Interim roadmap assessment: prior to step 4

Rosanna C. Barnard, Nicholas G. Davies, Mark Jit & W. John Edmunds
London School of Hygiene & Tropical Medicine
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We model Step 4 of the UK Government's Spring 2021 "Roadmap" out of lockdown in England. To capture behavioural changes in response to the easing of restrictions, we consider low, medium and high scenarios for mobility levels resulting from implementing Step 4 of the roadmap. We also consider a number of alternative policy options such as delaying roadmap Step 4, implementing circuit breaker lockdowns and reversing roadmap steps. As the Delta variant of concern (VOC) B.1.617.2 continues to spread in England, our analysis considers a third SARS-CoV-2 variant which exhibits different levels of immune escape and of increased transmissibility relative to the Alpha B.1.1.7 VOC.

There is considerable uncertainty over the properties of the Delta variant, but all scenarios considered project a third wave of infection peaking in the mid-to-late summer if roadmap Step 4 is enacted on 21st June. Delaying Step 4 by 2–9 weeks substantially reduces peak hospitalisations and deaths across all scenarios. Owing to the uncertainty over the properties of the Delta variant, further close monitoring of the COVID-19 burden associated with Delta is essential for robust decision making. The intensity of the third wave varies substantially depending upon the levels of transmissibility and immune escape exhibited by the Delta variant, and on the rate of social mixing due to policies enacted at Step 4 of the roadmap. This work builds upon modelling and assumptions used in our previous report. We make assumptions about the nature and impact of roadmap Step 4 which cannot be verified until policy decisions are finalised and behavioural responses can be measured.

Summary of findings

- Our results suggest that Step 2 of the roadmap likely increased the reproduction number (averaged across all three SARS-CoV-2 variants modelled) to just above 1 in April 2021. The additional easing of restrictions at roadmap Step 3 increased this further. Even without implementing Step 4 of the roadmap, a summer wave of infections, hospitalisations and deaths is likely.
- Implementing roadmap Step 4 as planned is likely to exacerbate this and lead to a third wave of infection, peaking in August or early September 2021. Under most scenarios, this summer wave would be smaller than the January 2021 wave, in terms of hospitalisations and deaths, but comparable to the April or October 2020 waves. Under more pessimistic scenarios of high immune escape and high transmissibility of Delta B.1.617.2 (70% more than Alpha B.1.1.7), it is possible that the summer wave could exceed the January 2021 peak in terms of hospitalisation and deaths. The size of the peak depends strongly upon the levels of mobility (and hence social mixing) reached following Step 4, and accordingly changes to Step 4 policies may have a large effect on the dynamics of the summer wave.
- The model projects that more than half of the hospitalisations and deaths occurring in the summer 2021 wave will be in unvaccinated individuals, with admissions being split relatively evenly between the 45-64, 65-74 and 75+ year age groups. Deaths are likely to be concentrated in the 75+ age group.
- Delaying Step 4 of the roadmap is likely to have an impact in the short term, reducing the impact of the summer wave. A two week delay has a modest impact, reducing deaths as measured until the end of October 2021 from 49,700 (35,600-67,200) to 48,500 (34,400-66,900) for the medium / central immune escape scenario and 50% increase in transmissibility for the Delta B.1.617.2 variant. Delaying Step 4 for 5 weeks, so that it coincides with the school vacation period is expected to have a larger effect in the short term helping to flatten the summer wave and reducing the number of deaths from 49,700 (35,600-67,200) to 43,500 (31,200-62,900) and peak deaths from 700 (500-1,200) per day to 500 (300-800) for the medium / central immune escape scenario and 50% increase in transmissibility for the Delta B.1.617.2 variant (Table 6).
- Taking further measures to reduce the summer wave, such as delaying Step 4 until all adults have had both vaccine doses, instigating a circuit-breaker lockdown or moving back to Step 2 measures is likely to largely negate the impact of the summer wave, unless pessimistic assumptions regarding immune escape and transmissibility are adopted (Tables 6 and 7 and Figures 9-12). Note, however, that the more stringent the short term measures are, then the larger the bounce-back in cases later in the year (Figures 9-12), when schools will be open and other seasonal factors are less favourable. Indeed, for these reasons even the 2 or 5 week delay to Step 4 can result in modest increases in morbidity and mortality when measured until the end of the year (Tables S3 and S4) as more cases are pushed back into the autumn. Over longer periods of time the epidemiology and policies are likely to change, however, and so in the base-case we report shorter term impacts in Tables 6 and 7.

- These projections are subject to considerable uncertainty. It is not possible to accurately predict how mobility and contacts will change following the easing of restrictions. We have presented our results in terms of low, medium and high assumptions for mobility, and these make a considerable difference to the results. For instance, taking the low/optimistic immune escape scenario and 50% increase in transmissibility of Delta B.1.617.2 variant over Alpha B.1.1.7 (Scenario I), then the median peak bed demand under the June 21st Step 4 scenario is 18,900 under the medium-mobility scenario. However, median demand is 12,700 beds under the low mobility scenario, and 29,200 under the high mobility scenario (over twice the bed demand of the low scenario).
- Furthermore, there remains enormous uncertainty in the characteristics of the Delta B.1.617.2 variant (in terms of immune escape and transmissibility) and the effectiveness of the vaccines at preventing infection and serious disease. A range of scenarios is presented both in the main text and in the appendices to cover these different possibilities. It is envisaged that further data on Delta B.1.617.2 will become available in the coming weeks to help reduce these critical uncertainties.

Summary of changes since May 2021

- The analysis in this report includes explicit consideration of the Delta B.1.617.2 variant of concern (VOC), also known as VOC-21APR-02, in addition to the wildtype variants circulating in early 2020 and the Alpha B.1.1.7 variant of concern (VOC-20DEC-01) which emerged in late 2020. The frequency of *S*-gene target failures up to 15th February 2021 is used to capture the spread of Alpha B.1.1.7 and genomic sequencing data up to 2nd June 2021 informs the proportion of the Delta B.1.617.2 variant. The model fits an introduction time for the Delta B.1.617.2 variant for each NHS England region, given specified levels of immune escape and relative transmissibility.
- We have updated our assumptions related to vaccine effectiveness against pre-existing and B.1.1.7 variants since the previous report. We now assume higher overall protection against mortality following the second dose of both AstraZeneca and Pfizer vaccines (see Table 1).
- We now include additional vaccine protection against onward transmission following breakthrough infections (see Table 1).
- Vaccine effectiveness assumptions against the Delta B.1.617.2 variant are calculated by scaling vaccine effectiveness assumptions against pre-existing and Alpha B.1.1.7 variants in Table 1. For this scaling, we use Public Health England (PHE) estimates on vaccine effectiveness against B.1.1.7 / S-gene negatives versus B.1.617.2 / S-gene positives split by vaccine product and vaccine dose (see Table 2).
- Roadmap Steps 1, 2 and 3 are modelled using historic Google Mobility data as recorded, rather than previous assumptions on behavioural changes.
- We have introduced an assumption of 20% peak to trough seasonality for central scenarios in this analysis.

Modelling limitations & uncertainties

- The extent of the threat that the Delta B.1.617.2 SARS-CoV-2 variant poses remains unclear. Evidence is still emerging on its inherent transmission advantage, the levels of protection provided by COVID-19 vaccines and natural immunity against different outcomes and on any potential increase in severity. We have based our scenarios related to Delta B.1.617.2 on the best available evidence, but this information may change as more data is collected.
- These results are dependent on as yet unverifiable assumptions regarding the impact of policy changes at roadmap Step 4 on individuals' behaviour. We are currently observing relatively high levels of mobility, which may be related to recent good weather, public holidays and schools being closed during the May/June 2021 half-term break. It is also unclear how predictive levels of mobility are on contact making behaviour that leads to transmission events, and in particular how this relationship might vary during different times of the year. It is also unclear that increases in transmission attributed to the Delta B.1617.2 SARS-CoV-2 variant apply uniformly to all types of contacts.
- It is unclear to what extent schools are contributing to transmission. We have assumed that the introduction of mass testing and mask wearing in schools in England from March 2021 resulted in an additional 30% reduction in transmission resulting from school related contacts. However, since the 17th of May 2021 face mask use is no longer required in secondary school classrooms, and it is unclear to what extent face mask wearing in secondary schools continues. We do not assume any increase in school related transmission since this policy change on the 17th of May.
- There is little evidence available related to the levels of cross protection that prior infection with pre-existing SARS-CoV-2 variants such as Alpha B.1.1.7 might provide against infection with Delta B.1.617.2. In our pessimistic scenario considering Delta B.1.617.2 with high levels of immune escape, we assume that prior infection with pre-existing or Alpha B.1.1.7 SARS-CoV-2 variants provides 90% protection against infection with Delta B.1.617.2.
- Levels of vaccine protection are assumed to be consistent across all age groups in the model. However, it is possible that vaccine protection differs across age groups.
- There is limited data regarding the effect that COVID-19 vaccines have on reducing onward transmission following breakthrough infections (when an individual with vaccine induced protection becomes infected). We rely on one study to parametrise our assumptions related to vaccine protection against onward transmission.
- In our modelling framework, only susceptible individuals can be immunised and provided with additional protection against SARS-CoV-2. We do not capture any additional vaccine protection provided to individuals who are either infected or recovered and then vaccinated.
- It is unclear how much seasonality affects SARS-CoV-2 transmission, both in relation to behavioural changes that influence transmission and in relation to the ability of the SARS-CoV-2 virus to persist and spread. For our central scenarios, we assume 20% peak to trough seasonality to capture these effects.

- There are a number of uncertainties related to the rollout of COVID-19 vaccines in England. Changes in the speed of vaccine rollout, the uptake of vaccines and policy changes such as vaccination of children will influence transmission dynamics. We do not consider the vaccination of children nor any additional booster vaccine doses in late 2021 which may provide additional protection against variants of concern such as Delta B.1.617.2.
- Our central scenario assumes that 15% of individuals with immunity conferred from prior infection with SARS-CoV-2 and from COVID-19 vaccination lose this protection within 6 months. There is limited evidence related to the timescales at which natural and vaccine induced immunity wanes, as well as any potential differences in rates of waning for natural and vaccine induced immunity. It is likely that protection against severe outcomes is longer lasting than protection against reinfection, but we do not model any additional protection against severe outcomes when an individual loses their immunity.
- While the model captures hospital admissions and bed occupancy well, it is currently overestimating COVID-19 deaths. There are a number of reasons why this may be the case. First, in-hospital mortality may have decreased as pressure on hospital services decreased following the January 2021 wave, and the model does not explicitly link mortality to hospital bed occupancy. Second, the model may be producing relatively more cases in older individuals, who are more likely to die from COVID-19, than have actually been observed, which could arise from the model underestimating transmission in schools. Third, the case fatality ratio may have decreased over time for reasons not related to hospital pressures, such as a frailty effect. It is also possible that part of the overestimation of deaths is because vaccines are more effective against mortality than we have assumed, but this does not account for the full difference between model-estimated and observed deaths, as the majority of model-estimated deaths are among individuals without vaccine protection. Trends in COVID-19 deaths should continue to be monitored in order to assess the extent to which this gap between model-estimated and observed deaths continues.

Methods & assumptions

Basic model assumptions

We use an age- and geographically-structured deterministic compartmental model of SARS-CoV-2 transmission. Geographic structure is by NHS England region and age groups are divided into 5-year age bands from 0–4 to 70–74 years with an additional age group comprising individuals aged 75 years and over. Further details of the model and how it has been fitted to data are given in Davies et al. 2020 (Lancet Inf Dis) and Davies et al. 2021 (Science). The model uses Google Community Mobility data to track mobility in various settings: workplaces, retail & recreation venues, transit stations, and grocery & pharmacy locations.

School openings and closings are accounted for in contacts among school-aged children, university-aged young adults and school/university staff. We assume that schools in England follow their traditional schedules (i.e. are closed during half-term periods and over summer holiday periods). However, to reflect the introduction of mass testing within educational facilities in the Spring of 2021, we have assumed an additional 30% reduction in transmission related to educational settings following the reopening of schools on 8th March 2021. This reduction in transmission is reflected in the model with a 30% reduction in school-related contacts. The relationship between mobility data and social contact rates is derived from the historical relationship between Google Community Mobility indices and social contact rates as measured by the CoMix study in 2020 (Davies et al. 2020, Lancet Inf Dis).

The model tracks three co-circulating SARS-CoV-2 variants: the Delta B.1.617.2, Alpha B.1.1.7 and pre-existing variants. The model structure has been extended from a similar two-variant model structure (Davies et al. 2021, Science) to consider three variants explicitly. The model is fitted to PCR prevalence as measured by the Office for National Statistics (ONS); seroprevalence as measured by REACT-2, UK Biobank, and the ONS; daily incidence of COVID-19 deaths, hospital admissions, hospital bed occupancy, and ICU admissions as provided by PHE and the NHS (Davies et al. 2020 Lancet Inf Dis); the frequency of *S* gene target failure up to 15th February 2021 to capture the spread of Alpha B.1.1.7 (Davies et al. 2021, Science); and the frequency of lineage B.1.617.2 in sequenced Pillar 2 cases up to 2nd June 2021 to capture the spread of Delta B.1.617.2.

We use PHE data recording the number of first and second vaccine doses delivered by age, geography and vaccine product from the 8th of December 2020 to the 1st of June 2021 to inform the fraction of vaccinated individuals in each age group, NHS England region and by vaccine type and dose over time. Vaccine schedules are generated by combining vaccines already delivered with future schedules generated based on a number of assumptions (see 'Vaccine assumptions') and ensuring that all first doses are followed up with equivalent second doses at most 8 weeks later for individuals aged 50 and above and 11 weeks later for individuals under 50 (see also 'Vaccine schedules' for a full description).

The age-specific probability of clinical symptoms is adopted from Davies et al (Nature Medicine, 2020) using data from 6 countries. The age-specific probability of hospital admission, ICU admission, and death given infection are fitted to data from England, with the relative rates by age group based on data collected by a large meta-analysis of the COVID-19 infection fatality rate (Levin et al., Eur J Epi 2020) and based on data collected by ISARIC (the CO-CIN study) for England (Davies et al., Lancet Inf Dis 2020). Each of these age-specific probabilities of severe outcomes is allowed to vary over the course of the epidemic in England and vary between pre-existing variants and B.1.1.7. For the third Delta variant B.1.617.2, the probability of severe outcomes is assumed to be the same as for B.1.1.7, except for our "high" immune escape scenario, in which we assume that the probability of hospitalisation and death is twice as high for Delta as for Alpha among unvaccinated individuals, in keeping with preliminary estimates from Public Health England and Public Health Scotland in PHE Technical Briefing 14.

Roadmap assumptions

We base our assumptions on how social contact rates might be expected to change at Step 4 of the Roadmap and in response to other policy changes considered by referring to historical Google Community Mobility data and making assumptions about future mobility changes (Figures 1 and 2). We consider “low”, “medium”, and “high” scenarios for future changes in mobility, with various assumptions made across four mobility indices (Grocery and pharmacy, Retail and recreation, Transit stations and Workplaces).

Grocery and pharmacy mobility is currently at or above baseline levels, so we assume this metric reaches 1.05 times baseline levels for “low”, “medium” and “high” scenarios implementing roadmap Step 4. For retail and recreation, our “low” scenario assumes mobility will return to the highest level recorded since the pandemic began (August 2020) following roadmap Step 4. We assume that retail and recreation mobility will reach 0.95 for the “medium” scenario and 1.05 for the “high” scenario following roadmap Step 4, assuming that pre-pandemic baseline levels are exceeded due to good weather and high spirits.

We do not expect either Transit or Workplace mobility to return to pre-pandemic baseline levels. Following roadmap Step 4, our “low” scenario assumes that transit-related mobility reaches similar levels to late September 2020. The “medium” and “high” scenarios assume transit-related mobility reaches 80 and 90% of baseline levels respectively. Workplace mobility levels are already at their highest point since pre-pandemic baseline levels were recorded in early 2020. Our “low” scenario assumes a slight increase of workplace mobility to 80% of baseline, whilst the “medium” and “high” scenarios assume workplace-related mobility reaches 85% and 90% of baseline levels, respectively.

Although we assume future mobility changes for “low”, “medium” and “high” scenarios, we assume that an additional level of control is maintained via contact tracing and social distancing (i.e. through physical distancing, mask wearing and hand hygiene), equivalent to a reduction in R of 30-40% in total, as fitted for each NHS England region during the summer of 2020. In addition to considering policy options for implementing roadmap Step 4 at different times, we include scenarios implementing a circuit breaker lockdown, splitting roadmap Step 4 into two separate policy changes (roadmap Steps 3.5 and 4) and reversing mobility to roadmap Step 2. For the circuit breaker lockdown scenario, we assume that mobility returns to levels seen during roadmap Step 1 from 21st June, before returning to roadmap Step 4 levels when schools close towards the end of July 2021. For the policy option splitting roadmap Step 4 into roadmap Steps 3.5 and 4, we assume that approximately half of the assumed Step 4 increase happens at Step 3.5 on the 21st of June, with the remaining half happening from 26th of July 2021. For the policy reversing mobility to levels recorded during roadmap Step 2, we only consider a “medium” scenario representing approximate levels of mobility between the implementation of roadmap Steps 2 and 3.

Vaccine schedules

Vaccine schedules are generated by combining PHE data on vaccines delivered up to 1st June 2021 in England with future schedules based on a number of assumptions related to vaccine effectiveness, vaccine supply and vaccine uptake (see 'Vaccine assumptions' section). The number of future doses supplied for each day in the schedule are distributed into the seven NHS England regions according to the population size of each region. The number of vaccine doses per region per day are initially allocated to age groups in the model according to the existing age distribution of all doses delivered. Beginning with the oldest age group, the allocated number of doses per day, per region and per age group are divided into specified proportions of vaccine products relevant to each age group (see 'Vaccine mix' section). Second doses are delivered at most 8 weeks later for individuals aged 50 and above and 11 weeks later for individuals under 50. Once all required second doses have been allocated, leftover doses for that day, region and age group are delivered as first doses up to the relevant age-specific uptake limit (set at 80% for individuals under 40 and as per vaccines delivered to date in 40+ year olds). If doses are remaining after second and first doses have been delivered, these leftover doses are carried over to either the next age group down, the next NHS England region, the next day, or are not allocated in the schedule and are recorded as leftover doses.

Vaccine assumptions

Vaccine effectiveness

We base our vaccine effectiveness assumptions on the latest available evidence. These may be subject to change in future work, as new evidence emerges. We currently treat individuals who have been and will be vaccinated with Moderna vaccines the same as individuals receiving Pfizer vaccines. We model individuals who have received different vaccine products (e.g. AstraZeneca and Pfizer/Moderna) and one or two vaccine doses separately, assuming separate efficacy estimates for each category. We model vaccine protection against five separate outcomes: infection, disease (i.e. symptomatic infection), hospitalisation, mortality and onward transmission following a breakthrough infection (i.e. when a vaccinated and protected individual becomes infected). We assume the same vaccine effectiveness for the first two SARS-CoV-2 variants in the model (pre-B.1.1.7 and Alpha B.1.1.7), shown in Table 1. Table S1 in the Supplementary Material section relates our assumptions on vaccine effectiveness against pre-B.1.1.7 and Alpha B.1.1.7 to those in PHE's week 22 COVID-19 vaccine surveillance report, with justification given for any differences between our assumptions and PHE's. Table S2 in the Supplementary Material section shows a summary of the relevant evidence we have used to guide our assumptions on vaccine effectiveness against B.1.1.7 and pre-existing variants of SARS-CoV-2.

A number of different scenarios are considered for vaccine effectiveness against the third SARS-CoV-2 variant in the model, Delta B.1.617.2, shown in Table 3. To arrive at estimates for vaccine protection against the Delta B.1.617.2 variant, we rely on PHE data calculating vaccine effectiveness against symptomatic infection for *S*-gene target negatives or B.1.1.7 and *S*-gene

target positives or B.1.617.2 (see reference in Table 2). We calculate the relative reduction in vaccine effect (against symptomatic infection) between B.1.1.7 or *S*-gene target negatives and B.1.617.2 or *S*-gene positives for each dose of each vaccine product. These estimates are then used to downgrade our assumed vaccine protection against pre- and B.1.1.7 variants shown in Table 1 to arrive at central, pessimistic and optimistic scenarios for vaccine effect against B.1.617.2 shown in Table 3. For vaccine protection against infection, disease and onward transmission, our optimistic, central and pessimistic scenarios assume 80%, 100% and 120% of the relative reduction in vaccine effect against symptomatic infection between Alpha B.1.1.7 and Delta B.1.617.2 for each vaccine product and dose calculated in Table 2. For vaccine protection against hospitalisation and mortality, our optimistic, central and pessimistic scenarios assume 0%, 50% and 100% of the relative reduction in vaccine effect against symptomatic infection between Alpha B.1.1.7 and Delta B.1.617.2 for each vaccine product and dose calculated in Table 2.

Table 1 - Assumptions for vaccine effectiveness against all outcomes (pre- and B.1.1.7)

Outcome	**Vaccine effectiveness**			
	*Pfizer-BioNTech**		*Oxford-AstraZeneca*	
	1 dose	2 doses	1 dose	2 doses
Infection	**0.7**	**0.85**	**0.67**	**0.68**
Disease	**0.7**	**0.89**	**0.67**	**0.78**
Hospitalisation	**0.845**	**0.9**	**0.845**	**0.9**
Mortality	**0.845**	**0.95**	**0.845**	**0.95**
Onward transmission	**0.49**	**0.6**	**0.38**	**0.5**
Delay to efficacy	28 days	14 days	28 days	14 days
*We assume that the Moderna mRNA-1273 vaccine confers the same levels of protection as the Pfizer-BioNTech vaccine				

Table 2 - Vaccine effectiveness for Pfizer BioNTech BNT162b2 and Oxford AstraZeneca ChAdOx1 vaccines against symptomatic infection with *S*-gene target negatives (B.1.1.7) and *S*-gene target positives (B.1.617.2), see Table 2 of Lopez Bernal et al.

