Potential profile of the COVID-19 epidemic in the UK under different vaccination roll out strategies [Ver 2.]

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Commission [N.B interpretation of parameters differs to the report dated 13th Jan 21]

The following assumptions specified by SPI-M were used for the main/central analysis:

1. **Transmissibility**: exploring two starting values of the reproduction number which gradually increases over time up to 1st July 2021 of 0.8 and 1.2. Note that in our model R is the reproduction number in the absence of immunity ($R\_excl\_immunity$).

2. **Vaccine efficacy**: for the main analysis assume protection against risk of
   a. Being **symptomatically infected,** we refer to this as clinical efficacy (e_{clin}) by:
      i. 88% for PF and 70% for AZ after dose 1; and
      ii. 94% for PZ and 88% for AZ after dose 2.
   b. Being **infected** (e_{inf}) by:
      i. 48% for both PF and AZ after dose 1; and
      ii. 60% for both PF and AZ after dose 2.

Summary

- Vaccination will have a large positive impact on the number of COVID-19 deaths with the doses administered to date (~2M) having a noticeable effect already.

- There is uncertainty around the total number of deaths. However, the impact will be substantially higher if optimistic, or even central vaccine roll out can be achieved, compared to pessimistic roll out (i.e. if vaccination can be rapidly ramped up from 1 to 2 or 3 million doses a week).

- For all gradual easing of NPI scenarios explored, unless vaccination is rapidly ramped up to 3 million doses a week, gradual lifting of NPIs from 1st March to 1st July will lead to a third wave of hospitalisations which will exceed our indicative threshold of 25,000 beds national hospital capacity.

- Given current estimates of Rt and the estimated increase in transmissibility of the new variant circulating in the UK, our most realistic scenario corresponds to R in the absence of immunity gradually increasing from $R_{\_excl\_immunity}$ = 1.2 to 4.0. Under this scenario, a rapid ramp-up of vaccination roll out to at least 3 million doses a week is critical to avoid exceeding national hospital capacity after the current wave (where it is already exceeded). This would still lead to an additional 130,800 (103,200 - 167,600) deaths between now and June 2022.

- Our results highlight the importance of speeding-up vaccine roll-out, and suggest that a more cautious approach to gradually lifting NPIs may need to be considered than the ones modelled in this report.

- Our sensitivity analyses suggest that at high levels of vaccine efficacy against symptomatic disease, different levels of vaccine impact on acquisition of infection would only have a moderate impact on hospitalisations or deaths.

Caveats and Key assumptions

- *Our results are directly dependant on the assumptions regarding vaccine efficacy.*
- Note that the reduction in the risk of being symptomatically infected (e_{clin}) 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}) as follows:

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

  We therefore calculated e_{sympt} as:

  $e_{sympt} = (e_{clin} - e_{inf}) / (1 - e_{inf})$

- In a small number of the proposed sensitivity analyses, some combinations of parameters were not compatible (as e_{inf} must be <= e_{clin}). In those cases, we adjusted e_{clin} upwards so that $e_{clin} = e_{inf}$.
- Degree-type protection from vaccination: all vaccinees have their likelihood of acquiring infection reduced by a factor of (*1 – vaccine efficacy*).
- We do not model health care workers, social workers and individuals at risk who may be prioritised for vaccination.
- We assume no dynamic replenishment of the care-home population.
- No loss of infection-induced or vaccine-induced immunity on the time horizon of the analysis.
- We assume the uptake is the same in all age groups and in care home workers and care home residents, at 85%. To mimic a potential decrease of uptake for second dose from 85% to 75%, efficacy of the second dose was adjusted downwards.
- We do not model the gradual building of the initial vaccination from December 2020 until today but model it as happening all in one go over two days at the start of our simulation.
- We considered 4 scenarios to reflect the possible NPIs in place during vaccine roll-out and their gradual easing, corresponding to each combination of:
  - Two <u>initial</u> R values from 5th January to end-February of R = 0.8 and R = 1.2
  - Two <u>final</u> R values as of 31st July of R = 2.8 and R = 4.0
  - With equally spaced step-wise changes in R on the 1st day of each month starting on 1st March (Figure 2).
- The gradual lifting of NPIs have been modelled as a step-wise increase in R, with each increase occurring on the first of the month from 1st March to 1st July 2021. We have not considered any potential corresponding policy changes that could reflect these changes such as reopening schools or non-essential retail.
- When quantifying hospital capacity thresholds, this analysis is done at the national level and region-specific capacity is not considered. Moreover, we note that given the physical and mental burden on frontline workers, assuming a constant maximum bed capacity for a prolonged period of time is in itself optimistic.

Conditions in the commission that <u>were not/could not</u> be modelled:

- We did not model lifting NPIs reactively when R = 1. Instead, we considered gradually lifting NPIs on the first day of each month starting 1st March 2021 onwards with full lifting on 1st July.

Methods

We used a stochastic compartmental model of SARS-CoV-2 transmission fitted to multiple data streams from each NHS region in the UK. The model is stratified into 17 five-year age groups (0-4, 5-9, …, 75-59, 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.imperial.ac.uk/mrc-global-infectious-disease-analysis/covid-19/report-41-rtm/). We used parameter values calibrated to data from the 11th January 2021.

The model was extended to include vaccination where each compartment in the model is further stratified to account for vaccination status. Table 1 details the scenarios explored with respect to doses administered per week and vaccine efficacy.

Table 1: Vaccination scenarios. In all scenarios, 1,959,151 vaccine 1st doses are assumed to have been delivered by 11th January 2021 in England, 78,005 in Northern Ireland, 163,377 in Scotland and 86,039 in Wales. (https://coronavirus.data.gov.uk/details/healthcare#card-people_who_have_received_vaccinations)

Scenario	Doses per week	Efficacy (first / second dose)
Central	- Jan 1~ = 1M doses/wk - Jan 25~ = 2M doses/wk	<u>Against being symptomatically infected (e_{clin})</u> *Pfizer* = 88% / 94% *Astra-Zeneca* = 70% / 88% <u>Against being infected (e_{inf})</u> 48% / 60%
Pessimistic	Jan 1~ = 1M doses/wk	*As above*
Optimistic	- Jan 1~ = 1M doses/wk - Jan 25~ = 2M doses/wk - Feb 1~ = 3M doses/wk	*As above*

1st dose vaccine roll-out

We assume 2,286,572 first doses were delivered in the UK by 11th January (1,959,151 in England, 78,005 in Northern Ireland, 163,377 in Scotland and 86,039 in Wales, see *https://coronavirus.data.gov.uk/details/healthcare#card-people_who_have_received_vaccinations*). We then assume a 1st dose roll out as in Table 1. As we start our simulation on 12th January, after the start of vaccination, we simulate a "catch-up" delivery of these December/January over two days 13 - 14th January (effectively delivering ~2.5M doses over the two-day period), and then move on to the roll-out described in Table 1.

