

Evaluating the Roadmap out of Lockdown for England: modelling the delayed step 4 of the roadmap in the context of the Delta variant

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1. Summary

This report summarises the findings of our evaluation of the easing of non-pharmaceutical interventions (NPIs) set out in the UK Government's Roadmap out of Lockdown, focusing on the delayed step 4 of the roadmap and the potential impact of the Delta variant (B.1.617.2). Full methods, data used, and parameter values assumed for forward projections are given in the technical appendix. Key parameters relevant to interpretation of findings are provided in the text.

1. Based on Public Health England (PHE) data available to 2 July 2021, 84% of the adult population in England have received one vaccine dose and 62% have received two doses.
2. Across all transmissibility and vaccine effectiveness (VE) scenarios explored, we estimate that lifting restrictions on 19 July in the context of Delta could lead to a significant third wave of hospitalisations and deaths.
3. The projected scale of the third wave is highly sensitive to small changes in assumptions about vaccine effectiveness. It is also sensitive to the assumed reproduction number of Delta following Step 4.
4. Under optimistic assumptions for both, the third wave is likely to lead to substantially lower numbers of hospitalisations and deaths than seen in the second wave last winter.
5. However, under more pessimistic assumptions, hospitalisations and deaths in the third wave could substantially exceed those seen in the second wave.
6. Our central scenarios suggest hospitalisation numbers comparable with, but deaths substantially lower than, the second wave.
7. If population contact rates only increase gradually between 19th July and 1st September, the third wave will be both delayed and reduced in size compared with a scenario where there is an abrupt change in contact rates following Step 4.
8. In comparison, delaying step 4 until 16 August with a sharp increase in transmissibility at that point, delays the third wave but has less of an impact on peak hospitalisations or total deaths.
9. Emphasis on, and good adherence to, baseline NPIs after 19 July may therefore play an important role in reducing hospitalisations and deaths as it could dampen and slow the increase in (potentially infectious) contact rates in the population.
10. There is considerable uncertainty regarding i) the levels of cross protection against Delta from prior infection with other variants; ii) the proportion of vaccine failure against Delta for severe outcomes (known to be small but unclear how small); and iii) the level of transmission after NPIs are lifted. This translates into large uncertainty in the possible future epidemic trajectory.

2. Introduction

The UK government has set out a roadmap for coming out of lockdown, with several defined stages for relaxing interventions that have been in place to control the spread of SARS-CoV-2. In this report we focus on the potential impact of the delayed “Step 4” of the roadmap hypothetically occurring on i) 19 July 2021; ii) 19 July but with a gradual increase in transmission due to high but waning adherence to baseline NPIs until 1 September; or iii) delayed until 16 August. Our analyses account for the Delta variant being now dominant in all regions of England.

Several key sources of data (as of 2 July 2021) feed into this analysis:

1. The degree of past infection over the course of the UK epidemic from January 2020. This determines the proportion of people who may have natural immunity due to prior infection and is estimated by fitting our transmission model [1] to data on infection prevalence surveys, serology, reported cases via Pillar 1 and Pillar 2 testing, reported hospitalisations and deaths within 28 days of a positive test, and now data on variants and mutations (VAM).
2. The proportion of cases due to the Delta variant over time between 1 May and 2 July 2021 by NHS region, as reported in the VAM data. Our model is fitted to these data to capture the emergence and spread of Delta in each region; the fitted parameters allow us to estimate the effective reproduction number for the Alpha and Delta variants in this time period and inform our assumptions about future transmissibility of the virus (see Methods).
3. PHE data on vaccination coverage over time by age and region, including the proportions receiving their first dose and second doses and the specific vaccine given to each age-group (see Figure 1 for current vaccine coverage).
4. The effectiveness of vaccination against Alpha and Delta variants. This is obtained from a review of clinical trial efficacy data and from UK and international studies on their real-world effectiveness (Table 1).

Forward projections require additional assumptions to be made about three further key determinants of the course of the epidemic:

1. The transmissibility of the circulating virus currently and as interventions are further relaxed at Step 4. We formulate this in terms of the reproduction number for Delta that would occur in the absence of natural- and vaccine-induced immunity ($R_{excl_immunity}$) (Table 4).
2. Future vaccination programme progress - including vaccine supply, roll-out speed, product mix and uptake in younger age-groups (Table 2 and Table 3).

2.1 Characteristics of the Delta variant

We explored the plausible future range of epidemic trajectories given the epidemiological characteristics of Delta, as supported by the current available scientific evidence.

Key factors considered include:

- Current levels of Delta in the community and transmissibility of Delta compared to the previously dominant Alpha variant. This is informed by fitting a multi-variant model to data between 1 May and 2 July (see Methods).

- Cross-protection from prior infection with wild-type or Alpha variants (Table 1).
- Vaccine effectiveness (VE) against Delta (Table 1).
- Increased severity of Delta relative to Alpha with a ~1.85x increased risk of hospitalisation [2].

We consider three scenarios with respect to the level of cross-protection from prior infection with non-Delta variants and vaccine effectiveness against Delta (Table 1) which are principally based on the latest PHE effectiveness studies against the Delta variant (see Vaccine Effectiveness (VE)).

2.2 Vaccine Effectiveness (VE)

Our assumptions regarding the mode of action and effectiveness for each vaccine reflect the most recent available evidence. Table 1 summarises these for the Pfizer, AstraZeneca and Moderna vaccines for Alpha and Delta variants. We assume that vaccine protection against symptomatic disease as determined from the original trials and real-world data also provides a similar level of protection against asymptomatic infection. In line with effectiveness studies, we assumed increasing protection against severe disease and death compared to symptomatic/mild disease. We further assume that, in those vaccinated individuals who do become infected, onward transmission is also reduced.

Note that for our central VE scenario, our values for VE against hospitalisation and death differ slightly from current PHE point estimates for Delta, though lie within the (wide) confidence intervals of the latter ([3,4]). Current PHE estimates apply only to hospitalisation of previously diagnosed Pillar 2 cases, while a substantial proportion of hospitalisations are not preceded by a Pillar 2 test. In addition, the PHE point estimates are higher than past estimates of the VE against death for Alpha. Our adjusted values are in-line with other studies where the VE against death is consistently higher than for hospitalisation. Our optimistic VE scenario uses the PHE point estimates and increases the assumed value of VE against death accordingly.

Note that assuming 100% cross protection from prior infection with the Alpha variant against infection/mild disease and hospitalisation due to Delta only had a 12-15% impact on infections, hospitalisations, and deaths under the central VE assumptions and a return to central R after NPI lifting.

Table 1: Cross-immunity and vaccine effectiveness assumptions for AstraZeneca (AZ), Pfizer (PF), and Moderna (Mod). “Optimistic”, “Central”, and “Pessimistic” cross protection or vaccine effectiveness refers to the degree to which Delta can escape vaccine induced immunity or immunity due to prior infection with non-Delta variants. We assume individuals ≥40 years will receive the mix of vaccines observed thus far and individuals under 40 years will receive PF or Moderna only. *100% protection = complete cross-protection, 0% = no cross-protection

		“Optimistic” cross protection	“Central” cross protection	“Pessimistic” cross protection		
Infection with VOC resulting in protection* vs Alpha		100%	100%	100%		
Infection with Alpha or earlier variants resulting in protection* vs Delta^	Infection/mild disease	100%	85%	75%		
	Hospitalisation	100%	95% (as PF 2 doses)	90% (as PF 2 doses)		
Vaccine Effectiveness (VE)	Vaccine	VE vs Alpha	Optimistic VE vs Delta	Central VE vs Delta	Pessimistic VE vs Delta	Informed by (Alpha/Delta)
Vs death	AZ (1)	80%	81%	80%	75%	Bernal 2021 [5]
	AZ (2)	95%	95%	95%	95%	Bernal 2021 [6]
	PF (1)	85%	93%	85%	80%	
	PF (2)	95%	98%	95%	95%	
	Moderna	Assume same as PF first and second dose				
Vs severe disease	AZ (1)	80%	81%	80%	75%	Vasileiou 2021 [7],
	AZ (2)	90%	94%	90%	85%	PHE [8], Hyams 2021 [9], Stowe 2021 [3]/ Assumed higher than against mild disease, similarly to Alpha
	PF (1)	85%	93%	85%	80%	Hyams 2021 [9]

						Hall 2021 [10], Stowe 2021 [3]
	PF (2)	95%	98%	95%	90%	PHE [11]/assumed higher than against mild disease, similarly to Alpha, Stowe 2021 [3]
	Moderna	Assume same as PF first and second dose				
Vs mild disease	AZ (1)	50%	45%	33%	20%	Voysey 2020 [12], Stowe 2021 [3]
	AZ (2)	74%	70%	58%	45%	Voysey 2021 [13]/ PHE [12-14]
	PF (1)	50%	45%	33%	20%	PHE [15] , Sheikh 2021 [2]
	PF (2)	93%	90%	85%	78%	Hall 2021 [10] / PHE [14]
	PF (2)	93%	90%	85%	78%	Hall 2021 [10]/ PHE [14], Sheikh 2021 [2]
	Moderna	Assume same as PF first and second dose				
Vs infection	AZ (1)	50%	45%	33%	20%	Assumed same as disease, Sheikh 2021 [2]
	AZ (2)	74%	70%	58%	45%	
	PF (1)	50%	45%	33%	20%	
	PF (2)	93%	90%	85%	78%	
	Moderna	Assume same as PF first and second dose				
Vs infectiousness if infected	AZ/PF/Mod (1)	45%	45%	40%	35%	Harris 2021 [16]/Assumed
	AZ/PF/Mod (2)	45%	45%	40%	35%	Harris 2021 [16]/Assumed

2.3 Vaccination Coverage

Data on vaccine uptake by age and product over time and for each NHS region were provided by PHE. Current uptake by age for England is summarised in Figure 1. Note that these data are the same as reported on the COVID-19 dashboard [17].

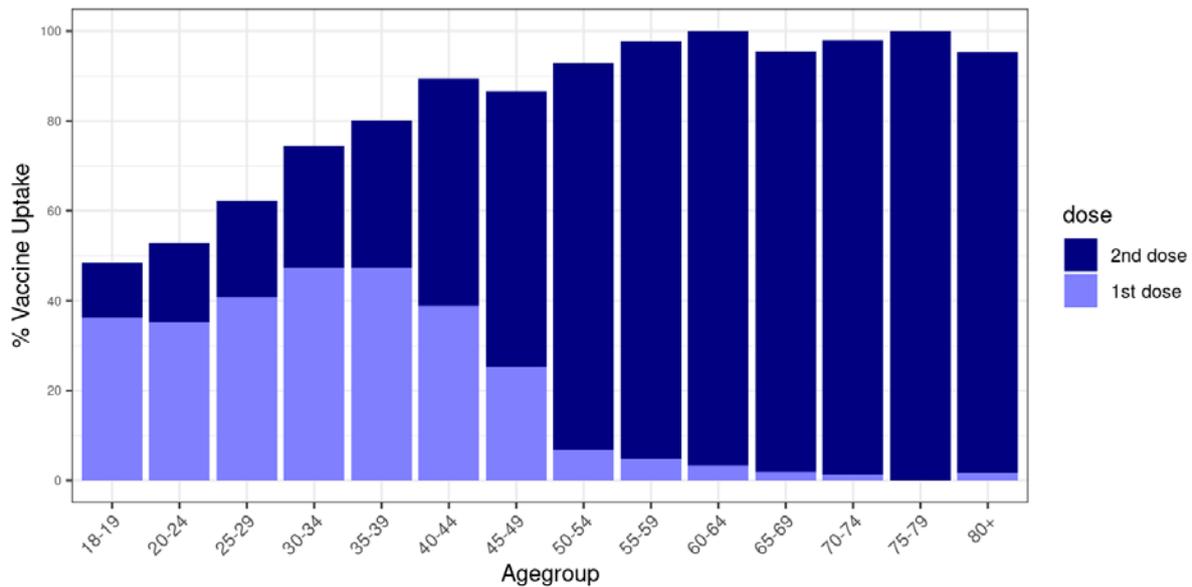


Figure 1: Cumulative vaccine uptake by 2 July 2021 by age for England shown for first (light blue) and second (dark blue) doses. Shown as the proportion of the population age group of England (ONS).

