Rapid Reviews COVID-19

Review 1: "Estimated transmissibility and severity of novel SARS-CoV-2 Variant of Concern 202012/01 in England"

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RR:C19 Evidence Scale rating by reviewer:

- **Potentially informative.** The main claims made are not strongly justified by the methods and data, but may yield some insight. The results and conclusions of the study may resemble those from the hypothetical ideal study, but there is substantial room for doubt. Decision-makers should consider this evidence only with a thorough understanding of its weaknesses, alongside other evidence and theory. Decision-makers should not consider this actionable, unless the weaknesses are clearly understood and there is other theory and evidence to further support it.

Review:

The novel SARS-CoV-2 Variant of Concern (VOC)-202012/01 first collected on September 20, 2020, in Kent, UK, is a rapidly growing lineage that in the second half of December 2020 constituted more than half of all SARS-CoV-2 genomes sequenced in England. In the reviewed manuscript, Nicholas G. Davies and collaborators have estimated that the VOC strain is 56% more transmissible (95% credible interval across three regions of England: 50-74%) than preexisting variants of SARS-CoV-2. To understand possible biological mechanisms of increased transmissibility authors considered four alternative hypotheses: increased infectiousness; immune escape; increased susceptibility among children; and shorter generation time, and found that the model based on increased infectiousness yields best agreement with data. Using the best-fitting model variant with increased transmissibility, the authors compared epidemic dynamics under different assumptions about control measures and progression of immunization from mid-December 2020 to the end of June 2021.

This is one of the first studies on the transmissibility of the VOC strain and for obvious reasons is based on incomplete data. In our opinion, because of the incompleteness of data and particular methodology, the authors underestimated the transmissibility of the VOC strain with respect to preexisting variants. The authors used data from the COG-UK Consortium to calculate the proportion of the VOC over time from October 1st to December 1st. Values were aggregated by NHS region and by day. As a consequence, the proportion of the VOC (to total), calculated based on very small numbers of daily collected genomes in each NHS region, is varying up-and-down more than twofold within any single week in the considered period, see Fig. 2A. In October 2020, only 70 VOC strain genomes were collected in the whole of England (based on GISAID, as of January 21, 2021). This makes the fitting of a sigmoid curve unreliable, as the fitting is based on averaging of, in a sense, nearly random numbers of daily ratios (especially in October period).

To illustrate our point, we analyzed England data aggregated by week, considering period of weeks 43–51 of 2020 (i.e. from October 19 till December 20). We chose to calculate the ratio of the VOC to the non-VOC sequenced genomes (instead of VOC to total) because this ratio is expected to grow exponentially (linearly in the logarithmic scale), which enables visual inspection of the persistence of the (linear) trend, see Fig. A (this review). One should notice that until week 46 there were days with no VOC genomes collected, which implies a daily ratio equal to zero.

Figure A. Ratio of the VOC to the non-VOC genomes sequenced in England

Data aggregated by week indicated that the VOC to non-VOC ratio, v , changes from $30:6708 = 0.0045$ in week 43 to $4544:3555 = 1.28$ in week 51, i.e. 286 times. This implies that v increased $286/8 \approx 2.03$ -fold per week. More rigorously, the fit in weeks 43–47 gives the weekly growth of v equal 2.38 [95% CI: 2.18–2.59], whereas the fit in weeks 43–51 gives the weekly growth of v equal 1.93 [95% CI: 1.78–2.09]. Thus, assuming that both strains have the same average serial interval of 6.73 days [Kochańczyk et al., R. Soc. Open Sci. 7, 200786, doi:10.1098/rsos.200786], one obtains $R_t^{\text{VOC}}/R_t^{\text{non-VOC}} = 2.38^{6.73/7} = 2.30$ [95% CI: 2.12–2.49] when fitting in the time span of weeks 43–47 and $R_t^{\text{VOC}}/R_t^{\text{non-VOC}} = 1.93^{6.73/7} = 1.88$ [95% CI: 1.74–2.03] for time span of weeks 43–51. One thus should expect that the replicative advantage of the VOC over preexisting strains is the range of 1.88–2.30, where the lower and the upper bounds correspond to the time span of weeks 43–51 and the time span of weeks 43–47, respectively.

Underestimation of the replicative advantage of the VOC strain likely resulted in the underestimation of the peak deaths in considered epidemic scenarios, Table 1. The authors predicted that under the tier 4 restrictions and 200k immunized per week the death peak in England will be in the range of (461

- 835). As of January 21, 2021, lockdown (with restrictions exceeding those of tier 4) is imposed, there are more than 1mln vaccinations per week, while the weekly average of COVID-confirmed deaths in England exceeds 1000 (coronavirus.data.gov.uk).