Evaluating the Roadmap out of Lockdown: Step 3

Raphael Sonabend, Lilith K Whittles, Natsuko Imai, Edward S Knock, Pablo N Perez-Guzman, Tara Mangal, Alexandra B Hogan, Erik M Volz, Azra Ghani, Neil M Ferguson, Marc Baguelin, Anne Cori
MRC Centre for Global Infectious Disease Analysis, Imperial College London

1. Summary

In this report, we summarise the findings of our evaluation of the successive easing of non-pharmaceutical interventions (NPIs) as set out in the UK Government's Roadmap out of Lockdown. 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. Results and assumptions refer to England unless otherwise specified.

1. We estimate the current level of transmission, R_{eff}, is approximately 1 in England. This estimate *may not* fully capture the impact of schools opening after Easter given the 3-week delay before changes in contact rates are reflected in surveillance data streams.
2. Based on PHE data available to 28 April 2021, 64% of the adult population in England have received at least one vaccine dose and 26% have received two doses. Under our central assumptions on vaccine effectiveness, this translates to 40% of adults (or 31% of the whole population) protected against symptomatic disease and 49% of adults (or 38% of the whole population) protected against severe disease (hospitalisation) via vaccination. Note this also includes individuals who are also protected due to recovery from past infection.
3. We estimate that an additional 15% of the population who are not protected through vaccination are currently protected due to recovery from past infection.
4. Assuming 2.7M vaccine doses/week are given up to 19 July (2.0M thereafter), we project that 52% of the whole population will be protected against symptomatic disease, and 60% against severe disease, due to either vaccination or recovery from infection by 21 June 2021.
5. We note that the coverage estimates given in point 2 above for first doses are lower than estimated in the most recent ONS survey (71% and 21% of adults in England having received one and two doses respectively as of 16/04/21 [1]) suggesting that the ONS survey participants may not be fully representative of the population as a whole.
6. Under our central scenario assumptions, and assuming steps 3 and 4 of the roadmap proceed, we expect a smaller third wave which is most likely to occur in the late summer to autumn. However, the timing and size of this third wave remains highly uncertain and depends on the levels of transmission that occur from 17th May and 21st June onwards.
7. The likelihood of the importation and spread of variants of concern (VOC) remains highly uncertain, as do the properties of such VOC. If a VOC emerges with similar transmissibility to B.1.1.7 and with a moderate degree of immune escape from both infection- and vaccine-induced immunity, a third wave substantially larger (both in hospitalisation and deaths) than the winter of 2021 could occur. This does not allow for the potential mitigating impact of booster vaccines and reintroduction of some NPIs.
8. Remaining at step 3 beyond 17 May is projected to maintain the effective reproduction number around 1 and keep hospitalisations and deaths at very low levels. It would also dampen a third wave due to VOC emergence.
9. Global collaborative efforts to control transmission abroad will be vital in preventing further emergence and importation of new VOCs which may trigger a third wave and necessitate a pause or reversal of the current roadmap. VOC importations over time should also be monitored carefully. Careful testing and quarantine measures will be critical as international travel restrictions are lifted.
10. Given the many uncertainties involved in making these projections, the impact of Step 3 must be carefully evaluated (and given enough time to do so) before committing to Step 4 which will pose the greatest risk to increased transmission.

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 upcoming "Step 3" of the plan due to take place not before 17th May 2021. We also consider the impact of further relaxation of measures from "Step 4", occurring not before 21st June 2021.

Several key sources of data (as of 1 May 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 will have natural immunity due to prior infection and is estimated by fitting our transmission model [2] to data on infection prevalence surveys, serology, reported cases via Pillar 1 and Pillar 2, reported hospitalisations and deaths within 28 days of a positive test (Figure S5).
2. PHE data on vaccination coverage over time- by age (Figure 1) and region, including the proportions receiving their first dose and second doses and the specific vaccine given to each age-group.
3. The effectiveness of vaccination against the circulating B1.1.7 variant in the UK. This is obtained from a review of clinical trial efficacy data and from UK and international studies on their real-world effectiveness (Table 3).

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

1. The transmissibility of the circulating virus as interventions are relaxed at Step 3 and Step 4. We formulate this in terms of the reproduction number, R, that would occur in the absence of natural- and vaccine-induced immunity ($R_{excl\_immunity}$) (Tables 4 and S1).
2. Future vaccination programme progress - including the vaccine supply, speed of roll-out, product mix and uptake in younger age-groups (Table 1 and 2).
3. The importation rate of VOCs from abroad and their transmissibility, severity and degree of immune escape compared with the currently dominant B.1.1.7 lineage (Table 5).

2.1 Vaccination Coverage

Data on vaccine uptake by age and product were provided by Public Health England. These data are summarised in Figure 1. Note that these data are the same as reported on the COVID-19 dashboard [3].

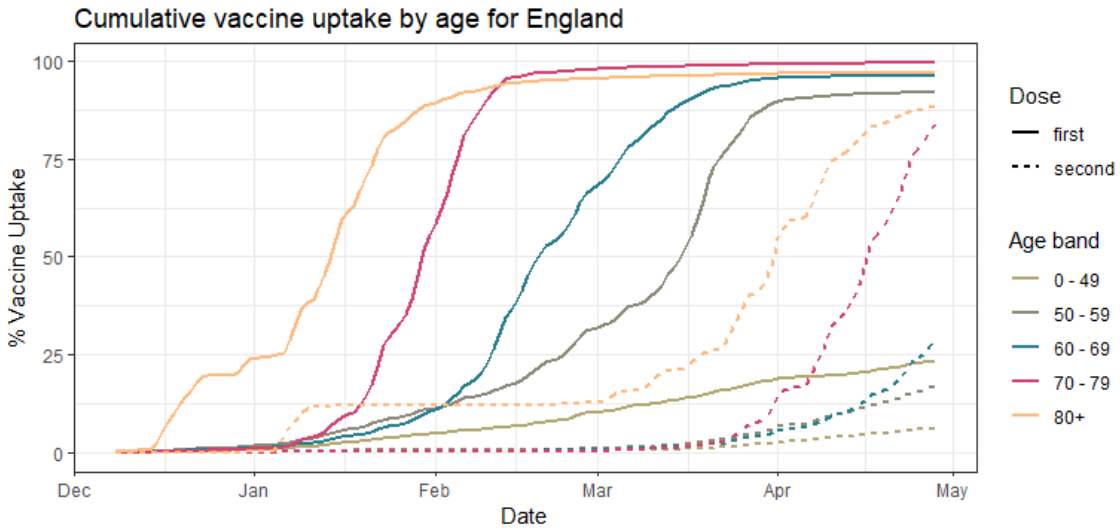


Figure 1: ***Cumulative vaccine uptake by 28 April 2021 by age for England shown for first (solid lines) and second (dashed lines) doses. Shown as the proportion of the population age group of England (ONS).***

Projections of vaccine roll-out provided by DHSC for this exercise are summarised in Table 1.

Table 1: Pre-specified vaccination schedule (million doses per week)

	Weeks commencing	Average doses per week
England	26 April 2021	2.7M
	19 July 2021 onwards	2.0M

For the forward projections, we model continued roll-out to all age-groups. The minimum uptake assumed to be achieved is summarised in Table 2. 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 2: Vaccine uptake assumptions by group or age for all nations.

Group	Central Scenario	Sensitivity analysis
Care home residents (CHR)	95%	95%
Care home workers (CHW)	85%	85%
80+ years*	95%	95%
50-79 years*	95%	95%
30-49 years*	90%	80%, 50%, 20%
<30 years*	80%	80%, 50%, 20%

* Not working or residing in a care home.

2.2 Vaccine Effectiveness

Based on the most recent evidence, we have updated our assumptions regarding the mode of action and effectiveness for each vaccine. Table 3 summarises these for the Pfizer, AstraZeneca and Moderna vaccines. 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. We further assume that, in those individuals who do become infected more than 21 days after vaccination, onward transmission is also reduced.

Table 3: Vaccine effectiveness assumptions for AstraZeneca (AZ), Pfizer (PF), and Moderna (Mod). We assume individuals ≥50 years will receive the mix of vaccines observed thus far; 30-49 years will receive 60% AZ and 40% PF or Moderna; and individuals under 30 years will receive PF or Moderna only.

	Vaccine	Central Scenario	Sensitivity Analysis	Informed by
Efficacy against severe disease	AZ (1 dose)	80%	70%	Vasileiou 2021 [4], PHE [5], Hyams 2021 [6]
	AZ (2 doses)	80%	70%	
	PF (1 dose)	80%	58%	Hyams 2021 [6] Hall 2021 [7]
	PF (2 doses)	95%	76%	PHE effectiveness data (unpublished)*
	Moderna	Assume the same as PF for 1 and 2 doses		
Efficacy against disease	AZ (1 dose)	63%	50%	Voysey 2020 [8]
	AZ (2 doses)	63%	50%	Voysey 2021 [9] [8,9][8,9][7,8]
	PF (1 dose)	65%	58%	PHE [10] Hall 2021 [7]
	PF (2 doses)	86%	76%	Hall 2021 [7]
	Moderna	Assume same as PF for 1 and 2 doses		
Efficacy against infection	AZ (1 dose)	63%	50%	assumed same as efficacy against disease
	AZ (2 doses)	63%	50%	
	PF (1 dose)	65%	58%	
	PF (2 doses)	86%	76%	
	Moderna	Assume same as PF for 1 and 2 doses		
Efficacy against infectiousness if infected	AZ/PF/Mod (1 dose)	45%	0%	[11]
	AZ/PF/Mod (2 doses)	45%	0%	[11]

*(33% additional protection in breakthrough infections)

2.3 Increases in population contact rates resulting from roadmap steps 3 and 4

To capture the gradual easing of restrictions at Steps 3 and 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 immunity (specified as a probability distribution, see Figure S6) that could occur at each stage. Table 4 summarises assumptions at Steps 3 and 4 for England. R is assumed to be 0.3 lower during the school holidays, due to lower contact rates between children. We assumed an average school holiday pattern across England (with half-term 29 May - 7 Jun, summer 24 Jul - 31 Aug). We do not model school holidays beyond summer 2021.

We examine two scenarios for the impact of step 4 – an increase of R to either 3.5 (which assumes ongoing control measures such as symptomatic case isolation and test-and-trace will reduce transmission by approximately 1/3 from an R_0 of 5 for B1.1.7 [12]) or 4.5 (which assumes ongoing control measures will reduce transmission by approximately 10%). We further assumed a slight seasonal trend in SARS-CoV-2 transmissibility throughout the year (see appendix 3).

