Roadmaps for Relaxation of NPIs, modelling impact of vaccine rollout. II
University of Warwick
15/02/2020

Executive Summary

1) We extend the original four different roadmap scenarios with two additional scenarios that different slightly in their timing. This is modelled for the seven NHS regions of England and then the data combined.

2) The new scenarios are contingent on levels of vaccine rollout making them more stable to uncertainties in delivery; however, they allow a moderate amount of within household during the early stages of relaxation – the modelling of this cannot be based upon existing data and generates considerable uncertainty within the models.

3) These roadmaps were modelled assuming an effective rollout of vaccination, with two assumptions: both achieve 4 million doses a week in April but the faster option maintains 3.9 million doses a week whereas the slower option drops to 2.0 million by June.

4) In addition to the speed of delivery 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 scenarios (2 sets of assumptions).

5) All of the relaxation scenarios 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) 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.

8) The new scenario(s) perform better than the original four roadmaps. The improvement is due to the new scenario(s) likely to generate two smaller waves of infection, rather than a single wave.

9) The uncertainty around the impact of some aspects of Step 2 (“one guest per day per household inside”) means that there is considerable uncertainty in the size of the first wave.

10) Seasonality is predicted to have a significant impact of the predicted pattern of infection, suppressing infection in the summer, and necessitating the need to consider longer time-scales and waning immunity.

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.

Methodology and Key Uncertainties.

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[3]	48.2%[2]	63.1% (51.8%-71.7%)[2]	60.2%[2]	82.4% (62.7%-91.7%)[2]
Central Assumptions	48%	70%	60%	88%
Cautious Assumptions	24%	56%	30%	70%

2) *Behaviour, NPIs and Estimates of Reproductive Number*. The previous document examined four different time-lines to relaxation of control. These are shown in purple, blue, red and yellow in all the following figures; the stages of these relaxation profiles were based on 'tier-like' control measures and had definitive start and end dates. The estimated level of NPIs (and compliance) is based on historical data for each region and therefore reflects uncertainty in parameter estimates as well as regional variation. Controls, timings and estimates of *R* (excluding immunity) for the original four road maps and the new scenario are given below; these values are illustrated graphically in Figure 5.

[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

	Roadmap 1	Roadmap 2	Roadmap 3	Roadmap 4	$R_{excluding\_immunity}$ (for Midlands)
Return to education	8 March – 29 March	8 March – 29 March	8 March – 5 April	8 March – 3 May	$1.94\ (1.35-2.57)$
Tier 3		29 March – 19 April	5 April – 3 May	3 May – 7 June	$2.16\ (1.70-2.71)$
Tier 2/3	29 March – 26 April				$2.31\ (1.96-2.80)$
Tier 2		19 April – 10 May	3 May – 7 June	7 June – 5 July	$2.47\ (2.16-2.90)$
Tier 1		10 May – 31 May	7 June – 5 July	5 July – 2 August	$2.73\ (2.38-3.09)$
Unlock	26 April onwards	31 May onwards	5 July onwards	2 August onwards	$3.18\ (2.62-3.71)$ low transmission

The new scenario investigated here (shown in green in all figures) has four main Steps, as outlined below. For the new scenario, the use of steps (3 and 4) that rely on vaccine targets makes this scenario far less sensitive to changes in vaccine delivery.

Step	Controls	$R_{excluding\_immunity}$ (for Midlands)
Step 1	reopening of primary and secondary schools from March 8th	$1.94\ (1.35-2.57)$
Step 2	close to the old Tier 3 restrictions except allowing "one guest per day per household inside" from March 29th	$2.54\ (2.23-2.94)$
Step 3	close to the old Tier 1 restrictions, and only comes into force three weeks after priority groups 1-9 have been vaccinated	$2.73\ (2.38-3.09)$
Step 4	unlock with long-term mitigations (as was assumed for the previous roadmap assumptions), this only happens once all adults are vaccinated	$3.18\ (2.62-3.71)$ low transmission

A second assumption (shown throughout in pink) is investigated with Step 3 only beginning once JCVI priority group 1-4 have been vaccinated twice, which is a slight delay to the original assumption. In general, this is only a small shift in dates and has a negligible impact on the epidemic.

What is clear from these changes is that the new scenarios achieve higher *R* values earlier in the relaxation process (Step 2 compared to Tier 2 or 3); this means that the new scenarios can experience a small-scale early outbreak, followed by a later outbreak when controls are finally relaxed. This two-humped third wave has the potential to generate a smaller total outbreak size than a single wave.

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% May completion (fast or slow)	85% July completion (fast or slow)	85% October completion (fast) December completion (slow)
Cautious Assumptions	95% May completion (fast or slow)	85% July completion (fast or slow)	75% September completion(fast) December completion (slow)

The roll-out of this vaccine follows a delivery schedule in which 3.9 million or 2.0 million doses a week can be administered from April 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 the main simulation, but this is examined in Figure 3 and 10. 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. An example of the potential impact of lower uptake is shown in Figure 4.

Predictions for Hospital Admissions & Deaths.