Projections of vaccine roll-out provided by DHSC for this exercise are summarised in Table 2.

Table 2: Pre-specified vaccination schedule (million doses per week)

	Weeks commencing	Average doses per week
England	up to 12 July 2021	1.9M
	19 July 2021 onwards	2.0M

For the forward projections, the modelled uptake is summarised in Table 3. For the older age-groups, we use the vaccine coverage that has been obtained for dose 1 if this is higher than the assumed uptake and we assumed the same uptake will be achieved for dose 2. For the younger age-groups where uptake remains below our assumed levels, we use these values for both dose 1 and dose 2.

Table 3: Latest vaccine uptake reported by the NHS and our assumptions by group or age for England.

Group	Reported NHS first dose uptake data up to 27 June [^]	Modelled first dose uptake at start of simulation (2 July)	Maximum uptake in the simulation
Care home residents (CHR)	-	92%	95%
Care home workers (CHW)	-	86%	86%
80+ years*	94.1%	96%	95%
75-79 years*	100% ⁺	99%	99%
70-74 years*	97.6%	99%	99%
65-69 years*	95.2%	97%	97%
60-64 years*	99.9%	99%	99%
55-59 years*	97.7%	98%	98%
50-54 years*	92.2%	95%	95%
45-49 years*	86.0%	89%	90%
40-44 years*	88.7%	91%	90%
35-39 years*	79.6%	81%	80%
30-34 years*	73.9%	76%	80%
25-29 years*	60.9%	64%	80%
18-24 years*	47.9%	20-24 years*: 53%	80%
		18-19 years*: 24%	80%

* Not working or residing in a care home. [^] [COVID-19 weekly announced vaccinations 1 July 2021 \(data up to 27 June\)](#). ⁺Signifies the number who have received their first dose exceeds the latest official estimate of the population from the ONS for this group.

2.4 Estimating contact rates following step 3

We fitted a multi-variant transmission model to a number of data streams including cases reported in the VAM data in each England NHS region between 1 May and 2 July 2021 to account for the joint transmission dynamics of the Alpha and Delta variant. We estimated the current effective reproduction numbers (R_{eff}) and the corresponding reproduction number excluding immunity ($R_{excl_immunity}$) separately for Alpha and Delta, which were used to inform assumptions about transmission in the future, formulated in terms of $R_{excl_immunity}$ for Delta; see appendix “Transmissibility associated with re-opening steps”. $R_{excl_immunity}$ for Delta was assumed to be 0.5 lower during the school holidays, due to lower contact rates between children. We assumed an average school holiday pattern across England until summer 2022.

2.5 Projected increases in population contact rates resulting from roadmap step 4

Table 4 summarises our assumptions for Step 4 for England. To capture the easing of restrictions at Step 4 in England, we do not model specific or detailed policy changes due to the uncertainty around their impact. Instead, we sample from a range of values for R in the absence of natural and vaccine-induced immunity (specified as a probability distribution, see Supplementary Figure 5) that could occur at that stage.

We examine three scenarios for the impact of step 4 – an increase of $R_{excl_immunity}$ for Delta to an average of 5.5 (central R after NPI lifting), 4.5 (low R after NPI lifting), or 7.0 (high R after NPI lifting). The central value corresponds to an approximate doubling of contacts at step 4, compared to step 3, while the low and high values assume contact rates at step 4 would be between 1.5- and 2.5-fold those at step 3 [18].

We assumed Step 4 would occur on 19 July or delayed 4-weeks until 16 August. As a sensitivity analysis, we also explored the impact of Step 4 occurring on 19 July, but with a gradual (rather than sudden) increase in transmissibility up to $R_{excl_immunity} = 5.5$ by 1 September 2021.

We further assumed a slight seasonal trend in SARS-CoV-2 transmissibility throughout the year (see appendix 2).

Table 4: Summary of NPI easing scenarios for England where restrictions are eased on specific dates resulting in an increase in transmissibility. The average R in the absence of immunity ($R_{excl_immunity}$) and 95% quantiles for the Delta variant at each stage are shown.

Delta $R_{excl_immunity}$ for the rest of Step 3	Date of full NPI lifting (step 4)	Delta $R_{excl_immunity}$ for Step 4
School holidays: 2.2 (1.4 – 3.3) School terms: 2.7 (1.9 – 3.8)	19 July	<u>Central scenario</u> School holidays: 5.0 (3.7 – 6.6) School terms: 5.5 (4.2 – 7.1)
		<u>Lower R following full NPI lifting</u> School holidays: 4.0 (2.7 – 5.7) School terms: 4.5 (3.2 – 6.1)
	16 August	<u>Higher R following full NPI lifting</u> School holidays: 6.5 (5.2 – 8.1) School terms: 7.0 (5.6 – 8.6)
	19 July (R increases gradually to 1 September*)	<u>Central scenario</u> School holidays: 5.0 (3.7 – 6.6) School terms: 5.5 (4.2 – 7.1)

*step 4 R values reached on 1 September

3. Results

In all scenarios modelled where Step 4 occurs on 19 July, R_{eff} is projected to rise from just above 1 to over 2.5 after step 4 of the roadmap (Figure 2), resulting in a third wave of infections. The magnitude of this wave is highly uncertain, depending on the assumed cross protection and vaccine effectiveness against Delta and the level of mixing after that step.

Despite assuming a high vaccine effectiveness against severe disease and death (Table 1), a substantial corresponding wave of hospitalisations and deaths could occur (Figure 4). The magnitude of hospitalisations is highly dependent on the level of cross protection, vaccine effectiveness, and contacts after 19 July, with peak admissions ranging from approximately a quarter to 6-fold higher than the winter wave (Figure 4).

In the most optimistic (optimistic VE and low R after NPI lifting) and pessimistic (pessimistic VE and high R after NPI lifting) scenarios considered, an additional 9,400 (95% CrI: 4,600, 19,800) to 115,800 (95% CrI: 81,700, 143,600) deaths could occur by 1 June 2022

respectively (Table 5), illustrating the high uncertainty in the total number of projected deaths across all scenarios (Figure 6).

If voluntary adherence to current step 3 restrictions wanes gradually over the summer to 1 September 2021, and assuming central R after NPI lifting, the resulting third wave is delayed by about a month (with a peak in September) and hospitalisations and deaths are dampened compared to the scenario with a steep increase in transmission on 19th July. Peak hospital admissions is reduced by >30%.

Delaying step 4 by 4 weeks until 16 August further delays the peak in hospitalisations until October allowing more time to implement additional measures such as booster vaccination campaigns.

In all scenarios, future deaths are projected to occur predominantly in individuals 75 years and above who have received two vaccine doses (due to very high uptake of an imperfect vaccine, Table 3). However, a substantial number of deaths are also projected to occur in fully vaccinated adults aged 50 – 74 years (Figure 7).

We did not model further mitigating measures such as booster doses; although their impact will depend on the speed of delivery, these may be critical to mitigate a third wave in the autumn if adherence to NPIs is high enough so that the third wave is delayed until then.

4. Conclusions

Our results highlight the large uncertainty regarding both the level of cross protection and vaccine effectiveness against Delta as well as the transmissibility after NPIs are lifted at step 4. This translates into large uncertainty on the possible future epidemic trajectory. However, all scenarios considered resulted in a substantial third wave of infections and hospitalisations. If adherence to current step 3 measures wanes gradually over the summer (rather than a sudden increase in transmissibility on 19 July), then the wave of hospitalisations and deaths can be substantially reduced and delayed. Therefore, whilst the impact of Test Trace Isolate (TTI), mask wearing, hand hygiene, and COVID security on R is difficult to quantify, it will be vital to emphasise the importance of normalising and ensuring adherence to all measures even after “full lifting” is achieved. For both scenarios where step 4 is delayed, or there is a gradual waning in adherence to step 3 measures, the projected third wave is delayed, allowing more time for further mitigating measures such as booster doses to be implemented.

Given the large uncertainty regarding the possible magnitude of the future wave, continuous careful monitoring of the epidemic trajectory will be critical as will further evidence on vaccine effectiveness against the Delta variant.

Preventing the further importation and spread of variants of concerns (VOC) with moderate to high immune escape properties will be critical as these could lead to future waves orders of magnitude larger than the ones experienced so far.

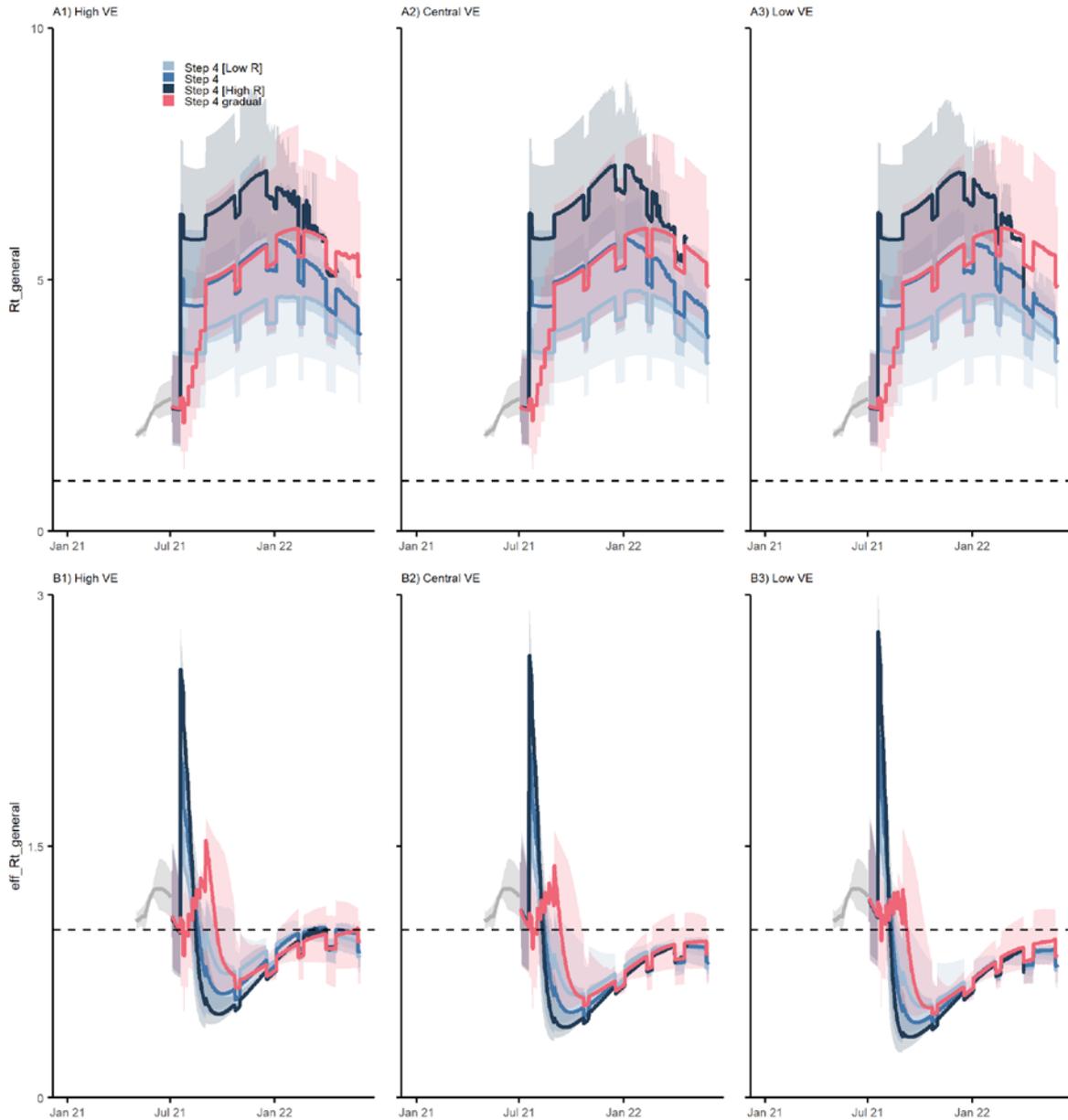


Figure 2: Reproduction number excluding immunity (top row) and the effective reproduction number R (bottom row) accounting for natural- or vaccine-induced immunity (overall for both Alpha and Delta) in England assuming Step 4 occurs on 19 July with central (blue), low (light blue) and high (dark blue) R after full NPI lifting or on 19 July but transmissibility increasing gradually to 1 September up to “central” R after NPI lifting (pink) (see Table 4), projecting forwards to 1 June 2022. We consider vaccine effectiveness against Delta to be from left to right: (High VE) optimistic; (Central VE) central; and (Low VE) pessimistic (see Table 1).

