Preliminary estimates of the international spreading risk associated with the SARS-CoV-2 VUI 202012/01

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Summary

In this report we provide a preliminary assessment of the potential spread of SARS-CoV-2, (VUI – 202012/01) outside the United Kingdom (UK) and provide a modeling analysis of the risk of its international dissemination. We provide a list of the top 20 countries at risk of introduction of the variant, and estimate the number of VUI – 202012/01 introductions outside UK considering different potential transmissibility increase for the variant.

Backgound

In the last two months, public health officials in the United Kingdom (UK) observed a rapid increase of COVID-19 cases in the South East of England and London. Despite a second national lockdown in November, the 14 day confirmation rates quadrupled since October (1). Detailed analyses attribute more than half of the cases in the region to a new variant of SARS-CoV-2 named *first Variant Under Investigation in December* (VUI – 202012/01), also known as lineage B.1.1.7 (1).

The new strain was detected in October from samples initially taken on September 20 in Kent and on September 21 London (2; 3). Official data from the Office for National Statistics (ONS), presented to the public in a press conference on December 19^{th}, show how the percentage of cases of the new variant in London, South East and East of England shifted, respectively, from 28%, 28% and 23% in mid November to 62%, 43% and 59% in the second week of December (4). Furthermore, the minutes of *New and Emerging Respiratory Virus*

Threats Advisory Group (NERVTAG) meeting on the 18^{th} of December paint a concerning picture (5). In fact, the growth rate of the new variant, estimated from genomic data, appears to be 71% ($95\%CI : 67\% - 75\%$) higher than others. Studies of the correlation between R_t and detection of the variant suggest an absolute increase of R_t from 0.39 to 0.93. PCR cycle threshold (ct) values show a decrease of around 2 and viral loads from several genome reads show a 0.5 increase in the median log_{10} values for the new variant. Furthermore, Public Health England estimates that an area with an effective reproductive number $R_t = 0.8$ without the new variant would have an $R_t = 1.32$ [95%CI 1.2-1.5] if only the new variant was present (6). A recent analysis, conducted by fitting a two strains model to the epidemic data from the most affected areas in England, suggests that the new variant is 56% more transmissible ($95\%CI : 50\% - 74\%$) (7). However, at the moment there is not enough evidence to draw conclusions about variations in age distribution of cases, disease severity or antigenic escape (5).

In terms of its spread the data is still fragmented. However, preliminary genomic analysis of the variant report, as of 15^{th} of December, 1619 genomes in the the B.1.1.7 lineage sampled: 519 in Greater London, 555 in Kent, 545 in other regions of the UK (3). Few days earlier, on Dec 13, the official number of confirmed cases of the new variant in the England was reported to be 1108 (6). As of December 14^{th} Wales confirmed 20 cases (8), while Scotland 18, as of December 21^{th} (9). To date, a few cases of the new variant have been reported by Australia (one), Belgium (four), Canada (two), Denmark (nine), France (one), Germany (one), Italy (two), Ireland, Israel (four), Japan (five), Lebanon, Netherlands (one), Singapore (one), Spain (four), and Sweden (one), Switzerland (three) (1; 10; 11; 12; 13; 14; 15; 16).

Starting on December 19, 2020, parts of England (including London) have been put under stricter measures to try to stop the spread, restricting movement within and between the most affected areas (17). In fact, a new tier, tier 4, has been introduced as result. Furthermore, as of December 20, 2020, more than 40 countries around the world have imposed a travel ban on UK arrivals (18).

Model

Here we use a detailed individual based mobility model to estimate the extent of the outbreak and the risk of international dissemination on a longer time scale. Our model simulates the mobility of people across more than 3,300 subpopulations in about 190 countries/territories. Subpopulations are defined by the catchment area of major transportation hubs. The mobility among subpopulations integrates the mobility by global air travel (obtained from the International Air Transport Association and Official Airline Guide databases) and the short-scale mobility between adjacent subpopulations, which represents the daily commuting patterns of individuals (see Data & Methods). We use year 2020 data on passengers traveling outside of the United Kingdom (origin-destination data) provided by OAG. The transmission dynamics take place within each subpopulation and assume a classic SLIR-like compartmentalization scheme for disease progression similar to those used in several large scale models of SARS-CoV-2 transmission (19). Each individual, at any given point in time, is assigned to a compartment corresponding to their particular disease-related state (being, e.g., susceptible, latent, infectious, removed). This state also controls the individual's ability

to travel. We assume that only individuals that do not test positive to SARS-CoV-2 tests can travel (approximated here by considering that only people in the Latent compartment travel). Individuals transition between compartments through stochastic chain binomial processes.

