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Preliminary analysis of SARS-CoV-2 importation & establishment of UK transmission lineages

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The COVID-19 pandemic was first reported in China and has spread rapidly, causing epidemics around the world. Cases of SARS-CoV-2 infections in the United Kingdom (UK) are the result of virus introductions from other countries, followed by local transmission within the UK[1]. **Here we provide estimates of trends through time in the number and sources of SARS-CoV-2 introductions into the UK.** We obtain these estimates by combining data on the numbers of inbound travellers to the UK, estimated numbers of infections worldwide, and large-scale virus genome sequencing undertaken by the COG-UK consortium. Our preliminary analysis provides a platform for evaluating future trends in virus introduction, however it does not attempt to measure the relative contributions to the UK epidemic of importation versus local transmission, nor model the possible impact of public health interventions on virus introduction.

The key conclusions of our analysis are as follows:

1. The UK epidemic comprises a very large number of importations due to inbound international travel [2]. We detect 1356 independently-introduced transmission lineages, however, we expect this number to be an under-estimate.
2. The speed of detection of UK transmission lineages via genome sequencing has increased through time.
3. Many UK transmission lineages now appear to be very rare or extinct, as they have not been detected by genome sequencing for >4 weeks.
4. The rate and source of introduction of SARS-CoV-2 lineages into the UK changed substantially and rapidly through time. The rate peaked in mid-March and most introductions occurred during March 2020.
5. We estimate that ≈34% of detected UK transmission lineages arrived via inbound travel from Spain, ≈29% from France, ≈14% from Italy, and ≈23% from other countries. The relative contributions of these locations were highly dynamic.
6. The increasing rates and shifting source locations of SARS-CoV-2 importation were not fully captured by early contact tracing.
7. Our results are preliminary and further analyses of these data are ongoing.

The COG-UK consortium has to date generated >20,000 SARS-CoV-2 genome sequences from infections in the UK. Phylogenetic analysis of these genomes, and those from other countries, can be used to identify individual UK transmission lineages.

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[1] As the UK's epidemic grew, it also became an exporter of virus lineages to other countries, e.g. to Iceland.

[2] On average, about 50% of inbound travellers during 2020 are British nationals.

Here we define a "*UK transmission lineage*" as two or more UK infection cases that (i) descend from a shared, single introduction of the virus into the UK from elsewhere, (ii) are the result of subsequent local transmission within the UK, and (iii) were present in our virus genome sequence dataset (Fig. 1). These lineages can be identified by reconstructing evolutionary trees (phylogenies) of the global pandemic from virus genome sequences sampled worldwide. Note that this concept is distinct to a *transmission cluster,* which in epidemiology commonly refers to a group of cases that occur close to each other in space and time (e.g. in a hospital or care home). Therefore a large UK transmission lineage may comprise many different individual transmission clusters.

We have detected 1356 transmission lineages in the UK to date[3]. **For methodological reasons[4] this is likely to be an underestimate of the actual number of times the virus has been introduced to the UK with subsequent onwards transmission.** Appendix 1 provides an illustration of the largest lineages in our data set. The size distribution of UK transmission lineages is provided in Appendix 2.

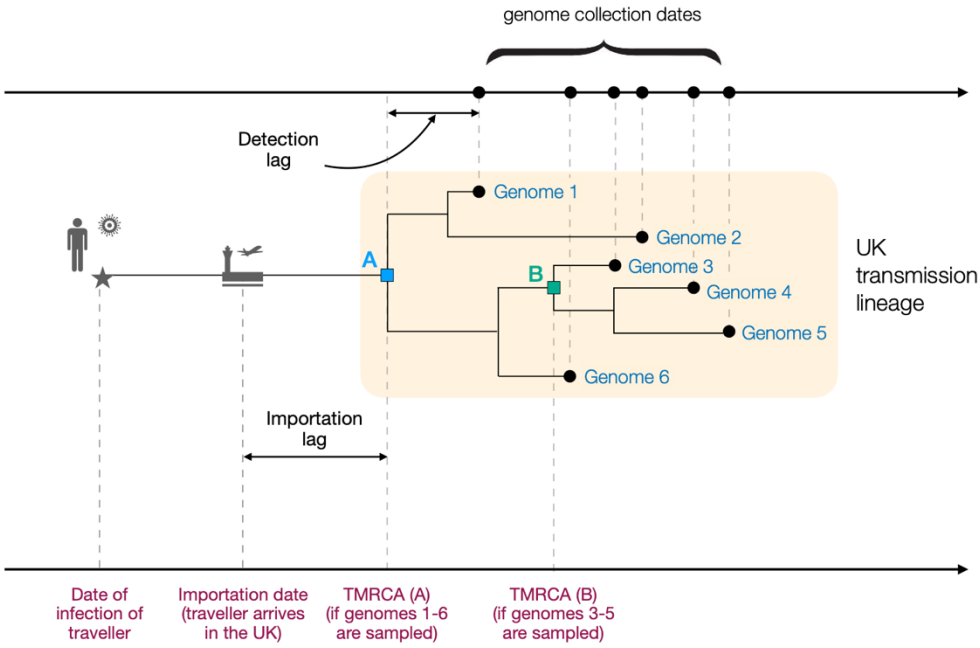


Figure 1: Figurative illustration of a UK transmission lineage detected through genome sampling. To be detected, a UK transmission lineage must contain two or more sampled genomes. The terms TMRCA, detection lag, and importation lag can be understood with reference to this figure. TMRCA A is observed if genomes 1–6 are sampled and TMRCA B is observed if genomes 3–5 are sampled.

[3] Our analysis is based on data available on 22/5/20, which comprised 16506 UK SARS-CoV-2 genomes and 11889 SARS-CoV-2 genomes sampled from other countries worldwide.

[4] Identifying UK-specific transmission lineages of SARS-CoV-2 is a complex problem. The estimated number of introduced lineages is likely to be conservative because we have virus genome sequences for only a small fraction of UK infections (perhaps 1-5%), hence many transmission lineages will have gone undetected; larger lineages are more likely to be detected than smaller ones. Furthermore (i) under-sampling of genomes from other countries will result in the mistaken aggregation of separately-introduced UK lineages, reducing the number of detected lineages, and (ii) 42% of UK genomes (n=6954) cannot be allocated to a UK transmission lineage on the basis of virus genetic relatedness (singletons). However, given the rate of SARS-CoV-2 genome evolution and the low fraction of sequenced, some of these singletons are likely to belong to UK transmission lineages (detected or undetected).

We combined genetic differences among the sampled virus genomes with a model of virus evolution to estimate the TMRCA (time of the most recent common ancestor) of each detected UK transmission lineage. The TMRCA is the date of the common ancestor of the sampled genomes in a transmission lineage (Fig. 1). While the TMRCA represents the earliest transmission event in the lineage revealed by the data, it does not necessarily represent the first transmission event in the lineage as a whole. Specifically, if the transmission lineage is well sampled then the TMRCA represents the date of the first transmission event in the UK lineage (TMRCA A in Fig. 1). However, if the transmission lineage is poorly sampled then the TMRCA may represent a later transmission event in the lineage (TMRCA B in Fig. 1). The "importation date" of each UK transmission lineage is the date that an infectious inbound traveller entered the UK. Figure 1 illustrates these and other terms used in this report.

The TMRCAs of the majority of UK transmission lineages are dated to mid-to-late March (Fig. 2; median=25th March, interquartile range = 17th March-1st April). It is important to note that these times represent the date of the first detected transmission event in each lineage, not the virus importation date (see Fig. 1). This distinction is explored further below.