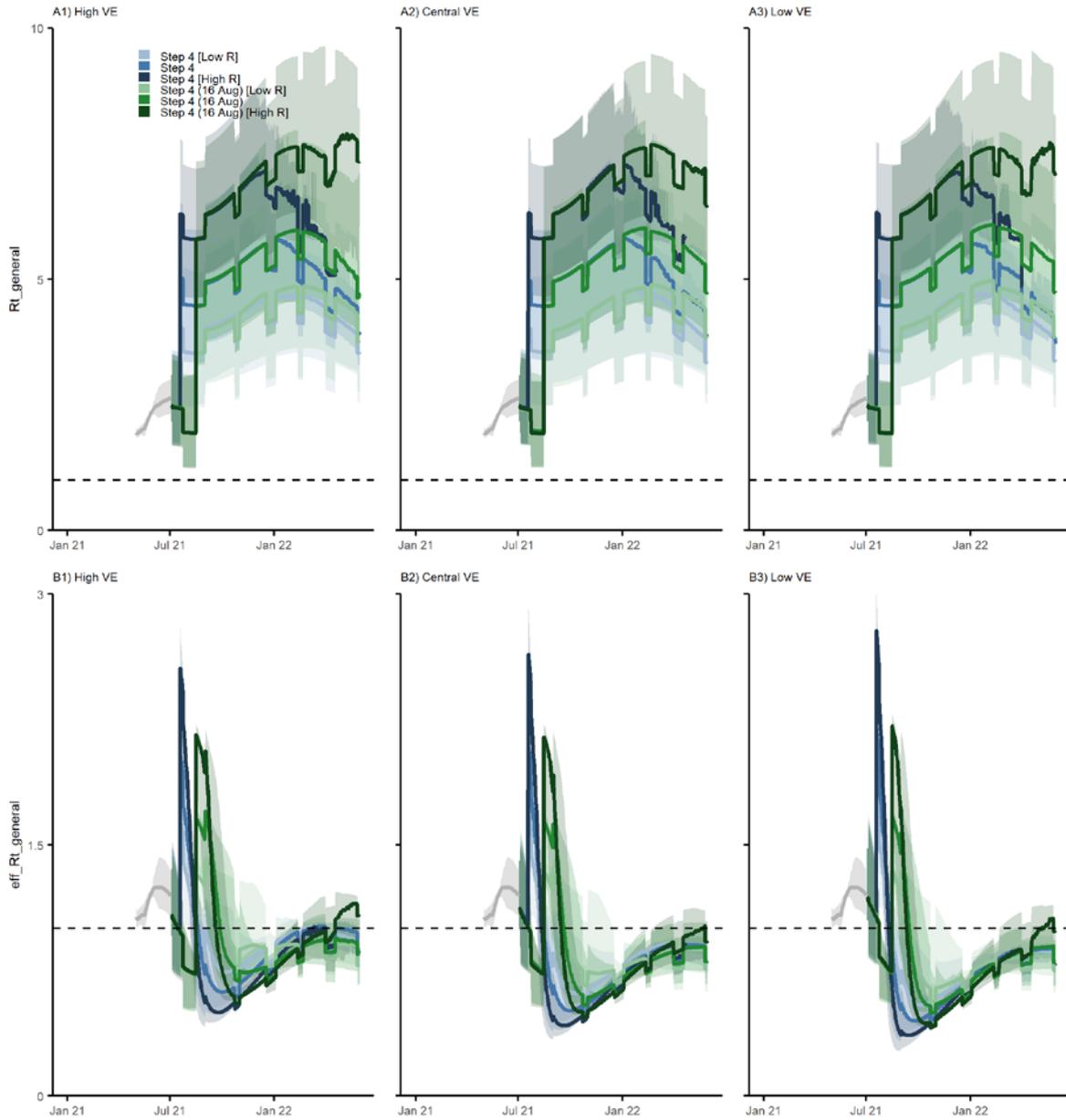


Figure 3: As Figure 2 but showing Step 4 at 19 July (blue) or delayed until 16 August (green) with low (light blue/light green), central (blue/green), or high (dark blue/dark green) R after full NPI lifting.

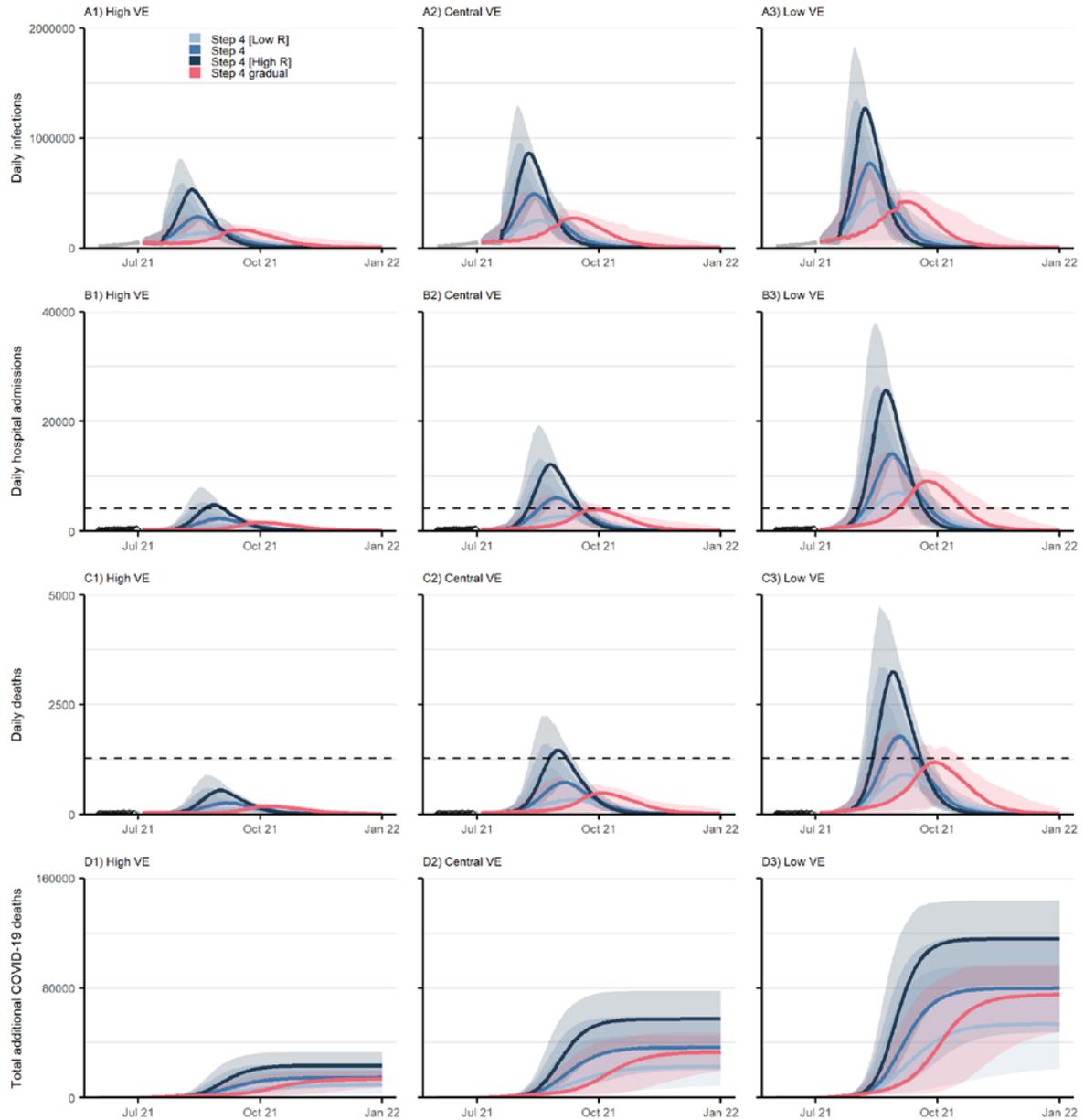


Figure 4: COVID-19 daily infections (top row), hospital admissions (second row), deaths (third row), and cumulative deaths from 2 July (bottom row) in England for Step 4 occurring on 19 July with central (blue), low (light blue), and high (dark blue) R after full NPI lifting or on 19 July but transmissibility increasing only gradually until 1 September up to “central” R after NPI lifting (pink) (see Table 4), projecting forwards to 1 January 2022. We consider vaccine effectiveness against Delta to be, from left to right: (High VE) optimistic; (central VE) central; and (Low VE) pessimistic (Table 1). The dashed horizontal lines show the peak of the winter wave for daily hospital admissions (second row) and deaths (third row). The coloured lines show the median and the shaded areas show 95% credible intervals. The points at the start of the plot show the data (admissions and deaths only) and the grey line the model fit (see Supplementary Figure 4). Note the y-axis scale is different in each row.