Table 4: Summary of two 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 of at each stage are shown. Further details are given in Table S1.

Scenario		
Step 3 only	Step 3 - 17 May '21	
	School holidays: 1.90 (1.54-2.32) School terms: 2.20 (1.83-2.62)	
Step 3 and 4	Step 3 - 17 May '21	Step 4 - 21 Jun '21
Central Scenario	School holidays: 1.90 (1.54-2.32) School terms: 2.20 (1.83-2.62)	School holidays: 3.20 (2.53 – 4.00) School terms: 3.50 (2.82 – 4.29)
Higher R following full NPI lifting	School holidays: 1.90 (1.54-2.32) School terms: 2.20 (1.83-2.62)	School holidays: 4.20 (3.51– 4.98) School terms: 4.50 (3.81 – 5.28)

2.4 Variants of Concern

The emergence and spread of VOCs remain highly uncertain. We therefore undertook many sensitivity analyses to understand the potential for further waves of infection if VOCs with partial immune escape to current vaccines were to establish in the UK population in the coming months. We note that these are all highly speculative and it is not possible to determine their likelihood at this time given the many associated uncertainties.

Key factors considered include:

- Rate of introduction - we assume a low level of importations up to Step 3 (May 17th) with this increasing thereafter to reflect the planned re-opening of borders.
- Transmissibility of the VOC compared to the current circulating variant (B1.1.7).
- Cross-protection from prior infection with wild-type or B1.1.7 variants.
- Severity of the VOC compared to B1.1.7.
- Vaccine efficacy against VOC.

Table 5 summarises the assumptions for the VOC dynamics. On average 5 cases a day of variants of concerns or variants under investigations have been reported among travellers entering the UK in the last few months [13]; we conservatively assumed only 1/3 of those would be detected and hence that there are currently 15 importations a day.

Table 5: Summary assumptions for Variants of Concern (VOC) for all nations

VOC characteristics	Central	Optimistic
Timing and rate of introduction	15 importations a day, increasing 10-fold at Step 3.	As central
Transmissibility relative to B1.1.7	As transmissible as B1.1.7.	20% less transmissible than B1.1.7
Cross-immunity from natural infection	Infection with VOC is fully (100%) protective against B1.1.7. Infection with B1.1.7 or earlier variants gives 55% protection against infection/mild disease and 70% protection against hospitalisation with VOC (similar to assumed efficacy of one dose of Pfizer).	As central

Table 6 summarises assumptions about vaccine efficacy against VOCs. These are principally based on a review of the (limited) data from vaccine efficacy and effectiveness studies for the B.1.351 variant, which currently is the VOC of greatest concern in relation to vaccine efficacy. We note that current data suggest that the mRNA vaccines are less vulnerable to VOCs than vectored vaccines.

Table 6: Vaccine efficacy assumptions for AstraZeneca (AZ), Pfizer (PF), and Moderna (Mod) against variants of concern (VOC). We assume individuals ≥50 years will receive the mix of vaccines observed thus far; 30-49 years will receive 60% AZ and 40% PF or Moderna; and individuals under 30 years will receive PF or Moderna only.

Vaccine efficacy	Vaccine	Central with VOC	Pessimistic VE against VOC	Optimistic VE against VOC	Informed by
Against severe disease	AZ (1)	40%	20%	64%	Assumed higher than against mild disease, similarly to B1.1.7
	AZ (2)	40%	20%	64%	
	PF (1)	70%	60%	80%	
	PF (2)	90%	85%	95%	
	Moderna	Assume same as PF for 1 and 2 doses			
Against mild disease	AZ (1)	10%	0%	50%	Madhi 2021 [14]
	AZ (2)	10%	0%	50%	
	PF (1)	55%	45%	65%	Assumed lower than 2 dose efficacy
	PF (2)	75%	55%	85%	PF press release [15]
	Moderna	Assume same as PF for 1 and 2 doses			
Against infection	AZ (1)	10%	0%	50%	Assumed same as disease
	AZ (2)	10%	0%	50%	
	PF (1)	55%	45%	65%	
	PF (2)	75%	55%	85%	
	Moderna	Assume same as PF for 1 and 2 doses			
Against infectiousness if infected	AZ/PF/Mod (1)	20%	0%	45%	Assumed
	AZ/PF/Mod (2)	20%	0%	45%	Assumed

3. Results

Under the central scenario defined by Tables 1-4, we project that 92% of the adult population and 72% of the population in England will have received at least one dose of the vaccine by 31 August 2021 when it plateaus, and 78% and 61% respectively will have received two vaccine doses. Given our assumptions regarding vaccine efficacy and the vaccine product mix that is planned, this would result in 72% of the English population being protected against severe disease through vaccination or recovery from previous infection by that date (Figure 2A). The remaining gap in protection (28% unprotected) stems from (a) not vaccinating <18-year-olds, and (b) imperfect vaccine efficacy. Whilst vaccine uptake in the adult population has been encouragingly high, as we enter autumn, children will remain susceptible to infection (Figure 4) and potentially contribute to continued transmission of any circulating virus.

Figure 2B shows the extent to which the population in England will be protected over time, through a combination of vaccination and immunity acquired through natural infection. Strategies which retain substantial NPIs (Step 3 only, where no further NPIs are released after 17 May 2021) can maintain the effective reproduction number below 1 (Figure 2D), keeping cases, hospitalisations, and deaths low (Table 7). Similarly, under our more optimistic assumptions about the impact of Step 3 and Step 4, we project that the effective reproduction number R should remain around 1 thereby mitigating against a future large wave of infection.

With our central assumptions, the current roadmap where all but baseline NPIs will be released sequentially in England after 17 May 2021 (Table 4, step 3 and 4) is projected to lead to another small wave of hospitalisations, with 9,000 (95%CrI: 5,100, 16,600) additional deaths by 1 June 2022. Given the high vaccine uptake observed so far, most deaths are predicted to occur in vaccinated individuals, because of imperfect vaccine efficacy (Figure 4). The number of additional deaths under this and other scenarios may not have stabilised by June 2022 thus further Covid-19 deaths beyond this date are possible. The projected deaths under our current central scenario are lower than those projected in our previous reports due to the much higher vaccine efficacy assumed in light of recent published studies. In particular, we now assume substantial reductions in infectiousness of vaccinated individuals who do become infected, and this further decreases the level of transmission in the population as a whole.

We estimate that the current level of transmission in the absence of immunity in England, R_{eff}, is approximately 1 (with large uncertainty). This *does not* fully reflect the impact on transmission of schools returning from Easter break, since R is a lagging indicator by at least 3 weeks. R_{eff} may therefore be higher by the time of the next set of releases on 17 May.

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.

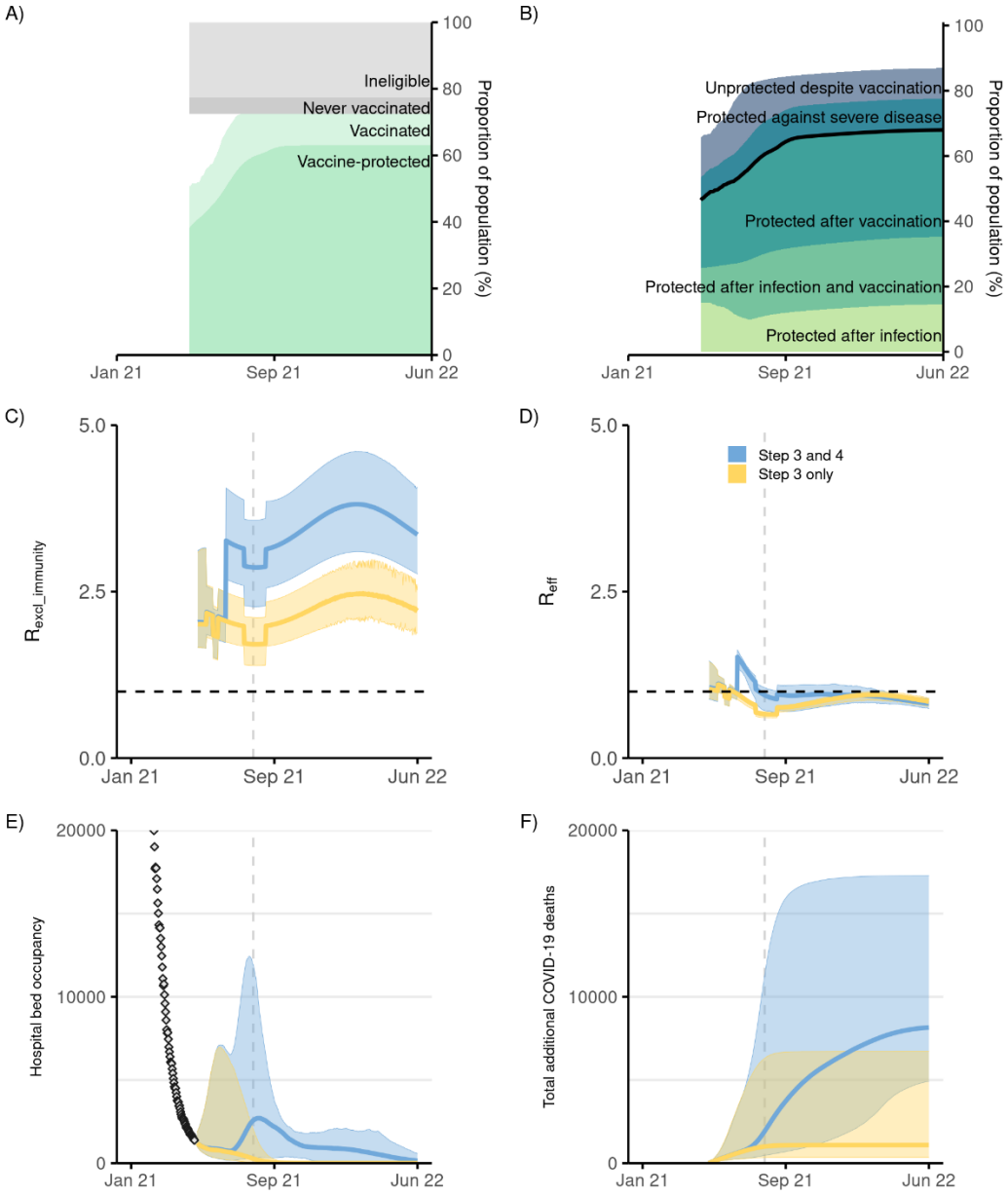


Figure 2: Impact of vaccine roll-out and roadmap Steps 3 and 4 on the epidemic in England assuming no VOC and central scenario. (A) Proportion of the whole population (including children) in England who have received at least one vaccine dose (light green) and who are protected against severe disease through vaccination (dark green shading). Light grey indicates <18 year-olds, who are currently ineligible for vaccination and dark grey those do not get vaccinated (Table 2). (B) Proportion of the population protected (from bottom to top): against infection through natural infection only, against infection from natural infection and also vaccinated, against infection after vaccination, against severe disease (but not against infection) after vaccination, and those unprotected despite vaccination. (C) Increase in R in the absence of natural- or vaccine-induced immunity due to Step 3 only or Steps 3 and 4 (note that curves reflect reduced transmission during the school holidays). Here final $R_{excl\_immunity}$ after Step 4 = 3.5 (schools open). (D) As C but showing effective reproduction number over time incorporating the impact of vaccination and natural immunity under the two release scenarios explored. (E) Projected COVID-19 hospital bed occupancy and (F) cumulative COVID-19 deaths (from 1 May 2021 onwards). In panel E, the points at the start show recent reported data. In panels C-F the coloured lines show the mean and the shaded areas show 95% credible intervals. The vertical dashed line denotes 9 Aug 2021, 12 weeks after the Step 3 release date.

