"Unlocking" Roadmap Scenarios for England v2

Lilith K Whittles, Natsuko Imai, Edward S Knock, Pablo N Perez-Guzman, Raphael Sonabend, Azra Ghani, Neil M Ferguson, Marc Baguelin, Anne Cori

Imperial College COVID-19 Response Team

Extended scenarios for England for lifting non-pharmaceutical interventions (NPIs) as set out by the Cabinet Office were explored. *Detailed/specific policy changes cannot be modelled.* Instead, the increase in transmissibility from successive easing of NPIs was translated as per Table 1, accounting for the considerable uncertainty in transmissibility associated with each step in our estimates of R. Vaccine roll out schedules (Table 3) were pre-specified. Current levels of transmissibility are based on our latest estimates for England at R_{eff} (including immunity) =0.75 (translating to $R_{excl\_immunity}$ =1.10 with an estimated 32% of the population currently protected via prior infection- and/or vaccine-induced immunity). Table 4 shows vaccine efficacy assumptions against severe disease, symptomatic disease and infection after each dose (Pfizer and Astra-Zeneca). Four sensitivity analyses were performed, using 1) slower vaccine roll out; 2) pessimistic vaccine efficacy; 3) lower adherence to NPI measures retained after full lifting (i.e. return to a higher baseline transmissibility) and 4) including seasonality in SARS-CoV-2 transmissibility. We assumed an age-dependent vaccine uptake (Table 5).

Summary

1. Due to eligibility and vaccine hesitancy, vaccination alone will not be sufficient to keep the epidemic under control. NPIs must be lifted slowly and cautiously to minimise the number of deaths and prevent high hospital occupancy, with some baseline NPIs remaining in place (and adhered to) throughout 2021 and beyond.
2. It is critical to achieve and maintain high vaccine uptake and roll out *before* easing NPIs.
3. Assuming optimistic vaccine efficacy, even if 3.2M vaccine doses/week are given up to 12 July (3.9M thereafter), only 46% of the population will be protected against disease (due to vaccination or recovery from infection) at the date of full NPI lifting in scenario 1 (26 April 2021), 60% in scenario 4 (2 August), and 65% in scenario 5a (16 July) (Fig 1A).
4. Relaxing too quickly (scenario 1) will result in peak hospital occupancy considerably higher than the current wave and substantial additional deaths (Fig 1E-F). This holds regardless of vaccine efficacy, roll out, adherence to baseline NPIs, and impact of seasonality.
5. Scenario 4 will still result in a substantial additional number of deaths (58,200, 95%CrI 31,000 - 95,300) by June 2022 in our main analysis.
6. Scenarios 5a and 5b where NPIs return to Tier-1 like restrictions on 27th April and 11th May 2021, and are fully lifted on 16th July 2021, result in a smaller but prolonged wave of hospitalisations compared to the current wave, and lead to an additional 55,000 (95%CrI:33,200 - 81,200) and 54,800 (95%CrI: 32,600 - 82,900) deaths, respectively.
7. Our results are highly dependent on the assumed (optimistic) vaccine efficacy, uptake, and roll-out speed. Due to the uncertainty surrounding these assumptions, it is critical to rapidly assess the true effectiveness of vaccination within the population as it may be lower than clinical efficacy reported in trial settings. Our results also assume no loss of infection- or vaccine-induced immunity on the time horizon of the analysis. Characterising the duration of vaccine-immunity will be critically important.
8. With a lower vaccine efficacy, all scenarios would lead to a third wave of hospitalisations larger than or comparable in magnitude to the current wave (Fig 3-A2).
9. A return to higher transmissibility levels after NPIs are lifted will also lead to a third wave of hospitalisations comparable in magnitude to the current wave (Fig 3-A1). 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.
10. Assessing the impact of each relaxation *before* committing to the next phase is critical. Impact of waning immunity and other VOC is particularly difficult to assess at present.

*Table 1: Summary of all NPI easing scenarios where some restrictions are eased on specific dates resulting in an increase in transmissibility. The **average** transmissibility at each stage is shown. For the overall transmissibility and associated uncertainty see Table 2.*

Date of NPI gradual release ("Full lift" still retains some baseline NPI measures such as TTI and hand hygiene^)

Scenario 1. "Very fast"	**8 March '21**	**29 March '21**	**26 April '21**			
Level of NPI lifting	All schools	Tier 3 & 2	Full lift			
*Average R (95% probability interval)**	1.60 (1.46-1.75)	2.10 (1.96-2.25)	3.00 (2.54-3.52) Lower adherence^: 4.00 (3.53-4.51)			
Scenario 2. "Fast"	**8 March '21**	**29 March '21**	**19 April '21**		**10 May '21**	**31 May '21**
Level of NPI lifting	All schools	Tier 3	Tier 2		Tier 1	Full lift
*Average R (95% probability interval)**	1.60 (1.46-1.75)	1.70 (1.56-1.85)	2.10 (1.96-2.25)		2.20 (2.06-2.35)	3.00 (2.54-3.52) Lower adherence^: 4.00 (3.53-4.51)
Scenario 3. "Medium"	**8 March '21**	**5 April '21**	**3 May '21**		**7 June '21**	**5 July '21**
Level of NPI lifting	All schools	Tier 3	Tier 2		Tier 1	Full lift
*Average R (95% probability interval)**	1.60 (1.46-1.75)	1.70 (1.56-1.85)	2.10 (1.96-2.25)		2.20 (2.06-2.35)	3.00 (2.54-3.52) Lower adherence^: 4.00 (3.53-4.51)
Scenario 4. "Gradual"	**8 March '21**	**5 April '21**	**3 May '21**	**7 June '21**	**5 July '21**	**2 Aug '21**
Level of NPI lifting	Primary schools	All schools	Tier 3	Tier 2	Tier 1	Full lift
*Average R (95% probability interval)**	1.35 (1.23-1.48)	1.60 (1.46-1.75)	1.70 (1.56-1.85)	2.10 (1.96-2.25)	2.20 (2.06-2.35)	3.00 (2.54-3.52) Lower adherence^: 4.00 (3.53-4.51)
Scenario 5. "New"	**8 March '21 / "Step 1"**	**29 March '21 / "Step 2"**		**"Step 3"**	**5a: 27 April '21 ** 5b: 11 May '21 ****	**"Step 4": Central roll out: 16 July 2021 ** Pessimistic roll out: 26 Sep 2021 ****
Level of NPI lifting	Schools + critical HE/FE, some children's activities	Tier 3-like + one guest per day per household indoors + outdoor hospitality		Tier 1-like		Full lift
*Average R (95% probability interval)**	1.60 (1.46-1.75)	1.90 (1.62-2.21)		2.20 (2.06-2.35)		3.00 (2.54-3.52) Lower adherence^: 4.00 (3.53-4.51)