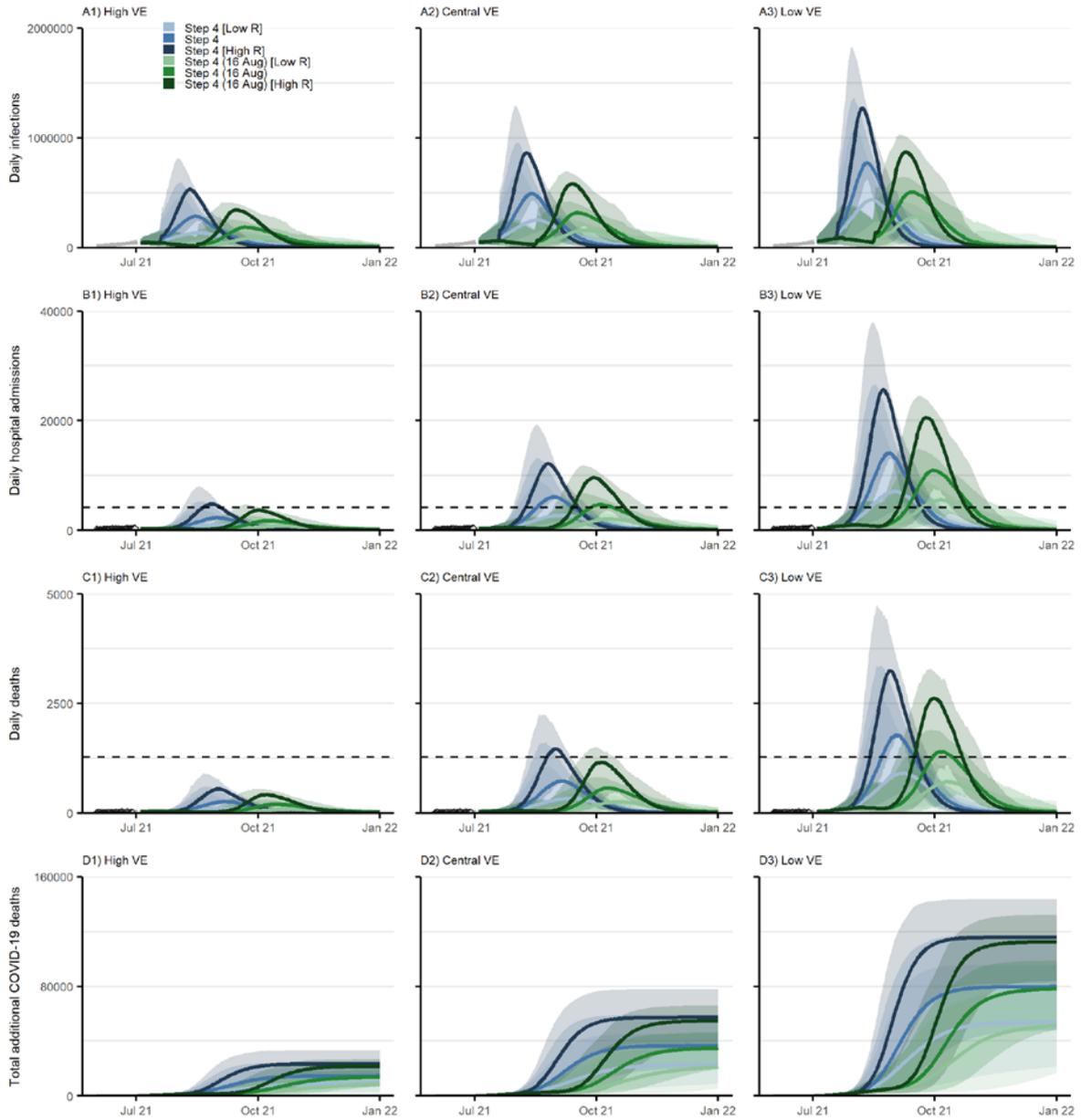


Figure 5: As Figure 4 but showing Step 4 at 19 July (blue) or delayed until 16 August (green) with low (light blue/light green), central (blue/green), or high (dark blue/dark green) R after full NPI lifting.

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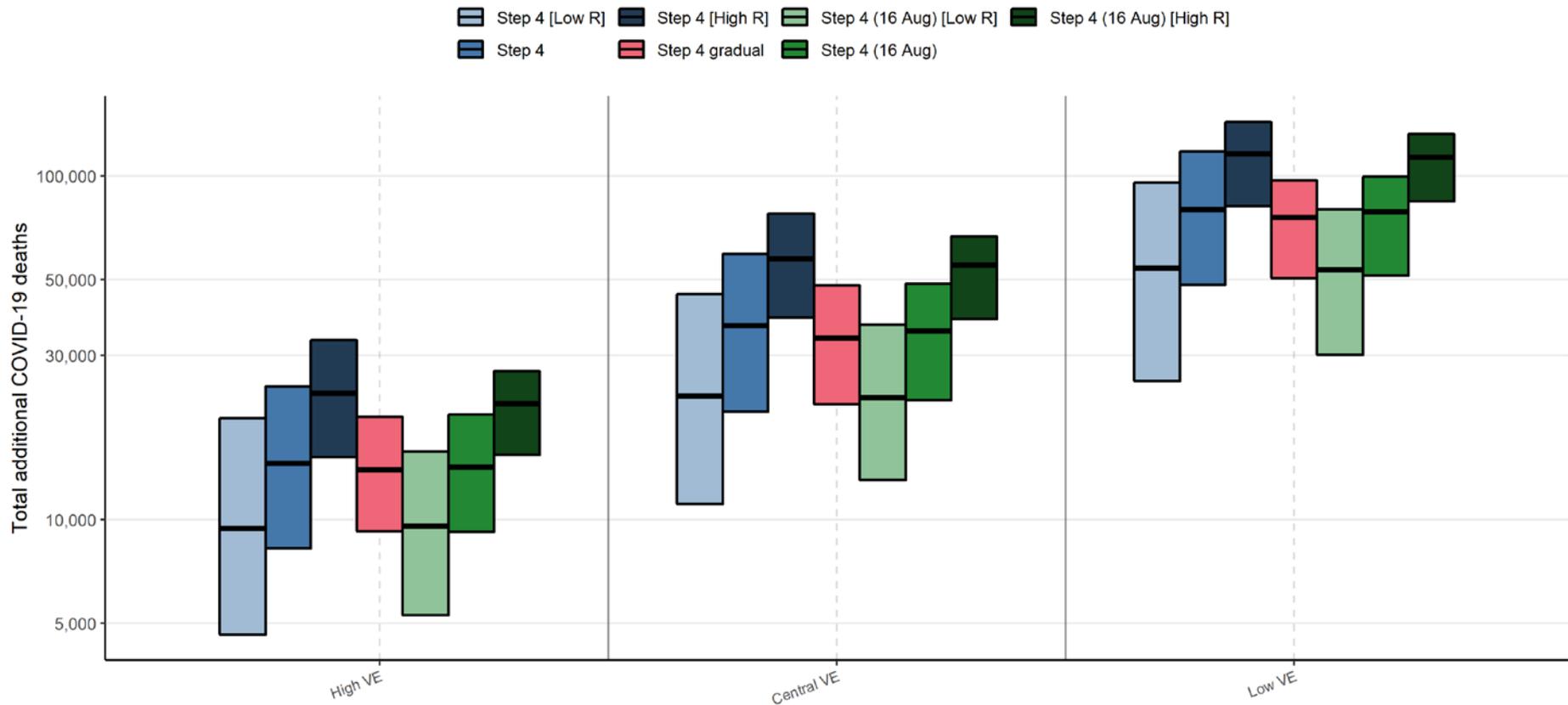


Figure 6: Sensitivity analysis showing cumulative COVID-19 deaths in England (counted from 2 July 2021 up to 1 June 2022). From left to right for each panel, Step 4 occurring on 19 July (blue: low, central, and high R after full NPI lifting), Step 4 on 19 July, but transmissibility increases gradually to 1 September (pink: central R after full NPI lifting), or delayed until 16 August (green: low, central, and high R after full NPI lifting) (see Table 4). Panels from left to right: (High VE) assume Delta has “optimistic”; (Central VE) “central”; (Low VE) “pessimistic” vaccine effectiveness respectively (see Table 1). Note that the y-axis is on a logarithmic scale.

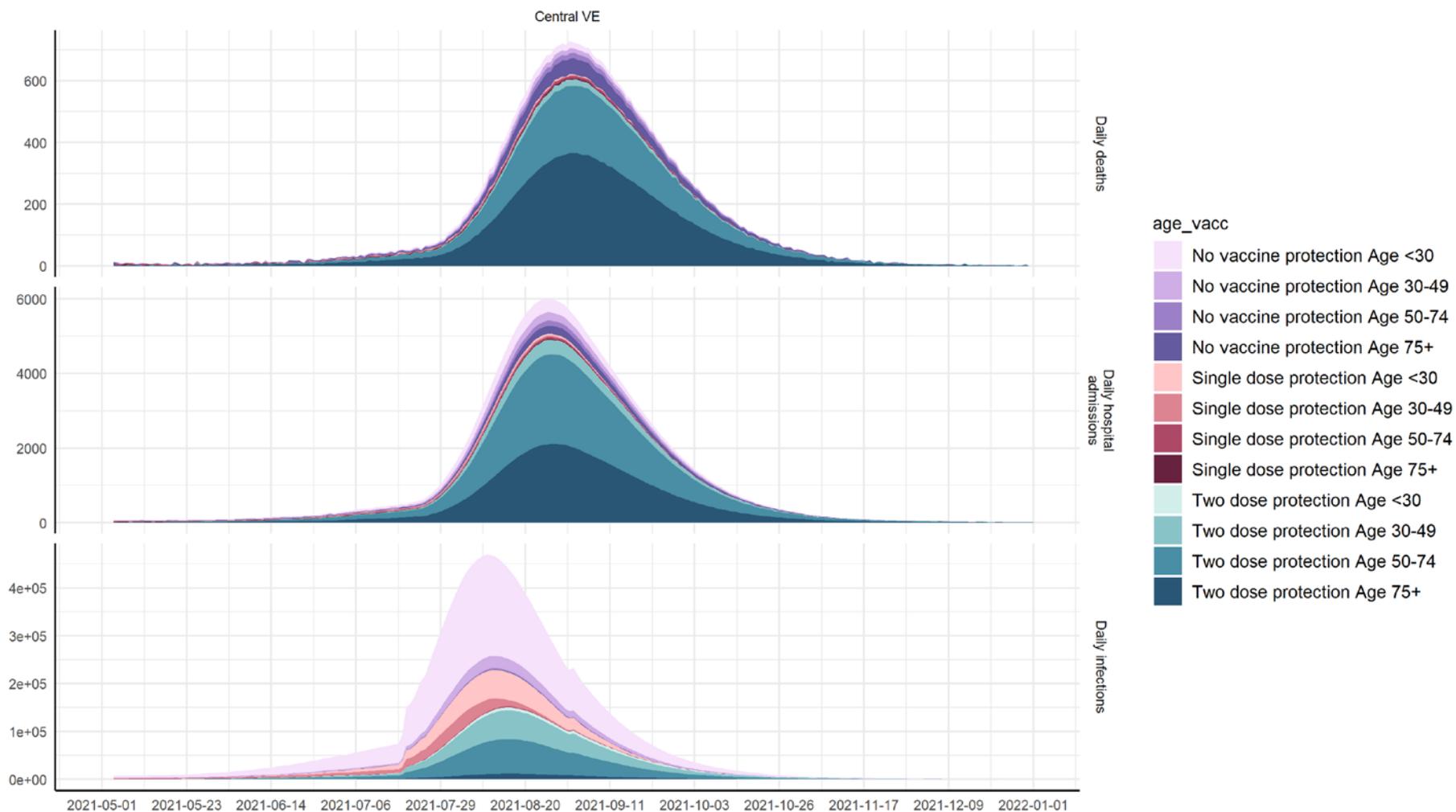


Figure 7: England COVID-19 daily (top) deaths, (middle) hospital admissions, (bottom) infections by age group and vaccination status assuming central vaccine effectiveness properties against Delta and Step 4 occurs on 19 July with a return to “central” R after NPI lifting (Table 1 and Table 4).

Table 5: Cumulative deaths, hospital admissions, and incidence in England (median (95% CrI), nearest 100) between 2 July 2021 and 1 June 2022. Results assume return to different baseline NPIs of $R_{excl_immunity}$ depending on the scenario (see Table 4 and appendix 2 for details). All scenarios assume a starting value of $R_{excl_immunity}$ of Delta of on average 2.7 for the rest of step 3 (schools open).