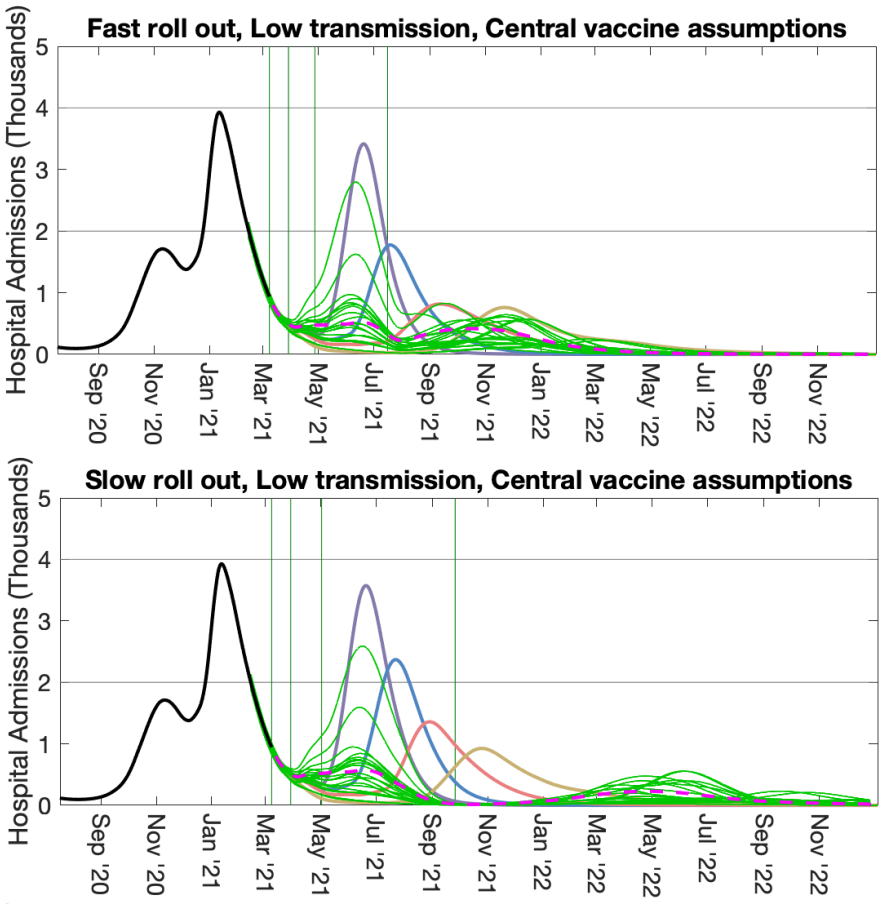


Figure 1 Daily Hospital Admissions for the four road maps and two new scenarios. The top graph is for fast roll-out, the bottom graph is for the slower roll-out. Here a sample of trajectories for the new scenario are shown to highlight the variability. Figure 6-8 capture this variability by shading the 95th and 50th percentiles.

Figure 1 shows the expected number of hospital admissions for the four original road maps and the two new scenarios assuming fast (3.9 million doses a week) and slow (2 million doses a week) vaccine delivery. Vertical lines show when different steps of the new scenario begin.

On average the new scenario compares favourably to the four roadmaps considered previously. The greater transmission in Step 2, means that a larger outbreak is predicted in the summer months (compared to Roadmap Three and Four), but this outbreak is not as extreme as for Roadmap One. By maintaining a level of control that is closer to $R_t \sim 1$, we experience small scale outbreaks as other relaxations occur, leading to lower deaths aggregated across future dates (Figure 2).

The uncertainty in the Step 2 surrounding how to model “one guest per day per household inside”, means that the 95% credible intervals (pale shaded area) are large for the first outbreak potentially exceeding the mean predictions for Roadmap Two (blue line Figure 1).

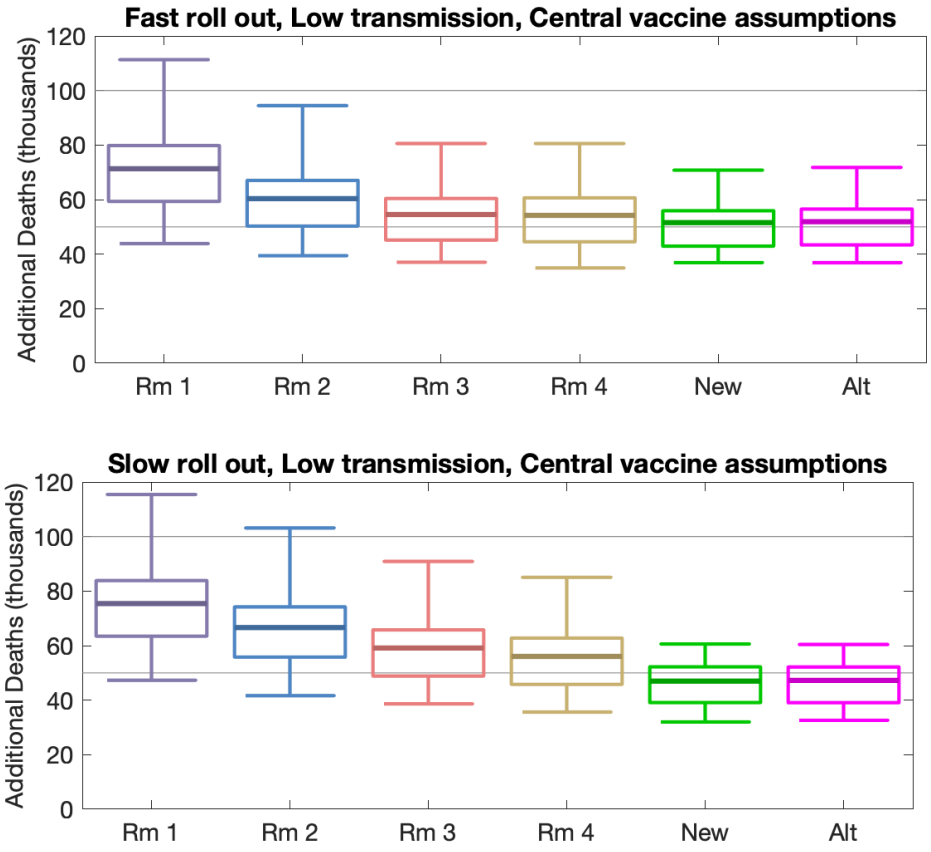


Figure 2 Total COVID-19 deaths from 8th March 2021 for the four road maps and two new scenarios. The top graph is for fast roll-out, the bottom graph is for the slower roll-out. 95th and 50th percentiles are shown for each relaxation option.

We expand these simulations by considering the sensitivity to multiple assumptions in combination: (fast or slow vaccination delivery) × (central or cautious vaccine parameter assumptions) × (low or high transmission in the final stage of relaxation). These 8 combinations are shown in Figures 5-9. As shown in previous work, the uncertainty in vaccine parameters has by far the largest impact (rows 2 and 4).

We consistently find that the two new scenarios often generate two smaller scale but more prolonged outbreaks (figure 6), which leads to a lower total number of deaths (figure 9). Examining the number of infections (symptomatic and asymptomatic, figure 8), we can more easily relate growth rates to different steps of relaxation. This clearly shows that steps 1 and 2 in combination, and step 3, generate two small-scale waves of infection.

Given that the timing of steps 3 and 4 under the new scenarios is tied to achieving specific vaccine targets rather than set dates, these comparatively perform far better that the roadmaps when vaccination delivery is slow.

