Preliminary results of the transmissibility of novel SARS-CoV-2 Variant of Concern 202012/01 in Belgium

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Data sources

- sequencing data of S-dropout samples (weeks 49-53 2020, weeks 1-2 2021)
- counts of tests showing S dropout as a share of all positive tests (1-22 Jan 2021)
- to minimise bias in our results, data from UZ Ghent & UZA were excluded, as these labs were heavily involved in pro-active screening of UK variant infection clusters, and data from ULG - FF 3.x were excluded due to low sample size
- COG-UK sequence data (version of 22nd of December, aggregated by NHS region)

Methods

- The increase over time in share of S-dropout samples that are actually 501Y.V1 are estimated from sequencing data of S-dropout samples using a binomial generalized linear mixed model (GLMM) with sample date included as a covariate and an observation-level random effect included to take into account overdispersion
- The estimated growth rate advantage of the 501Y.V1 variant (i.e. the difference in Malthusian growth rate per day of 501Y.V1 minus that of the wild type variants) is estimated from the S gene dropout data using a binomial GLMM of the proportion of cases that are consistent with being 501Y.V1. This model uses the counts of S dropout samples, multiplied by the estimated probability of being 501Y.V1 (as estimated by a separate binomial GLMM fit on S gene dropout sequencing data in function of sample data), as a proportion of the count of all positive tests on a given day. Sample date and laboratory were included as fixed effects and an observation-level random effect was included to take into account overdispersion. A model with or without an interaction effect between laboratory and sample date were both fitted to test if the rate at which 501Y.V1 displaces other strains occurs at the same rate throughout Belgium or not. The growth rate advantage is given by the slope in function of time in this binomial GLMM (Davies et al. [1]).
- The estimate transmission advantage (increase in infectiousness in terms of multiplicative effect on the effective reproduction number *Rt*), assuming an identical generation time, can be shown to be equal to $\exp(\Delta r \, . \, T)$ [1], where T is the mean generation interval (here taken to be 4.7 days, Nishiura et al. 2020 [2], which is the value that historically has been used throughout the epidemic by Sciensano, and therefore provides the best point of reference).

Preliminary results

Increase over time in share of S-dropout samples that are 501Y.V1

Sequencing results of S-dropout samples show that the share of S-dropout samples that are actually the 501Y.V1 UK SARS-CoV2 variant has been rapidly increasing (Figure 1), with the percentage that is 501Y.V1 among newly diagnosed S dropout samples as of today (26/1/2021) being estimated at 97% [89-99%] 95% CLs, or among new infections (curve shifted ca. 7 days to the left) at 99% [93.7-99.8%] 95% CLs. S-dropout in Belgium can therefore now be used as a reliable proxy for a sample being the 501Y.V1 variant.

