Roadmaps for Relaxation of NPIs.
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Executive Summary

1) We examine four different roadmap scenarios that begin relaxation of current restrictions on 8th March and end with full unlock and baseline NPIs. This is modelled for the seven NHS regions of England and then the data combined.

2) These roadmaps were modelled assuming an effective rollout of vaccination, achieving four million doses a week from March 2021.

3) We consider two key uncertainties: vaccine efficacy both against disease and infection (2 sets of assumptions); and the level of control remaining at the end of the roadmaps (3 sets of assumptions).

4) We consider hospital admissions, hospital occupancy and daily deaths due to COVID-19 as the three key public health measures of greatest concern.

5) All of the relaxation roadmaps lead to a third wave of infections, the scale of this wave and the implications for health services and loss of life are critically dependent on the two key uncertainties.

6) The results are most sensitive to changes in vaccine efficacy. The more cautious assumptions of lower efficacy allow cases to rise at an earlier stage of relaxation and generates larger peaks at earlier dates. Changes to the final level of control have a significant but smaller impact on the epidemic.

7) While vaccine efficacy parameters will be better determined by on-going studies, the behaviour of the population as measures are relaxed cannot be pre-determined.

8) Further uncertainties that may only be resolved over longer time periods include: the uptake of vaccine by region, risk-group and age; other aspects of behavioural response; and the impact of climate and seasonality.

9) We have also assumed that there is good and continuing adherence to current restrictions, leading to a continued decline. Any change to adherence will have implications for the timing of relaxation.

10) In this work we are not accounting for waning immunity either due to natural infection or vaccination, which will begin to play a significant role over longer time scales.

11) The large number of uncertainties suggest that a period of monitoring may be necessary before restrictions can be further released. Changes in epidemic behaviour take at least 2 weeks to be realised in the data, and then a further 2 weeks is required before there is statistical confidence in estimates of epidemic growth/decay.

The Brief

To model four roadmap scenarios and predict the likely interaction between vaccination coverage and relaxation of NPIs in each case.

To explore key uncertainties including behaviour and vaccine efficacy.

We model the dynamics using an age-structured model which has been matched to data from the seven NHS regions. This model explicitly includes multiple actions of vaccination (infection and disease blocking), differential mixing due to school terms and holidays, and the increased transmission of the new variant. The model does not include waning immunity nor seasonality, neither of which has been rigorously quantified. The model explores the full (posterior) parameter space inferred from matching to epidemiological data (hospital admissions, hospital occupancy, daily deaths within 28 days of a positive COVID test, and proportion of Pillar 2 tests that are positive) on 29th January.
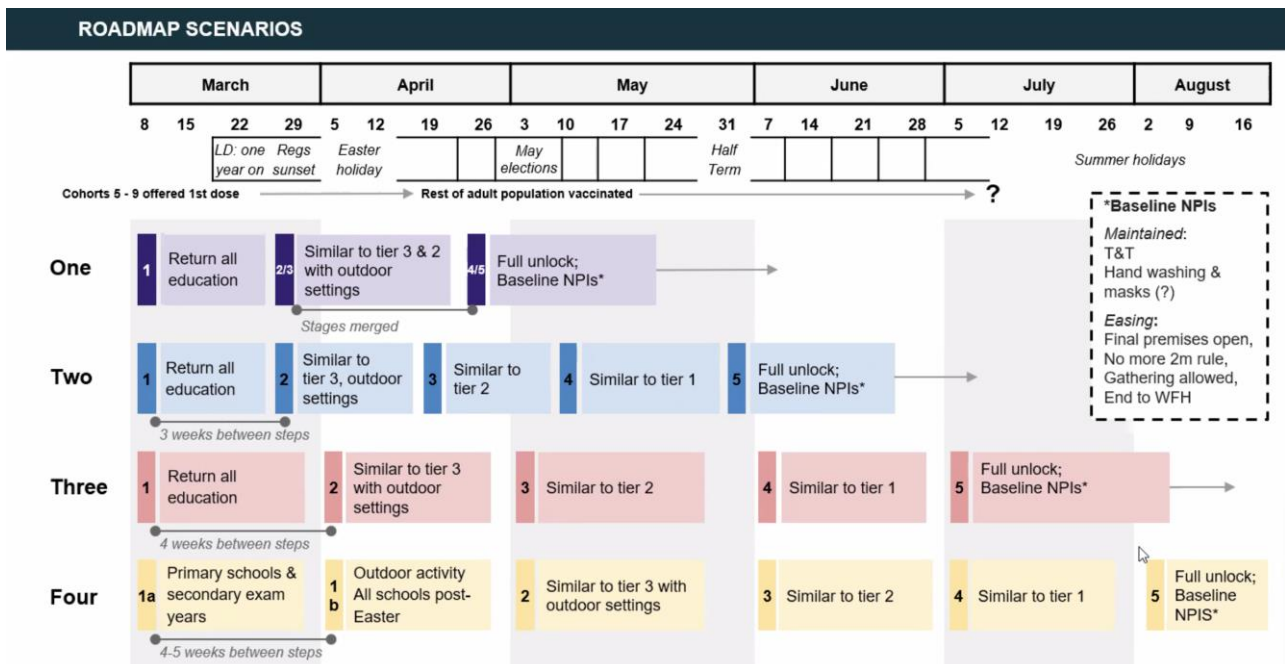
Key Uncertainties and Caveats.

1) *Vaccine action*. Having been vaccinated, the protection generated can affect multiple components of the infection, illness and transmission process. We have concentrated on the action of the vaccine in blocking infection and preventing disease (supplementary figures show the behaviour if vaccines provide additional protection against severe disease, hospitalisation and death). Despite detailed Phase 3 trials and continued research, there is still considerable uncertainty in the precise parameters (see table below for our assumptions in comparison to available vaccine data), in particular estimates of infection blocking are difficult to obtain in observational studies.

	Infection blocking 1st dose	Vaccine efficacy against disease 1st dose	Infection blocking 2nd dose	Vaccine efficacy against disease 2nd dose
Pfizer vaccine	53% (32%-68%)	89% (52%-97%)[1]	-	95% (90.3%-97.6%)[2]
Ox/AZ vaccine	48.2%[3]	63.1% (51.8%-71.7%)[3]	60.2%[3]	82.4% (62.7%-91.7%)[3]
Central Assumptions	48%	70%	60%	88%
Cautious Assumptions	24%	56%	30%	70%

2) *Behaviour in Stages 1-5 of the roadmaps*. While there are some local-scale data on the growth or decline of cases under different Tiers, there is still considerable uncertainty in projecting the recommendations in each stage to changes in *R*. In particular, we may expect very different behaviour as control measures are relaxed in an improving environment compared to the available data on tightening restrictions when cases were increasing.

It is also extremely difficult to make predictions about Stage 5 (Full unlock with baseline level NPIs); this has not occurred at any point in the pandemic so there is an absence of data. It is anticipated that there will be some continued caution amongst the population for some time even in the absence of strict government control, but the precise nature of this is difficult to predict. We therefore consider three different scenarios regarding the impact of NPIs and hence the degree of transmission in this period.

We approximate the realised level of NPIs in each of the five stages as follows:

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[1] https://www.gov.uk/government/publications/prioritising-the-first-covid-19-vaccine-dose-jcvi-statement/optimising-the-covid-19-vaccination-programme-for-maximum-short-term-impact

[2] Polack et al (2020) Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. *N Engl J Med* 2020; 383:2603-2615

[3] Voysey et al (2021) Single dose administration, and the influence of the timing of the booster dose on immunogenicity and efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine. *The Lancet* https://doi.org/10.1016/S0140-6736(21)00432-3

Stage	Description	Assumption
Stage 1	Current controls + return to education	Current control levels as estimated by fitting to data. Interaction between pupils increased (80% of pre-COVID levels).
Stage 2	Similar to Tier 3	70% Stage 1 & 30% Stage 4.
Stage 3	Similar to Tier 2	30% Stage 1 & 70% Stage 4.
Stage 4	Similar to Tier 1	Control levels as in mid-September estimated by fitting to data.
Stage 5	Full unlock + baseline level NPIs	Three assumptions: Low transmission, $R_{no\ immunity} \approx 3$ Medium transmission, $R_{no\ immunity} \approx 3.6$ High transmission, $R_{no\ immunity} \approx 4$

3) *Vaccine Uptake*. The uptake of the vaccine in care homes and the over 80s has been exceptionally high, although there are communities and regions that have been more difficult to reach. Predicting the general level of uptake in younger age groups is again uncertain although we hope that the current pattern continues. We make two assumptions that are used in tandem with our assumptions about the protection offered by the vaccine.

	Uptake in >80s	Uptake in 50-80	Uptake in <50
Central Assumptions	95% April completion	85% July completion	85% October completion
Cautious Assumptions	95% April completion	85% July completion	75% September completion

The roll-out of this vaccine follows a delivery schedule in which 4 million doses a week can be administered from March onwards, leading to the completion dates given in the table above. (The earlier complete date under the cautious assumptions is due to the lower coverage but the same delivery schedule). Any slippage in this goal will inevitably delay the programme and lead to lower levels of population immunity. A secondary assumption is that vaccination will follow the JCVI priority groups, both in terms of vaccinating the highest risk groups first and in terms of leaving a 12-week separation between doses. It is clear from the existing data that there is already some blurring of priority groups, with those 70-74 or 75-79 being vaccinated before the over 80s are complete. Operationally this is entirely sensible (getting vaccine into as many people as possible is key), but theoretically it does mean that the actual roll-out is slightly less effective in the short-term than predicted, in the later stages of vaccination this variation will be absorbed however.

4) *Seasonality*. Like many respiratory infections we expect there to be a considerable degree of seasonality, both due to climatic factors (which affect the virus's ability to persist) but also in terms of behaviour (less indoor mixing and greater ventilation in the summer). There is limited data on this aspect of transmission, which has therefore not been incorporated in current simulations. This may cause issues with an over optimistic response following monitoring of the situation in summer, however, and will need further consideration at this time.