4. Sensitivity analyses

Our results are highly dependent on the underlying assumptions about vaccine roll-out, transmissibility after NPI lifting and vaccine effectiveness. Results from sensitivity analyses varying these assumptions are shown in Figures 3, S1-S4, and Tables 7-8.

Assuming a return to higher values of R after full lifting of NPIs, a lower vaccine effectiveness, or low vaccine uptake in the <50-year-olds could lead to a larger third wave of hospitalisations and deaths, with a peak hospital bed occupancy which might reach or even exceed that of the most recent wave in England.

Seasonality in transmission did not substantially affect the results but reduced and broadened the peak of hospitalisations compared to a scenario with no seasonality.

We also examined the potential impact of a hypothetical variant of concern (VOC) on the magnitude of the simulated epidemics. We varied the level of transmissibility of that VOC (same as B.1.1.7 or 20% lower) as well as its degree of immune escape (see Table 5 and 6). Under the low immune escape assumption, the predicted third wave was still smaller than the most recent wave in England. However, under the central and high immune escape assumptions, the predicted third wave was orders of magnitude larger, with a peak hospital bed occupancy up to nearly 10 times that experienced in early 2021. In the range of parameters we examined, immune escape properties of the VOC affected the magnitude of the third wave more than assumptions about transmissibility.

5. Conclusions

Our results suggest that with a continued rapid roll-out and high uptake of the vaccines, and assuming recent high estimates of vaccine effectiveness on infectiousness hold, the current roadmap out of lockdown would likely lead to a moderate wave of infections, hospitalisations and deaths between the summer and the autumn of 2021. However, preventing the importation 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.

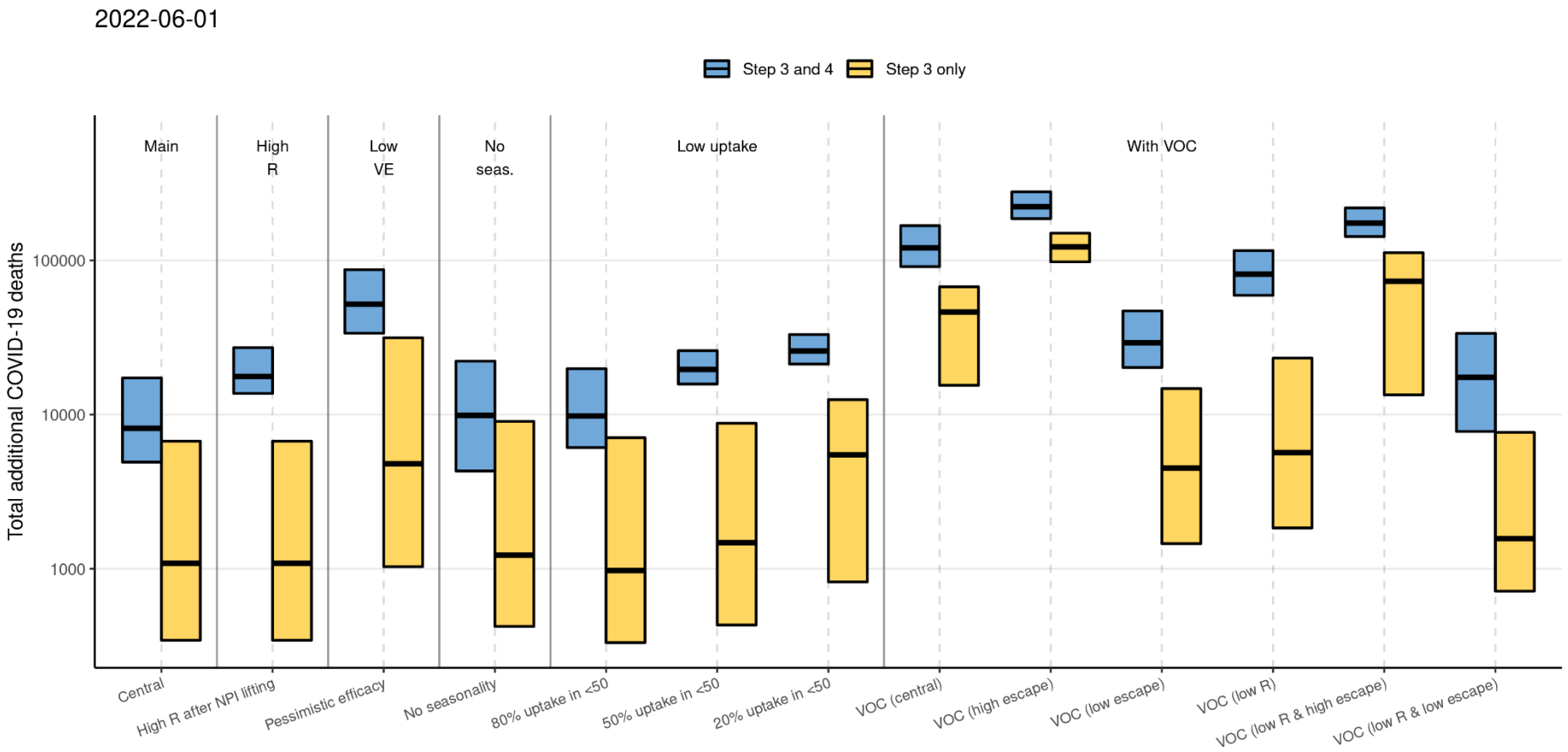


Figure 3: Sensitivity analysis showing cumulative COVID-19 deaths in England (counted from 1 May 2021 up to 1 Jun 2022) for Step 3 only (yellow) and Steps 3 and 4 (blue). Results from left to right: (main) central scenario defined by Tables 1-4 (high R) a higher R after NPIs are "fully" lifted as shown in Table 4 (not applicable for step 3 only); (low VE) lower vaccine effectiveness (notably no vaccine effectiveness against onwards transmission) as set out in Table 3; (no seas) no effect of seasonality on transmission; (low uptake) lower vaccine uptake amongst <50 yrs of 80%, 50%, and 20% respectively; (with VOC) assumes transmission of VOC with "central" immune escape and transmissibility properties, VOC with high immune escape and central transmissibility, VOC with low immune escape and central transmissibility, VOC with low transmissibility and "central" immune escape, VOC with low transmissibility and high immune escape, VOC with low transmissibility and low immune escape (see Table 5 and 6). Note that the y-axis is on a logarithmic scale.

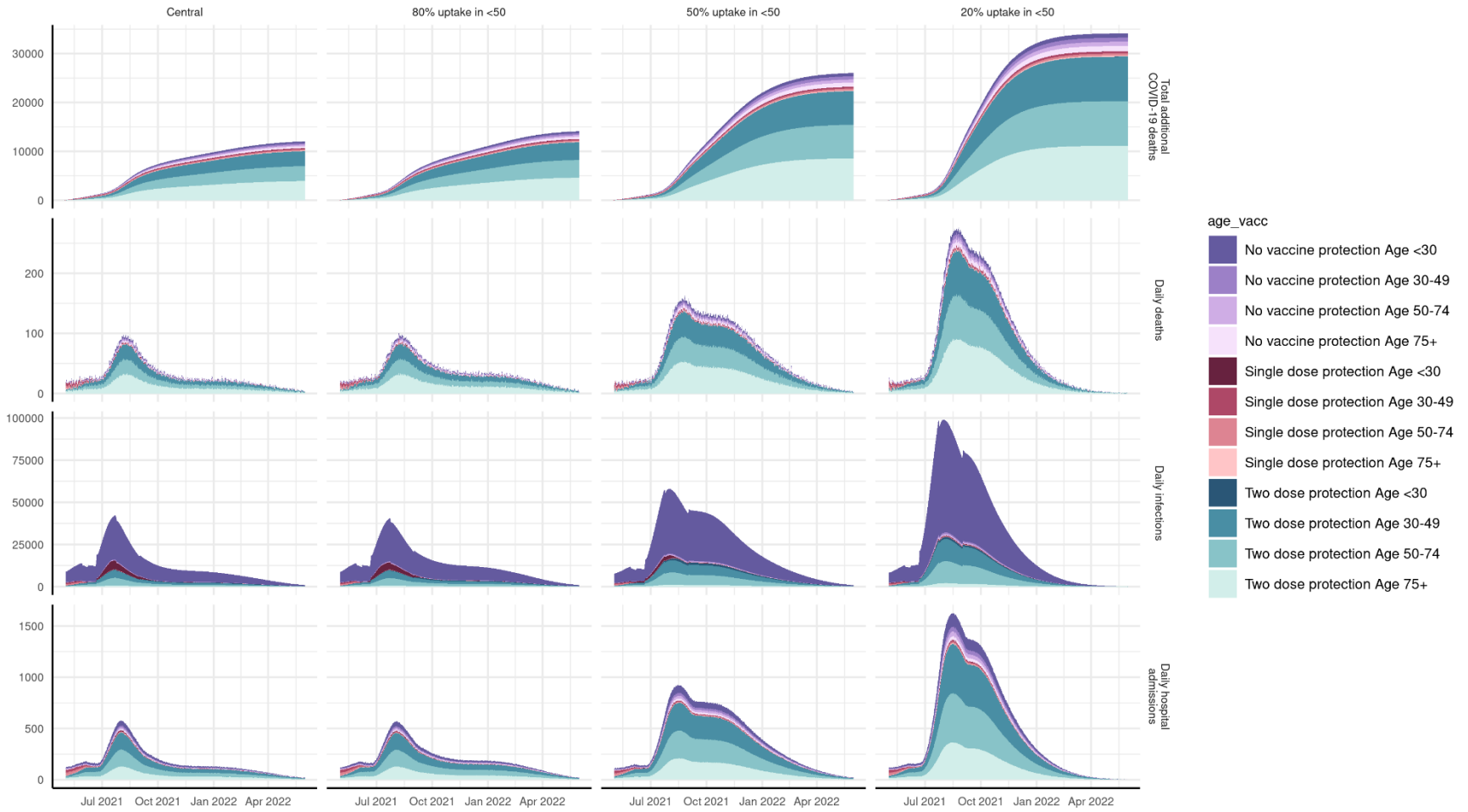


Figure 4: England COVID-19 (top row) cumulative deaths (counted from 1 May 2021 to 1 June 2022), (second row) daily deaths, (third row) daily infections, and (bottom row) daily hospital admissions by age group and vaccination status. Single dose and two dose protection refers to individuals vaccinated with one and both vaccine doses respectively after the onset of dose-specific vaccine efficacy. From left to right: (Central) "central" analysis with a "central" transmissibility after NPI lifting where moderate baseline NPIs are retained (see Table 4), "central" vaccine effectiveness (see Table 3), central vaccine roll-out and uptake described in Tables 1 and 2, and accounts for seasonality in transmission; (80% uptake, 50% uptake, 20% uptake) lower vaccine uptake amongst <50 yrs of 80%, 50%, and 20% respectively.