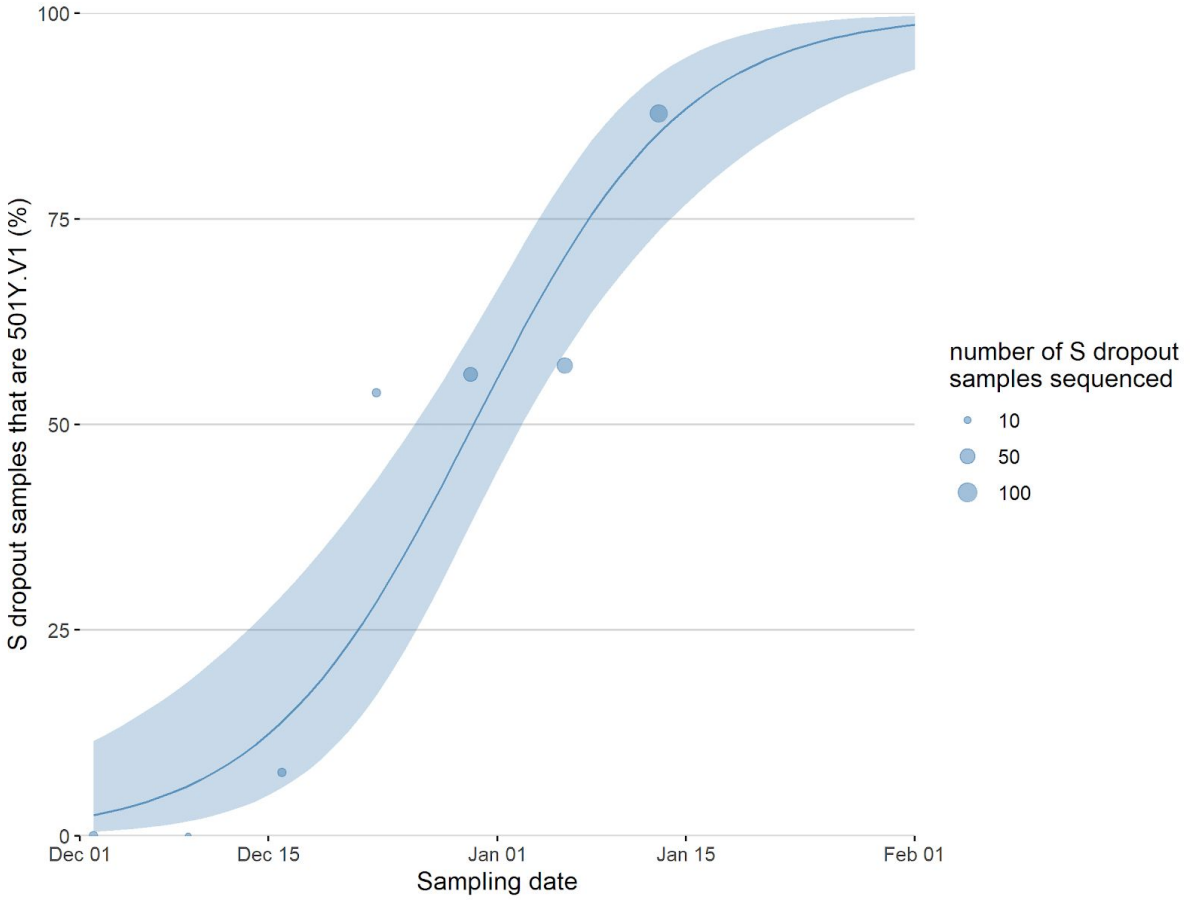


Figure 1. The increase in the proportion of S dropout samples that are actually the 501Y.V1 variant (binomial GLMM with 95% confidence intervals).

Growth rate advantage and increased infectiousness of variant 501Y.V1

A common-slope binomial GLMM fitted the available data best based on the Bayesian Information Criterion (BIC). In addition, in a model with separate-slopes per laboratory (region), there were no significant differences in the inferred slopes of the binomial GLMM in function of time across the different laboratories (Tukey posthoc tests for differences in slopes, calculated using R's *emtrends* function in the *emmeans* package, all $p > 0.05$). Hence, we can conclude that the variant 501Y.V1 is displacing other strains at approximately

the same rate across the whole of Belgium. The common-slope binomial GLMM had a marginal slope of 0.12 [0.09-0.16] 95% CLs (observation-level random effect variance: 0.45), which implies that the 501Y.V1 variant has a 12% [9-16%] higher growth rate than the previous SARS-CoV2 wild types. This estimate is compatible with other international data, which demonstrate a growth rate advantage of the 501Y.V1 variant of 11% [10-12%] in the UK (Davies et al. Table S1, [1], range 9-15% across different NHS regions), 8% [7-10%] in Denmark (Davies et al. Table S1, [1]), 8% [7-10%] in Portugal (Borges et al., [3]) and 8% [7.5-9.5%] in the US (T. Bedford, pers. comm.).