5) *Local-Scale Heterogeneity*. The model is formulated and matched to data for the seven NHS regions, and therefore captures many of the broader-scale spatial heterogeneities. However, this may mask many smaller-scale differences in both vaccine uptake, social mixing and adherence to control measures. When the regional R_t value is close to one, it is likely that some pockets of infection will grow, reflecting smaller scale structures. This could be compounded by local-scale variation in vaccine uptake.

Results

Here we present results for the number of individuals admitted to hospital across the whole of the UK, very similar patterns are found if the scope is restricted to England only. Results for hospital occupancy and predicted daily deaths can be found in the Appendices.
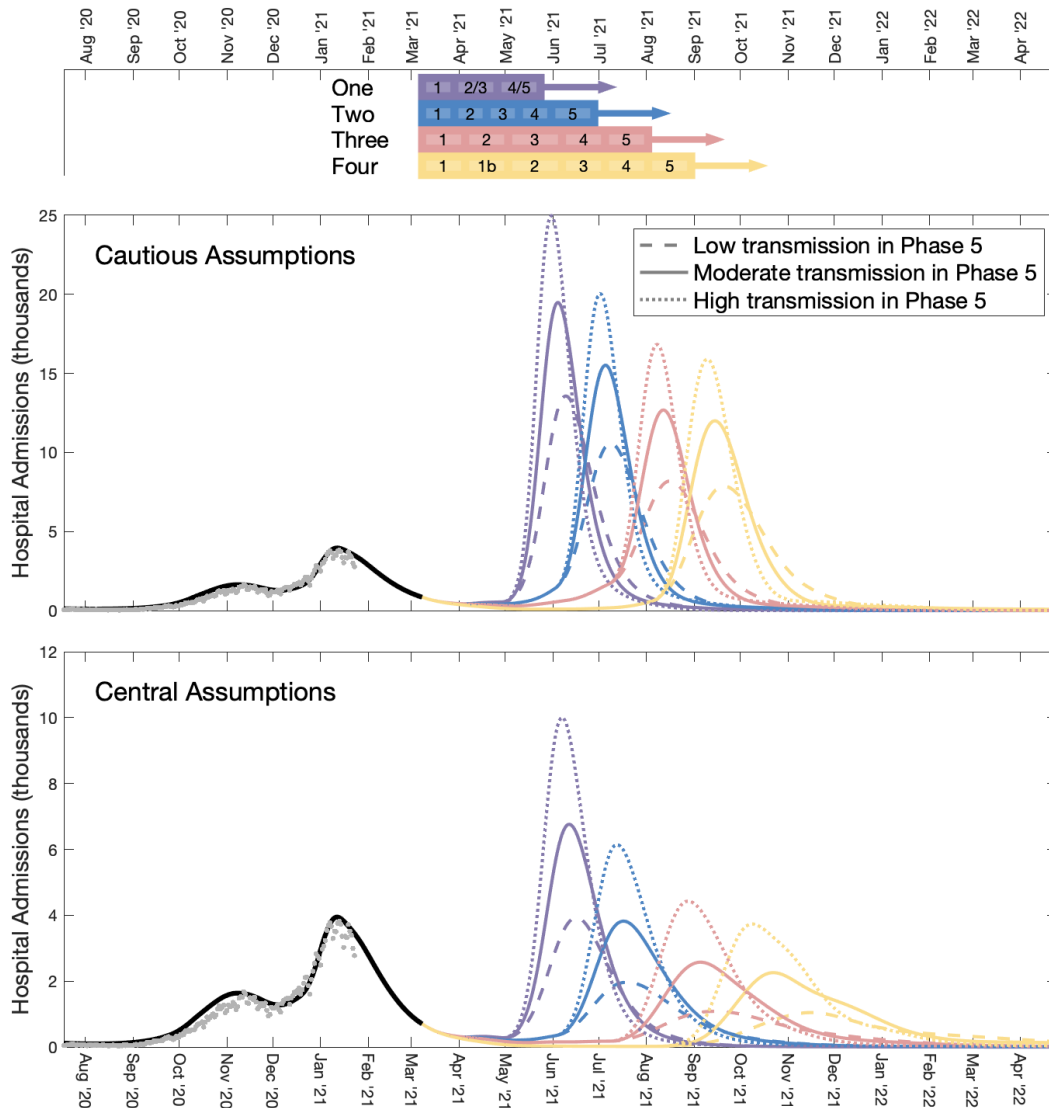
Figure 1. Predicted number of hospital admissions for the four strategies (colours), under two assumptions about vaccine action and uptake (upper & lower graphs) and under three assumptions about the degree of control in Stage 5 (line type). The period before 8th March is shown in black, and the available data is shown as grey dots.

Figure 1 shows the mean predicted dynamics across a range of scenarios and assumptions; there is considerable uncertainty to the baseline assumptions on vaccine efficacy and the level of

transmission that occurs in Phase 5 of the roadmap. These results are expanded in the Appendices where we show the prediction intervals associated with the simulations.

For the central assumptions and under moderate transmission in Phase 5 (solid lines) both reopening roadmaps One and Two generate peak hospital admissions that exceed those observed in January 2021 (Appendix 3). Under the central assumptions for vaccine efficacy, growth first occurs at Stage 4/5 for Roadmap One, at Stage 4 for Roadmap Two, and at Stage 5 for Roadmaps Three and Four (Appendix 1). Only for the most optimistic assumption of low transmission in Stage 5 and for roadmaps Three and Four does the predicted range of hospital admission lie below the January peak (Appendix 2).

For the more cautious set of vaccination assumptions, the lower uptake in those under 50 years old coupled with the weaker protection against disease and onward transmission, generate large increases in growth rate as we enter Stages 4 and 5 (Appendix 1). For all roadmaps and all assumptions about transmission in Stage 5, peak hospital admissions surpass those experienced in January.

A more prolonged relaxation of controls has the additional benefit that it provides time for the impact of any changes to be assessed and for the relaxation to be further slowed if necessary.

As an alternative to considering the dynamics over time, we can compare scenarios by considering the peak hospital occupancy (Figure 2). These values can be compared to the actual hospital occupancy which reached over 34,000 on 18th January.
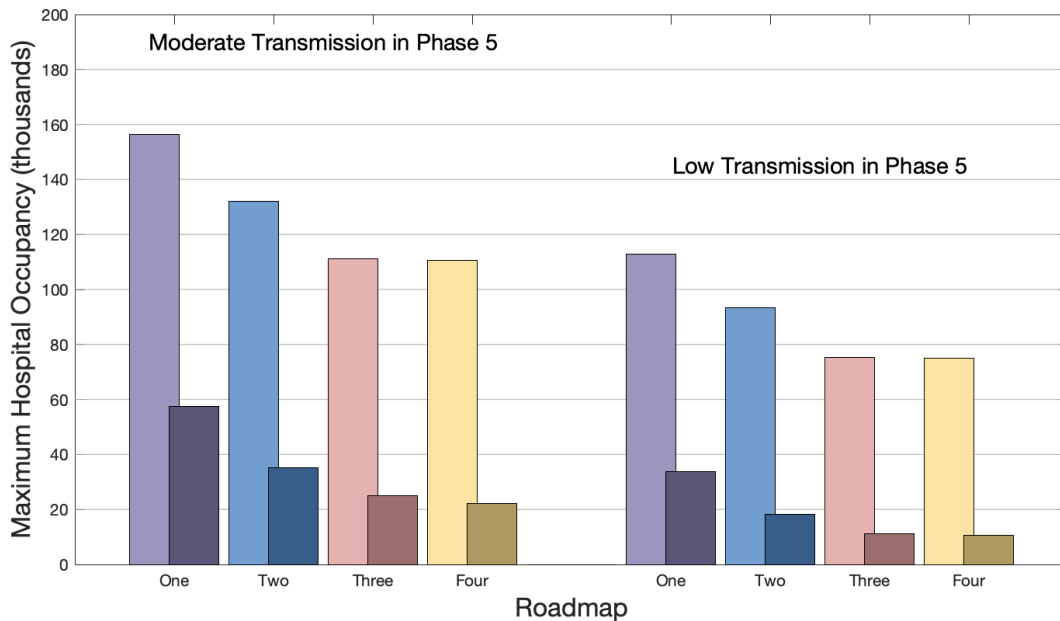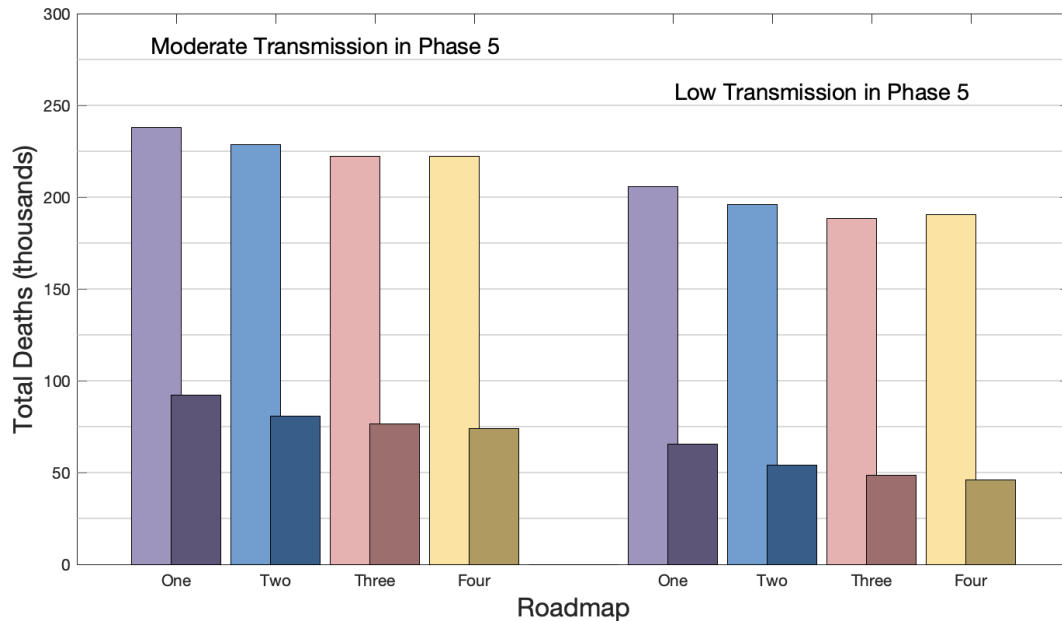
Figure 2: The maximum hospital occupancy and total deaths (from March 8th 2021) predicted under the four relaxation roadmaps, and for the low and moderate transmission in phase 5. Darker bars represent the results from the central vaccination assumptions, while the total height of the bars shows the results from the cautious assumptions.