Seasonality

One issue that has been highlighted as a potential limitation of the models used so far is their lack of seasonality. Following the work of Baker *et al* 2020[4], we relate the potential level of seasonality to specific humidity (q):

$$\beta(t) \sim \exp(a \times q(t) \times [R_0^{max} - R_0^{min}])$$

Using the values obtained by Baker *et al* for the scaling parameter a (-32.5 for coronavirus OC43, and -227.5 for coronavirus HKU1), we estimate that the seasonality is either 6% or 14% in the UK - measured as the relative peak to trough variation. The pattern from specific humidity can be closely matched by a sinusoidal function with a minimum in mid-August:

$$\beta(t) = 1 - \frac{\phi}{2} - \frac{\phi}{2}\cos\left(\frac{2\pi(t-T)}{365}\right)$$

Where T is the middle of August (day 228) and ϕ is the strength of the seasonality.

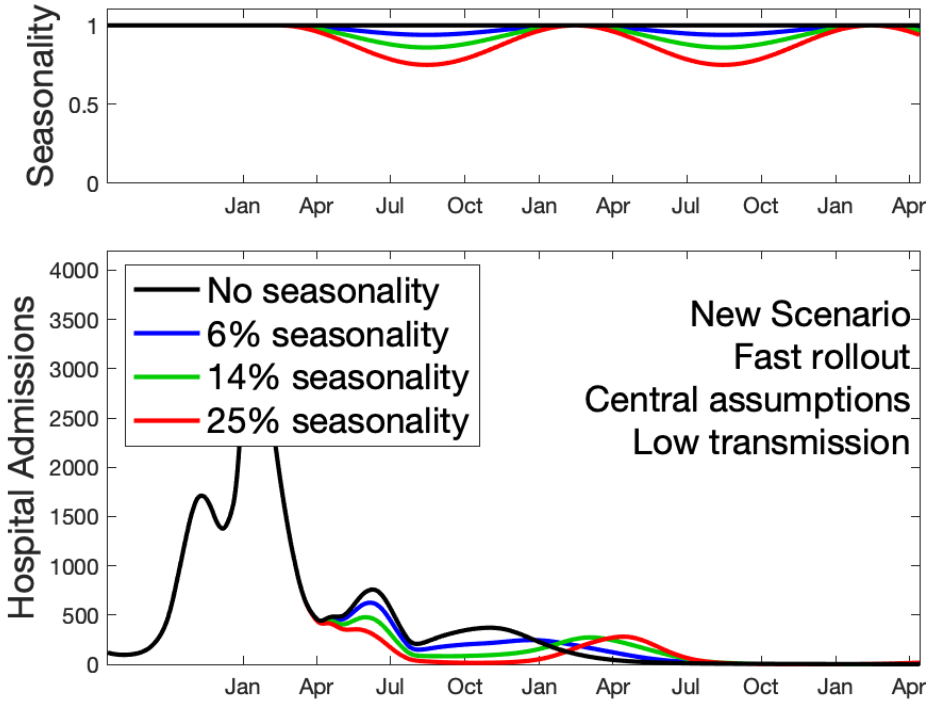


Figure 3. Impact of seasonality on the new scenario, showing 0, 6%, 14% and 25% strengths of seasonality. These are within the bounds estimated by other researchers[5], while 6% and 14% come directly from the work of Baker *et al*.

The implications of seasonality interacting with the other sensitivities (speed of deployment, vaccine parameters and final transmission) are explored in Figure 10. While seasonality has a pronounced impact of the shape of the infection waves, it has a more limited impact on the total scale of deaths – although given the time-scales involved waning of immunity will begin to play a substantial role.

[4] Baker, Yang, Vecchi, Metcalf & Grenfell (2020) Susceptible supply limits the role of climate in the early SARS-CoV-2 pandemic. *Science* **369** 315-319.

[5] Kissler, Tedijanto, Goldstein, Grad & Lipsitch (2020) Projecting the transmission dynamics of SARS-CoV-2 through the postpandemic period. *Science* **368** 860-868

Heterogeneity in Vaccine Uptake.

Finally, the vaccine uptake data show multiple LTLAs where the uptake in the over 80's is substantially below the national average. We show that pockets of low vaccine uptake could generate substantial small-scale pockets of high infection (figure 4); here we plot admissions per hundred thousand, as the likely size of these low-uptake pockets is uncertain.

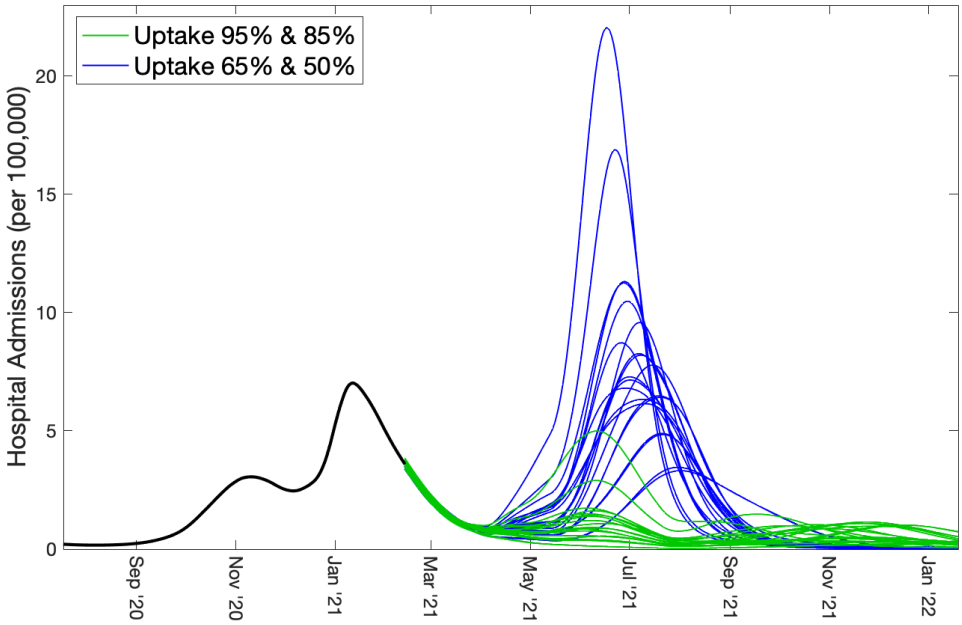


Figure 4. Impact of heterogeneity in vaccine uptake for the new relaxation scenario. Comparing the standard assumption about vaccine uptake (95% in the over 80s and 85% for those under 80) with a much lower extreme that matches recorded uptake in some LTLAs (65% in the over 80s and an assumed 50% in other age groups).