We assumed 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*

For each compartment in the model, 6 successive vaccination stages (duration of each stage and efficacy of vaccine in each stage are shown on Figure 1):

- Unvaccinated
- Vaccinated with 1st dose before onset of vaccine efficacy
- Vaccinated with 1st dose with partial efficacy from 1st dose
- 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 partial efficacy from 2nd dose
- Vaccinated with 2nd dose with full efficacy from 2nd dose

Figure 1: 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 below and Table 1) but we always assume:

- No efficacy in the 7 days following a dose
- Half the dose efficacy between 7 and 14 days following the dose
- Full dose efficacy from 14 days following the dose

Vaccine efficacy

Against being symptomatically infected (e_{clin})

Efficacy against being symptomatically infected (defined as the relative reduction in the probability that a vaccinated individual becomes symptomatic if infected, compared to an unvaccinated) was assumed to be:

- First dose efficacy: 88% for PF and 70% for AZ
- Second dose efficacy: 94% for PF and 88% for AZ

with no heterogeneity by age.

Against being infected (e_{inf})

Efficacy against being infected (defined as the relative reduction in the probability of becoming infected when exposed of a vaccinated individual, compared to an unvaccinated) was assumed to be:

- First dose efficacy: 48% for both PF and AZ
- Second dose efficacy: 60% for both PF and AZ

with no heterogeneity by age.

Note that the reduction in the risk of being symptomatically infected (e_{clin}) 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}) as follows:

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

We therefore calculated e_{sympt} as:

$$\boldsymbol{e_{sympt} = (e_{clin} - e_{inf}) / (1 - e_{inf})}$$

We considered the above in our main analyses, and also considered as a sensitivity analysis (labelled f) a more pessimistic efficacy of 66% that of the vaccine efficacy against being symptomatically infected in the main analysis. This was only run for the central daily doses scenario. We also considered as sensitivity analyses (labelled h, I and j) different impacts on transmission blocking:

h. Assume above but **transmission blocked** (acquisition of infection blocked) at **dose 1 is 32% and dose 2 is 40%**
i. Assume above but **transmission blocked** (acquisition of infection blocked) at **dose 1 is 60% and dose 2 is 75%**
j. Assume above but with **0% of transmission blocked** (acquisition of infection blocked).

Vaccine uptake

We assume the uptake is the same in all age groups and in care home workers and care home residents, at 85%. To mimic a potential decrease of uptake for second dose from 85% to 75%, we adjusted the efficacy of the second dose downwards.

Background levels of transmission

We consider four scenarios for the changing levels of transmissibility ($\boldsymbol{R_{\_excl\_immunity}}$, i.e. the reproduction number in the absence of immunity in the population) whilst the vaccine 1st doses are being rolled out. The scenarios considered are summarised in Figure 2 below.
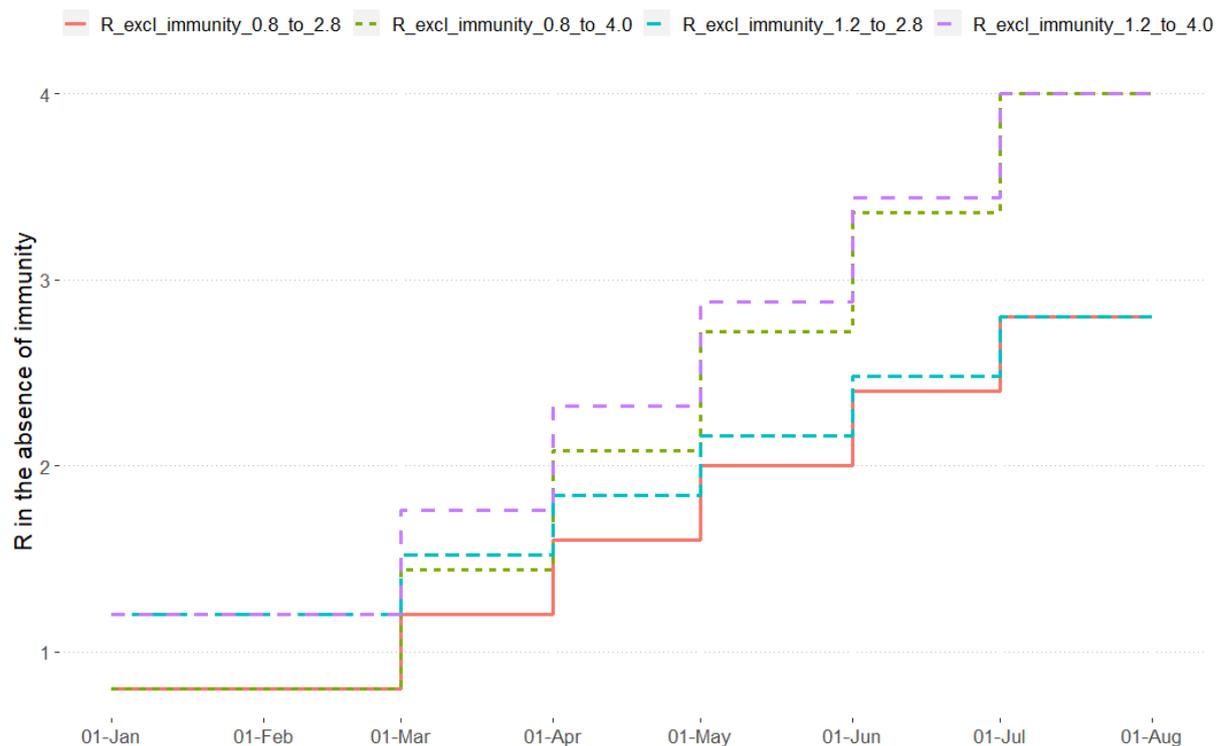
Figure 2: Assumed changes in the transmissibility (the reproduction number in the absence of immunity, $R_{excl\_immunity}$) over time for each of the four transmissibility scenarios. We assume two starting values of $R_{excl\_immunity} = 0.8$ OR 1.2 and two final values of $R_{excl\_immunity} = 2.8$ OR 4.0. Starting on the 1st March 2021, the gradual lifting of NPIs is then modelled by an equally spaced step-wise increase in transmissibility on the first of each month up to 1st July 2021.

Results

The figures below show results through to 30th June 2022. The sensitivity analyses are only shown for the scenario where transmissibility gradually increases from $R_{excl\_immunity} = 1.2$ to 4.0 as R is unlikely to be <1 currently and to account for the increased transmissibility of the new variant of concern.

As expected, the faster vaccination can take place and the more stringent NPIs can remain in place whilst this happens, the lower the number of hospitalisations and deaths (Table 2, Figure 4 and 5), resulting from the increased transmission within the population following the lifting of NPIs.