Only predictions assuming the central estimates of vaccine efficacy (dark bars in Figure 2) and low transmission in the final Stage 5 of the relaxation roadmaps can keep hospital occupancy to manageable levels. This plot highlights the importance of robustly determining the precise vaccine property if long-term policy decisions are to be based on predictions for the current roll-out programme.

Finally, we consider the vaccine status to provide an understanding of the factors contributing to hospital admissions (Figure 3). We show both the raw predicted number of hospital admissions (left) and the proportion of hospital admissions (right), and which of these is attributable to those that remain unvaccinated and those that have received one or two doses. We contrast central assumptions about vaccination and low transmission in Phase 5 with more cautious assumptions, as these generate very different scales of future cases. Despite this difference in the magnitude of the third wave, both show remarkably similar behaviour in terms of proportions, with between 40% and 60% of the hospital admissions in the third wave in those that have had two doses of the vaccine.
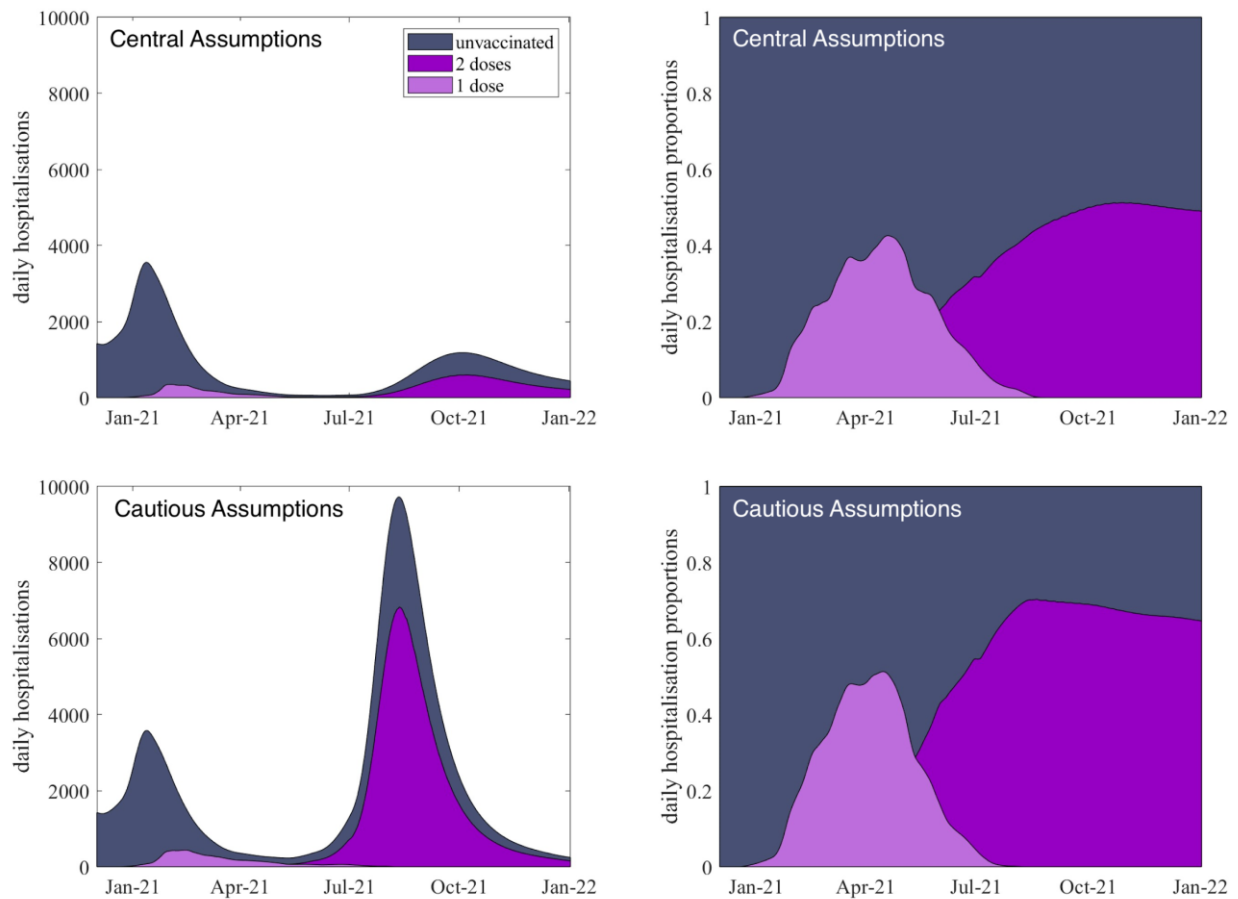
Figure 3: The distribution hospital admissions between those that are unvaccinated, those that have received one dose and those that have received both doses. Graphs on the left show the raw number of admissions, those on the right show proportions; the top graphs are for the central assumptions, while the lower graphs are for the cautious assumptions. All results are for Roadmap Four and low transmission in Phase 5.

Conclusions

All of the relaxation roadmaps lead to a third wave of infections. The scale of this wave and the implications for health services and loss of life are critically dependent on the two key uncertainties: the vaccine efficacy (against disease and infection) and the level of transmission at the end of the relaxation period.

Our results are most sensitive to changes in vaccine efficacy. The more cautious assumptions of lower efficacy mean that cases rise at an earlier stage of relaxation and larger peaks are generated at earlier dates. Changes to the final level of control have a significant but smaller impact on the epidemic. Far more optimistic assumptions about vaccine efficacy are shown in Appendix 13.

The large number of uncertainties – many of which can only be determined during the relaxation programme - suggest that a period of monitoring may be necessary before restrictions can be further released. Changes in epidemic behaviour take at least 2 weeks to be realised in the data, and then a further 2 weeks is required before there is statistical confidence in estimates of epidemic growth/decay.

Appendix 1. Total level of Infection

Showing the total level of infection (both symptomatic and asymptomatic) over time for the four relaxation roadmaps, the two assumptions about vaccination and the three assumptions concerning transmission in Phase 5 of the relaxation.