		Adjusted vaccine effectiveness, B.1.1.7 or S-gene target negative	Adjusted vaccine effectiveness, B.1.617.2 or S-gene target positive	Relative reduction in vaccine effect
Pfizer BioNTech BNT162b2	Dose 1	49.2% (42.6% to 55.0%)	33.2% (8.3% to 51.4%)	**32.5%**
	Dose 2	93.4% (90.4% to 95.5%)	87.9% (78.2% to 93.2%)	**5.9%**
Oxford AstraZeneca ChAdOx1	Dose 1	51.4% (47.3% to 55.2%)	32.9% (19.3% to 44.3%)	**36.0%**
	Dose 2	66.1% (54.0% to 75.0%)	59.8% (28.9% to 77.3%)	**9.5%**

Table 3 - Assumptions for vaccine effectiveness against all outcomes (Delta / B.1.617.2)

Outcome	Vaccine effectiveness			
	*Pfizer-BioNTech**		*Oxford-AstraZeneca*	
	1 dose	2 doses	1 dose	2 doses
Infection^	**0.4725** (0.427, 0.518)	**0.7999** (0.7898, 0.8098)	**0.4288** (0.3806, 0.4770)	**0.6154** (0.6025, 0.6283)
Disease^	**0.4725** (0.427, 0.518)	**0.8375** (0.8270, 0.8480)	**0.4288** (0.3806, 0.4770)	**0.7059** (0.6911, 0.7207)
Hospitalisation^	**0.7077** (0.5704, 0.845)	**0.8735** (0.8469, 0.9)	**0.6929** (0.5408, 0.845)	**0.8573** (0.8145, 0.9)
Mortality^	**0.7077** (0.5704, 0.845)	**0.9220** (0.8940, 0.95)	**0.6929** (0.5408, 0.845)	**0.9049** (0.8598, 0.95)
Onward transmission^	**0.3308** (0.2989, 0.3626)	**0.5646** (0.5575, 0.5717)	**0.2432** (0.2158, 0.2706)	**0.4525** (0.443, 0.462)
Delay to efficacy	28 days	14 days	28 days	14 days

*We assume that the Moderna mRNA-1273 vaccine confers the same levels of protection as the Pfizer-BioNTech vaccine

^Central assumptions are shown in bold, with pessimistic and optimistic assumptions shown below in brackets. For central assumptions, we reduce vaccine effectiveness against infection, disease and onward transmission by the appropriate relative reduction in vaccine effect shown in Table 2. We reduce vaccine effectiveness against hospitalisation and mortality by half of the same relative reduction. For pessimistic assumptions, we reduce vaccine effectiveness against infection, disease and onward transmission by 1.2 times the relative reduction in Table 2 and vaccine effectiveness against hospitalisation and mortality by the relevant relative reduction in Table 2. For optimistic assumptions, we reduce vaccine effectiveness against infection, disease and onward transmission by 0.8 times the appropriate relative reduction in vaccine effect shown in Table 2, but assume protection against hospitalisation and mortality remains at the same levels as for B.1.1.7, shown in Table 1.

Vaccine uptake

Vaccine uptake is modelled as per vaccine uptake to date (using data up to 1st June 2021) for individuals aged 40 years and above, and is assumed to be 80% for individuals under 40 years old.

Vaccine rollout

Future vaccine rollout follows a Cabinet Office agreed scenario with an average of 2.15 million doses per week in England until the 25th July 2021 and then 2 million doses per week thereafter. We assume that future second doses are delivered at most 8 weeks following equivalent first doses for individuals aged 50 and over, and assume a maximum of an 11 week dosing gap for individuals under 50 years old.

Vaccine mix

The following proportions of each vaccine product are used in the vaccine schedules projected forwards:

- 75% Pfizer and 25% Moderna for <40 year olds
- 60% AstraZeneca, 30% Pfizer and 10% Moderna for 40-49 year olds
- Actual mix of AstraZeneca, Pfizer and Moderna first doses already delivered to 50+ year olds (using data on vaccines delivered up to 1st June 2021)

Waning immunity

Our central scenarios consider waning protection from SARS-CoV-2 infection developed from natural infection and vaccination. For all scenarios with waning immunity, we assume that rates of waning are identical for all three virus variants considered in the model. We assume that both natural and vaccine induced immunity wane at identical rates (Table 4). We further assume that waning of immunity against different endpoints (infection, disease, hospitalisation, deaths and onward transmission) occurs at the same rate. We also assume that rates of waning are identical across all age groups. Many of these assumptions are likely to not hold in practice, but there is currently an absence of data on differential rates of immunity against different outcomes, from different routes (vaccines and naturally occuring) and for different population groups. For details including relevant evidence related to waning immunity, please refer to Table S4 in our previous report.

Table 4 - Waning immunity scenarios

Description	Assumed values (**waning**)	Assumed values (**no waning**)
Waning of natural immunity	log(0.85)/-182.5, corresponding to 85% protection after 365 / 2 days = 6 months	0
Waning of vaccine induced immunity (second dose to susceptible / naive)	log(0.85)/-182.5, corresponding to 85% protection after 365 / 2 days = 6 months	0
Waning of vaccine induced immunity (first dose to susceptible / naive)	0	0
Waning of vaccine induced immunity (second dose to first dose)	0	0

Variant of concern Delta B.1.617.2

Our analysis considers a third SARS-CoV-2 variant which has been parametrised in relation to the Delta / B.1.617.2 variant of concern, also referred to as VOC-21APR-02. We use sequenced Pillar 2 cases to inform the proportion of the Delta B.1.617.2 variant circulating versus the proportion of pre-B.1.1.7 and B.1.1.7. There is uncertainty surrounding the relative transmissibility of the B.1.617.2 variant in comparison to B.1.1.7 and other pre-existing variants. We consider three scenarios for increased transmissibility of B.1.617.2 compared to B.1.1.7: 30%, 50% and 70% increases. We also consider optimistic, central and pessimistic scenarios for immune escape properties of the Delta variant, comprising different levels of cross protection conferred from prior infection with pre-existing SARS-CoV-2 variants and different assumptions related to the effectiveness of COVID-19 vaccines against the Delta B.1.617.2 variant. These scenarios and relevant values are summarised in Tables 3 and 5. For each combination of assumed increased transmissibility and immune escape, and for each NHS England region, we allow the model to fit the optimal introduction time of the Delta B.1.617.2 variant in order to maximise the likelihood of the model fit to both the proportion of Delta over time and to disease outcomes (hospitalisations, ICU admissions, and deaths). Accordingly, the model fits shown are a compromise between fitting the observed spread of the Delta variant and observed health outcomes.

Table 5 - Overview of scenarios considered for immune escape of the Delta B.1.617.2 variant of concern VOC-21APR-02

		Optimistic	Central	Pessimistic
	Cross protection	100%	100%	90%
Outcome	**Vaccine**	**Vaccine protection**		
Infection	Pfizer dose 1	0.518	0.4725	0.427
	Pfizer dose 2	0.8098	0.7999	0.7898
	AZ dose 1	0.4770	0.4288	0.3806
	AZ dose 2	0.6283	0.6154	0.6025
Disease	Pfizer dose 1	0.518	0.4725	0.427
	Pfizer dose 2	0.8480	0.8375	0.8270
	AZ dose 1	0.4770	0.4288	0.3806
	AZ dose 2	0.7207	0.7059	0.6911
Hospitalisation	Pfizer dose 1	0.845	0.7077	0.5704
	Pfizer dose 2	0.9	0.8735	0.8469
	AZ dose 1	0.845	0.6929	0.5408
	AZ dose 2	0.9	0.8573	0.8145
Mortality	Pfizer dose 1	0.845	0.7077	0.5704
	Pfizer dose 2	0.95	0.9220	0.8940
	AZ dose 1	0.845	0.6929	0.5408
	AZ dose 2	0.95	0.9049	0.8598
Onward transmission	Pfizer dose 1	0.3626	0.3308	0.2989
	Pfizer dose 2	0.5717	0.5646	0.5575
	AZ dose 1	0.2706	0.2432	0.2158
	AZ dose 2	0.462	0.4525	0.443

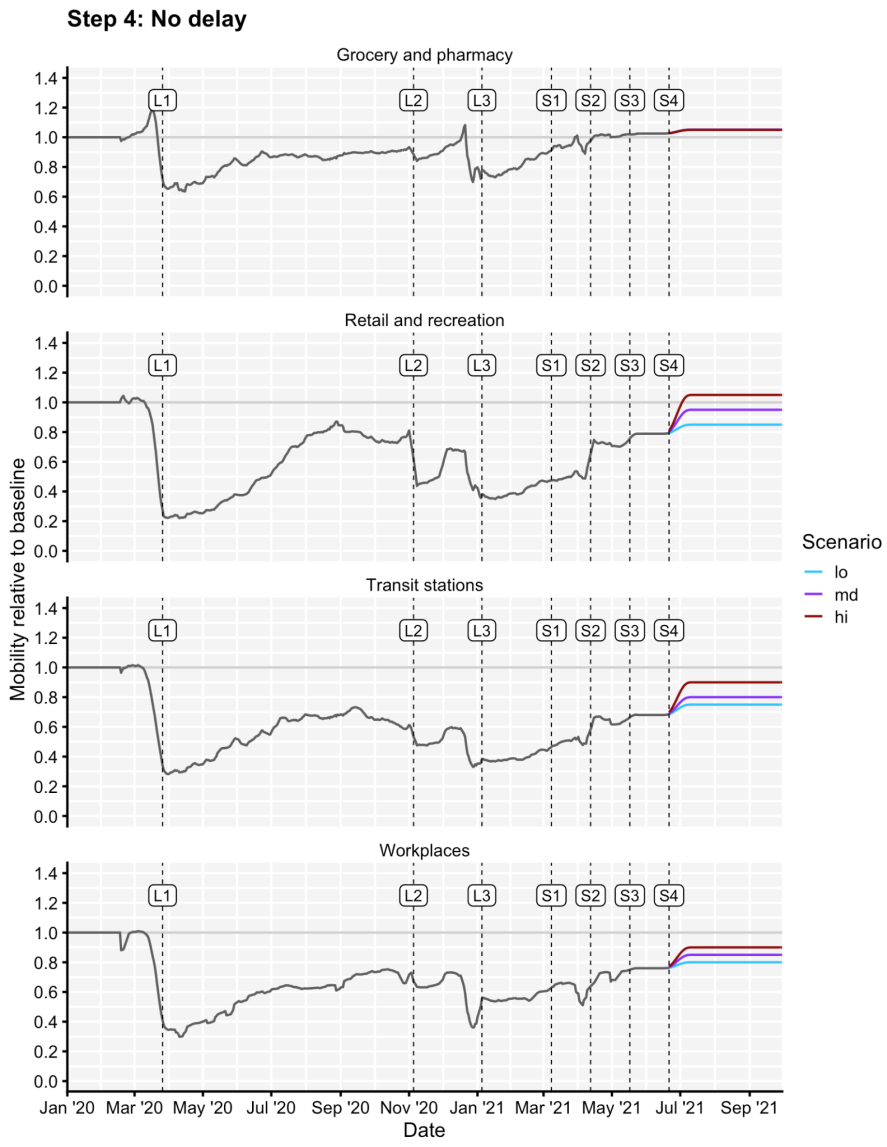

Figure 1 - Historic Google Community Mobility data (grey) and assumed future mobility in England for low (blue), medium (purple) and high (red) scenarios used for model projections implementing roadmap Step 4 as planned on 21st June 2021. Mobility indices are measured relative to baseline mobility levels recorded during early 2020, prior to the COVID-19 pandemic. The beginning of each lockdown and each roadmap Step is marked with a vertical dashed line.

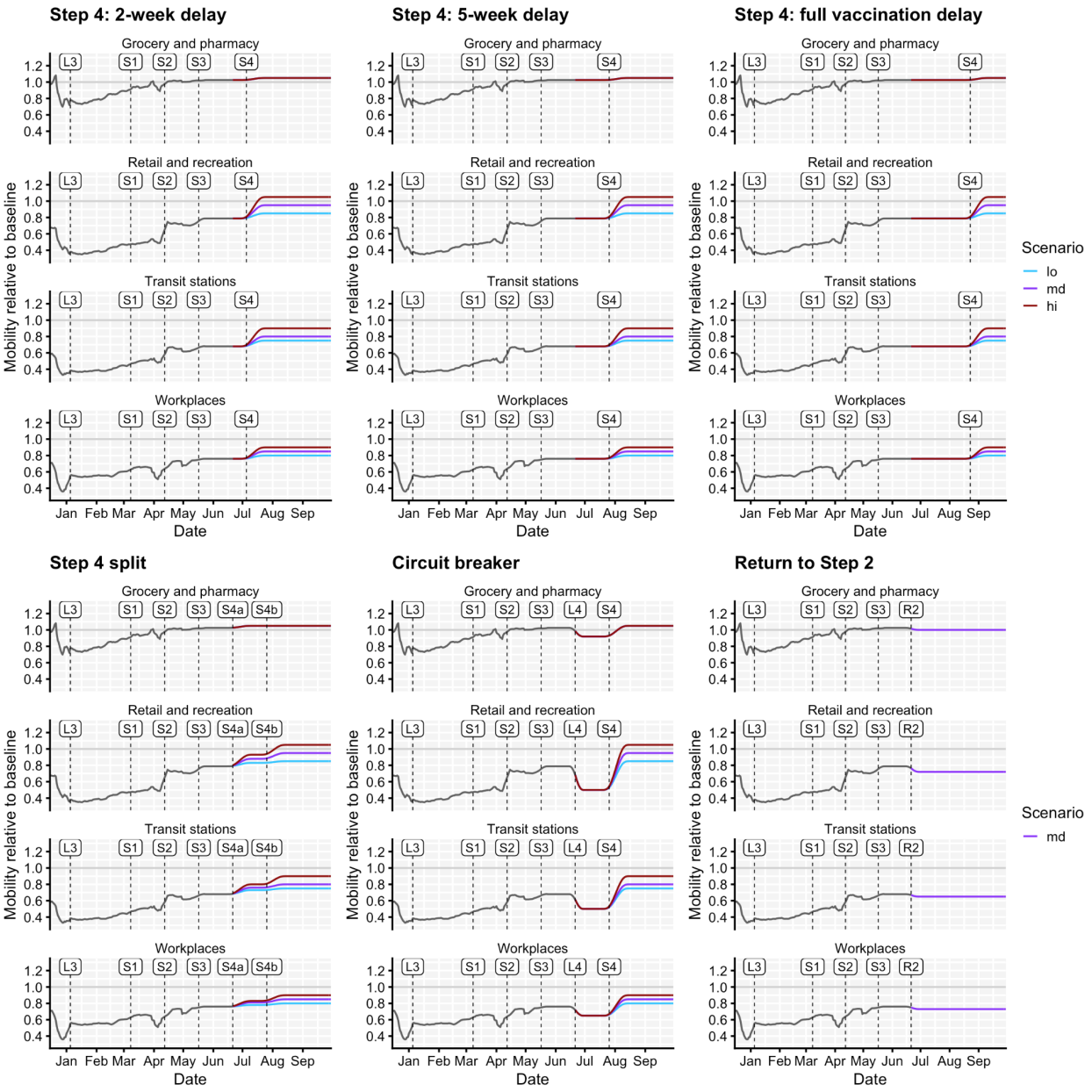

Figure 2 - Google Community Mobility data (grey) between December 2020 and June 2021 and assumed future mobility in England for low (blue), medium (purple) and high (red) scenarios used for model projections implementing various policy changes instead of roadmap Step 4 as planned on 21st June 2021. From left to right and top to bottom, we show assumed mobility scenarios for: a 2-week delay to Step 4, a 5-week delay to Step 4, a delay to Step 4 until all adults up to assumed uptake limits are projected to have received their second vaccine dose, splitting roadmap Step 4 into two policy changes (Step 4a on the 21st of June and 4b on the 26th of July 2021), a circuit breaker lockdown between 21st June and 26th of July 2021 and a return to Step 2 levels of mobility from the 21st of June 2021 onwards. The beginning of each lockdown and each roadmap Step is marked with a vertical dashed line.

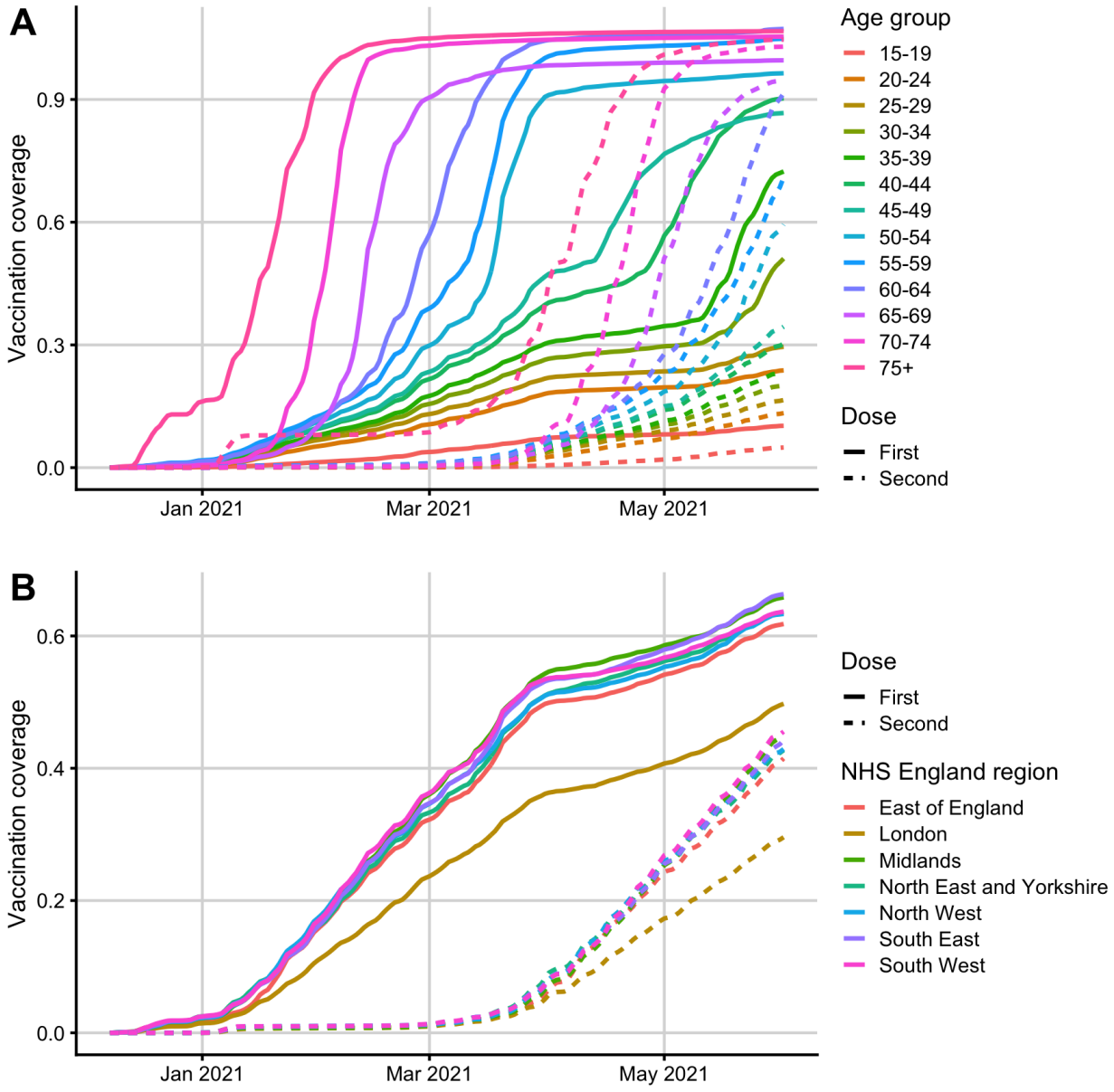

Figure 3 - COVID-19 vaccine coverage in England between 8th December 2020 and 1st June 2021, by age group (A) and NHS England region (B), using PHE data from 2nd June 2021. Solid lines show first dose coverage and dashed lines show second dose coverage, with coverage being calculated across all three vaccine products (Pfizer, AstraZeneca and Moderna) currently being administered in England. Low vaccine coverage for London is partly due to the lower average age of inhabitants of London, and may be partly due to an overestimation of the number of people living in London, as the population size estimates used date to mid-2018.

Results & discussion

The projected effect of implementing roadmap Step 4 as planned on the 21st of June 2021 is shown in Figures 4-8, with consideration given to various combinations of immune escape and increased transmissibility of the Delta B.1.617.2 VOC. We also include a sensitivity analysis with and without waning of natural and vaccine-induced immunity (Figures 5 and 6). We contrast four main scenarios for the Delta variant:

I. Low immune escape, with an additional 50% increase in transmissibility;
II. Medium immune escape, with an additional 50% increase in transmissibility;
III. High immune escape, with an additional 30% increase in transmissibility;
IV. Medium immune escape, with an additional 70% increase in transmissibility.

Scenarios I-III were chosen to explore the range of modelled assumptions for immune escape (low, medium, or high); we paired each with the transmissibility increase (30%, 50%, or 70%) which maximised model likelihood across both (a) the growth of the Delta variant relative to other variants and (b) the observed burden (hospitalisations and deaths) in England. This resulted in “compromise” scenarios in which the growth of the Delta variant was not accurately captured (Figures 4–7), but which were better fitting to observed COVID-19 burden. We also included Scenario IV, with medium immune escape and a 70% transmissibility increase, as this better captured the relative growth of Delta (Figure 8).

In the supplementary material, we include results for all combinations of low/medium/high immune escape and 30% / 50% / 70% transmissibility increase (Figures S2–S10).