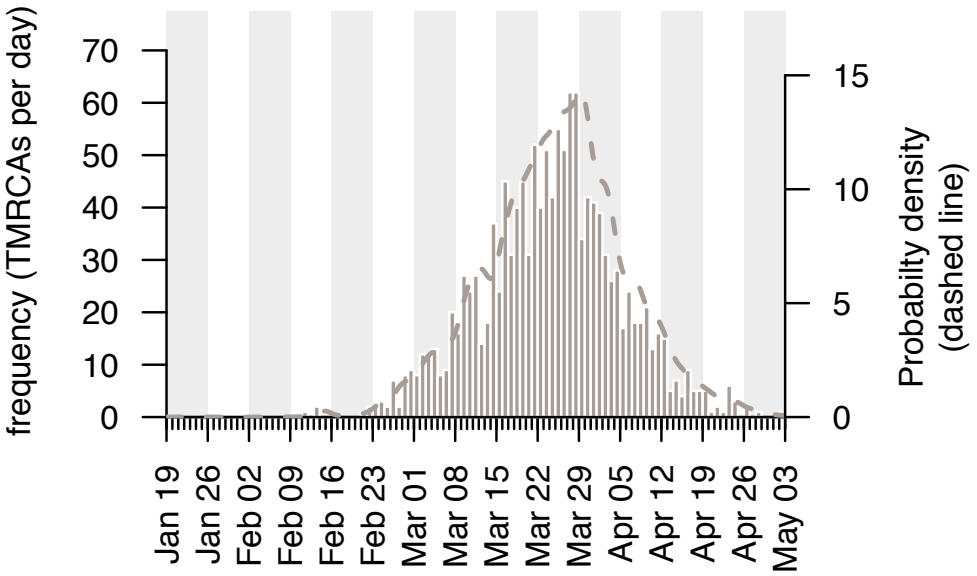


Figure 2: Estimated TMRCAs of detected UK transmission lineages (histogram; left hand axis). These dates are concentrated in mid-to-late March. The bars show the histogram for the median TMRCA of each lineage. The dotted line shows the corresponding probability density of TMRCA estimates after incorporating some aspects of phylogenetic uncertainty (right hand axis).

We can use the TMRCA values to estimate the genomic "detection lag" for each UK transmission lineage, which represents the length of time that a transmission lineage went undetected before it was first sampled by genome sequencing (see Figure 1 for explanation). This detection lag has decreased through time as the cumulative number of UK virus genomes generated by the COG-UK project has increased (Fig. 3).

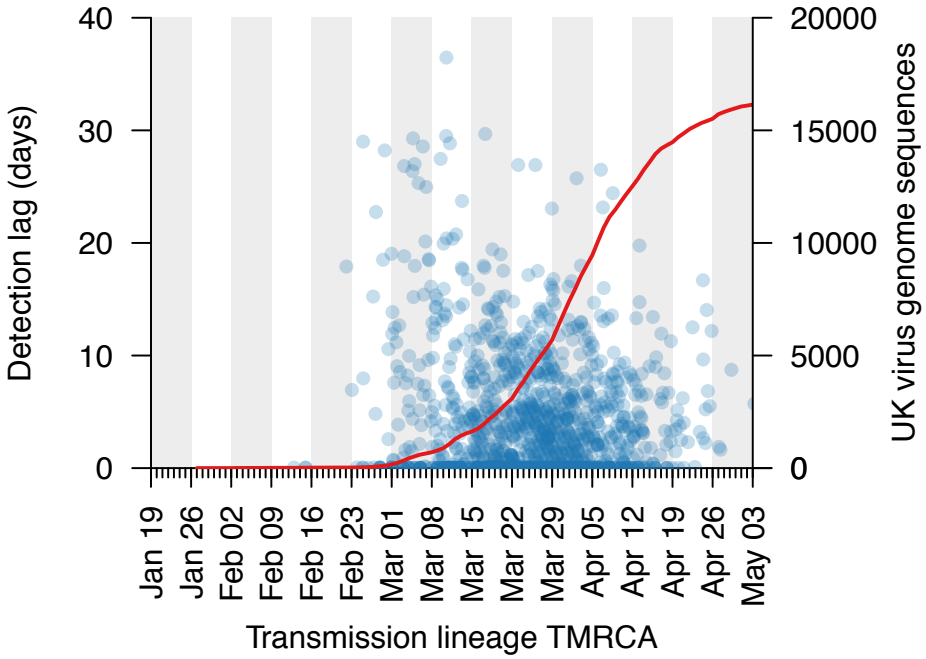


Figure 3: The genomic detection lag has decreased through time (blue points, Pearson correlation coefficient, r=-0.12), coincident with the accumulation of sampled UK virus genomes (red line).

In addition to having different dates of establishment (TMRCAs), UK transmission lineages vary in duration. Many have not been sampled for several weeks and are therefore very rare or gone extinct, most likely as a result of the interventions such as social distancing that led to reductions in the numbers of new cases. Fig. 4 shows how the composition of UK transmission lineages has changed through time. In early March the epidemic mostly comprised lineages that had been newly-detected for the first time, whilst by late April most transmission lineages had not been detected by genomic sampling for more than a week (see Appendix 1).

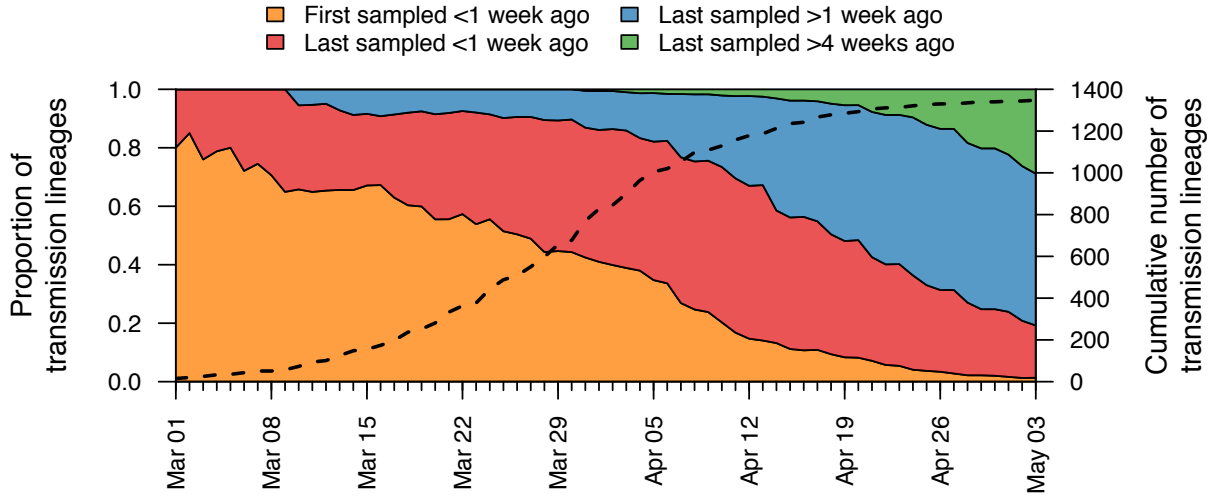


Figure 4: Trends through time in the detection of UK transmission lineages. The dotted line shows the cumulative number of detected lineages. For each day, all lineages detected up to that day were grouped into four categories (colours) depending on when genomes in that lineage were first, or most recently, sampled.