To help identify the impact of the different Phases, the start of each new phase is marked with a dot on the appropriate line. As expected the three assumptions concerning phase 5 only deviate in this last time period.
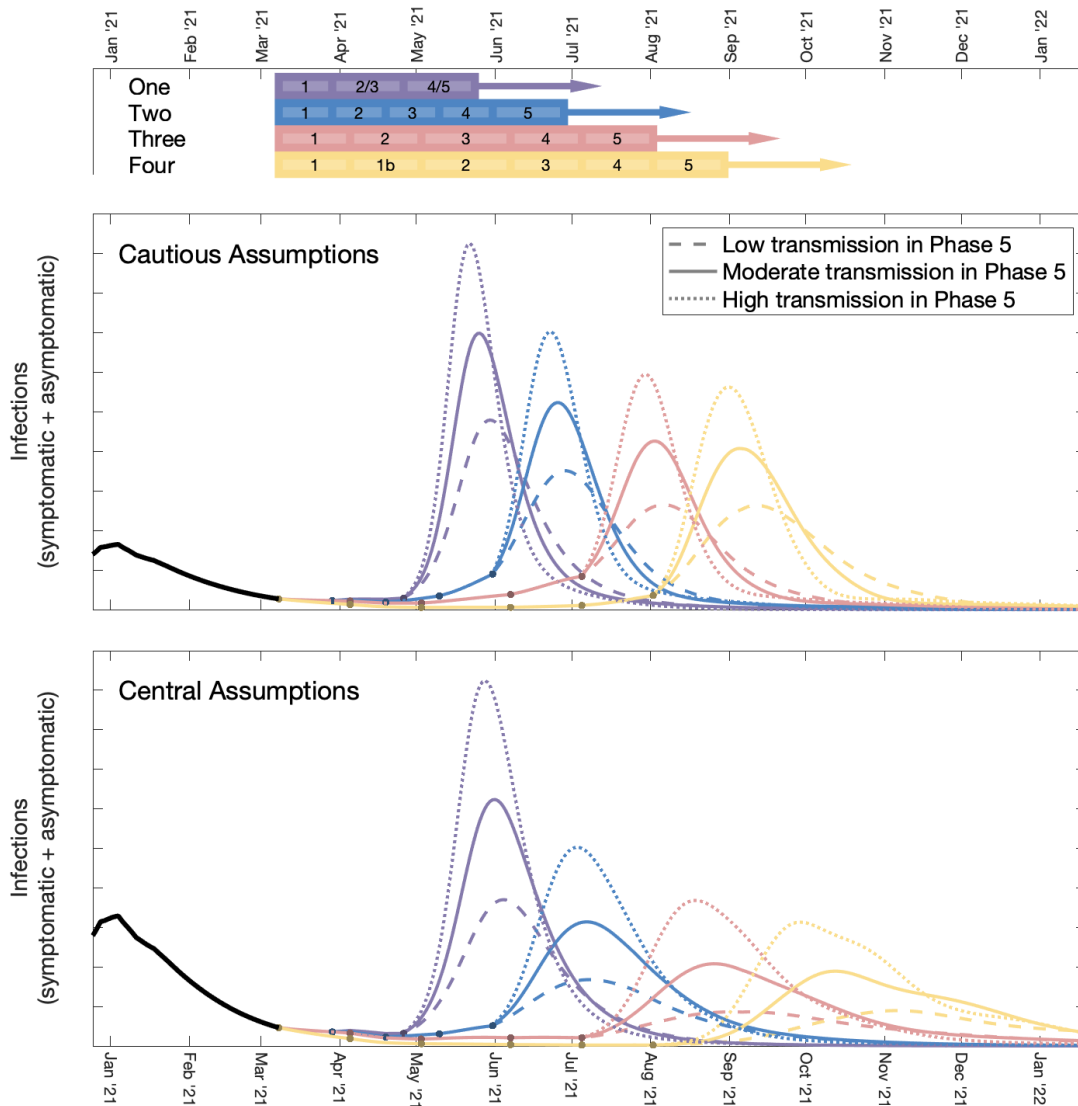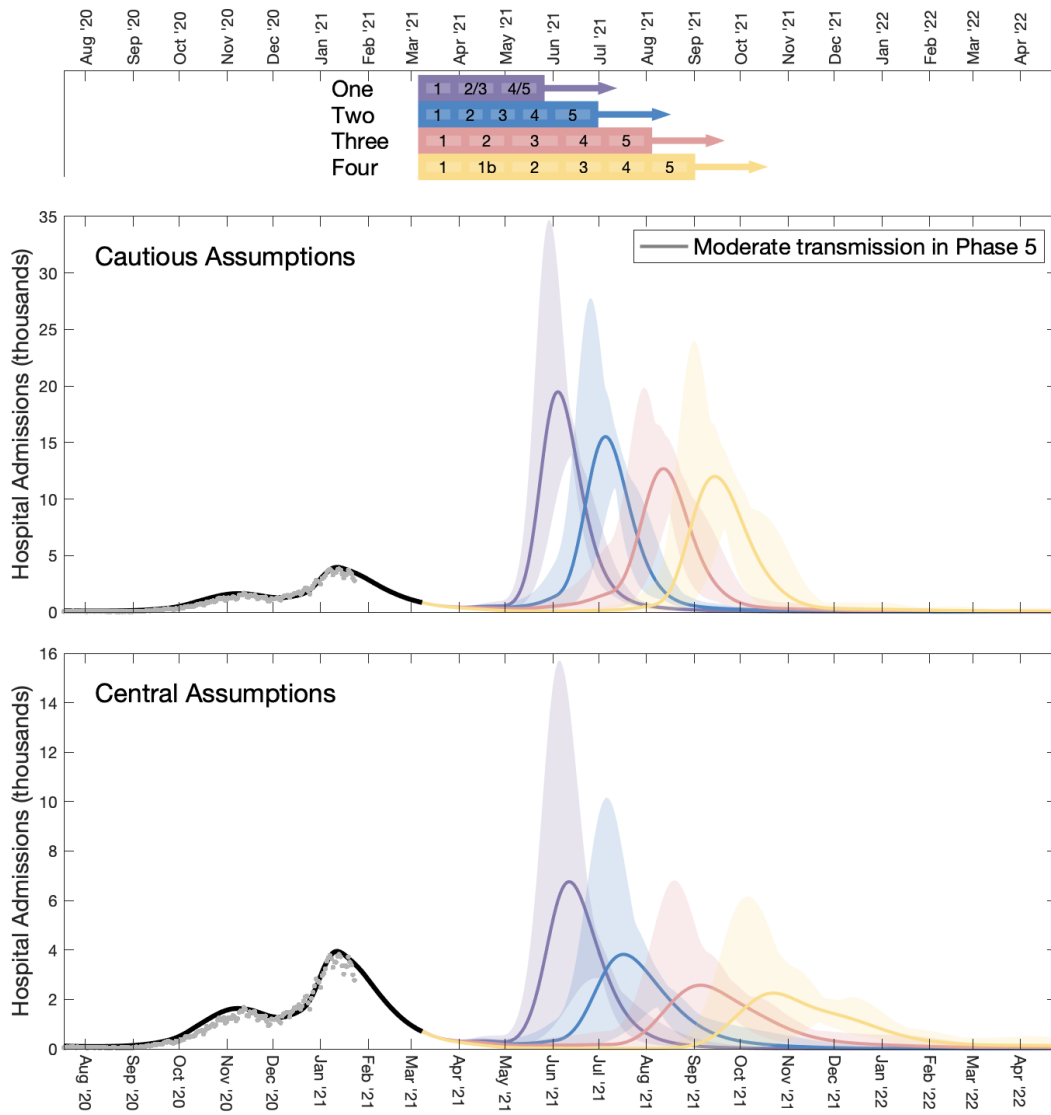
Appendix 2. Hospital Admissions, Low Transmission in Phase 5