In the scenario with low / optimistic immune escape and 50% increased transmissibility of the Delta B.1.617.2 VOC (Scenario I), the continued easing of restrictions on the 21st of June is projected to lead to a significant third wave of transmission occurring during the late summer months of 2021, with “high” mobility assumptions projected to lead to hospital admissions and hospital beds occupied at or above peak levels recorded during the previous wave in January 2021 (Figure 4). An increase in the extent of immune escape of the Delta B.1.617.2 variant (Scenario II) results in similar dynamics but with higher peaks in hospital admissions, bed occupancy and deaths (Figure 5).

A scenario with high / pessimistic immune escape, even with the most cautious assumption of a 30% increase in relative transmissibility of Delta B.1.617.2 (Scenario III), leads to very significant waves of transmission, particularly for the “high” mobility scenario (Figure 7). For this scenario, the “medium” and “low” mobility scenarios are projected to lead to less extreme but more protracted waves of transmission, lasting into the winter of 2021. However, the model with high immune escape but only 30% increased transmissibility is not able to fit a rapid enough increase in the frequency of the VOC to Delta B.1.617.2 sequencing data.

A scenario assuming Delta B.1.617.2 has 70% increased transmissibility relative to Alpha B.1.1.7 and medium / central levels of immune escape (Scenario IV) is able to achieve a better

fit to sequencing data (Figure 8). This scenario is projected to lead to a large wave of transmission over the summer months, with both the “medium” and “high” mobility scenarios exceeding peak levels of hospital admissions, bed occupancy and deaths recorded in January 2021. Tables 6 and 7 summarise the projected total number of deaths, peak number of deaths, total hospitalisations and peak number of hospital beds occupied for the four aforementioned scenarios with waning immunity, across all seven policy options considered in relation to roadmap Step 4, between 21st June and 31st October 2021. Tables S3 and S4 in the Supplementary Material show the same metrics calculated until the end of December 2021.

As a sensitivity analysis, we explored a model fit without waning immunity (Scenario IIb). Projections without waning of natural or vaccine-induced immunity result in a lower peak occurring slightly later during the summer of 2021 (Figure 6).

Figures 9-12 show the projected effects of implementing different policy options in relation to roadmap Step 4, for the four scenarios (I-IV) which most closely fitted the observed data. Delays to roadmap Step 4 are projected to flatten the third wave and reduce peak hospitalisations and deaths, whilst circuit breaker lockdowns may result in resurgences later in 2021. Full results for all 9 scenarios are provided in the Supplementary Material (Figs S2-S10), including model fits to hospital admissions, hospital bed occupancy and deaths (Fig S1). Plots by NHS England region for the control scenario of Step 4 with no delay, for scenarios I-IV, are provided in Figs. S11-S14.

I. Low / optimistic immune escape, 50% increased transmissibility

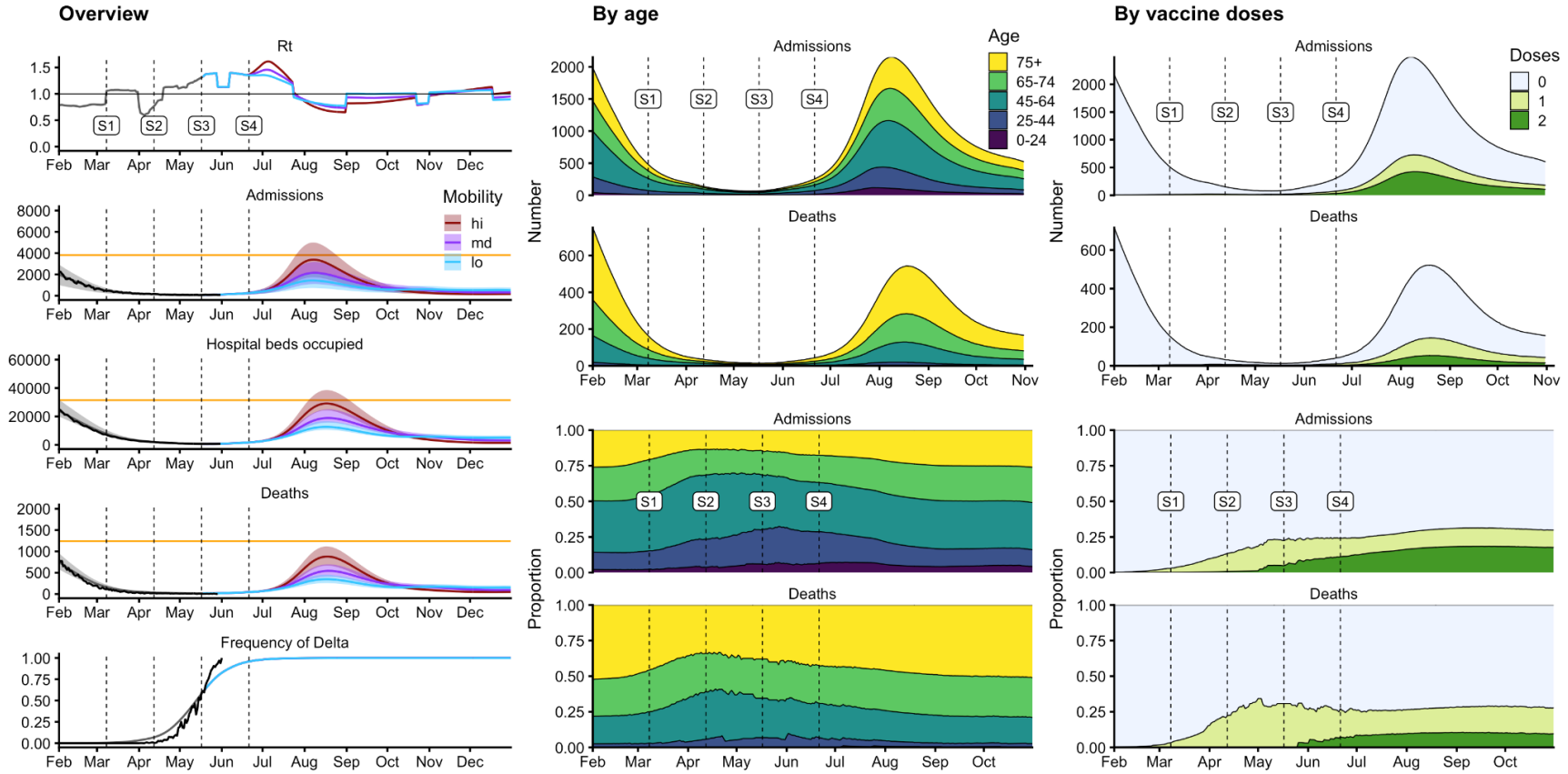

Figure 4 - Model projections implementing roadmap Step 4 on 21st June 2021, Delta B.1.617.2 scenario with low / optimistic immune escape (Table 5) and 50% increased transmissibility relative to the Alpha B.1.1.7 variant, with waning of natural and vaccine-induced immunity. The Overview panel shows model projections of the effective reproduction number (Rt), hospital admissions, the number of hospital beds occupied, the daily number of deaths and frequency of the Delta B.1.617.2 variant over time for England overall. The beginning of each roadmap Step is marked with a vertical dashed line; orange horizontal lines mark peak admissions, bed occupancy, and deaths in England during the second wave (January 2021). Data (black) and model fits (grey) are shown up to the date of the latest available data. Low (blue), medium (purple) and high (red) mobility scenarios are used to project forwards from June to December 2021. The “By age” and “By vaccine doses” panels show model projections for the medium (central) mobility scenario only, with the number and proportion of hospital admissions and deaths split by age group and vaccine status.

II. Medium / central immune escape, 50% increased transmissibility

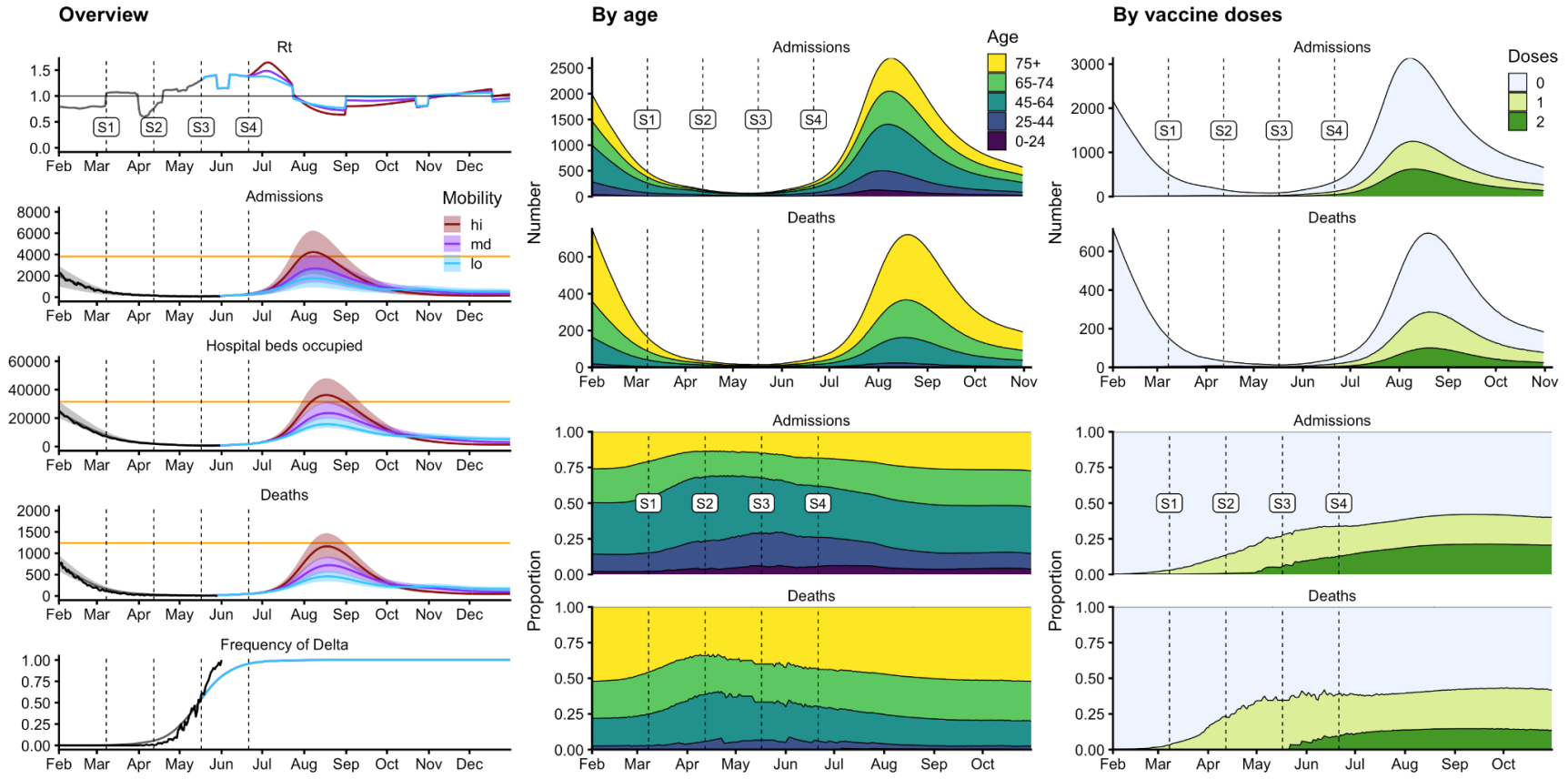

Figure 5 - Model projections implementing roadmap Step 4 on 21st June 2021, Delta B.1.617.2 scenario with medium / central immune escape (Table 5) and 50% increased transmissibility relative to the Alpha B.1.1.7 variant, with waning of natural and vaccine-induced immunity. The Overview panel shows model projections of the effective reproduction number (Rt), hospital admissions, the number of hospital beds occupied, the daily number of deaths and frequency of the Delta B.1.617.2 variant over time for England overall. The beginning of each roadmap Step is marked with a vertical dashed line; orange horizontal lines mark peak admissions, bed occupancy, and deaths in England during the second wave (January 2021). Data (black) and model fits (grey) are shown up to the date of the latest available data. Low (blue), medium (purple) and high (red) mobility scenarios are used to project forwards from June to December 2021. The “By age” and “By vaccine doses” panels show model projections for the medium (central) mobility scenario only, with the number and proportion of hospital admissions and deaths split by age group and vaccine status.

IIb. Sensitivity with no waning: Medium / central immune escape, 50% increased transmissibility

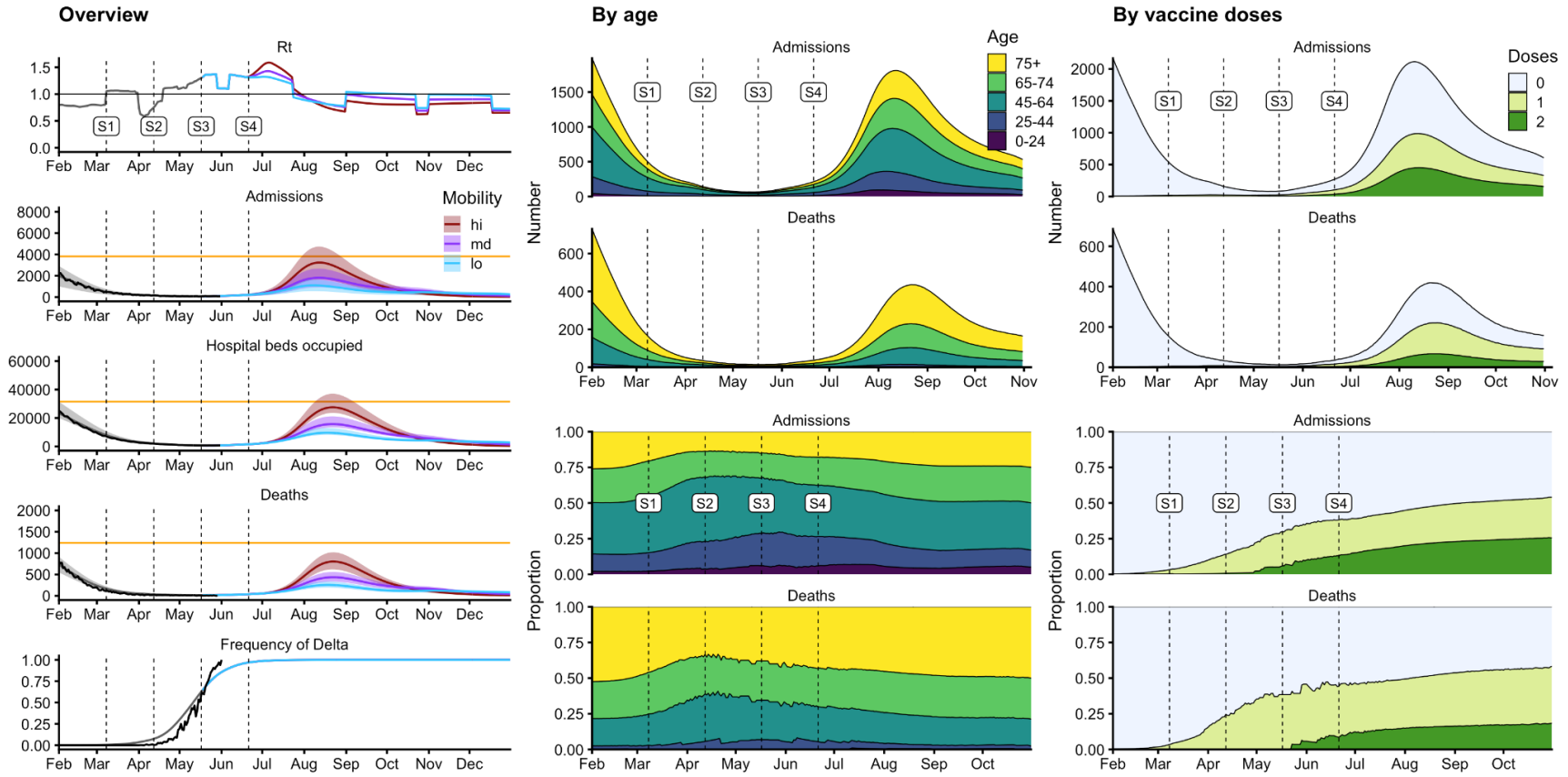

Figure 6 - Model projections implementing roadmap Step 4 on 21st June 2021, Delta B.1.617.2 scenario with medium / central immune escape (Table 5) and 50% increased transmissibility relative to the Alpha B.1.1.7 variant, with no waning of natural or vaccine-induced immunity. The Overview panel shows model projections of the effective reproduction number (Rt), hospital admissions, the number of hospital beds occupied, the daily number of deaths and frequency of the Delta B.1.617.2 variant over time for England overall. The beginning of each roadmap Step is marked with a vertical dashed line; orange horizontal lines mark peak admissions, bed occupancy, and deaths in England during the second wave (January 2021). Data (black) and model fits (grey) are shown up to the date of the latest available data. Low (blue), medium (purple) and high (red) mobility scenarios are used to project forwards from June to December 2021. The “By age” and “By vaccine doses” panels show model projections for the medium (central) mobility scenario only, with the number and proportion of hospital admissions and deaths split by age group and vaccine status.

III. High / pessimistic immune escape, 30% increased transmissibility

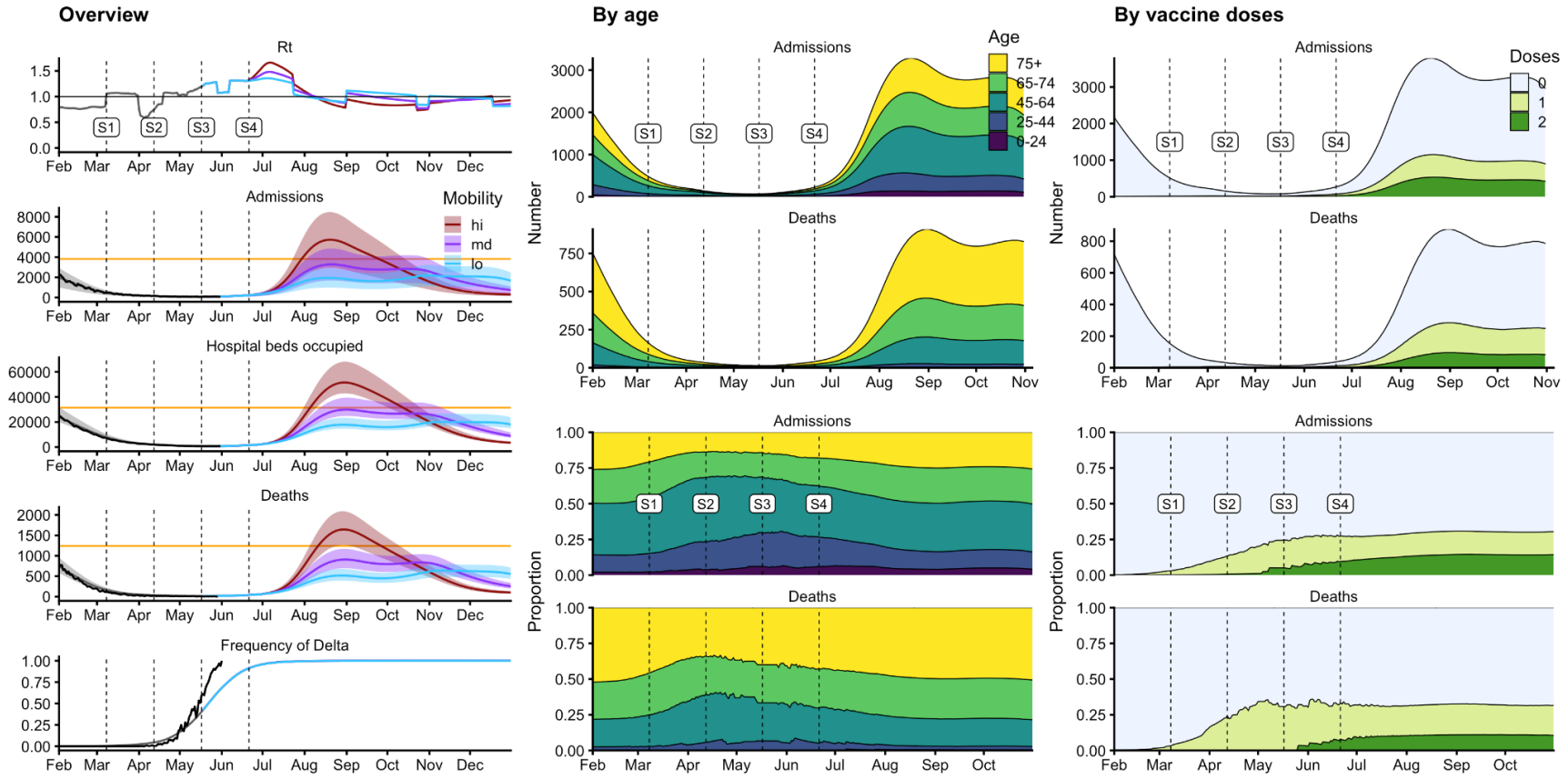

Figure 7 - Model projections implementing roadmap Step 4 as planned on 21st June 2021, Delta B.1.617.2 scenario with high / pessimistic immune escape (Table 5) and 30% increased transmissibility relative to the Alpha B.1.1.7 variant, with waning of natural and vaccine-induced immunity. The Overview panel shows model projections of the effective reproduction number (Rt), hospital admissions, the number of hospital beds occupied, the daily number of deaths and frequency of the Delta B.1.617.2 variant over time for England overall. The beginning of each roadmap Step is marked with a vertical dashed line; orange horizontal lines mark peak admissions, bed occupancy, and deaths in England during the second wave (January 2021). Data (black) and model fits (grey) are shown up to the date of the latest available data. Low (blue), medium (purple) and high (red) mobility scenarios are used to project forwards from June to December 2021. The “By age” and “By vaccine doses” panels show model projections for the medium (central) mobility scenario only, with the number and proportion of hospital admissions and deaths split by age group and vaccine status.