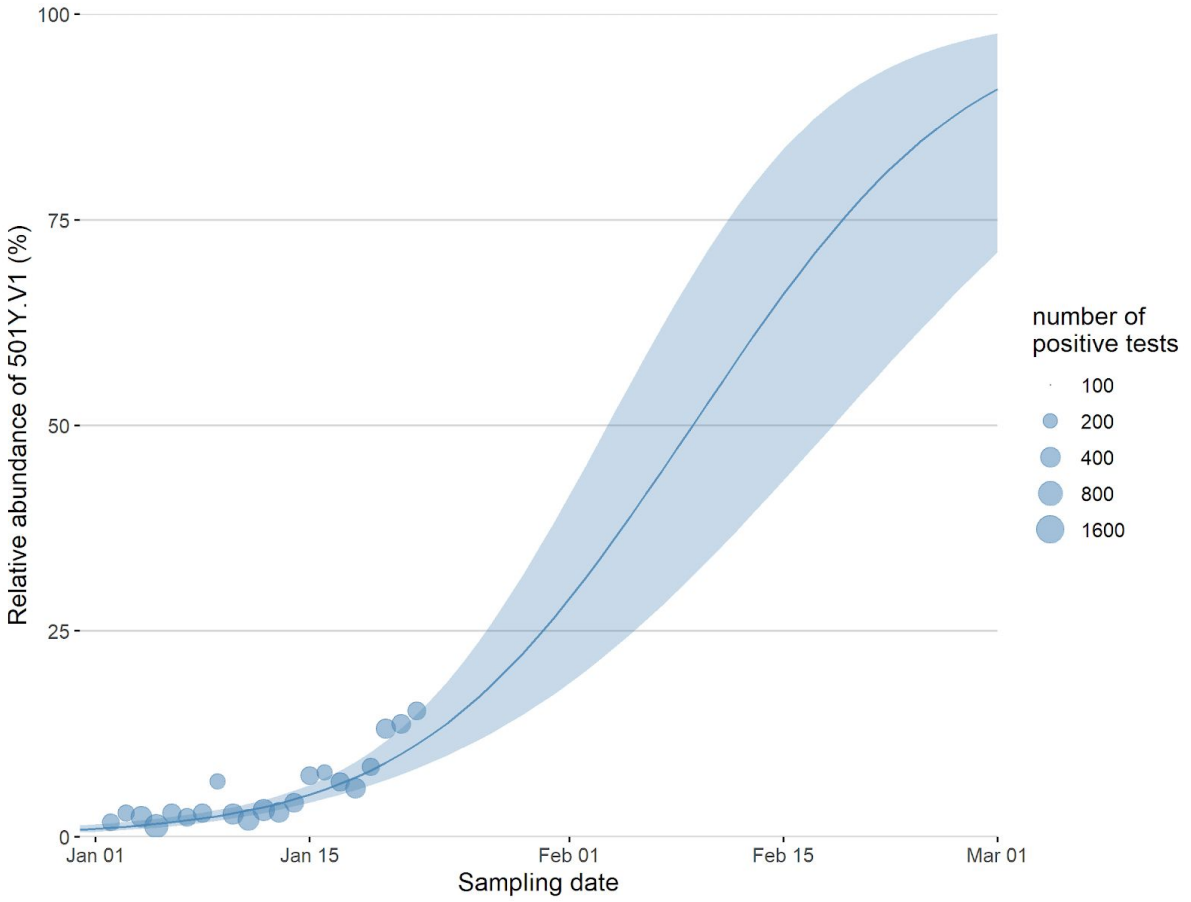


Figure 2. Estimated increase in the relative abundance of the 501Y.V1 variant in Belgium based on S dropout data (mean and 95% confidence intervals, binomial GLMM with random intercept for laboratory and an observation-level random effect to take into account overdispersion, with correction for the expected proportion of true positives). An extrapolation up to the first of March is shown.

If we assume that the 501Y.V1 variant has the same generation as the SARS-CoV2 wild type (which epidemiological models have shown is likely, Davies et al. [1]), and assuming a generation interval of T=4.7 days (following Nishiura et al. 2020 [2]), the estimated growth rate advantage Δr for Belgium would be expected to have a multiplicative effect on the effective reproduction number Rt of exp($\Delta r \,.\, T$)=1.79 [1.55-2.08] 95% CLs, implying an increased infectiousness of 79% [55-108%] 95% CLs. The fitted model indicates that at this moment (26/1/2021), 17% [12-24%] 95% CLs of all newly diagnosed infections are compatible with being variant 501Y.V1, whilst among all new infections (taking into account a time of approx. 7 days between time of infection and diagnosis), already 31% [20-45%]

would be estimated to be with variant 501Y.V1. By February 3d [28th of January - 12th of February] 95% CLs, we estimate that >50% of all new infections will be by variant 501Y.V1 (at time of infection), while by the 22nd of February [12th of February - 9th of March], we estimated that >90% of all new infections will be by this variant.

