Autumn and Winter 2021-2022: potential COVID-19 epidemic trajectories

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A. Part 2: Retrospective evaluation of the roadmap in the context of the Delta variant

England's COVID-19 "roadmap out of lockdown" policy set out the timeline and conditions for the stepwise lifting of non-pharmaceutical interventions (NPIs) from March to July 2021 as vaccination roll-out continued.

1. Introduction

Below we provide a retrospective assessment of the stepwise lifting of NPIs from March to July 2021. The model is described in [1].

Based on results from Sonabend *et al* [1] we can estimate the reproduction number excluding immunity ($R_{excl\_immunity}$) over time (Fig 1) and the relative contact rate $\beta(t)$ (Fig 2). $R_{excl\_immunity}$ is estimated by combining Alpha and Delta variant specific reproduction numbers $R^{\mathrm{A}}_{excl\_immunity}$ and $R^{\Delta}_{excl\_immunity}$ derived from the model fits using data up to 24 September 2021. It describes the reproduction number in the absence of any immunity from past infections or vaccination. The relative contact rate $\beta(t)$ is a measure of the change in contact rates combined with the contact matrix and potential transmission advantage of the circulating variants to define the age specific force of infection. Its change over time captures the impact of NPIs and adherence to Covid-safe behaviours (e.g. mask wearing or working from home). Importantly it accounts for the transmission advantage of the currently circulating variant, and captures the impact of each step of the roadmap.

2. Estimating the change in transmission during the roadmap

The third lockdown in January 2021 led to a sharp decline in transmission, which remained roughly constant during the lockdown. Step 1A (school re-opening) was associated with a sharp increase in transmission (+27.6% compared to lockdown period) followed by a decline during the Easter holidays. The relative contact rate does not seem to increase following step 2 and step 3 (Figure 2, blue curve). There is a "bump" at the end of step 3, concurrent with the Euros football tournament, which could explain the increased contacts. Following the increase, a sharp decline can be seen, likely due to school children having exams thus mixing less, or individuals self-isolating following the COVID app "ping-demic". Note that children self-isolating will decrease their contact rates but also impact the contact of their peers still attending school.

The lack of increase in the relative contact rate following the emergence of Delta inferred by the model means that the increase in $R_{excl\_immunity}$ is attributed only to the transmission advantage of Delta over Alpha in the model. This is derived using the observed frequency of Alpha and Delta cases over time [1], akin to observing variant specific growth rates of cases. The translation of these variant specific growth rates into variant specific reproduction numbers linked by a transmission advantage depends on the assumed serial interval [2]. In particular, a longer serial interval, will increase the estimated transmission advantage and reduce the transmission coefficient.

Our assumed serial interval (6.3 days on average based on [3]) and resulting estimated transmission advantage (180%) are higher than estimated or assumed by other groups [4]. Our estimated relative contact rates (Fig 2) are consistent with the COMIX study [5] up until the emergence of the Delta variant, after which they diverge. This suggests that part of the increase in $R_{excl\_immunity}$ attributed to the transmission advantage should be attributed to an increase in relative contact rates and thus the actual transmission advantage is smaller than inferred by our model. This is likely a consequence of the longer serial interval assumed in our model.

3. Impact of accounting for a potential smaller transmission advantage

Based on an analysis presented in the methods section below, we tested the impact of a slightly smaller 150% transmission advantage on the inferred transmission coefficients $\beta(t)$ associated with each step of the roadmap.

Using a smaller transmission advantage results in a more marked increase in relative contact rates associated with each step of the roadmap (Table 1 and Fig 2 red curve). We estimate that the relative contact rate was on average 28.6% higher during Step 1A than during the third lockdown. Step 1B saw a smaller average increase in relative contacts compared to Step 1A (+8.4%). Levels remained relatively constant during Step 2 (-0.7%). There was a 13.9% increase from Step 2 to Step 3. Thus far, Step 4 is associated with a 5.6% increase from Step 3. Note that the relative contact rate might vary substantially during each associated step. For example, schools were closed for a large part of Step 4.

Table 1: Estimated mean and standard deviation of $R_{\_excl\_immunity}$, relative contact rate (beta), and inflated contact rates associated with the different steps of the Roadmap

Start	End	School	Step	$R_{\_excl\_immunity}$ mean	$R_{\_excl\_immunity}$ s.d.	Beta mean	Beta s.d.	Beta inflated mean	Beta inflated s.d.
05/01/2021	07/03/2021	Closed	Lockdown 3	1.16	0.042	0.0427	0.00153	NA	NA
08/03/2021	31/03/2021	Opened	Step 1.A	1.48	0.119	0.0545	0.00437	0.0549	0.00402
01/04/2021	18/04/2021	Closed	Step 1.B	1.63	0.047	0.0593	0.00207	0.0595	0.00194
19/04/2021	16/05/2021	Opened	Step 2	1.80	0.194	0.0556	0.00086	0.0591	0.00222
17/05/2021	18/07/2021	Opened	Step 3	2.68	0.317	0.0561	0.00537	0.0673	0.00662
19/07/2021	30/09/2021	Both	Step 4	2.90	0.273	0.0592	0.00544	0.0711	0.00667