To understand the delay between importation and subsequent onward transmission within the UK, we quantified the dynamics of virus importation by combining data on the number of

inbound travellers into the UK with estimates of SARS-CoV-2 cases worldwide. Figure 5 shows how the number of inbound travellers and global SARS-CoV-2 prevalence changed through time. Until the beginning of March, the UK received ≈1.75m inbound travellers per week. This baseline increases by ≈10% at the end of the February half-term school holidays and varies predictably according to the day of the week. The number of inbound passengers fell rapidly and continuously after 8th March, leading to a ≈95% reduction in inward international travel by the beginning of April that has been maintained. The UK government advised against all non-essential overseas travel on 17th March and advised British travellers overseas to return to the UK on 23rd March. The estimated global prevalence of SARS-CoV-2 rose rapidly in March. Notably there was a period in mid-March when inbound travel to the UK was still substantial and coincided with high numbers of active cases elsewhere.

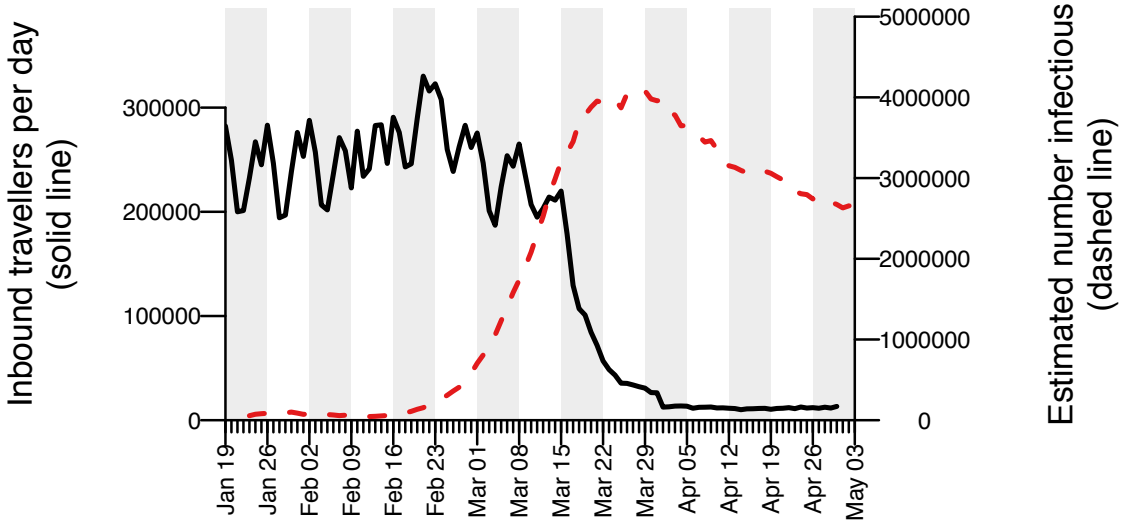


Figure 5: Estimated total number of inbound travellers to UK per day (black line) and the estimated number of infectious cases worldwide (dashed red line).

We combine the trends shown in Figure 5 to generate an empirical estimate of the daily intensity of SARS-CoV-2 importation into the UK (Fig. 6). This estimated importation intensity (EII) to the UK rises rapidly in early March, peaks around 15th March, then quickly declines to a low level in April.

The temporal profile of the EII closely matches, but precedes, that of the TMRCAs of UK transmission lineages (Fig. 6). The difference between the two curves represents the time elapsed between a virus importation and the first observation of UK transmission in the lineage that results from that importation (denoted “importation lag” in Figure 1).

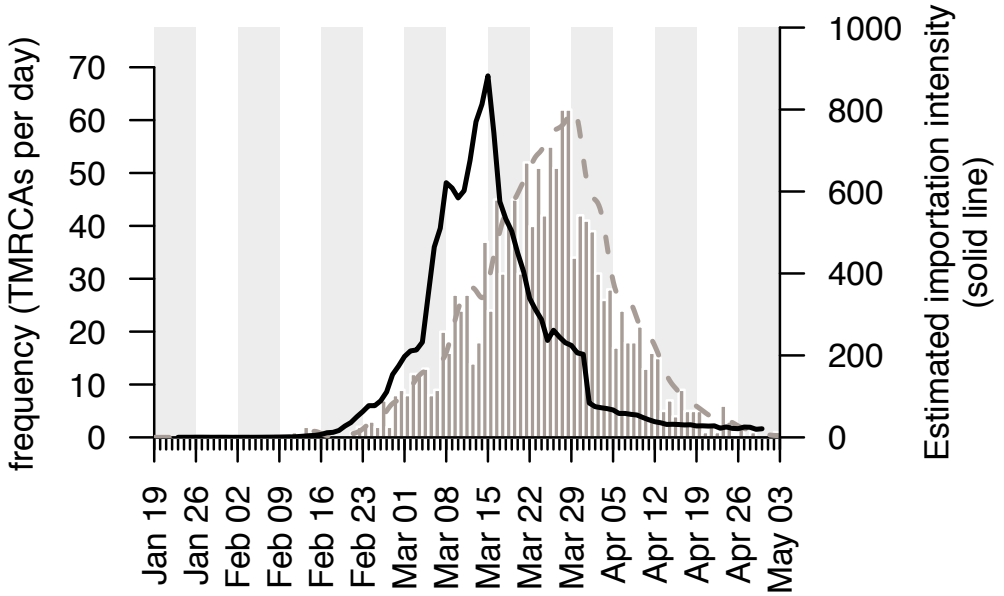


Figure 6: The estimated importation intensity (EII) curve (black line), and the histogram of UK transmission lineage TMRCAs. The average "importation lag" between the two curves is 10.7 days.

Using a statistical model we estimate the duration of the importation lag to be 10.7 days on average for all transmission lineages. However, the importation lag is expected to be shorter for large transmission lineages because the earliest transmission events within a lineage are much more likely to be observed if the lineage is well sampled (Fig. 1). Our data supports this: the estimated lag is 11.9 days for lineages of 2-5 genomes, 9.4 days for lineages of 6-15 genomes and 4.2 days for lineages >15 genomes. The latter value (4.2 days) is our best estimate of the duration between arrival of an inbound infected passenger and the first onward transmission event in the UK, and is similar to the estimated serial interval of SARS-CoV-2. By combining this statistical lag model with the estimated TMRCAs **we estimate that 80% of the importation events that give rise to detectable UK transmission lineages occurred between 28th February and 29th March 2020** (the remaining 20% of imports occurred before or after these dates).

The EII is highly dynamic because it is the product of two values (number of inbound travellers and epidemic size in countries of embarkation) that vary over orders of magnitude within a matter of weeks. In early March there was a high volume of arrivals into the UK, however the countries from which most of these arrivals originated had comparatively small numbers of active infections. Towards the end of March the situation was reversed with large epidemics in many countries but a low volume of international arrivals. The mid-March peak in importation occurred because moderate levels of inbound travel coincided with highly active transmission in several European countries.

To investigate the contributions to virus introduction of travellers arriving into the UK from different countries we estimated the number of inbound travellers for those countries with both high numbers of inbound travellers and COVID-19 deaths between Jan-Apr 2020 (Appendix 3). The greatest number of inbound travellers originated from Spain and France (≈30,000 per day from each before travel declined). Italy, The Netherlands, Germany, Poland, USA, Republic of Ireland[5], and Switzerland also contribute relatively high numbers of inbound travellers (Appendix 3). The volume of inbound travel (20,000 inbound passengers

[5] Our estimates do not include travel across the land border with the Republic of Ireland. See Summary of Methods for details.

per day from Spain in mid-March) shows that individual events, such as football matches, likely made a negligible contribution to the overall number of imports at that time. Large-scale and longer-term trends in prevalence and mobility are much more important.