** Here R denotes the reproduction number in the absence of immunity $R_{\_excl\_immunity}$, see methods "Definitions of the reproduction number" for definitions. The 95% probability interval is given as the 2.5 and 97.5 percentiles of a lognormal distribution, see Table 2. ** These were chosen to roughly correspond to the below timings with an additional delay to account for the vaccination of (non-care home) heath care workers and other priority groups (e.g. younger but fragile) which we do not model explicitly. These dates are therefore in-line with Warwick's lifting dates: i) 3 weeks after everyone in JCVI groups 1-9 received 1st dose (step 3, scenario 5a), ii) everyone in JCVI groups 1-4 received 2 dose2 (step 3, scenario 5b), iii) all adults (18+) vaccinated with one dose (step 4 scenarios 5a and 5b).*

Table 2: Overview of transmissibility and uncertainty associated with each tier-like restriction, accounting for immunity (R_{eff}) and excluding immunity ($R_{excl\_immunity}$) (see Methods "Definitions of the reproduction number"), assuming 68% of the population in England is currently susceptible to infection after accounting for infection-induced and vaccine-induced population immunity. See methods Table 7 for full distribution.

	$R_{\_excl\_immunity}$: mean (95% CI)	**Corresponding R_{eff}***: mean (95% CI)**
Current level	1.10 (1.00-1.20)	0.75 (0.68-0.82)
School reopening* (Step 1)	1.60 (1.46-1.75)	1.09 (0.99-1.19)
Tier 3	1.70 (1.56-1.85)	1.16 (1.06-1.26)
Step 2	1.90 (1.62-2.21)	1.29 (1.10-1.50)
Tier 2	2.10 (1.96-2.25)	1.43 (1.33-1.53)
Tier 1 (Step 3)	2.20 (2.06-2.35)	1.50 (1.40-1.60)
Baseline NPI (Step 4)	3.00 (2.54-3.52) (*moderate baseline NPIs retained*)	2.04 (1.73-2.39)
	4.00 (3.53-4.51) (*lower adherence to baseline NPIs***)	2.72 (2.40-3.07)

*Refers to fully opening all schools. We assumed that opening primary schools only would lead to an increase in $R_{\_excl\_immunity}$ from its "current level" which is half the increase obtained with full "school reopening" (see methods[1]). **"Lower adherence to baseline NPIs" values were used for sensitivity analyses only. ^Assumes some control such as TTI and hand hygiene continue. ***R_{eff} was calculated assuming 68% of the population in England is susceptible to infection

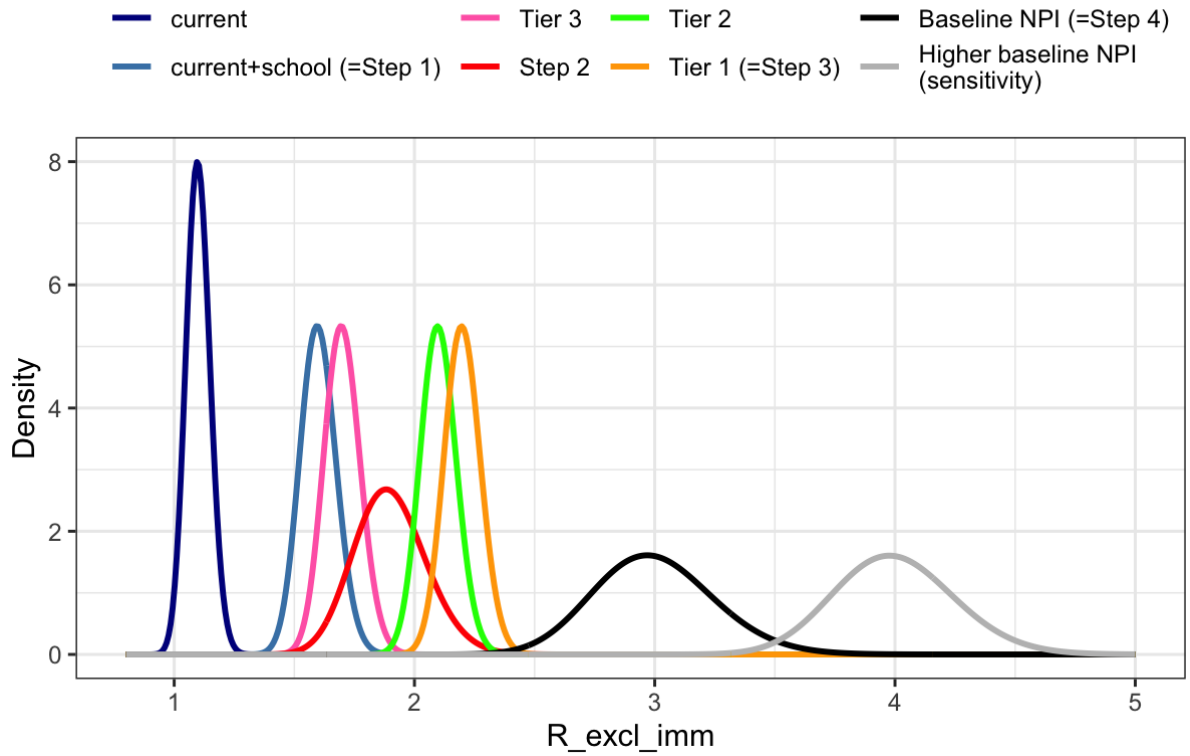

Figure 1: Distributions of transmissibility ($R_{excl\_immunity}$) associated with each step of NPI lifting (Table 2 and Table 7). Values of $R_{\_excl\_immunity}$ were constrained so they could only increase over time.

[1] https://cmmid.github.io/topics/covid19/comix-schools.html

Table 3: Pre-specified vaccination schedule (million doses per week)

Weeks commencing	England doses / week Central (main analysis)	Slower roll out (sensitivity analysis)
22-Feb to 05 Jul	Average 3.2 M	Average 2.7 M
12-Jul onwards	3.9 M	2.0 M

Table 4: Vaccine efficacy assumptions for Astra-Zeneca (AZ, assumed to be 80% of the vaccine doses distributed) and Pfizer (PF, assumed to be 20% of the vaccine doses distributed)

	Vaccine	Central (Main analysis)	Pessimistic*
Efficacy against severe disease	AZ (1 dose)	80%	70%
	AZ (2 doses)	80%	70%
	PF (1 dose)	86%	55%
	PF (2 doses)	98%	90%
Efficacy against disease	AZ (1 dose)	63%	50%
	AZ (2 doses)	63%	50%
	PF (1 dose)	65%	55%
	PF (2 doses)	94%	90%
Efficacy against infection	AZ (1 dose)	63%	50%
	AZ (2 doses)	63%	50%
	PF (1 dose)	65%	55%
	PF (2 doses)	94%	90%

* Pessimistic values were used for sensitivity analyses only.