IV. Medium / central immune escape, 70% increased transmissibility

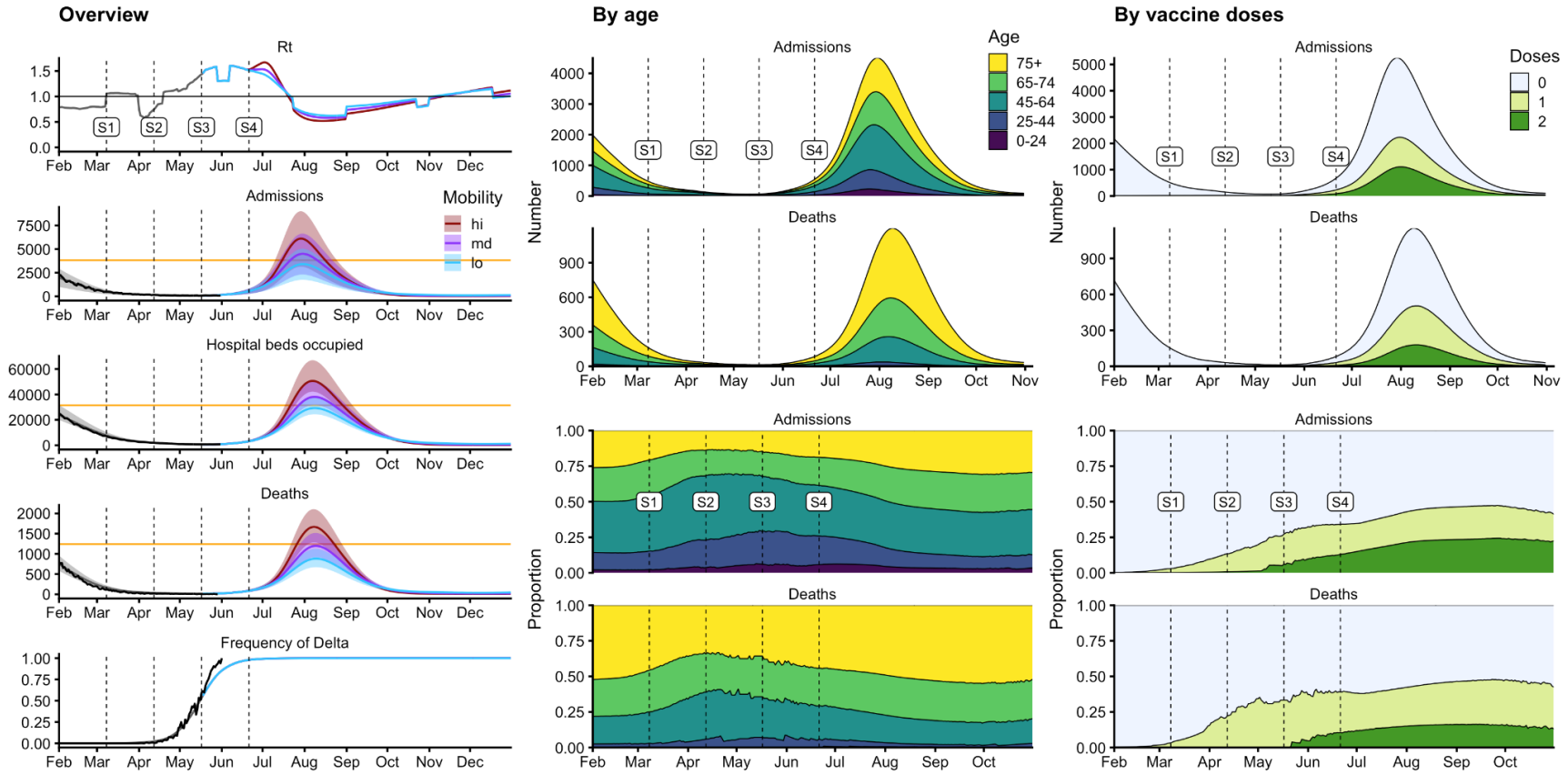

Figure 8 - Model projections implementing roadmap Step 4 as planned on 21st June 2021, Delta B.1.617.2 scenario with medium / central immune escape (Table 5) and 70% increased transmissibility relative to the Alpha B.1.1.7 variant, with waning of natural and vaccine-induced immunity. The Overview panel shows model projections of the effective reproduction number (Rt), hospital admissions, the number of hospital beds occupied, the daily number of deaths and frequency of the Delta B.1.617.2 variant over time for England overall. The beginning of each roadmap Step is marked with a vertical dashed line; orange horizontal lines mark peak admissions, bed occupancy, and deaths in England during the second wave (January 2021). Data (black) and model fits (grey) are shown up to the date of the latest available data. Low (blue), medium (purple) and high (red) mobility scenarios are used to project forwards from June to December 2021. The “By age” and “By vaccine doses” panels show model projections for the medium (central) mobility scenario only, with the number and proportion of hospital admissions and deaths split by age group and vaccine status.

Table 6 - Summary of projections for total COVID-19 deaths, peak daily COVID-19 deaths, total COVID-19 hospitalisations, and peak hospital bed occupancy for England, over the time period 21st June – 31st October 2021, assuming the Delta B.1.617.2 variant has a 50% increase in transmissibility relative to the Alpha B.1.1.7 variant, and with waning immunity. Medium mobility assumptions are shown, with low and high mobility assumptions shown below in brackets where relevant.

I. Low / optimistic immune escape

Indicator	Step 4, no delay (21st June)	Step 4, two week delay	Step 4, five week delay	Step 4, 2 doses for all adults	Step 4, split	Circuit breaker	Return to Step 2
Total deaths	38,400 (27,200-52,200)	37,400 (26,200-52,200)	33,200 (23,700-48,900)	23,700 (19,900-31,800)	36,100 (26,000-49,400)	25,900 (15,200-45,300)	12,500
Peak deaths	500 (300-900)	500 (300-800)	400 (200-700)	400 (200-800)	400 (300-600)	700 (400-1,000)	200
Total hospitalisations	150,000 (110,200-196,300)	147,400 (107,000-196,400)	134,900 (98,400-189,300)	101,400 (84,200-136,700)	142,900 (106,100-188,000)	114,600 (70,000-184,400)	53,300
Peak hospital beds occupied	18,900 (12,700-29,200)	16,100 (11,300-25,100)	13,300 (8,900-21,100)	12,200 (8,500-22,800)	15,000 (11,300-21,100)	21,700 (12,300-31,300)	6,300

II. Medium / central immune escape

Indicator	Step 4, no delay (21st June)	Step 4, two week delay	Step 4, five week delay	Step 4, 2 doses for all adults	Step 4, split	Circuit breaker	Return to Step 2
Total deaths	49,700 (35,600-67,200)	48,500 (34,400-66,900)	43,500 (31,200-62,900)	31,300 (26,200-42,000)	46,900 (34,100-63,400)	34,800 (20,500-59,300)	16,200
Peak deaths	700 (500-1,200)	600 (400-1,000)	500 (300-800)	500 (300-1,000)	600 (400-800)	900 (500-1,300)	200
Total hospitalisations	183,700 (136,400-238,800)	180,700 (132,900-238,200)	166,900 (122,800-230,000)	127,200 (105,400-170,600)	175,300 (131,700-227,900)	145,500 (89,900-227,300)	66,100
Peak hospital beds occupied	23,600 (15,700-36,200)	20,200 (14,100-31,500)	16,000 (11,100-25,800)	15,500 (10,500-27,900)	18,800 (14,100-26,400)	27,000 (16,100-37,900)	7,700

Table 7 - Summary of projections for total COVID-19 deaths, peak daily COVID-19 deaths, total COVID-19 hospitalisations, and peak hospital bed occupancy for England, over the time period 21st June – 31st October 2021, with waning immunity. Medium mobility assumptions are shown, with low and high mobility assumptions shown below in brackets where relevant.

III. High / pessimistic immune escape; +30% transmissibility

Indicator	Step 4, no delay (21st June)	Step 4, two week delay	Step 4, five week delay	Step 4, 2 doses for all adults	Step 4, split	Circuit breaker	Return to Step 2
Total deaths	81,000 (49,800-121,500)	77,100 (47,600-120,100)	66,100 (42,500-107,500)	44,400 (34,300-65,300)	75,100 (47,300-115,700)	44,800 (24,700-83,900)	17,800
Peak deaths	900 (600-1,600)	1,000 (700-1,500)	1,200 (700-1,900)	1,100 (600-2,100)	1,000 (600-1,500)	1,400 (800-2,300)	200
Total hospitalisations	307,700 (198,300-431,900)	297,600 (191,200-432,000)	263,900 (174,200-403,800)	188,900 (144,500-276,900)	290,900 (190,000-420,600)	195,900 (114,500-340,100)	75,300
Peak hospital beds occupied	29,900 (19,400-51,500)	31,700 (20,800-48,500)	37,600 (21,900-56,700)	32,900 (19,300-59,300)	31,500 (20,300-46,800)	42,700 (25,600-67,000)	6,900

IV. Medium / central immune escape; +70% transmissibility

Indicator	Step 4, no delay (21st June)	Step 4, two week delay	Step 4, five week delay	Step 4, 2 doses for all adults	Step 4, split	Circuit breaker	Return to Step 2
Total deaths	63,600 (51,100-79,900)	60,800 (49,300-76,300)	53,500 (45,200-67,500)	43,500 (40,900-49,300)	58,600 (49,100-70,400)	52,400 (37,300-74,100)	31,400
Peak deaths	1,200 (900-1,700)	1,000 (800-1,400)	700 (600-800)	600 (600-600)	1,000 (800-1,200)	800 (600-1,200)	500
Total hospitalisations	228,400 (188,400-278,500)	218,600 (182,500-266,000)	196,600 (169,300-240,800)	166,100 (156,000-188,100)	212,200 (181,700-248,700)	197,700 (147,700-263,800)	122,700
Peak hospital beds occupied	38,100 (29,300-50,600)	32,800 (26,600-43,100)	22,900 (22,500-25,100)	22,200 (22,200-22,200)	31,700 (27,000-37,300)	22,600 (16,000-33,200)	17,700

I. Low / optimistic immune escape, 50% increased transmissibility

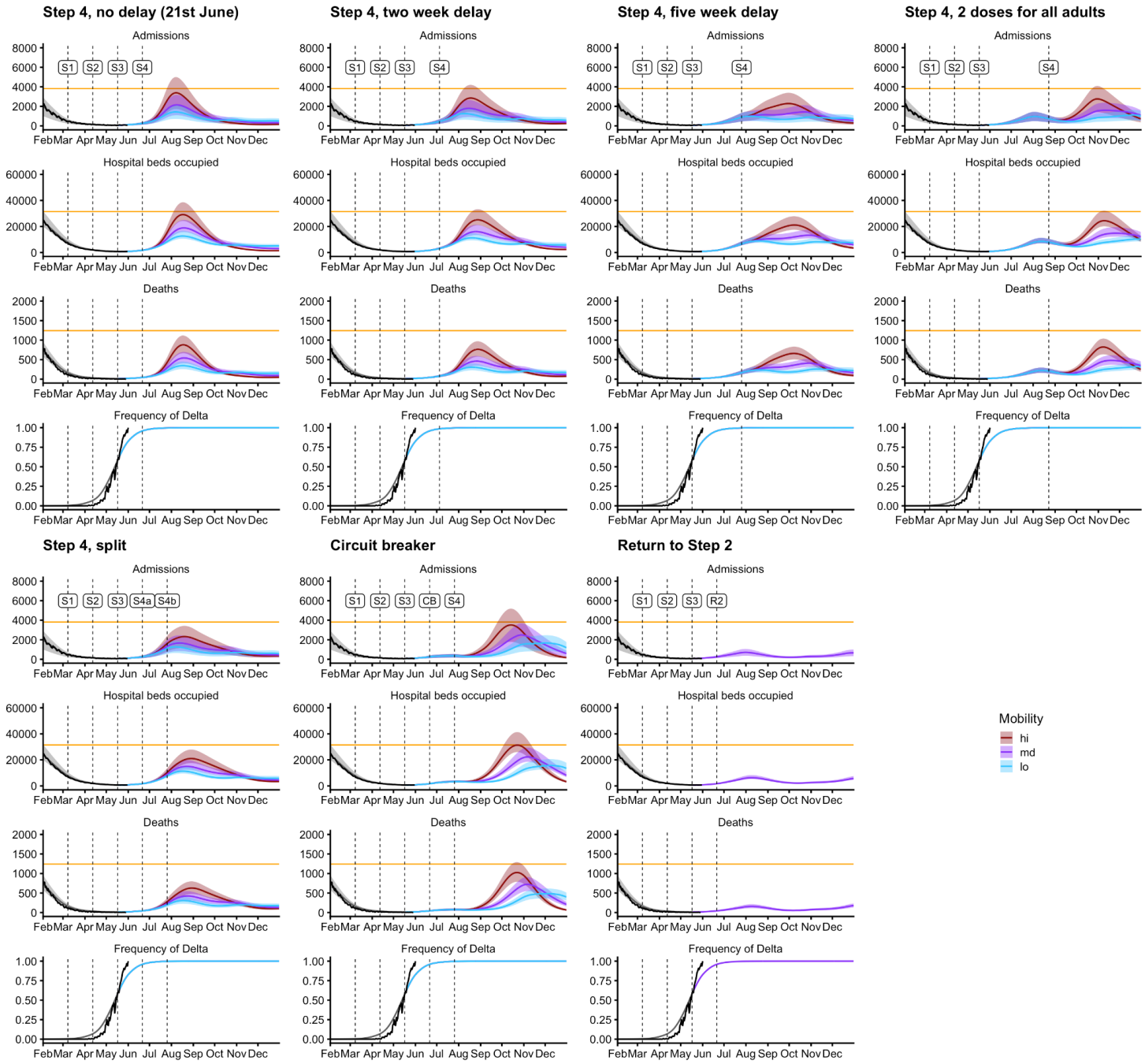

Figure 9 - Overview of scenarios considering different policy options for control of the projected third wave of transmission, Delta B.1.617.2 scenario with low / optimistic immune escape (Table 5) and 50% increased transmissibility relative to the Alpha B.1.1.7 variant, with waning of natural and vaccine-induced immunity. For each policy option considered we show projected hospital admissions, the number of hospital beds occupied, the daily number of deaths and frequency of the Delta B.1.617.2 variant over time for England overall. The beginning of each roadmap Step, circuit breaker lockdown (CB) and roadmap Step reversal (R2) are marked with a vertical dashed line; orange horizontal lines mark peak admissions, bed occupancy, and deaths in England during the second wave (January 2021). Data (black) and model fits (grey) are shown up to the date of the latest available data. Low (blue), medium (purple) and high (red) mobility scenarios are used to project forwards from June to December 2021.

II. Medium / central immune escape, 50% increased transmissibility

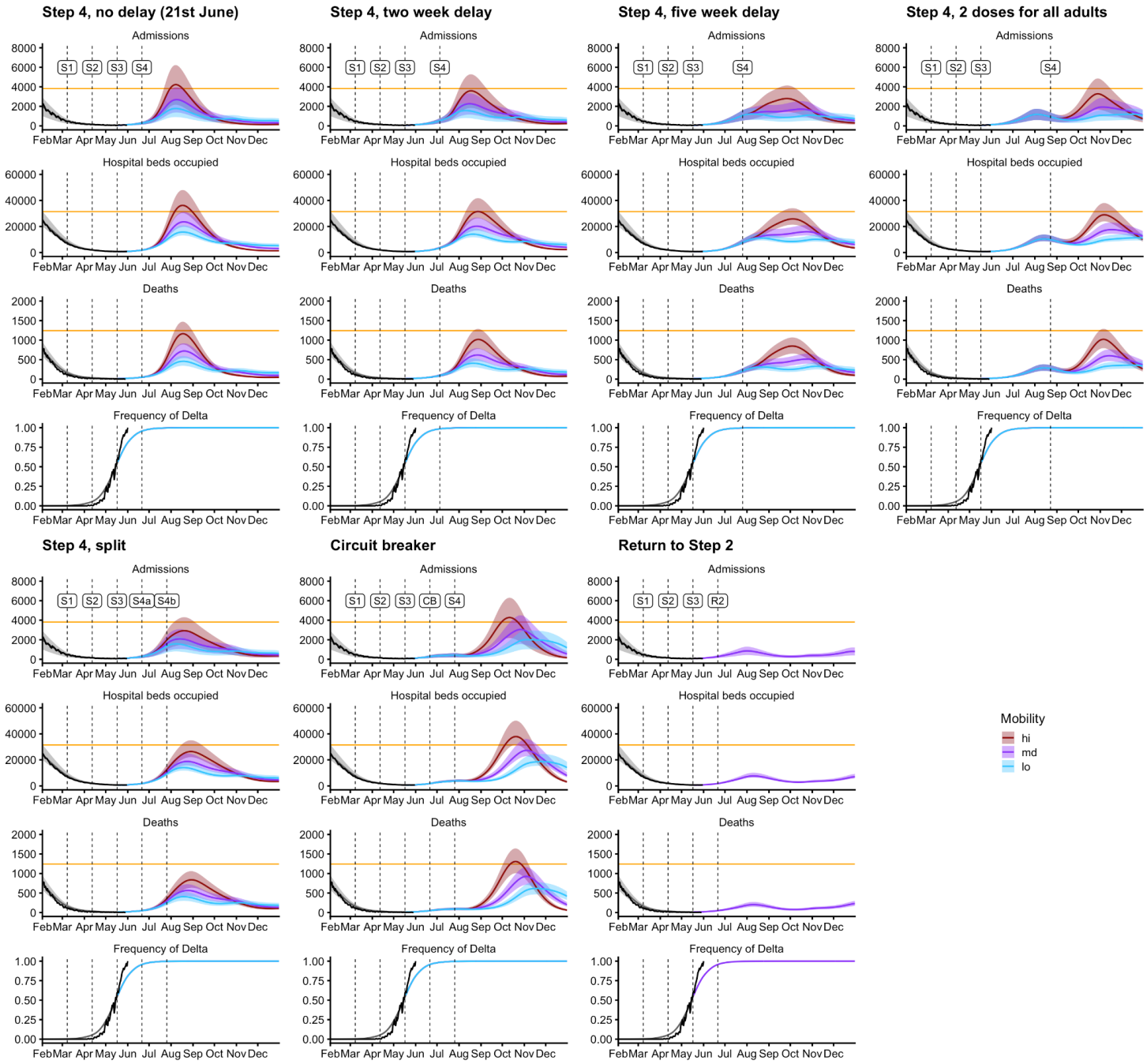

Figure 10 - Overview of scenarios considering different policy options for control of the projected third wave of transmission, Delta B.1.617.2 scenario with medium / central immune escape (Table 5) and 50% increased transmissibility relative to the Alpha B.1.1.7 variant, with waning of natural and vaccine-induced immunity. For each policy option considered we show projected hospital admissions, the number of hospital beds occupied, the daily number of deaths and frequency of the Delta B.1.617.2 variant over time for England overall. The beginning of each roadmap Step, circuit breaker lockdown (CB) and roadmap Step reversal (R2) are marked with a vertical dashed line; orange horizontal lines mark peak admissions, bed occupancy, and deaths in England during the second wave (January 2021). Data (black) and model fits (grey) are shown up to the date of the latest available data. Low (blue), medium (purple) and high (red) mobility scenarios are used to project forwards from June to December 2021.

III. High / pessimistic immune escape, 30% increased transmissibility

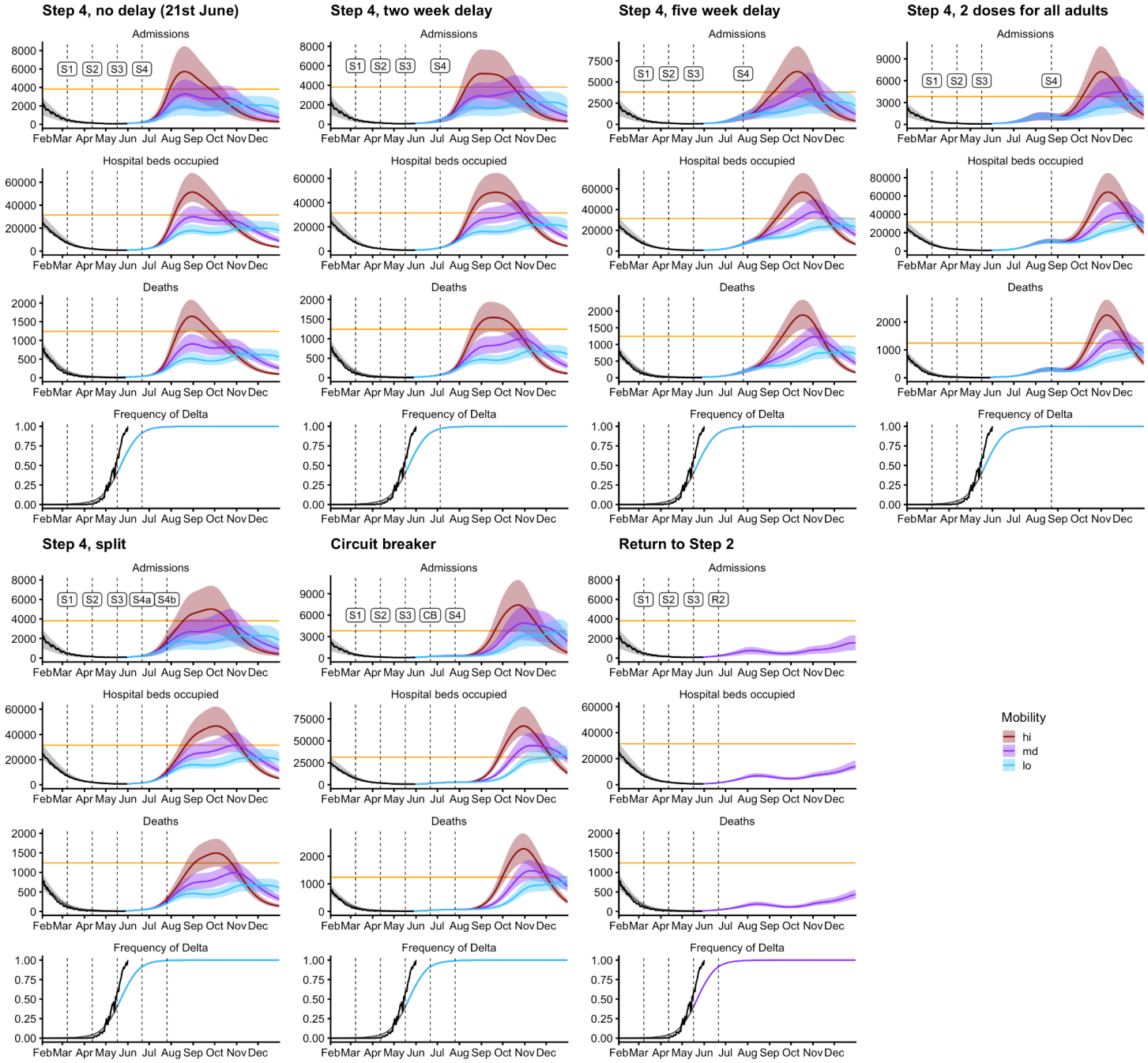

Figure 11 - Overview of scenarios considering different policy options for control of the projected third wave of transmission, Delta B.1.617.2 scenario with high / pessimistic immune escape (Table 5) and 30% increased transmissibility relative to the Alpha B.1.1.7 variant, with waning of natural and vaccine-induced immunity. For each policy option considered we show projected hospital admissions, the number of hospital beds occupied, the daily number of deaths and frequency of the Delta B.1.617.2 variant over time for England overall. The beginning of each roadmap Step, circuit breaker lockdown (CB) and roadmap Step reversal (R2) are marked with a vertical dashed line; orange horizontal lines mark peak admissions, bed occupancy, and deaths in England during the second wave (January 2021). Data (black) and model fits (grey) are shown up to the date of the latest available data. Low (blue), medium (purple) and high (red) mobility scenarios are used to project forwards from June to December 2021.