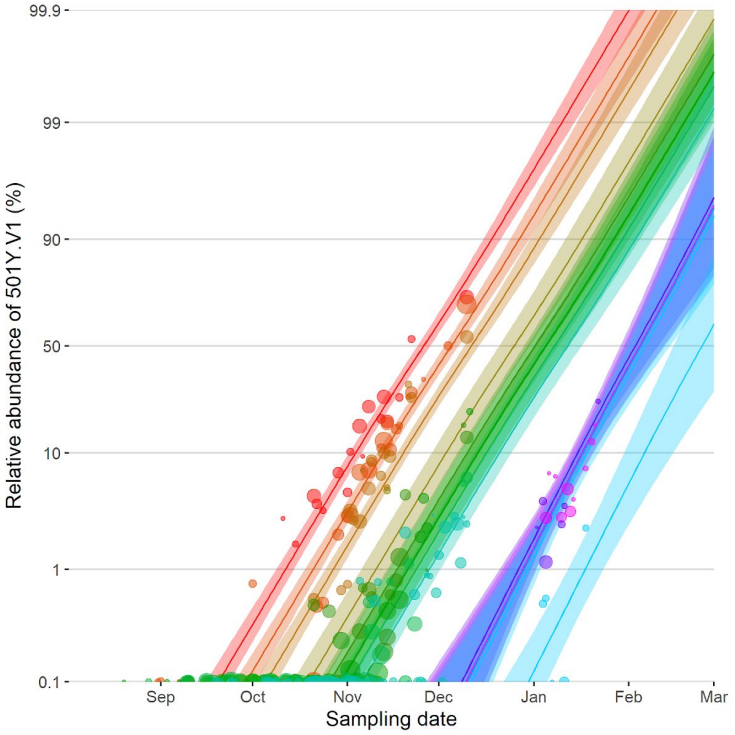
Given that the estimated growth trajectory of the 501Y.V1 variant still has relatively broad confidence intervals, we also carried out a combined analysis of the Belgian S-dropout data and the COG-UK sequencing data (data August 1 2020 - December 17 2020), to be able to further narrow down the predictions. In these analyses, we fitted two binomial GLMMs in which we either allowed separate slopes per country or not, whilst using common slopes per region within each country (NHS region for UK or hospitals for Belgium). As before, we also included an observation-level random effect to take into account overdispersion. These analyses show that a model with a constant slope per country and region was most parsimonious, having the lowest BIC value. With such a model, we estimated a growth advantage of the 501Y.V1 variant across the UK and Belgium of 10.6% per day [10-11%] (observation-level random effect variance: 0.39), which with a generation time of 4.7 days would translate to an increased infectiousness of 65% [60-70%]. Based on this model, we estimate that by February 2nd [29th of January - 6th of February] 95% CLs, we estimate that >50% of all new infections will be by variant 501Y.V1 (at time of infection), while by the 24th of February [19th of February - 1st of March], we estimated that >90% of all new infections will be by this variant. In the model with separate slopes per country, the growth advantage of the 501Y.V1 variant was 12.5% [9.5-15.5%] for Belgium and 10.6% [9.9-11.2%] for the UK (observation-level random effect variance: 0.38). The differences in slope across both countries, however, were not significant (z ratio=1.23, p = 0.22), thereby suggesting that the 501Y.V1 variant is spreading at the same rate in Belgium as in the UK. Model predictions for this model with separate slopes by country are shown in Figure 3.

Conclusion

We can conclude that although data on the relative rate of spread of the 501Y.V1 variant is still somewhat limited for Belgium, it is already plain clear that the variant will become the dominant strain in a very short timespan, being projected to reach 90% of all newly diagnosed infections before the end of February, and being estimated to already make up 31% of all new infections at this moment (26/1/2021). The growth advantage relative to other strains is on the order of 11% per day, or even slightly higher, which would translate to an increased infectiousness of ca. 65%. This increase in infectiousness is entirely in line with estimates that can be made for other countries based on the observed growth advantage there (typically 8-11% per day, cf. above). These figures are worrisome, as they would imply that under the current measures, which causes the Rt value of the old SARS-CoV2 variants in Belgium to be around 1, the Rt value would likely increase to a value of ca. 1.65 by the time that 501Y.V1 will become the dominant variant (i.e. before the end of February).