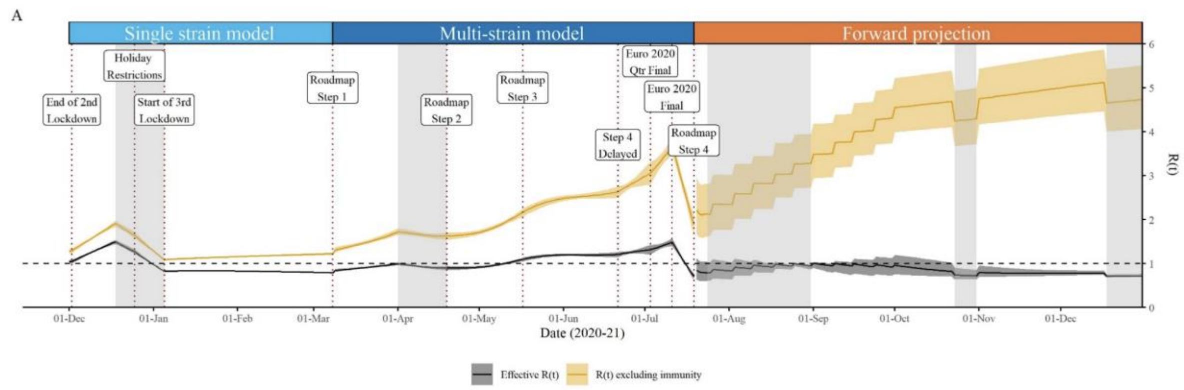

Figure 1: Prevalence weighted (black) effective reproduction number and the reproduction number excluding infection- or vaccine-induced immunity ($R_{excl\_immunity}$, orange) over time: estimated values from the end of the second national lockdown up to 19 July 2021 ("roadmap step 4" vertical line) and assumed values thereafter. The solid line shows the R(t) median and the shaded area the 95% CrI. The vertical dashed lines show key dates of the roadmap steps and the shaded area the school holidays (excluding half term), note we do not explicitly model the impact of school closures for the period 23 July-31 August in order to capture the overall gradual increase in contacts from 19 July-1 October. The 'forward projection' section of the figure corresponds to the central immunity scenario. Note that our central projected trend is the median across all daily projections and is not a single trajectory.

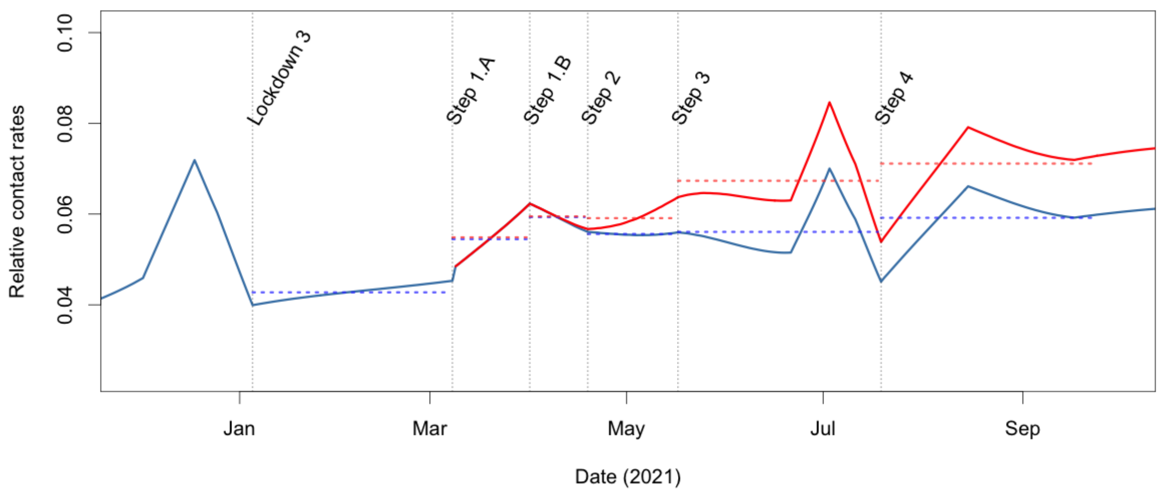

Figure 2: Estimated relative contact rates (beta) over each step of the roadmap (blue line, bottom). The red line (top) shows the "inflated" contact rates adjusted for the lower transmission advantage for Delta. The vertical dashed lines show key roadmap dates or steps. The horizontal dashed lines show the average estimated beta over that time period as reported in Table 1.

4. Conclusions

There are many key unknowns that make it difficult to anticipate the potential level of restrictions required in the coming months. A key uncertainty is the level of mixing over winter 2021-22. However, the spike in transmission and transmissibility estimated just prior to step 4 of the roadmap (Figure 2) highlight the potential transmission levels that could be reached.