Showing the dynamics of hospital admissions over time for a single assumption about transmission in Phase 5 of the roadmaps for relaxation; in these figures the 95% prediction intervals for each of the roadmaps is also presented.
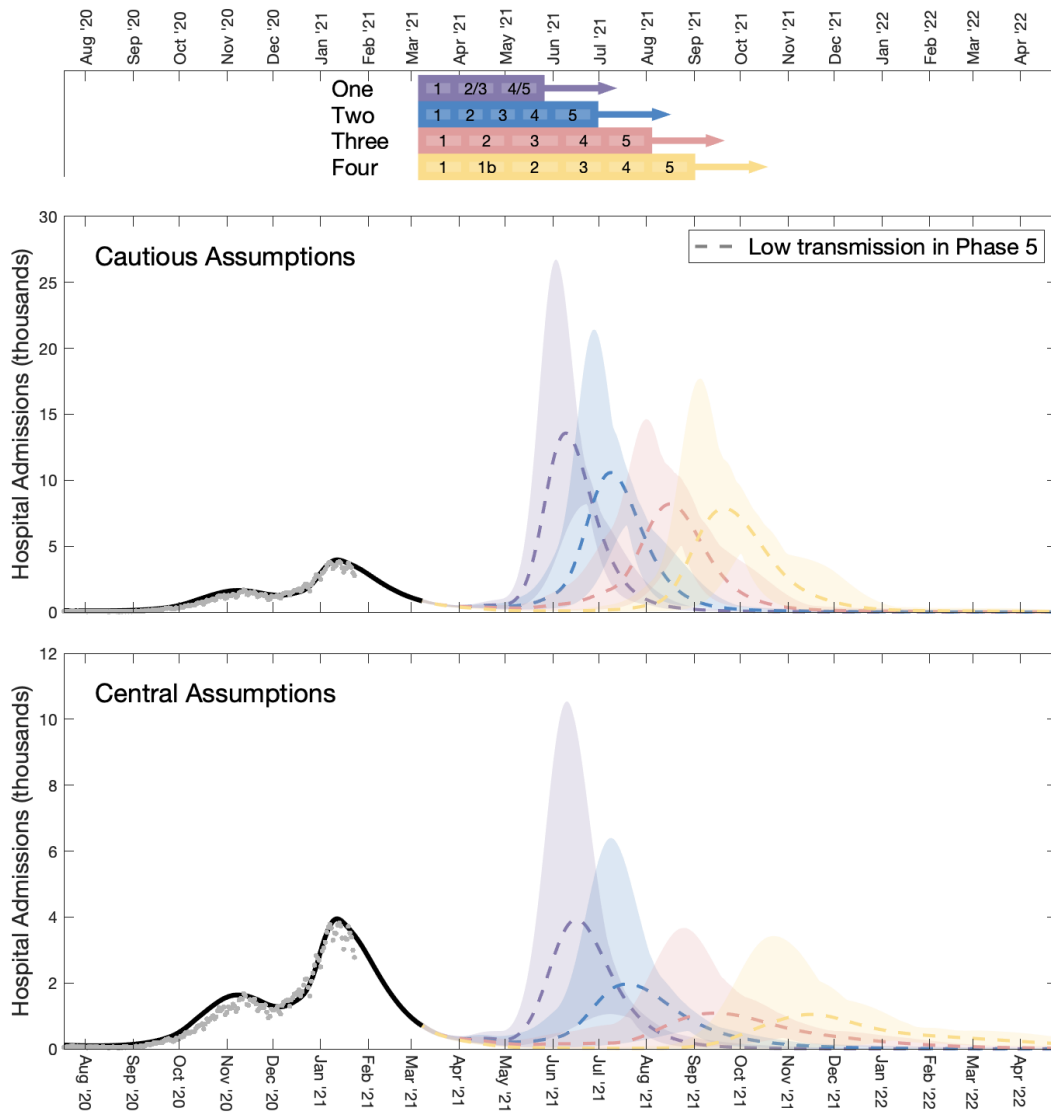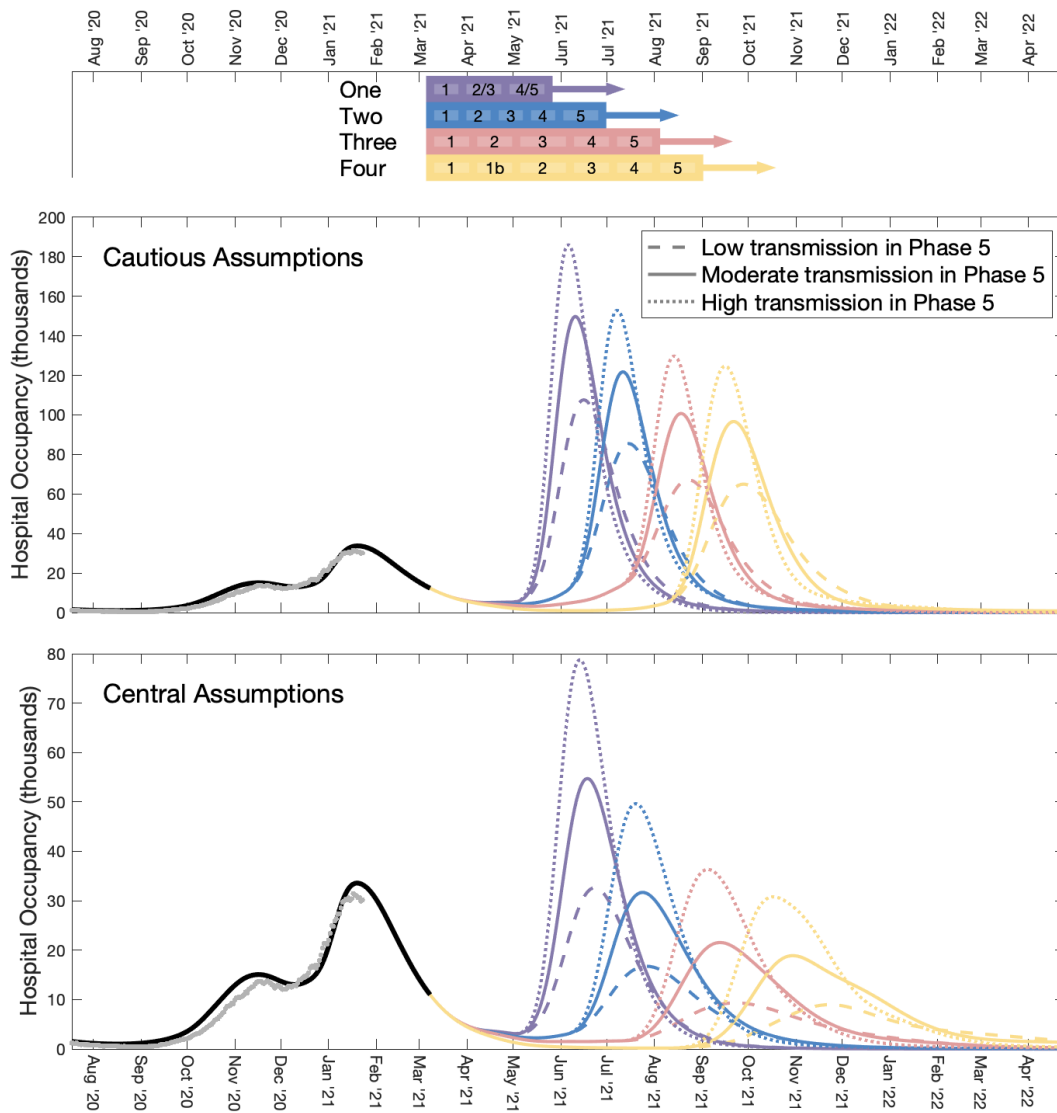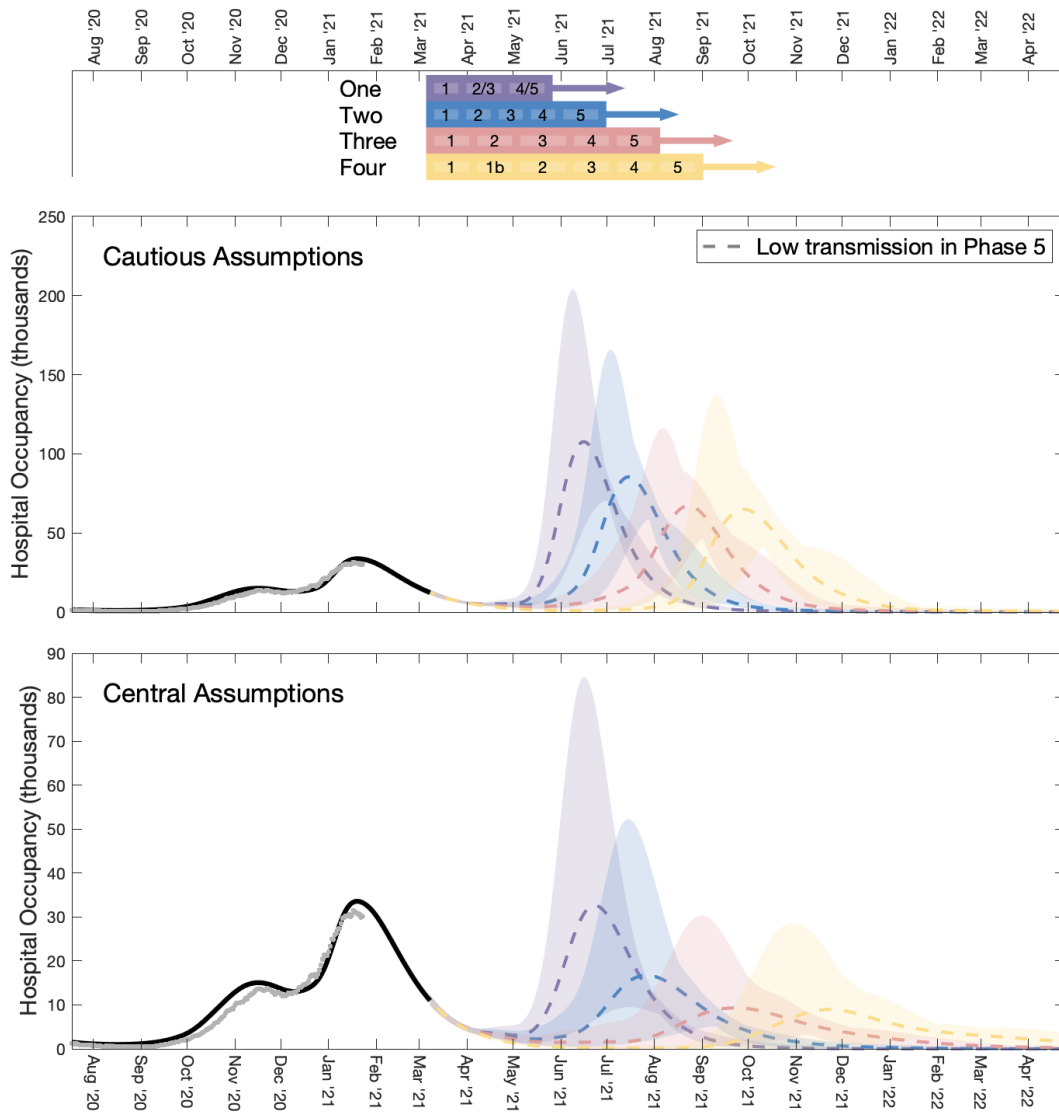
Appendix 3. Hospital Admissions, Medium Transmission in Phase 5

Showing the dynamics of hospital admissions over time for a single assumption about transmission in Phase 5 of the roadmaps for relaxation; in these figures the 95% prediction intervals for each of the roadmaps is also presented.