We found that under the pessimistic vaccine roll out scenario, hospital capacity (assumed to be ~25,000 beds in the UK) was breached for the 4 NPI lifting scenarios considered. This highlights that a distribution of 2-3M doses per week must be reached to prevent considerable mortality in the third wave.
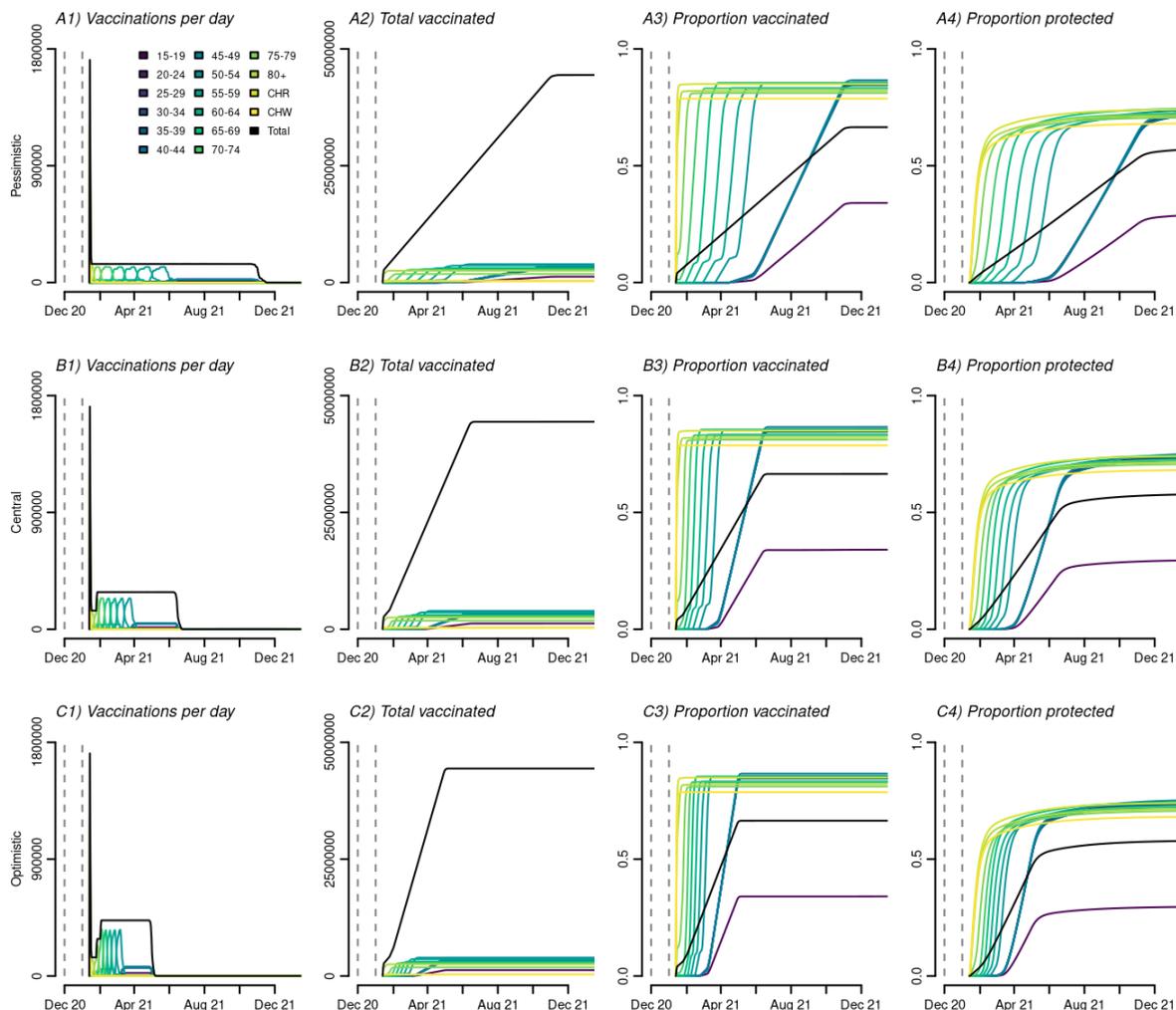
Figure 3: Plot shows for each vaccination scenario (top, middle and bottom rows correspond to optimistic, central and pessimistic vaccine roll out respectively, with central vaccine efficacy, as defined in Table 1). (A1, B1, C1) Daily number of people vaccinated with the first dose over time. (A2, B2, C2) Cumulative number of first doses delivered over time. (A3, B3, C3) Proportion of the population having received at least one dose of the vaccine over time. (A4, B4, C4) Proportion of the population effectively protected, accounting for partial protection after the first dose, and for delays between the two doses and between injection and onset of efficacy (Note that only efficacy against acquisition is accounted for here, not impact of the vaccine on onwards transmission). In all panels, the colours correspond to age groups as well as care home residents (CHR) and care home workers (CHW); black lines show the total across all age groups, CHR and CHW in the population. Note that age groups under 15 are not shown individually as they do not receive vaccination, but they contribute to the population totals used as denominators in panels A3, B3, C3, A4, B4 and C4.
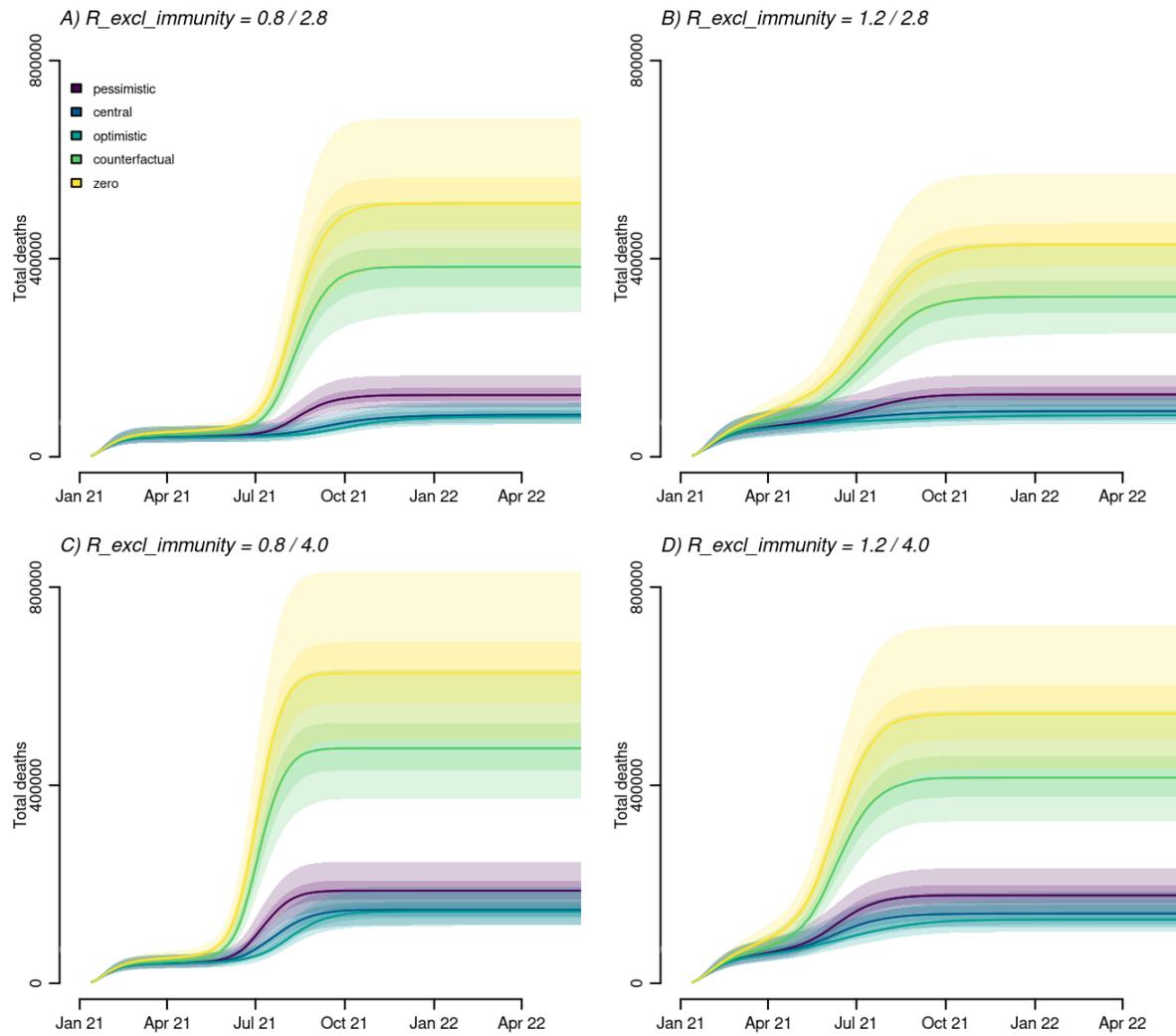
Figure 4: Cumulative UK COVID-19 deaths under a pessimistic (purple), central (blue), and optimistic (dark green) vaccine roll-out scenarios as described in Table 1. The light green shows the counter-factual where no additional vaccines beyond those already distributed up to 11th Jan are administered. Yellow shows the scenario where "zero" vaccinations are administered. Each panel shows the impact of vaccination according to different levels of NPI relaxation translating to a gradual increase in the transmissibility ($R_{excl\_immunity}$) with stepwise changes on the first of each month starting 1st March to 1st July 2021. $R_{excl\_immunity}$ A) increasing from 0.8 to 2.8; B) increasing from 1.2 to 2.8; C) increasing from 0.8 to 4.0; and D) increasing from 1.2 to 4.0 as shown in Figure 3.