ADDITIONAL FIGURES

Figure 5. Timing of the changes in R (excluding immunity) for the Roadmaps and new scenarios. The mean lines are the same in each graph, but the individual graphs show the variation (95th and 50th percentiles) in the underlying assumptions.

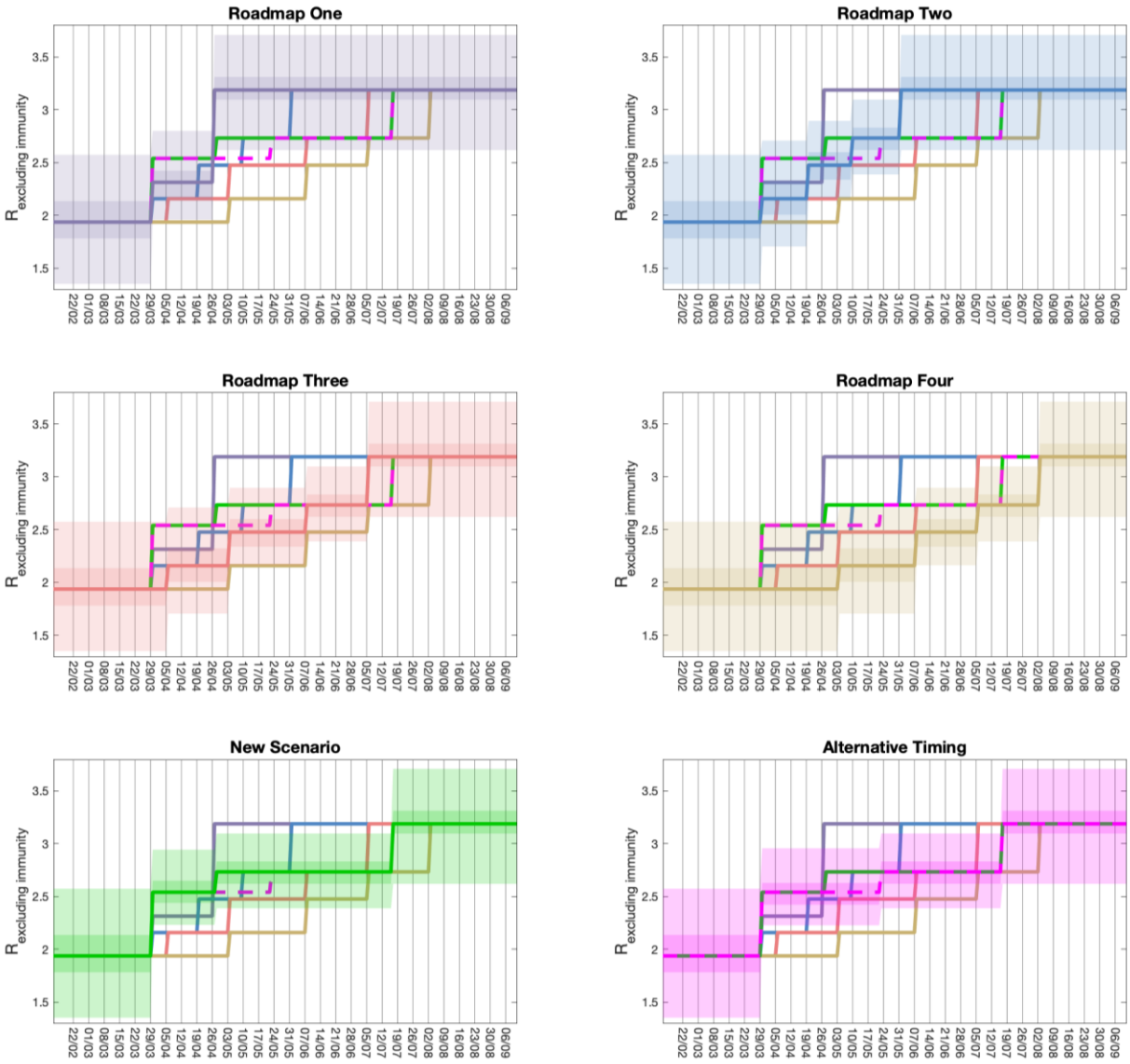


Figure 6. Hospital Admissions. New scenarios in Green (with 95% and 50% CIs) and Pink.