Table 5: Vaccine uptake assumptions by group or age. Uptake was assumed to be the same for vaccine doses 1 and 2.

Group	Uptake	YouGov survey week 33 results^
Care home residents (CHR)	95%	-
Care home workers (CHW)	85%	-
80+ years*	95%	93.9% (70.4 - 99.8%)
50-80 years*	85%	85.7% (82.1 – 88.9%)
<50 years*	75%	71.4% (67.0 – 75.4%)

* not working or residing in a care home. ^YouGov COVID-19 survey results, weighted proportion (95% CI) of individuals who responded “Strongly agree” or “Agree” to the question “If a Covid-19 vaccine were made available to me this week, I would definitely get it” in week 33.

Caveats and Key assumptions

1. We have not explicitly modelled the impact of Higher Education return.
2. We assume **no loss of infection-induced or vaccine-induced immunity** over the time horizon of the analysis (*optimistic)*.
3. We assume that vaccine roll out pace of 3.9M doses/week from 12 July 2021 onwards can be maintained (*unclear*)
4. We assume high vaccine uptake across all age groups (*optimistic*).
5. We assume "step 3" to occur on 27 April 2021 for scenario 5a and 11 May 2021 for scenario 5b. We assume that "step 4/full lift" for scenarios 5a and 5b to occur on 16 July 2021 in the central vaccine roll-out scenario and on 26 September 2021 in the slow vaccine roll-out scenario. These were chosen to roughly correspond to: 3 weeks after everyone in JCVI groups 1-9 received 1st dose (step 3, scenario 5a), everyone in JCVI groups 1-4 received 2 dose2 (step 3, scenario 5b), and all adults (18+) vaccinated with one dose (step 4 scenarios 5a and 5b) respectively. Note that in our model these targets may be achieved earlier than those dates because we do not model vaccination of health care workers, (non-care home) social workers and individuals at risk who may be prioritised for vaccination. We therefore added an additional delay to account for this making our dates more in line with Warwick's lifting dates as specified above.
6. We **assume a higher vaccine efficacy than our previous report** (*optimistic*)
7. We **assume the vaccines provide some protection from severe disease requiring hospitalisation or death** *(optimistic).*
8. 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** *(unclear).*
9. We assume that mixing patterns under each Tier are the same as in autumn 2020 and these levels are fixed *(unclear)*.
10. We do not explicitly model school holidays *(unclear)*.
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** *(unclear)*.
13. We **do not model health care workers, (non-care home) social workers and individuals at risk** who may be prioritised for vaccination *(unclear).* Explicit modelling of these groups would mean "Step 3" and "Step 4" of scenarios 5a and 5b happening later than assumed here.
14. We assume **no dynamic replenishment of the care-home population** *(optimistic).*
15. We assume that some level of transmission control remains even after "fully lifting" NPIs (Table 1) through measures such as TTI and hand hygiene *(optimistic)*.

Results

With the central vaccine roll-out set out in Table 3, and the uptake assumed (see Table 5), the proportion of the population protected against severe disease through vaccination will stabilise and plateau at around 51% during the summer 2021 (Figure 1A). This relatively low value stems from 1) not vaccinating the <18-year-olds, and imperfect vaccine 2) efficacy (see Table 4) and 3) uptake (see Table 5). ***[77.3% population eligible for vaccination x average 79.1% uptake amongst those eligible x 83.6% ("central") efficacy against severe disease with 2 doses = 51%].*** Note that this leaves a large pool of children (<18 years) who are not eligible for vaccination and who contribute to transmission.

Figure 1B shows, for our central assumptions, the extent to which the population will be protected over time, through a combination of vaccination and natural infection. This illustrates that vaccination alone is unlikely to be sufficient to bring the epidemic under control.

Strategies involving very rapid lifting of NPIs (scenario 1, Figure 1C) will lead to mixing and transmissibility increasing faster than population immunity, which will build-up incrementally until the summer (Figure 1A). This will lead to high values of the effective reproduction number *(R_{eff})* in the spring 2021 (Figure 1D), leading in turn to a large wave of infections, hospitalisations and deaths over the spring or summer 2021 (Figure 1E-F and Table 6). This result holds across our (rather optimistic) main analysis, as well as all the sensitivity analysis considering lower adherence to baseline NPI, lower vaccine efficacy, slower vaccine-roll-out, and seasonality in transmission (Figure 3 and S1).

Strategies which lift NPIs more gradually (scenario 4) will lead to increases in mixing that are closer to being offset by the increases in population immunity (Figure 1A), leading to lower values of the effective reproduction number in the spring 2021 (Figure 1C), and in turn to a wave of infections, hospitalisations and deaths predicted to be smaller on average than the current one, although with large associated uncertainty (Figure 1E-F).

The “new” strategy (scenario 5a and 5b) where NPIs will return to Tier-1 like restrictions on 27 April 2021 (three weeks after JCVI groups 1-9 receive 1 dose) or on 11 May 2021 (when JCVI groups 1-4 receive both doses), and full lifting of NPIs (after all eligible adults receive their first dose) on 16 July 2021, leads to a wave of hospitalisation on average slightly smaller compared to the first wave and that currently experienced. It is also similar in magnitude to those predicted under scenarios 3 and 4, but with an earlier predicted peak in late June 2021. This new strategy is estimated to result in an additional 55,000 (95% CrI:33,200 - 81,200) to 54,800 (95% CrI:32,600 - 82,900) deaths.

In summary, all lifting strategies will lead to a resurgence of transmission, but for strategies 3, 4, 5a and 5b, the corresponding peak of hospitalisations and deaths is likely to be smaller than seen in January 2021 (Figure 1E-F and Table 6).

Our results depend on the underlying assumptions about vaccine roll out, mixing/transmissibility after NPI lifting (see Table 2) and vaccine efficacy (note that we have used more optimistic vaccine efficacy assumptions than the previous report, see Table 4).