The data described above enable us to estimate a separate importation intensity (EII) for each country (Appendix 4). The date when EII peaks varies among countries. Peak importation intensity was highest for Spain because there was a window of time when large numbers of inbound travellers from Spain coincided with high prevalence there (Appendix 3). France has the second highest peak EII. These results contrast with media coverage of importations that focussed more on the earliest importation events, from China and east and southeast Asia. Early importations were indeed likely to originate from those locations but constitute a tiny fraction of all importation events that resulted in detectable UK transmission lineages. Individual-level information about travel history acquired by contact tracing will mostly relate to infections acquired before March, when importation rates were low and before the importation intensity from Spain, France, and other European countries rapidly increased. Although inbound travel from France is as frequent as from Spain (Appendix 3), the epidemic in France occurred later, by which point there were many fewer inbound travellers, hence the EII for France is lower than that for Spain.

These trends are summarised in Fig. 7, which displays, for each day, the estimated number of importation events[6] (that led to a detected UK transmission lineage) that can be attributed to inbound travellers from each source country[7]. Early importations from China and Italy are, by early March, surpassed in number by importations from inbound travellers from Spain. The diversity of source locations also increases in March, with smaller numbers of importations attributed to a growing range of countries. In late March, the number of imports declines whilst the estimated relative contribution of travellers from France increases. The relative contribution of cross-channel movement to all international arrivals likely increased through time due to the collapse in inbound air travel.

[6] These are inferred dates of importation (obtained by combining the estimated TMRCAs with the importation lag model).

[7] Note that these estimates are *not* based on virus phylogeography (a technique we have used in previous studies). We find that, for many UK transmission lineages, the virus phylogeny is currently not sufficiently informative about likely locations of origin, due to low virus genetic variation relative to rates of international movement, and to variable rates of genome sampling among locations. Further genome sequencing around the world may improve this situation in the future.

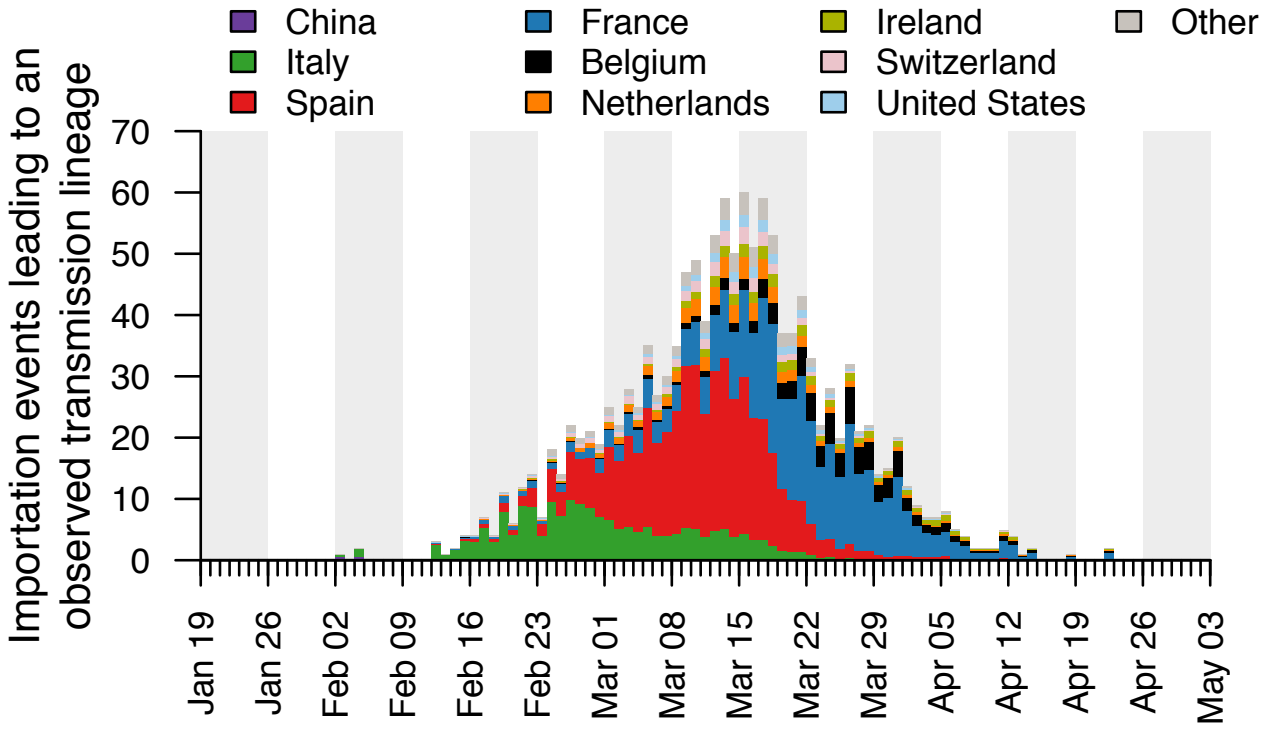


Figure 7: The estimated number of importation events that are attributable to inbound travellers from each of several source countries. Values shown are per day and not cumulative. Estimated dates of importations are obtained by combining the size-dependent importation lag model with the TMRCAs. Note that this is a statistical inference of the overall importation process, and cannot ascribe a specific source location to any given UK lineage[7].

By compiling the estimated importations through time, we estimate the fraction of detected UK transmission lineages that can be attributed to each country (Fig. 8). We estimate that ~34% of lineages arrived via inbound travel from Spain, 29% from France, 14% from Italy, and 23% from other countries[8]. Notably the contribution of China and other Asian countries to the number of detected transmission lineages was very small.

In summary, intensive sequencing of SARS-CoV-2 genomes reveals a high frequency of virus importations that led to onward transmission within the UK. Both the rate and source of virus importations fluctuate rapidly through time. We expect that similar trends in SARS-CoV-2 importation also occurred in other countries and regions that are highly connected by international travel, although these trends may be less apparent if fewer virus genomes are generated from those locations. The relative contributions of SARS-CoV-2 importation and local transmission to early epidemic growth in each country therefore warrants further investigation. These dynamics should be taken into account when planning and modelling future public health actions in the context of international travel.

[8] Since the sizes of transmission lineages vary considerably, this result does *not* imply that 34% or 29% of UK cases were descended from importations from Spain or France, respectively.

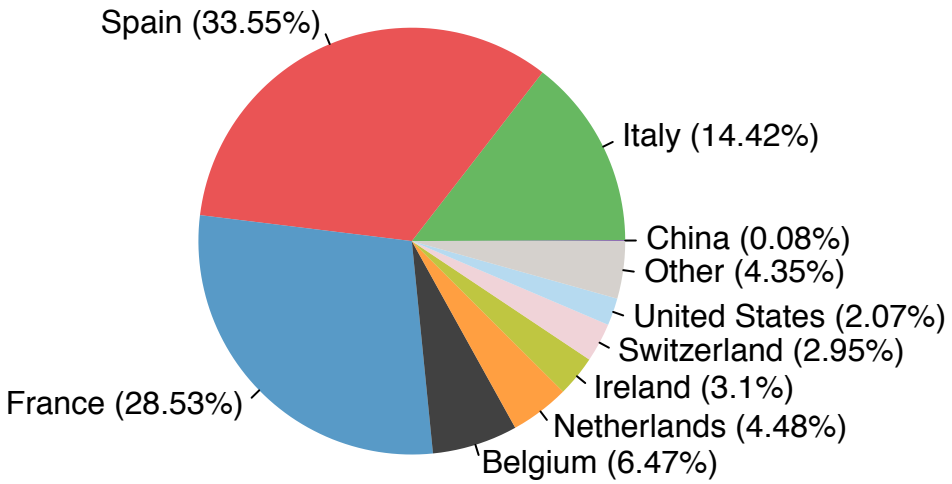


Figure 8: The estimated fraction of importation events that are attributable to inbound travellers from each country.