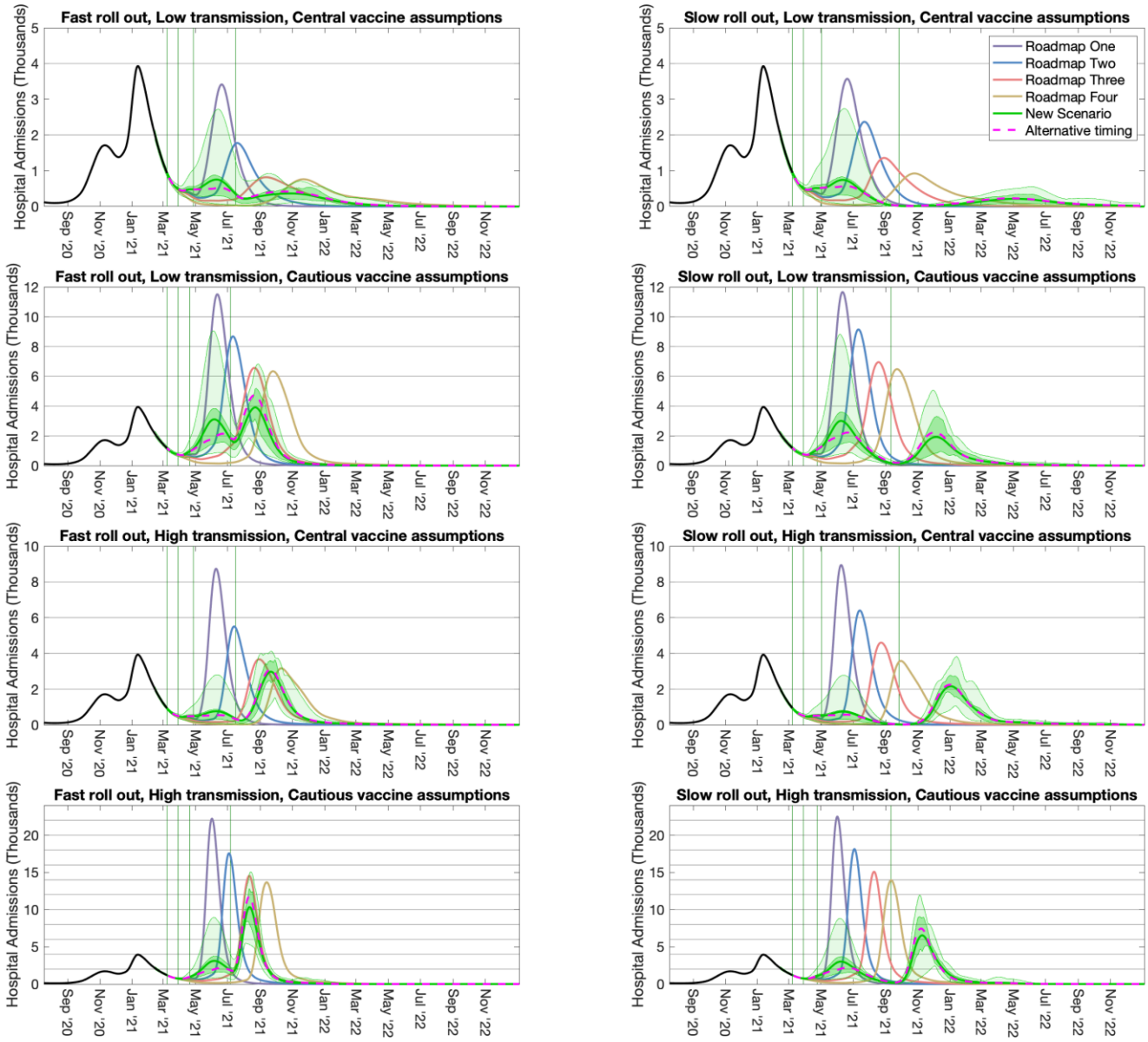


Figure 7. Hospital Occupancy. New scenarios in Green (with 95% and 50% CIs) and Pink

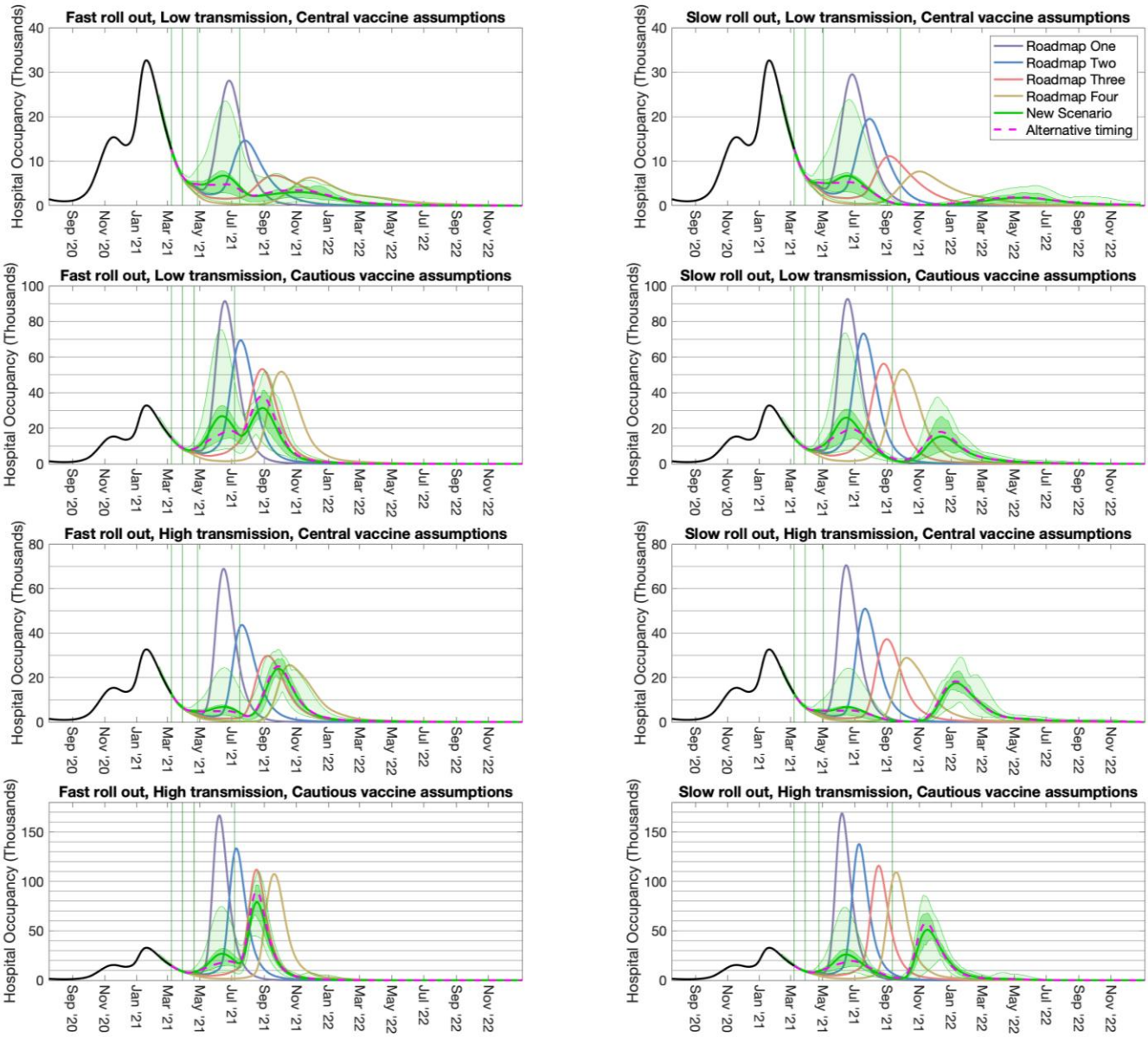


Figure 8. Infections to show timing. New scenarios in Green (with 95% and 50% CIs) and Pink