Qualitatively, results were very similar across scenarios 1, 2, 3, and 4 with a slower roll out of vaccination (still assuming >2M doses a week, see Table 3). For scenarios 5a and 5b, where the last step of NPI lifting occurs at a given coverage of vaccine rather than at a given date, the slower vaccine roll-out in fact led to fewer predicted hospitalisations and deaths; this is because the slow roll out means it takes longer to reach the given vaccine coverage threshold. Therefore, the return to baseline NPIs occurred at a later date on 26 September 2021 (compared to 16 July 2021 in the fast roll-out scenario).

Assuming more pessimistic values for either vaccine efficacy or mixing/transmissibility after NPI lifting would lead, with NPI lifting strategies 5a and 5b, to a third wave of hospitalisations and deaths of magnitude comparable to the current one (Figures 3 & S1).

Allowing for some level of seasonality in transmission did not substantially affect the results (Figures 3 & S1).

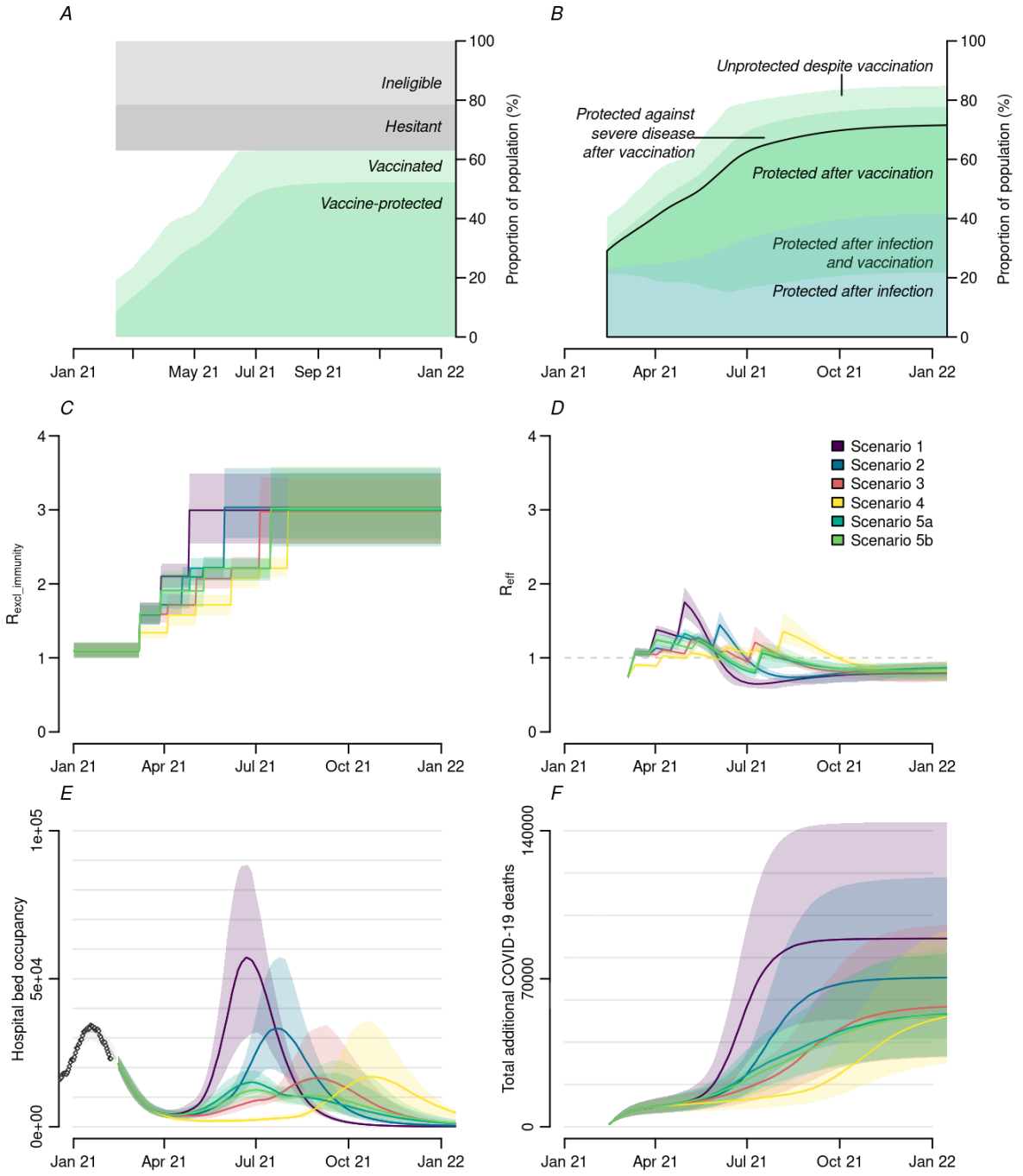

Figure 2: Impact of vaccine roll-out and NPI lifting on the epidemic dynamic in England. *(A) Proportion of the population in England protected against severe disease through vaccination over time (dark green shading) and vaccinated (having received one dose) over time (light green shading) (Table 4). The grey shaded areas show the proportion of the population ineligible for vaccination (i.e. <18 years, light grey) and those who are vaccine hesitant and not taking the vaccine (dark grey) (see Table 5). (B) Proportion of the population protected (from bottom to top): after natural infection, after natural infection and vaccination, after vaccination, against severe disease (but not against infection) after vaccination, and those unprotected despite vaccination over time. (C) Increase in mixing (measured as $R_{\_excl\_immunity}$, coloured lines) under different release strategies over time and (D) Effective reproduction number over time under different release strategies. (E) COVID-19 hospital occupancy (general wards and ICU) and (F) cumulative COVID-19 deaths (counted from 1st Feb 2021) under different release strategies. In panel E, the points at the start (Jan 21) show the recent reported data and the grey line the model fit. The release strategies considered are scenario 1 (purple), 2 (blue), 3 (pink), 4 (yellow), and 5 (green) as set out in Table 1. In panels C-D the coloured lines show the mean; in panels E-F the coloured lines show the median. In panels C-F the shaded areas show the 95% credible intervals. This figure shows results assuming moderate baseline measures are retained after NPI lifting (see Table 2), "central" vaccine efficacy, and vaccine roll-out and uptake described in Tables 3 and 5. See methods for definitions of R_{eff} and $R_{excl\_immunity}$.*