Limitations

A limitation of this preliminary analysis is that our estimates do not capture all the statistical uncertainty involved. The analytical framework used here is newly developed and it will take time before we can incorporate all sources of uncertainty in a statistically rigorous manner. The estimates reported here are preliminary and we focus on reporting results that we believe are robust. We have undertaken sensitivity analyses for several parameters and have compared our estimates of SARS-CoV-2 prevalence with those from more sophisticated model-based approaches. We are undertaking further work to explore the sensitivity of our results to the different ways in which UK-specific subtrees (lineages) are identified within the global SARS-CoV-2 phylogeny. Our estimates of the number of infectious individuals in each country are naïve and could be improved. For example, we assume that the probability of a traveller from country *X* being infectious is the same as that of a member of the general population of country *X* on the same day. This may be unrealistic when prevalence and rate of inbound travel vary among regions in a country. Our estimates of international rail passenger numbers are more uncertain than those for air and sea travel. The EII represents the varying likelihood of the introduction of infections into the UK but does not model the probability that an infectious arrival will initiate a local transmission lineage. Further work is needed to understand what factors might affect this probability of establishment. We intend to explore further how the number and size of UK transmission lineages observed in our sample relates to the actual number and size of transmission lineages in the general population.

Summary of Methods

UK transmission lineages were identified from SARS-CoV-2 genomes generated by the COG-UK consortium and genomics teams in other countries worldwide. Virus genomes used in this study are publicly available from https://www.cogconsortium.uk/data and https://www.gisaid.org.

All available virus genome sequences with appropriate metadata as of 22nd May 2020 were collated and aligned. Large-scale phylogenetic trees were estimated separately using IQTree v1.6.12 for the following global lineages: A (n=2056), B (n=3330), B.1 (n=7505), B.1.X (n=8408), B.1.Y.X (n=4157), and B.2 (n=2943). UK transmission lineages within these

large-scale trees were identified using a parsimony reconstruction of a two-state character (UK, non-UK). Many internal phylogeny nodes are polytomies comprising multiply sequenced identical genomes. If the genomes at such nodes had both UK and non-UK states, then the polytomy character state was conservatively reconstructed as non-UK. The UK genomes that exist at such polytomies were labelled as singletons. This approach aims to be conservative, i.e. it will likely underestimate the number of detected UK transmission lineages. The approach used here is specifically designed to identify UK transmission lineages descended from distinct introductions and is different from the "UK lineage" designation used within the COG-UK consortium for other purposes.

Each of these large-scale phylogenies was converted into a time-scaled tree by applying an externally-estimated posterior distribution of the rate of SARS-CoV-2 genome evolution (see below). The posterior rate had a mean of 9.41×10^{-4} nucleotide substitutions per site per year and a standard deviation of 4.99×10^{-5}. This rate was estimated from an alignment of 710 SARS-CoV-2 genomes sampled longitudinally through time using an HKY substitution model, a strict molecular clock model, and a skygrid coalescent prior, as implemented in BEAST 1.10. The conversion to time-scaled trees was performed using the strict molecular clock approach implemented in *treedater* (minimum branch length = 0.01 days). Molecular clock estimation was replicated 150 times for each large-scale phylogenetic tree, using 150 random resolutions of polytomies and 150 random rates drawn from the posterior distribution described above. The resulting distribution of TMRCA values therefore incorporates uncertainty in the estimated clock rate and polytomy resolution.

To estimate temporal trends in SARS-CoV-2 importation intensity we sought information on (i) the number of travellers entering the UK from each source country (comprising both British nationals and resident and visiting citizens of other countries) and (ii) the prevalence (i.e. number of infectious individuals) in each source country on each day.

Estimates for item (i) were generated by combining multiple data sources. The first source was a Home Office report providing numbers of inbound travellers arriving in the UK by air on each day during Jan-Apr 2020[9]. The second source was the percentage of inbound flight journeys to the UK that start from each country. These percentages are calculated from IATA data on a monthly basis, for January, February and March 2020. The proportions of inbound passengers from each country vary little between countries through time, so the percentages for March were extrapolated to April (for which no data is available). We combined these two data sources to estimate the number of air passenger arrivals in the UK from each country on each day. Third, we augmented the air passenger numbers with estimated numbers of travellers arriving per day by short-sea ferry and rail. The numbers of ferry passengers from France, Netherlands and the Republic of Ireland, and the number of Eurotunnel vehicle movements, were obtained from publicly available monthly records. Inbound rail travellers from France and Belgium were estimated from historical data and adjusted as far as possible for post-pandemic reduction in travel. Estimates of short-sea ferry arrivals in April, and of rail arrivals on all months, are less certain than those for travellers by air. Note, we have not incorporated estimates of land-border movements with the Republic of Ireland.

Estimates for item (ii) were obtained by back-extrapolating time series of cumulative deaths due to COVID-19 in each country. Cumulative death numbers were extracted from the Johns Hopkins University database (containing data from January 23rd to May 30th). Time series of reported deaths related to COVID-19 reported deaths were used rather than confirmed cases

[9] https://www.gov.uk/government/statistics/statistics-relating-to-covid-19-and-the-immigration-system-may-2020

as we are primarily interested in temporal dynamics rather than absolute values, and counts of deaths are believed to be less sensitive to changes in case definition and the level of surveillance. The difference in the number of cumulative cases on each day was used as the number of deaths on that day, truncated as zero for days where the cumulative value decreased (due to changes in reported numbers). On 17th April, 1290 additional deaths were added to the cumulative number of deaths in China that had occurred since the beginning of the epidemic but were not previously part of the database. Without a reliable way to distribute them across the time series, the count on this day was set to the same value as the preceding and subsequent days: zero. Estimates of the time after infection that an individual becomes infectious and experiences symptoms, the infectious duration, and the time between symptom onset and death (among those who will die from COVID-19) were taken from peer-reviewed sources[10]. Specifically we assumed an individual becomes infectious 3 days after being infected, symptoms begin 2 days later, the infectious period ends 5 days after that, and for those who will die, they do so 18 days after the onset of symptoms. Since the numbers of deaths is large, the variation in these timings among individuals will be averaged out and is not considered. Accounting for the amount of time each fatal case was infectious and how many fatalities there were on each day, we estimated the total number of infectious individuals (who would subsequently be reported as having died due to COVID-19) on each day. We estimated the total number of infectious individuals on each day as the number of infectious individuals (who would eventually die) on that day multiplied by the reciprocal of the infection fatality rate, which was set to be 1% (a value broadly consistent with those found in the literature for China, France, and passengers aboard the Diamond Princess; Verity *et al* (2020), Russel *et al* (2020), Roques *et al* (2020)). However, the main results presented here are invariant to the value of this scalar. Due to right censoring of the time series (i.e. recent dates do not incorporate those who will, but have not yet, died), the last 25 days were ignored and we only consider data up to May 5th.