Table 7: Cumulative deaths, hospital admissions, incidence, and peak hospital occupancy in England (median (95% CrI), nearest 100) between 1 May 2021 and 9 Aug 2021 for Step 3 only under different scenarios considered (as Figure 3). Unless otherwise specified in "Analysis Type", results assume "central" values of vaccine efficacy (incl. 50% efficacy against infectiousness), vaccine roll-out, return to baseline NPIs of $R_{excl\_immunity}$ = 3.5 (when schools are open), and account for seasonality.

Analysis type	NPI lifting scenario	Cumulative deaths (95%CrI)	Cumulative hospital admissions (95%CrI)	Cumulative incidence (95%CrI)	Peak hospital occupancy (95%CrI)
		Up to 9 Aug 2021			
Central scenario	Step 3 only (no further lifting after 17 May)	1,500 (400, 6,200)	10,500 (2,000, 46,900)	1,007,200 (159,400, 4,397,100)	1,700 (1,000, 6,900)
Higher $R_{excl\_immunity}$ after full NPI lifting* = 4.5		As above	As above	As above	As above
Lower vaccine efficacy**		5,800 (900, 27,500)	35,700 (5,100, 162,500)	2,108,400 (296,600, 8,245,200)	4,600 (1,000, 23,400)
Without seasonality		1,800 (400, 7,800)	12,200 (2,400, 54,500)	1,203,500 (190,300, 5,125,500)	1,800 (1,000, 7,500)
Lower (80%) vaccine uptake in <50 yrs		1,400 (300, 5,700)[Δ]	9,800 (2,000, 39,900)	928,400 (152,700, 3,754,500)	1,600 (1,000, 5,700)
Lower (50%) vaccine uptake in <50 yrs		1,600 (400, 7,100)	11,200 (2,200, 49,200)	1,072,200 (186,800, 4,414,300)	1,700 (1,000, 6,900)
Lower (20%) vaccine uptake in <50 yrs		2,000 (400, 8,500)	14,300 (2,300, 58,700)	1,418,300 (187,800, 5,488,400)	2,000 (1,000, 7,700)
Central VOC R[+] and central VOC immune escape[++]		2,700 (800, 9,900)	18,500 (4,700, 73,000)	1,718,800 (389,700, 6,651,800)	2,800 (1,000, 8,700)
Central VOC R[+] and high immune escape[++]		5,300 (1,500, 14,900)	38,100 (10,200, 110,800)	3,088,400 (725,000, 9,137,800)	10,600 (2,400, 28,900)
Central VOC R[+] and low immune escape[++]		1,800 (500, 6,900)	12,000 (3,000, 46,500)	1,208,700 (276,200, 4,360,200)	1,700 (1,000, 6,800)
Low VOC R[+] and central VOC immune escape[++]		1,800 (500, 7,800)	12,400 (3,000, 52,000)	1,170,500 (244,200, 4,607,300)	1,800 (1,000, 7,600)
Low VOC R[+] and high immune escape[++]		2,200 (700, 6,700)	14,900 (4,000, 49,800)	1,298,100 (281,600, 4,545,800)	2,000 (1,000, 5,800)
Low VOC R[+] and low immune escape[++]		1,500 (400, 6,300)	10,600 (2,400, 45,900)	1,042,700 (214,800, 4,298,500)	1,700 (1,000, 7,100)

* $R_{\_excl\_immunity}$ used after NPI relaxation (see Tables 4, S1, and SI text for details). **See Table 3 for details. [+] Central VOC R = VOC as transmissible as B1.1.7, Low VOC R = VOC 20% less transmissible than B1.1.7 (see Table 5 for details). [++]See Table 6 for VOC vaccine efficacy details. [Δ] Projected deaths in this scenario are lower than in the central scenario despite lower vaccine uptake; this is because of stochastic effects and because of younger groups (who may contribute more to transmission) being vaccinated earlier when uptake is lower but vaccination schedule remains the same.

Table 8: as Table 7 but for roadmap Steps 3 and 4. All outputs are measured between 1 May 2021 and 1 June 2022.

Analysis type	NPI lifting scenario	Cumulative deaths (95%CrI)	Cumulative hospital admissions (95%CrI)	Cumulative incidence (95%CrI)	Peak hospital occupancy (95%CrI)
Up to 1 June 2022					
Main analysis	Steps 3 and 4 (full lift 21 Jun)	9,000 (5,100, 16,600)	54,900 (31,100, 104,100)	5,306,700 (3,268,900, 9,134,900)	4,200 (1,100, 12,200)
Higher $R_{excl\_immunity}$ after full NPI lifting* = 4.5		18,500 (13,700, 27,000)	111,900 (87,400, 169,600)	9,657,200 (7,944,400, 13,301,200)	13,100 (6,200, 26,900)
Lower vaccine efficacy**		53,600 (34,100, 86,300)	285,300 (184,500, 452,900)	12,618,700 (8,632,800, 18,344,400)	27,300 (7,700, 65,700)
Without seasonality		10,900 (4,400, 22,100)	65,800 (27,400, 141,700)	6,170,300 (2,832,500, 11,323,800)	6,500 (1,400, 20,200)
Lower (80%) vaccine uptake in <50 yrs		10,600 (6,200, 19,600)	65,500 (39,700, 112,200)	6,027,600 (3,901,400, 9,622,100)	4,600 (1,800, 13,300)
Lower (50%) vaccine uptake in <50 yrs		20,000 (16,000, 25,500)	128,100 (105,800, 165,400)	10,669,900 (8,904,400, 12,735,300)	9,400 (5,500, 20,200)
Lower (20%) vaccine uptake in <50 yrs		26,300 (21,300, 33,000)	171,800 (148,200, 213,900)	14,341,300 (12,113,900, 16,249,100)	16,300 (10,200, 31,100)
Central VOC R^+ and central VOC immune escape^{++}		124,000 (91,300, 164,800)	670,800 (522,000, 908,000)	30,158,100 (23,039,400, 39,789,000)	95,300 (54,000, 145,800)
Central VOC R^+ and high immune escape^{++}		225,400 (186,400, 275,900)	1,175,500 (1,017,800, 1,410,100)	40,428,400 (34,118,700, 49,591,800)	233,400 (157,500, 323,200)
Central VOC R^+ and low immune escape^{++}		30,700 (20,300, 46,100)	182,800 (126,600, 285,600)	13,986,500 (9,582,600, 21,366,000)	15,200 (8,000, 25,100)
Low VOC R^+ and central VOC immune escape^{++}		83,200 (59,700, 114,700)	460,000 (341,100, 644,100)	22,491,500 (15,904,600, 31,232,200)	36,500 (22,400, 55,800)
Low VOC R^+ and high immune escape^{++}		176,500 (143,200, 215,600)	927,500 (782,900, 1,080,100)	34,029,200 (27,729,100, 41,665,300)	127,000 (83,400, 170,400)
Low VOC R^+ and low immune escape^{++}		18,100 (7,900, 33,600)	109,800 (49,100, 198,400)	9,629,300 (4,747,400, 16,517,900)	5,300 (2,600, 14,300)

* $R_{excl\_immunity}$ used after NPI relaxation (see Tables 4 and S1, and SI text for details). **See Table 3 for details. $^+$ Central VOC R = VOC as transmissible as B1.1.7, Low VOC R = VOC 20% less transmissible than B1.1.7 (see Table 5 for details). $^{++}$See Table 6 for VOC vaccine efficacy details.

6. Appendix 1: Caveats and key assumptions

1. We assume **no loss of infection-induced or vaccine-induced immunity** over the time horizon of the analysis (*optimistic)*.
2. Our central scenario **incorporates seasonality in transmission** with a +/-10% relative change in transmissibility throughout the year.
3. We assume that vaccine roll-out pace of 2.0M doses/week from 19 July 2021 onwards can be maintained (unclear). Note that this roll-out speed is much slower than assumed previously for informing the UK Government's "Roadmap out of lockdown for England".
4. We assume **high vaccine uptake across all age groups** (*optimistic*) and further assume that uptake is homogeneous within and across regions.
5. We assume the vaccines provide protection against infection in addition to protection from severe disease and death *(optimistic)*.
6. We assume the vaccines prevents to a certain extent, an infected person who is vaccinated from transmitting the virus *(optimistic, assumed as part of "central" assumptions*)*.
7. The gradual lifting of NPIs has been modelled as a step-wise 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**.
8. We assume that mixing patterns under each Tier or step are the same as in autumn 2020.
9. We model school holidays by assuming an average decrease in $R_{\_excl\_immunity}$ of 0.3 whilst schools are closed*.
10. We do not model school holidays beyond September 2021 when evaluating outcomes up to June 2022 under Step 3 and 4 releases (*pessimistic)*.
11. 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)*.
12. We do not model differential infectivity or susceptibility by age.
13. We assume no dynamic replenishment of the care-home population *(optimistic)*.
14. We assume that some level of transmission control remains even after "fully lifting" NPIs (Tables 4 and S1) through measures such as TTI and hand hygiene *(optimistic)*. We **assume a higher $R_{\_excl\_immunity}$ than previously*** of 4.5 (see Tables 4 and S1) (*pessimistic*)
15. We only capture cases, hospitalisations and deaths occurring up to 9 August 2021 in Table 7 for Step 3 only scenarios where no further release steps are taken after 17 May 2021.
16. Note that not all scenarios under "Step 3 and 4" have reached an equilibrium with respect to the number of additional deaths by June 2022.
17. We additionally model distribution of the Moderna vaccine* and assume it has the same vaccine efficacy as Pfizer.
18. We do not model any "booster" vaccines designed to be efficacious against VOC (*pessimistic*).
19. We assume that all individuals under 30 years will now receive the Pfizer or Moderna vaccine*, 30-49 year olds will receive 60% AZ and 40% Pfizer or Moderna*, and 50+ will continue to receive the distribution of vaccines observed thus far (more PF than the 20% assumed previously)* .
20. We have not modelled a slower vaccine roll-out (*optimistic)**
21. We now model the potential impact of an immune escape VOC importation and establishment (*pessimistic*)*. Note that these are highly speculative scenarios.
22. Rates of VOC importation were assumed constant within each NPI release step.