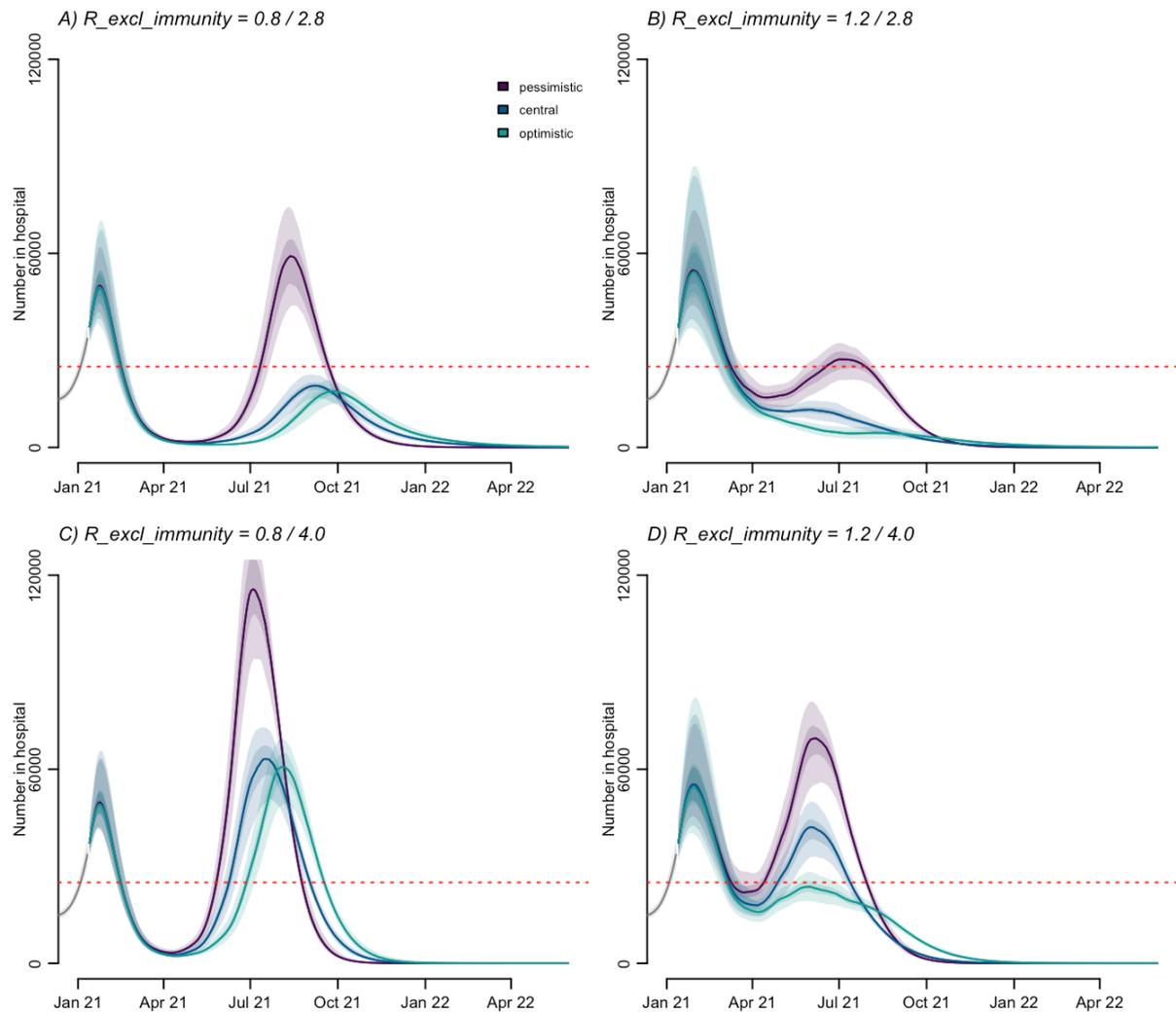
Figure 5: UK COVID-19 hospital occupancy (general wards and ICU) under a pessimistic (purple), central (blue), and optimistic (dark green) vaccine roll-out scenarios as described in Table 1. Each panel shows the impact of vaccination according to different levels of NPI relaxation translating to a gradual increase in the transmissibility (R_excl_immunity) with stepwise changes on the first of each month starting 1ˢᵗ March to 1ˢᵗ July 2021. R_excl_immunity A) increasing from 0.8 to 2.8; B) increasing from 1.2 to 2.8; C) increasing from 0.8 to 4.0; and D) increasing from 1.2 to 4.0 as shown in Figure 3. The horizontal red dashed line denotes a threshold of 25,000 beds in the UK indicative of considerable stress for hospital capacity. N.B the y-axis is truncated to allow scenarios to be better differentiated. Thus, the peak is not shown for some scenarios.
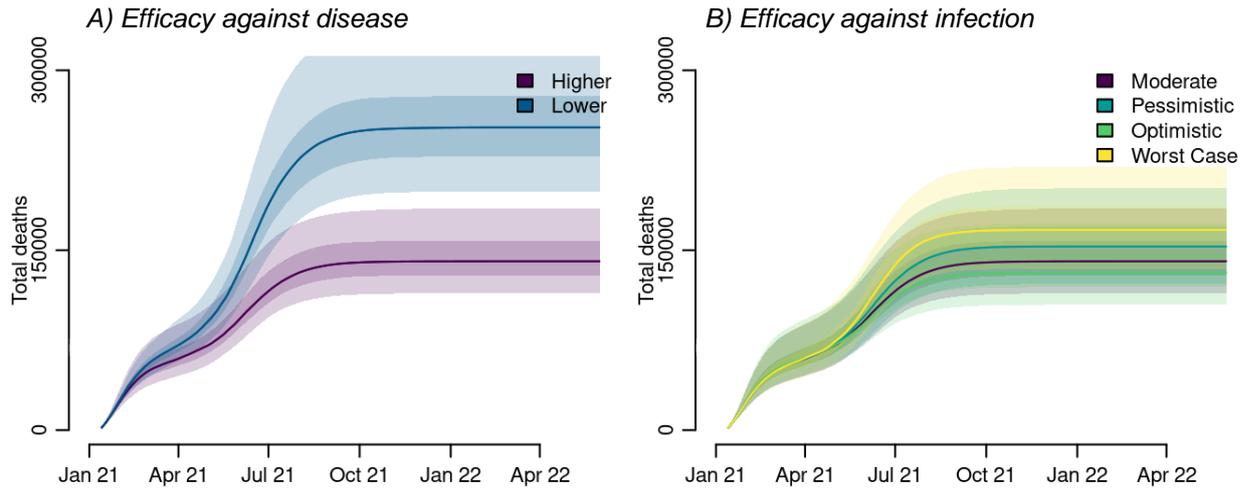
Figure 6: Cumulative UK COVID-19 deaths under different assumptions of vaccine efficacy against (left panel) symptomatic disease and (right panel) acquisition of infection. [Left panel] Purple shows the higher vaccine efficacy against symptomatic disease (first dose efficacy: 88% for PF and 70% for AZ, second dose efficacy: 94% for PF and 88% for AZ) and blue a more pessimistic efficacy of 66% that of the vaccine efficacy. [Right panel] Purple shows the moderate/central vaccination efficacy (first dose/second dose) against acquisition of infection of 48% / 60% for both PF and AZ, blue the pessimistic where efficacy is 32% / 40%; green the optimistic where efficacy is 60% / 75%; and yellow a worst-case efficacy of 0% / 0%. We assume levels of NPI relaxation translating to a gradual increase in the transmissibility ($R_{excl\_immunity}$) with stepwise changes on the first of each month starting 1ˢᵗ March to 1ˢᵗ July 2021 increasing from 1.2 to 4.0 as shown in Figure 3, and a central vaccine roll-out scenario as described in Table 1.
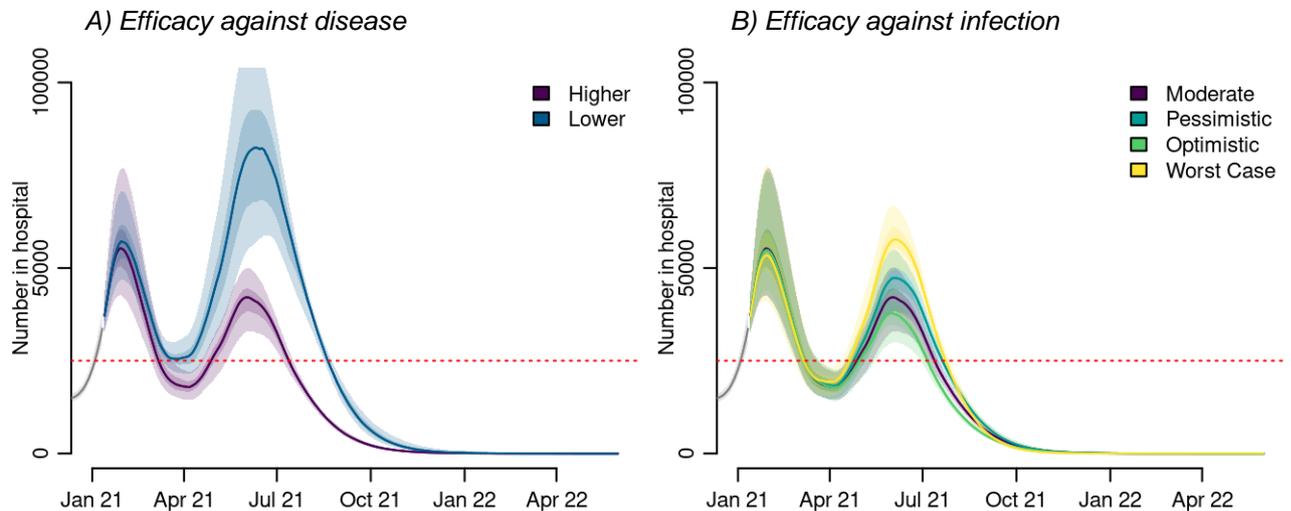