IV. Medium / central immune escape, 70% increased transmissibility

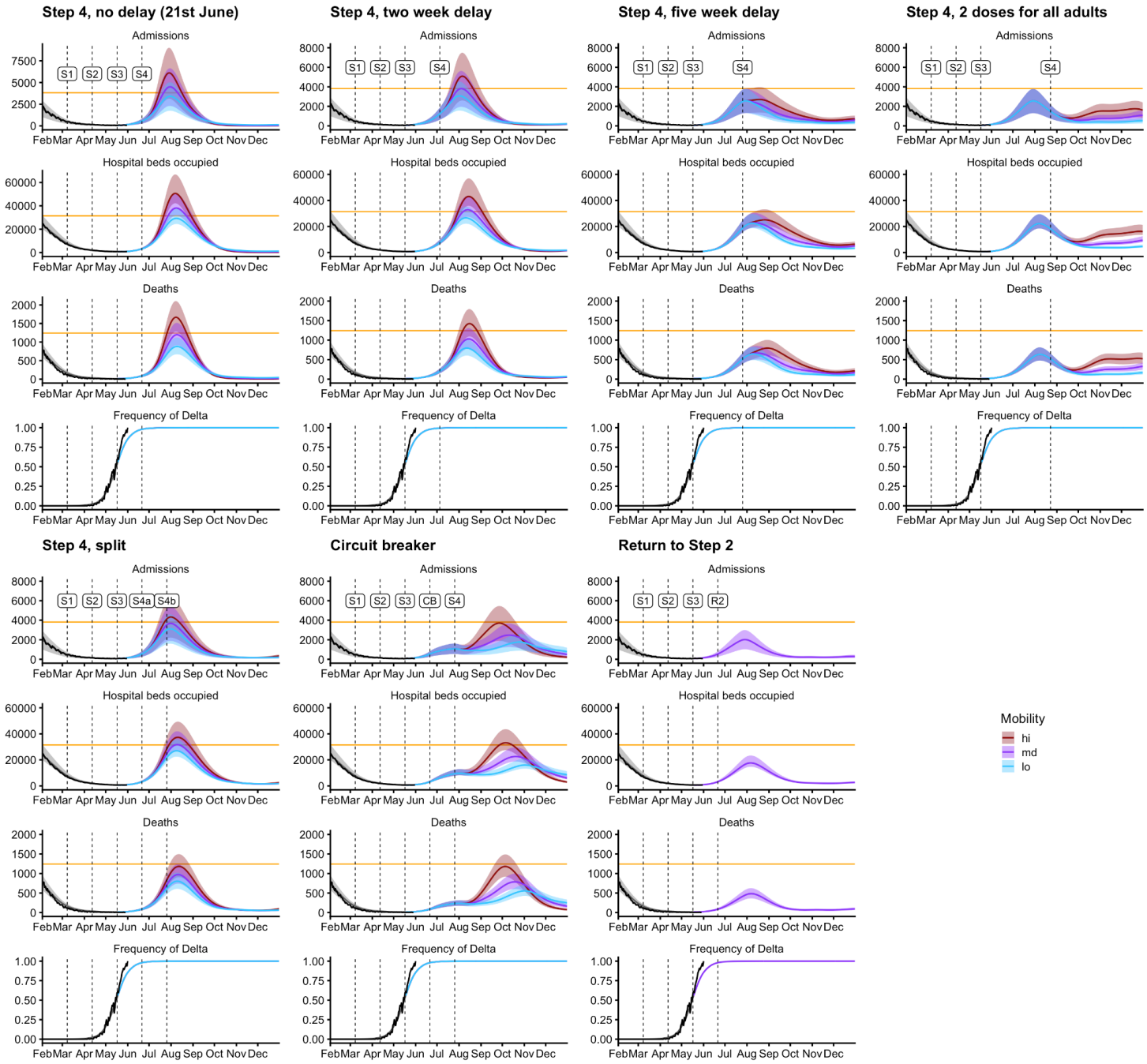

Figure 12 - Overview of scenarios considering different policy options for control of the projected third wave of transmission, Delta B.1.617.2 scenario with medium / central immune escape (Table 5) and 70% increased transmissibility relative to the Alpha B.1.1.7 variant, with waning of natural and vaccine-induced immunity. For each policy option considered we show projected hospital admissions, the number of hospital beds occupied, the daily number of deaths and frequency of the Delta B.1.617.2 variant over time for England overall. The beginning of each roadmap Step, circuit breaker lockdown (CB) and roadmap Step reversal (R2) are marked with a vertical dashed line; orange horizontal lines mark peak admissions, bed occupancy, and deaths in England during the second wave (January 2021). Data (black) and model fits (grey) are shown up to the date of the latest available data. Low (blue), medium (purple) and high (red) mobility scenarios are used to project forwards from June to December 2021.

Supplementary material

Table S1 - Comparison of modelling assumptions for vaccine effectiveness against all outcomes (pre- and B.1.1.7) and related values from Public Health England's COVID-19 vaccine surveillance report, week 22 (ref). Estimates which are not in line with the PHE report are highlighted in yellow. Relevant explanations for these discrepancies are given at the bottom of the table.

Outcome	**Vaccine effectiveness**			
	Pfizer-BioNTech		*Oxford-AstraZeneca*	
	1 dose	2 doses	1 dose	2 doses
Infection	70%	85%	67%	68%
Infection (PHE)	55-70%	70-90%	60-70%	No data
Disease	70%	89%	67%	78%
Symptomatic disease (PHE)	55-70%	85-90%	55-70%	65-90%
Hospitalisation	84.5%	90%	84.5%	90%
Hospitalisation (PHE)	75-85%	90-95%	75-85%	No data
Mortality	84.5%*	95%	84.5%*	95%
Mortality (PHE)	75-80%*	95-99%	75-80%*	No data
Onward transmission	49%[+]	60%[+]	38%[+]	50%[+]
Onward transmission (PHE)	45-50%	No data	35-50%	No data

*Dagan et al. estimate vaccine effectiveness against mortality of 84% (44–100%) 21 to 27 days after first dose of Pfizer-BioNTech BNT162b2 vaccine. Lopez Bernal et al. B estimated a hazard ratio of 0.56 (0.47 - 0.68) for cases vaccinated with one dose of Pfizer compared to unvaccinated cases, indicating an additional 44% (32-53%) protection against death given becoming a case for individuals vaccinated with one dose of Pfizer. Using the aforementioned estimate of a 44% increase and assuming this in addition to assumed protection against infection/disease of 0.7**,** we get overall protection against mortality of 0.832. Lopez Bernal et al. B estimated a hazard ratio of 0.45 (0.34 - 0.59) for cases vaccinated with one dose of Oxford-AstraZeneca compared to unvaccinated cases, indicating an additional 55% (41-66%) protection against death given becoming a case for individuals vaccinated with one dose of AZ. Using the aforementioned estimate of a 55% increase and assuming this in addition to protection against infection/disease of 0.67**,** we get overall protection against mortality of 0.8515.

[+]Harris et al. estimate an odds ratio of infection for contacts of index cases vaccinated with

ChAdOx1 (AstraZeneca) matched to contacts of unvaccinated index cases of 0.62 (95% 0.48-0.79) and an odds ratio of infection for contacts of index cases vaccinated with BNT162b2 (Pfizer-BioNTech) matched to contacts of unvaccinated index cases of 0.51 (95% 0.42-0.62), where the vaccinated index cases received their vaccine dose at least 21 days before testing positive. In the absence of any data, we assumed a modest improvement in efficacy against infectiousness for 2 vaccine doses relative to 1 vaccine dose. We also assume the vaccines provide the same reduction in onward transmission for all breakthrough infections, regardless of whether they are symptomatic or asymptomatic; note that the source study only assessed the relative infectiousness of breakthrough symptomatic infections.

Table S2 - Vaccine effectiveness against pre-B.1.1.7 and B.1.1.7 relevant evidence

Description	Relevant evidence, assumed value shown in bold
Overall protection against infection for AstraZeneca dose 1	Shrotri et al. results, secondary analyses, paragraph 1, p.8 adjusted hazard ratio 0.33 (0.16, 0.68) at 28-34 days post vaccination. Pritchard et al. supplementary Table 7, adjusted odds ratio >=21 days after first dose of AZ 0.36 (0.3, 0.45). **0.67 (+28 days)**
Overall protection against disease for AstraZeneca dose 1	Lopez Bernal et al. Table 3, ChAdOx1 adjusted odds ratio d1:28-34 0.4 (0.27-0.59), adjusting 0.6 up to equivalent estimate for protection against infection (see cell above) **0.67 (+28 days) as for infection**
Overall protection against hospitalisation for AstraZeneca dose 1	Vasileiou et al. Table 2, vaccine programme effect for ChAdOx1 21-27 days post first vaccine is 81% (72 to 87%), 28-34 days post first vaccine is 88% (75-94%), 35-41 days post first vaccine is 97% (63-100%). Smaller numbers. Table 3 splits analysis into age groups for ChAdOx1: 65-79 years 21-27 days post first dose 68% (31 to 85%), 80+ years 21-27 days post first dose 77% (63 to 86%) and 28-34 days post first dose 81% (60 to 91%). Small numbers for 65-79 years old and for 18-64 years old, so difficult to directly compare but overall the vaccine effect appears stronger in the younger (65-79 years) cohort than the older (80+) cohort, for the first three time points which enable comparison. Effect reversed for fourth time point. Ismail et al. estimate vaccine effectiveness against hospitalisation of 73% (60-81%) for 80+ year olds and 84% (74-89%) for 70-79 year olds, 28 days following the first dose of AZ. When analysis is not split across vaccine products, the same study estimates efficacy against hospitalisation of 80% (74-85%) for 80+ year olds and 82% (75-87%) for 70-79

	year olds. **0.845 (+28 days)**
Overall protection against mortality for AstraZeneca dose 1	Lopez Bernal et al. B estimated a hazard ratio of 0.45 (0.34 - 0.59) for cases vaccinated with one dose of AZ compared to unvaccinated cases, indicating an additional 55% (41-66%) protection against death given becoming a case for individuals vaccinated with one dose of AZ. Using the aforementioned estimate of a 55% increase and assuming this in addition to protection against disease of **0.67,** we get overall protection against mortality of 0.8515 **0.845 (+28 days)**
Overall protection against onward transmission for AstraZeneca dose 1	Harris et al. estimate an odds ratio of infection for contacts of index cases vaccinated with ChAdOx1 (AstraZeneca) matched to contacts of unvaccinated index cases of 0.62 (95% 0.48-0.79), where the vaccinated index cases received their vaccine dose at least 21 days before testing positive. **0.38 (+28 days)**
Overall protection against infection for AstraZeneca dose 2	Shrotri et al. results, secondary analyses, paragraph 1, p.8 adjusted hazard ratio 0.32 (0.15, 0.66) at 35-48 days post vaccination **0.68 (+14 days)**
Overall protection against disease for AstraZeneca dose 2	Voysey et al. A randomised controlled trial for ChAdOx1 nCoV-19 vaccine AZD1222, Table 3, average of efficacies more than 14 days after a second dose for LD/SD and SD/SD in 'COV002 (UK), age 18–55 years with >8 weeks' interval between vaccine doses*' row -> 0.778 = (0.9+0.656)/2 **0.78 (+14 days)**
Overall protection against hospitalisation for AstraZeneca dose 2	Ismail et al. estimate vaccine effectiveness against hospitalisation of 92% (87-95%) 14 days after a second dose across both AZ and Pfizer vaccines **0.9 (+14 days)**
Overall protection against mortality for AstraZeneca dose 2	**0.95 (+14 days)**

Overall protection against onward transmission for AstraZeneca dose 2	**0.5 (+14 days)**
Overall protection against infection for Pfizer dose 1	Hall et al. Table 2, full cohort adjusted hazard ratio d1>=21 days 0.30 (0.15-0.45). Pritchard et al. supplementary Table 7, adjusted odds ratio >=21 days after first dose of Pfizer 0.33 (0.28, 0.39) **0.7 (+28 days)**
Overall protection against disease for Pfizer dose 1	Lopez Bernal et al. Table 2, odds ratio vs day 4-9, d1:28-34 0.30 (0.22-0.41) **0.7 (+28 days)**
Overall protection against hospitalisation for Pfizer dose 1	Hyams et al. Table 2, adjusted vaccine effectiveness for one dose of BNT162b2 71.4% (43.1 - 86.2%). When the analysis of the effectiveness of one dose of BNT162b2 was restricted to the period covered by the ChAdOx1nCoV-19 analysis after the end of 2020, the observed adjusted estimate was 79.3% (95% CI 47.0-92.5) (P=0.0014). Dagan et al. estimate vaccine effectiveness against hospitalisation of 74% (56–86%) 14-20 days after first dose and 78% (61–91%) 21 to 27 days after first dose. Vasileiou et al. Table 2, vaccine effect for BNT162b2 21-27 days post first vaccine is 78% (71 to 83) and 28-34 days post first vaccine is 91% (85 to 94). Estimated vaccine effect against hospitalisation is reduced for later time points to 78% and 77%. Ismail et al. estimate vaccine effectiveness against hospitalisation of 81% (76-85%) for 80+ year olds and 81% (73-87%) for 70-79 year olds, 28 days following the first dose of Pfizer. When the analysis is not split across vaccine products, the same study estimates protection against hospitalisation of 80% (74-85%) for 80+ year olds and 82% (75-87%) for 70-79 year olds, 28 days following the first vaccine dose **0.845 (+28 days)**
Overall protection against mortality for Pfizer dose 1	Dagan et al. estimate vaccine effectiveness against mortality of 72% (19–100%) 14-20 days after first dose and 84% (44–100%) 21 to 27 days after first dose. Lopez Bernal et al. B estimated a hazard ratio of 0.56 (0.47 - 0.68) for cases vaccinated with one dose of Pfizer compared to unvaccinated cases, indicating an additional 44% (32-53%) protection against death given becoming a case for individuals vaccinated with one dose of Pfizer. Using the aforementioned estimate of a

	44% increase and assuming this in addition to protection against disease of **0.7,** we get overall protection against mortality of 0.832 **0.845 (+28 days)**
Overall protection against onward transmission for Pfizer dose 1	Harris et al. estimate an odds ratio of infection for contacts of index cases vaccinated with BNT162b2 (Pfizer-BioNTech) matched to contacts of unvaccinated index cases of 0.51 (95% 0.42-0.62), where the vaccinated index cases received their vaccine dose at least 21 days before testing positive. **0.49 (+28 days)**
Overall protection against infection for Pfizer dose 2	Hall et al. Table 2, full cohort adjusted hazard ratio d2>=7 days 0.15 (0.04-0.26). Pritchard et al. supplementary Table 7, adjusted odds ratio post second dose of Pfizer 0.28 (0.21, 0.36). Haas et al. estimate vaccine protection against SARS-CoV-2 infection (both asymptomatic and symptomatic and symptoms unknown) of 95.3% (94.9-95.7%) **0.85 (+14 days)**
Overall protection against disease for Pfizer dose 2	Lopez Bernal et al. Table 2, odds ratio vs day 4-9, d2:14+ 0.11 (0.07-0.15). Haas et al. estimate vaccine protection against symptomatic COVID-19 >7 days after second dose of 97% (96.7-97.2%) **0.89 (+14 days)**
Overall protection against hospitalisation for Pfizer dose 2	Dagan et al. estimate vaccine effectiveness against hospitalisation of 87% (55–100%) >7 days after second dose. Haas et al. estimate vaccine protection against COVID-19 related hospitalisation >7 days after second dose of 97.2% (96.8-97.5%). Ismail et al. estimates vaccine protection against hospitalisation of 93% (89-95%) for individuals aged 80+ years 14 days after receiving their second dose of Pfizer. When the analysis is not split by vaccine type, the same study estimates protection against hospitalisation of 92% (87-95%) for 80+ year olds 14 days after second dose **0.9 (+14 days)**
Overall protection against mortality for Pfizer dose 2	Dagan et al. estimate vaccine effectiveness against mortality of 72% (19–100%) 14-20 days after first dose and 84% (44–100%) 21 to 27 days after first dose. Haas et al. estimate vaccine protection against death >7 days

	after second dose of 96.7% (96.0-97.3%). Lopez Bernal et al. B estimated a hazard ratio of 0.31 (0.14 - 0.69) for cases vaccinated with two doses of Pfizer compared to unvaccinated cases, indicating an additional 69% (31-86%) protection against death given becoming a case for individuals vaccinated with two doses of Pfizer. Using the aforementioned estimate of a 69% increase and assuming this in addition to protection against disease of **0.89,** we get overall protection against mortality of 0.9659 **0.95 (+14 days)**
Overall protection against onward transmission for Pfizer dose 2	**0.6 (+14 days)**

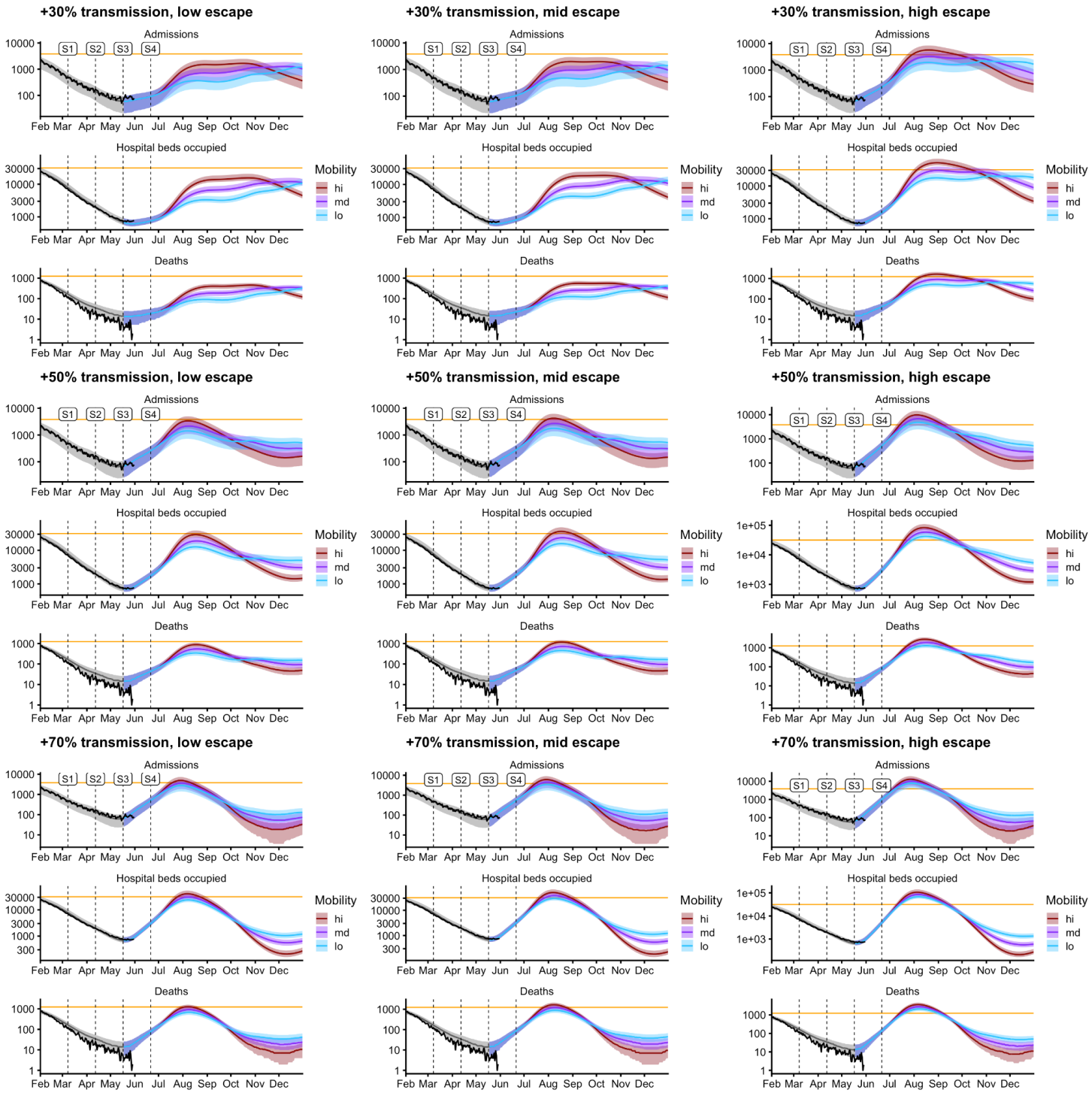

Figure S1 - Log scale showing model fits (grey) to hospital admissions, hospital beds occupied and deaths data (black) for all 9 combinations of immune escape (Table 5) and increased relative transmissibility of the Delta B.1.617.2 variant and with waning of natural and vaccine induced immunity - note that deaths are overpredicted by the model. Model projections implementing roadmap Step 4 on the 21st of June 2021 are shown for low (blue), medium (purple) and high (red) mobility scenarios from June to December 2021. The beginning of each roadmap Step is marked with a vertical dashed line; orange horizontal lines mark peak hospital admissions, bed occupancy, and deaths in England during the second wave (January 2021).