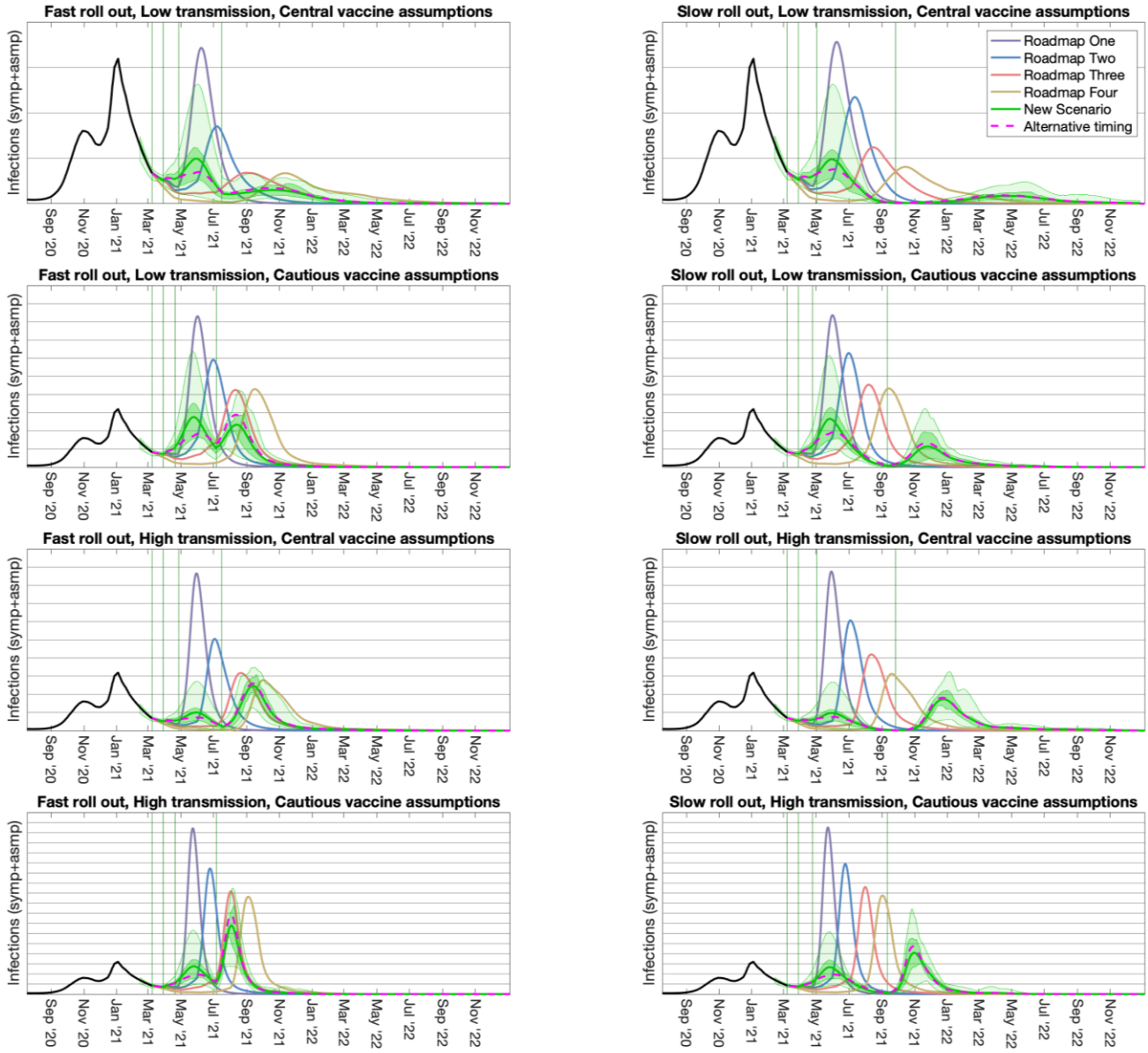
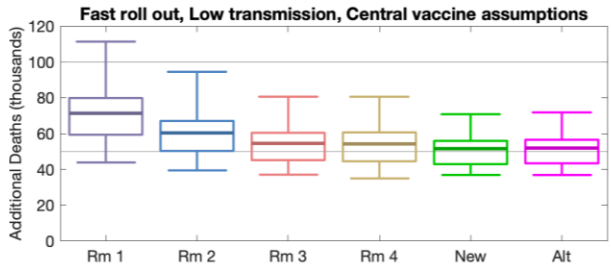
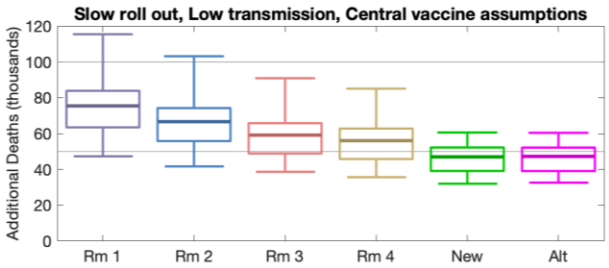
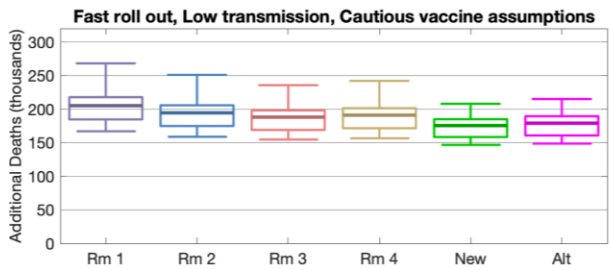
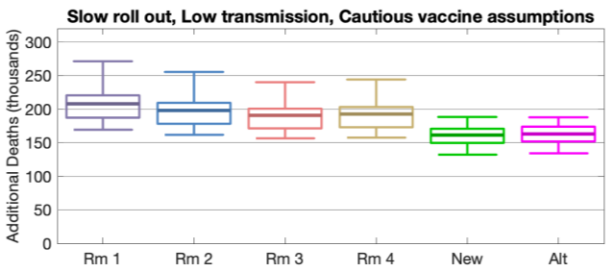


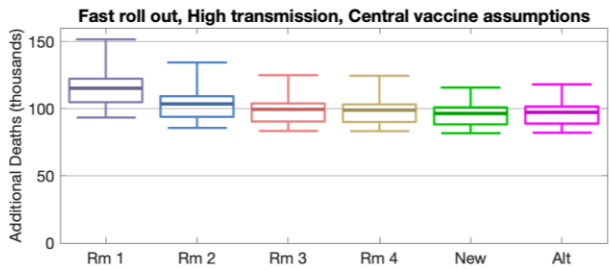
Figure 9. Total Deaths from 8th March 2021. New scenarios in Green and Pink. All have 95%, 50% CIs and means.