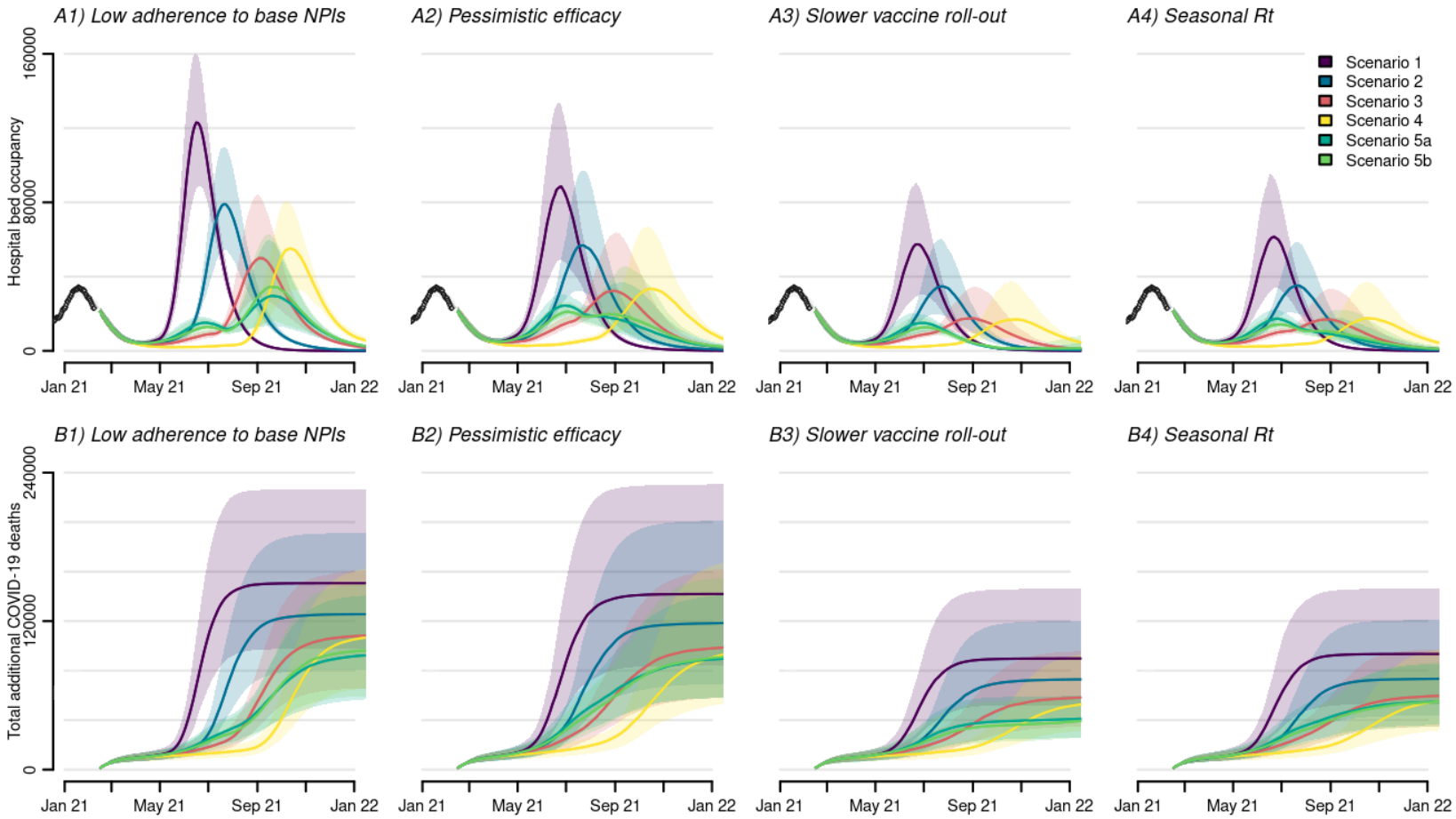

Figure 3: Sensitivity analyses. *England COVID-19 (top: A1, A2, A3, A4) hospital occupancy (general wards and ICU) and (bottom: B1, B2, B3, B4) cumulative deaths (counted from 12th Feb 2021) assuming scenario 1 (purple), 2 (blue), 3 (pink), 4 (yellow), and 5 (green) release of NPIs over time as set out in Table 1, with vaccine roll out and uptake assumptions as in Tables 3 and 5 respectively. A1 and B1 assume a higher transmissibility level after NPIs are "fully" lifted (lower adherence to baseline NPIs) ($R_{excl\_immunity}$ = 4) as shown in Table 2. A2 and B2 assume a "pessimistic" vaccine efficacy as set out in Table 4. A3 and B3 assume a slower vaccine roll out as set out in Table 3. A4 and B4 assume seasonality in transmission as outlined in Methods (+/-10% relative change in transmissibility throughout the year). The points at the start of panel A1-A3 (Jan 21) show the recent reported data and the grey line the model fit. 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 1E-F*

Table 6: Cumulative deaths (mean (95% CrI), nearest 100) between 12th Feb 2021 and 30th Jun 2022 under different vaccination scenarios considered. Unless otherwise specified in "Analysis Type", results assume "central" values of vaccine efficacy, vaccine roll out, return to baseline NPIs of $R_{excl\_immunity}$ = 3, and no seasonality.