Appendix 4. Hospital Admissions, High Transmission in Phase 5

Showing the dynamics of hospital admissions over time for a single assumption about transmission in Phase 5 of the roadmaps for relaxation; in these figures the 95% prediction intervals for each of the roadmaps is also presented.
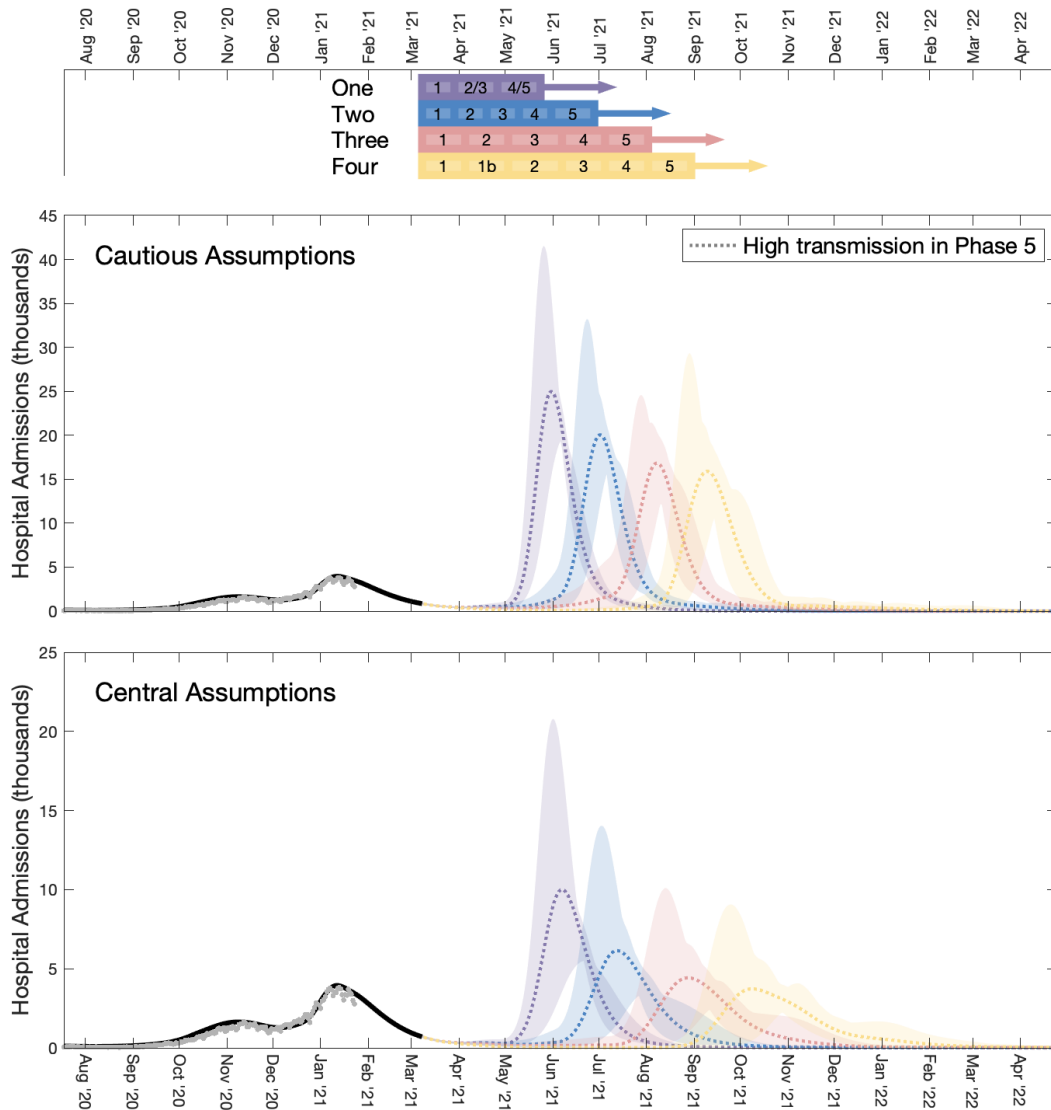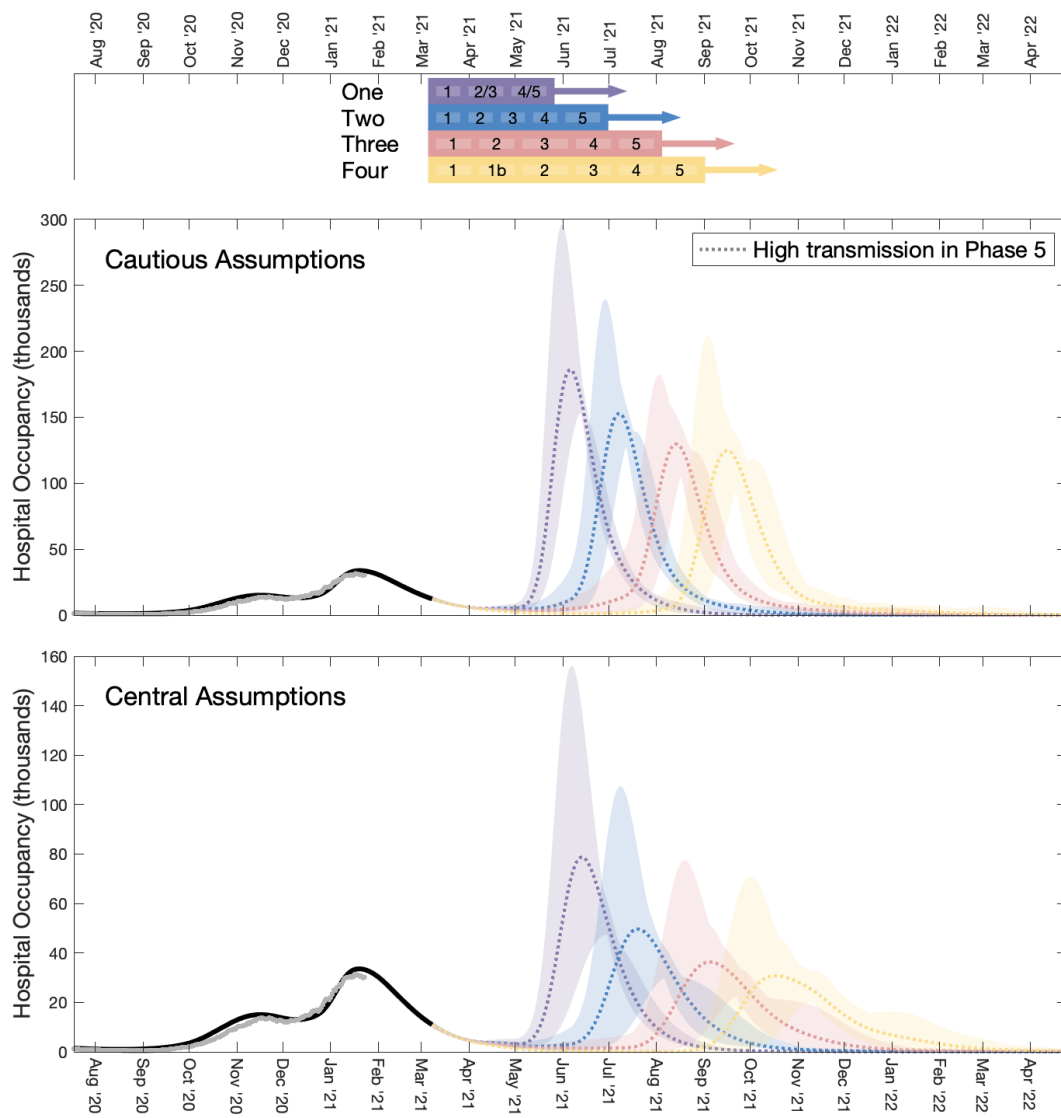
Appendix 5. Hospital Occupancy.

Showing the dynamics of hospital occupancy for the four relaxation roadmaps, the two assumptions about vaccination and the three assumptions concerning transmission in Phase 5 of the relaxation.

Appendix 6. Hospital Occupancy, Low Transmission in Phase 5

Showing the dynamics of hospital occupancy over time for a single assumption about transmission in Phase 5 of the roadmaps for relaxation; in these figures the 95% prediction intervals for each of the roadmaps is also presented.
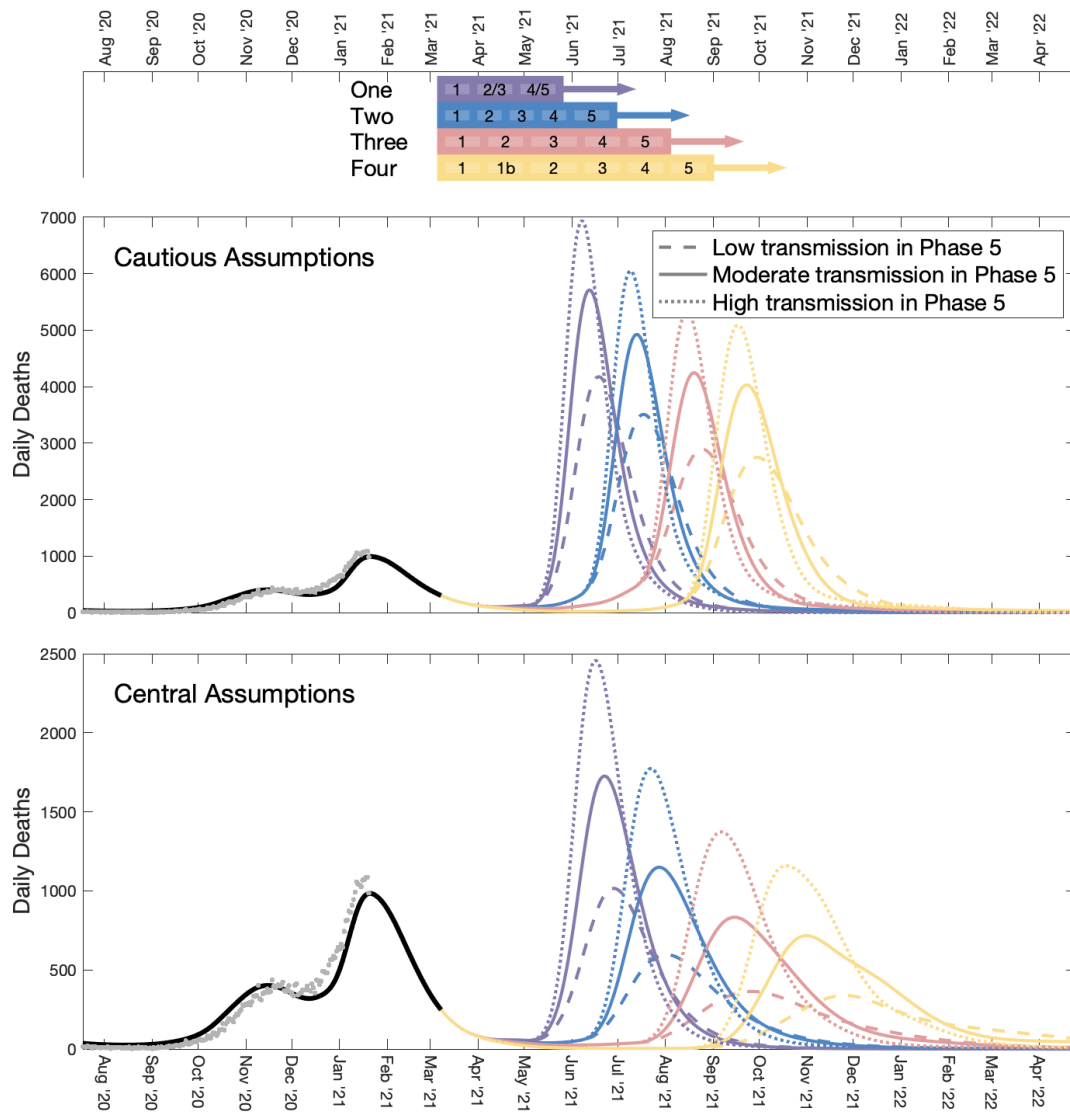
Appendix 7. Hospital Occupancy, Medium Transmission in Phase 5