The model considers the emergence of the VUI – 202012/01 in mid September in the London area. As UK sequences about 5% to 10% of positive cases (20), we assume a conservative initial conditions for a cluster of symptomatic/exposed infectious individuals drawn from a Poisson distribution with mean value of 10 symptomatic individuals for the collection of the first VUI – 202012/01, on September 20, 2020. We also assumed that the new variant has the same characteristic times (latency, generation time etc.) observed for SARS-CoV-2 so far. We explore the VUI – 202012/01 transmissibility in the range of $R_t = 1.3$ to $R_t = 1.8$ during the simulation time.

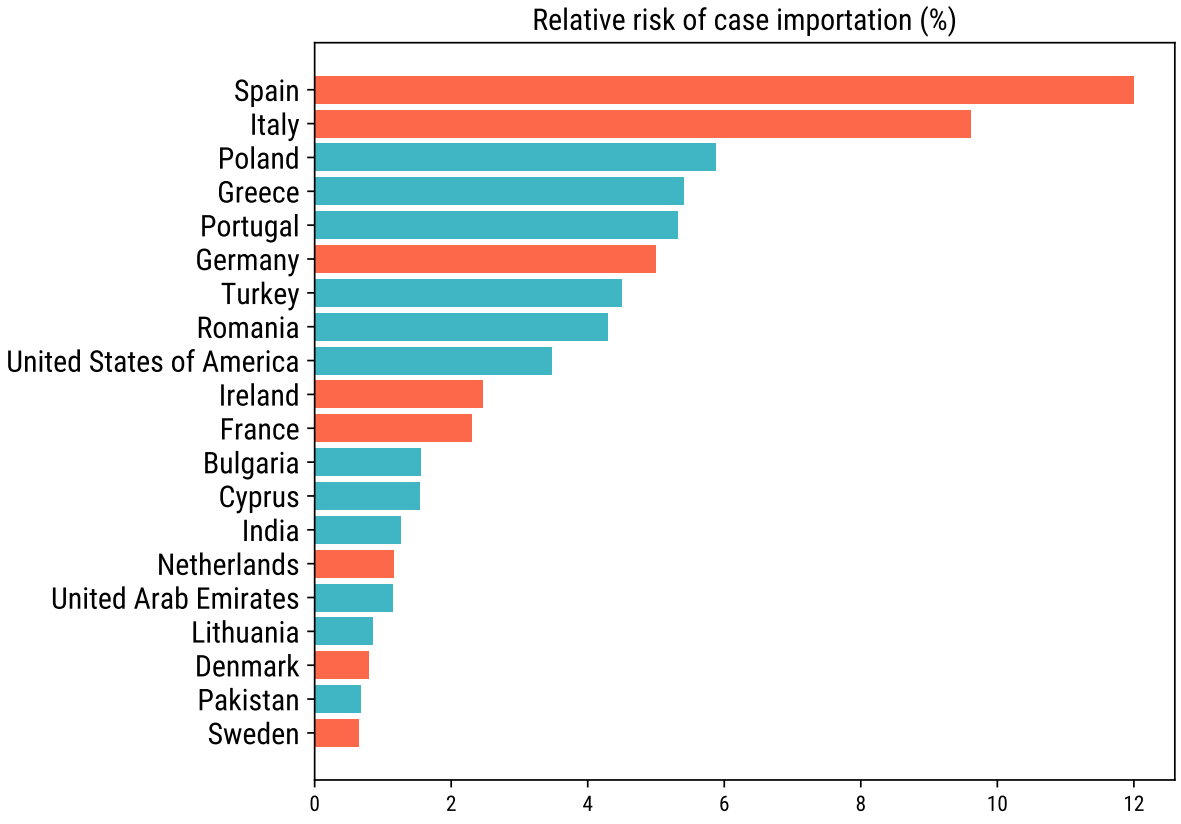

Figure 1: Relative risk of case importation for the top 20 countries. The countries highlighted in orange have already detected cases of the VUI – 202012/01.

Results

The model estimates two main quantities:

VUI–202012/01 R_t in the UK	Worldwide introductions (median)	(95% CI)
1.3	11	[2 – 35]
1.4	25	[3 – 75]
1.5	63	[8 – 175]
1.6	158	[23 – 422]
1.7	394	[63 – 1000]
1.8	978	[192 – 2,389]

Table 1: Estimated median number of introductions of VUI – 202012/01 outside the UK as of December 20, 2020 for the different UK transmissibility scenarios considered.