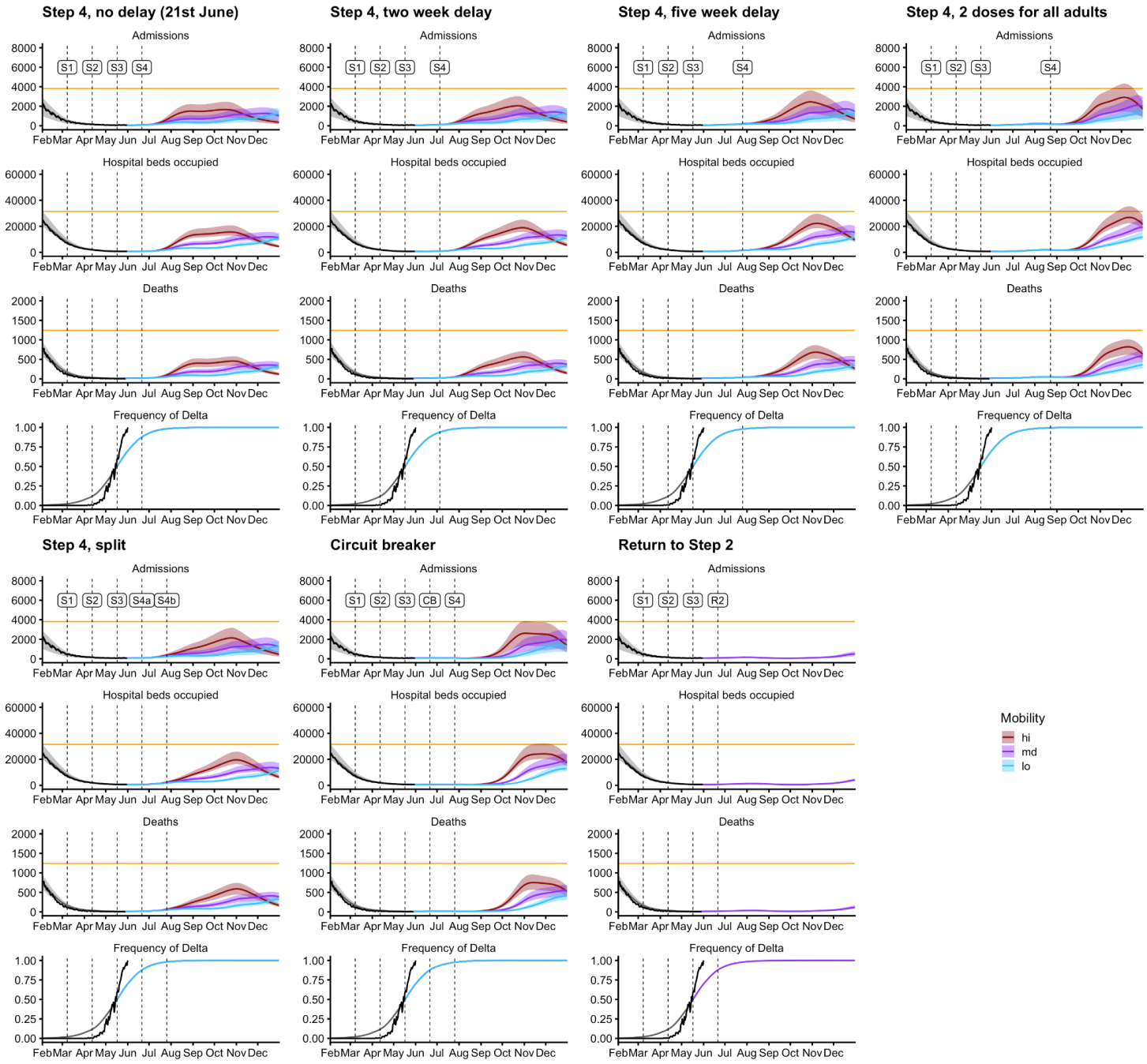

Figure S2 - Overview of scenarios considering different policy options for control of the projected third wave of transmission, Delta B.1.617.2 scenario with low / optimistic immune escape (Table 5) and 30% increased transmissibility relative to the Alpha B.1.1.7 variant, with waning of natural and vaccine-induced immunity. For each policy option considered we show projected hospital admissions, the number of hospital beds occupied, the daily number of deaths and frequency of the Delta B.1.617.2 variant over time for England overall. The beginning of each roadmap Step, circuit breaker lockdown (CB) and roadmap Step reversal (R2) are marked with a vertical dashed line; orange horizontal lines mark peak admissions, bed occupancy, and deaths in England during the second wave (January 2021). Data (black) and model fits (grey) are shown up to the date of the latest available data. Low (blue), medium (purple) and high (red) mobility scenarios are used to project forwards from June to December 2021.

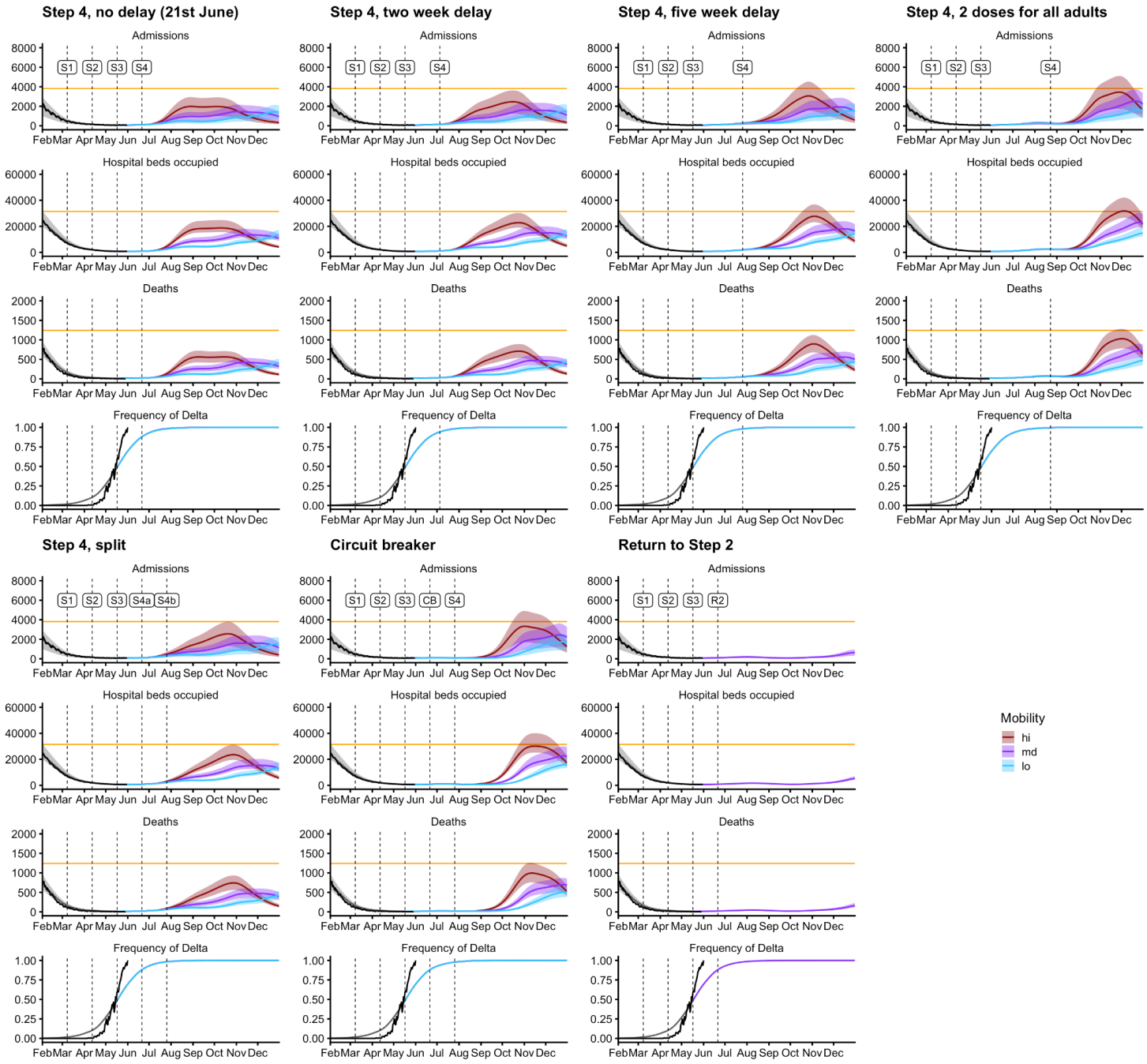

Figure S3 - Overview of scenarios considering different policy options for control of the projected third wave of transmission, Delta B.1.617.2 scenario with medium / central immune escape (Table 5) and 30% increased transmissibility relative to the Alpha B.1.1.7 variant, with waning of natural and vaccine-induced immunity. For each policy option considered we show projected hospital admissions, the number of hospital beds occupied, the daily number of deaths and frequency of the Delta B.1.617.2 variant over time for England overall. The beginning of each roadmap Step, circuit breaker lockdown (CB) and roadmap Step reversal (R2) are marked with a vertical dashed line; orange horizontal lines mark peak admissions, bed occupancy, and deaths in England during the second wave (January 2021). Data (black) and model fits (grey) are shown up to the date of the latest available data. Low (blue), medium (purple) and high (red) mobility scenarios are used to project forwards from June to December 2021.

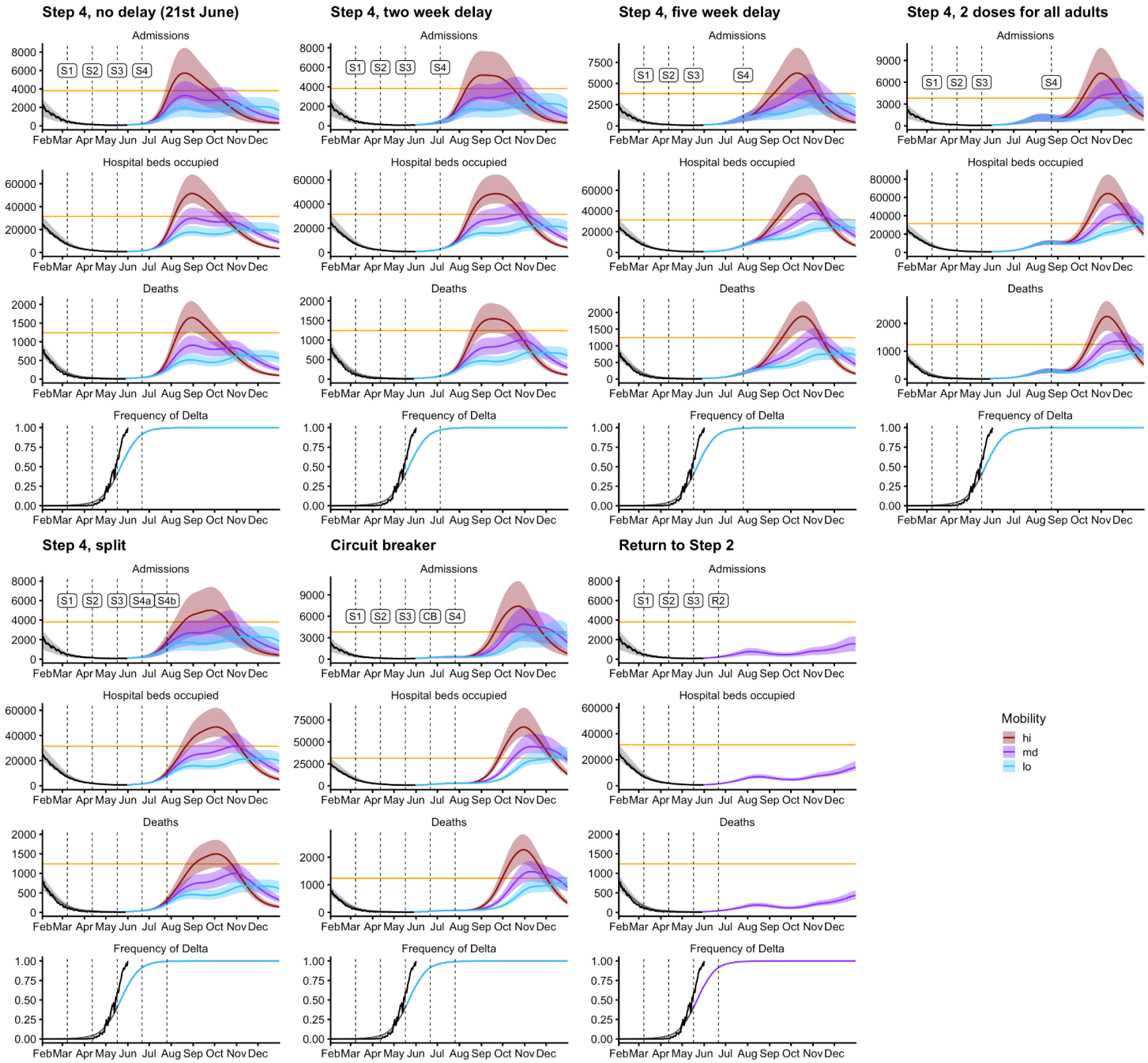

Figure S4 - Overview of scenarios considering different policy options for control of the projected third wave of transmission, Delta B.1.617.2 scenario with high / pessimistic immune escape (Table 5) and 30% increased transmissibility relative to the Alpha B.1.1.7 variant, with waning of natural and vaccine-induced immunity. For each policy option considered we show projected hospital admissions, the number of hospital beds occupied, the daily number of deaths and frequency of the Delta B.1.617.2 variant over time for England overall. The beginning of each roadmap Step, circuit breaker lockdown (CB) and roadmap Step reversal (R2) are marked with a vertical dashed line; orange horizontal lines mark peak admissions, bed occupancy, and deaths in England during the second wave (January 2021). Data (black) and model fits (grey) are shown up to the date of the latest available data. Low (blue), medium (purple) and high (red) mobility scenarios are used to project forwards from June to December 2021.

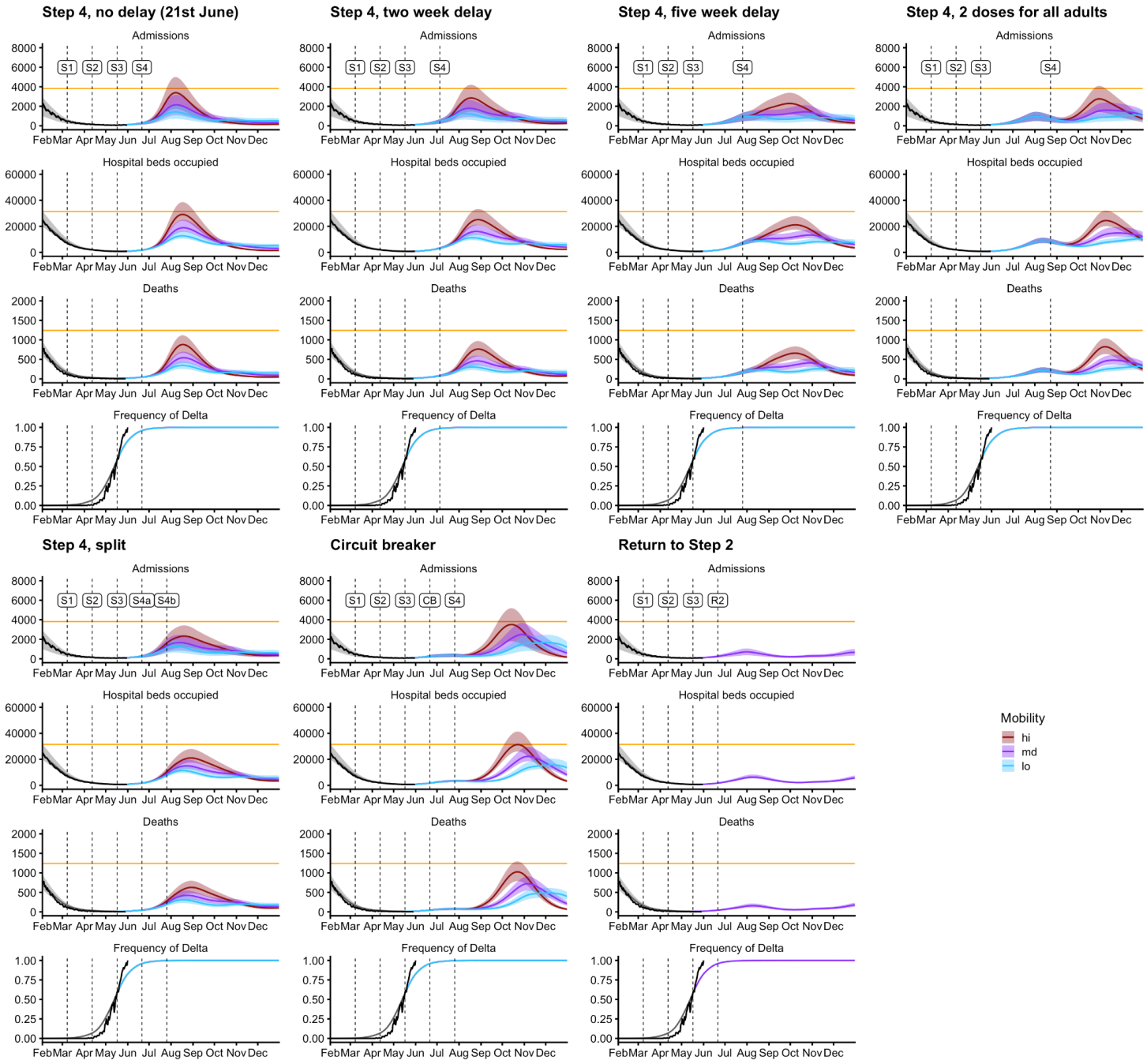

Figure S5 - Overview of scenarios considering different policy options for control of the projected third wave of transmission, Delta B.1.617.2 scenario with low / optimistic immune escape (Table 5) and 50% increased transmissibility relative to the Alpha B.1.1.7 variant, with waning of natural and vaccine-induced immunity. For each policy option considered we show projected hospital admissions, the number of hospital beds occupied, the daily number of deaths and frequency of the Delta B.1.617.2 variant over time for England overall. The beginning of each roadmap Step, circuit breaker lockdown (CB) and roadmap Step reversal (R2) are marked with a vertical dashed line; orange horizontal lines mark peak admissions, bed occupancy, and deaths in England during the second wave (January 2021). Data (black) and model fits (grey) are shown up to the date of the latest available data. Low (blue), medium (purple) and high (red) mobility scenarios are used to project forwards from June to December 2021.