*change since last report

7. Appendix 2: Supplementary Results

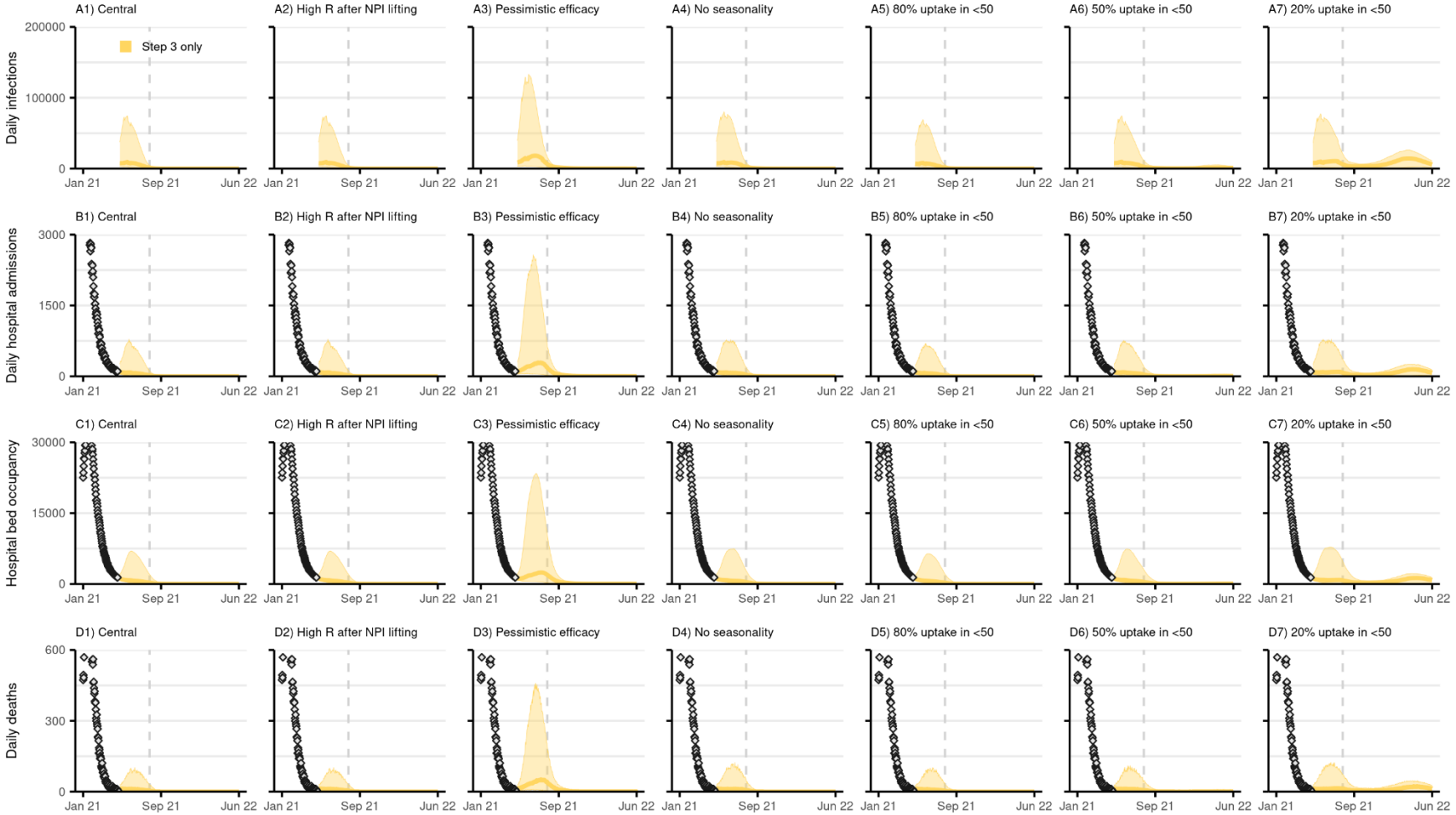


Figure S1: England COVID-19 daily (A1-A7) infections, (B1-B7) hospital admissions, (C1-C7) hospital bed occupancy, and (D1-D7) deaths assuming step 3 only (yellow) release of NPIs over time as set out in Table 4. All analyses shown in this figure assume no variant of concern (VOC). Columns show a subset of the scenarios detailed in Figure 3 and Tables 7 and 8. Note that in this figure the first two columns are identical as in the step 3 only release of NPIs the latest R increase is not occurring. The points at the start of the panels B, C and D (Jan-Apr 2021) show the recent reported data. The coloured lines show the median and the shaded areas the 95% credible intervals. Note the y-axis scale is different to that in Figure 2E-F and differs for each row. The vertical dashed line denotes 9 Aug 2021, 12 weeks after the Step 3 release date.

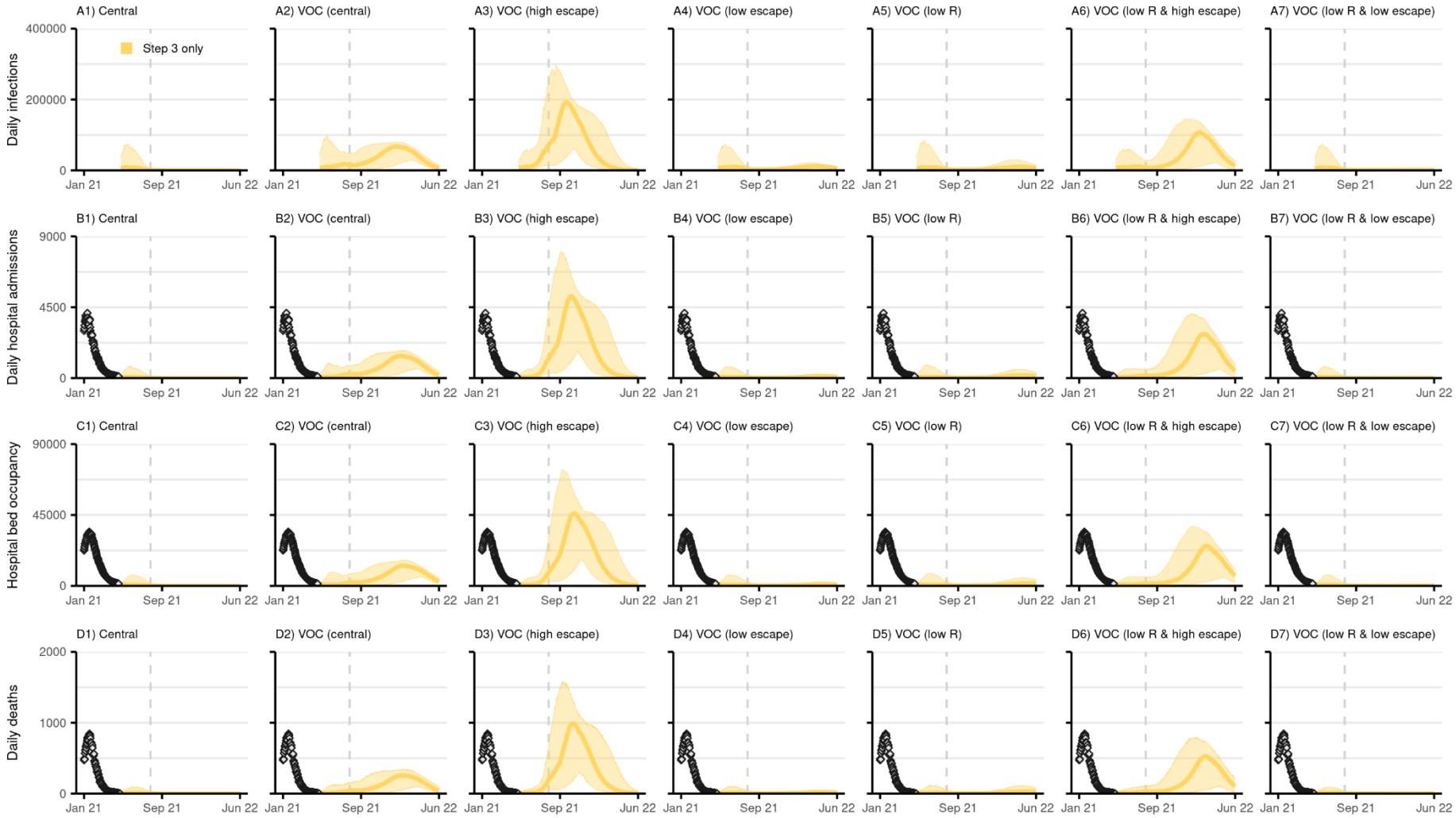


Figure S2: As Figure S1 but showing scenarios including a VOC with partial immune escape from natural and vaccine-induced immunity (see Figure 3 and Tables 7 and 8 for details on each scenario).