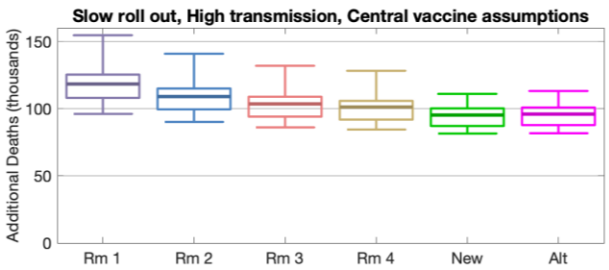


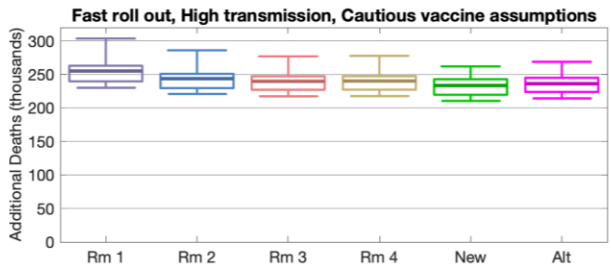












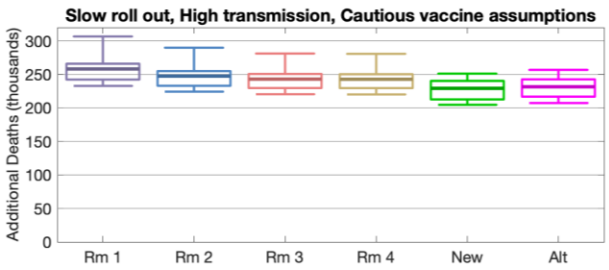
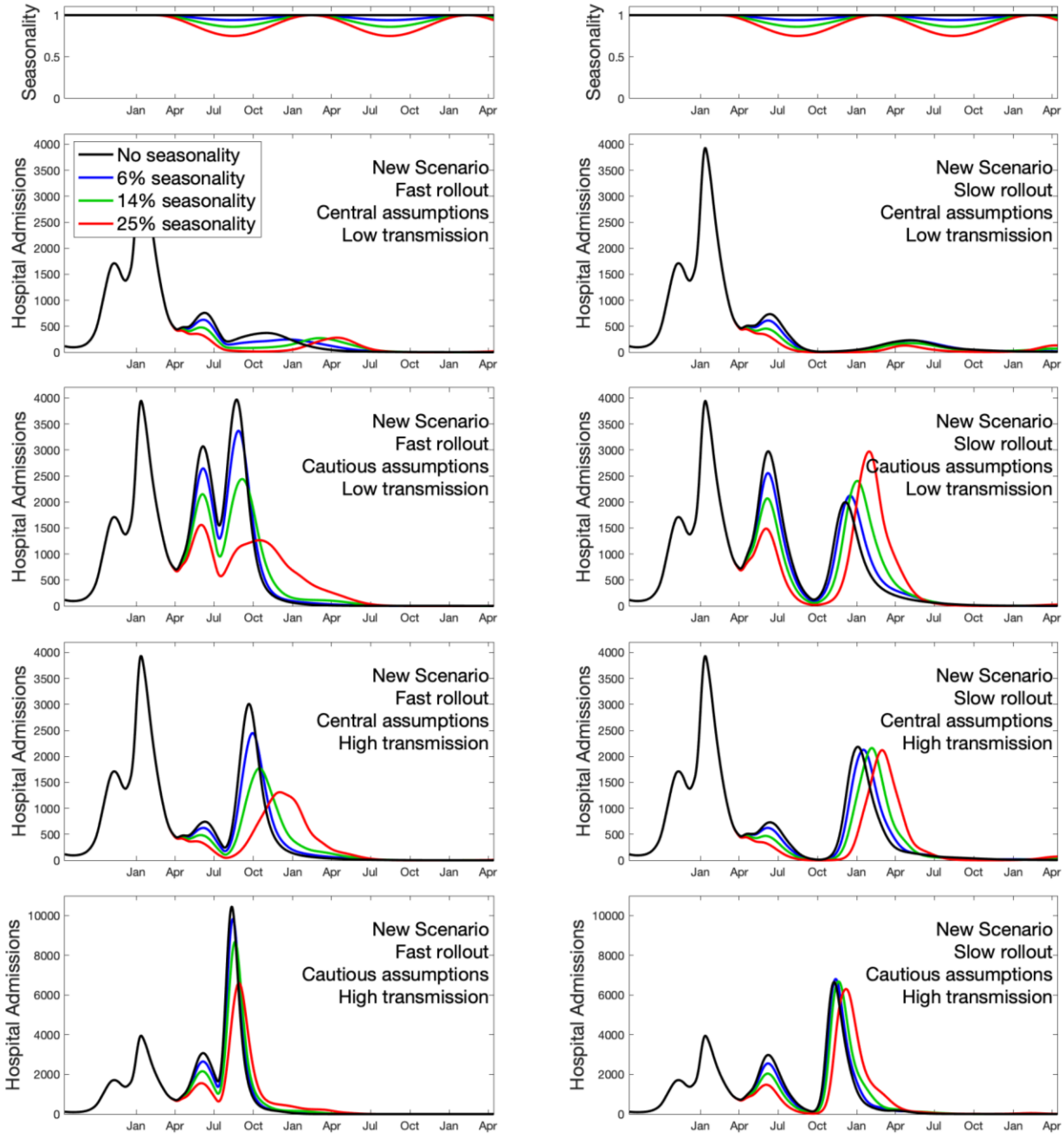
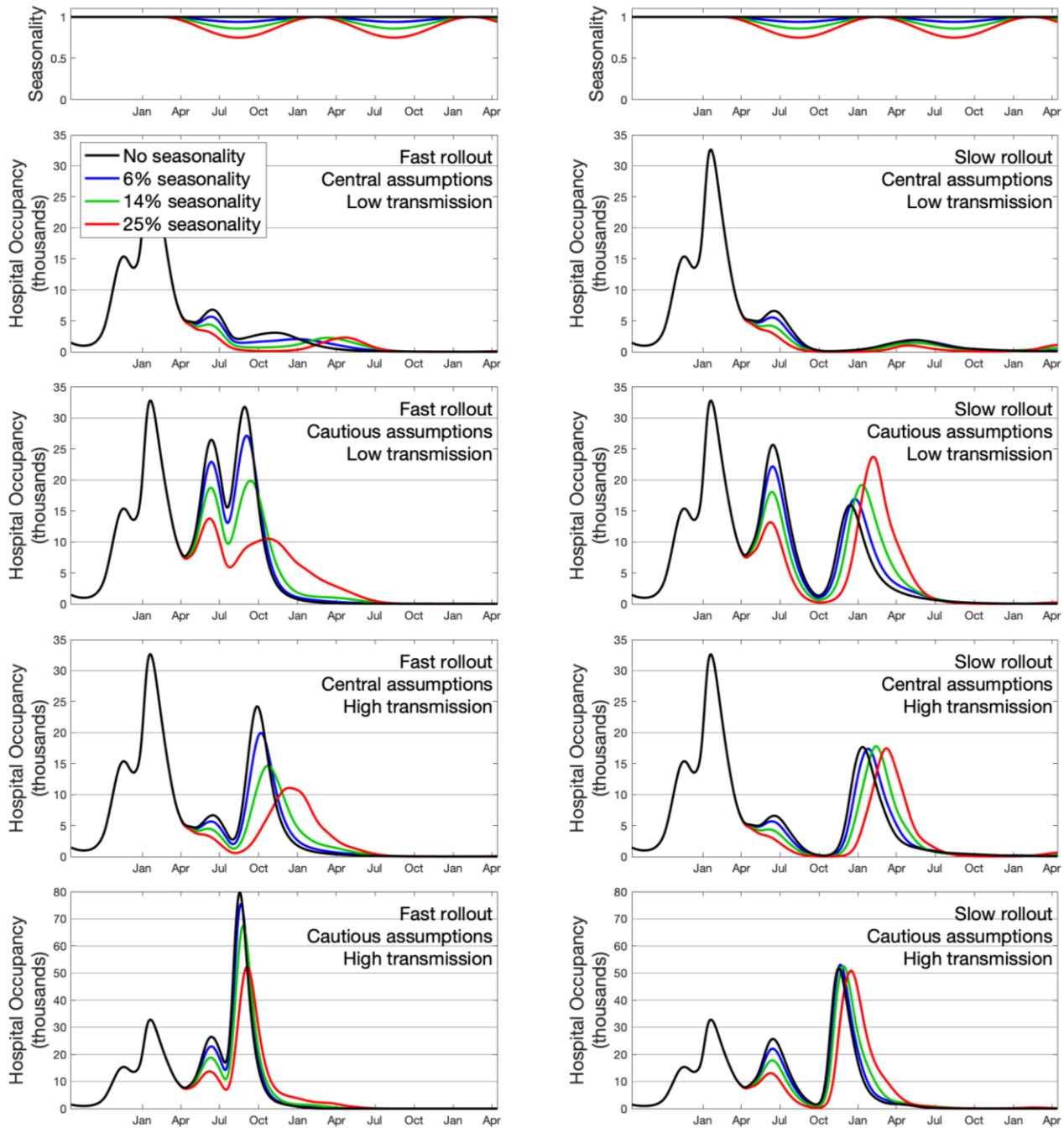
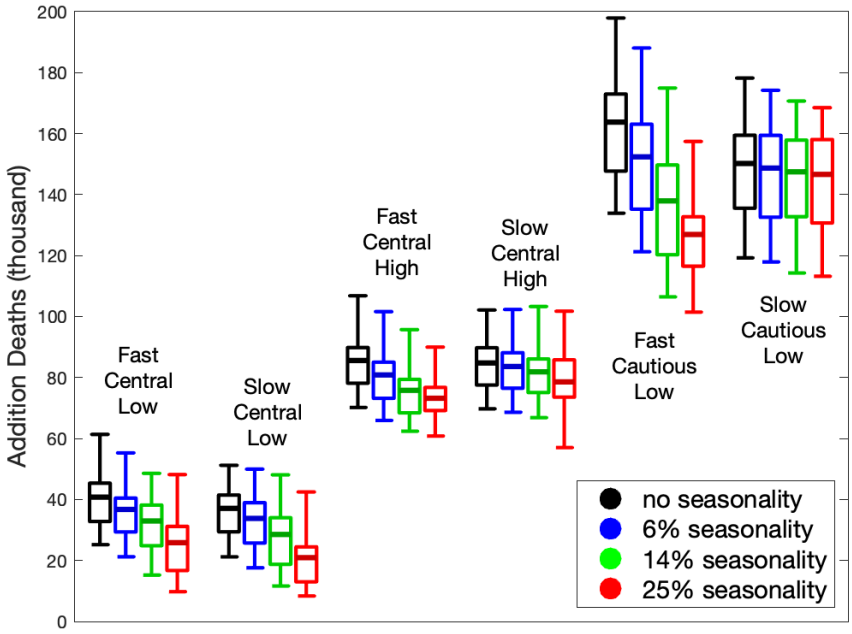


Figure 10. Impact of Seasonality on hospital admissions and total deaths from March 8th 2021.




Seasonality
Hospital Occupancy (thousands)
No seasonality
6% seasonality
14% seasonality
25% seasonality
Fast rollout
Central assumptions
Low transmission
Slow rollout
Central assumptions
Low transmission
Fast rollout
Cautious assumptions
Low transmission
Slow rollout
Cautious assumptions
Low transmission
Fast rollout
Central assumptions
High transmission
Slow rollout
Central assumptions
High transmission
Fast rollout
Cautious assumptions
High transmission
Slow rollout
Cautious assumptions
High transmission
Jan
Apr
Jul
Oct


Addition Deaths (thousand)
200
180
160
140
120
100
80
60
40
20
0
Fast Central Low
Slow Central Low
Fast Central High
Slow Central High
Fast Cautious Low
Slow Cautious Low
no seasonality
6% seasonality
14% seasonality
25% seasonality