Analysis type				Cumulative deaths (95%CrI)	Cumulative hospital admissions (95%CrI)	Cumulative incidence (95%CrI)		
VE vs Delta*	Vaccinated age groups	Date of NPI lifting	R after full lift***	Up to 1 June 2022				
Optimistic	18+	19 July	Low	9400 (4600, 19800)	77500 (38700, 155100)	9557400 (5457700, 16120900)		
			Central	14600 (8200, 24400)	118600 (69400, 196100)	13158300 (8776100, 18732100)		
			High	23300 (15200, 33300)	184600 (127000, 257700)	17780100 (13636800, 21987600)		
				19 July w/ gradual increase in R to 1 Sep	Central	14000 (9200, 19900)	112500 (79800, 158900)	12122100 (9525600, 16143800)
		16 August	Low	9600 (5300, 15800)	78900 (43200, 127400)	9435100 (5869400, 13633400)		
			Central	14200 (9200, 20200)	114500 (79300, 159800)	12154000 (9511300, 15657200)		
			High	21700 (15400, 27100)	172600 (132900, 212400)	15794700 (13290500, 18453200)		
		Central	18+	19 July	Low	22900 (11100, 45300)	179600 (87500, 347900)	14732600 (8309000, 23999900)
					Central	36700 (20600, 59200)	283500 (161800, 445400)	20426300 (13389500, 27866200)
High	57300 (38700, 77700)				431600 (304000, 580100)	26934100 (21150100, 32306100)		
				19 July w/ gradual increase in R to 1 Sep	Central	33700 (21600, 48000)	258300 (173600, 360000)	18302300 (13683600, 24075900)
16 August	Low			22700 (13000, 36900)	175900 (102600, 287100)	13921000 (9366200, 20565500)		
	Central			35300 (22200, 48700)	270600 (178400, 370200)	18597000 (13881300, 23683300)		
	High			55000 (38300, 66600)	414100 (308600, 500700)	24461800 (19946900, 28160500)		

Pessimistic	18+	19 July	Low	53900 (25300, 95600)	397800 (187100, 689000)	21999600 (12091300, 32496900)		
			Central	79700 (48100, 117500)	579100 (355400, 832000)	28607100 (19874000, 36073400)		
			High	115800 (81700, 143600)	820700 (620200, 1034400)	35619400 (29544000, 40587000)		
				19 July w/ gradual increase in R to 1 Sep	Central	75500 (50400, 97200)	546000 (375600, 691800)	26391400 (19750100, 32098500)
		16 August	Low	53300 (30100, 79800)	389200 (222200, 581300)	20622700 (13594900, 28132000)		
			Central	78700 (51200, 99400)	566700 (382200, 721200)	26623100 (19974400, 32048400)		
			High	113000 (84200, 132300)	815300 (645200, 932600)	33699400 (28478200, 36694200)		

* See Table 1 for Delta vaccine effectiveness/cross protection details. *** $R_{excl_immunity}$ used after NPI relaxation (see Table 4, and appendix 2 for details).

5. Appendix 1: Caveats and key assumptions ^{*}*new since last report*

1. The lifting of NPIs has been modelled as a stepwise increase in R. We do not model any specific policy change, rather an assumed change in the corresponding level of transmission. Note that there is **considerable uncertainty around these assumptions**.
2. We assume that baseline control measures such as face coverings, case isolation (and TTI), and hand hygiene are retained and adhered to even after “fully lifting” NPIs (Table 4) (*optimistic*). If such measures are not kept, we would expect a larger wave of hospitalisations and deaths than projected.
3. We do not model any “booster” vaccines designed to enhance protection against Delta or other VOCs (*pessimistic*).
4. We have not modelled different dosing schedules by age group.
5. We model the potential impact of Delta, but we note that there remains uncertainty regarding the effectiveness of vaccines against Delta infection, severe disease, death and onward transmission [14]. Vaccine effectiveness against these endpoints (VE vs death being newly introduced) have been updated (higher) since the last report based on newly available evidence^{*}.
6. We assumed infection with the **Delta variant was more severe than Alpha** with the risk of hospitalisation increasing ~1.85 times [2].
7. Our current estimates of the duration of hospital stay range from 6.6 days (95% CrI: 5.5, 8.3) in the South West, to 14.8 days (95%CrI: 13.1, 18.1) in London.
8. We estimate the current values of R_{eff} and $R_{excl_immunity}$ for Alpha and Delta by fitting a multi-variant compartmental model to the VAM data set between 1 May and 2 July 2021, in England.
9. We assume **infection-induced immunity wanes exponentially over time**, with an average time to loss of protection of 3 years (*pessimistic*).
10. Our central scenario **incorporates seasonality in transmission** with a +/-10% relative change in transmissibility throughout the year.
11. We assume that vaccine roll-out pace of 2.0M doses/week from 19 July 2021 onwards can be maintained (unclear).
12. We assume **high vaccine uptake for both doses** (*optimistic*).
13. We assume the vaccines provide protection against infection in addition to protection from severe disease and death (*optimistic*).
14. We assume the vaccines prevent to a certain extent, an infected person who is vaccinated from transmitting the virus (*optimistic, assumed as part of “central” assumptions*).
15. We model school holidays by assuming an average decrease in $R_{excl_immunity}$ for Delta of 0.5 whilst schools are closed.
16. We model transmissibility at step 3 as lower than previously assumed^{*}
17. We assume **no correlation between vaccine uptake and risk of severe infection**. If uptake were to be lower in groups at higher risk of severe disease (e.g. ethnic groups), our results would be too optimistic in terms of hospitalisations and deaths (*optimistic*).
18. We do not model differential infectivity or susceptibility by age.
19. We assume no dynamic replenishment of the care-home population (*optimistic*).
20. We fit our stochastic model to multiple data sources simultaneously. In our latest iteration, the model has captured hospitalisation trends well, including deaths within hospital. There is still considerable uncertainty to how well we are predicting deaths

outside hospitals. Additional data regarding vaccine effectiveness against severe disease caused by Delta may help to capture these trends more robustly.

21. We model Moderna vaccine distribution assuming it has the same effectiveness as Pfizer (*unclear*).
22. We assume that all individuals under 40 years will now receive the Pfizer or Moderna vaccine and 40+ will continue to receive the distribution of vaccines observed thus far.
23. We have not modelled a slower vaccine roll-out (*optimistic*).

6. Appendix 2: Methods

We used a stochastic compartmental model of SARS-CoV-2 transmission fitted to multiple data streams from each NHS region in England. The model is stratified into 17 five-year age groups (0-4, 5-9, ..., 75-79, 80+), a group of care home residents (CHR) and a group of care home workers (CHW). The model has been described in detail elsewhere [1]. The model was extended to include vaccination where each compartment in the model is further stratified to account for vaccination status. We used parameter values calibrated to data from 2 July 2021. The model was fitted with vaccination (both first and second doses) as reported by DHSC to SPI-M (Figure 1).

Definitions of the reproduction number

Throughout, we consider two definitions of the reproduction number:

- **The reproduction number in the absence of immunity, $R_{excl_immunity}$** , defined as the average number of secondary infections that an infected individual would generate in a large population with no immunity. $R_{excl_immunity}$ depends on the virulence of the pathogen and the contact patterns in the population, but not the level of population immunity. We use different values of $R_{excl_immunity}$ to reflect different levels of mixing associated with different levels of restrictions, irrespective of the level of immunity in the population (see next section). $R_{excl_immunity}$ also captures the increase in transmissibility resulting from the emergence of the Alpha variant during the autumn.
- **The effective reproduction number, R_{eff}** , defined as the average number of secondary infections that an infected individual will generate with current levels of population immunity. R_{eff} depends on the virulence of the pathogen, the contact patterns in the population and the level of immunity in the population. We use R_{eff} to characterise the extent to which the epidemic is under control, with $R_{eff} > 1$ in a growing epidemic and $R_{eff} < 1$ in a declining epidemic.

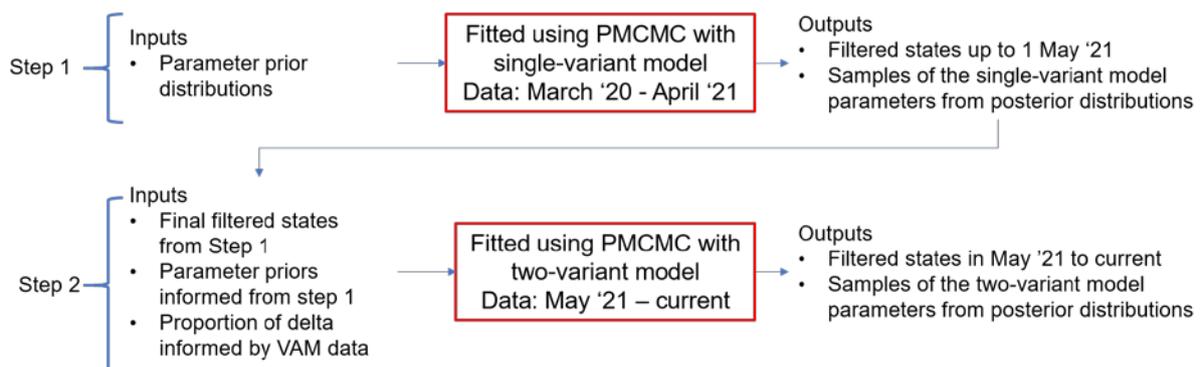
$R_{excl_immunity}$ and R_{eff} are linked through the proportion of the population who is immune (because of infection- or vaccine-induced immunity) p_{immune} , with $R_{eff} = R_{excl_immunity} * (1 - p_{immune})$.

Transmissibility associated with re-opening steps

We modelled levels of restrictions in line with the reopening steps set out in the roadmap [19]. For step 4, this includes baseline NPIs with TTI, hand washing & masks and some Covid-secure measures in places such as public transport and crowded indoor spaces.

To account for the emergence of the Delta variant, our dynamic transmission model is calibrated in two steps (Supplementary Figure 1). We first run the inference using a single variant model until 1 May. While the model only includes one variant, some of the fitted epidemiological parameters (such as the transmission parameters or the probability of dying in hospitals) are time-varying. These time-varying parameters capture the trends observed in the data following changes in behaviour, in treatment practice, or the displacement of the wild-type virus by the Alpha variant. After 1 May, we switch to a two-variant model and propagate the information from the first inference step in two ways.

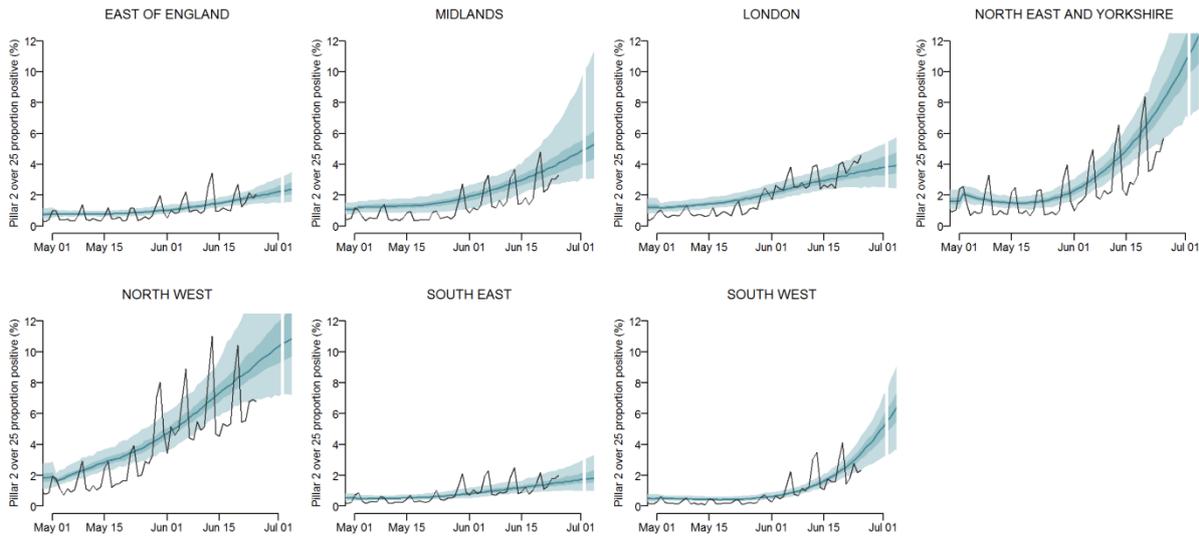
First, we propagate the sample of filtered end model states on 1 May (obtained with the particle MCMC algorithm [1]) and use it as the initial distribution of the two-variant model. To capture the regional heterogeneities in the proportion of Alpha and Delta cases on 1 May, we also fit to the initial proportion of Delta variant cases. Second, we propagate the information from the fitted posterior distributions of parameters common between step 1 and 2. We fit a functional form to each of the parameters using the samples from the marginal posterior distributions from step 1 using maximum likelihood. These distributions are then used as priors for step 2.