Showing the dynamics of hospital occupancy over time for a single assumption about transmission in Phase 5 of the roadmaps for relaxation; in these figures the 95% prediction intervals for each of the roadmaps is also presented.
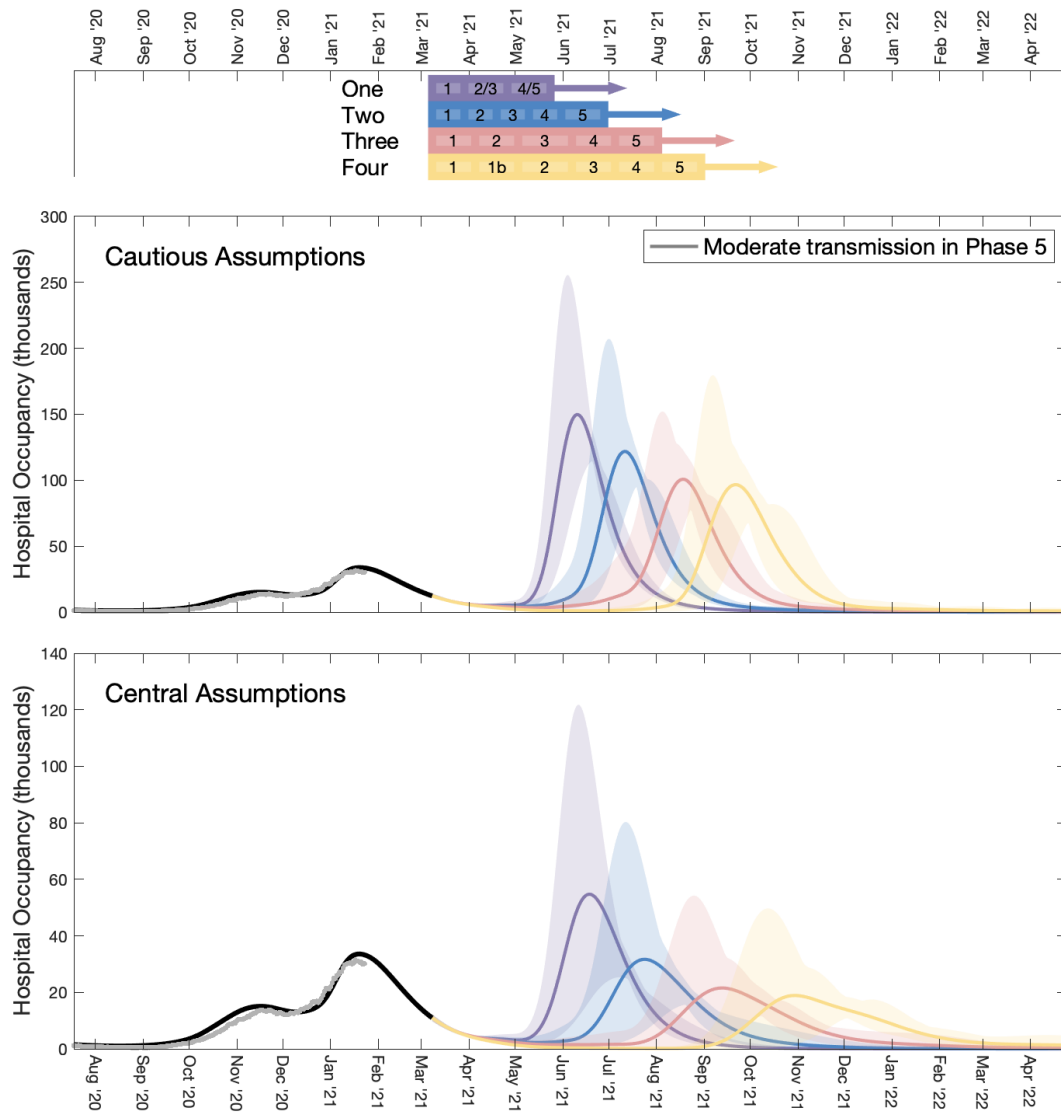
Appendix 8. Hospital Occupancy, High Transmission in Phase 5

Showing the dynamics of hospital occupancy over time for a single assumption about transmission in Phase 5 of the roadmaps for relaxation; in these figures the 95% prediction intervals for each of the roadmaps is also presented.
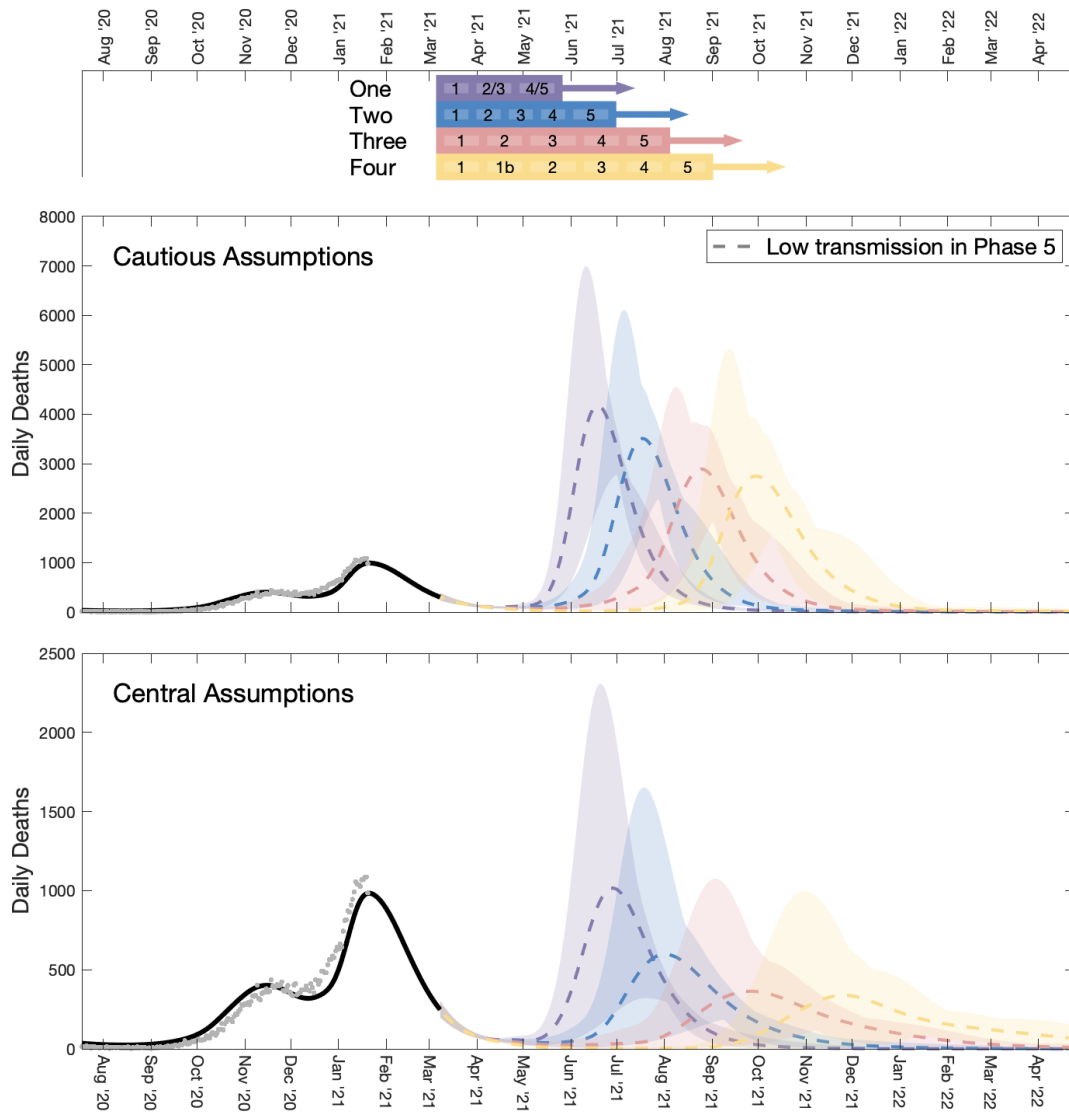
Appendix 9. Daily Deaths

Showing the dynamics of deaths for the four relaxation roadmaps, the two assumptions about vaccination and the three assumptions concerning transmission in Phase 5 of the relaxation.
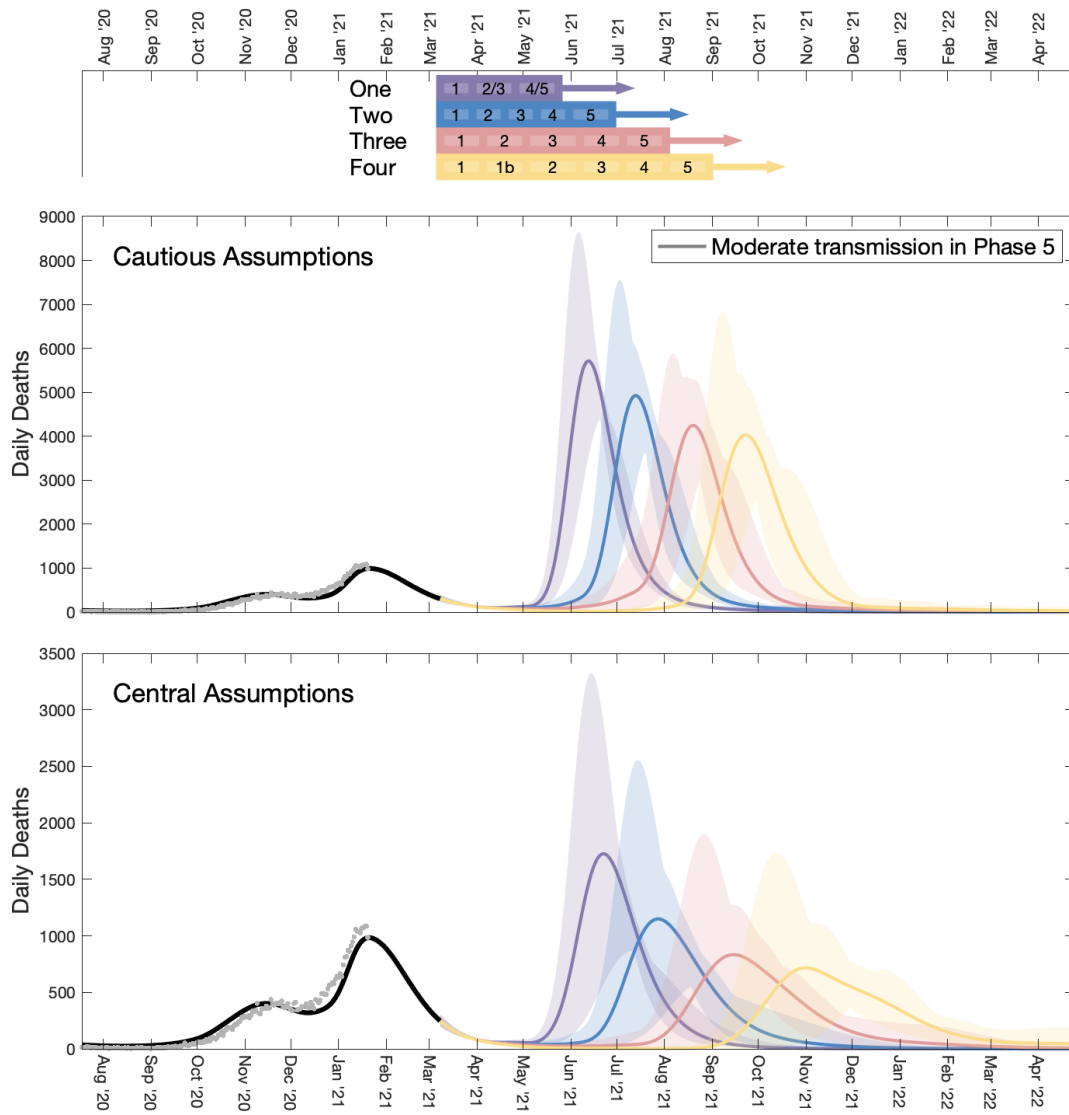
Appendix 10. Daily Deaths, Low Transmission in Phase 5

Showing the dynamics of daily deaths over time for a single assumption about transmission in Phase 5 of the roadmaps for relaxation; in these figures the 95% prediction intervals for each of the roadmaps is also presented.