Figure 7: UK COVID-19 hospital occupancy (general wards and ICU) under different assumptions of vaccine efficacy against (left panel) symptomatic disease and (right panel) acquisition of infection. [Left panel] Purple shows the higher vaccine efficacy against symptomatic disease (first dose efficacy: 88% for PF and 70% for AZ, second dose efficacy: 94% for PF and 88% for AZ) and blue a more pessimistic efficacy of 66% that of the vaccine efficacy. [Right panel] Purple shows the moderate/central vaccination efficacy (first dose/second dose) against acquisition of infection of 48% / 60% for both PF and AZ, blue the pessimistic where efficacy is 32% / 40%; green the optimistic where efficacy is 60% / 75%; and yellow a worst-case efficacy of 0% / 0%. We assume levels of NPI relaxation translating to a gradual increase in the transmissibility ($R_{excl\_immunity}$) with stepwise changes on the first of each month starting 1ˢᵗ March to 1ˢᵗ July 2021 increasing from 1.2 to 4.0 as shown in Figure 3, and a central vaccine roll-out scenario as described in Table 1.

Table 2: Cumulative deaths, deaths averted and potential for hospital capacity to be exceeded in the UK between 12th January 2021 and 30th June 2022 under different vaccination scenarios considered. Values shown are mean (95% CrI) and are all rounded to the nearest hundred. National hospital capacity threshold is assumed to be 25,000 patients.*