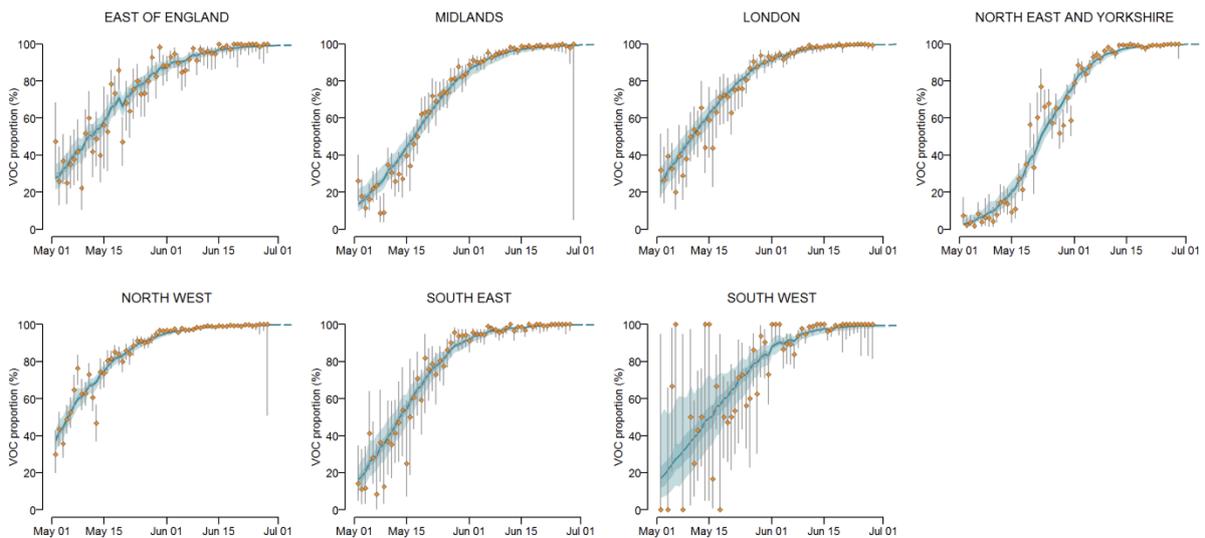
Supplementary Figure 1: Two-step fitting procedure used to calibrate the model to the emergence of the Delta variant. VAM data = variant and mutation data.

Additionally, to the data streams such as the proportion of pillar 2 positive cases aged 25+ years and other hospital data streams (Supplementary Figure 2 and Supplementary Figure 4) used to fit from March 2020 to April 2021, from 1 May to 2 July, the two-variant model was fitted to the variant and mutation (VAM) dataset which gives an indication of the proportion of Alpha and Delta cases by NHS region (Supplementary Figure 3).

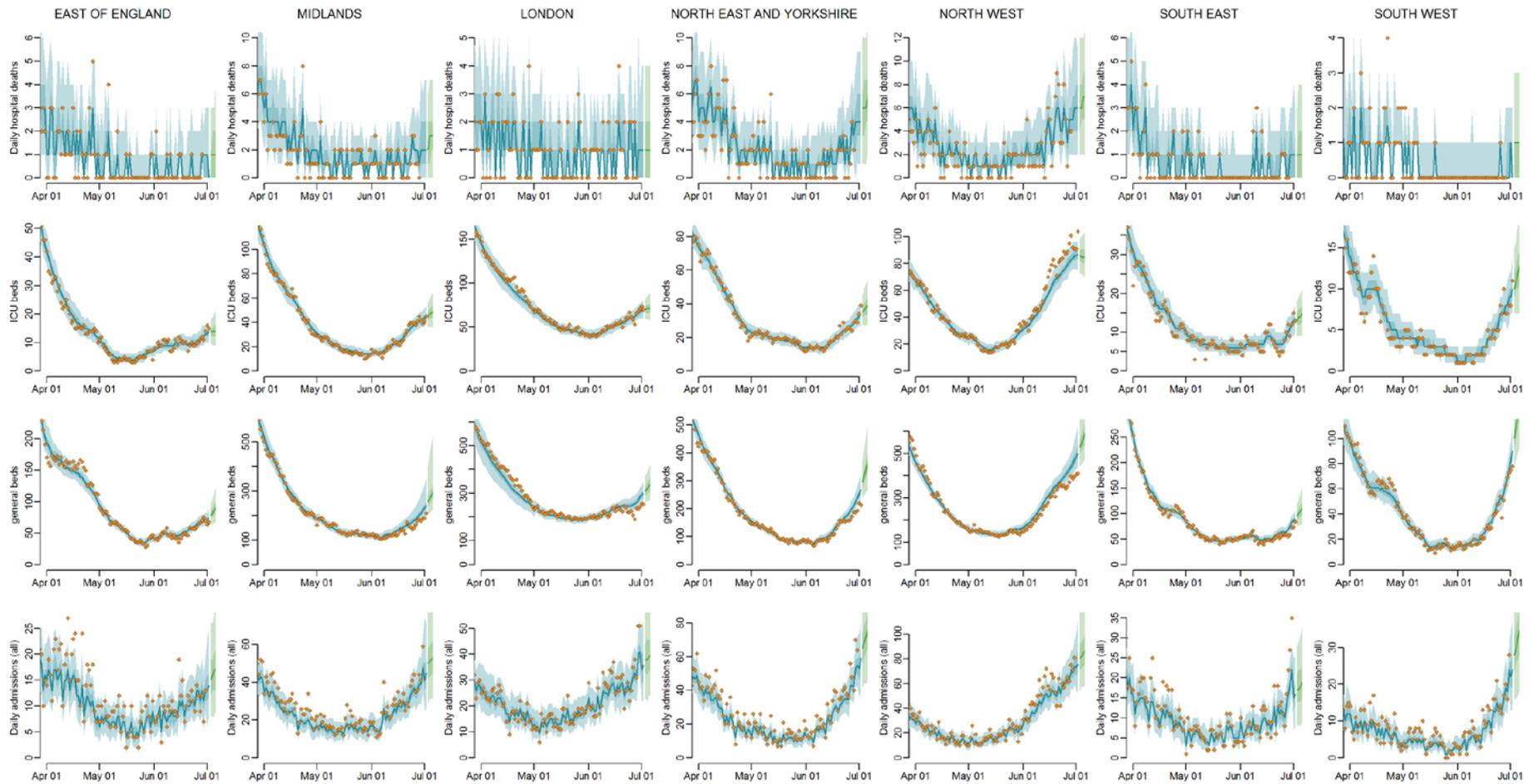
We used the resulting estimated R_{eff} for Alpha and Delta, and the proportion of the population protected against each of the variants, as estimated from our dynamic transmission model, to determine the reproduction number excluding immunity ($R_{excl_immunity}$) for both variants, reflecting the current level of mixing after step 3, and the transmission advantage of Delta, compared to Alpha. This corresponded to a reproduction number excluding immunity ($R_{excl_immunity}$) for Delta of 2.7 for schools opened during step 3. This reproduction number was then used for the whole period until step 4.



Supplementary Figure 2: Model fit to the proportion of pillar 2 positive cases aged 25+ years between 1 May and 2 July 2021 in NHS regions in England. The line show the data, the blue solid line shows the model fit, and the light and dark blue shaded area the 50% and 95% CrI respectively.



Supplementary Figure 3: Model fit to the proportion of Delta variant cases between 1 May and 2 July 2021 in NHS regions in England. The points show the data, the bar the 95% CI, the blue solid line shows the model fit to these data, and the light and dark blue shaded area the 50% and 95% CrI respectively.



Supplementary Figure 4: Model fits from April – July 2021 to hospital data streams by NHS region. Model fits to daily hospital deaths (deaths within 28 days of a positive test, top row), ICU bed occupancy (second row), general bed occupancy (third row), and all daily admissions (bottom row) by region (columns). The points show the data, the solid line the median model fit and the shaded area the 95% CrI.

There is substantial uncertainty around the level of transmissibility associated with specific policy changes. To capture this uncertainty, we assumed $R_{excl_immunity}$ under each level of restrictions was distributed around the mean values described above, using lognormal distributions shown in Supplementary Figure 5.

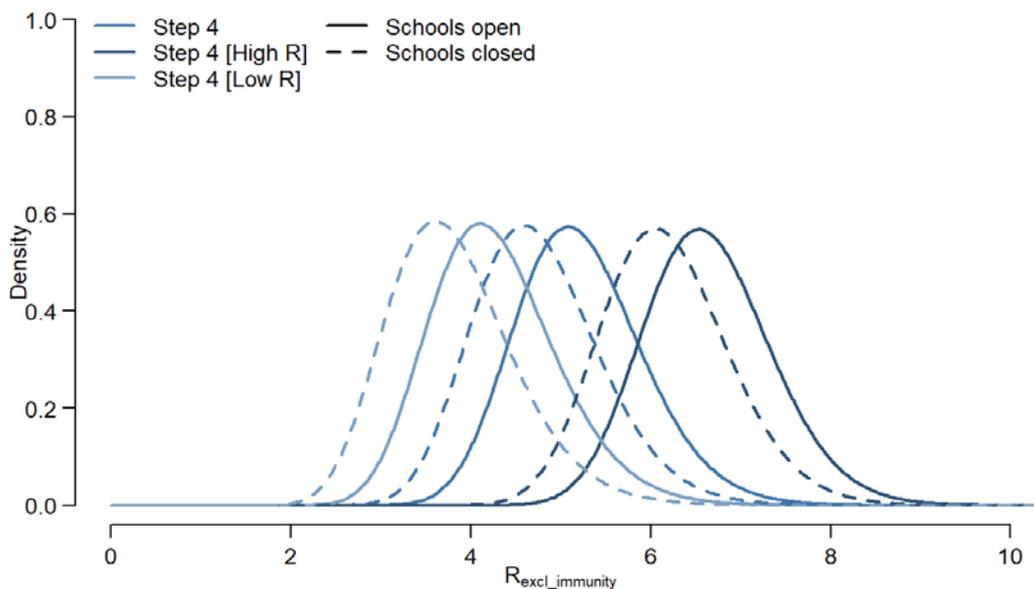
We model three scenarios for the final step of NPI lifting (step 4):

1. Step 4 occurs on 19 July and $R_{excl_immunity}$ increases to 5.5 on that date
2. Step 4 occurs on 19 July, and transmissibility increases gradually in stepwise weekly increments from 19 July to $R_{excl_immunity} = 5.5$ by 1 September 2021.
3. Step 4 is delayed by four weeks until 16 August and $R_{excl_immunity}$ increases to 5.5 on that date.