- Relative importation risk: for each destination Y, the model estimates the probability $P(Y)$ that a single infected individual travels from the UK to a specific destination country Y. In other words, given the occurrence of one traveling infected individual, $P(Y)$ is the probability that the disease carrier will appear in country Y, with respect to any other possible country.

- Exported cases: the model estimates the probability $P(n)$ of introducing n infections in countries outside of the UK. To calculate the distribution P we simulate mechanistically the model and record the number of introduction observed for the different increase of the variant transmissibility (varying R_t).

We used the model to estimate first the relative risk of case importation at the country level. In Fig. 1 we report the top 20 countries across the world ranked according to probability importation $P(Y)$. The countries colored in orange have already detected the new variant.The ranking of countries is depending on the relative volume of the International origin-destination travel patterns and it is not changing with the transmissibility of the new variant. The volume of introduction worldwide is instead strongly dependent on the growth of the number of cases within the UK. In Table 1 we report for each potential value of R_t the estimated median number of introduction and the 95%CI observed in 10,000 stochastic simulations.

Discussion

The model highlights the relative risk of observing the SARS-CoV-2 variant VUI–202012/01, around the world. We observe that the number of potential international introductions of the variant is strongly depending on the potential increase in transmissibility, that is encoded in the effective R_t characterizing the variant's spreading. We are not specifying what is the mechanism for this increase that could be biological or due to other changing conditions related to SARS-CoV-2 mitigation in the affected areas.

Even for moderate estimates of potential increase of transmissibility, we estimate an appreciable number of international introductions. The SARS-CoV-2 variant VUI–202012/01 could thus be already present in several countries across the world. It is important to stress that the separate introductions are not necessarily leading to transmission chains, thus it is not possible to estimate precisely how many countries may already experience

VUI–202012/01 active transmission. It is also worth remarking that if any of the introductions has led to local transmission chains, the variant could be spreading also from other countries and not just from the UK. Lack of extensive sequencing in many countries makes it very hard to detect possible introductions unless large clusters of transmission of the new variant are already taking place.

Larger increase in transmissibility ($R_t > 1.5$) indicates with high confidence that the variant may be already spreading outside the UK. Airline traffic restrictions and border control will contribute to slow the spreading of the variant by limiting the future number of introductions in other countries across the world. However, it is important to consider the economic cost of travel limitations and trade-off with the likelihood that the variant is likely already present in several countries worldwide. Travel bans aimed only at the UK could be ineffective if other countries are already experiencing VUI–202012/01 ongoing transmission.

Limitations

We assume a fixed transmissibility during the simulations period, although variations of R_t could have occurred in the area due to changes in the non-pharmaceuticals interventions. The variant's mutations could lead to changes in the characteristic times describing the course of the disease, notably in the incubation and generation time. We are not considering the detection of asymptomatic/presymptomatic individuals due to testing requirements (COVID-free flights, international travel policies etc.). We assume that travel probabilities are homogeneous across all individuals in the UK. This implies that the travel probability is independent of age, risk of exposure, and specific location within the UK. Furthermore, the model assumes statistically independent case introductions. Thus events with the introduction of multiple but related cases, such as family clusters, are considered as single importation events. Even given the above limitations we hope that this preliminary analysis of the new strain outbreak and the associated risk of international spread provided here may be useful to national and international agencies.

Data & Methods

Data. The airline transportation data used in the platform are based on origin-destination traffic flows from the Official Aviation Guide (OAG)(21) and IATA(22) databases. We use the average number of daily passengers traveling outside of the United Kingdom (origin-destination data) during the month of October 2020. Commuting flows are derived by the analysis and modeling of commuting data collected from the Offices of Statistics for 30 countries on 5 continents. The full dataset contains about 80 thousand administrative regions on five continents and over 5 million commuting flow connections between them (23). Population data are obtained from the high-resolution population database of the Gridded Population of the World project from the Socioeconomic Data and Application Center at Columbia University (`sedac.ciesin.columbia.edu`). The model considers geographical cells of 0.25° x 0.25°, corresponding to an approximately 25km x 25km square for cells along Earth's equator. Cells are then grouped into subpopulations defined by a Voronoi-like tessellation of the Earth's surface centered around major transportation hubs in different urban

areas. The model includes over 3,300 subpopulations in roughly 200 different countries and territories (numbers vary by year). The full model is described in detail in Ref. (19).

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