To estimate the importation lag, the number of transmission lineage TMRCAs on each day was modelled as a constant fraction of the total number of importation events on each day up until then, where the propensity of a new importation to begin a transmission lineage is Poisson-weighted by how long ago it arrived. For example, for an average lag of 2 days, a transmission lineage whose TMRCA is on Friday could be due to an importation event on Monday or Tuesday, but is more likely to be due to an importation event on Wednesday. Due to the statistical properties of the TMRCA of a random sample from a subtree, the importation lag is expected to be longer for smaller transmission lineages. To account for this we fitted one lag for transmission lineages with 2-5 genomes (estimated to be 11.9 days), one lag for lineages with 6-15 genomes (9.4 days) and another lag for lineages >15 genomes (4.2 days).

For each country, the estimated daily importation intensity (EII) is computed by multiplying the estimated proportion of people in each country who are infectious on each day (see item (ii) above) and the number of people entering the UK from that country on that day (see item (i) above). We estimated country-specific EII curves for all countries. We display the curves for those countries with the greatest net contribution to virus introduction (see Appendix 4). The EII curves for remaining countries were calculated and then aggregated into a single category "Other". Here we use the EII as a measure of relative intensity through time and among countries. It is possible to interpret the global or country-specific EII values as the expected number of people entering the UK per day who are infectious. However, that interpretation requires us to assume that (i) the infection fatality rate used is accurate and constant across countries, and (ii) the probability of a traveller being infectious is the same as

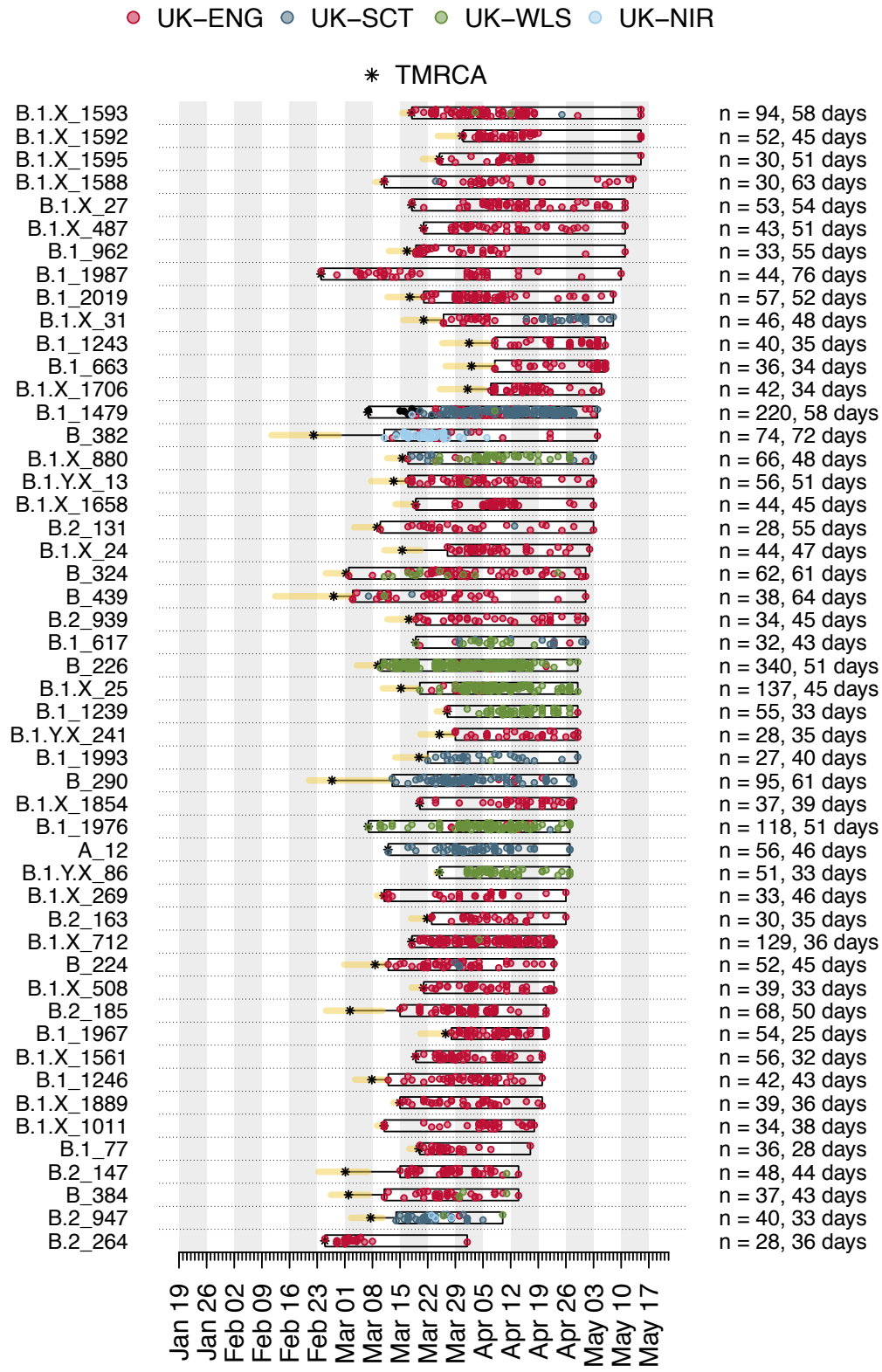
[10] Nature Medicine 26:672–675 (2020); The Lancet Infectious Diseases 20:669-677 (2020)

the proportion of the source country's population that is infectious on the same day. We caution that further work is needed to evaluate whether these assumptions are reasonable.

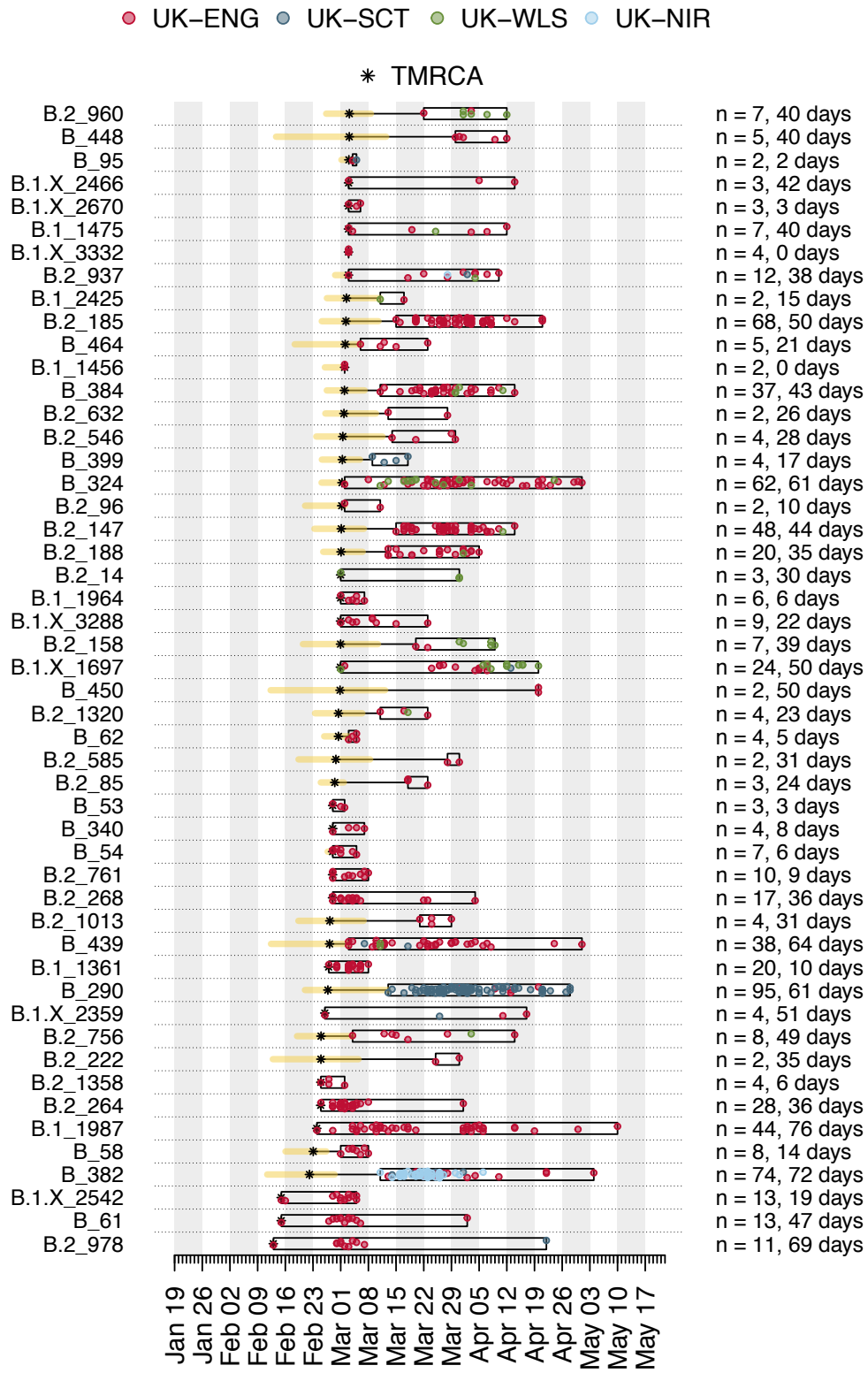
No personal or individual-level information was used or analysed in this study.