Note that the re-introduction of measures is unlikely to have exactly the same impact compared to when first introduced. However, introduction of measures may have a more immediate impact on transmission than the lifting of interventions.

We estimate that current contact rates may already be higher than this time last year (autumn/winter 2020). The continued roll-out of vaccination including booster doses and expansion of eligibility to 12–15-year-olds will help to offset the higher transmission from increased contact rates.

We anticipate that re-introducing working from home guidance may have at least a 6% impact on average transmission levels (note that the impact is likely to be higher as relative contact rates estimated for step 4 in our analysis includes the summer holidays and we have not yet observed the full impact of step 4).

Methods (B: Part 2)

Inflation of inferred contact rate for a variant with a different transmission advantage

The reproduction number excluding immunity over time $R_{excl\_immunity}$ is given by

$$R_{excl\_immunity} = (1 - \zeta(t))R^{A}_{excl\_immunity} + \zeta(t)R^{\Delta}_{excl\_immunity} \quad (1)$$

where $\zeta(t)$ is the contribution of delta variant based on the incidence of cases with Alpha or Delta, $R^{A}_{excl\_immunity}$ the reproduction number excluding immunity over time for the Alpha variant and $R^{\Delta}_{excl\_immunity}$ the reproduction number excluding immunity over time for the Delta variant.

We can calculate $\zeta(t)$ based on the output of our model using:

$$\zeta(t) = \frac{R_{excl\_immunity} - R^{A}_{excl\_immunity}}{R^{\Delta}_{excl\_immunity} - R^{A}_{excl\_immunity}}.$$

Figure S1 shows the estimated $\zeta(t)$ from our model showing the fast emergence of the Delta variant during May and June 2021 in England.

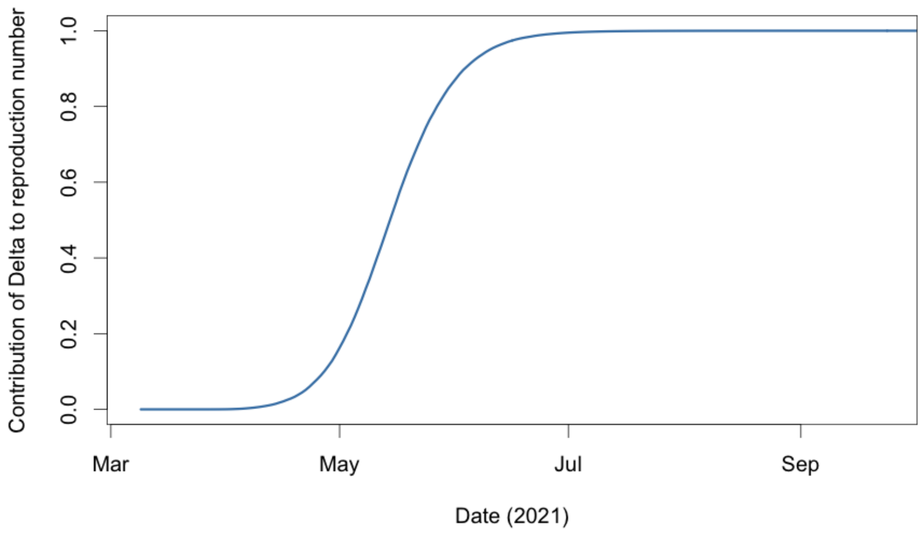

Figure S1: Contribution of Delta to the reproduction number based on incidence of infections by the Alpha and Delta variant in England.

We also assume that $R^{\Delta}_{excl\_immunity}$ and $R^{\mathrm{A}}_{excl\_immunity}$ are linked by η the transmission advantage of Delta over Alpha such that:

$$R^{\Delta}_{excl\_immunity} = \eta R^{\mathrm{A}}_{excl\_immunity}. \tag{2}$$

If we also assume that the reproduction number of a given variant is proportional to the relative contact rate $\beta(t)$, we have

$$R^{\mathrm{A}}_{excl\_immunity} = c^{\mathrm{A}}\beta(t). \tag{3}$$

Combining equations (1), (2) and (3) we can derive the relative contact rate $\beta(t)$ as a function of the transmission advantage, the contribution of delta variant and the observed $R_{excl\_immunity}$:

$$\beta(t) = \frac{R_{excl\_immunity}}{c^{\mathrm{A}}(1 - \zeta(t) + \eta\zeta(t))}.$$

For a given $R_{excl\_immunity}$ profile over time with contribution ζ(t) from variant Delta, it is thus possible to work out how a different transmission advantage would impact the transmission. In the following equation we derive the inflated relative contact rate under a transmission advantage η_2 using the estimated relative contact rate $\beta_{\eta_1}(t)$ calculated using a transmission advantage η_1:

$$\beta_{\eta_2}(t) = \frac{1 - \zeta(t) + \eta_1\zeta(t)}{1 - \zeta(t) + \eta_2\zeta(t)}\beta_{\eta_1}(t). \tag{4}$$

B. References

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