Appendix 11. Daily Deaths, Medium Transmission in Phase 5

Showing the dynamics of daily deaths over time for a single assumption about transmission in Phase 5 of the roadmaps for relaxation; in these figures the 95% prediction intervals for each of the roadmaps is also presented.

Appendix 12. Daily Deaths, High Transmission in Phase 5

Showing the dynamics of daily deaths over time for a single assumption about transmission in Phase 5 of the roadmaps for relaxation; in these figures the 95% prediction intervals for each of the roadmaps is also presented.
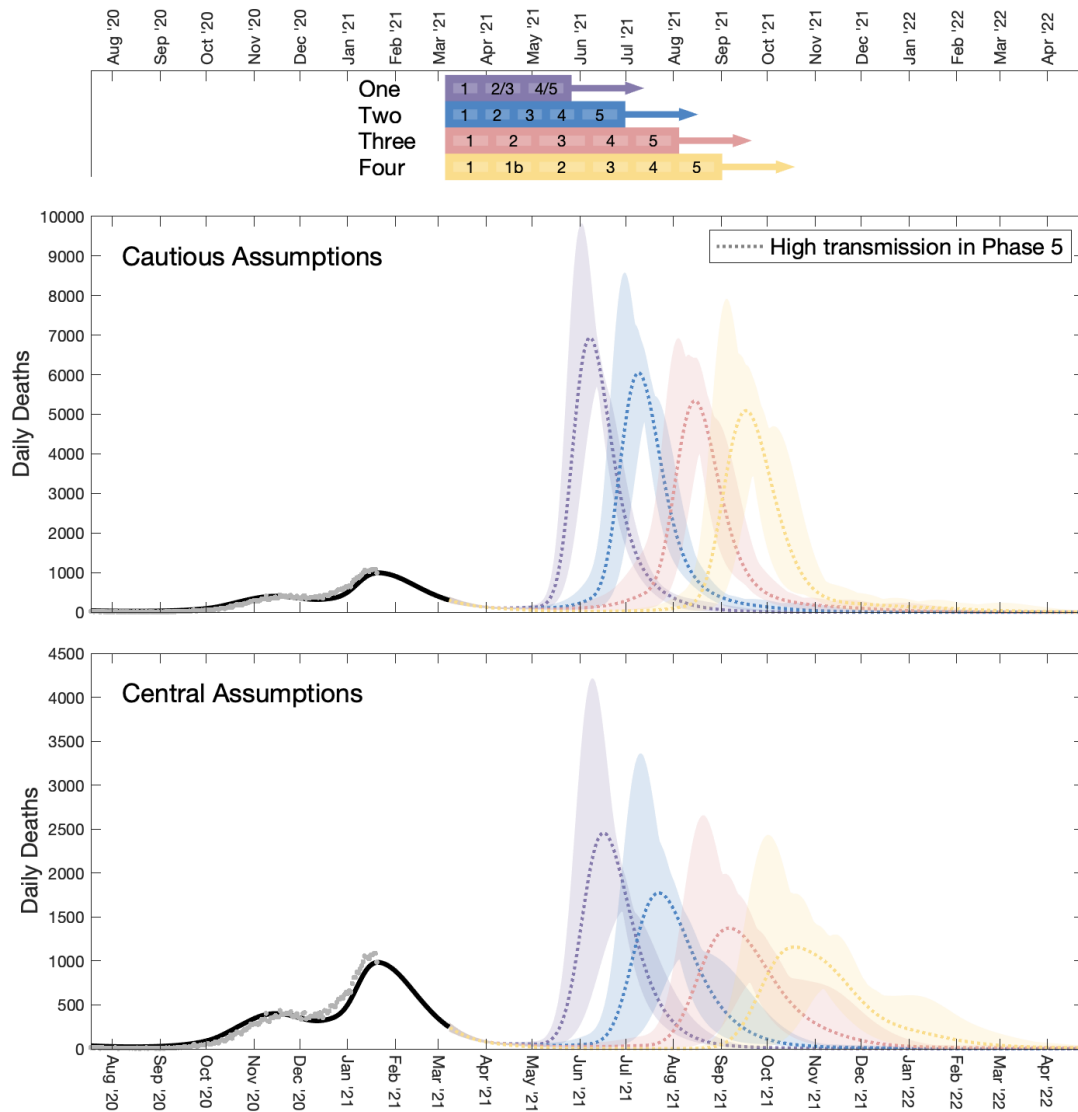
Appendix 13. Hospital Admissions and Occupancy. Vaccine prevents all severe disease.
Showing the dynamics of hospital admissions and occupancy over time for the extremely optimistic
assumption that two doses of the vaccine can block 99% of all severe illness – and hence prevent
a large proportion of hospital admissions and deaths. All admission in this figure therefore come
from the fraction of the population that have not yet received two doses of vaccine.
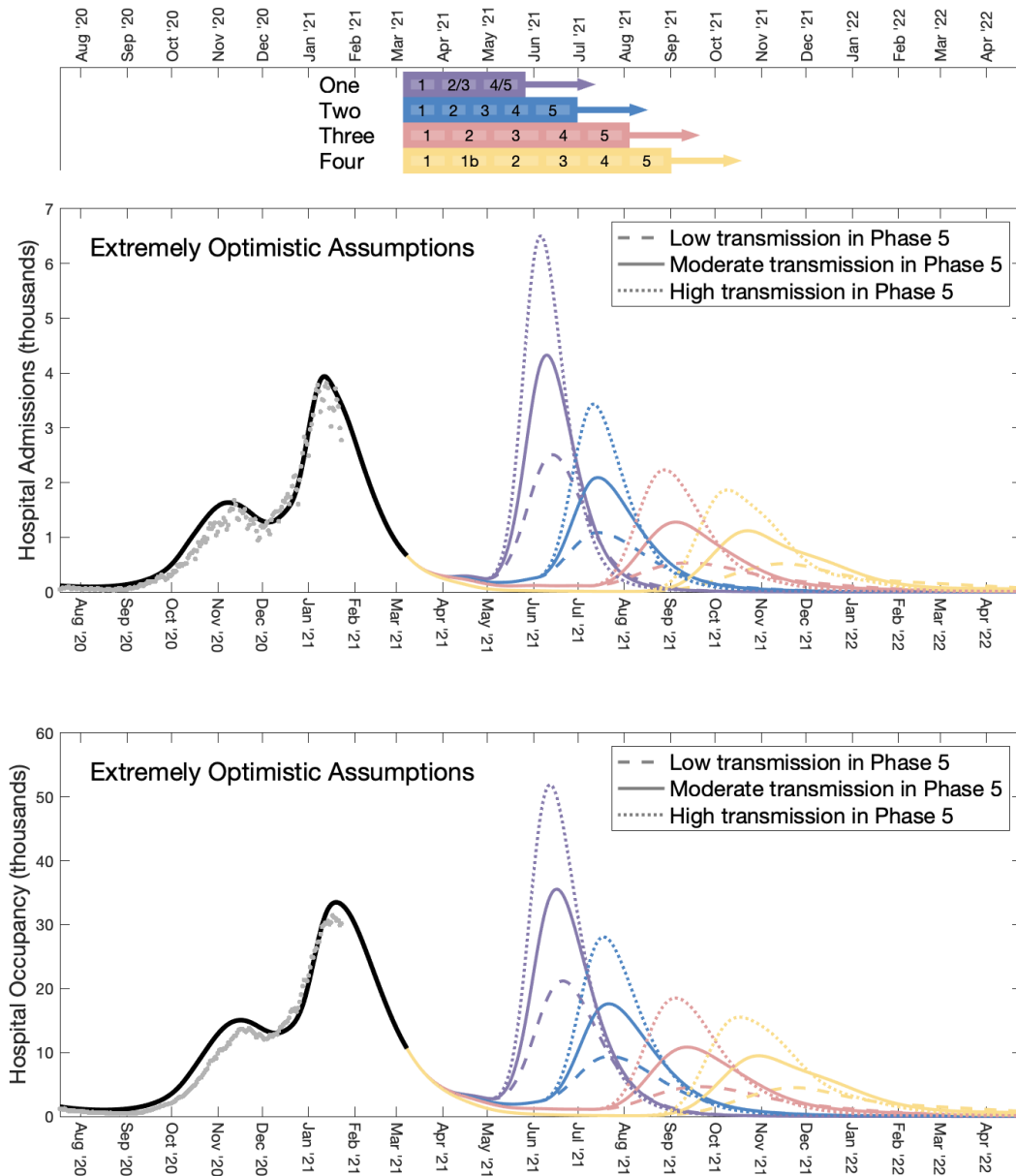
Appendix 14. Warwick's Results plotted at the same scale as Imperial's.