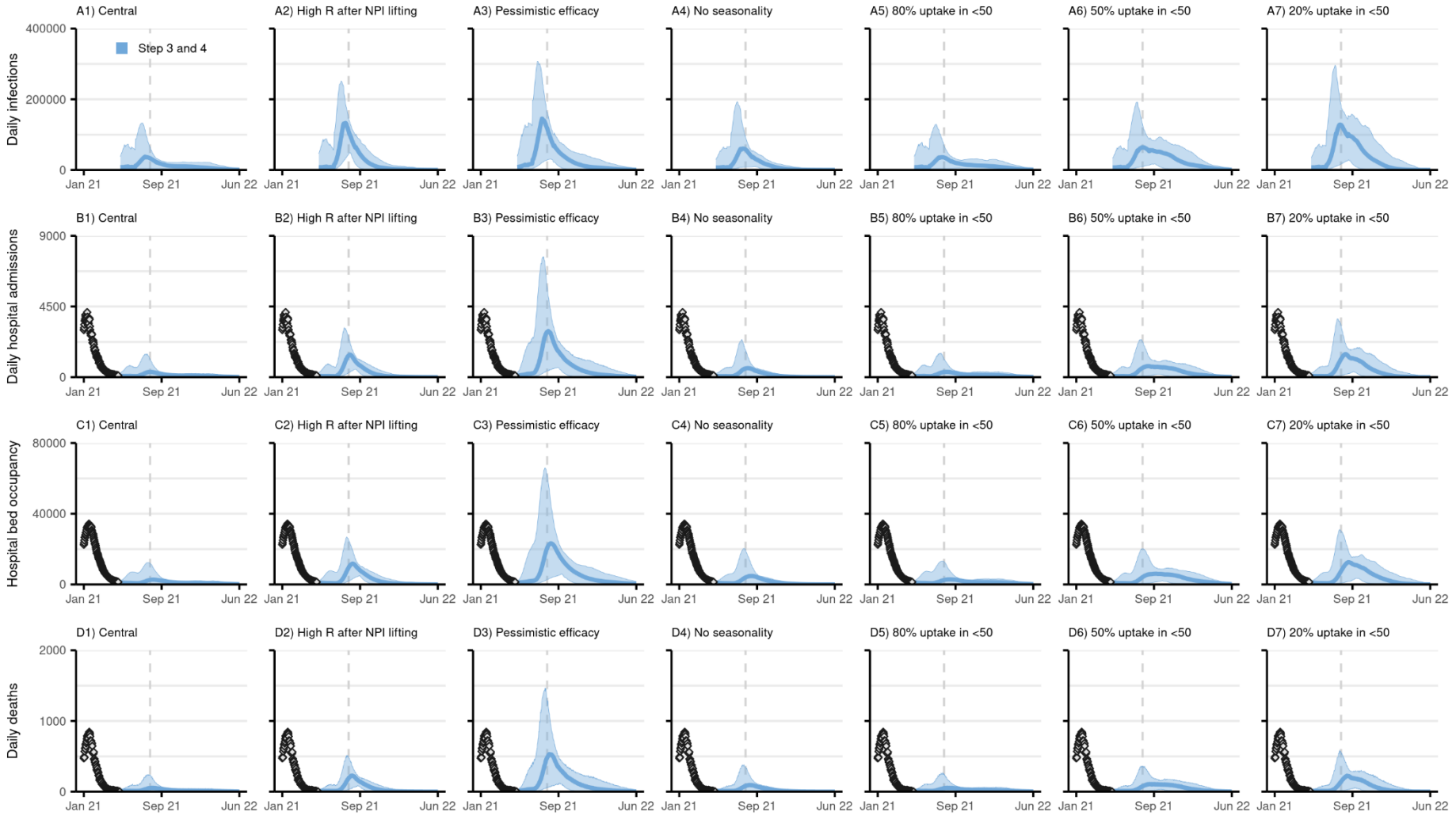


Figure S3: As Figure S1 (results with no VOC) but showing impact of Steps 3 and 4.

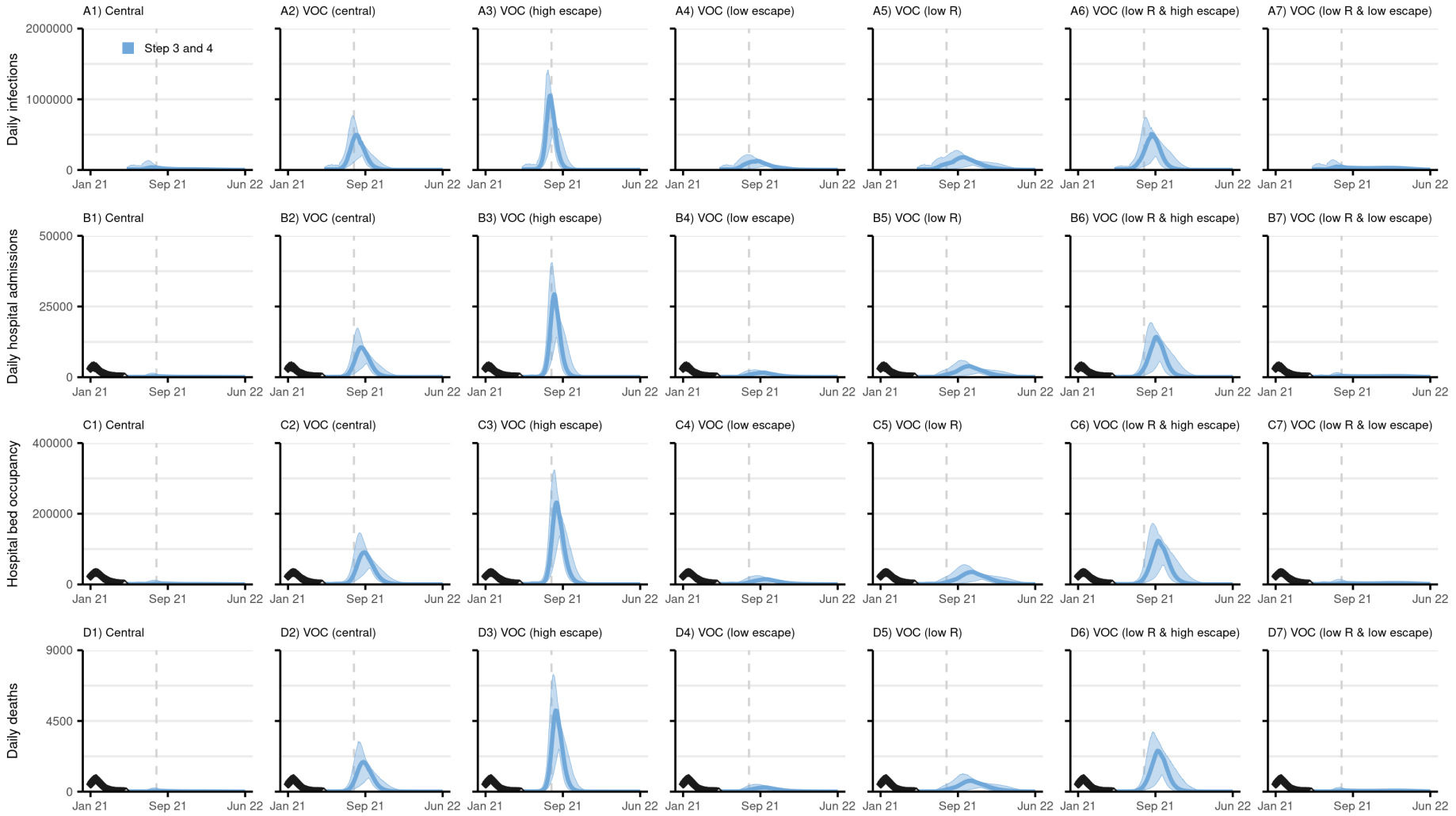
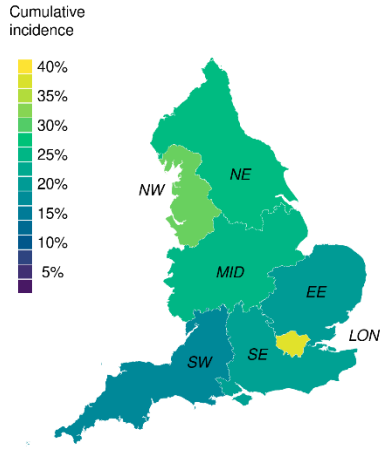


Figure S4: As Figure S2 (results with VOC) but showing impacts of Steps 3 and 4.

8. Appendix 3: 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 [2]. 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 1 May 2021. The model was fitted with vaccination (both first and second doses) as reported by DHSC to SPI-M (Figure 1). Figure S5 shows the estimated cumulative incidence in England by NHS region.



Region	Estimated cumulative proportion of the population infected up to 1 May 2021	
	Median	95%CrI
East of England (EE)	20%	16-24%
Midlands (MID)	25%	22-27%
London (LON)	38%	33-44%
North East and Yorkshire (NE)	26%	22-29%
North West (NW)	31%	27-34%
South East (SE)	21%	19-24%
South West (SW)	17%	14-22%

Figure S5: Estimated cumulative proportion of the population infected by NHS England Region up to 1 May 2021. The map shows the median; the table shows the median and 95% credible intervals rounded to the nearest percent.

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 B.1.1.7 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

England

We modelled levels of restrictions in line with the reopening steps set out in the roadmap [16]. These have been matched as closely as possible to what has been implemented in the past during this pandemic. While we cite policies in place during the Tier system implemented last autumn, we do not model any specific policy change but instead an assumed change in the corresponding level of transmission.

- Step 3: Similar to tier 1, i.e. rule of six in place, working from home when possible, hospitality curfew;
- Step 4: Baseline NPIs with TTI, hand washing & masks and some Covid-secure measures in places such as public transport and crowded indoor spaces.

The reproduction number for step 2 is set to the latest estimated value of the reproduction number based on data up to 1 May 2021 (see Table S1). *However, this estimate does not fully capture the impact of schools re-opening after Easter on transmission as R lags by at least 3 weeks*.

We modelled step 3 as similar to transmission levels seen for tier 1 in 2020 (further details in the previous report [17]).

The final baseline transmissibility once all NPIs are lifted is assumed to be on average $R_{\_excl\_immunity}$ = 3.5 consistent with an increase in transmissibility due to B1.1.7 (wild type R0 ~2.8 to 3.0, relative increase in B1.1.7 transmissibility ~75% [12]) but with a ~30% reduction due to residual measures such as hand hygiene and TTI. To capture the considerable uncertainty in predicting the behaviour of individuals after lifting most restrictions, we also consider a baseline $R_{\_excl\_immunity}$ of 4.5 (~10% marginal effect of remaining measures) as a sensitivity analysis.

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 with parameters shown in Table S1 and Figure S6.

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 $R_{\_excl\_immunity}$ by an average -0.3. This is based on the consensus value from SPI-M accounting for the increase in transmission due to the B.1.1.7 variant. This is consistent with the impact seen during Step 2 and slightly lower than the value (-0.5) assumed in previous iterations of this work. As some of the "not before" dates for the next step of NPI release overlap with school holidays, we adjusted the assumed transmissibility during this time accordingly with an average -0.3 in $R_{\_excl\_immunity}$ when schools are closed.

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 (shown in Figure 2C) may therefore differ slightly from those shown in Table S1 and Figure S6 because of this additional constraint.