We should note that earlier preprints in which the increased infectiousness of 501Y.V1 were estimated do not always use correct procedures and often use differing generation times, which is a major cause of the differences in the estimates obtained [4]. For example, Volz et al. [5] calculated an additive change in the Rt value based on the product of the difference in growth rate and generation time, while the actual relationship is multiplicative [1]. Likewise, Walker et al. [6] analysed ONS S gene dropout data from the UK, but forgot to filter out samples with single-gene amplifications (indicative of random gene dropout due to very low

virus titers, e.g. linked to old infections), which resulted in an underestimation of the current incidence of the 501Y.V1 variant (ca. 60% prevalence across England among new infections now vs. >90% shown by the Pillar 2 S gene target failure data) as well as the contagiousness of the 501Y.V1 variant (K. Pouwels, pers. comm.). This is currently being addressed by the study authors, in consultation with the ONS, who would be required to adapt their definition of S dropout samples. As shown above, if the same procedure is used to estimate the growth and transmission advantage of the 501Y.V1 variant then highly concordant estimates are obtained across different countries and regions. We therefore believe these conclusions to be reliable and robust.



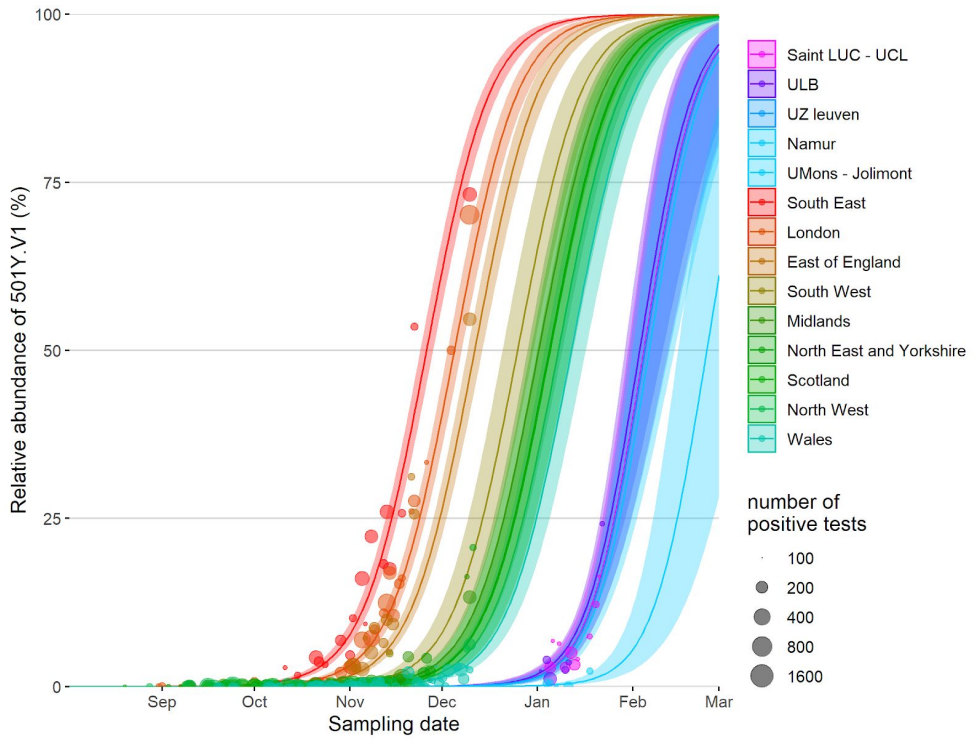


Figure 3. Estimated increase (plus 95% confidence intervals) in the relative abundance of the 501Y.V1 variant in the UK and Belgium, based on a joint analysis of S dropout data for Belgium and COG-UK sequencing data for the UK (binomial GLMM with separate slopes per country, but identical slopes per region within each country). The plots are shown either on a logit link (top) or a backtransformed response scale (bottom). The introduction of the 501Y.V1 variant clearly occurred with a delay compared to the spread in the UK, and also happened somewhat later in Mons.

Outlook

To further minimise bias related to the selection of samples tested and sequenced, more data on the reason for testing and whether data pertain to specific outbreaks are needed. Further in-depth-analyses are only possible with good quality data. Patient meta-data are also urgently needed to be able to estimate possible differential age-susceptibility and estimate possible effects on hospitalisation or mortality rates.

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