Acknowledgements
We thank all partners of and contributors to the COG-UK consortium, who are listed at https://www.cogconsortium.uk/about/. We acknowledge support from the Oxford Martin School. We thank Prof Christopher Dye for helpful comments and feedback. We thank Alexander Watts, Kamran Khan and Isaac Bogoch for assistance with global aviation statistics. We also acknowledge the important work of SARS-CoV-2 genome data producers globally contributing sequence data to the GISAID database.

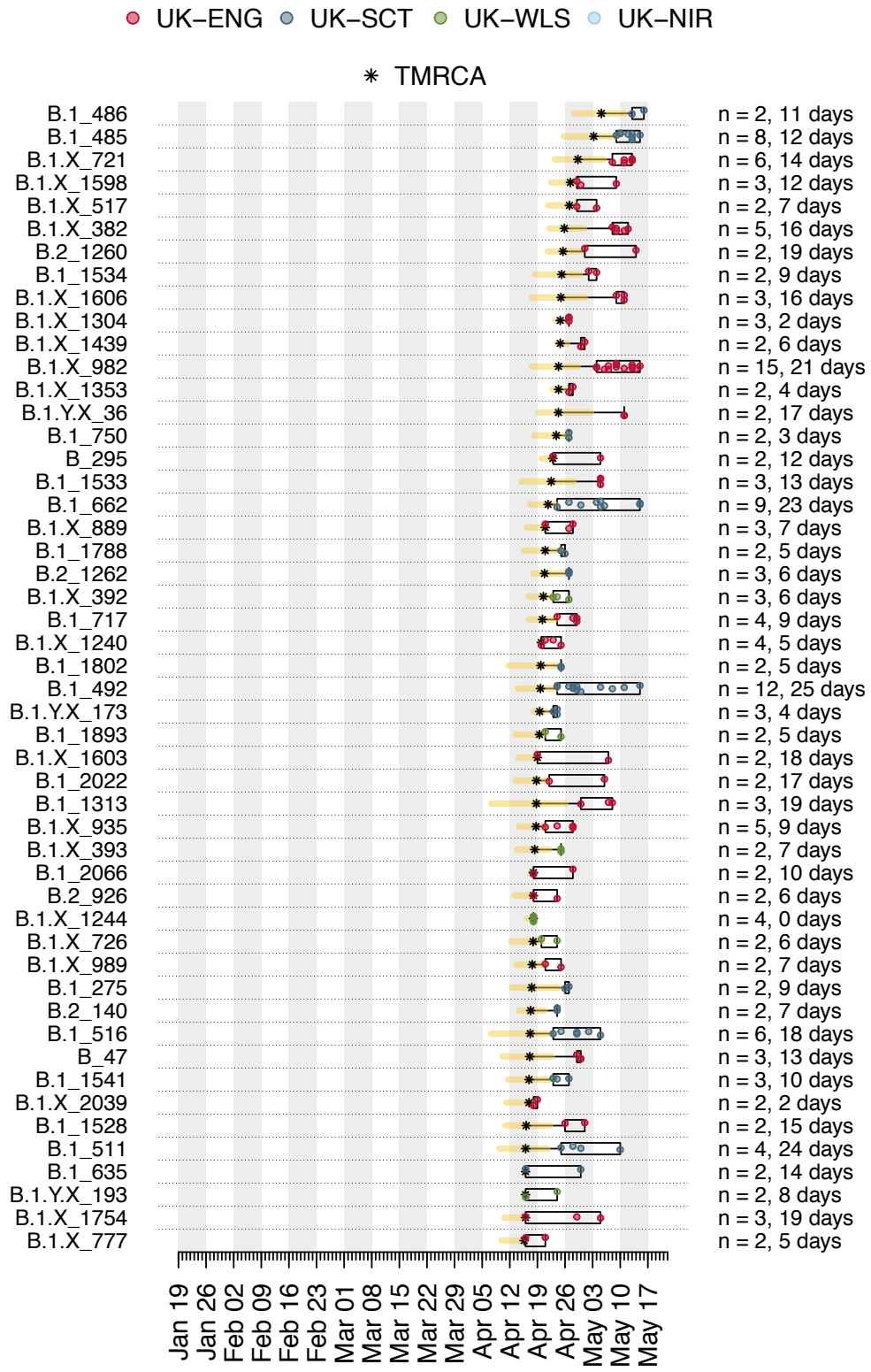
Appendix 1a: Illustration of the time course of the largest UK transmission lineages. Each row is a transmission lineage. Dots are genome sampling times (coloured by sampling location) and boxes show the range of sampling times for each transmission lineage. Asterisks show the median TMRCA of each lineage and the yellow bars show the 2.5% to 97.5% percentile range of each TMRCA. On the right, n indicates the number of genomes in the lineage, and the duration in days between the median TMRCA and most recently sampled genome is given.