Analysis type	NPI lifting scenario (date return to baseline, 2021)	Cumulative deaths by 30 June 2022 (95%CrI)	Cumulative hospital admissions to 30 June 2022 (95%CrI)	Cumulative incidence to 30 June 2022 (95%CrI)	Peak hospital occupancy to 30 June 2022 (95%CrI)
Main analysis	1 (26 Apr)	91,300 (52,500 - 146,400)	348,600 (236,200 - 468,100)	16,312,200 (11,671,300 - 20,766,200)	59,200 (32,100 - 89,800)
	4 (2 Aug)	58,200 (31,000 - 95,300)	213,000 (140,400 - 301,000)	10,331,600 (6,978,000 - 13,735,300)	18,300 (7,000 - 35,500)
	5a (16 Jul)	55,000 (33,200 - 81,200)	207,700 (159,200 - 261,300)	10,600,400 (8,406,000 - 13,150,200)	15,800 (11,500 - 20,500)
	5b (16 Jul)	54,800 (32,600 - 82,900)	205,800 (159,000 - 270,800)	10,449,500 (8,350,700 - 13,438,800)	14,100 (10,000 - 22,100)
Higher transmissibility after NPI lifting* ($R_{excl\_immunity}$= 4)	1 (26 Apr)	154,000 (96,000 - 222,400)	587,200 (485,700 - 688,500)	23,993,300 (21,105,800 - 26,674,400)	124,900 (91,100 - 160,900)
	4 (2 Aug)	112,600 (67,600 - 167,900)	420,400 (328,100 - 516,300)	17,851,500 (14,803,200 - 20,678,600)	55,200 (32,800 - 81,700)
	5a (16 Jul)	94,700 (58,900 - 143,400)	361,100 (288,700 - 449,800)	16,431,700 (13,963,200 - 19,228,900)	31,800 (16,500 - 57,200)
	5b (16 Jul)	98,100 (58,500 - 148,100)	373,400 (294,000 - 470,400)	16,780,000 (13,989,500 - 19,518,200)	35,900 (17,100 - 63,200)
Lower vaccine efficacy**	1 (26 Apr)	146,000 (82,300 - 232,100)	531,900 (357,900 - 712,000)	19,368,100 (14,191,100 - 23,838,100)	91,400 (51,100 - 137,500)
	4 (2 Aug)	103,800 (56,100 - 172,500)	369,000 (232,200 - 512,800)	14,007,800 (10,005,000 - 18,927,000)	35,600 (13,600 - 67,300)
	5a (16 Jul)	94,000 (56,300 - 141,500)	342,700 (255,900 - 442,500)	13,685,200 (10,791,400 - 16,888,800)	26,400 (20,600 - 42,900)
	5b (16 Jul)	94,400 (58,300 - 146,700)	342,800 (262,300 - 471,500)	13,606,400 (10,831,900 - 17,546,000)	25,100 (17,300 - 45,200)
Slower vaccine roll out***	1 (26 Apr)	92,300 (53,100 - 148,100)	353,000 (240,500 - 470,000)	16,517,900 (11,710,600 - 20,781,700)	59,400 (31,400 - 91,500)
	4 (2 Aug)	58,600 (30,800 - 96,800)	214,500 (143,200 - 306,200)	10,412,400 (7,145,200 - 13,675,400)	18,600 (7,200 - 35,900)
	5a (26 Sep)	44,300 (28,100 - 62,900)	166,700 (136,400 - 205,200)	8,812,800 (7,262,300 - 10,448,500)	15,600 (10,700 - 21,100)
	5b (26 Sep)	43,300 (27,600 - 62,900)	162,200 (133,400 - 194,000)	8,562,500 (7,138,900 - 10,349,500)	13,200 (9,300 - 17,300)
Including seasonality^	1 (26 Apr)	95,600 (54,200 - 152,800)	365,900 (248,700 - 487,200)	16,980,500 (12,240,400 - 21,245,800)	63,400 (34,300 - 98,800)
	4 (2 Aug)	60,300 (34,400 - 97,400)	221,500 (150,600 - 314,300)	10,717,400 (7,493,300 - 14,260,500)	19,000 (7,500 - 36,700)
	5a (16 Jul)	57,100 (35,000 - 84,300)	216,500 (168,600 - 266,200)	11,035,300 (8,975,300 - 13,398,500)	17,700 (12,900 - 21,700)
	5b (16 Jul)	56,700 (35,400 - 84,000)	214,100 (170,100 - 269,400)	10,860,400 (8,775,500 - 13,728,500)	15,500 (10,700 - 21,300)

* $R_{\_excl\_immunity}$ used after NPI relaxation (see Tables 1 and 2 and text for detail). **See table 4 for details. ***See table 3 for details. ^See methods "Seasonality in Transmissibility".