Analysis type	Vaccine roll out scenario	Background transmissibility $R_{excl\_immunity}$	Vaccine efficacy against disease	Vaccine efficacy against infection	Cumulative number of deaths by 30 June 2022 (95% CrI)	Cumulative number of deaths averted by 30 June 2022 (95% CrI)	Number of days above hospital capacity in current wave^	Will hospital capacity be exceeded in future waves (by 30 June 2022)?**
Main analysis	Central	1.2 to 4	Higher	Moderate	143,200 (113,400 - 183,700)	408,700 (317,000 - 536,700)	66	Yes
Varying vaccine roll out	Optimistic	1.2 to 4	Higher	Moderate	130,800 (103,200 - 167,600)	421,100 (325,500 - 556,300)	63	Yes
	Pessimistic				180,500 (142,100 - 231,500)	371,400 (286,500 - 488,900)	203	No (as current wave never drops within hospital capacity)
Varying background transmissibility	Central	0.8 to 4	Higher	Moderate	150,300 (117,300 - 193,300)	483,700 (372,800 - 635,400)	41	Yes
		1.2 to 2.8			93,700 (72,400 - 124,500)	338,200 (247,900 - 451,300)	64	No
		0.8 to 2.8			85,800 (67,400 - 110,200)	429,300 (320,100 - 574,000)	42	No
	Optimistic	0.8 to 4			146,700 (115,500 - 189,100)	487,300 (376,500 - 640,100)	40	Yes
		1.2 to 2.8			85,900 (65,800 - 116,000)	346,000 (253,500 - 462,600)	63	No
		0.8 to 2.8			82,900 (64,800 - 107,000)	432,200 (322,800 - 578,800)	42	No
	Pessimistic	0.8 to 4			189,500 (147,800 - 244,700)	444,500 (342,300 - 584,900)	40	Yes
		1.2 to 2.8			127,800 (101,000 - 164,300)	304,100 (224,900 - 403,300)	69	Yes
		0.8 to 2.8			126,700 (99,800 - 163,400)	388,400 (292,900 - 517,900)	39	Yes
Varying vaccine efficacy vs acquisition	Central	1.2 to 4	Lower	Moderate	254,700 (198,100 - 334,800)	297,200 (235,000 - 384,700)	225	No (as current wave never drops within hospital capacity)
Varying impact of vaccine on transmission	Central	1.2 to 4	Higher	Pessimistic	155,500 (121,100 - 200,600)	396,400 (306,800 - 522,200)	67	Yes
				Optimistic	133,300 (103,900 - 171,500)	418,600 (323,100 - 549,700)	66	Yes
				Worst case	170,100 (133,500 - 218,500)	381,700 (293,300 - 505,100)	68	Yes

* To ensure all deaths from the third wave (after NPIs are lifted) are captured in this table, we show deaths and deaths averted between 12 January 2021 and 30th June 2022. For each scenario, deaths averted are calculated compared to a scenario with same background transmissibility but no or "zero" vaccine doses distributed. ^As national hospital capacity is currently at its limit, we define "current wave" as the length of time (up to June 2022) until the number of patients in hospital decreases below this threshold. **Hospital capacity is defined as exceeded if at least 5% of simulated epidemics for that scenario exceed the capacity for at least one day.
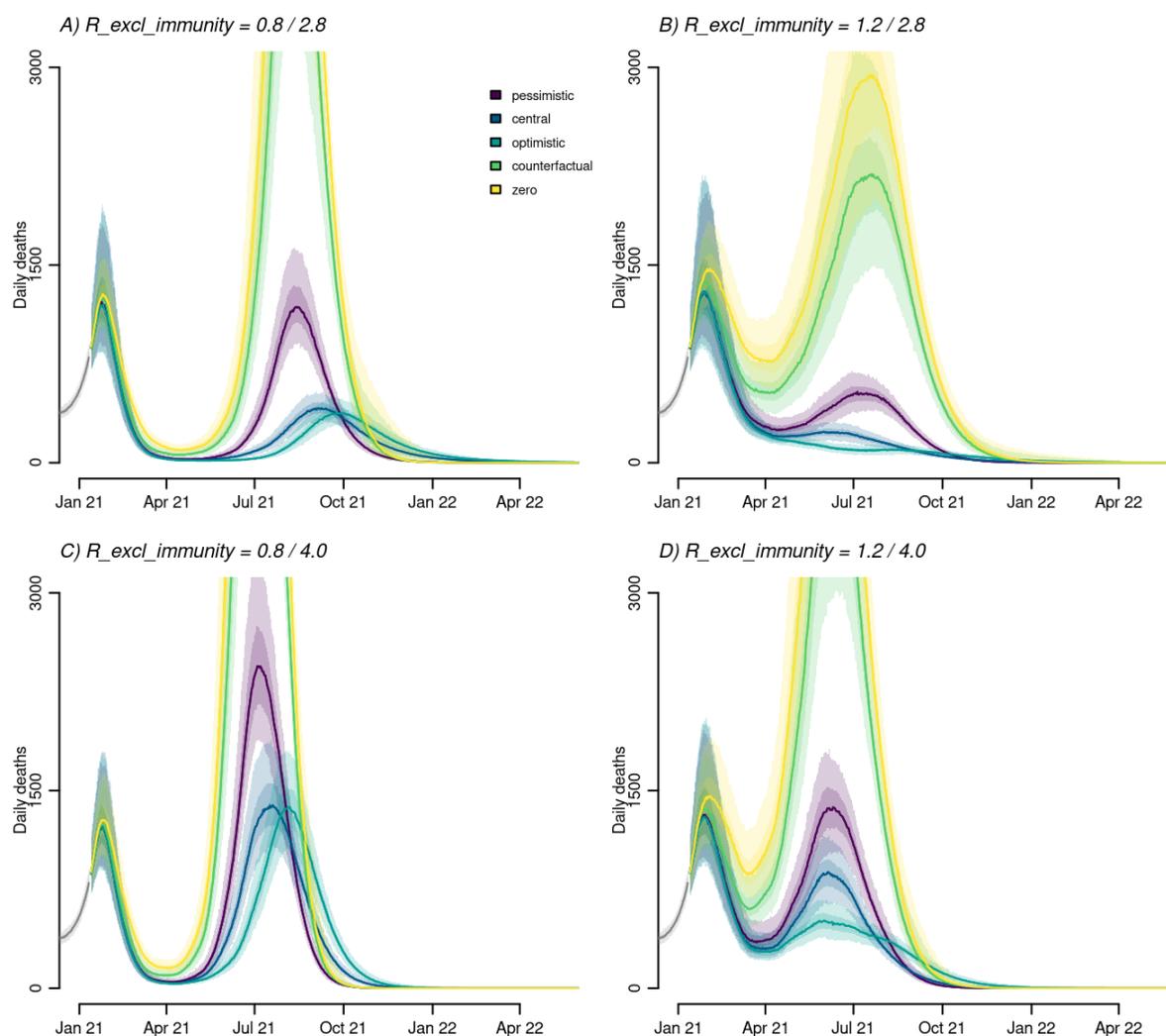
Supplementary Results