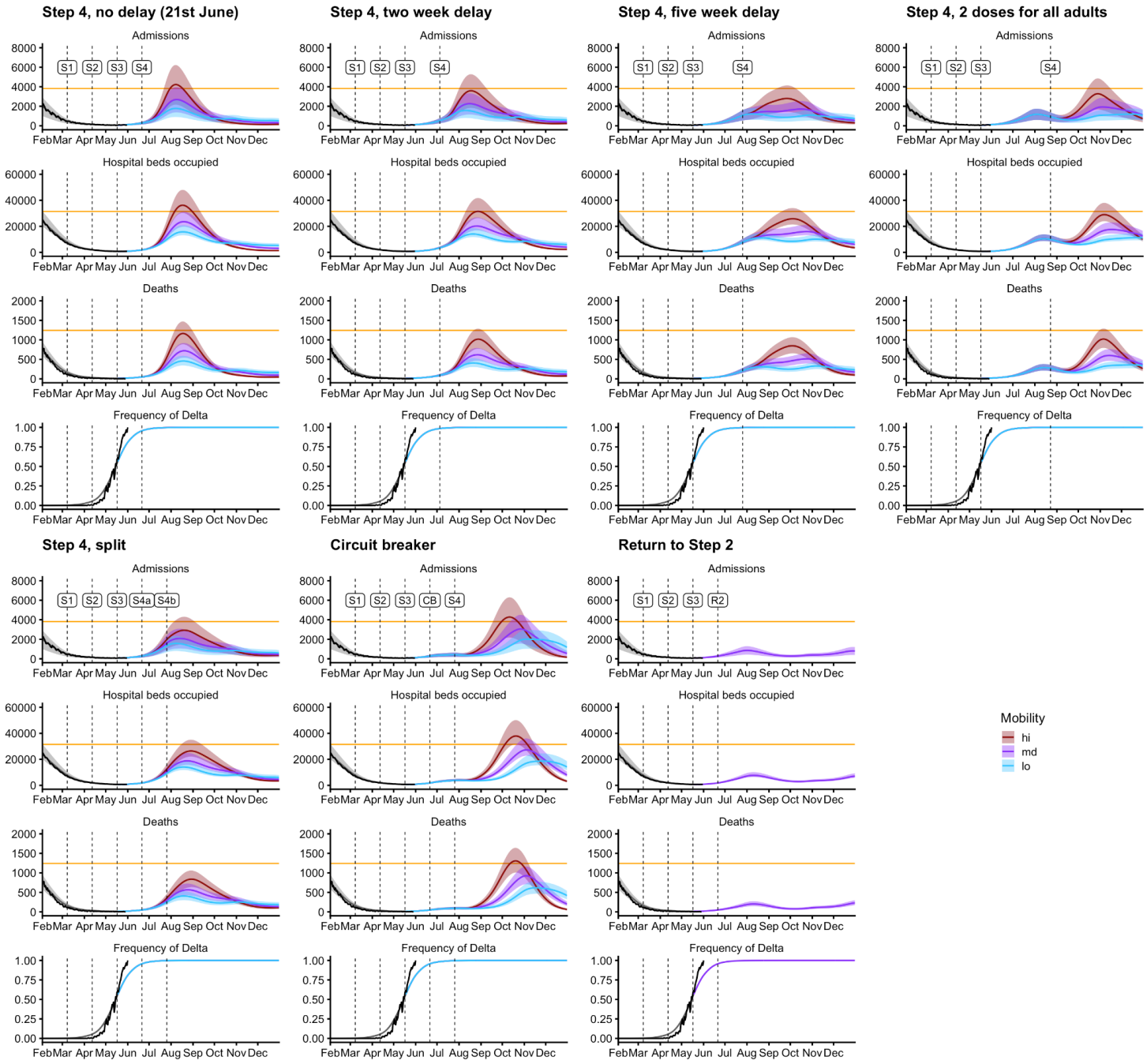

Figure S6 - Overview of scenarios considering different policy options for control of the projected third wave of transmission, Delta B.1.617.2 scenario with medium / central immune escape (Table 5) and 50% increased transmissibility relative to the Alpha B.1.1.7 variant, with waning of natural and vaccine-induced immunity. For each policy option considered we show projected hospital admissions, the number of hospital beds occupied, the daily number of deaths and frequency of the Delta B.1.617.2 variant over time for England overall. The beginning of each roadmap Step, circuit breaker lockdown (CB) and roadmap Step reversal (R2) are marked with a vertical dashed line; orange horizontal lines mark peak admissions, bed occupancy, and deaths in England during the second wave (January 2021). Data (black) and model fits (grey) are shown up to the date of the latest available data. Low (blue), medium (purple) and high (red) mobility scenarios are used to project forwards from June to December 2021.

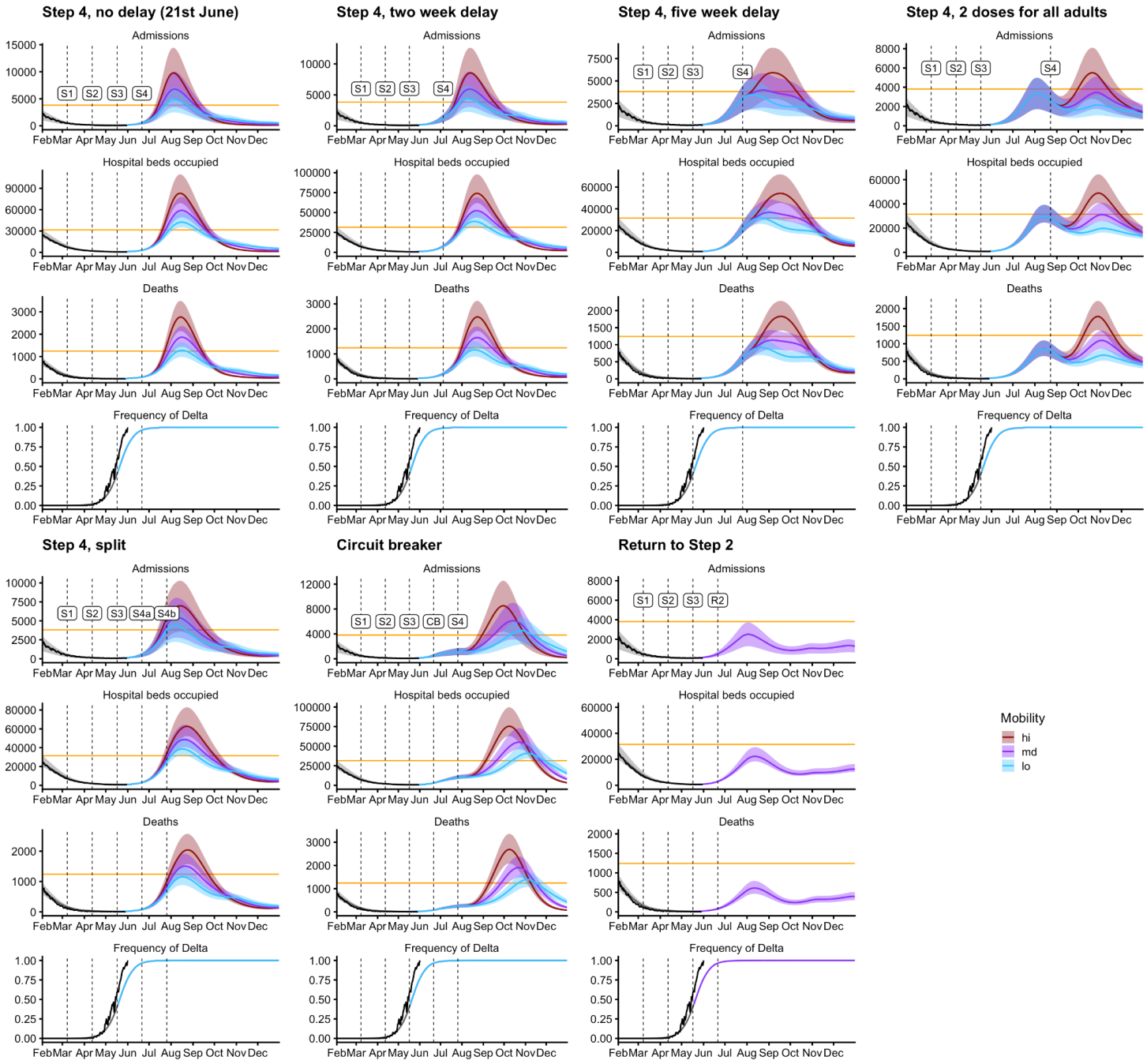

Figure S7 - Overview of scenarios considering different policy options for control of the projected third wave of transmission, Delta B.1.617.2 scenario with high / pessimistic immune escape (Table 5) and 50% increased transmissibility relative to the Alpha B.1.1.7 variant, with waning of natural and vaccine-induced immunity. For each policy option considered we show projected hospital admissions, the number of hospital beds occupied, the daily number of deaths and frequency of the Delta B.1.617.2 variant over time for England overall. The beginning of each roadmap Step, circuit breaker lockdown (CB) and roadmap Step reversal (R2) are marked with a vertical dashed line; orange horizontal lines mark peak admissions, bed occupancy, and deaths in England during the second wave (January 2021). Data (black) and model fits (grey) are shown up to the date of the latest available data. Low (blue), medium (purple) and high (red) mobility scenarios are used to project forwards from June to December 2021.

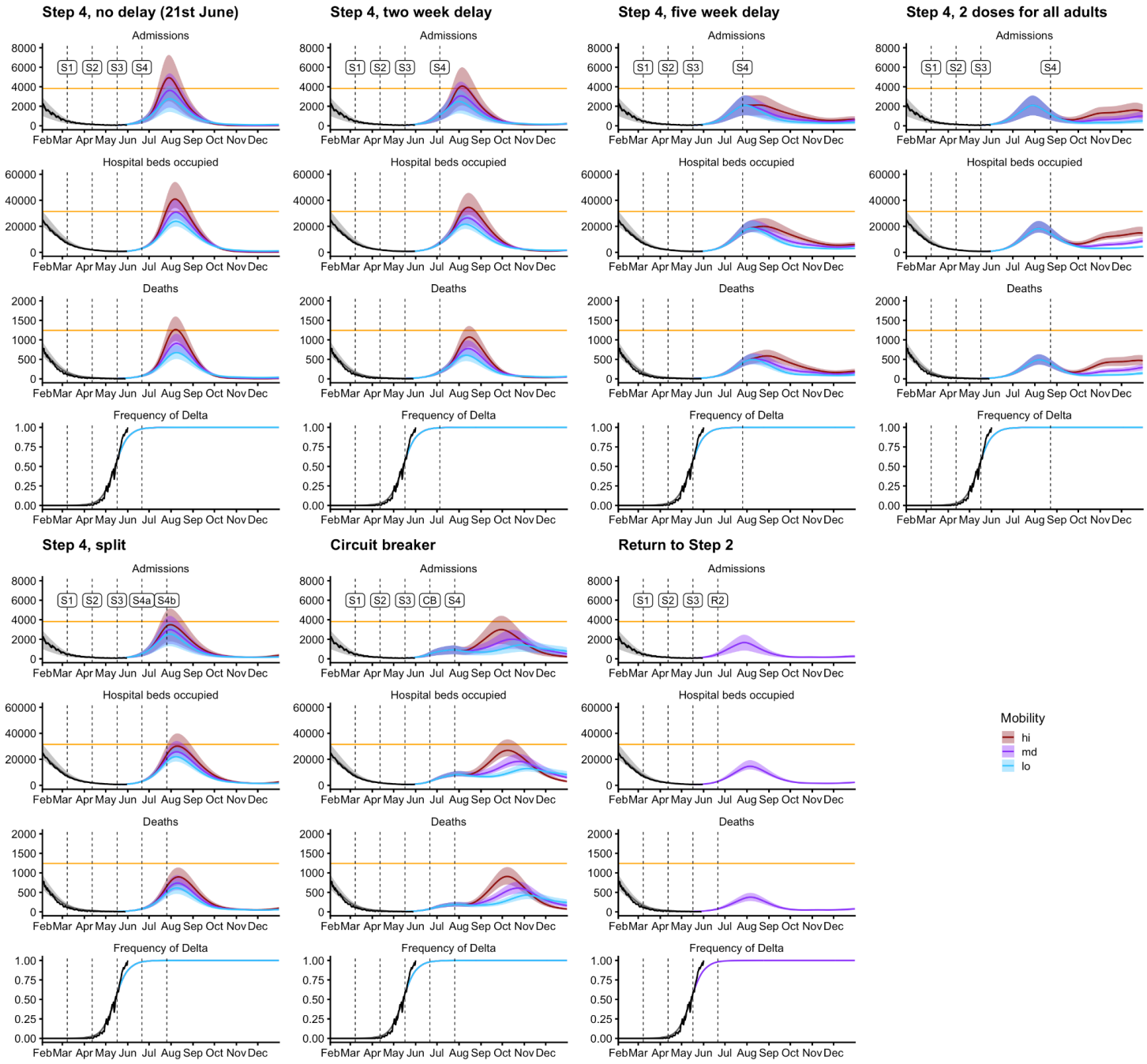

Figure S8 - Overview of scenarios considering different policy options for control of the projected third wave of transmission, Delta B.1.617.2 scenario with low / optimistic immune escape (Table 5) and 70% increased transmissibility relative to the Alpha B.1.1.7 variant, with waning of natural and vaccine-induced immunity. For each policy option considered we show projected hospital admissions, the number of hospital beds occupied, the daily number of deaths and frequency of the Delta B.1.617.2 variant over time for England overall. The beginning of each roadmap Step, circuit breaker lockdown (CB) and roadmap Step reversal (R2) are marked with a vertical dashed line; orange horizontal lines mark peak admissions, bed occupancy, and deaths in England during the second wave (January 2021). Data (black) and model fits (grey) are shown up to the date of the latest available data. Low (blue), medium (purple) and high (red) mobility scenarios are used to project forwards from June to December 2021.

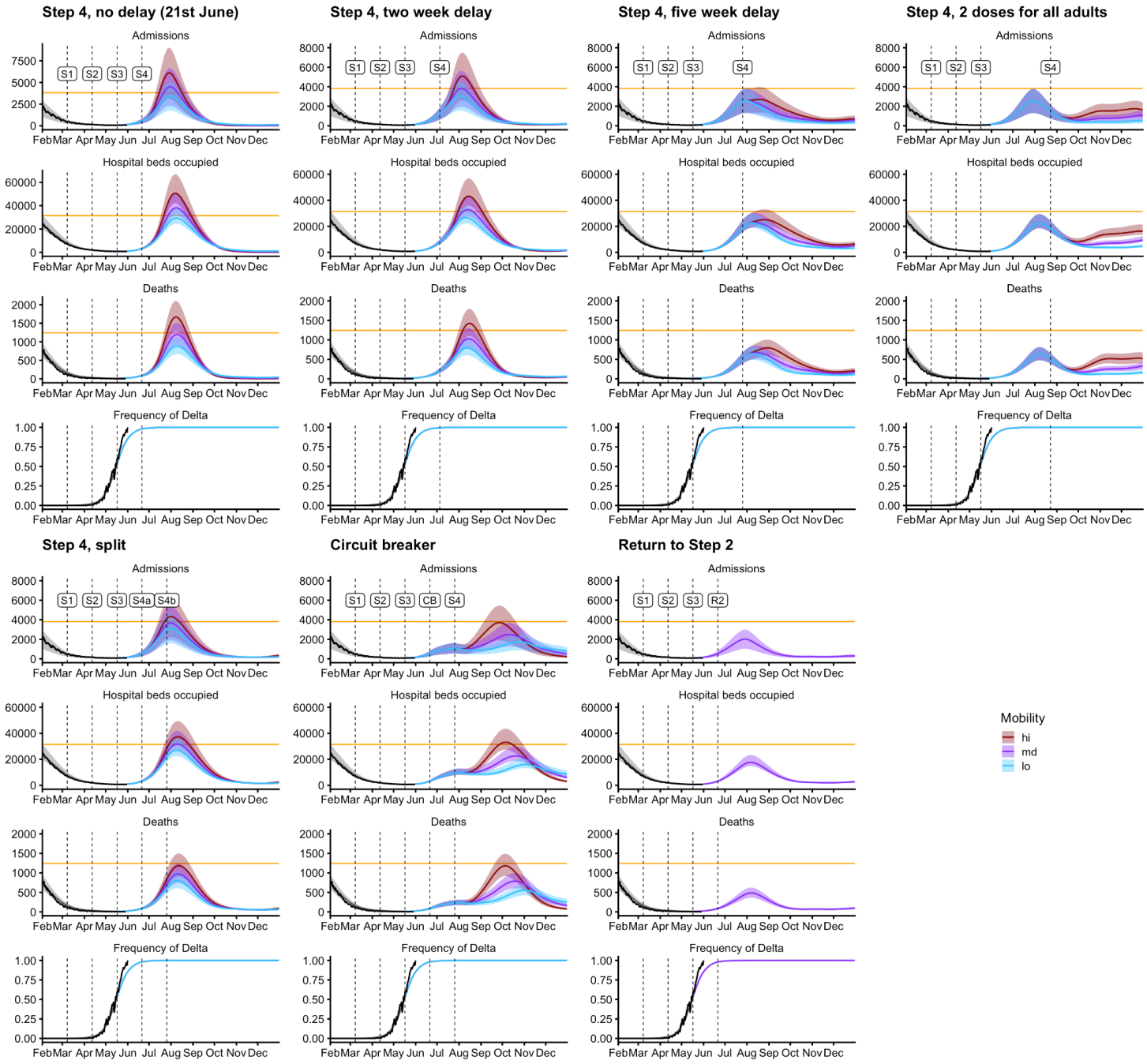

Figure S9 - Overview of scenarios considering different policy options for control of the projected third wave of transmission, Delta B.1.617.2 scenario with medium / central immune escape (Table 5) and 70% increased transmissibility relative to the Alpha B.1.1.7 variant, with waning of natural and vaccine-induced immunity. For each policy option considered we show projected hospital admissions, the number of hospital beds occupied, the daily number of deaths and frequency of the Delta B.1.617.2 variant over time for England overall. The beginning of each roadmap Step, circuit breaker lockdown (CB) and roadmap Step reversal (R2) are marked with a vertical dashed line; orange horizontal lines mark peak admissions, bed occupancy, and deaths in England during the second wave (January 2021). Data (black) and model fits (grey) are shown up to the date of the latest available data. Low (blue), medium (purple) and high (red) mobility scenarios are used to project forwards from June to December 2021.

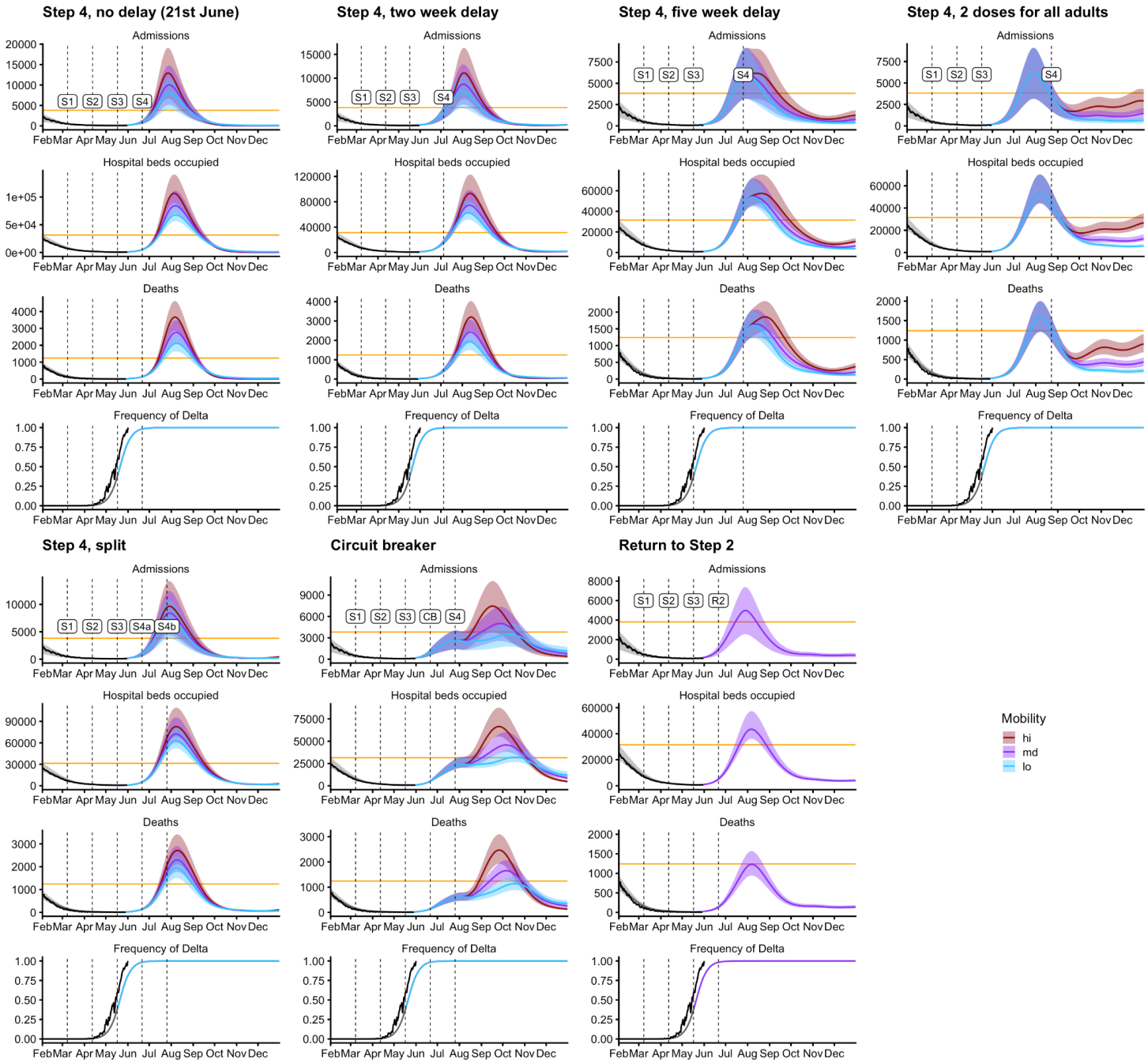

Figure S10 - Overview of scenarios considering different policy options for control of the projected third wave of transmission, Delta B.1.617.2 scenario with high / pessimistic immune escape (Table 5) and 70% increased transmissibility relative to the Alpha B.1.1.7 variant, with waning of natural and vaccine-induced immunity. For each policy option considered we show projected hospital admissions, the number of hospital beds occupied, the daily number of deaths and frequency of the Delta B.1.617.2 variant over time for England overall. The beginning of each roadmap Step, circuit breaker lockdown (CB) and roadmap Step reversal (R2) are marked with a vertical dashed line; orange horizontal lines mark peak admissions, bed occupancy, and deaths in England during the second wave (January 2021). Data (black) and model fits (grey) are shown up to the date of the latest available data. Low (blue), medium (purple) and high (red) mobility scenarios are used to project forwards from June to December 2021.

Table S3 - Summary of projections for total COVID-19 deaths, peak daily COVID-19 deaths, total COVID-19 hospitalisations, and peak hospital bed occupancy for England, over the time period 21st June – 31st December 2021, assuming the Delta B.1.617.2 variant has a 50% increase in transmissibility relative to the Alpha B.1.1.7 variant, and with waning immunity. Medium mobility assumptions are shown, with low and high mobility assumptions shown below in brackets where relevant.