Table S1: Overview of transmissibility and uncertainty associated with each release step in England, excluding immunity ($R_{excl\_immunity}$) (see Methods "Definitions of the reproduction number").

	$R_{\_excl\_immunity}$: mean (95% CI)	sd	meanlog	sdlog
Step 2 current level	1.05 (0.86-1.46)	0.13	-	-
Step 3 Schools closed	1.90 (1.54-2.32)	0.2	0.636	0.105
Schools open	2.20 (1.83-2.62)	0.2	0.784	0.0907
Step 4 (full lift)^ Schools closed	3.20 (2.53-4.00) (moderate baseline NPIs retained)	0.375	1.16	0.117
	4.20 (3.51-4.98) (higher R after full NPI lifting**)	0.375	1.43	0.0891
Schools open	3.50 (2.82-4.29) (moderate baseline NPIs retained)	0.375	1.25	0.107
	4.50 (3.81-5.28) (higher R after full NPI lifting**)	0.375	1.5	0.0832

**Higher R after full NPI lifting or "Lower adherence to baseline NPIs" values were used for sensitivity analyses only. ^Assumes some control such as TTI and hand hygiene continue.

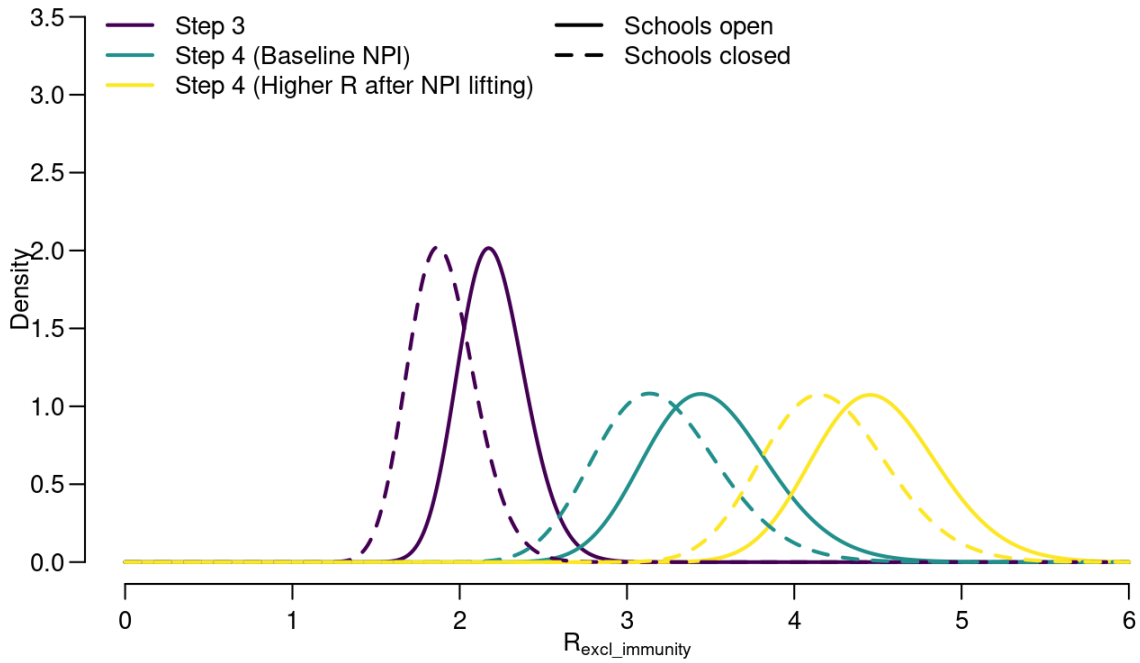


Figure S6: Distributions of transmissibility ($R_{excl\_immunity}$) associated with each step of NPI lifting in England. Values of $R_{\_excl\_immunity}$ were constrained so they could only increase over time except during school holidays when $R_{\_excl\_immunity}$ was decreased on average by -0.3. (For full details see Table S1).

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 (Figure S7) to $R_{excl\_immunity}$ in each phase (see Tables 4 and S1).

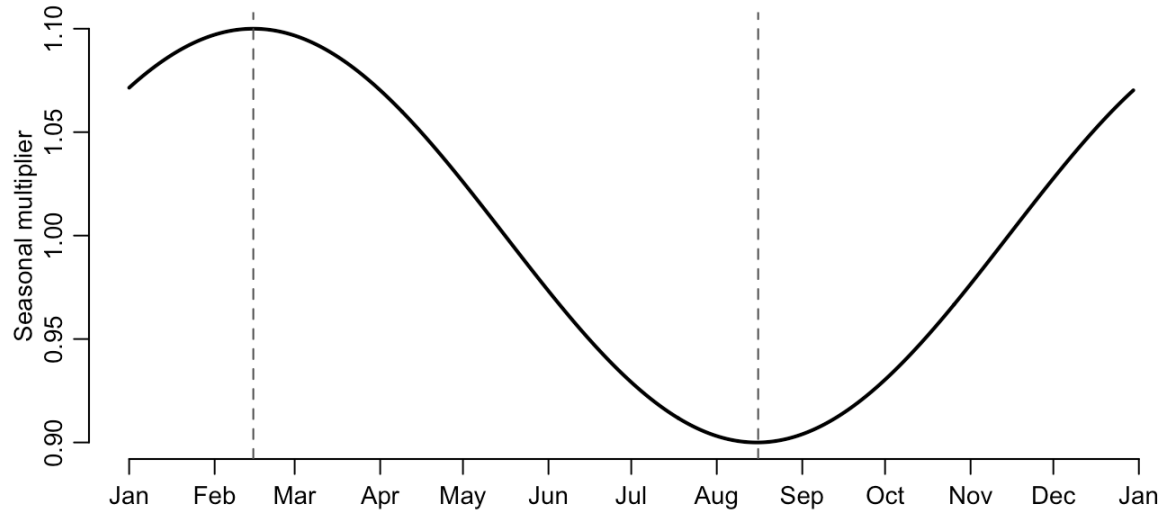


Figure S7: Seasonal daily multiplier for transmissibility ($R_{excl\_immunity}$) applied to each phase (Table S1).

We also performed a sensitivity analysis where we assumed no seasonal patterns of transmission.

First dose vaccine roll-out

We assume first doses were delivered in England between 8 December 2020 and 1 May 2021 as reported in data received from PHE and DHSC via SPI-M. We then assume a vaccine dose roll-out as in Table 1. 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 1 May 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 50+ years. For 30-49 year olds we assumed a 60% AZ and 40% PF or Moderna mix, and <30 years will receive PF 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. 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 efficacy after each dose

We assume degree-type protection from vaccination: all vaccinees have their likelihood of acquiring infection reduced by a factor of (*1 – vaccine efficacy*), see section on vaccine efficacy below for more detail.

For each compartment in the model, 4 successive vaccination stages (duration of each stage and efficacy of vaccine in each stage are shown on Figure S8):

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

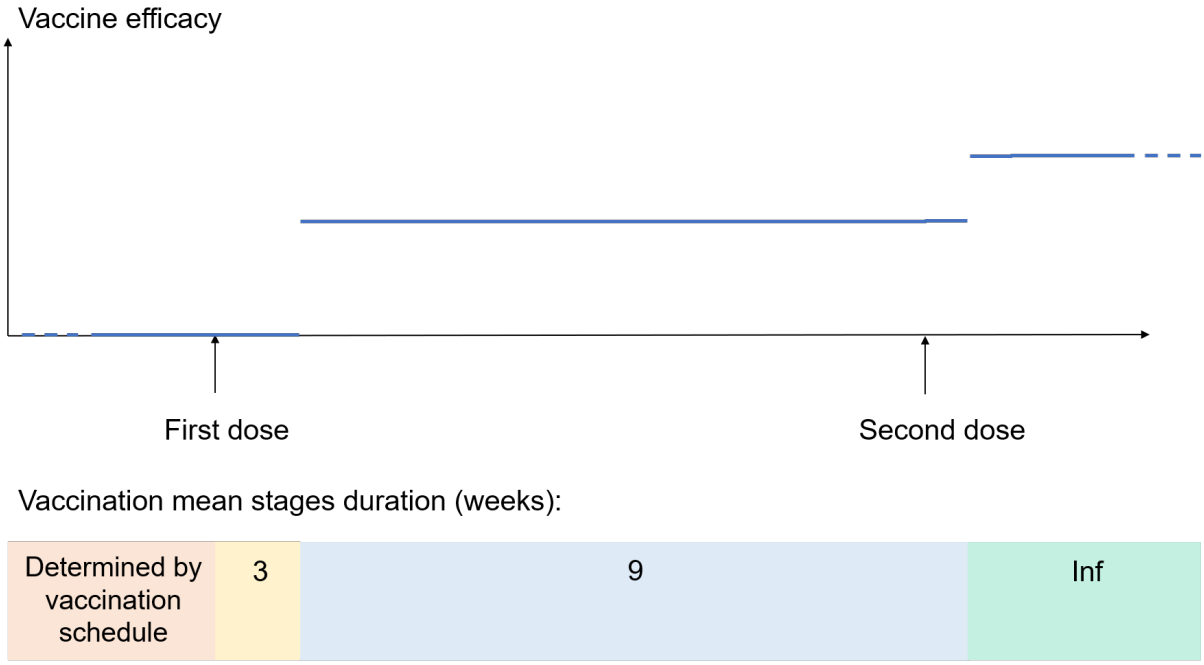


Figure S8: Vaccination stage duration and associated vaccine efficacy. The lower panel depicts mean duration of vaccination stages in weeks (numbers denote number of weeks in each stage). The top panel shows the associated vaccine efficacy and delays to protection over time.

Vaccine efficacy after first and second dose was varied across scenarios (see Table 3), but we assume:

- No efficacy in the 21 days following the first dose
- No efficacy 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 [23,24]. We therefore assumed a 21-day (respectively 7-day) delay between receiving the first (respectively second) dose and the onset of dose-specific efficacy.

Vaccine effectiveness

We assumed that the vaccine has four effects (Table 3):

1. Efficacy *against infection,* e_{inf}: Reducing the risk of infection in vaccinated individuals, compared to those not vaccinated.
2. Efficacy *against symptoms conditional on infection,* $e_{sympt\,|\,inf}$: Reducing the risk of symptoms in vaccinated individual who become infected, compared to those non vaccinated who become infected.
3. Efficacy *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 non vaccinated who become infected and symptomatic.
4. Efficacy against *onward transmission conditional on infection* $e_{transmit\,|\,inf}$: Reducing the risk of onward transmission from a vaccinated individual who became infected, compared to those non vaccinated who became infected (used in sensitivity analysis only)

The first two effects combined reduce the risk of symptomatic infection ("Efficacy *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 ("Efficacy *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 3. 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:

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

Vaccine uptake

We assume vaccine uptake was age dependant, as shown in Table 2. We assumed every individual having received their first dose would go on to also receive a second dose.