Figure S1: UK daily COVID-19 deaths under a pessimistic (purple), central (blue), and optimistic (dark green) vaccine roll-out scenarios as described in Table 1. The light green shows the counter-factual where no additional vaccines beyond those already distributed up to 11th Jan are administered. Yellow shows the scenario where "zero" vaccinations are administered. Each panel shows the impact of vaccination according to different levels of NPI relaxation translating to a gradual increase in the transmissibility ($R_{excl\_immunity}$) with stepwise changes on the first of each month starting 1st March to 1st July 2021. $R_{excl\_immunity}$ A) increasing from 0.8 to 2.8; B) increasing from 1.2 to 2.8; C) increasing from 0.8 to 4.0; and D) increasing from 1.2 to 4.0 as shown in Figure 3.
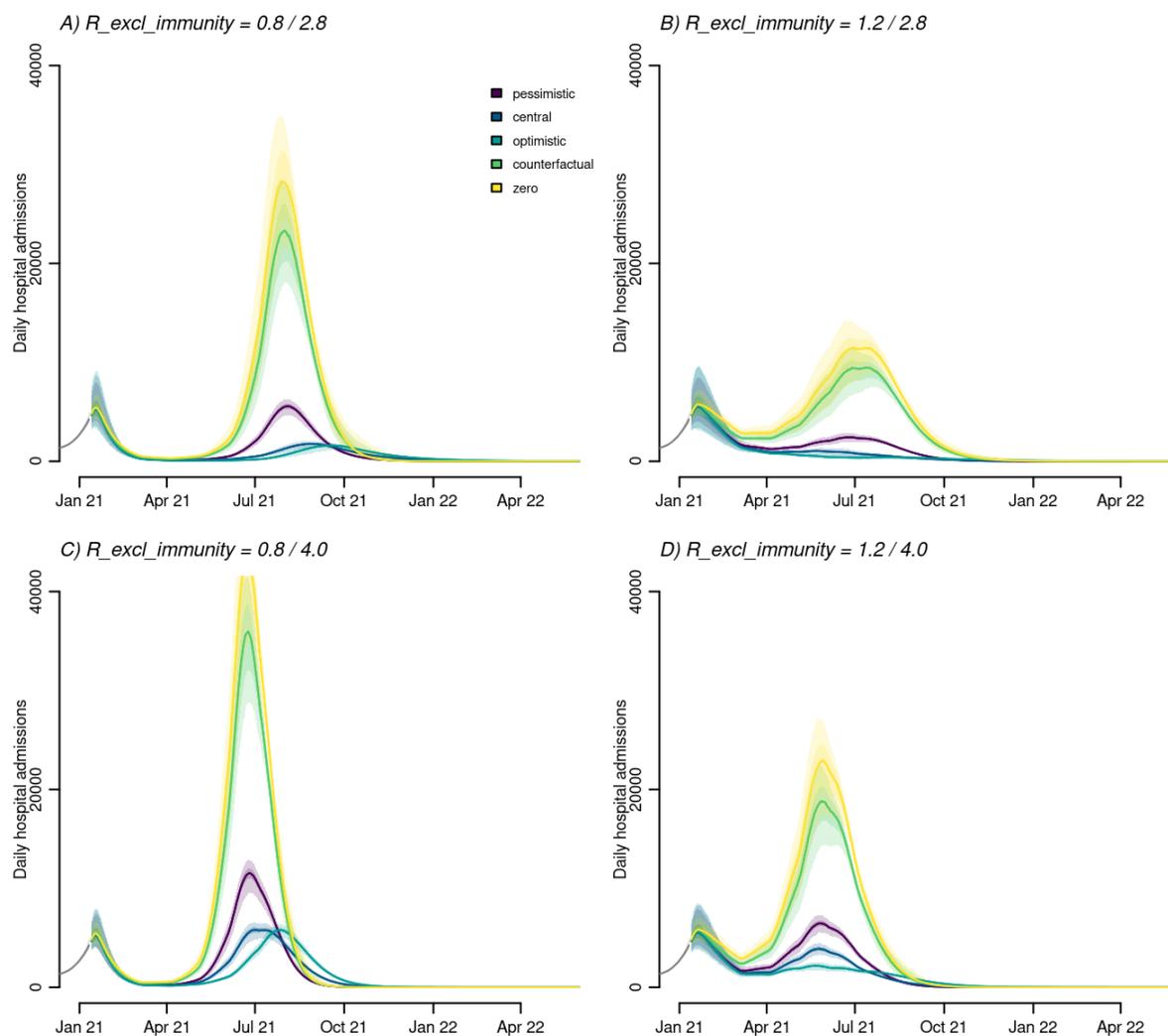
Figure S2: UK daily COVID-19 hospital admissions under a pessimistic (purple), central (blue), and optimistic (dark green) vaccine roll-out scenarios as described in Table 1. The light green shows the counter-factual where no additional vaccines beyond those already distributed up to 11th Jan are administered. Yellow shows the scenario where "zero" vaccinations are administered. Each panel shows the impact of vaccination according to different levels of NPI relaxation translating to a gradual increase in the transmissibility ($R_{excl\_immunity}$) with stepwise changes on the first of each month starting 1st March to 1st July 2021. $R_{excl\_immunity}$ A) increasing from 0.8 to 2.8; B) increasing from 1.2 to 2.8; C) increasing from 0.8 to 4.0; and D) increasing from 1.2 to 4.0 as shown in Figure 3.
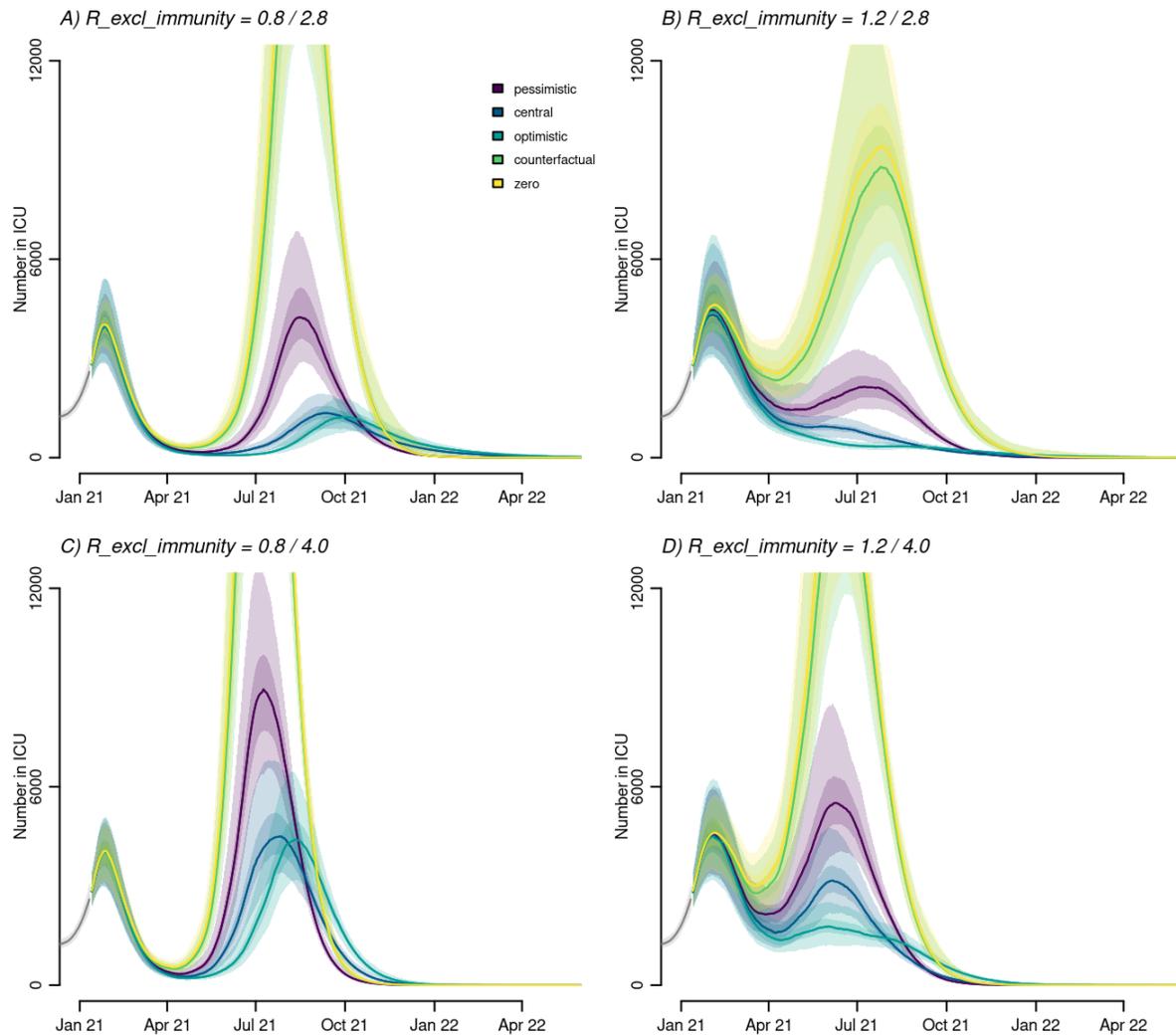