For scenarios 1 and 3 described above, we also explored a return to two alternative (low and high) levels of $R_{excl_immunity}$ (see Table 4) on the date of NPI lifting.

The reproduction numbers assumed in the steps above are assuming schools are opened. In addition, we assumed that closing schools, e.g. during school holidays, will decrease $R_{excl_immunity}$ for Delta by an average -0.5.

For each NPI lifting scenario, we sampled from the relevant distributions of $R_{excl_immunity}$ at each step of lifting (including school holidays) and generated sampled trajectories of $R_{excl_immunity}$ over time by matching the ranked values obtained for each step. This constraint was added to ensure that $R_{excl_immunity}$ could only increase over time except for the time period when schools were closed. The resulting distributions of R over time may therefore differ slightly from those shown in Supplementary Figure 5 because of this additional constraint. Supplementary Table 1 shows the estimated weekly growth rates after step 4.



Supplementary Figure 5: Distributions of transmissibility ($R_{excl_immunity}$) for Delta associated with step 4 of NPI lifting in England. Values of $R_{excl_immunity}$ were constrained so they could only increase over time except during school holidays when $R_{excl_immunity}$ was decreased on average by -0.5.

Supplementary Table 1: Estimated daily growth rates (given to 3 dp) after step 4 NPI releases under different vaccine effectiveness and cross protection assumptions (see Table 1) and different values of R after full NPI lifting (see Table 4).

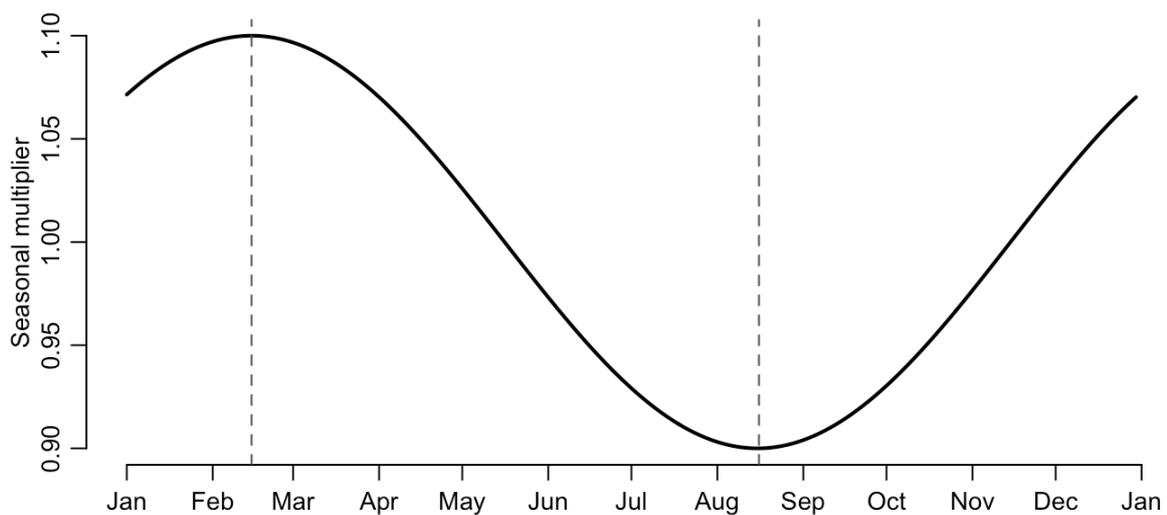
			Growth rate (95% CrI) at week beginning			
Date of NPI lifting	Vaccine effectiveness	R after full lift	19 July	26 July	2 August	9 August
19 July	Optimistic	Low	0.079 (0.034, 0.114)	0.049 (0.004, 0.074)	0.036 (0.001, 0.044)	0.021 (-0.017, 0.026)
		Central	0.117 (0.079, 0.141)	0.085 (0.051, 0.097)	0.063 (0.035, 0.069)	0.041 (-0.023, 0.047)
		High	0.160 (0.127, 0.177)	0.126 (0.098, 0.131)	0.093 (0.036, 0.102)	0.043 (-0.040, 0.078)
	Central	Low	0.084 (0.040, 0.115)	0.053 (0.011, 0.069)	0.037 (0.004, 0.043)	0.018 (-0.030, 0.023)
		Central	0.121 (0.084, 0.144)	0.088 (0.060, 0.096)	0.062 (0.019, 0.066)	0.031 (-0.048, 0.045)
		High	0.166 (0.136, 0.185)	0.128 (0.104, 0.132)	0.086 (0.017, 0.101)	0.025 (-0.068, 0.073)
	Pessimistic	Low	0.095 (0.048, 0.127)	0.060 (0.018, 0.074)	0.037 (0.003, 0.043)	0.016 (-0.052, 0.022)
		Central	0.131 (0.091, 0.151)	0.094 (0.060, 0.101)	0.063 (0.003, 0.069)	0.023 (-0.070, 0.046)
		High	0.176 (0.146, 0.191)	0.133 (0.100, 0.138)	0.081 (-0.003, 0.102)	0.006 (-0.101, 0.065)
Gradual increase in R from 19 July to 1 Sep	Optimistic	Central	0.010 (-0.057, 0.066)	-0.001 (-0.058, 0.040)	0.014 (-0.037, 0.038)	0.026 (-0.014, 0.036)
	Central	Central	0.015 (-0.046, 0.072)	0.002 (-0.058, 0.041)	0.019 (-0.033, 0.035)	0.025 (-0.020, 0.033)
	Pessimistic	Central	0.024 (-0.038, 0.084)	0.013 (-0.047, 0.049)	0.021 (-0.028, 0.034)	0.026 (-0.016, 0.032)

Seasonality in transmissibility

In our main analyses we assumed a slight seasonal trend in SARS-CoV-2 transmissibility throughout the year in England with 20% relative peak to trough variation. We computed a daily multiplier for transmissibility which was:

- Maximal at 1.1 in mid-February of each year (10% relative increase compared to the mean transmissibility)
- Minimal at 0.9 on in mid-August (day 228) of each year (10% relative decrease compared to the mean transmissibility)

We then applied this daily seasonal multiplier (Supplementary Figure 6) to $R_{excl_immunity}$ in each phase (see Table 4).



Supplementary Figure 6: Seasonal daily multiplier for transmissibility ($R_{excl_immunity}$) applied to each phase.

First dose vaccine roll-out

We assume first doses were delivered in England between 8 December 2020 and 2 July 2021 as reported in data received from PHE and DHSC via SPI-M. We then assume a vaccine dose roll-out as in Table 2. To account for second doses, we assumed that the number of available first doses on a given day is given by the total available doses on that day and subtract the number of first doses administered 77 days (11 weeks) prior. If the resulting value was negative, this was set to 0. From 2 July onwards, we assumed first doses are split between NHS regions in proportion of their population size. We assumed that a mixture of Pfizer and AstraZeneca vaccines as observed thus far in each age group continue to be distributed to individuals 40+ years and <40 years will receive Pfizer or Moderna only.

We assume doses are distributed following the JCVI priority list i.e. to:

1. Care home workers and residents

2. Individuals 50 or over by decreasing 5-year age band priority as well as health care workers (we assume a fraction of the working age population to be within this group) and vulnerable individuals (also modelled as a fraction of the population)
3. Individuals under 50

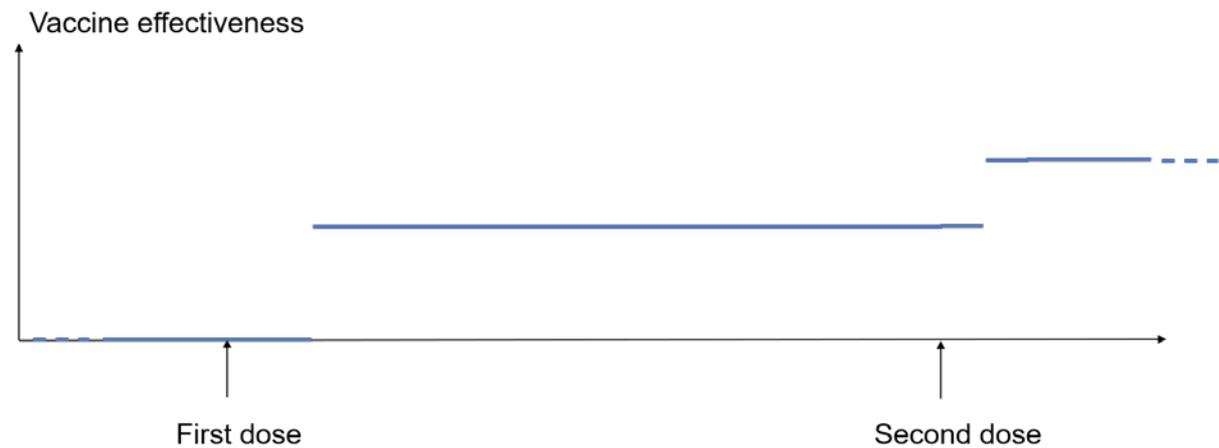
Children under 18 years are not vaccinated in our main analyses. As our model is stratified using 5-year age classes, we model the vaccination of individuals aged 18-19 by assuming the uptake in the 15-19 age group is 2/5 of the uptake in the 20-24 year olds.

2nd dose vaccine roll-out and vaccine effectiveness after each dose

We assume degree-type protection from vaccination: all vaccinees have their likelihood of acquiring infection reduced by a factor of $(1 - \text{vaccine effectiveness})$, see section on vaccine effectiveness below for more detail.

For each compartment in the model, 4 successive vaccination stages (duration of each stage and effectiveness of vaccine in each stage are shown on Supplementary Figure 7):

- Unvaccinated
- Vaccinated with 1st dose before onset of vaccine effectiveness
- Vaccinated with 1st dose with full effectiveness from 1st dose – this includes individuals having received the second dose before the onset of effectiveness of the second dose
- Vaccinated with 2nd dose with full effectiveness from 2nd dose



Vaccination mean stages duration (weeks):

Determined by vaccination schedule	3	9	Inf
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Supplementary Figure 7: Vaccination stage duration and associated vaccine effectiveness. The lower panel depicts mean duration of vaccination stages in weeks (numbers denote number of weeks in each stage). The top panel shows the associated vaccine effectiveness and delays to protection over time.

Vaccine effectiveness after first and second dose was varied across scenarios (see Table 1), but we assume:

- No effectiveness in the 21 days following the first dose
- No effectiveness of the second dose for the 7 days following dose 2

Phase 2 PF and AZ vaccine trial results indicated substantial increase in immunogenicity only after 2 to 3 weeks post-dose 1, and one-week post-dose 2 [20,21]. We therefore assumed a 21-day (respectively 7-day) delay between receiving the first (respectively second) dose and the onset of dose-specific effectiveness.

7. Vaccine effectiveness

We assumed that the vaccine has five effects (Table 1):

1. Effectiveness *against infection*, e_{inf} : Reducing the risk of infection in vaccinated individuals, compared to those not vaccinated.
2. Effectiveness *against symptoms conditional on infection*, $e_{sympt | inf}$: Reducing the risk of symptoms in vaccinated individuals who become infected, compared to those not vaccinated who become infected.
3. Effectiveness *against severe symptoms requiring hospitalisation, conditional on symptomatic infection*, $e_{hosp | sympt}$: Reducing the risk of severe symptoms requiring hospitalisation in a vaccinated individual who becomes infected and symptomatic, compared to those not vaccinated who become infected and symptomatic.
4. Effectiveness *against death, conditional on disease severe enough to require hospitalisation*, $e_{death | hosp}$: Reducing the risk of death in a vaccinated individual who becomes infected, symptomatic, and requires hospitalisation, compared to those not vaccinated who become infected and require hospitalisation.
5. Effectiveness *against onward transmission conditional on infection* $e_{transmit | inf}$: Reducing the risk of onward transmission from a vaccinated individual who becomes infected, compared to those non vaccinated who become infected.

