidence of one or both variant.

In France, we were able to estimate the combined transmission advantage for the beta and gamma variants compared to the wild type (figure Heatmap and errorbar from SI), which was comparable to the transmission advantage of the alpha variant. Using our joint estimation, we estimate the transmission advantage at 1.25 (95%CrI 1.24 ; 1.27). Again relying solely on independent daily estimates of the reproduction number, the estimate of transmission advantage were comparable but with much wider confidence intervals (median 1.16, 95%CrI 0.69 ; 1.74). As previously, the pattern were very consistent across regions, but less so across quarters, reflecting period of low incidence of one or both variant.