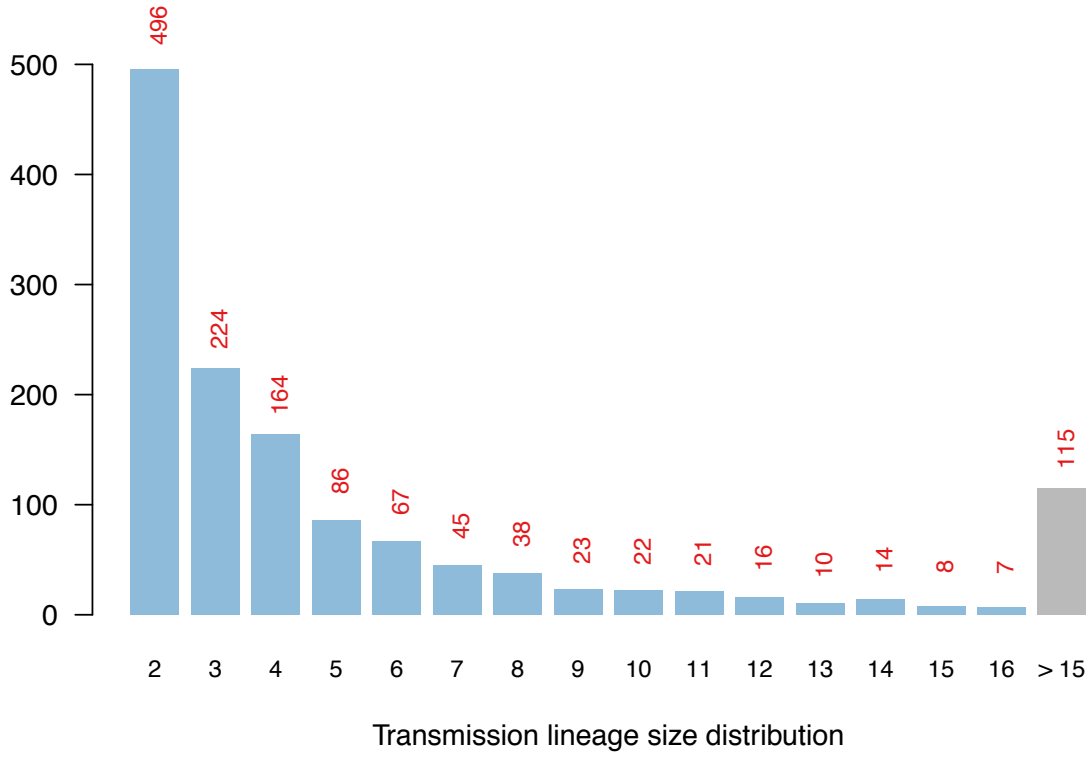
Appendix 1b: Illustration of the time course of the earliest UK transmission lineages. Each row is a transmission lineage. Dots are genome sampling times (coloured by sampling location) and boxes show the range of sampling times for each transmission lineage. Asterisks show the median TMRCA of each lineage and the yellow bars show the 2.5% to 97.5% percentile range of each TMRCA. On the right, n indicates the number of genomes in the lineage, and the duration in days between the median TMRCA and most recently sampled genome is given.



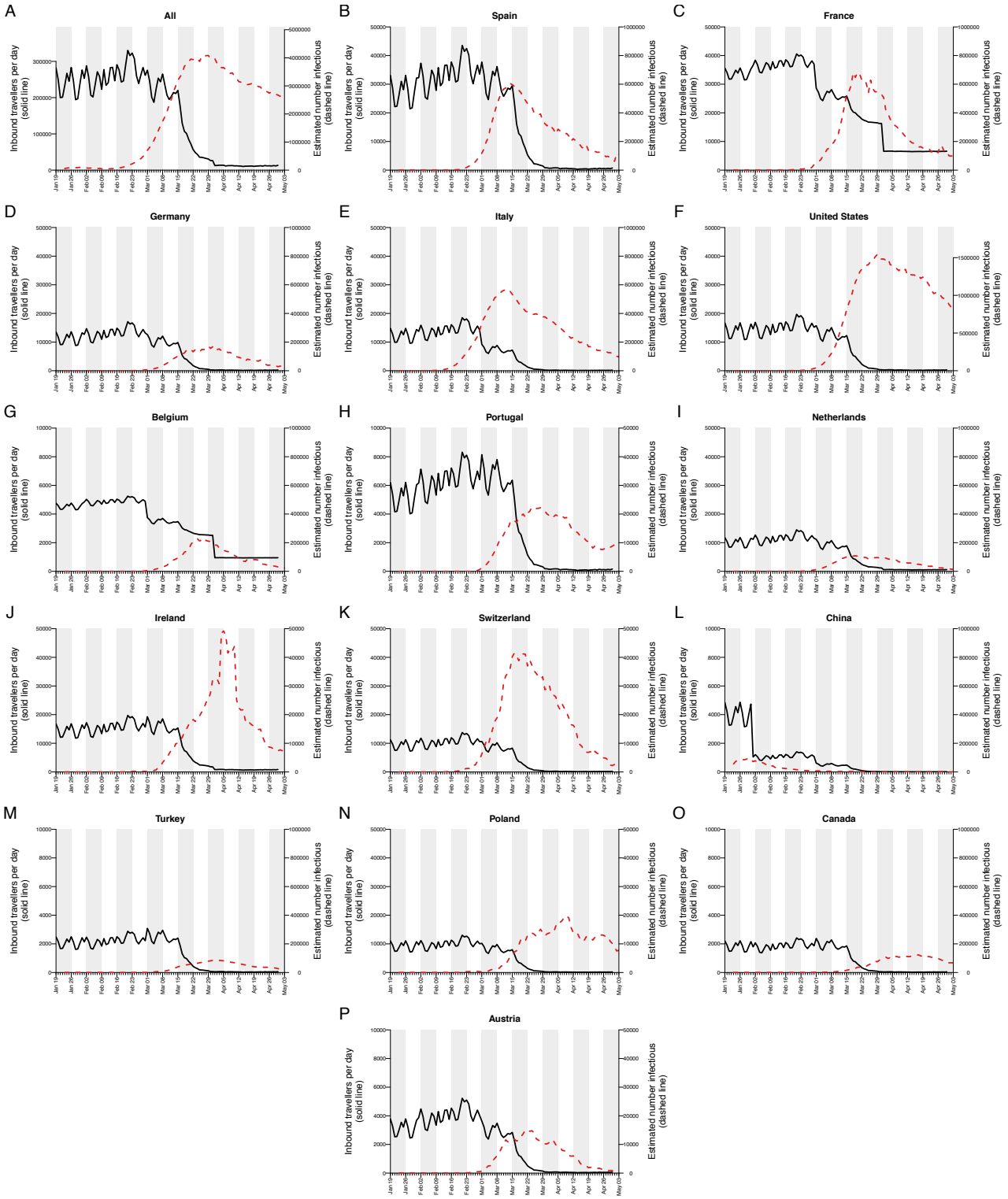
Appendix 1c: Illustration of the time course of the most recent UK transmission lineages. Each row is a transmission lineage. Dots are genome sampling times (coloured by sampling location) and boxes show the range of sampling times for each transmission lineage. Asterisks show the median TMRCA of each lineage and the yellow bars show the 2.5% to 97.5% percentile range of each TMRCA. On the right, n indicates the number of genomes in the lineage, and the duration in days between the median TMRCA and most recently sampled genome is given.



Appendix 2: Histogram of UK transmission lineage sizes (number of sampled virus genomes in each lineage). The number of lineages of each size is shown on the vertical axis and also in red text. In addition there were 6954 UK virus genomes that could not be reliably allocated to a transmission lineage due to either (i) limited virus genetic variation, or (ii) because only one genome had been sampled from the lineage. Many of these singletons will, in reality, belong to detected and undetected UK transmission lineages. The maximum number of detected transmission lineages that could be formed by these singletons is 3477. For related discussion see Footnote 4 in the main text.



Appendix 3: Estimated numbers of inbound travellers per day, and estimated number of active infections per day, for a range of countries (panels B-P). Panel A shows the total numbers for all countries combined (same as Figure 5).



Appendix 4: Estimated importation intensity (EII) curves for a range of countries with large COVID-19 epidemics or which experience high travel volumes with the UK (panels B-D). Panel A shows the EII for all countries (black line) and for all countries not in panels B-D (dotted line).