The first two effects combined reduce the risk of symptomatic infection (“Effectiveness *against symptomatic infection*, e_{sympt} “, non-conditional on infection) in vaccinated individuals, compared to those not vaccinated. The first three effects combined reduce the risk of severe infection (“Effectiveness *against severe infection*, e_{hosp} “, non-conditional on symptomatic infection) in vaccinated individuals, compared to those not vaccinated.

Assumed values of effectiveness for e_{inf} , and e_{sympt} and e_{hosp} are shown in Table 1.

The reduction in the risk of being symptomatically infected (e_{sympt}), as reported in clinical trials, is determined by both the reduction in the risk of being infected (e_{inf}) and the reduction in the risk of becoming symptomatic if infected ($e_{sympt | inf}$) as follows:

$$e_{sympt} = e_{inf} + (1 - e_{inf}) * e_{sympt | inf}$$

Similarly, the reduction in the risk of being severely infected (e_{hosp}), as reported in some clinical trials, is determined by the reduction in the risk of being infected (e_{inf}), the reduction in the risk of becoming symptomatic if infected ($e_{sympt | inf}$), and the reduction in the risk of developing severe symptoms if infected and symptomatic ($e_{hosp | sympt}$) as follows:

$$e_{hosp} = e_{sympt} + (1 - e_{inf}) * (1 - e_{sympt | inf}) * e_{hosp | sympt}$$

Similarly, the reduction in the risk of death (e_{death}), as listed in Table 1, is determined by the reduction in the risk of being infected (e_{inf}), and of severe disease warranting hospitalisation

(e_{hosp}), the reduction in risk of becoming symptomatic if infected ($e_{sympt | inf}$), the reduction in risk of developing severe symptoms if infected and symptomatic ($e_{hosp | sympt}$), and the reduction in risk of death if displaying severe symptoms ($e_{death | hosp}$) as follows:

$$e_{death} = e_{hosp} + (1 - e_{inf}) * (1 - e_{sympt | inf}) * (1 - e_{hosp | sympt}) * e_{death | hosp}$$

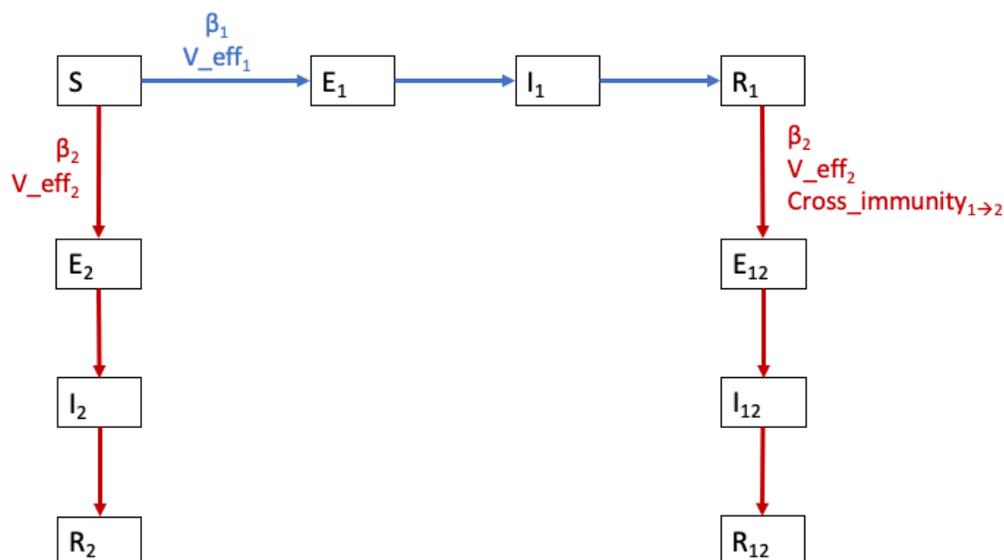
Vaccine uptake

We assume vaccine uptake was age dependant with 80% uptake in those aged 18-39 years unless current uptake for dose 1 was higher. We further assumed that every individual who received their first dose would go on to also receive a second dose.

Modelling the introduction and spread of the Delta variant

We model the potential introduction and spread of Delta in England by extending our model to a two-variant model (see section Transmissibility associated with re-opening steps). Variant 1 represents the previously dominant variant in circulation, i.e. Alpha in the UK; variant 2 represents Delta. Transmissibility, effectiveness of vaccines and natural immunity differ between the two variants.

A simplified flowchart for our two-variant model is shown in Supplementary Figure 8. The age/care home structure and vaccine class structure for the second variant is equivalent to that for the first.



Supplementary Figure 8: Flowchart summarising the two-variant structure of the model. S denotes susceptibles, E exposed (infected not infectious), I infectious and R recovered. Indexes denote infection with variant 1 (e.g. E1), variant 2 (e.g. E2) or variant 1 and 2 in turn (e.g. E12). In the model, each compartment is further split by age/care home resident/care home worker class (as described in [1]), and by vaccination class, not shown in this figure. The I compartment is also further split to distinguish between symptomatic and asymptomatic cases, and to describe in detail the hospital pathways of severely affected cases [1]. Deaths are not pictured on this figure but are also modelled as described in [1]. Blue and red arrows denote infection and clinical progression for the first and second variant respectively. Parameters next to an arrow denote parameters which influence the risk of infection for that

arrow and include b_i , the transmission rate for variant i , $\text{cross_immunity}_{j \rightarrow i}$, the cross protection against variant i provided by prior infection with the other variant (j), and $V_{\text{eff},i}$, the vaccine effectiveness against variant i . Note that vaccine effectiveness will also alter the probability of symptomatic and severe infection and death.

Transmissibility of Delta

Transmissibility for Delta is modelled as proportional to that for the first variant, with a constant multiplier through time estimated from fitting the transmission model to the data (see section Transmissibility associated with re-opening steps). Unless otherwise specified, numbers of infections, hospitalisations, bed occupancy and deaths are shown for both variants together.

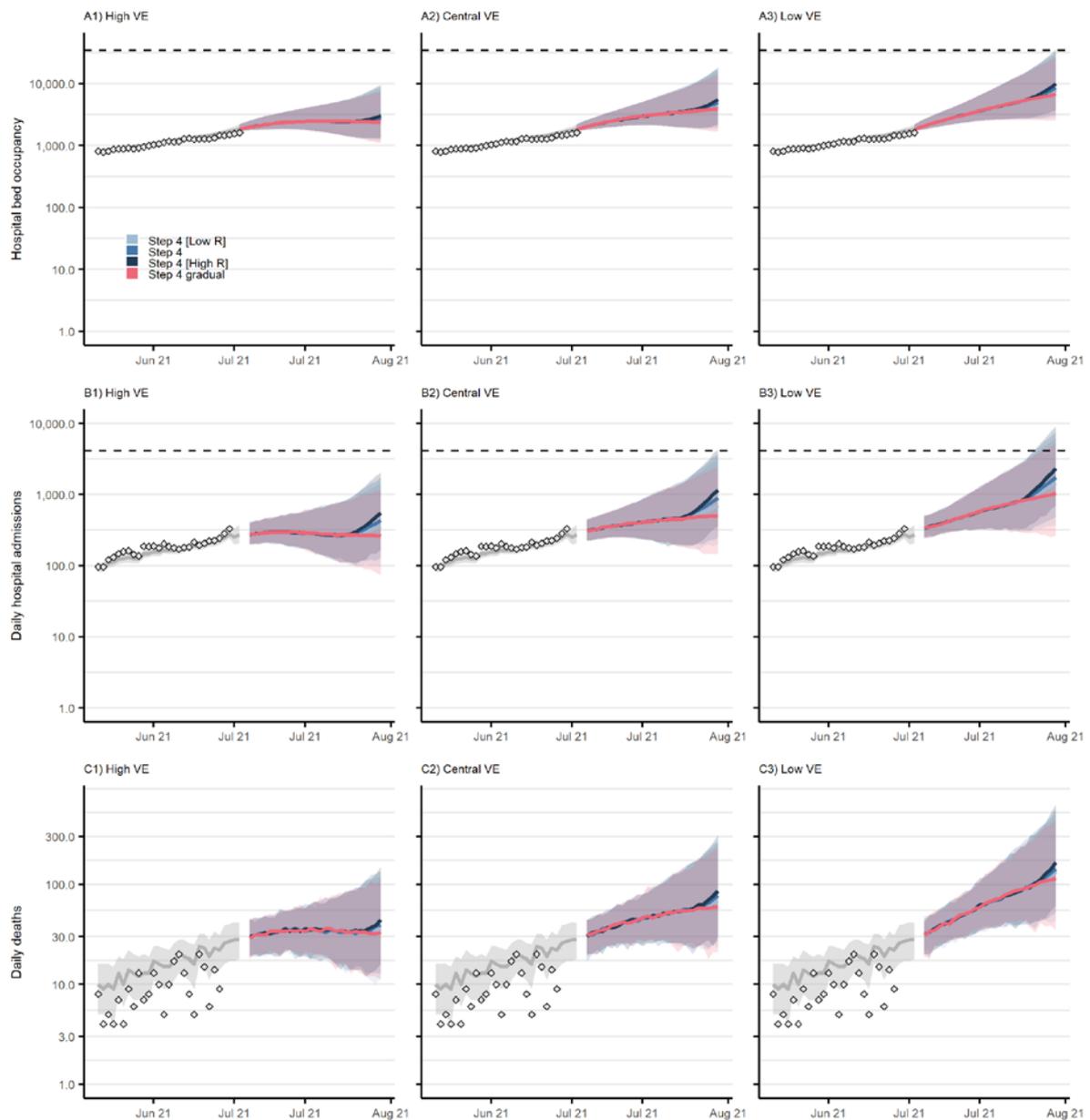
Immune escape properties of Delta

We assume that vaccines may be less efficacious against Delta (Table 1). We also model a non-symmetrical cross immunity between the two variants; we assume that infection with Delta confers perfect immunity to previously circulating variants, but infection with variant 1 (i.e. Alpha or previous variants) is only partially protective against infection with Delta (Table 1). In addition, for individuals infected by each variant in turn, we assume that if the second infection is symptomatic, the probability of hospitalisation is reduced compared to individuals with no prior infection history (Table 1).

Severity of Delta

In line with recent evidence, we assume that infection with the Delta variant is more severe than Alpha. This is modelled as an 1.85-fold risk of hospitalisation for symptomatic Delta variant infections [2].

8. Supplementary Results



Supplementary Figure 9: COVID-19 daily (top row) hospital bed occupancy, (second row) hospital admissions, and (third row) deaths in England shown on a log-scale for Step 4 occurring on 19 July with central (blue), low (light blue), or high (dark blue) R after full NPI lifting, or on 19 July with only a gradual increase in transmissibility to 1 September to a “central” R after NPI lifting (pink) (see Table 4), projecting forwards to 30 July 2021. We consider vaccine effectiveness against Delta to be from left to right: (High VE) optimistic; (Central VE) central; and (Low VE) pessimistic. The horizontal dashed lines show the peak of the winter wave. See Table 1 for Delta properties. The coloured lines show the mean and the shaded areas show 95% credible intervals. Note the y-axis scale is different in each row. The points show the data and the grey line the model fit (grey shaded area shows the 95% CrI of the model fit).

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