Supplementary Results

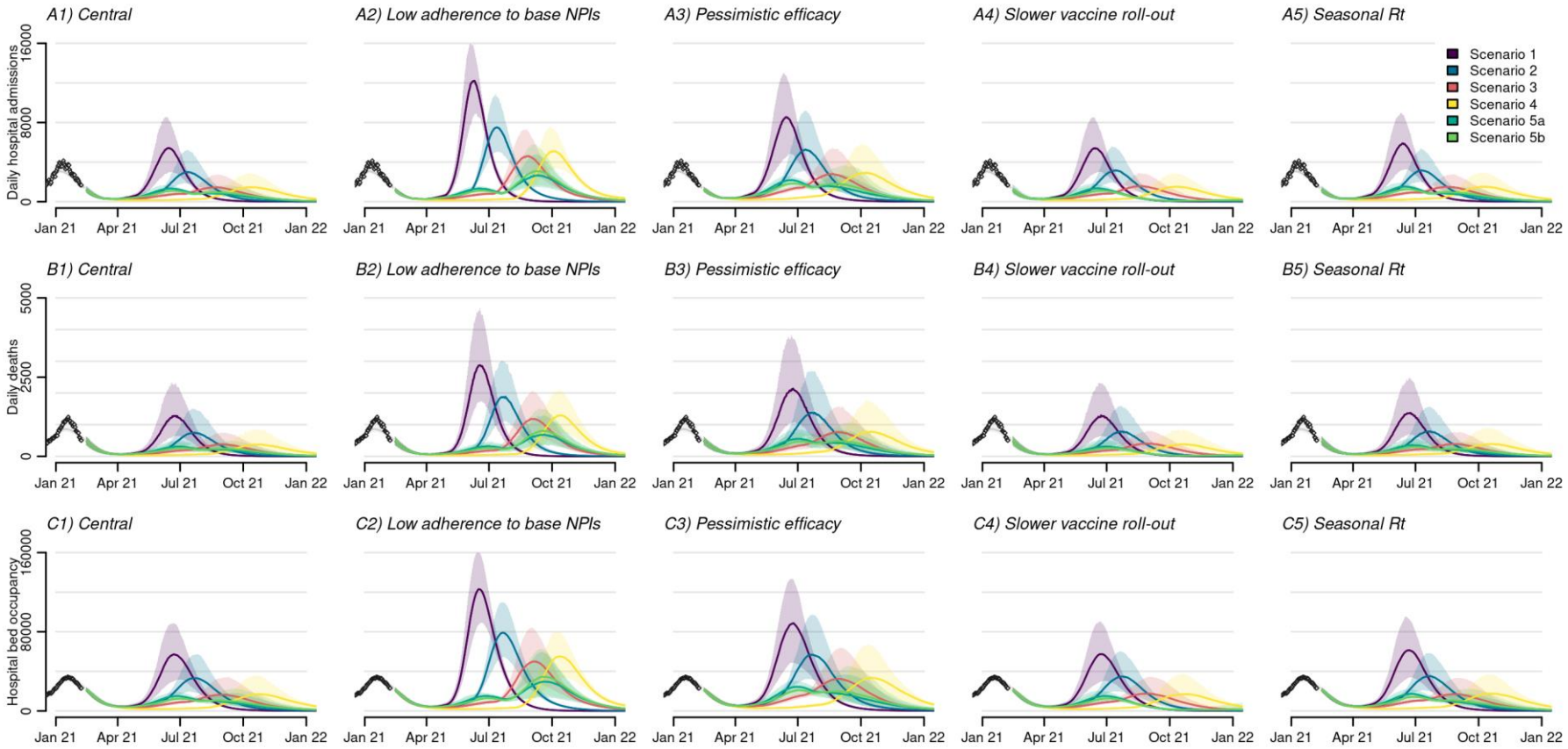

Figure S1: *England COVID-19 daily (A1-A5) hospital admissions, (B1-B5) deaths and (C1-C5) hospital occupancy assuming scenario 1 (purple), 2 (blue), 3 (pink), 4 (yellow), and 5 (green) release of NPIs over time as set out in Table 1. A1-C1 show our main analysis with a "central" transmissibility after NPI lifting where moderate baseline NPIs are retained (see Table 2), "central" vaccine efficacy (see Table 4), and central vaccine roll-out and uptake described in Tables 3 and 5. A2-C2 show sensitivity analyses assuming a higher transmissibility level after NPIs are "fully" lifted with lower adherence to baseline NPIs ($R_{excl\_immunity}$ = 4) as shown in Table 2. A3-C3 show sensitivity analyses assuming a "pessimistic" vaccine efficacy as set out in Table 4. A4-C4 show results with a slower vaccine roll out as set out in Table 3. A5-C5 show sensitivity analyses with seasonality in transmission as outlined in Methods (+/-10% relative change in transmissibility throughout the year). The points at the start of the panels (Jan 21) show the recent reported data and the grey line the model fit. 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 1E-F.*

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 (https://www.medrxiv.org/content/10.1101/2021.01.11.21249564v1). 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 the 12th February 2021. The model was fitted with vaccination as reported.

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).
- **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 Tiers

We modelled 7 levels of restrictions from 1 (lowest level of restrictions) to 7 (highest). These have been matched to the ask and 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.

- Level 1: Baseline NPIs with TTI, hand washing & masks and some Covid-secure measures in places such as public transport and crowded indoor spaces;
- Level 2: Similar to tier 1, i.e. rule of six in place, working from home when possible, hospitality curfew;
- Level 3: Similar to tier 2, i.e. measures from level 2 plus no indoor mixing between households and travel reduced;
- Level 4: Intermediate between tier 2 and 3 (tier 3 + one person indoors per household per day and outdoor hospitality);
- Level 5: Similar to tier 3, i.e. measures of level 4 plus local travel only, and pubs and bars closed;
- Level 6: Similar to the autumn lockdown, i.e. measures of level 4 plus non-essential shops being closed;
- Level 7: Full lockdown with schools closed.

We assume that going from level 7 to level 6 (opening schools) will increase $R_{\_excl\_immunity}$ by an average +0.5 (+0.25 if opening only primary schools). This is based on the consensus value from SPI-M accounting for the increase in transmission due to the B.1.1.7 variant. The impact of switching from level 6 to 5 is difficult to quantify but is likely to be small, and we assume an increase of on average +0.1 in $R_{\_excl\_immunity}$.

To model the average change of transmission between level 5, 3 and 2, we used the analysis by Laydon et al. (unpublished, previously presented at SPI-M) which estimated level 3 and 4 as having respectively 94% and 74% of the level of transmission of level 2.

We modelled level 4 as an intermediate between levels 3 and 5 (i.e. tier 2 and tier 3), with an average $R_{\_excl\_immunity}$ taken as the mean of the values used for levels 3 and 5.

Lastly, the final baseline transmissibility once all NPIs are lifted is assumed to be on average $R_{\_excl\_immunity} = 3$, consistent with an increased in transmissibility due to B.1.1.7 but with a slightly lower level of transmission due to baseline NPIs. Due to the uncertainty in predicting the behaviour of individuals after the lifting of most of the restrictions, we also consider a baseline $R_{\_excl\_immunity}$ of 4 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 7 and Figure 1.

For each NPI lifting scenario, we sampled from the relevant distributions of $R_{\_excl\_immunity}$ at each step of lifting, with the added constraint that $R_{\_excl\_immunity}$ could only increase over time. The resulting R distributions (shown in Figure 2C) may therefore differ slightly from those shown in Table 2 and Figure 1 because of this additional monotonic constraint.

Table S2: Overview of transmissibility and distribution associated with each tier-like restriction, accounting for immunity (R_{eff}) and excluding immunity ($R_{excl\_immunity}$) (given to 3dp, see Methods "Definitions of the reproduction number"), assuming 68% of the population in England is currently susceptible to infection due to a combination of infection-induced and vaccine-induced immunity.

	$R_{\_excl\_immunity}$ **mean (95% CI)**	**sd**	**meanlog**	**sdlog**	R_{eff} **mean (95% CI)**
Current level	1.10 (1.00-1.20)	0.050	0.094	0.045	0.75 (0.68-0.82)
School reopening* (Step 1)	1.60 (1.46-1.75)	0.075	0.469	0.047	1.09 (0.99-1.19)
Tier 3	1.70 (1.56-1.85)	0.075	0.530	0.044	1.16 (1.06-1.26)
Step 2	1.90 (1.62-2.21)	0.150	0.639	0.079	1.29 (1.10-1.50)
Tier 2	2.10 (1.96-2.25)	0.075	0.741	0.036	1.43 (1.33-1.53)
Tier 1 (Step 3)	2.20 (2.06-2.35)	0.075	0.788	0.034	1.50 (1.40-1.60)
Baseline NPI (Step 4)	3.00 (2.54-3.52) *(moderate baseline NPIs retained)*	0.250	1.095	0.083	2.04 (1.73-2.39)
	4.00 (3.53-4.51) *(lower adherence to baseline NPIs**)*	0.250	1.384	0.062	2.72 (2.40-3.07)

* Refers to fully opening all schools. We assumed that opening primary schools only would lead to an increase in $R_{\_excl\_immunity}$ from its "current level" which is half the increase obtained with full "school reopening" (see methods[2]). ** "Lower adherence to baseline NPIs" values were used for sensitivity analyses only. ^Assumes some control such as TTI and hand hygiene continue.

[2] https://cmmid.github.io/topics/covid19/comix-schools.html

Seasonality in transmissibility

In our main analyses we assumed no seasonality in SARS-CoV-2 transmissibility. We performed a sensitivity analysis where we assumed seasonal patterns of transmission throughout the year was 20% in the UK measured as the relative peak to trough variation. We computed a daily multiplier for transmissibility which was:

- Maximal at 1.1 on 1st December of each year (10% relative increase compared to the mean transmissibility)
- Minimal at 0.9 on 1st June of each year (10% relative decrease compared to the mean transmissibility)

We then computed a monthly multiplier as the average of the daily multiplier for each calendar month (February 2021, March 2021, etc). We then applied this monthly seasonal multiplier (Figure S2 blue line) to $R_{excl\_immunity}$ in each phase (see Table S2).