Modelling the introduction and spread of a variant of concern (VOC)

Overview

We model the potential introduction and spread of a hypothetical variant of concern (VOC) in England by extending our model to a two-variant model. Variant 1 represents the dominant variant in circulation, i.e. B.1.1.7 in the UK; variant 2 represents a hypothetical VOC. Transmissibility, efficacy of vaccines and natural immunity differ between the two variants. We only model the introduction of variant 2 after 1 May 2021, with daily seeding of new cases of variant 2 modelled with a Poisson distribution with rate specified in Table 5.

A simplified flowchart for our two-variant model is shown in Figure S9. The age/care home structure and vaccine class structure for the second variant is equivalent to that for the first.

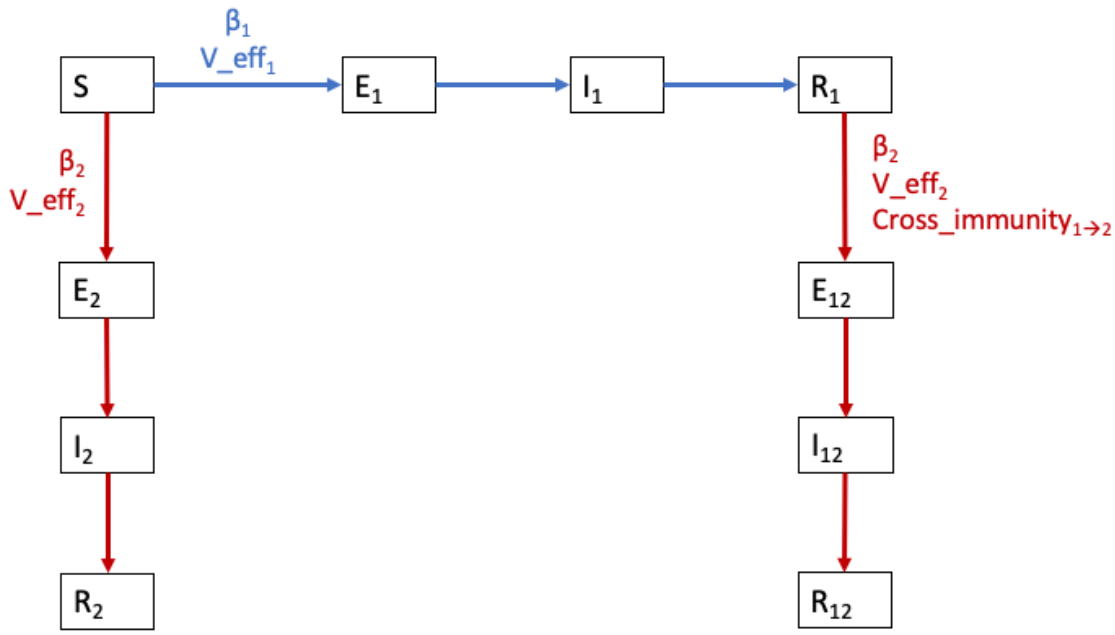


Figure S9: Flowchart summarising the two-variant structure of the model. S denotes susceptibles, E exposed (infected not infectious), I infectious and R recovered. Indexes denote infection with variant 1 (e.g. E1), variant 2 (e.g. E2) or variant 1 and 2 in turn (e.g. E12). In the model, each compartment is further split by age/care home resident/care home worker class (as described in [2]), 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 [2]. Deaths are not pictured on this figure but are also modelled as described in [2]. 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 β_i, the transmission rate for variant i, $cross\_immunity_{j->i}$, the cross protection against variant i provided by prior infection with the other variant (j), and V_eff_i, the vaccine efficacy against variant i. Note that vaccine efficacy will also alter the probability of symptomatic and severe infection.

Transmissibility of the VOC

Transmissibility for the second variant is modelled as proportional to that for the first variant, with a constant multiplier through time (Table 5). Therefore, increases in the reproduction number for the first variant automatically triggers corresponding increases in the reproduction number for the second variant. Unless otherwise specified, values of the reproduction numbers (both excluding immunity and effective) described in the text and in Figures and Tables all correspond to B1.1.7. When presenting reproduction numbers across the two variants, we compute these as the weighted average between the reproduction number for each variant, with weights given by the total force of infection for each variant. Unless otherwise specified, numbers of infections, hospitalisations, bed occupancy and deaths are shown for both variants together.

Immune escape properties of the VOC

We assume that vaccines may be less efficacious against the VOC (Table 6). We also model a non-symmetrical cross immunity between the two variants; we assume that infection with variant 2 (the VOC) confers perfect immunity to variant 1, but infection with variant 1 is only partially protective against infection with variant 2 (see Table 5). 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 (see Table 5).

9. *References*

1. Office for National Statistics. Coronavirus (COVID-19) antibody and vaccination data for the UK - Office for National Statistics [Internet]. [cited 3 May 2021]. Available: https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/datasets/coronaviruscovid19antibodydatafortheuk
2. Knock S, Whittles LK, Lees JA, Perez-Guzman PN, Verity R, FitzJohn RG, et al. The 2020 SARS-CoV-2 epidemic in England: key epidemiological drivers and impact 1 of interventions 2 Short title: Epidemiology of SARS-Cov-2 in England 3. medRxiv. Cold Spring Harbor Laboratory Press; 2021; 2021.01.11.21249564.
3. UK Government. Vaccinations | Coronavirus in the UK [Internet]. [cited 4 May 2021]. Available: https://coronavirus.data.gov.uk/details/vaccinations
4. Vasileiou E, Simpson CR, Shi T, Kerr S, Agrawal U, Akbari A, et al. Interim findings from first-dose mass COVID-19 vaccination roll-out and COVID-19 hospital admissions in Scotland: a national prospective cohort study. Lancet. Elsevier; 2021;0.
5. Public Health England. Public Health England vaccine effectiveness report. 2021.
6. Hyams C, Marlow R, Maseko Z, King J, Ward L, Fox K, et al. Assessing the Effectiveness of BNT162b2 and ChAdOx1nCoV-19 COVID-19 Vaccination in Prevention of Hospitalisations in Elderly and Frail Adults: A Single Centre Test Negative Case-Control Study. SSRN Electron J. Elsevier BV; 2021;
7. Hall VJ, Foulkes S, Saei A, Andrews N, Oguti B, Charlett A, et al. Effectiveness of BNT162b2 mRNA Vaccine Against Infection and COVID-19 Vaccine Coverage in Healthcare Workers in England, Multicentre Prospective Cohort Study (the SIREN Study). SSRN Electron J. 2021;
8. Voysey M, Clemens SAC, Madhi SA, Weckx LY, Folegatti PM, Aley PK, et al. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. Lancet. Elsevier; 2020;0.
9. Voysey M, Costa Clemens SA, Madhi SA, Weckx LY, Folegatti PM, Aley PK, et al. Single-dose administration and the influence of the timing of the booster dose on immunogenicity and efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine: a pooled analysis of four randomised trials. Lancet. Elsevier B.V.; 2021;397: 881–891.
10. Public Health England. PHE monitoring of the early impact and effectiveness of COVID-19 vaccination in England. 2021.
11. Harris RJ, Hall JA, Zaidi A, Andrews NJ, Kevin Dunbar J, Dabrera G. Impact of vaccination on household transmission of SARS-COV-2 in England.
12. Volz E, Mishra S, Chand M, Barrett JC, Johnson R, Geidelberg L, et al. Assessing transmissibility of SARS-CoV-2 lineage B.1.1.7 in England. Nature. Nature Publishing Group; 2021; 1–17.
13. Public Health England. SARS-CoV-2 variants of concern and variants under investigation in England.
14. Madhi SA, Baillie V, Cutland CL, Voysey M, Koen AL, Fairlie L, et al. Efficacy of the ChAdOx1 nCoV-19 Covid-19 Vaccine against the B.1.351 Variant. N Engl J Med. Massachusetts Medical Society; 2021; NEJMoa2102214.
15. Pfizer-BioNTech. Pfizer and BioNTech Confirm High Efficacy and No Serious Safety Concerns Through Up to Six Months Following Second Dose in Updated Topline Analysis of Landmark COVID-19 Vaccine Study | Business Wire [Internet]. [cited 8 Apr 2021]. Available: https://www.businesswire.com/news/home/20210401005365/en/
16. Cabinet Office UK Government. COVID-19 Response - Spring 2021 - GOV.UK. 2021.
17. Whittles LK, Imai N, Knock ES, Perez-Guzman PN, Sonabend R, Ghani AC, et al. Imperial College London: Unlocking roadmap scenarios for England, 18 February 2021 - GOV.UK. 2021.
18. Scottish Borders Council. School term dates for 2020-21 | Term, holiday and closure dates | Scottish Borders Council [Internet]. [cited 30 Apr 2021]. Available: https://www.scotborders.gov.uk/info/20009/schools_and_learning/621/term_holiday_and_closure_dates

19. Welsh Government. School terms, holidays and closures | Sub-topic | GOV.WALES [Internet]. [cited 30 Apr 2021]. Available: https://gov.wales/school-terms-holidays-and-closures

20. Wales Primary School. Wales Primary School: Term Dates 2020-2021 [Internet]. [cited 30 Apr 2021]. Available: https://www.walesprimary.co.uk/page/term-dates-2020-2021/71816

21. Education Authority Northern Ireland. School Holidays | Education Authority Northern Ireland [Internet]. [cited 30 Apr 2021]. Available: https://www.eani.org.uk/school-management/policies-and-guidance/school-holidays

22. BBC News. Covid: What's the roadmap for lifting lockdown? - BBC News [Internet]. [cited 30 Apr 2021]. Available: https://www.bbc.co.uk/news/explainers-52530518

23. Mulligan MJ, Lyke KE, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. Phase I/II study of COVID-19 RNA vaccine BNT162b1 in adults. Nature. Nature Research; 2020;586: 589–593.

24. Ramasamy MN, Minassian AM, Ewer KJ, Flaxman AL, Folegatti PM, Owens DR, et al. Safety and immunogenicity of ChAdOx1 nCoV-19 vaccine administered in a prime-boost regimen in young and old adults (COV002): a single-blind, randomised, controlled, phase 2/3 trial. Lancet. Lancet Publishing Group; 2020;396: 1979–1993.