Figure S3: UK COVID-19 ICU occupancy under a pessimistic (purple), central (blue), and optimistic (dark green) vaccine roll-out scenarios as described in Table 1. The light green shows the counter-factual where no additional vaccines beyond those already distributed up to 11th Jan are administered. Yellow shows the scenario where "zero" vaccinations are administered. Each panel shows the impact of vaccination according to different levels of NPI relaxation translating to a gradual increase in the transmissibility ($R_{excl\_immunity}$) with stepwise changes on the first of each month starting 1st March to 1st July 2021. $R_{excl\_immunity}$ A) increasing from 0.8 to 2.8; B) increasing from 1.2 to 2.8; C) increasing from 0.8 to 4.0; and D) increasing from 1.2 to 4.0 as shown in Figure 3.
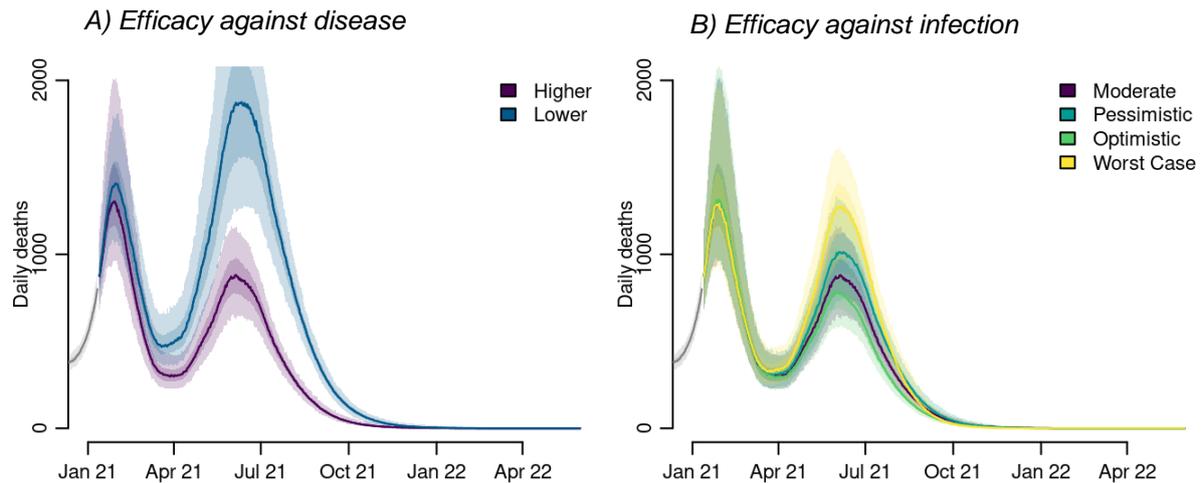
Figure S4: UK daily COVID-19 deaths under different assumptions of vaccine efficacy against (left panel) symptomatic disease and (right panel) acquisition of infection. [Left panel] Purple shows the higher vaccine efficacy against symptomatic disease (first dose efficacy: 88% for PF and 70% for AZ, second dose efficacy: 94% for PF and 88% for AZ) and blue a more pessimistic efficacy of 66% that of the vaccine efficacy. [Right panel] Purple shows the moderate/central vaccination efficacy (first dose/second dose) against acquisition of infection of 48% / 60% for both PF and AZ, blue the pessimistic where efficacy is 32% / 40%; green the optimistic where efficacy is 60% / 75%; and yellow a worst-case efficacy of 0% / 0%. We assume levels of NPI relaxation translating to a gradual increase in the transmissibility ($R_{excl\_immunity}$) with stepwise changes on the first of each month starting 1st March to 1st July 2021 increasing from 1.2 to 4.0 as shown in Figure 3, and a central vaccine roll-out scenario as described in Table 1.