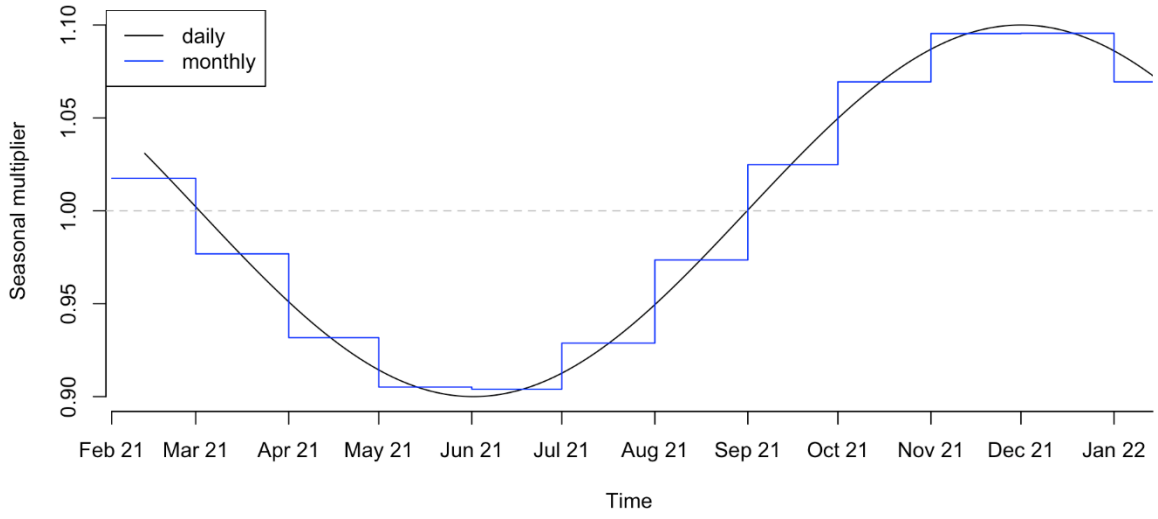

Figure S2: Seasonal multiplier for transmissibility ($R_{excl\_immunity}$). Daily multipliers (black line) were averaged by calendar month (blue line) and applied to each phase (Table 2).

1st dose vaccine roll-out

We assume first doses were delivered in England between 8th December 2020 and 12th February 2021 as reported in data received from PHE and DHSC via SPI-M. We then assume a vaccine dose roll out as in Table 3. 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 84 days (12 weeks) prior. If the resulting value was negative, this was set to 0. From 13th February onwards, we assumed first doses are split between NHS regions in proportion of their population size. We assumed a mixture of 20% of Pfizer and 80% of AstraZeneca vaccine doses are distributed, with no difference between age groups or care home workers and residents being modelled.

We assume doses are distributed in priority order to:

1. Care home workers and residents
2. Individuals 50 or over by decreasing 5-year age band priority

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 other groups under 50 years old.

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 S3):

- 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

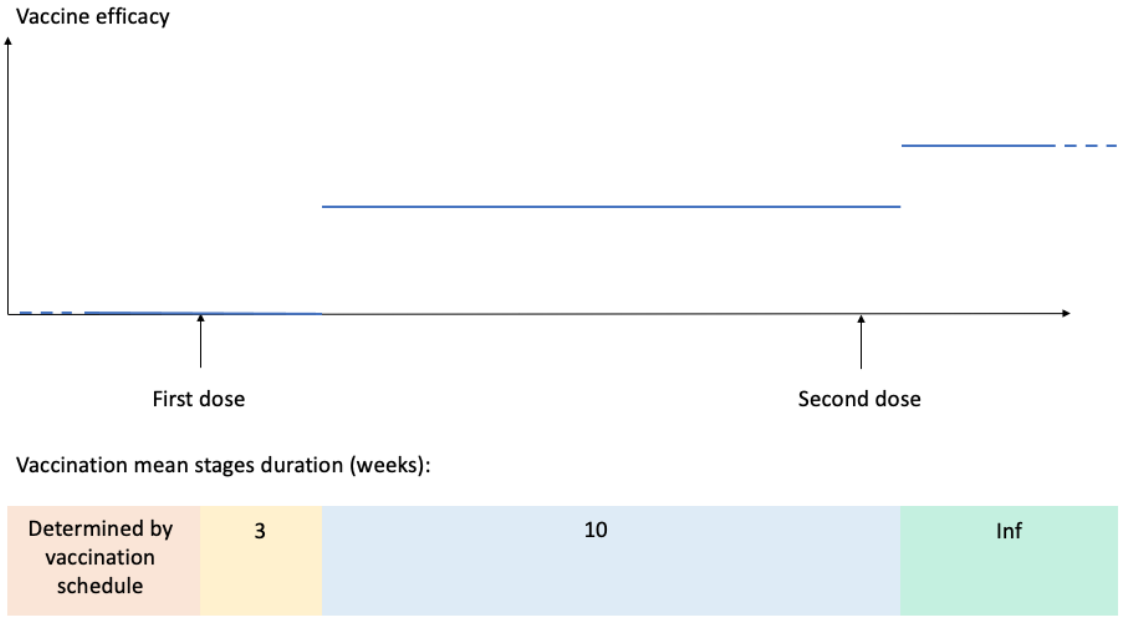

Figure S3: Vaccination stage duration and associated vaccine efficacy. The lower panel depicts mean duration of vaccination stages in weeks (numbers denote number of weeks in each stage). The top panel shows the associated vaccine efficacy and delays to protection over time.

Vaccine efficacy after first and second dose was varied across scenarios (see Table 4), 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[3,4]. 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 efficacy

We assumed that the vaccine has three effects:

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,* $e_{sympt \mid inf}$: 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,* $e_{hosp \mid sympt}$: 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.

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 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 efficacy for e_{inf} , and e_{sympt} and e_{hosp} are shown in Table 4. 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 ($e_{sympt \mid inf}$) as follows:

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

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

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

Vaccine uptake

We assume vaccine uptake was age dependant, as shown in Table 5. We assumed every individual having received their first dose would go on to also receive a second dose.

[3] Mulligan et al. (2020). https://www.nature.com/articles/s41586-020-2639-4
[4] Ramasamy et al. (2020). https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32466-1/fulltext