I. Low / optimistic immune escape; +50% transmissibility

Indicator	Step 4, no delay (21st June)	Step 4, two week delay	Step 4, five week delay	Step 4, 2 doses for all adults	Step 4, split	Circuit breaker	Return to Step 2
Total deaths	45,400 (36,900-55,800)	47,400 (37,800-58,600)	49,900 (38,400-62,900)	50,400 (37,200-67,000)	46,700 (37,300-57,900)	56,400 (43,200-69,400)	19,300
Peak deaths	500 (300-900)	500 (300-800)	400 (300-700)	500 (300-800)	400 (300-600)	700 (500-1,000)	200
Total hospitalisations	172,100 (142,700-206,700)	178,700 (145,800-215,400)	187,100 (148,200-228,800)	190,200 (145,100-242,700)	176,600 (144,100-214,100)	206,600 (165,400-246,300)	79,800
Peak hospital beds occupied	18,900 (12,700-29,200)	16,100 (11,300-25,100)	13,300 (8,900-21,100)	14,800 (10,400-24,400)	15,000 (11,300-21,100)	22,300 (15,700-31,300)	6,300

II. Medium / central immune escape; +50% transmissibility

Indicator	Step 4, no delay (21st June)	Step 4, two week delay	Step 4, five week delay	Step 4, 2 doses for all adults	Step 4, split	Circuit breaker	Return to Step 2
Total deaths	57,400 (46,800-70,900)	59,600 (47,900-73,700)	62,300 (48,600-78,300)	62,800 (47,300-82,700)	58,700 (47,300-72,500)	70,200 (54,800-86,200)	25,400
Peak deaths	700 (500-1,200)	600 (400-1,000)	500 (300-800)	600 (400-1,000)	600 (400-800)	900 (600-1,300)	200
Total hospitalisations	206,500 (172,100-248,800)	213,400 (175,500-257,200)	222,400 (178,200-271,400)	226,100 (175,300-286,300)	210,800 (173,700-254,700)	245,300 (199,600-292,300)	100,100
Peak hospital beds occupied	23,600 (15,700-36,200)	20,200 (14,100-31,500)	16,000 (11,100-25,800)	17,600 (11,300-29,000)	18,800 (14,100-26,400)	27,300 (18,600-37,900)	7,700

Table S4 - Summary of projections for total COVID-19 deaths, peak daily COVID-19 deaths, total COVID-19 hospitalisations, and peak hospital bed occupancy for England, over the time period 21st June – 31st December 2021, with waning immunity. Medium mobility assumptions are shown, with low and high mobility assumptions shown below in brackets where relevant.

III. High / pessimistic immune escape; +30% transmissibility

Indicator	Step 4, no delay (21st June)	Step 4, two week delay	Step 4, five week delay	Step 4, 2 doses for all adults	Step 4, split	Circuit breaker	Return to Step 2
Total deaths	112,300 (87,500-137,400)	115,800 (88,400-143,400)	119,800 (88,500-151,600)	119,800 (84,700-159,500)	115,000 (87,900-143,000)	124,800 (84,500-162,900)	35,900
Peak deaths	900 (600-1,600)	1,000 (700-1,500)	1,200 (800-1,900)	1,400 (1,000-2,200)	1,000 (700-1,500)	1,500 (1,100-2,300)	400
Total hospitalisations	398,200 (323,000-473,200)	409,000 (326,600-490,200)	422,600 (328,200-513,700)	428,600 (319,100-539,700)	407,200 (324,800-490,000)	442,700 (319,900-545,000)	145,600
Peak hospital beds occupied	29,900 (20,100-51,500)	31,700 (21,600-48,500)	37,800 (24,900-56,700)	41,500 (30,100-64,300)	31,500 (21,600-46,800)	44,700 (34,100-67,000)	14,100

IV. Medium / central immune escape; +70% transmissibility

Indicator	Step 4, no delay (21st June)	Step 4, two week delay	Step 4, five week delay	Step 4, 2 doses for all adults	Step 4, split	Circuit breaker	Return to Step 2
Total deaths	65,000 (53,700-80,400)	64,000 (53,200-78,700)	63,000 (51,700-79,900)	60,000 (49,200-80,800)	62,000 (52,700-74,300)	75,200 (61,300-90,700)	35,900
Peak deaths	1,200 (900-1,700)	1,000 (800-1,400)	700 (600-800)	600 (600-600)	1,000 (800-1,200)	800 (600-1,200)	500
Total hospitalisations	232,100 (195,800-279,800)	227,900 (193,700-273,100)	226,100 (189,100-279,700)	218,300 (181,900-286,700)	222,300 (192,300-260,800)	261,300 (218,300-306,800)	137,000
Peak hospital beds occupied	38,100 (29,300-50,600)	32,800 (26,600-43,100)	22,900 (22,500-25,100)	22,200 (22,200-22,200)	31,700 (27,000-37,300)	22,600 (16,000-33,200)	17,700

I. Low / optimistic immune escape; +50% transmissibility

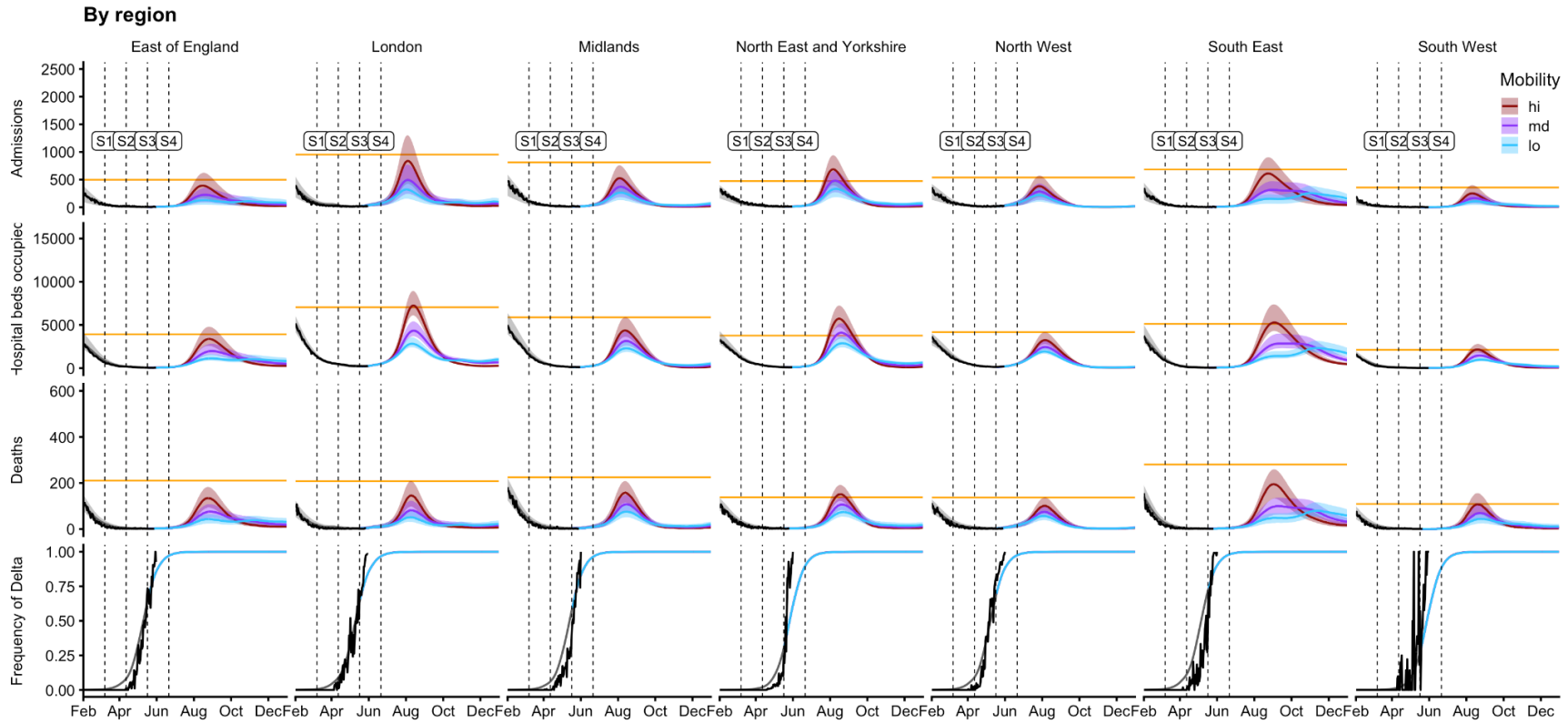

Figure S11. Projections by region, Delta B.1.617.2 scenario with low / optimistic immune escape (Table 5) and 50% increased transmissibility relative to the Alpha B.1.1.7 variant, with waning of natural and vaccine-induced immunity. For roadmap step 4 occurring on June 21st, we show projected hospital admissions, the number of hospital beds occupied, the daily number of deaths and frequency of the Delta B.1.617.2 variant over time for England overall. The beginning of each roadmap Step is marked with a vertical dashed line; orange horizontal lines mark peak admissions, bed occupancy, and deaths in England during the second wave (January 2021). Data (black) and model fits (grey) are shown up to the date of the latest available data. Low (blue), medium (purple) and high (red) mobility scenarios are used to project forwards from June to December 2021.

II. Medium / central immune escape; +50% transmissibility

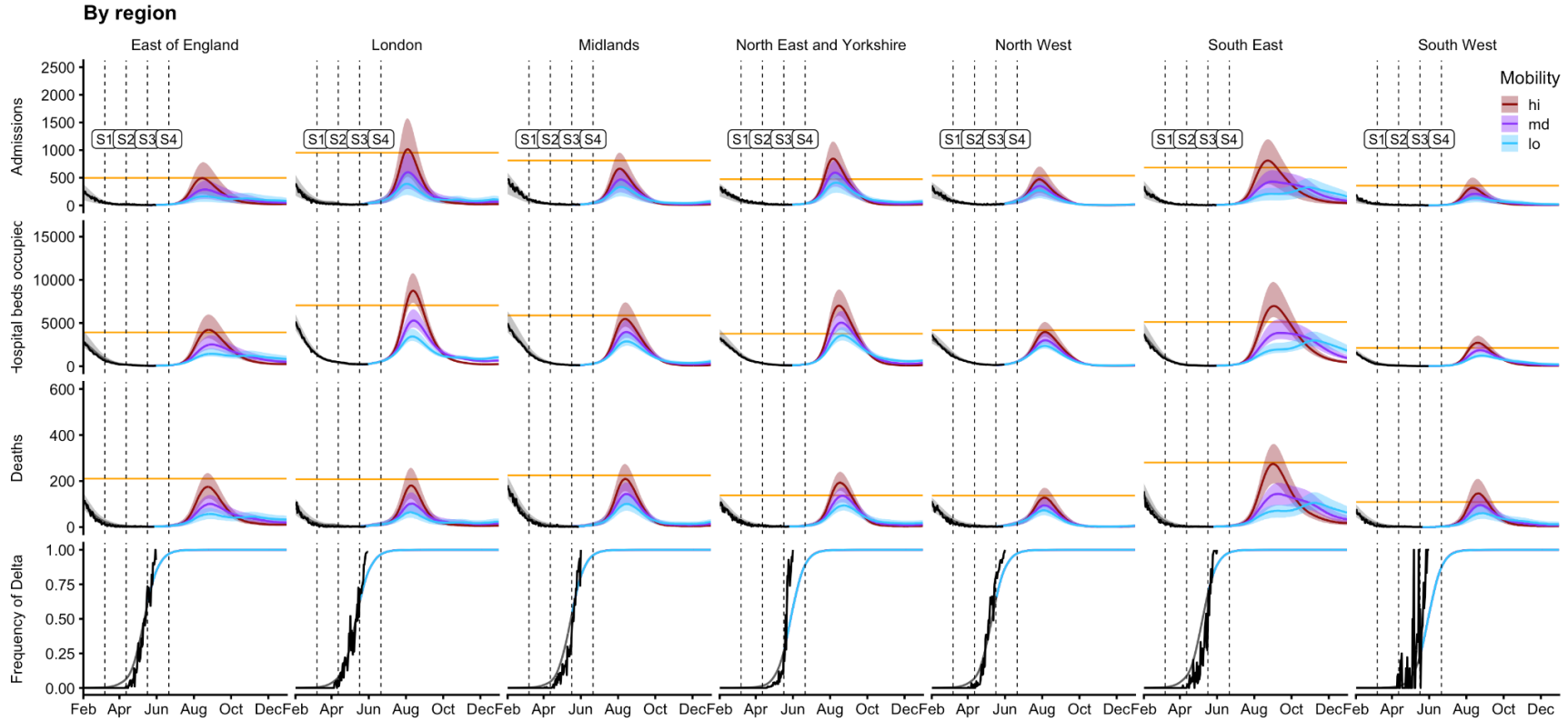

Figure S12. Projections by region, Delta B.1.617.2 scenario with medium / central immune escape (Table 5) and 50% increased transmissibility relative to the Alpha B.1.1.7 variant, with waning of natural and vaccine-induced immunity. For roadmap step 4 occurring on June 21st, we show projected hospital admissions, the number of hospital beds occupied, the daily number of deaths and frequency of the Delta B.1.617.2 variant over time for England overall. The beginning of each roadmap Step is marked with a vertical dashed line; orange horizontal lines mark peak admissions, bed occupancy, and deaths in England during the second wave (January 2021). Data (black) and model fits (grey) are shown up to the date of the latest available data. Low (blue), medium (purple) and high (red) mobility scenarios are used to project forwards from June to December 2021.

III. High / pessimistic immune escape; +30% transmissibility

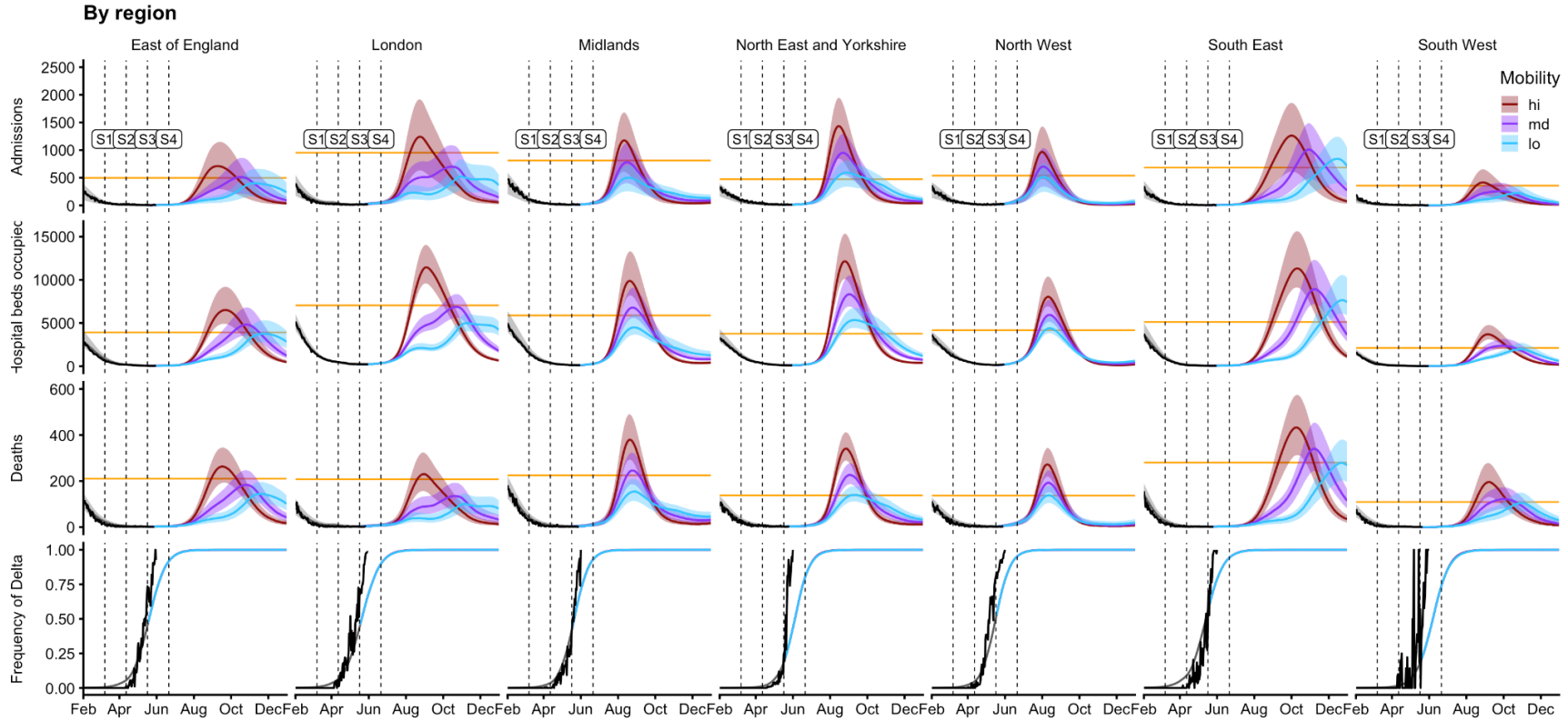

Figure S13. Projections by region, Delta B.1.617.2 scenario with high / pessimistic immune escape (Table 5) and 30% increased transmissibility relative to the Alpha B.1.1.7 variant, with waning of natural and vaccine-induced immunity. For roadmap step 4 occurring on June 21st, we show projected hospital admissions, the number of hospital beds occupied, the daily number of deaths and frequency of the Delta B.1.617.2 variant over time for England overall. The beginning of each roadmap Step is marked with a vertical dashed line; orange horizontal lines mark peak admissions, bed occupancy, and deaths in England during the second wave (January 2021). Data (black) and model fits (grey) are shown up to the date of the latest available data. Low (blue), medium (purple) and high (red) mobility scenarios are used to project forwards from June to December 2021.

IV. Medium / central immune escape; +70% transmissibility

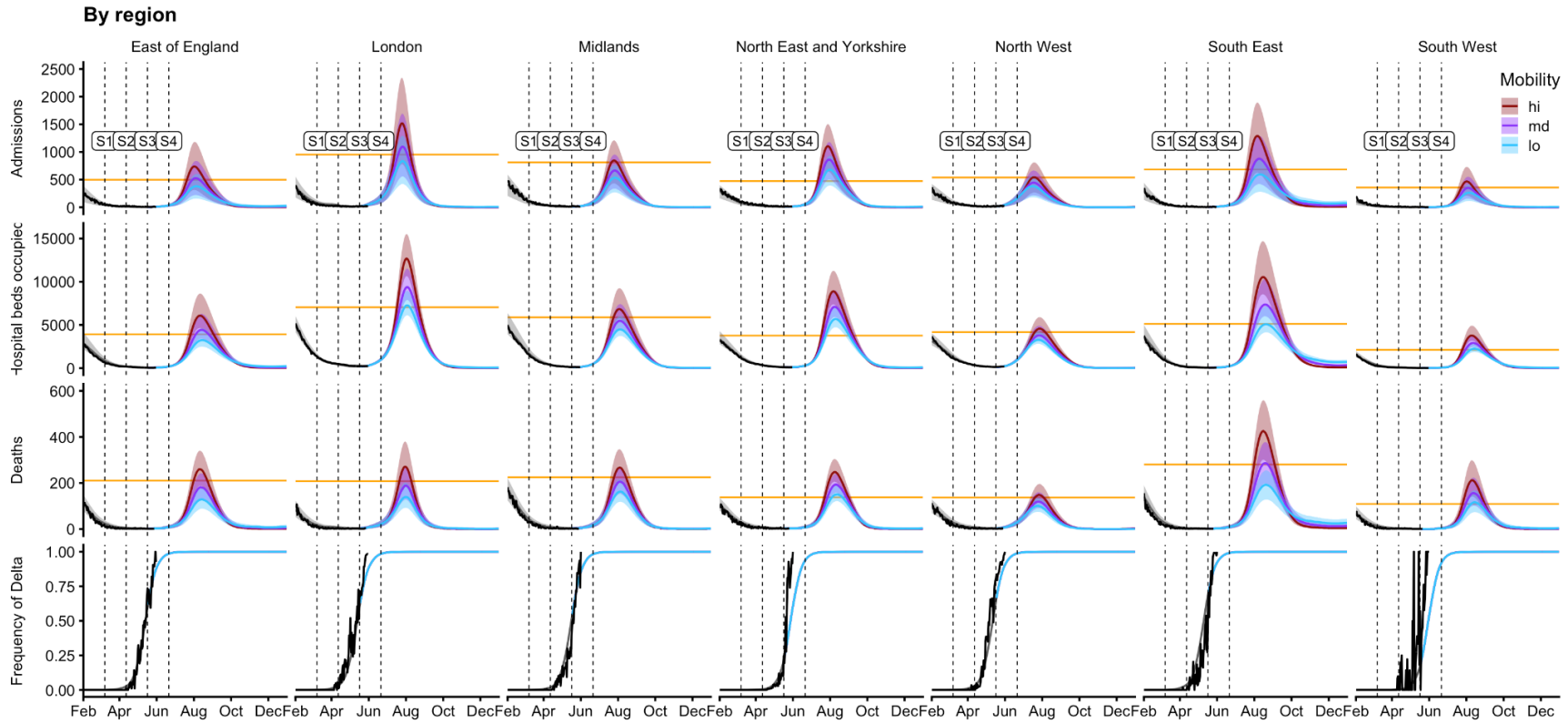

Figure S14. Projections by region, Delta B.1.617.2 scenario with medium / central immune escape (Table 5) and 70% increased transmissibility relative to the Alpha B.1.1.7 variant, with waning of natural and vaccine-induced immunity. For roadmap step 4 occurring on June 21st, we show projected hospital admissions, the number of hospital beds occupied, the daily number of deaths and frequency of the Delta B.1.617.2 variant over time for England overall. The beginning of each roadmap Step is marked with a vertical dashed line; orange horizontal lines mark peak admissions, bed occupancy, and deaths in England during the second wave (January 2021). Data (black) and model fits (grey) are shown up to the date of the latest available data. Low (blue), medium (purple) and high (red) mobility scenarios are used to project forwards from June to December 2021.